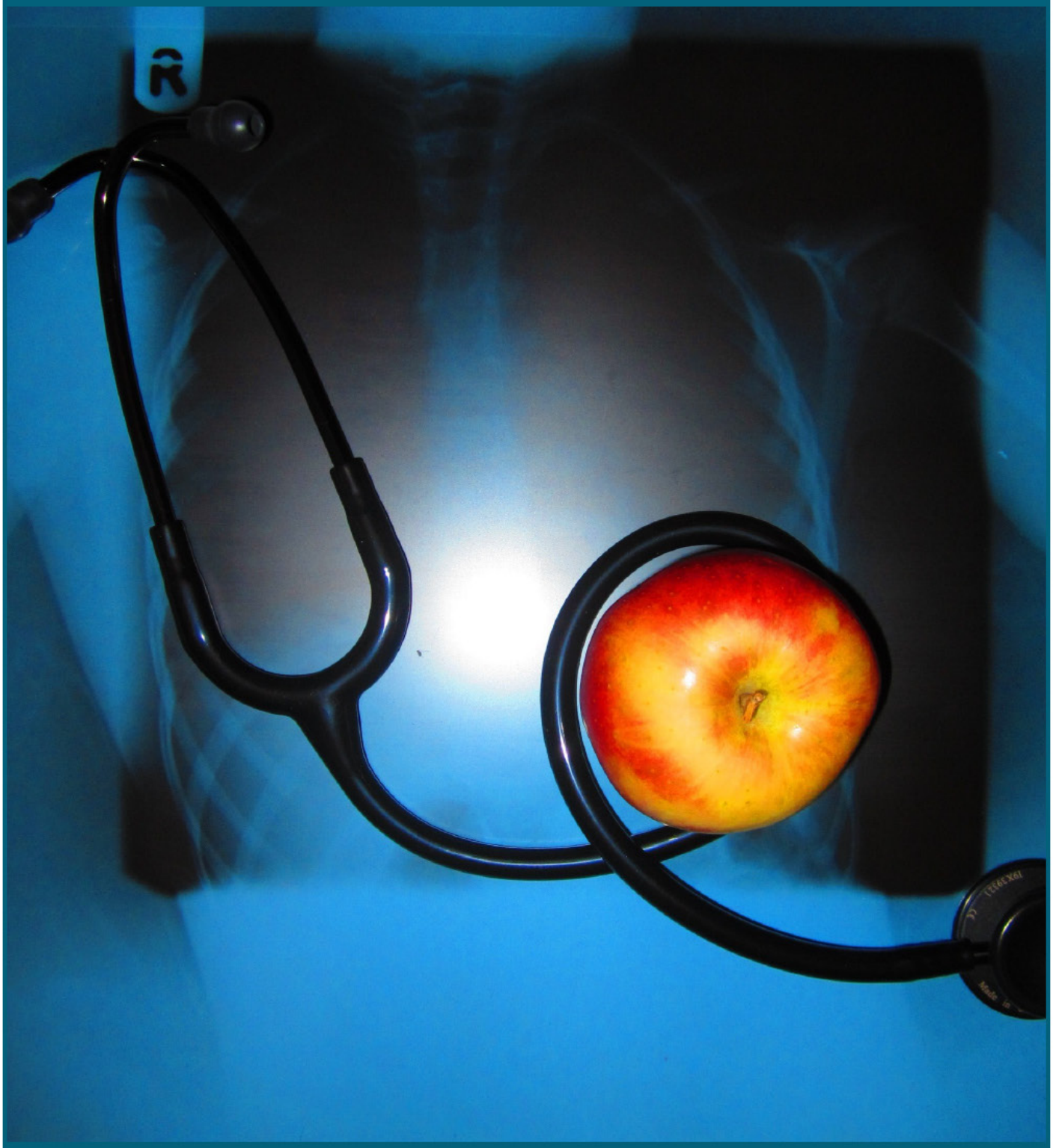
Minima Medicamenta



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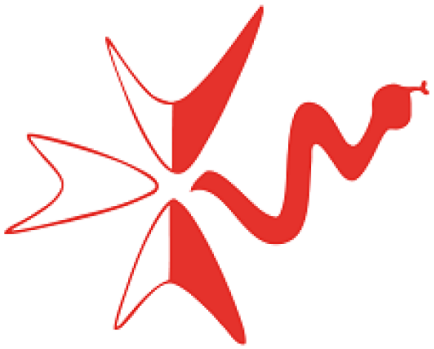


MMSA

Malta Medical Students' Association

L-Għaqda tal-Istudenti tal-Mediċina ta' Malta

www.mmsa.org.mt

Minima Medicamenta

Editors: Isaac Bertuello and Maria Grazia Grech
Cover: Naomi Mercieca
Proof-reading: Stephanie Vella

Message from the Dean of Medicine and Surgery

The Malta Medical Students' Association (MMSA) has once again taken on the task of putting together and publishing the *Minima Medicamenta.*

This second compilation of this project of unusual clinical cases that students encounter during their ward rounds is recognized by the International Federation of Medical Students' Associations. It provides our students with an opportunity to develop the necessary skills in presenting and rationalising patient cases.

Various areas are represented in these case studies, and include amongst others, surgery, oncology, paediatrics, neurology, obstetrics and orthopaedics. This project provides students with an educational experience and strengthens their clinical knowledge and reasoning skills.

I must commend MMSA as well as the contributing students for embarking on this project. A heartfelt thank you goes to colleagues for their on-going support of this initiative.

Professor G. LaFerla
Dean, Faculty of Medicine and Surgery

Message from the President of the Malta Medical Students' Association

The Malta Medical Students' Association (MMSA) represents all the medical students studying at the University of Malta, and it is through this holistic representation that the union and efforts of the medical students lead to proactive results and projects. Minima Medicamenta has been launched last year, and therefore this is the second edition of the project.

Through this publication, medical students are encouraged to participate in scientific papers and appreciate the diversity within the presentation of disease. The case reports are written by medical students themselves, thus increasing student involvement within their own medical education.
I would like to thank all those who contributed to this publication, especially the coordinating team and the Medical Education Officer who worked with great dedication and passion towards medical education and their association by means of this project, which is also recognised by the International Federation of Medical Students' Associations.

Hard work breeds success – This is a perfect example of medical students working towards their holistic development, on the way to becoming holistic doctors.

Daniel Vella Fondacaro
MMSA President 2012-13
Malta Medical Students' Association

Message from the Malta Medical Students' Association Medical Education Officer

MMSA's Standing Committee on Medical Education (SCOME) aims at making the student's educative experience as holistic as possible. We encourage active participation during our five years of medical school by offering opportunities to attend interesting seminars, training workshops and to take leading roles in publications. Furthermore, SCOME takes pride in representing the students and acting as their pillar of support.

Minima Medicamenta is a publication that depicts SCOME's aims to the full. It has encouraged many students to delve deeper into their clinical rotations and has aroused an interest in writing and publications. In this second edition, we have added more interesting cases and have made radical changes to the format in order to allow readers a more comfortable and informative learning experience.

As head of SCOME, I would like to extend my appreciation to Isaac Bertuello and Maria Grazia Grech, who have taken it upon themselves to direct this excellent initiative. Furthermore, a heartfelt thanks goes to Robert Cachia for his invaluable help and support throughout the project.

I hope that you will find this publication useful, enjoyable and worthwhile.

Myranda Attard
MMSA Medical Education Officer 2012-13
Malta Medical Students' Association

Message from the Editors

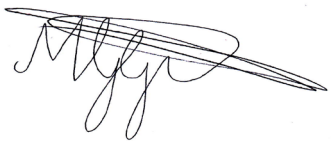
This is the second time that Minima Medicamenta is being published, following last year's successful launch. It is an International Federation of Medical Students' Association (IFMSA) recognised project undertaken by the Malta Medical Students' Association (MMSA). The scope of such an initiative is to aid student participation in the publication of a scientific paper as well as sharing of medical and scientific information.

Through this project, participants have gained the ability to seek out interesting cases, write a report and also obtain knowledge via the sharing of different educational experiences. Those who have submitted the cases have shown that they are dedicated and motivated to work, thus being worthy ambassadors of the Medicine and Surgery course at the University of Malta.

The readers will get a holistic view from varied and different branches of medicine and will also get knowledge of rare and interesting cases as well as learning about the methods used to gain information for a diagnosis to be made and also about the approaches taken to treat and manage the patient.

We hope that you will enjoy reading these cases, which are the result of a lot of hard work for both the students and those who are teaching and helping them. We would also like to extend our thanks to all those who contributed to making this publication a reality including Myranda Attard, Robert Cachia, Naomi Mercieca, Stephanie Vella and last but not least, the students themselves and the doctors who supported them throughout.

Isaac Bertuello
Minima Medicamenta Editor 2013
Malta Medical Students' Association



Maria Grazia Grech
Minima Medicamenta Editor 2013
Malta Medical Students' Association

Index

Case Number 1
Guillain-Barré Syndrome (GBS)

Maria Angela Grima
Reviewed by: Dr. Nicola Aquilina

Case summary:

Demographic details:
Mr. JS, male, Gudja
Referred from: GP

A 57-year-old Caucasian gentleman presented with bilateral progressive distal upper limb paraesthesiae, which he described as a feeling of "heaviness" followed by distal lower limb and mild tongue parasthaesia. He complained of dysaesthetic symptoms in his upper limbs with intermittent burning and tingling and autonomic disturbances such as excessive sweating of the face, hands and legs. He later developed epigastric pain that radiated to the chest, which was not related to exercise. According to the patient, symptoms got worse after taking the influenza vaccine. On examination, he had gait disturbance with weaker left lower limb muscles. During his stay in hospital, he also developed slight dysarthria and diplopia, together with urinary retention and constipation. He had had a similar, though much less severe, episode six years previously where he was diagnosed with Guillain-Barré Syndrome based on his clinical features, EMG result and his high protein levels in the CSF (more than 8g/L). He was treated with IVIG and recovered completely. This was his second presentation of neuromuscular weakness and he was referred for immunoglobulin treatment and intensive physiotherapy.

Presenting complaint:

JS presented with progressive bilateral parasthaesia of the upper extremities. It was followed by bilateral lower limb and later, tongue parasthaesia. He had been referred to hospital due to epigastric pain that progressed to chest pain. His chest pain was associated with slight sweating and it did not radiate anywhere. It was exacerbated by inspiration.

History of presenting complaint:

He suffered from a similar episode six years previously where he was diagnosed with GBS. He recovered completely after being treated with intravenous immunoglobulins (IVIG) and had no symptoms until this second presentation.

Past medical and surgical history:

Past medical history:

- Hypertension
- Diabetes
- Hypercholesterolemia
- Gastro-oesophageal reflux disease

Drug history:

Drug	Dosage	Frequency	Type	Reason
Metformin	500mg	TDS	Anti-diabetic	Treatment for Diabetes Mellitus type 2
Perindopril	4mg	Nocte	ACE Inhibitor	Treatment of hypertension
Simvastatin	20mg	Nocte	Lipid lowering agent	Treatment of hypercholesterolaemia
Aspirin	75mg	Once Daily	Analgesic	Ischaemic Heart Disease

Family history:

Father died of a myocardial infarction.
Mother suffers from arthritis.

Social history:

A married public transport driver. He is a non-smoker and drinks socially.

Systemic inquiry:

- General Health: looks well in general
- Cardiovascular System: no abnormalities
- Respiratory System: clear chest
- Gastrointestinal System: constipation, bloated
- Genitourinary System: urinary retention
- Central Nervous System: unstable gait, cannot walk on toes and heels, needs help to stand, impaired sensation in a glove and stocking distribution, reduced power of muscles L>R
- Musculoskeletal System: chest pain especially on inspiration
- Endocrine System: no abnormalities

Current Therapy:

Immunoglobulins via IV route were given for 5 days in order to suppress the acute inflammatory demyelination of the peripheral nervous system.

Discussion of results of general and specific examination:

Neurological examination:

General: The patient did not have any nystagmus or facial asymmetry, but had a slight dysarthria.

Tone: There was reduced tone in both his upper and lower limbs.

Power: Power assessment showed marked weakness in both upper and lower limbs, being more pronounced in the lower limbs, with the left more severe than the right.

Upper limb examination of power:

Muscle	Right Limb	Left Limb
Deltoid	4	3
Triceps	4	3

Lower limb examination of power:

Muscle	Right limb	Left limb
Glutei	3	2
Quadriceps	3	2
Hamstrings	3	2
Iliopsoas	3	2

Reflexes: Reflexes of both upper and lower limbs were reduced.

Coordination: Upper and lower limb coordination examination was normal.

Sensation: He had reduced sensation in both his upper and lower limbs.

Gait: He had mild difficulty raising himself from a sitting position. His gait was unstable and was unable to walk on his toes or heels.

Differential diagnosis:

- GBS
- Mononeuritis multiplex

Diagnostic procedures:

Laboratory exams:

Test: Lumbar Puncture
Justification for test: In order to obtain CSF composition.
Result: Raised protein (889 mg/L) with no cells diagnostic of GBS.
Conclusion: GBS

Instrumental exams:

Test: Nerve Conduction Studies and Electromyography
Justification for test: To show any evidence and distribution of a neuropathy
Result: Findings are consistent with a severe sensori-motor predominantly demyelinating polyneuropathy that is compatible with an acute inflammatory neuropathy
Conclusion: GBS

Therapy:

Drugs:

Drug Name (Generic)	Dosage	Frequency	Type	Reason
IVIG	0.4g/kg	Once daily	Immunoglobulin	Suppression of demyelination

Diagnosis:

This gentleman's symptoms were suggestive of GBS. The typical clinical presentation consists of lower limb symmetrical parasthaesia that ascends to the upper limbs, progressing to weakness. However, this patient's presentation was atypical since he first complained of a "heavy" feeling of his upper extremities which later progressed to parasthaesia. The same later occurred in the lower limbs, thus his presentation had a 'descending' pattern rather than 'ascending'. Together with that, he had tongue parasthaesia which progressed to dysarthria. In view of these signs and symptoms, a lumbar puncture was done to assess the CSF. Elevated protein levels, in the absence of high white blood cell count, was indicative of GBS. EMG is a specific and sensitive investigation for GBS since the results were consistent with demyelination.

Final treatment and follow ups:

The patient was started on IVIG which was continued for five days. However he had minimal immediate benefit and required intensive rehabilitation. He complained of constipation, urinary retention and diplopia. He was transferred to rehab for further physical therapy.

Fact Box 1

Title: Guillain–Barré syndrome

General overview: GBS is an acute inflammatory immune-mediated disorder affecting the peripheral nervous system[1]. GBS typically manifests as sudden distal symmetrical parasthaesia that ascends to the upper limbs and progresses to weakness. A few patients undergo sensory dysfunction especially in the demyelinating forms of GBS[2]. About a third of hospitalised patients are mechanically ventilated due to diaphragmatic, respiratory and oropharyngeal muscle weakness[3].

Long term signs and symptoms: GBS patients may have persistent weakness, areflexia, ataxia and sensory loss. About 7-15% of patients suffer from permanent neurologic sequelae such as bilateral foot-drop, intrinsic hand muscle wasting, ataxia and dysaesthesia. Moreover, they may experience long-term functional impairment and differences in pain intensity[4].

Epidemiology: GBS is made up of different subtypes with variable incidence rates in different countries. In Europe, acute inflammatory demyelinating polyradiculoneuropathy (AIDP) contributes to 90% of the cases. This subtype includes predominantly motor, bilateral facial and pharyngeal disturbances, with occasional abnormal sensory and autonomic manifestations[5].

Risk factors: Usually, a bacterial or viral infection such as Campylobacter jejuni, Mycoplasma pneumonia, CMV, EBV or influenza virus precede the onset of GBS [6, 7]. Surgery has also been shown as a risk factor[8]. Several vaccines have been associated with GBS (mainly past rabies vaccination[9], swine flu (H1N1) influenza vaccine used in 1976-77 and oral polio vaccination[10]), but controversy remains for the influenza vaccines[11]. A recent study, however, found an increased risk of GBS with the seasonal influenza vaccination[12]. Moreover, the risk increases with age[13].

Prognosis: Up to 85% achieve a full functional recovery within 6-18 months [14]. Acute relapse occurs in about 10% after initial improvement after treatment [15]. Some undergo clinical fluctuations during their treatment course. Recurrence of Guillain-Barré syndrome is rare but has been reported in 2-5% of patients [16, 17]. Mortality is rare, 2-12% and this occurs due to GBS complications: acute respiratory distress syndrome, sepsis, pneumonia, venous thromboembolism, cardiac arrhythmias and arrest. The most common cases are due to severe autonomic instability or from the complications of prolonged intubation and paralysis [18-21].

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Case Number 2
Kawasaki Disease

Francesca Spiteri
Reviewed by: Dr. Valerie Zammit

Case summary:

Demographic details:
Patient: YB, Male.
Resident in Attard.
Age: 2 years
Referred by: GP

Patient YB is a two-year-old boy who presented to A&E with a 7 day history of fever up to 101.8^{o}F associated with symptoms of an upper respiratory tract infection with cough, vomiting and diarrhoea and bilateral non-purulent conjunctivitis and fissuring of the lips. Based on clinical findings the patient was diagnosed with Kawasaki Disease and was treated accordingly.

Presenting complaint:

Pyrexia up to101.8^{o}F: 7 days
Non-Purulent conjunctivitis: 7 days.
Cracked lips: 7 days.

History of presenting complaint:

The patient developed coryzal symptoms and cough associated with a temperature which persisted for 7 days. He was also vomiting and passing loose stools. Concomitantly he developed a non-purulent conjunctivitis with fissuring and crusting of his lips. He was seen by the GP who prescribed an antibiotic, a mucolytic agent and antipyretics. However, the fever persisted with no clinical improvement and the patient was admitted to hospital.

Past medical and surgical history:

Past medical history:

Bronchiolitis: 7 weeks prior to current admission

Drug history:

Drug	Dosage	Frequency	Type	Reason
Augmentin 457mg/5ml Syrup	2.5ml	BD	Penicillin Antibiotic	Treatment of secondary bacterial infection
Paracetamol Suppositories	125-250mg	4-6 hourly	Antipyretic and Analgesic	Brings about a reduction in fever

Ambroxol hydrochloride Syrup	2.5ml	TDS	Mucolytic-cough preparation	Secretolytic agent and Mucolytic agent which helps in the breakdown and thinning of mucus.

Table 1[1] Treatment on admission

The patient has no known drug allergy.

Family history:

Both parents are unrelated and healthy. There is no significant family history.

Social history:

The boy has a fraternal twin sister, lives with his family and attends playschool.

Systemic inquiry:

- General Health: the patient was feverish and irritable.
- Cardiovascular System: nil of note
- Respiratory System: nil of note
- Gastrointestinal System: few episodes of vomiting, an episode of loose stools.
- Genitourinary System: the patient was passing normal volumes of urine.
- Central Nervous System: nil of note
- Musculoskeletal System: nil of note
- Endocrine System: nil of note
- Others: non-purulent conjunctivitis, mild cervical lymphadenopathy.

Discussion of results of general and specific examinations:

The patient was lying down in bed, miserable and irritable. He was not pale, jaundiced or cyanosed and was well-hydrated. There were no evident rashes. He had a normal respiratory rate. Mild cervical lymphadenopathy was noted. His temperature was 101.8^{o}F (febrile). There was no generalised oedema but the hands were noted to be swollen. The tonsils were enlarged with no pus but a generalised erythema of the oral mucosa was noted. Healing perioral excoriations and satellite lesions on the nose were evident.

Cardiovascular examination revealed normal heart sounds S1+S2+0 and a pulse of 148 beats per minute of good volume.

Respiratory examination showed equal air entry in both right and left lungs with normal vesicular breath sounds. No added sounds were noted.

The abdomen moved with respiration and there were no swellings or scars. It was soft, with no guarding or rebound tenderness. No masses were felt and there was no organomegaly. Normal bowel sounds were auscultated and stools were normal.

Differential diagnosis:

- Kawasaki Disease
- Stephen Johnson Disease
- Measles
- Scarlet Fever
- Drug reactions
- Other febrile viral exanthems
- Toxic Epidermal Necrolysis
- Rocky Mountain Spotted fever
- Staphylococcal Scalded skin Disease
- Juvenile Idiopathic Arthritis
- Leptospirosis
- Mercury Poisoning [2]

Diagnostic procedures:

Laboratory exams:[3-4]

Test: Complete blood count, including platelet count.
Justification for test: May help with differential diagnosis specifically assessing white blood cell count and differential, which is likely to be elevated and the presence of anaemia. A marked thrombocytosis in the second week of illness is a typical finding.
Result: Normocytic anaemia, with an elevated white cell count and thrombocytosis.
Conclusion: These results are often seen in Kawasaki Disease.

Test: Urea & Electrolytes
Justification for test: These tests help assess state of hydration and electrolyte imbalances.
Result: Normal
Conclusion: This excludes any Renal Disease.

Test: C- Reactive Protein
Justification for test: Acute phase reactant.
Result: Elevated
Conclusion: This is usually elevated to a degree not typically found in common viral infections and can be an indication of Kawasaki disease or other invasive bacterial conditions.

Test: Erythrocyte Sedimentation Rate
Justification for test: Nonspecific marker of inflammation.
Result: Elevated
Conclusion: This is usually elevated to a degree not typically found in common viral infections and can help differentiate between connective tissue diseases and other bacterial infections.

Test: Blood cultures
Justification for test: This is done to detect the presence of actively multiplying bacteria or fungi in the bloodstream, to identify the microorganism(s) present and to guide antimicrobial treatment.
Result: Negative
Conclusion: Bacterial sepsis is excluded.

Instrumental exams:

Test: Echocardiogram (ECHO) [2-3,5]
Justification for test: Kawasaki Disease affects the coronary arteries in 1/3 of affected children within the first 6 weeks of illness leading to aneurysm formation. These are best visualised by echocardiography. In the acute phase of illness, coronary artery abnormalities include lack of tapering, perivascular brightness and ectasia. Echocardiography may also reveal decreased ventricular function, mild valvular regurgitation and pericardial effusion.
Result: The ECHO was found to be normal. Mitral, coronary or cardiac involvement was excluded.
Conclusion: The disease did not involve the coronary arteries in this patient.

Therapy:

Drugs:[1]

Drug	Dosage	Frequency	Type	Reason
Immunoglobulin	2g/kg IVI	2 g/kg over 10 hours; preferably within the first 10 days of the illness	Human pooled Immunoglobulin	Suppresses inflammatory response which may lead to coronary artery damage
Paracetamol Suppositories	250mg PR	Every 4-6 hours	Antipyretic and analgesic	Provides symptomatic relief
Aspirin Tablets	7.5 -12.5 mg/ kg/dose = 150 mg PO	QDS for 2 weeks or until afebrile; dose reduced to 2-5mg/ kg od for 6-8 wk	NSAID Anti -Inflammatory	Antiplatelet and anti-inflammatory effect preventing coronary artery damage
Ranitidine Syrup 25mg/ml	2-4 mg/kg/dose = 4mls PO	BD	Histamine H2-receptor antagonist	This is used as prophylaxis against dyspepsia and risk of gastrointestinal bleeding caused by high dose aspirin

Diagnosis:

Kawasaki Disease is a systemic vasculitis which predominantly affects children under the age of 5 years. The etiology of Kawasaki disease remains unknown, although an infectious agent is strongly suspected based on clinical and epidemiologic features. The diagnosis of Kawasaki Disease cannot be made by a single laboratory test or combination of tests. Physicians make the diagnosis after carefully examining a child, observing signs and symptoms and eliminating the possibility of other, similar diseases.
To diagnose Kawasaki Disease the child must have a persistent fever of 5 days and 4 out of 5 of the criteria below:

- Polymorphous rash
- Bilateral (non-purulent) conjunctival injection
- Mucous membrane changes, e.g. reddened or dry cracked lips, strawberry tongue, diffuse redness of oral or pharyngeal mucosa
- Peripheral changes, e.g. erythema of the palms or soles, oedema of the hands or feet, and in convalescence desquamation

- Cervical lymphadenopathy (> 15 mm diameter, usually unilateral, single, non-purulent and painful). In this case the child presented with a 7 day history of fever, a bilateral conjunctival injection, cracked lips, swollen hands and cervical lymphadenopathy and therefore fulfilled the criteria of diagnosis of Kawasaki Disease[2-3,5-7].

Final treatment and follow up:

The patient was treated as shown in Table 2. He was also prescribed intravenous fluids - 5% dextrose in 0.9% saline at maintenance rate. These intravenous solutions are indicated for use in paediatric patients as sources of electrolytes, calories and water for hydration [8]. Oral fluids were encouraged and the patient was placed on a soft diet.

Renal profile tests were carried out and repeated as necessary. Parameters including fluid input and output were monitored at regular intervals.

Since no coronary artery abnormalities were noted at presentation, an echocardiogram is to be repeated at two weeks and at six to eight weeks after diagnosis[2]. The risk of developing significant heart disease is less once the fever subsides[3].

The patient was kept in hospital until the fever subsided. He was then discharged and reviewed at regular intervals.

The patient should be re-evaluated one week post-discharge and then have a repeat echocardiogram[3].

Fact Box 2:

Name of Condition: Kawasaki Disease[5,6,7]
Also known as: Mucocutaneous lymph node Disease; Infantile polyarteritis

Risk factors:

- Age: Children under 5 years old are most at risk of Kawasaki Disease.
- Sex: Boys are slightly more likely than girls are to develop Kawasaki Disease.
- Ethnicity: Children of Asian descent, such as Japanese or Korean, have higher rates of Kawasaki Disease.

Symptoms and Signs:

Children with Kawasaki Disease usually present with:

- A persistent fever of 5 days and 4 out of 5 of the criteria below:
- Polymorphous rash
- Bilateral (non-purulent) conjunctival injection
- Mucous membrane changes, e.g. reddened or dry cracked lips, strawberry tongue, diffuse redness of oral or pharyngeal mucosa
- Peripheral changes, e.g. erythema of the palms or soles, oedema of the hands or feet, and in convalescence desquamation
- Cervical lymphadenopathy (> 15 mm diameter, usually unilateral, single, non-purulent and painful)

Prevention: Kawasaki Disease cannot be prevented, but usually has tell-tale symptoms and signs that appear in phases.

Complications : Heart complications include:

- Inflammation of the heart muscle (myocarditis)
- Heart valve problems (mitral regurgitation)
- Abnormal heart rhythm (dysrhythmia)
- Inflammation of blood vessels (vasculitis), usually the coronary arteries, that supply blood to the heart

For a small percentage of children with Kawasaki Disease, this can result in death in spite of treatment.

Treatment:

Immunoglobulins: Infusion of an immune protein (gamma globulin) through a vein (intravenously) can lower the risk of coronary artery problems [9].
Aspirin: High doses of aspirin may help treat inflammation. Aspirin can also decrease pain and joint inflammation, as well as reduce the fever. Kawasaki treatment is a rare exception to the rule against aspirin use in children.

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Case Number 3
A Univentricular Heart: Tricuspid Atresia

Simon Mifsud and Emma Schembri
Reviewed by: Prof. V. Grech

Case summary:

Demographic details:
Master TA, male, Balluta
Referred from: MDH

A two-year-three-month-old boy was diagnosed with tricuspid atresia. This condition requires three surgical interventions, of which he has already had two. He has now presented to hospital with shortness of breath. This implies that he might now benefit from the third operation. Investigations, which were planned beforehand, will assess whether he is a candidate for this operation, that will improve his symptoms and hence his quality of life.

Presenting complaint:

Shortness of breath
Reduced exercise tolerance

History of presenting complaint:

The shortness of breath has been present for about a year, but has been noticed to have increased progressively during the last three months. Furthermore, during vigorous physical activity, the child ends up vomiting. Nevertheless the child is still very active. There were no other associated symptoms, such as cough, fever, or chest pain.

Past medical and surgical history:

The patient was diagnosed with tricuspid atresia on the third day of life. This was confirmed with an echocardiogram which showed a heart with a missing patent tricuspid valve. This echocardiogram was indicated due to the presence of perioral cyanosis, clubbing of the fingers and toes and a pan-systolic murmur grade 3 and a loud second heart sound (S2). During crying episodes, the patient was noted to become dusky but without any hypercyanotic spells. The oxygen saturations recorded at this point in time were 85% on air.

Two weeks later, the child presented with mild cyanosis and a fever of 38.1^{o}C. Investigations revealed that the oxygen saturations were 78% but all other investigations including the septic screen were negative. As a result the child was administed low flow oxygen, together with ceftriaxone, amoxillin and rocycline.

The dramatic fall in the patient's oxygen saturations initiated a cascade of surgical interventions. The first was the Modified Right-Blalock Interposition Shunt carried out at 24 days of life. This operation involved the temporary insertion of a 3.5mm shunt between the subclavian and pulmonary arteries. Furthermore, the interatrial septum was obliterated by an atrial septectomy. After this intervention, the oxygen saturation improved to 89%.

The second operation was carried out at 9 months of age. This was the Bi-directional Superior Cavopulmonary Anastomosis (BSCA). In this procedure, the previous shunt was removed and the superior vena cava was connected to the pulmonary artery. The saturations improved after this procedure (i.e.: from 74% to 79%) but the increase was not as dramatic as that after the shunt insertion.

Gestational history:

The child was born at 39 weeks of gestation by normal vaginal delivery with a birth weight of 3.47kg. The patient appeared cyanosed at birth due to a slightly traumatic vaginal delivery, but otherwise there were no other significant complications. The Apgar score was 9. The mother had a miscarriage prior to this birth. The parents were not exposed to harmful chemicals during gestation.

Drug history:

Drug	Dosage	Frequency	Type	Reason
Aspirin	50mg	PO, once daily	Anti-platelet agent	Prevents thrombosis

He is also following the national immunisation schedule.
There are no known drug allergies.

Family history:

No family history of congenital cardiac problems.

Social history:

The patient lives at home with his parents and younger sister. He is sociable and plays with peers of the same age.

Systemic inquiry:

- General Health: looks well in general.
- Cardiovascular System: tricuspid atresia
- Respiratory System: shortness of breath, reduced exercise tolerance
- Gastrointestinal System: vomiting during vigorous exercise
- Genitourinary System: nil to note
- Central Nervous System: nil to note
- Musculoskeletal System: nil to note
- Endocrine System: nil to note

Current therapy:

The patient was starved from morning prior to the pre-Total Cavo-Pulmonary Connection (TCPC) diagnostic catheter.

Discussion of results of general and specific examinations:

On general inspection, the patient appeared well. He had a respiratory rate of about 30 breaths per minute, i.e.: slightly tachypnoeic. The pulse rate was 130 beats per minute, which is normal for a child of his age. He had a median sternotomy scar from his previous operations. Clubbing of the fingers and toes was

observed. This is a feature of cyanotic congenital heart disease.
On palpation, the apex beat was not displaced and no heaves or thrills were felt. On auscultation of the chest, a grade 1 pansystolic murmur was heard with radiation to the axilla. The pansystolic murmur may be consistent with mild mitral regurgitation due to mitral annular dilatation. This could be explained by the fact that there might be some volume overload to the left ventricle, therefore resulting in dilatation. Auscultation of the lung fields revealed normal air entry and no inspiratory crackles.

Differential diagnosis:

- Previous corrections of the Tricuspid Atresia (i.e.: BSCA) cannot keep up with the child's demands thus highlighting the need for the third and final operation regarding this condition.
- Anaemia.

Diagnostic procedures:

Laboratory exams:

Test: Pulse Oximetry
Justification for test: To monitor the oxygen saturation of the patient's haemoglobin.
Result: The patient had an oxygen saturation of 76%.
Conclusion: The normal oxygen saturation in a child should be greater than 94%, implying that the patient has low oxygen saturations.

Test: Arterial Blood Gases (ABGs)
Justification for tests: To check for arterial oxygen (and carbon dioxide) partial pressures, pH and base deficit.
Result: Arterial oxygen saturation was 100mmHg (75-100mmHg) and carbon dioxide arterial saturations were 49mmHg (35-45mmHg). pH values were 7.276 (7.35-7.45).
Conclusion: The ABG results are practically within normal limits, when one takes into consideration the child's condition.

Before undergoing the third operation, the patient must satisfy the Fontan's "ten commandments". These ten criteria define the ideal candidate for the operation and should ideally be satisfied, in order to ensure a low level of morbidity and mortality after undergoing the Fontan or TCPC operation. These "ten commandments"/criteria are:

1. Age older than 4 years
2. Sinus rhythm
3. Normal systemic venous return
4. Normal right atrial volume
5. Mean Pulmonary Pressure less than 15mmHg
6. Pulmonary Arteriolar Resistance less than 4 wood units/m^2
7. Pulmonary Artery-Aorta ratio more than 0.75
8. Left Ventricular Function and Ejection Fraction more than 60%
9. Competent Mitral Valve
10. Absence of Pulmonary Artery Distortion

The following instrumental exams were done in order to ensure that the patient satisfies the above "ten commandments".

Instrumental exams:

Test: ECG

Justification for test: Tricuspid Atresia is associated with right atrial volume overload and dilatation, left ventricle hypertrophy and left axis deviation. These three cardiovascular structural changes can be picked up using the ECG.

Result: The ECG confirmed that the patient is in sinus rhythm and none of the above features were recorded.

Conclusion: The patient is in sinus rhythm (Criterion Number 2), with no right atrial dilatation (Criterion Number 4) or left ventricular hypertrophy (Criterion Number 8). The BSCA operation was performed to redirect venous blood from the superior vena cava to the pulmonary artery. In doing so, venous blood from the superior vena cava is bypassing the right atrium and the left atrium and left ventricle, meaning that there is less blood going to these chambers. This helps to prevent the above mentioned changes from taking place inside the heart. It also shows that prior to the operation there were no major dilatations of the right atrium or hypertrophy of the left ventricle.

Test: Echocardiogram

Justification for test: To assess heart movements, heart size and pressure gradients.

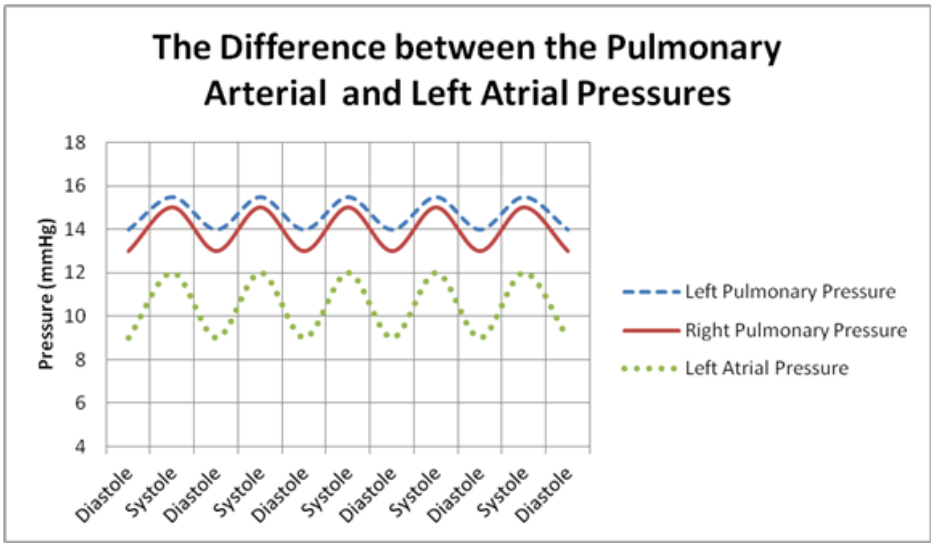
Result: Good Left Ventricular function
Mild mitral regurgitation
Large Atrial Septal Defect
Normal Aorta and Pulmonary arteries

Conclusion: The pansystolic murmur that was referred to the axilla is consistent with mild mitral regurgitation. This does not completely satisfy Criterion Number 9, but if need be, the trivial abnormalities of the mitral valve can be corrected by surgery implying that the patient can still be an ideal candidate for the TCPC Operation. The echocardiogram ensured that the patient has good left ventricular function with an ejection fraction of 86.3% (Criterion Number 8). Moreover, the echocardiogram confirmed the presence of normal aorta and pulmonary arteries (Criteria Numbers 7 and 10). The latter two criteria are not as important as once thought, as nowadays, surgical intervention can correct such abnormalities.

Test: Pre-TCPC Diagnostic Catheter

Justification for test: To assess whether he is a candidate for this operation by measuring the mean pressure gradient between the pulmonary arteries and the left atrium.

Result: The mean pulmonary arterial pressure is 14.38 mmHg (Criterion Number 5) and the mean left atrial/pulmonary venous pressure is 10.5 mmHg. The pressure gradient between the pulmonary arteries and the left atrium is around 4 mmHg (<6mmHg for the TCPC operation to be succesful)[1]. This is depicted in Graph 1. The gap between the pulmonary and left atrial pressures in Graph 1 shows that there is a low pressure gradient between the pulmonary arteries and left atrium. This ensures that blood flows across the pulmonary circulation in order to become oxygenated. If the gap between the pulmonary arterial and left atrial pressures was significant, this would imply that there is high pulmonary vascular resistance. In the Fontan operation, blood flow to the lungs is driven passively without any help from the right ventricle. Thus the presence of a low mean pulmonary arterial pressure (<15mmHg) and a transpulmonary gradient of less than 6mmHg ensures that there is no major pulmonary vascular resistance and that blood flow to the lungs will occur easily.



Graph 1: The Difference between the Pulmonary Arterial and Left Atrial Pressures.

Conclusion: Since the transpulmonary pressure gradient is less than 6, the child will benefit from a TCPC operation, but the operation can be postponed until he is older.

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Enalapril	2.5g	Once daily	ACE-inhibitor	To preserve left ventricular function, by reducing afterload and systemic vascular resistance.

Diagnosis:

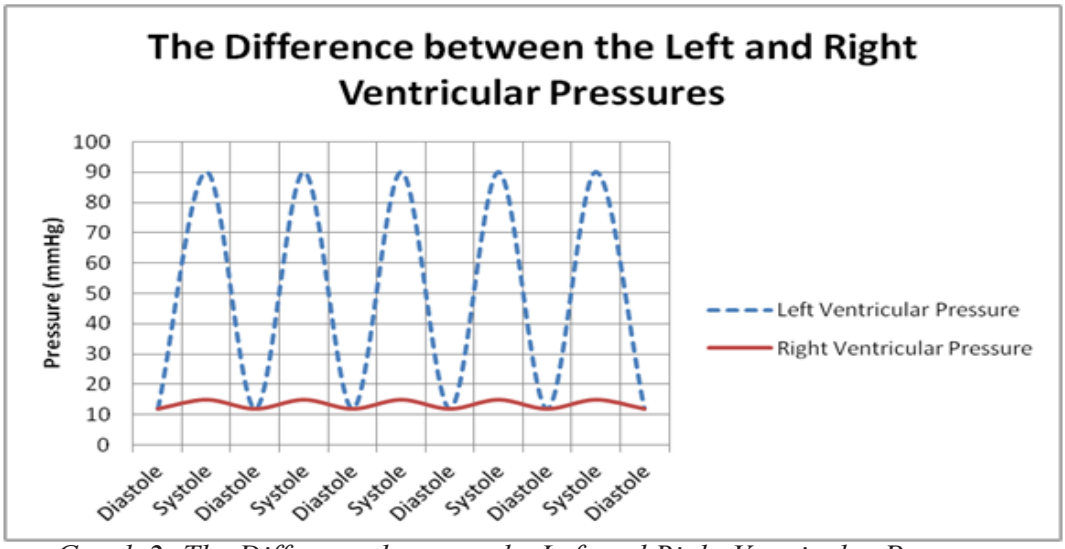
Tricuspid atresia is a type of univentricular heart and is the third most common cyanotic congenital heart disease. There are different subtypes of tricuspid atresia, but this goes beyond the scope of this case report[2]. As the name infers, these patients lack a tricuspid valve between the right atrium and right ventricle[3]. This does not allow blood to flow from the right atrium to the right ventricle and it therefore acts as an obstructive lesion[4].

As a result, the right ventricle does not receive any blood from the right atrium and so remains hypoplastic and undeveloped leaving the left ventricle as the only functional ventricle. Hence the name: univentricular heart. The cause of tricuspid atresia is not known, but it occurs during the first eight weeks of fetal development, when the heart starts to form (i.e.: organogenesis)[3]. Patients with tricuspid atresia depend on an atrial septal defect (ASD) together with a ventricular septal defect (VSD) to maintain an adequate circulation. In fact almost all patients with a tricuspid atresia have these defects i.e.: ASD and a VSD.

Blood reaching the right atrium goes to the left atrium across the ASD. As a result, the deoxygenated blood from the right atrium mixes with the oxygenated blood from the pulmonary veins inside the left atrium. This mixing explains the cyanosis associated with tricuspid atresia. This mixed blood then passes into the left ventricle. Once inside the left ventricle, most of the blood passes into the aorta during left ventricular systole, but some blood also passes through the VSD into the hypoplastic right ventricle and eventually into the pulmonary arteries.

Furthermore, some blood from the aorta flows through the patent ductus arteriosus (PDA) into the pulmonary arteries thus allowing more blood to reach the lungs. A PDA initially allows the patient to live with minimal cyanosis. However problems begin, when the ductus arteriosus closes and since the VSD tends to be restrictive, blood flow to the pulmonary arteries is reduced with a resultant increase in cyanosis. If the blood supply to the lungs is highly restricted, the patient might collapse suddenly. This patient lacked a PDA and as a result presented with perioral cyanosis after birth.

The pan-systolic murmur (referred to as a flow murmur) that was heard soon after birth occurs due to the restrictive VSD. Since the left ventricle is well developed and more muscular than the right ventricle, it generates a larger amount of pressure i.e.: circa 90 mmHg during systole. The hypoplastic right ventricle generates very little pressure during systole i.e.: circa 15 mmHg. During diastole the pressures generated by the right and left ventricles are very similar. Therefore it is only during systole that a large pressure gradient exists between the two ventricles. Therefore left-to-right shunting of blood occurs mostly during systole, causing a pan-systolic murmur to be heard. This principle is depicted in Graph 2.



Graph 2: The Difference between the Left and Right Ventricular Pressures

Final treatment and follow ups:

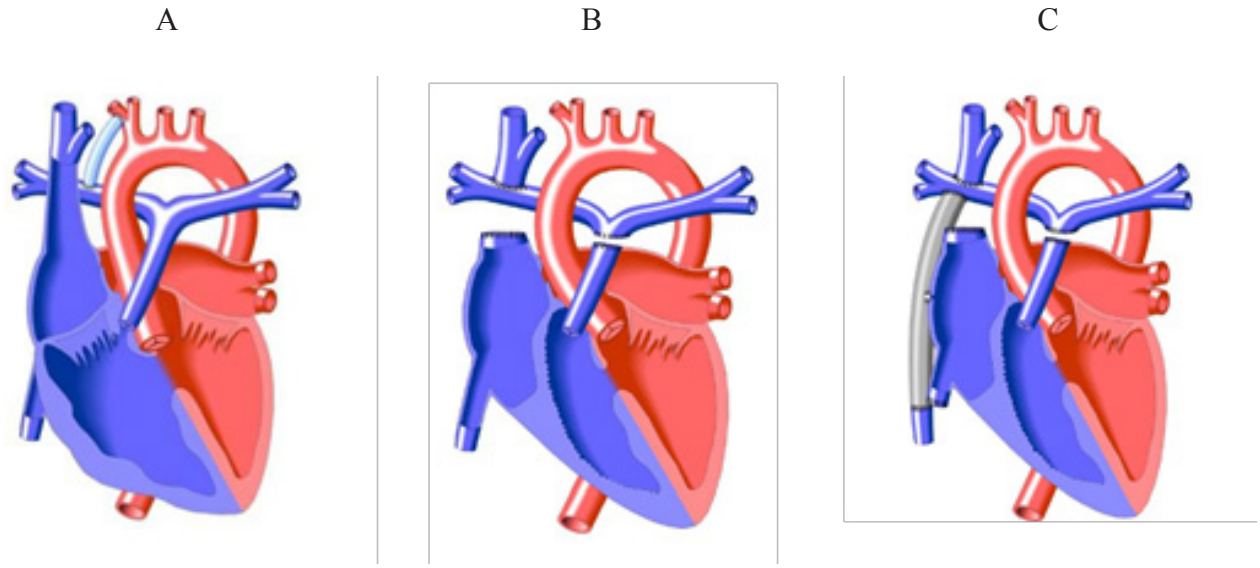


Figure 1: Surgical Interventions in Patients with Tricuspid Atresia. The above figure is a summary of the three surgical opererations required for palliation of Tricuspid Atresia[5]. Key to Figure 1:
A. Modified Right Blalock Interpositional Shunt (Right Subclavian Artery to Right Pulmonary Artery)
B. SCA (Superior Vena Cava to Right branch of Pulmonary Artery)
C. TCPC (Inferior Vena Cava to Right branch of Pulmonary Artery)

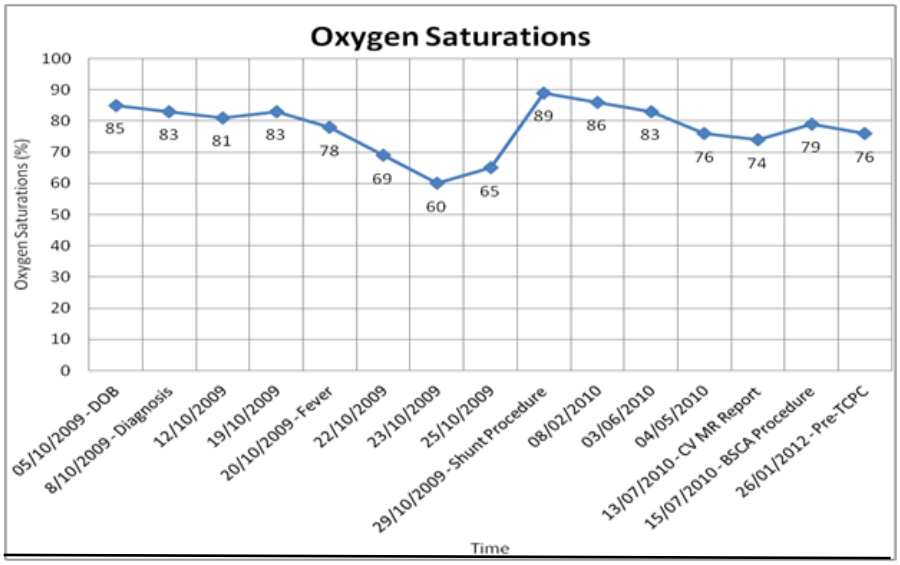
The first operation for tricuspid atresia was done to adjust pulmonary blood flow. Since this child lacked a PDA and appeared cyanosed at birth, his pulmonary blood flow needed to be increased. This increase in pulmonary blood flow was achieved by the insertion of a shunt between the right subclavian artery and the right pulmonary artery i.e.: Modified Right Blalock Interpositional Shunt. This shunt was a temporary one, until the second operation took place. The shunt mimics the function of a PDA, as it allows blood from the aorta via the right subclavian artery to flow into the right pulmonary artery. The shunt tries to compensate for the reduction in the left-to-right shunt across the restrictive VSD.

During this operation, an atrial septectomy was also done. This involved inserting a balloon catheter to enlarge the ASD. The septectomy helps to increase the right-to-left shunt across the atria, in order to prevent right atrial dilatation and allow more blood to reach the left ventricle. This means that the left ventricle has a greater end-diastolic volume and according to the Frank-Starling Relationship, there is a greater stroke volume. This increase in stroke volume is important to make up for the blood that is shunted across the Blalock-Interposition Shunt. The aim of this procedure was to increase the saturations and in fact these increased to 89% at rest, from the previous 65% prior to the operation.

The second (BSCA) and third (TCPC) operations are done separately, rather than together, to reduce morbidity and mortality[1].

The second operation, known as BSCA (or Bi-directional Glenn or Hemi-Fontan), involves connecting the superior vena cava (SVC) to the right branch of the pulmonary artery and removing the Blalock-Taussig Interposition Shunt since it's no longer required. The scope of the BSCA is to shift the blood supply to the pulmonary circulation from one of a high pressure (from the left ventricle) to one of a low pressure (directly from the superior vena cava).

With the Blalock-Taussig Interposition Shunt, the pulmonary circulation is receiving high pressurised blood from the left ventricle meaning that the pulmonary arteries may become thick walled and hard. These changes may result in an increased resistance to blood flow. If this is left for a significant period of time, the resistance offered by the pulmonary circulation, might not allow the patient to be an ideal candidate for the BSCA or TCPC Operations.



Graph 3: Oxygen Saturations. This shows how the oxygen saturations varied during different life events of this patient. Key to Graph 3: DOB – date of birth, CV MR – Cardiovascular Magnetic Resonace, BSCA – Bidirectional Superior Cavopulmonary Anastomosis, TCPC – Total Cavopulmonary Connection.

In the BSCA, the SVC is detached from the right atrium and attached to the right branch of the pulmonary artery. In this way, venous blood directly from the SVC will flow passively into the pulmonary arteries. Without any pump, blood flow across the pulmonary circulation is driven by the central venous pressure and enhanced by the negative intrathoracic pressures that occur during inspiration. As a result this system necessitates a low pulmonary vascular resistance. Further stressing this fact is the age at which this operation is carried out i.e.: at 6 - 9 months. This is the optimum age as the pulmonary vascular resistance would have decreased considerably when compared to that of birth. In this case, the operation was performed at nine months of age. The saturations increased to 79% on air from 74%.

Graph 3 depicts how the onset of fever caused the patient's oxygen saturation to drop dramatically and initiate a cascade of surgical interventions. Overall, after every intervention, the patient's oxygen saturations improved (especially after the insertion of the Blalock-Taussig Interposition Shunt), but with the child growing and becoming more active, the intervention's benefits become limited due to the continuosly increasing demands made by the patient's active body. This explains the gradual drop of oxygen saturations that occur after every intervention.

The third and final operation is known as the TCPC or Fontan procedure. Prior to this operation, a pre-operative assessment is performed with a diagnostic cardiac catheter. The main aim of this test is to establish whether the patient will be likely to benefit from the TCPC operation on the basis of a transpulmonary gradient which is less than 6mmHg. As discussed earlier the results from the pre-TCPC diagnostic catheter show that the child is a candidate for the Fontan operation[1].

After this assessment the child was prescribed enalapril, an Angiotensin Converting Enzyme (ACE) inhibitor, to be taken until the TCPC is done. This was prescribed in order to preserve left ventricular function, by decreasing both afterload and systemic vascular resistance. In doing so, the left ventricle does not have to generate high pressures to eject blood during systole, thus reducing the risk of left ventricular hypertrophy.

The TCPC is planned to take place when the child is about four years of age. In the TCPC the inferior vena cava (IVC) will be connected to the right branch of the pulmonary artery. In the end the right branch of the pulmonary artery will end up attached to the SVC and IVC. The TCPC reduces the volume overload presented to the left ventricle, improves oxygen saturations as it is arranged in such a way that there is no longer any mixing of blood and it finally attaches the low pressure pulmonary system with a low pressure systemic venous system.

This child's mother has recently set up an assocation, known as Beating Hearts Malta. This will help to increase the awareness and show support to patients living with a congenital heart defect. More information about this association can be found on their Facebook Page - Beating Hearts Malta.

Figure 2: The logo of Beating Hearts Malta.

Fact Box 3:

Name of Condition: Tricuspid Atresia

Tricuspid atresia is the third most common cyanotic congenital heart disease. Patients with tricuspid atresia lack a tricuspid valve between the right atrium and right ventricle. Therefore, there is no right atrioventricular communication and as a result the right ventricle remains hypoplastic and undeveloped. These patients are thus left with only one functioning ventricle i.e.: the left ventricle, hence the term univentricular heart. Other defects that are present in patients with tricuspid atresia include an atrial septal defect (ASD), a ventricular septal defect (VSD) and possibly a patent ductus arteriosus (PDA).

Risk Factors: The exact aetiology of tricuspid atresia is unknown, however there are a number of risk factors that may increase the chances of a person developing this condition. These include:

- A Family History of Congenital Heart Defects
- Antenatal problems such as an infection with the Rubella virus, uncontrolled diabetes mellitus during pregnancy and alcohol consumption during pregnancy.
- The use of certain teratogenic drugs during pregnancy such as Lithium, Sodium Valproate, Carbamezapine and other anticonvulsants.
- The presence of Trisomy 13, 18 and 21 is associated with a greater likelihood of the presence of congenital heart defects.

Clinical Features: At birth the patient may be well or have some minimal cyanosis as there is the PDA which augments pulmonary blood flow. However the PDA usually closes 24 to 48 hours after birth and when it closes, there is reduced blood flow to the lungs, and the patient may become severely cyanosed and breathless and may also collapse.

Symptoms of Tricuspid atresia include:

- Breathlessness
- Fatigue
- Poor exercise tolerance and weakness
- Poor Feeding

Signs of Tricuspid Atresia include:

- Cyanosis
- A Pansystolic murmur
- Tachypnoea
- Poor weight gain and slow growth

Diagnosis and Management: The diagnosis of tricuspid atresia is confirmed by an echocardiogram. Once the diagnosis of tricuspid atresia is established, one has to ensure that there is adequate pulmonary blood flow. If there is a PDA, one can start the patient on a prostaglandin E1 infusion to maintain the ductus arteriosus patent. On the other hand, if there is no PDA, the surgical insertion of a left-to-right shunt is required. The latter procedure is known as a Modified Right Blalock Interpositional Shunt. This involves the insertion of a shunt between the right subclavian artery and the right pulmonary artery branch. This operation is usually carried out within the first few days of life.

The second operation occurs when the patient is 4 to 9 months old and involves the removal of the previous Blalock shunt and the connection between the superior vena cava and the right branch of the pulmonary artery. This is known as a Bi-directional Superior Cavopulmonary Anastomosis (BSCA). The

third and final operation is the Total Cavopulmonary Connection (TCPC) and involves the connection of the inferior vena cava and the right branch of the pulmonary artery. This is normally performed when the patient is 1 to 4 years of age. The BSCA and TCPC operations help to improve the patient's oxygen saturations, relieve the patient from cyanosis, and reduce the volume overload presented to the left ventricle.

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Case Number 4
Pre-eclampsia Toxaemia

Caroline Galdes & Roberta Bugeja
Reviewed by: Dr. Karl Cutajar

Case summary:

Demographic details:

Mrs. KG, female, Żejtun
Referred from: GP

Mrs. KG, a 33 year old primagravida rhesus positive woman was referred to the Emergency Department by her family doctor at 27 weeks gestation. At 25 weeks of gestation, she had been diagnosed with hypertension and was started on labetalol therapy. At 27 weeks of gestation she was admitted in view of persistently raised blood pressure which was not being controlled with Labetalol, generalised (facial, hands and lower limbs) oedema and frequent frontal headaches. The patient also complained of photophobia. Following examination it was found that the patient was suffering from pre-eclampsia toxaemia. Delivery was expedited in view of the developing complications.

Presenting complaint:

Facial, hands and bilateral lower limb oedema: 2 weeks
Frontal headaches: 3 days
Photophobia: 3 days
Raised Blood Pressure

History of presenting complaint:

The patient presented with facial, hand and bilateral lower limb oedema which started 2 weeks before. She reported that facial oedema was worse in the morning but then subsided during the day. Frontal headaches had occurred in the past three days and were worse when lying down. Her blood pressure started to rise during the first trimester, at 15 weeks gestation; this indicated that the patient was suffering from essential hypertension.

Present obstetric history:

Mrs. KG is a primagravida. Her last menstrual period was on the 28th of April 2012, computing her expected date of delivery to the 5th of February 2013. She is known to suffer from polycystic ovarian syndrome.

Mrs. KG did not have any problems during the first trimester, except that at 15 weeks gestation, her blood pressure was found to be 140/80mmHg and she was referred for closer monitoring by the family doctor. The patient was on Folic acid during the first trimester and did not report any vaginal bleeding during the first three months. All routine investigations (complete blood count; Syphilis, Hepatitis B and C, HIV screen, blood glucose) were reported within the normal ranges. Her blood group was A Rhesus positive.

She had no problems during the second trimester except for repeatedly borderline high blood pressure which was being monitored by her family doctor. In the late second trimester at 25 weeks gestation, the

patient presented to the antenatal clinic with significant lower limb oedema. Urine testing revealed a trace of albumin in the urine. Her blood pressure was 160/100mmHg. She was admitted to an obstetric ward for 4 hourly blood pressure charting. Pre-eclampsia toxaemia bloods were taken: complete blood count, urea and electrolytes, serum creatinine, uric acid, liver function tests, coagulation profile, random blood glucose and 24-hour urinary collection to test for proteinuria. The results showed elevated uric acid and proteinuria was greater than 300g/24hrs. An abdominal ultrasound and Doppler umbilical blood flow velocimetry were also done. The abdominal ultrasound reported the fetus to be above the 90th centile indicating macrosomia and the need for closer monitoring.Umbilical artery flow had an aqeduate pulsatility index, resistence index and systolic/diastolic ratio. The fact that the child was above the 90th centile, in itself ensures adequate blood supply to the fetus; should the blood supply have been diminished, the fetus would have been on the lower end of the centile chart. She was discharged on 200mg Labetalol daily and her blood pressure was stable on discharge. She was asked to revisit her family doctor for further blood pressure monitoring.

Past gynaecological history:

Patient had her menarche at 14 years of age, her menses were irregular ranging from 40 to 60 days. She had regular smear tests; her last being in 2011 and reported to be normal. She was never on the oral contraceptive pill or on any other formulation of contraception. She had a history of infertility attributable to polycystic ovarian syndrome, for which she was started on clomiphene. This treatment was successful in her achieving a pregnancy.

Past medical and surgical history:

Past medical history:

Polycystic ovarian syndrome

Past surgical history:

Left axillary cystectomy

Drug history:

Drug	Dosage	Frequency	Type	Reason
Folic acid	5mg	Once daily	Vitamin B9	Prevents neural tube defects. Taken during the first trimester.
Pregnatal		Once daily	Multi-vitamins	Helps to cover any nutritional gaps in the mother's diet. Taken from the second trimester onwards.

Family history:

Her mother is known to suffer from essential hypertension. Two of her aunts are known to suffer from type 2 diabetes mellitus.

Social history:

She is married and lives with her husband. She works as a teacher. She does not smoke or drink alcohol and does not exercise regularly.

Systemic inquiry:

- General Health: looks oedematous
- Cardiovascular System: nil to note
- Respiratory System: shortness of breath on exertion
- Gastrointestinal System: nil to note
- Genitourinary System: nil to note
- Central Nervous System: frontal headaches, photophobia
- Musculoskeletal System: nil to note
- Endocrine System: nil to note
- Others: nil to note

Current therapy:

Labetalol 100mg BD – to lower the patient's blood pressure.

Discussion of results of general and specific examinations:

At 27 weeks of gestation: On inspection, the patient looked ill and severely oedematous; involving the face, both hands and both lower limbs up to the knees. The patient's blood pressure was found to be 152/83mmHg and her pulse was 110 beats/min regular.

Blood pressure and pulse monitoring were carried out 4 hourly in order to check if the patient was worsening or getting better. Her blood pressure readings were quite labile and were not adequately controlled with therapy.

On auscultation, the chest was clear. There was adequate air entry on both sides of the chest. No bibasal crackles were heard which would have been a sign of pulmonary oedema – a complication of pre-eclampsia toxaemia.

On abdominal examination, the abdomen was distended compatible with pregnancy. The foetus was palpable in a longitudinal lie and the presentation was cephalic. The fetal heart rate was audible and of normal rate. The abdomen was soft and non-tender. No pain was elicited in the right upper quadrant. Right upper quadrant pain is a sign of impending eclampsia due to capsular pain from the liver.

From the neurological examination, the patient was noted to have hyper-reflexia which was most marked in the knee jerk on both sides. There was also one tap of clonus. Together with the symptoms of photophobia and frontal headaches, symptomatology pointed to central nervous system involvement.

Differential diagnosis:

- Pre-eclampsia toxaemia
- Pregnancy-induced hypertension with a urinary tract infection
- Nephrotic Syndrome

Diagnostic procedures:

Laboratory exams:

Test: Complete blood count.
Justification for test: To look for anaemia (haemolysis) and thrombocytopenia (platelet count <100x10^9/L), both signs of haematological disturbances, part of pre-eclampsia[5].
Result: At diagnosis (25^{+2} weeks gestation): Hb – 12.5g/dL, Platelets – 332x10^9/L
Pre-operative (29^{+2} weeks gestation): Hb – 12.3g/dL, Platelets – 338x10^9/L
Post-operative: Hb – 11.2g/dL (low), Platelets – 380x10^9/L
Conclusion: Both the haemoglobin level and the platelet count were normal throughout her pregnancy hence demonstrating a lack of haematological disturbances due to pre-eclampsia.

Test: Uric acid
Justification for test: In women with pre-eclampsia, serum uric acid is elevated (mean: 6.2 +/- 1.4mg/dl)[8], however it has been shown to be a weak predictor of pre-eclampsia and severe hypertension[9]. It may be a predictor of renal tubular dysfunction, but is not a specific marker[10].
Result: At diagnosis (25^{+2} weeks gestation): 257umol/L
Pre-operative (29^{+2} weeks gestation): 348umol/L (high)
Post-operative: 446umol/L (high)
Conclusion: An elevation of the patient's uric acid level in the serum at 29^{+2} weeks gestation could be an indicator decreased renal perfusion or increased uric acid production by the poorly perfused tissue[12], hence a demonstration of multisystem involvement in pre-eclampsia. This also shows a progression to the worse in our patient, despite the treatment given, and hence could have contributed to the decision to carry out an elective cesarean section so early on in pregnancy. Since the pre-eclamptic state does not resolve immediately after the birth of the child (up to 6 weeks post-partum), the level of serum uric acid was persistently high even post-operatively.

Test: Urea and Electrolytes
Justification for test: To look for renal dysfunction; serum creatinine >90µmol/L[5].
Result: At diagnosis (25^{+2} weeks gestation): creatinine – 53umol/L, urea-3mmol/L; electrolytes within range
Pre-operative (29^{+2} weeks gestation): creatinine – 66umol/L, urea – 3.4mmol/L; electrolytes – within range
Post-operative: creatinine – 76umol/L, urea – 4.7mmol/L; electrolytes – within range
Conclusion: Despite the elevation of uric acid levels in the serum, serum creatinine, urea and electrolyte levels were continuously within the normal range. Being good predictors of renal function, such results indicate very little kidney damage if any, as indicated previously from the elevated uric acid levels.

Test: Liver function tests
Justification for test: To look for elevated liver enzymes, which would indicate liver malfunction as part of the multisystem effects seen in pre-eclampsia: ALT >32 IU/L, AST >30 IU/L 5.
Result: At diagnosis (25^{+2} weeks gestation): ALT – 12 IU/L, ALP – 85 IU/L
Pre-operative (29^{+2} weeks gestation): ALT – 15 IU/L, ALP – 109 IU/L (high)
Post-operative: ALT – 22 IU/L, ALP – 77 IU/L
Conclusion: Normal aminotransferase levels show lack of liver involvement in the patient's condition. It is also an indicator for HELLP syndrome.

Test: APTT/INR

Justification for test: These tests are only done if liver function tests and platelet count are abnormal. They may be abnormal in consumptive coagulopathies and disseminated intravascular coagulation, both known complications of severe pre-eclampsia[10].

Result: At diagnosis (25^{+2} weeks gestation): APTT – 29.9s (high), INR – 0.87 (low)
Pre-operative (29^{+2} weeks gestation): APTT – 26.7s; INR – 0.86 (low)
Post-operative: APTT – 28.3s, INR – 0.87 (low)

Conclusion: APTT and INR values were borderline, and hence the results are not significant of an underlying coagulopathy.

Test: Thyroid function tests

Justification for test: Abnormal TSH levels could be associated with pre-eclampsia. A U.S. study found a rise in TSH levels in pre-eclamptic females, when compared to normotensive patients. The findings suggest that there is the possibility of developing hypothyroidism during pre-eclampsia, but more so 20 years after birth of the child[11]. Thyroid function tests in pregnancy need to be carefully interpreted since can be due to serum and functional physiological changes.

Result: Post-operative: TSH – 1.95mIU/L, free T4 – 11.6pmol/L

Conclusion: Thyroid function was found to be normal.

Test: Urinalysis, microscopy and culture

Justification for test: Urinalysis may be used as a screen for proteinuria[10]. Microscopy is used to detect the presence of cells and casts in the urine which could be a beneficial diagnostic tool, while culture is indicated for screening for a possible urinary tract infection.

Result: Pre-operative (29^{+2} weeks gestation): proteins – 150mg/dL (very high); erythrocytes – 0-5/mm^3, leukocytes – 0-5/mm^3, casts-absent, MC and S – Acinetobacter baumannii cultivated.
Post-operative: proteins – 25mg/dL (high); erythrocytes – negative, leukocytes – negative, casts - absent.

Conclusion: The increased glomerular permeability characteristic of pre-eclampsia was the cause of the significant proteinuria the patient experienced[12]. An increasing proteinuria and worsening blood pressure recordings indicate a declining condition and hence point towards the choice to deliver the child.

Instrumental exams:

Test: Cardiotocography

Justification for test: It is a screening test to monitor foetal well-being. It shows acute cardiac changes in the foetus reflecting placental flow. It indicates acute hypoxia and foetuses in danger of developing hypoxia[15].

Result: At diagnosis (25^{+2} weeks gestation): Baseline rate: 150bpm, Variability: >5 beats per minute, accelerations: present and concordant with uterine contractions, decelerations: nil.
Pre-operative (29^{+2} weeks gestation): Baseline rate: 140bpm, variability: >5 beats per minute, accelerations; present and concordant with uterine contractions, decelerations: nil.

Conclusion: The cardiotocograms done were normal. According to the NICE guidelines, the four categories of variables: baseline rate, variability, accelerations and decelerations fall within the reassuring ranges[13].

Test: Doppler ultrasound

Justification for test: It is used to evaluate the feto-placental unit in order to assess placental insufficiency – a known complication of pre-eclampsia. If the placenta is functioning well, the blood flows easily. If there is placental insufficiency, there would be resistance to blood flow. In extreme cases where the resistance is too high, there may be periods

of reverse blood flow from the fetus to the umbilical blood vessels. Umbilical cord flow together with symptomatology can indicate the severity of the disease.

Result: At diagnosis (25^{+2} weeks gestation): pulsatility index, resistance index and systolic/diastolic ratio were within the normal ranges.
Pre-operative (29^{+2} weeks gestation): pulsatility index, resistance index and systolic/diastolic ratio were within the normal ranges.

Conclusion: The ultrasounds indicated that the foetus was receiving an adequate blood supply.

Test: 24-hour urinary collection

Justification for test: It is a quantitative method to measure proteinuria[1]. This test was done to confirm the diagnosis of pre-eclampsia[3].

Result: At diagnosis (25^{+2} weeks gestation): 211.2mg/24hr (high)
Pre-operative (29^{+2} weeks gestation): 1257mg/24hr (very high)

Conclusion: Both results indicate that there was significant proteinuria in concordance with the diagnosis.

Test: Oral glucose tolerance test

Justification for test: On Doppler ultrasound the foetus was found to be greater than the 90th centile indicating macrosomia. This may be caused by diabetes mellitus[4]. The patient also had a history of polycystic ovarian syndrome which may be associated with the development of diabetes [2].

Result: At 28 weeks gestation: Fasting blood glucose: 4.1mmol/L; at 1hr: 8.88mmol/L; at 2hr: 7.88mmol/L.

Conclusion: The results obtained were within the normal ranges except the 2 hour glucose which is slightly above the higher limit of normal (7.8mmol/L) which indicates impaired glucose tolerance[14].

Therapy:

In view of her uncontrolled hypertension and symptoms, the patient was started on the following drug regime:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Labetalol	100mg	BD	Alpha/Beta blocker	Lowers high blood pressure
Nifedipine	20mg	BD	Calcium channel blocker	Lowers high blood pressure
Hydralazine	10mg	QDS	Vascular smooth muscle relaxant	Lowers high blood pressure

At 29^{+2} weeks of gestation: Despite the change introduced in her drug therapy the patient's condition remained uncontrolled. Her condition continued to worsen. Her blood pressure was found to be 180/110mmHg. On inspection, she had facial, hand and lower limb oedema. She had bibasal crackles on chest auscultation – a sign of pulmonary oedema. On urinalysis there was 3 + protein and macroscopic haematuria. The patient was catheterised and a urinometer was attached in order to measure urine output accurately. A decision was taken to perform a lower segment Caesarian section due to worsening blood pressure and the developing complications. Pre-operatively, pre-eclampsia toxaemia bloods were taken. Blood was cross-matched and grouped and saved. She was administered two doses of dexamethasone 12mg via intramuscular route at 12hrs apart to try and stimulate foetal pulmonary type 1 pneumocyte conversion to type 2 pneumocyte for surfactant release. She was also started on low molecular weight heparin since pre-eclampsia is associated with a high risk of thrombotic events. The patient was started on continuous cardiotocographic monitoring, in order to monitor foetal well-being. She was continued on Labetalol and Nifedipine whilst Hydralazine (PO) was added to her drug regime.

Surgery:

Emergency lower segment Caesarian section was done at 29^{+2} weeks gestation, under epidural anaesthesia. It was remarked that both ovaries were polycystic and the Fallopian tubes were normal.

Diagnosis:

The patient was diagnosed with pre-eclampsia toxaemia; defined as an elevation of blood pressure above 140/90, with proteinuria or oedema of the hands, feet and face[4]. It predominantly affects primagravida females[5] and is more common at increasing gestational age[4]. The patient was preganant with her first child, and had various other risk factors for developing this condition; including: polycystic ovarian syndrome and a family history of essential hypertension[6]. After previously being diagnosed with hypertension and started on treatment, at 27 weeks of gestation, she presented to her family doctor with generalised oedema, and frontal headaches. She later developed photophobia and also complained of shortness of breath. On examination however, no basal crackles were heard, which would have hinted the presence of pulmonary oedema. She did have hyperreflexia on examination – which is a sign of cerebral irritation, a blood pressure 152/83 mmHg, and proteinuria on urine dipstick and in the 24hr urine collection test. Pre-eclampsia is diagnosed when hypertension with blood pressure ≥140/90 and proteinuria; defined as ≥300mg/day in a single specimen or ≥ 1+ on urine dipstick, are detected for the first time after 20 weeks' gestation. Being a multi-organ disease, the diagnosis of pre-eclampsia becomes more certain if symptoms and signs associated with organ system malfunction are diagnosed in addition to the hypertension and proteinuria[7]. Such symptoms and signs include:

Symptoms:
- Persistent severe headache
- Persistent epigastric pain
- Disturbances in vision
- Vomiting
- Severe swelling of the face, hands and feet, of sudden onset

Signs:
- Hyperreflexia (Neurological disturbance)
- Serum Creatinine concentration ≥110mmol/L (Renal insufficiency)
- Thrombocytopenia; platelet count $\leq 100 \times 10^9$/L (Haematological disturbance)
- Disseminated intravascular coagulation (Haematological disturbance)
- Elevated liver enzymes (Liver disease)

Many of the above mentioned signs and symptoms were present in this patient, hence pointing towards the diagnosis of pre-eclampsia toxaemia. Thus the patient was admitted for closer monitoring of her condition and the investigations listed previously were conducted. From the results of the investigations, the diagnosis of pre-eclampsia was confirmed.

Final treatment and follow ups:

Severe pre-eclamptic hypertension is a risk factor for placental abruption and fetal growth restriction, while risking hepatic rupture and development of eclampsia in the mother[12]. Thus, after all measures were taken to control her condition and delay birth as much as possible, an elective C-section was performed in view of severe Pre-eclampsia toxemia and the maternal complications.

She had been on labetalol and nifedipine treatment, despite which, her hypertension continued to worsen. Pre-operatively her blood pressure varied between 145/85 – 170/90mmHg. She also developed bibasal

crackles; a sign of pulmonary oedema, and haematuria; a sign of renal tubular damage. Thus she was given corticosteroid therapy, in hope for improving fetal lung maturation, and started on 40mg clexane prophylactically. The epidural procedure was commenced and 4g of magnesium sulfate in 100mLs of normal saline was administered to the patient pre-operatively (to reduce the risk of convulsions in the presence of hyper-reflexia and increased cerebral excitability) and the C-section was performed, to prevent an eclamptic episode. Delivery by C-section was preferred since child was pre-term. A female infant weighing 1180 grams was born. She had an Apgar score of 6 and 8 at 1 and 5 minutes respectively. The infant was intubated and transferred to the neonatal paediatric intensive care unit.

The risk of development of eclampsia or continuation of the pre-eclamptic state does not resolve immediately after delivery of the child[7]. Thus the patient was kept on labetalol treatment post-partum, as indicated in the NICE guidelines[9]. The patient was also given oxygen via nasal prongs. In addition, she was put on an intravenous infusion of magnesium sulfate (2mL/hr) therapy, which was continued for 24 hrs, and was kept on a slow intravenous infusion of saline. The mother was also monitored for signs of toxaemia, including; hypotension, respiratory depression, oliguria and loss of reflexes. Her blood pressure was monitored every four hours, Pre-eclamptic Toxaemia (PET) blood tests were once again taken post-operatively, and fluid balance was continuously monitored. Patient was sent home after 8 days in view of blood pressure 130/80 mmHg, stable blood tests and improving clinical picture of her condition.

After discharge from hospital, patient was advised to have her blood pressure checked at least every 1-2 days for up to two weeks after discharge. Antihypertensive therapy should be adjusted by her doctor according to her blood pressure readings. The patient was offered a post-natal review 6 weeks after birth, to check her blood pressure readings, and whether or not she is still on antihypertensive therapy, which would then be an indiction for further investigations and management[9].

Fact Box 4:

Title: Pre-eclampsia toxaemia

This is a multi-system disorder which manifests as hypertension and proteinuria after 20 weeks of gestation. The disease originates from the placenta and is cured by delivery. There is blood vessel endothelial damage with a maternal inflammatory response which leads to vasospasm, increased capillary permeability and clotting dysfunction which account for hypertension, proteinuria, reduced placental blood flow and reduced cerebral perfusion resulting in eclampsia.

Risk factors:

- Nulliparity
- Previous history
- Family history
- Older maternal age
- Chronic hypertension
- Diabetes
- Twin pregnancies
- Autoimmune disease
- Renal disease
- Obesity

Symptoms: Usually asymptomatic.
At a late stage:

- Headaches
- Drowsiness
- Visual disturbances
- Nausea and vomiting
- Epigastric pain

Signs:

- Hypertension
- Gross and non-postural oedema
- Epigastric tenderness
- Proteinuria on urinalysis
- Hyperreflexia
- Clonus

Prevention:

All pregnant women, should have regular blood pressure and urinalysis checks. Low dose aspirin (75mg) starting from 16 weeks reduces the risk of pre-eclampsia and is recommended in women at risk.

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Case Number 5
Anton's Syndrome

Luke Portelli
Reviewed by: Dr. Pierre Ellul

Case Summary:

Demographic details:

Mr. AS, male, Nadur
Referred from: Gozo General Hospital

57-year-old male admitted to ITU with a severe Community Acquired Pneumonia. Stayed in ITU for about three weeks and during this period suffered an episode of deterioration which was attributed to multiple venous infarcts of the brain. This caused the patient to become blind.

Presenting complaint:

Sudden onset blindness.

History of presenting complaint:

The blindness occurred suddenly and with no warning. Patient became increasingly disoriented and was clearly blind although adamantly kept saying that he was able to see normally. At the time the patient had been in ITU for about three weeks.

Past medical and surgical history:

Past medical history:

- Severe Community Acquired Pneumonia lasting three weeks, exactly preceding the blindness. Patient had to be admitted to ITU due to the severity of the pneumonia.
- Mild Hypertension.

Past surgical history:

- Patient did not have any major operations.

Drug history:

Drug	Dosage	Frequency	Type	Reason
Tazocin Piperacillin/Tazobactam	Piperacillin 4g Tazobactam 0.5g	TDS	Antibiotic	Treatment for pneumonia
Levofloxacin	500mg	Dly	Antibiotic	Treatment for pneumonia
Doxycycline	100mg	BD	Antibiotic	Treatment for pneumonia

Antibiotics were later switched due to the possibility of a viral pneumonia.

Drug	Dosage	Frequency	Type	Reason
Ganciclovir	300mg - IV	BD	Antiviral	Treatment for CMV pneumonia

Patient received IV ganciclovir for 12 days and was later switched to oral valganciclovir.

Family history:

The patient did not have any major illnesses in the family. His father had hypertension, as did his uncle but other than that nil of note.

Social history:

Patient used to smoke cigarettes and drink alcohol on occasions. Patient did not divulge the actual amount of cigarettes and alcohol he consumed.

Systemic inquiry:

- General Health: patient looks very thin and showed cachexia due to the long stay in ITU.
- Cardiovascular System: relatively normal except for mild hypertension.
- Respiratory System: patient was still short of breath even after the pneumonia was resolving. Patient also had a cough and was on occasions bringing up sputum.
- Gastrointestinal System: relatively normal. Patient had a NG tube.
- Genitourinary System: urine output was normal and not painful.
- Central Nervous System: normal.
- Musculoskeletal System: very weak due to the cachexia. Patient was unable to stand by himself.
- Endocrine System: normal.
- Others: pupillary light reflex and fundoscopy were normal.

Current therapy:

After the period in ITU and the occurrence of the blindness, the patient recovered considerably. However he was still given the antivirals for complete elimination of the CMV infection.

Discussion of results of general and specific examination:

The pupillary light reflex of the patient was normal, suggesting that his anterior visual pathway was intact and functioning normally. This indicated that the blindness was arising from a problem in the posterior visual pathway or maybe the occipital lobe. Patient was clearly blind however he insisted that he was seeing things normally. After some days he began to recognise some shades of color but other than that he remained blind.

General examination was normal. Chest was clear suggesting that the patient was recovering from the pneumonia.

Differential diagnosis:

- Regarding the pneumonia, at first it was thought that it was bacterial in nature, however diagnosis changed to CMV infection since CMV was detected by PCR.
- The blindness was probably caused by an injury to the brain during the patient's stay at ITU. Due to the complexity of the symptoms and their relative rarity, the diagnosis was still unknown.

Diagnostic procedures:

Laboratory Exams:

Test: Cell pathology.
Justification: Exclusion of malignancies.
Result: Scattered bronchial epithelial cells, many of which exhibited hyperplastic changes and few macrophages are present on a background of erythrocytes.
Conclusion: No malignant cells seen.

Instrumental Exams:

Test: CT Thorax.
Justification: Detection of pneumonia.
Results: Inflammatory changes of the lung are noted bilaterally basally and in the left upper lobe. Some pleural effusion is noted but there is no abscess formation. Lymphadenopathy is seen but there was no evidence of malignancy.
Conclusion: Pneumonia is confirmed.

Test: CT Brain.
Justification: Finding the cause of blindness.
Result: Multiple hypo dense zones of the brain are noted bilaterally.
Conclusion: These changes are most probably due to a post-infarctive process.

Test: MRI Head.
Justification: Finding the cause of blindness.
Result: Multiple bilateral abnormal cerebral foci. These appearances are suggestive of multifocal haemorrhages infarcts with associated haemorrhages changes, worse in the occipital regions bilaterally. Normal appearance of the Circle of Willis. No evidence of aneurysm and no evidence of venous sinus thrombosis.
Conclusion: Multifocal bilateral haemorrhagic infarcts.

Therapy:

Drugs:

Drug Name	Dosage	Frequency	Type	Reason
Lactulose	10mls	Dly	Synthetic, non-digestible sugar	Treatment of constipation
Omeprazole	40mg	Dly	PPI	Upset stomach

Patient received the last dose of oral anti-viral on the day of discharge.

Diagnosis:

Due to the pupillary light reflex being normal, it was concluded that the problem did not arise from the anterior visual pathway, as most cases of blindness do. The CT scans and MRI showed infarcts in the occipital lobe and this suggested that the problem was arising from the occipital cortex itself. Cortical blindness is defined as visual inability in the presence of normal light reflexes and normal fundoscopy[1]. This observation led to the diagnosis of Anton's syndrome, which is a very rare case of blindness. This syndrome is characterised by a phenomenon called confabulation[1]. Patients suffering from Anton's syndrome adamantly say that they can see when they obviously cannot and also speak as if they had normal vision[2]. This denial of vision problems is called visual anosognosia[2].

Cortical blindness was first described in detail by Gabriel Anton, who was an Austrian neurologist. This is why this syndrome now bears his name[3].

Final Treatment and Follow ups:

The treatment in this case is very limited. Follow-ups included visits from speech language pathologists, physiotherapy teams and occupational therapists. The patient was suggested to have a repeat CT Thorax, two weeks after the first one and to be regularly followed up at the stroke clinic.

Fact Box 5:

Title: Anton's Syndrome

Anton's Syndrome is a very rare type of brain damage that occurs in the occipital lobe. People with the condition suffer from cortical blindness.

Risk Factors: Since Anton's Syndrome is technically a stroke, its risk factors include:

- Hypertension
- Diabetes
- Smoking
- Alcohol consumption
- Prolonged periods of inactivity

Symptoms:

- Blindness (although the patient denies his blindness)
- Headaches
- Confusion.

Signs: A very specific sign of Anton's Syndrome is confabulation. Confabulation is a way by which the patient denies his blindness, walking and trying to move as he still sees normally. Confabulation is made very clear when the patient stars to describe objects and people in his vicinity that are in fact not there.

Prevention: This consists mainly in preventing cerebrovascular disease which include a healthy life style, controlled blood pressure, no smoking and alcohol consumption and others.

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Case Number 6
Pancreatic Ductal Adenocarcinoma

Daniel Debattista & Sarah Bezzina
Reviewed by: Mr N. Spiteri & Mr A. Attard

Case summary:

Demographic details:
Mr. SS, male, Tarxien
Referred from: Polyclinic

A 61-year-old gentleman who lives with his wife and 20-year-old son, presented to the polyclinic with a four week history of pruritus. On examination he was found to be jaundiced and his LFTs were high. Consequently he was referred to Mater Dei Hospital where, following ERCP and MRCP, he was found to have a tumour of the head of the pancreas, causing a stricture of the common bile duct, with consequent obstructive jaundice. The patient was planned for Whipple's operation (pancreatico-duodenectomy), which was extended to total pancreatectomy, splenectomy and cholecystectomy. The operation was successful and the patient is recovering.

Presenting complaint:

Pruritus: 4 weeks

History of presenting complaint:

The patient reported generalised itching for four weeks. The itching woke him up at night and disturbed his sleep. The patient was jaundiced and reported passing dark urine and pale stools which were difficult to flush. Recent weight loss and decreased appetite were also reported. The patient denied any back pain or abdominal pain. Moreover, he did not experience any chills or rigors. He reported reflux and dyspepsia following a meal. He did not complain of any nausea, vomiting or haematemesis.

Past medical and surgical history:

Past medical history:

- Hypertension
- No history of diabetes, ischaemic heart disease, asthma, chronic heart failure or epilepsy.
- No previous history of jaundice.

Drug history:[1]

Drug	Dosage	Frequency	Type	Reason
Amlodipine	5mg PO	Dly	Calcium Channel Blocker	Hypertension
Enalapril	20mg PO	Dly	ACE-Inhibitor	Hypertension
Burinex	2mg PO	Dly	Loop Diuretic	Hypertension

Family history:

Father died of a myocardial infarction at the age of 66.
Mother died of pulmonary embolism.
Siblings and children do not suffer from any medical condition.
No family history of cancer.

Social history:

The patient is a married pensioner, father of three, who lives with his wife and youngest son. He used to do clerical work. He is a non-smoker and drinks socially. He does not abuse of drugs.

Systemic inquiry:

- General Health: looks well in general; reported recent weight loss and decreased appetite
- Cardiovascular System: nil to note
- Respiratory System: nil to note
- Gastrointestinal System: GORD and bloating after a meal; pale stools which are difficult to flush
- Genitourinary System: dark urine (though occasionally it is clear)
- Central Nervous System: nil to note
- Musculoskeletal System: nil to note
- Endocrine System: nil to note

Pre-operative therapy:

- Vitamin K supplements (10mg/Dly, IV) were given in view of the fact that the coagulation cascade may be deficient in such patients[1].
- Prophylactic Clexane® (enoxaparin) therapy was given pre-operatively in view of increased risk of deep vein thrombosis in patients undergoing surgery[1].
- Phenergan® (promethazine hydrochloride) was given for symptomatic treatment of pruritus[1].

Discussion of results of general and specific examinations:

Feature	Discussion
Jaundice, pruritus, pale stools and dark urine	Indicative of an obstructive lesion in the biliary tree. The conjugated hyperbilirubinaemia causes the itchiness in the skin and yellow discolouration in the skin and sclera. Since no bile is secreted from the common bile duct, the stools are pale. Conjugated hyperbilirubinaemia is water soluble and thus is excreted in greater amounts in the urine, turning it dark.
Steatorrhoea	Indicates that lipid absorption is impaired because of an obstruction to the biliary tree, thus inhibiting pancreatic enzymes (including lipase) from being secreted into the small intestine. Lipids are not digested and are passed with the stool, making it difficult to flush.
Weight loss and anorexia	May indicate a chronic illness such as a tumour.
No abdominal pain	Shows that the condition is unlikely to be inflammatory.
Soft abdomen	Excludes peritonitis.
No chills or rigors	Absence of pyrexia makes infective cause unlikely.

Differential diagnosis:[3,4]

Differential diagnosis is from other causes of painless obstructive jaundice[3], such as:

Differential Diagnosis	Features
Tumour of the head of pancreas, periampullary malignant tumours	Biliary ducts appear dilated on ultrasound. This is characterised by painless jaundice, weight loss, and obstruction within head of pancreas, which is confirmed via ERCP and MRCP.
Common bile duct stones	Characterised by tenderness in the right upper quadrant, and dilatation of biliary ducts on ultrasound. However, abdominal pain may be absent.
Benign strictures of the common bile duct	May be due to surgical damage or inflammation caused by a previous stone. Obstructive features are similar to carcinoma of the head of pancreas.
Intrahepatic cholestasis	Mainly caused by viral hepatitis. Low grade jaundice is due to systemic sepsis.
Primary biliary cirrhosis	Hepatomegaly and possible splenomegaly, xanthomas and arthralgia. This disease is characterised by a positive test for anti-mitochondrial antibody and serum IgM. Cirrhosis is confirmed via liver biopsy.
Drugs, such as phenothiazines, anabolic steroids and erythromycin	Discontinuing such drugs will relieve symptoms of obstructive jaundice.
Alcoholic hepatitis	A history of excessive alcohol intake is needed. Presents with features of chronic liver disease, such as spider naevi.
Sclerosing cholangitis	Presence of beading in intra- and extra-hepatic bile ducts on ERCP
Dubin-Johnson syndrome	Characterised by decreased excretion of conjugated bilirubin, intermittent jaundice and pain in the right hypochondrium. Increased urinary bilirubin and pigment granules on liver biopsy.

Diagnostic procedures:

Instrumental exams:

Test: Ultrasound Abdomen (Figure 1)
Justification for test: Patient with pruritus and abnormal LFTs; suspecting stone in biliary tree
Result: Dilated biliary tree and pancreatic duct
Conclusion: Further investigation recommended – referred for CT scan

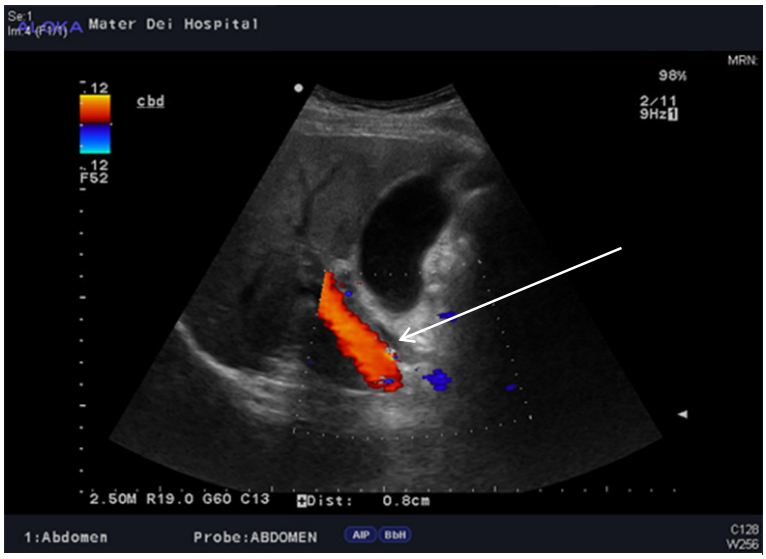

Figure 1: Ultrasound Image, showing the dilated (0.8cm) common bile duct (arrow)

Test: CT Abdomen (Figure 2)
Justification for test: Patient with painless jaundice and dark urine; post ultrasound abdomen findings, suspecting gall stone
Result: Pancreatic duct dilatation and evidence of distal biliary obstruction; no calculi or significant mass lesion
Conclusion: Suspecting vater papilla process and ampullary tumour; ERCP recommended

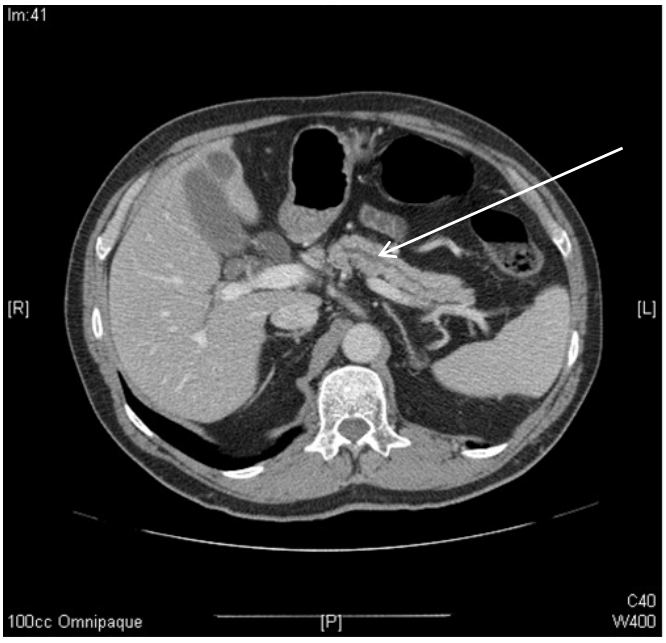

Figure 2: Preoperative CT Abdomen - showing the dilated pancreatic duct (arrow)

Test: ERCP (Endoscopic Rertrograde Cholangiopancreatography) (Figure 3)
Justification for test: To rule out pancreatic head pathology
Result: Ampulla appeared flat and normal; suspected common bile duct stricture
Conclusion: Result inconclusive – patient referred for MRCP

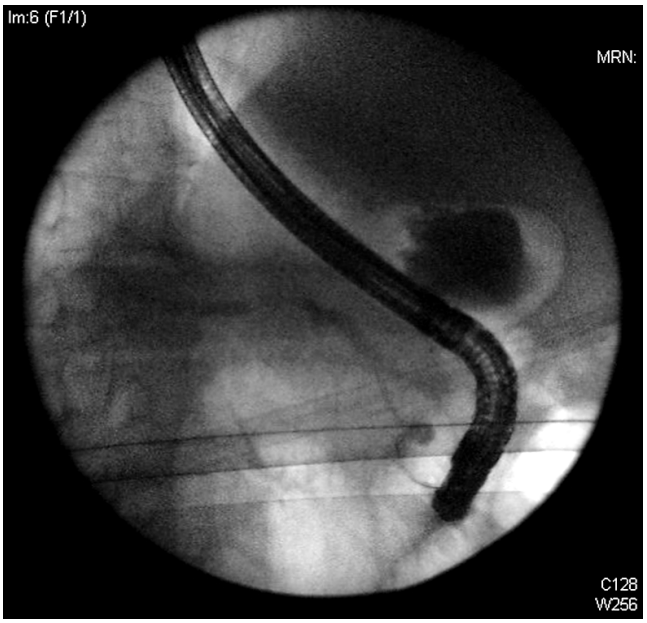

Figure 3: ERCP, showing the biliary tree

Test: MRCP (Magnetic Resonance Cholangiopancreatography) (Figure 4)
Justification for test: Confirm ERCP findings
Result: Common bile duct stricture, noted to be possibly malignant
Conclusion: Suspicion of obstruction of the common bile duct within the head of pancreas confirmed. Surgery needed to resect pancreatic head pathology

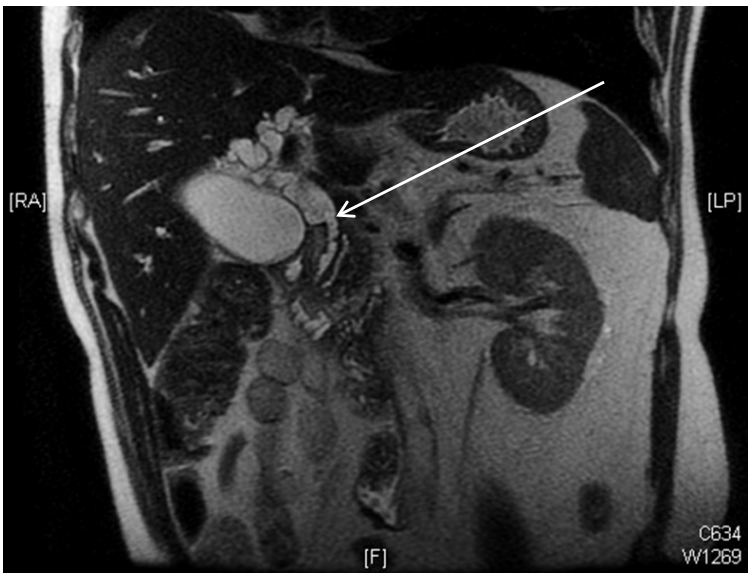

Figure 4: MRCP showing stricture at common bile duct (arrow), with proximal dilatation

Therapy:

Drugs:[1]

Drug	Dosage	Frequency	Type	Reason
Promethazine Hydrochloride (Phenergan®)	50mg PO	TDS	Antihistamine	Symptomatic relief treatment of pruritus
Bumetanide	1mg PO	Dly	Loop Diuretic	Hypertension

Enalapril	20mg PO	Dly	ACE-Inhibitor	Hypertension
Amlodipine	5mg PO	Dly	Calcium Channel Blocker	Hypertension
Vitamin K	10mg IV	Dly	Vitamin supplements	Aids the clotting cascade as this may be deficient in such patients
Enoxaparin Sodium (Clexane®)	40mg SC	Dly	Parenteral angicoagulant	Prophylaxis of deep-vein thrombosis in surgical patients
Actrapid	Continuous Infusion according to blood glucose level	Continuous Infusion according to blood glucose level	Soluble Insulin	Insulin deficiency due to pancreatectomy
Cefuroxime (Zinacef®)	750mg IV	TDS	Cephalosporin	Prophylaxis post-splenectomy and post-laparotomy
Metronidazole	500mg IV	TDS	Antimicrobial	Post distal gastrectomy and roux-en-Y anastomosis
Paracetamol	1g PO	6hrly	Analgesic	Pain Relief
Octreotide	25mcg infusion	Hrly	Somatostatic analogue	Prevent complications of pancreatic surgery

Surgical therapy:

Pre-operative: Admitted two days early due to episode of vomiting. Was given IVI N saline and 10cc 20% KCl 1L 8-hourly, in order to compensate for fluid loss and low sodium concentration in the blood. In addition, promethazine hydrochloride was given. All hypertensive drugs were continued, except for burinex. On the day prior to surgery, the patient started fasting, BP was monitored and bloods were sent for crossmatch.

Operation: A total pancreatectomy, duodenectomy, splenectomy, cholecystectomy, distal gastrectomy and roux-en-Y anastomosis were performed. On operating, a tumour of the head of pancreas was identified. There was no evidence of metastasis.

The duodenum was mobilised and the common bile duct, the common hepatic duct and the portal vein were dissected. An enlarged lymph node was found at the porta hepatis and sent to frozen section. Fortunately this was found to be benign. The gall bladder was dissected fundus first and the cystic artery was divided using sutures.

The neck of the pancreas was dissected off the portal vein and divided. The common bile duct was divided and the biliary stent removed. The duodeno-jejunal flexure was mobilised and divided. The head of pancreas was removed together with the duodenum, gall bladder and distal third of the stomach.

Completion of pancreatectomy and splenectomy were performed. Roux-en-Y anastomosis was performed using a loop of jejunum. Choledochojejunostomy (anastomosis between common bile duct and jejunum) was performed using stapling device. Jejuno-jejunostomy was performed using side to side anastomosis with stapling device. Mesenteric defects were then closed, a drain was inserted and the wound was closed.

The following specimens were sent to histology:

- Head of pancreas and distal stomach
- Distal pancreas and spleen
- Gall bladder

Post-operation: The patient was transferred to ITU and was administered the drug treatment listed in the table above. IVI and analgesia were given as required. In view of total pancreatectomy, the patient was to be given continuous actrapid infusion even if glucose levels were to be normal initially. Vaccines were planned post-splenectomy – these include prophylactic immunisation with pneumococcal, meningococcal and H. influenza type B vaccines[2]. In addition, cefuroxime (prophylaxis active against haemophilus influenzae) was given post-splenectomy. Metronidazole (effective Helicobacter pylori eradication) was given in view of partial gastrectomy and roux-en-Y anastomosis.

Laboratory findings postoperatively:

- A frozen section taken from a possible metastatic lesion was found to be benign.
- Mild fibrous cholecystitis was found at the fundus of the gall bladder.
- No evidence of tumour infiltration at the pancreatic tail.
- Spleen and splenic hilum were found to be normal.
- A well differentiated invasive pancreatic ductal carcinoma was found at the head of pancreas and encroaching the ampulla. The invasive tumour was associated with widespread pancreatic intraepithelial neoplasia and intraductal carcinoma. Extensive perineural and lymphovascular invasion was found. Foci of intraductal carcinoma extend to less than 1mm from both the superior mesenteric vessel margin and the posterior margin. The anterior margin is clear of tumour.
- Three out of eleven regional pancreatic lymph nodes show metastatic adenocarcinoma. Two greater curve lymph nodes were sampled and were found to be free of tumour. A single focus of malignant cells was found at the perineurum of a large nerve.

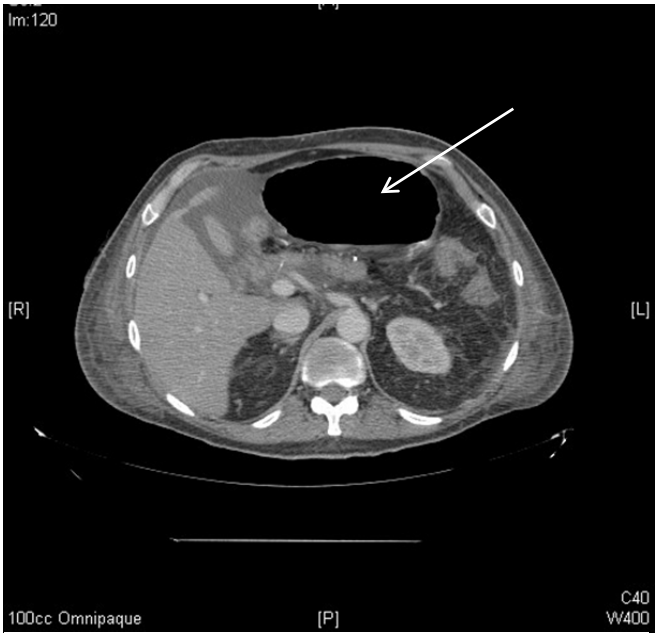

Figure 5: Post op CT Abdomen, showing extensive ascites in the subhepatic region (arrow)

Diagnosis:

Based on laboratory findings from specimen of excised organs, the following diagnosis was elicited:
Grade 1 pancreatic ductal adenocarcinoma. The tumour at the pancreatic duct traversing the head of

pancreas resulted in compression of the common bile duct, with consequent features of obstructive jaundice. Pancreatic cancer is renowned for its rapid progression and poor prognosis. Often treatment is palliative due to extensive metastasis. However, in rare cases such as this one, early presentation with the lesion confined to the head of the pancreas, curative surgical resection is possible.

Final treatment and follow ups:

In the days that followed the operation, the patient passed altered blood PR (malaena), experienced nausea and brought up coffee ground vomit. These were managed by administering omeprazole (proton pump inhibitor) and ranitidine (H2-receptor blocker); and antiemetic therapy - metoclopramide hydrochloride (maxolon®). In addition, an OGD was performed, with findings of slight erythema, without active bleeding in the body of the stomach and normal post-operative appearance of the gastro-jejunostomy, without any signs of bleeding.

A diabetologist was consulted in order to manage the insulin regimen.

A CT scan of the thorax, abdomen and pelvis was performed 9 days post-operatively in order to investigate confusion post-total pancreatectomy. Findings included extensive bilateral pleural effusion, atelectatic changes in the lower lobes of the lungs and extensive ascites, mainly in the subhepatic region (Figure 5). However, no lymphadenopathy was noted and the liver was homogenous in structure.

Furthermore, a CT scan of the brain was carried out, in which no focal lesions were found and midline structures were not displaced.

Fact Box 6:

Title: Pancreatic Ductal Adenocarcinoma

Pancreatic ductal adenocarcinoma is a highly malignant tumour which arises from the cells lining the pancreatic duct. It is the fifth commonest tumour worldwide. It has a high mortality and is often diagnosed late.

Risk factors:

- Family history of tumour
- Smoking

Signs and Symptoms:

- Jaundice
- Dull epigastric pain which may radiate to the back
- Itching
- Recent onset diabetes
- Thrombophlebitis
- Migraines
- Anorexia
- Weight loss

Treatment: In most cases this is palliative, either via a surgical bypass or insertion of a stent through the common bile duct. A curable surgical resection involves Whipple's pancreaticoduodenectomy.

Prognosis: Poor, most cases are not operable. In the case of those which are operable, surgery is associated with a high mortality and few survive for more than 5 years.

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Case Number 7
Liver Abscess following ingestion of a foreign object

Keith Borg Xuereb and Lauren Abela
Reviewed by: Mr. Dennis T. Gatt F.R.C.S., L.R.C.P.(Lond.), F.R.C.S.(Eng.), F.R.C.S.(Edin.)

Case summary:

Demographic details:

Ms. MB, female.
Referred from: home

A 31 year old, previously healthy female presented to A&E on 24/07/2012 with a 2 day history of colicky epigastric pain and spiking fever; however on investigation no pathology was found except for an ovarian cyst of 4cm. It was concluded that it was unlikely that the cyst was causing pain and fever and the patient was discharged. She was given proton pump inhibitors for 2 weeks and pain improved, however on stopping therapy, the pain became much more severe, with radiation to the back. She presented to A&E again on 05/08/2012. A more detailed history elicited the fact that she had ingested half a toothpick by mistake 3 weeks previously. Imaging showed the formation of an abscess between the stomach and liver; which needed drainage.

Presenting complaint:

Epigastric pain: 3 weeks
Low grade fever: 3 days

History of presenting complaint:

The epigastric pain started gradually on 22/07/12 and was colicky in nature with no radiation.
The patient was nauseated but did not vomit and pain killers had no effect. The pain was unrelated to food intake, position and breathing and was described as quite severe (6/10). The patient had also been febrile for 3 days. Omeprazole therapy was initiated on 24/07/12, and the pain improved somewhat but persisted. On stopping omeprazole on 01/08/12, the pain worsened to 8/10. The patient presented again to A&E on 05/08/12 complaining of epigastric pain with radiation to the right hypochondrium and back. The pain was colicky in nature and also persisted through the night preventing sleep and associated with severe belching. By this time the patient had become anorexic with chills, rigors and a spiking fever.

Past medical and surgical history:

Past medical history:

Previously healthy. Nil of note.

Past surgical history:

Ovarian cyst (Last seen on CT abdo/pelvis on 24/07/12, unchanged from previous CT scans)
Laparoscopy for ovarian freezing
Liposuction
Tummy tuck

No reported adverse reactions to anaesthesia.

Drug history:

Drug	Dosage	Frequency	Type	Reason
Paracetamol	1g	PRN	Analgesic	Relief for epigastric pain
Omeprazole	20mg	BD	PPI	Relief of acid reflux

Family history:

No family history of specific illnesses

Social history:

MB lived with her husband and children. She reported smoking approximately 20 cigarettes daily and drank only socially. There was no history of binge drinking or drug abuse.

Systemic inquiry:

First Hospital Event 24/7/12

- General Health: she looked well in general but with the anorexia there was evidence of weight loss over the past 3 weeks. Lethargy, rashes, sleep disturbances
- Cardiovascular System: chest pain, palpitations, SOB, Orthopnea, PND, syncope
- Respiratory System: cough, wheeze, sputum
- Genitourinary System: dysuria, haematuria
- Central Nervous System: headaches, seizures, blurring of vision/visual problems, tinnitus
- Musculoskeletal System: muscle aches, claudication
- Endocrine System: hot/cold intolerance, excessive sweating, tremor

Discussion of results of general and specific examinations:

Physical Examination: On presentation her pulse was regular at a rate of 85 beats per minute. The Blood Pressure was 130/70 but she was pyrexial at 100.3°F with her SpO2 98% on air. She was alert, oriented and not jaundice.

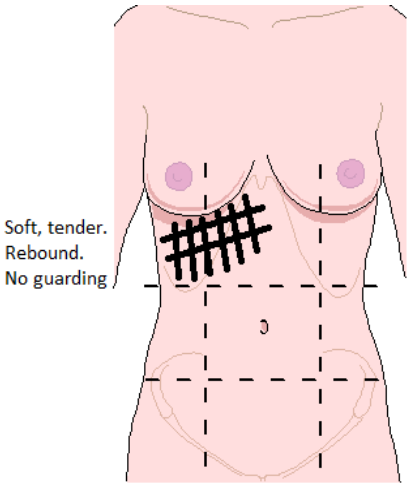

Diagram 1

Examinations of the cardiovascular and respiratory systems were unremarkable, with the main findings being in the abdomen. Her abdomen was soft but with tenderness in the epigastrium and right hypochondrium with rebound tenderness but no guarding or rigidity (Diagram 1). The rest of the abdominal examination including hernial orifices and rectum were normal.

In view of the history of ovarian cyst she underwent a full gynaecological assessment but this was within normal limits.

Differential diagnosis:

- Peptic Ulcer Disease particularly perforated duodenal ulcer
- Acute Cholecystitis
- Pancreatitis
- Appendicitis
- Musculoskeletal pain
- Liver abscess
- Ovarian cyst

Diagnostic procedures:

Laboratory Investigations:

Test: Urinalysis 24/07/12:
Results: Protein: Trace
Blood: +++

Test: Urine Microscopy 24/07/12:
Results: Erythrocytes: 150 U/L
Nitrites: Negative
White blood cells: Negative

Test: Blood tests 24/07/12:
Justification for test: To take baseline values and make a diagnosis according to the clinical findings
Results: CBC: Normal
Coagulation screen: Normal
Renal profile: Normal
Amylase: Normal
Calcium and phosphate: Normal

Imaging Investigations:

Test: Abdominal X-Ray 24/07/12
Justification for test: Basic investigation and to identify possible pathology:
Result/Conclusion: No abnormality detected

Test: Chest X-Ray 24/07/12:
Justification for test: Basic investigation and to identify possible pathology
Result/Conclusion: No abnormality detected

Test: Ultrasound abdomen 24/07/12
Justification for test: To diagnose or rule out abdominal pathologies

Result: Avascular area adjacent to liver; may represent a distended gastric antrum. Mildly distended gallbladder (common bile duct not seen).
Test: CT abdomen & pelvis 24/07/12:
Justification for test: To identify abdominal or pelvic abnormalities.
Result: No pulmonary lesion is seen in the lung bases. No free gas, abscess or signs of bowel obstruction are seen. The pancreas, liver, gall bladder, spleen, both adrenals, kidneys and urinary bladder are normal. The abdominal and retroperitoneal lymph nodes are not enlarged. No ascites is present. There is a 4cm cystic formation in left ovary.
Conclusion: All findings normal except 4cm cystic lesion in the left ovary.

Second Hospital Event 5/8/12

Test: Ultrasound Abdomen & Pelvis: Day 1:
Justification for test: Reassessment of patient on her second admission.
Result: Difficult examination due to patient habitus and abundant bowel gas in the upper abdomen. The liver is normal in size and echotexture. An ill-defined hypoechoic avascular area is seen adjacent to the liver in the vicinity of the stomach. No intra- or extrahepatic bile duct dilatation is seen. Normal flow is seen in the portal vein. The gall bladder is mildly distended (4.5cm width) but no stones or signs of inflammation are seen. The common bile duct could not be visualized due to abundant bowel gas. Both kidneys are normal in size, shape and parenchymal thickness. No stones or hydronephrosis are seen. The right kidney measures 12.5cm and the left kidney measures 12.1cm (interpolar dimensions). The urinary bladder is unremarkable. The spleen has a normal echotexture and size. No free fluid is seen in the abdomen and pelvis.
Conclusion: An ill-defined hypoechoic avascular area is seen adjacent to the liver in the vicinity of the stomach. This may represent a distended gastric antrum. Mildly distended gall bladder.

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Hartmann's solution	1L	8 hourly	Rehydration IV solution	To ensure good hydration
Cefuroxime	750mg	TDS	IV antibiotics	To clear possible infective agent
Ranitidine	50mg	TDS	Histamine receptor antagonist	Inhibits acid production in the stomach
Maalox	20ml	TDS	Antacid	Neutralises acid in stomach
Clexane	40mg	DLY	Anticoagulant	Thromboprophylaxis in a high risk patient (smoker, relatively immobile)

Management:

Day 2: The patient improved with analgesia but still had chills and rigors even though she was tolerating a light diet.

Physical Examination: Pulse 80 bpm
BP: 125/70
Temperature: 99.3°F
SpO2 on air: 99%
She was haemodynamically stable, alert, oriented and not jaundiced.

Abdomen: Tenderness epigastrium and right hypochondrium, with soft abdomen and no guarding.

Day 3: CT Abdomen & Pelvis: The lung bases are clear. The spleen, pancreas, adrenals and kidneys are normal. There is a large ill-defined hypodense lesion in the left liver lobe measuring about 56 x 42mm. No enlarged nodes, free air, or free fluid are seen. The uterus and uterine bladder are normal. There is complex left ovarian mass measuring 36mm due to probably dermoid. Impression: Liver abscess that requires drainage.

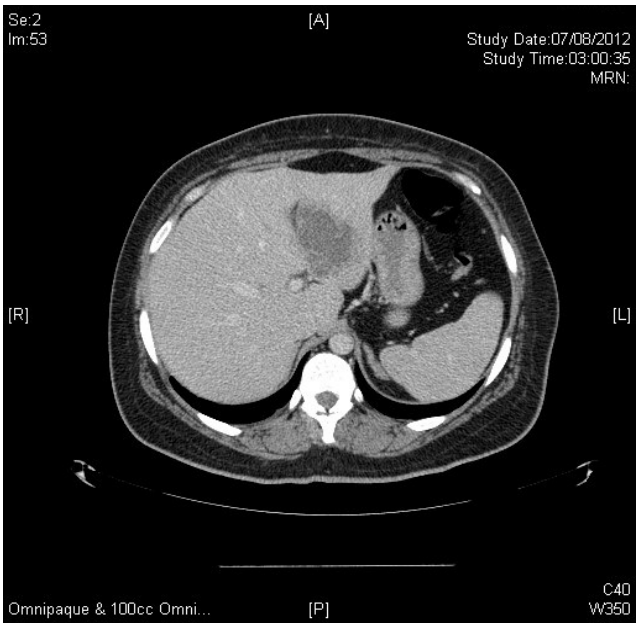

Image 1: Abscess visible within left lobe of liver

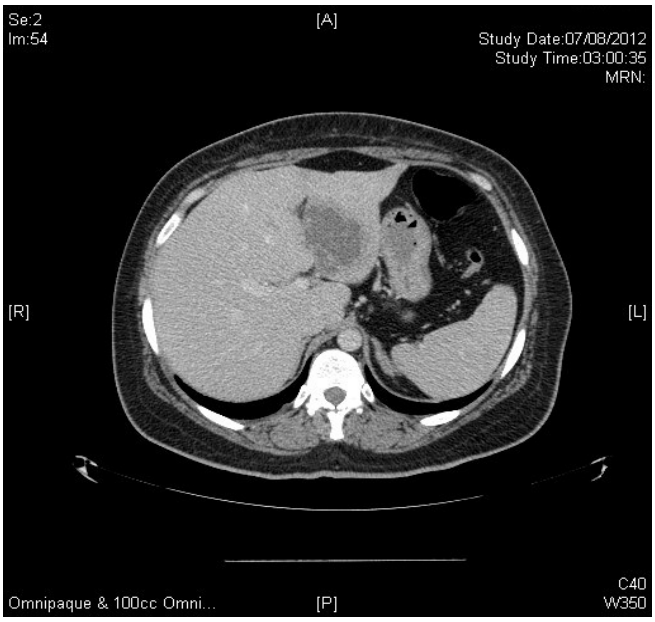

Image 2: Abscess visible within left lobe of liver

Operation: Day 3:
CT guided cyst drainage

Procedure:

- Drainage and insertion of pigtail catheter into liver abscess under CT control
- 10F catheter inserted
- 30ml of pus aspirated

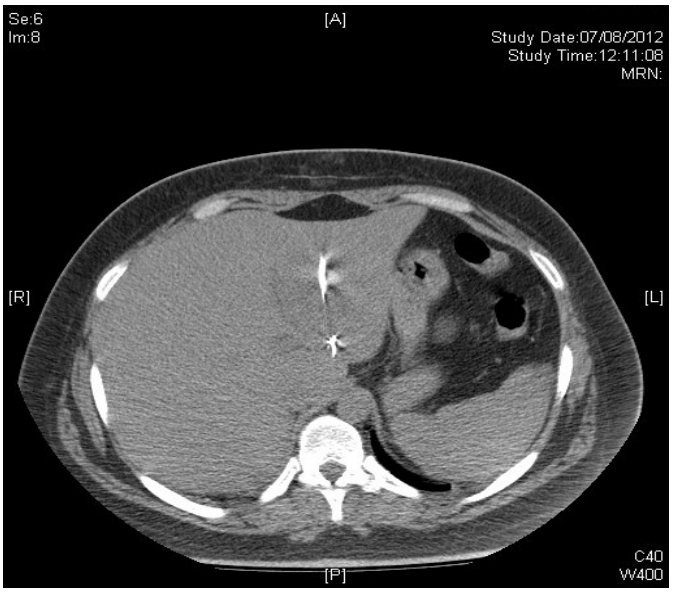

Image 3: Drainage under CT control

Patient stable post-procedure. Analgesia PRN.
Gentamycin given, calculated according to patients weight (355mg 8 hourly).

Day 4: Following this procedure the patient became afebrile for the first time. She remained well with no further complications until discharge. As at this stage the diagnosis was still obscure so a further CT scan was scheduled for day 7 to try to identify the cause of the perforation that led to the subhepatic and hepatic abscess. The investigation however confirmed the presence of a resolving abscess with a drain within but no other foreign bodies were visible. A follow-up CT scan, taken 19 days post-procedure showed that the abscess was healing well. The image is shown below (Image 4).

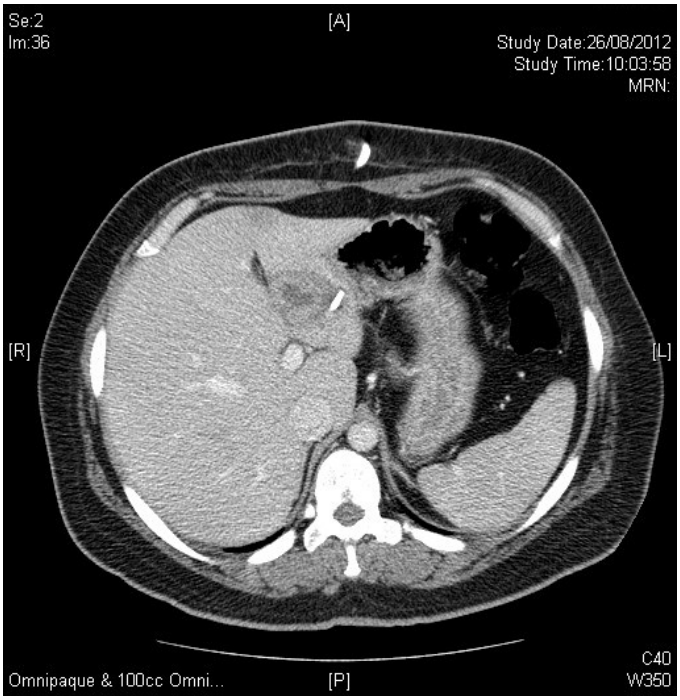

Image 4: Healing abscess with drain within

In view of the fact that the patient had been previously perfectly healthy and the history of inadvertent ingestion of half a toothpick 3 weeks previously there was little doubt that the sequence of events was of perforation of the lesser curvature of the stomach with the ingested toothpick and subsequent subhepatic and intrahepatic abscess formation.

Diagnosis:

This is a case of liver abscess following accidental ingestion of a foreign body, namely half a toothpick. Unintentional ingestion of foreign bodies is common in daily life. Ingested foreign bodies pass through the gastro-intestinal system undiscovered within a week in approximately 80-90% of cases[1-3]. In the remainder of cases, obstruction is the likeliest cause of symptoms[1-2].

Perforation is a rare finding in 1% of cases. The areas which are commonly affected are the ileocecal region, the rectosigmoid region and the duodenum[2-5]. Development of a hepatic abscess is even rarer. Between the first reported case in 1898 and 2007 only 47 cases were reported globally[6]. The commonest sites of perforation of the gut are the stomach and duodenum[5].

Establishing the diagnosis is difficult as the patients may be unaware of their ingestion and presentation is often late as the migrating foreign body can remain silent until an abscess has formed[1,3,4]. Symptoms are usually non specific, with abdominal pain, fever, nausea and vomiting, anorexia and weight loss. Furthermore, the classical presentation of hepatic abscess (i.e. fever, abdominal pain and jaundice) is

only present in a few cases[5-7]. In 1955, Griffiths described a case of septic shock and subsequent death following the ingestion of a needle. So far, only two cases of death were reported, both by Griffiths[8]. Laboratory findings are also non specific and identification on plain radiography is not possible unless the foreign body is radio-opaque[3,4]. CT scan is preferred technique for the diagnosis due to its high resolution and accuracy. The second best option is an abdominal ultrasound[1]. In the vast majority of such cases treatment includes drainage and antibiotic therapy and does not require more extensive surgical procedures[3].

A literature review by Santos et al found that fish bones were the most common foreign body and the stomach was the principal site of perforation[11]. Abscess formation occurs more commonly on the left lobe. Isolated microorganisms on abscess or fluid cultures are usually part of the normal flora of human oropharynx. Prognosis depends on a rapid diagnosis[6, 9-11].

From a total of 47 reported cases of abscess formation secondary to ingestion of a foreign object, 12 cases (25.5%) were due to toothpick ingestion. Of these 12 cases there was only one mortality. 58% of these cases reported a perforation through the stomach, 33% reported a perforation through the duodenum whilst in 9% the perforation was through the colon. The left lobe was the most commonly affected lobe (66%). Presenting complaints included epigastralgia, fever, vomiting and shock. Management involved removal of the toothpick with abscess drainage in all cases except one. This patient refused surgery and was consequently treated with antibiotics[11].

Final treatment and follow ups:

Following CT drainage of the abscess, the patient made a rapid and unremarkable recovery with the post-procedure CT confirming resolution of the abscess. The patient was discharged on day 8 post-admission with lifestyle advice regarding smoking cessation, reduction of coffee intake and to eat small frequent fat free meals and to pay more attention while eating.

Fact Box 7:

Title: Liver Abscess

Short description of condition:

A liver abscess is a pus-filled cavity within the liver which is normally caused by a biliary tract source but can also be due to other intra-abdominal processes, including diverticulitis, and hematogenous spread. In this case hepatic abscess occurred following perforation of the gastrointestinal tract caused by ingested foreign body.

Risk factors: Inflammatory bowel disease, especially Crohn's disease, due to loss of integrity of the mucosal barrier

- Liver cirrhosis
- Hepatic transplant
- Hepatic artery embolization
- Institutionalization
- Immunocompromise / Immunodeficiency syndromes
- Older age (particularly associated with biliary sepsis)
- Malnutrition, malignancy, pregnancy, steroid use, and excessive alcohol intake

Symptoms:

- Chills and rigors
- Right upper quadrant pain
- Anorexia
- Malaise
- Referred pain to the right shoulder is also possible
- Irritation of the diaphragm may also cause cough or hiccoughs however this is unlikely

Signs:

- Fever (either continuous or spiking)
- Right upper quadrant tenderness
- Hepatomegaly
- A mass may be palpable
- One forth of cases may present with jaundice and this is usually associated with biliary tract disease or the presence of multiple abscesses
- A pleural or hepatic friction rub are uncommon but may be associated with diaphragmatic irritation or inflammation of Glisson capsule

Prevention:

- Prompt treatment of biliary, gastrointestinal, pelvic, and systemic infections that may spread to the liver
- Minimize alcohol intake to maintain hepatic cellular integrity

Prognosis: Liver abscess is almost uniformly fatal if left untreated. Timely treatment, which includes drainage and antibiotics reduces mortality to approximately 5%.

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Fact Box:

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Case Number 8
Congenital Neuroblastoma

Dillon Mintoff & Christine Mizzi
Reviewed by: Dr. J. Mizzi MD, MRCP, MRCPCH

Case summary:

Demographic details:
Baby D, female, Swieqi

Baby D is a 3-day-old baby girl who was noted to have abnormal posture and paucity of movement of the left foot. Examination revealed flaccid weakness of the left lower limb. The rest of the neurological examination was normal. MRI revealed an extramedullary extradural intracanalicular lesion extending from caudal to the 10th thoracic vertebral body to L4 and a paraspinal mass from level of L1 to L4 vertebral bodies which was in continuity with the intracanalicular mass through the right L1/L2 neural foramen. This was diagnosed as congenital dumbbell neuroblastoma.

Presenting Complaint:

Left foot flaccid paralysis and dorsiflexion weakness since birth.

History of Presenting Complaint:

Baby D is a 3-day-old baby girl. She was born at 38^{+2} weeks gestation by normal vaginal delivery. Her birth weight was 3.36kg, which is on the 50th centile. Her weight was appropriate for gestational age. Her parents noted that the baby was not moving her left lower limb. Clinical examination revealed flaccid paralysis of the left lower limb. The rest of the neonatal and neurological examination was normal.

Past medical and surgical history:

The patient has no previous medical or surgical history.

Drug history:

Drug	Dosage	Frequency	Type	Reason
Paracetamol	30mg	QID	Analgesic	Pain relief

Family history:

Mother suffered two miscarriages before giving birth to Baby D.

Systemic inquiry:

Apart from the left lower limb paralysis, Baby D was completely healthy on neonatal examination.

Current therapy:

Baby D is currently receiving therapy at Great Ormond Street Hospital for Children in London.

Discussion of results of general and specific examinations:

General examination: The patient looked comfortable at rest and did not appear to have any dysmorphic features. The patient weighed 3.10kg. She was noted to be slightly plethoric but not jaundiced. Examination of the cardiovascular system revealed normal heart sounds (S1+S2+0) and a radial pulse rate of 150 beats per minute. The femoral arteries were palpated and there was a normal liver edge. The lungs were clear, with air entry on the left equal to that on the right. Respiratory rate was 40 breaths per minute. The hips were symmetrically abducted. Galiazzi, Barlow and Ortolani tests were negative.

Neurological examination: Upper limbs: Normal tone, power and sensation.
Trunk: Normal tone.
Lower limbs: Right side: normal tone, power and sensation. Left side: flaccid weakness below left knee with foot drop and inversion. The knee jerk was equivocal and the ankle jerk could not be elicited. The left leg seemed to be thinner than the right but had the same length. The anal sphincter was intact. The bladder was not distended and there was no leakage of urine.

Differential diagnosis:

- Birth trauma
- Tumours: Neuroblastoma
  Schwannoma
  Paraganglioma
  Ganglioneuroblastoma
  Ganglioneuroma
  Glioblastoma

Diagnostic procedures:

Laboratory exams:

Test: Complete Blood Count
Justification for test: To exclude bone marrow involvement from a possibly malignant lesion
Results: White blood cell count: 9.10 x 10^9/L
Neutrophils: 7.5 x 10^9/L (High)
Lymphocytes: 8.49 x 10^9/L
Monocytes: 2.29 x 10^9/L (High)
Eosinophils: 0.73 x 10^9/L
Basophils: 0.13 x 10^9/L (High)
Red Cell Count: 5.60 x 10^9/L
Haemoglobin: 19.2 g/dL
Haematocrit: 53.6%
Mean Cell Volume: 95.5 fL
Mean Cell Hb: 34.2 pg (High)
Mean Cell Hb concentration: 35.8 g/dL
Red Cell distribution Width: 17.9% (High)
Platelets: 233 x 10^9/L
Mean Platelet volume: 9.2 fL

Reticulocytes: 208.10 x 10^9/L (Low)

Serum Urea: 8 mmol/L
Serum Creatinine: 79 mmol/L
Serum Sodium: 145 mmol/L
Serum Potassium: 5.45 mmol/L (High)
Serum Chloride: 105.5 mmol/L
Serum Bilirubin: 193.00 umol/L

Conclusion: The blood results were normal overall, with the slight abnormalities being insignificant. Other laboratory tests which could have been included, given this case in particular, are LFTs to show any involvement of the liver in case of metastases, along with urine catecholamine metabolites, neuron specific enolase and LDH as tumour markers.

Instrumental exams:

Test: X-ray of left lower limb.
Justification for test: To exclude any trauma or abnormalities in the lower limb, which could possibly explain the paralysis.
Result: No pathology noted.
Conclusion: The paralysis is not due to a lesion in the lower limb itself.

Test: MRI head.
Justification for test: To exclude an upper motor neuron lesion in the right motor cortex, which could possibly give rise to left lower limb paralysis. Although the weakness in the limb was flaccid and the reflexes were absent, suggesting a lower motor neuron problem, this test was still justified as a motor cortical lesion may present with hypotonia and absent reflexes in the acute stages.
Result: The brain and CSF spaces showed normal intensity. No focal lesion was seen.
Conclusion: The lower limb motor defect is not the result of a brain lesion.

Test: MRI whole spine.
Justification of test: To identify any lesion in the spinal cord which could be the cause of left lower limb paralysis.
Result: An extramedullary extradural intracanalicular lesion extending from caudal to the 10th thoracic vertebral body to L4 is noted. This displaced the cord and cauda to the left, taking up most of the intracanalicular space. A dumbbell paraspinal mass, 3.2cm (craniocaudally) by 2cm (anteroposteriorly), extends from the level of L1 to L4 vertebral bodies. This appears to be in continuity with the described intracanalicular mass through the right L1/L2 neural foramen. Fullness is also noted at the left L1/L2 neural foramen with no associated extracanalicular extension. (See figures 1 to 6).
Conclusion: There is a paraspinal tumour which has extended to the spinal canal and caused spinal cord compression, leading to left lower limb paraplegia. Histological confirmation of the tumour was not done locally because Baby D was referred to a tertiary centre for further investigations where a biopsy specimen was taken at laparoscopy.

Therapy:

Drug	Dosage	Frequency	Type	Reason
Paracetamol	30mg	QID	Analgesic	Pain relief

Diagnosis:

Diagnosis: Congenital Neuroblastoma

Neuroblastoma is the commonest malignant neoplasm in foetuses and neonates and the second commonest solid tumour in children, following brain tumours[5]. It has an incidence of 1 in 7000 live births[11]. 96 % of cases occur before the age of 10 years[2]. More young children die of neuroblastoma than any other cancer[11].

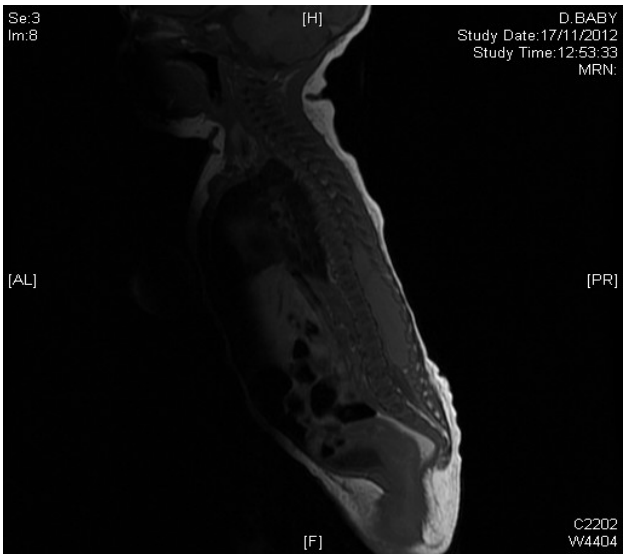

Figure 1

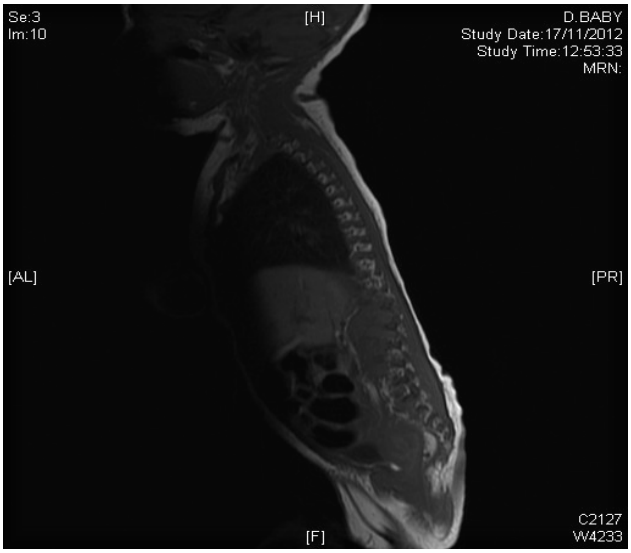

Figure 2

MRI spine. Fig 1 shows an extramedullary extradural lesion to extend from caudal to the 10th thoracic vertebral body to L4. Figure 2 shows a 3.2cm (craniocaudally) x 2cm (anteroposteriorly) paraspinal mass extending from L1 to L4 vertebral body.

Neuroblastoma is a malignant embryonic tumour derived from the primordial neural crest cells. These cells eventually inhabit the sympathetic ganglia along the neural tube and the adrenal medulla. Since both of these produce cathecholamines they can be used as a biomarker for diagnosis of neuroblastoma. Neuroblastoma can arise anywhere along the migratory path of the neural crest cells. The most common site of primary tumour at presentation is the adrenal gland, followed by the retroperitoneum, paraspinal ganglia, posterior mediastinum and with the least common being the pelvis and cervical region[5]. In this particular case, the tumour evolved from the paravertebral ganglia which link with the spinal cord. As the dumbbell neuroblastoma grew, it infiltrated the intervertebral foramina and compressed the spinal cord and the intraspinal part of the spinal nerves with possible involvement of the vertebral bodies, which eventually gave rise to the paraplegia noted on neonatal examination. The incidence of intraspinal involvement from peripheral neuroblastoma extension is between 6% and 24%[10]. Although in this particular case, the spinal neuroblastoma was in the lumbar area, the thoracic spine is the most frequent level of spinal compression[3].

The majority of neuroblastoma cases are sporadic. Amplification and overexpression of the MYCN proto-oncogene occurs in approximately 20% of neuroblastomas. MYCN gene codes for N-myc protein which controls the cell cycle and several microRNAs[1]. In such sporadic cases, there may also be alterations in the p53 pathway and amplification and polymorphism of the MDM2 oncogene. Familial tumours represent only 1-2% of cases. They are transmitted in an autosomal dominant fashion with incomplete penetrance, with germline mutation in Phox2b and ALK. ALK is critical in the development of the nervous system and Phox2b is involved in the formation of cells of the sympathoadrenal lineage[11]. Familial cases can present with two or more neuroblastoma tumours in different sites. Most probably, congenital neuroblastoma is

multifactorial, having both an environmental and a genetic input in its aetiology[7]. It is associated with cardiac defects in 20% of cases[4].

Neuroblastoma consists of undifferentiated small round-shaped sympathetic cells with scanty cytoplasm, hyperchromatic nuclei and indistinct nucleoli. These cells are called neuroblasts and are surrounded by neutopil[12]. Neuroblastoma is one of the small, round, blue cell tumours of childhood (SRBCT)[11]. The neuroblasts may form clusters called Horner–Wright rosettes which are characteristic of neuroblastoma. Calcification and schwannian stroma are also sometimes seen[12].

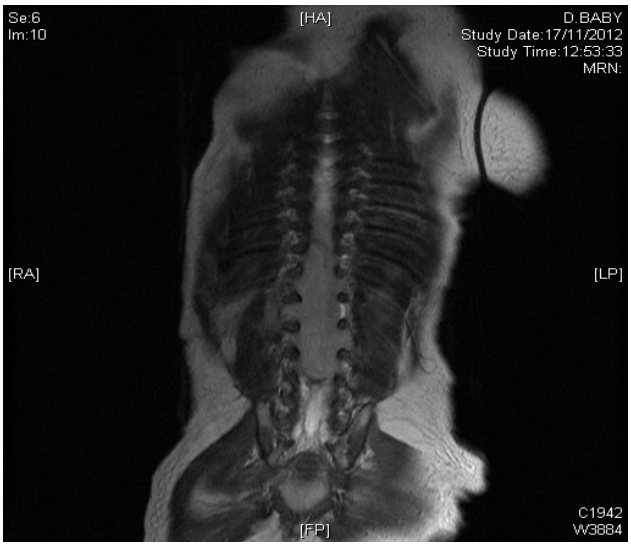

Figure 3

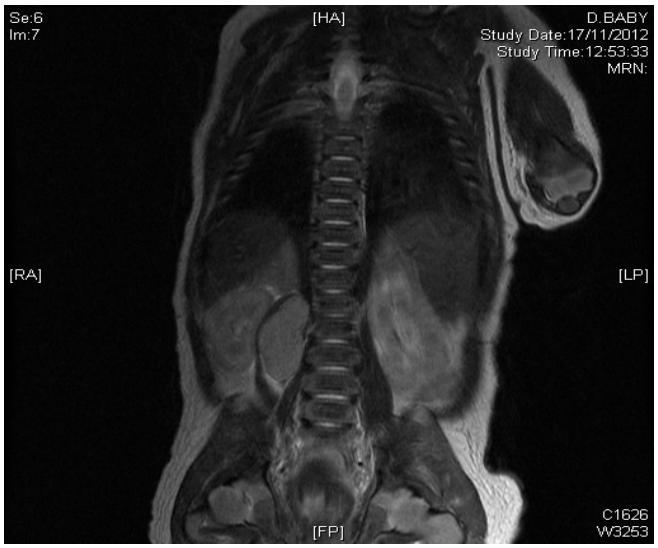

Figure 4

Figure 3 and 4 show the masses described in figure 1 and 2 in coronal section

Neuroblastoma has a range of clinical presentations. It can present as an indolent abdominal or chest mass. If it has infiltrated bone it can present with pallor secondary to anaemia, pain or a limp. The rare cervical neuroblastomas can present with Horner's syndrome, a neck mass, stridor and dysphagia. Periorbital ecchymosis, proptosis and blindness occur with metastases to the orbital bones[11]. Spinal neuroblastomas give back or radicular pain, sensory deficits, motor deficits and sphincteric dysfunctions[3]. Paraneoplastic syndrome is another presentation of neuroblastoma, specifically opsoclonus-myoclonus ataxia, hypertension, flushing, tachycardia, sweating (in adrenal tumours) or intractable diarrhoea (as a result of VIP secretion), irritability, vomiting and loss of appetite[12]. The main site of metastases is the liver[5]. Sometimes neuroblastoma is asymptomatic and discovered incidentally during imaging for other reasons[12].

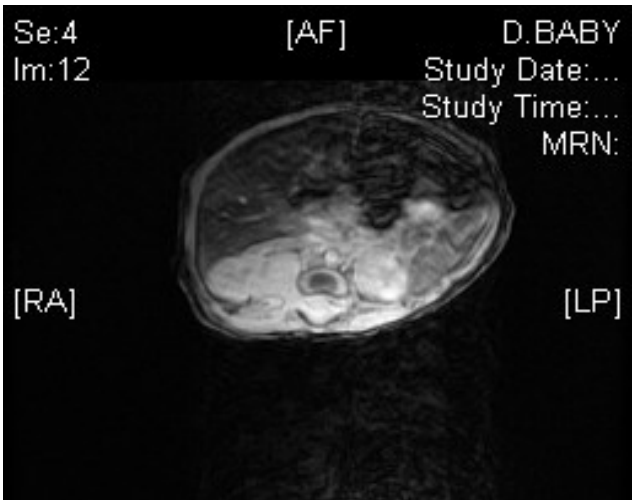

Figure 5

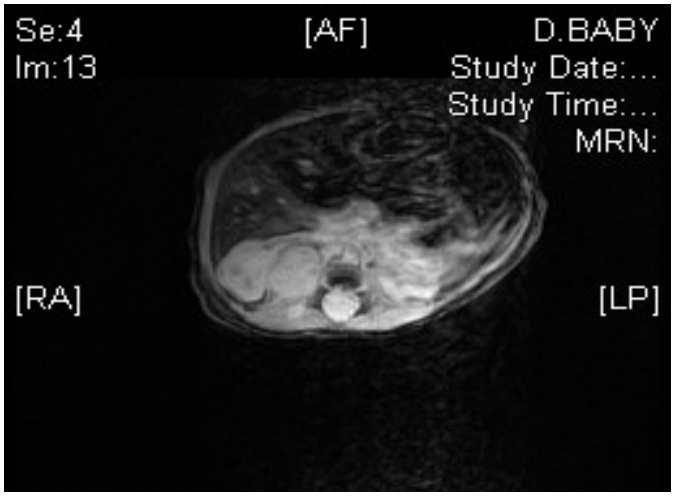

Figure 6

Figures 5 and 6 show the masses described in figure 1 and 2 in transverse section

Poor prognostic factors in neuroblastoma are the presence of MYCN gene, deletion of 11p23, poor differentiation, advanced stage, diploid tumour (rather than hyperploid), noncystic, diagnosis after birth as opposed to antenatal diagnosis, age greater than 18 months, a high mitosis-karyorrhexis index (MKI), poor stromal maturity, high serum levels of lactate dehydrogenase, neuron specific enolase and ferritin and a low ratio of vanillylmandelic acid to homovanillic acid[5,6,12,13].

The International Neuroblastoma Risk Group Staging System (INRGSS) is used to stage neuroblastoma. It is based on risk factors identified by imaging at diagnosis, biopsies and laboratory tests. Stage L includes a localised tumour that does not involve vital structures and is confined to one body component. Stage L2 refers to a locoregional tumour with the presence of one or more image-defined risk factors. Stage M means that there are distant metastasis[11]. Cytogenetics of neonatal tumours are different to those of older children, which explains their different clinical behaviour and the better prognosis[7]. Taking this into consideration, such cases are classified as stage MS which refers to metastatic disease in children younger than 18 months in whom the secondaries are limited to the skin, liver and bone marrow. Low-risk neuroblastoma patients have a 5-year survival rate of 95%, whereas with high risk groups this falls to 30-50%[11].

It is thought that foetuses presenting with neuroblastoma have a better outcome than if the disease occurs later on in childhood[4]. This is because children older than 1 year usually turn out to have extensive metastases at presentation which tends to progress despite intensive treatment[2]. On the other hand, if congenital or diagnosed before the age of 1, the tumour is usually localised[8]. Moreover, neuroblastoma in neonates tends to have a normal MYCN copy number and a hyperdiploid DNA index, both of which indicate a good prognosis[5]. However, although survival with dumbbell neuroblastoma appears to be good in many cases, neurological outcome is usually poor[8]. The most common neurological deficit is irreversible flaccid paralysis of lower limbs that does not respond to therapy[5]. When the patient presents with paraplegia, as was the case with this particular baby, it is almost always irreversible[3].

Final treatment and follow ups:

Although neuroblastoma is the commonest extra-cranial tumour in childhood, it is still a rare disease. The rarity of this disease means that there are few controlled trials researching the management of this condition[6]. It is know that the clinical behaviour varies from spontaneous regression to widespread disseminated disease[11]. Therefore, expectant management is not suggested for neonates with neuroblastoma because the natural history of the disease is unpredictable[4]. Baby D is currently receiving therapy at Great Ormond Street Hospital for Children in London.

Treatment of neuroblastoma is usually a combination of chemotherapy, radiotherapy and surgical resection[9]. The stage of the tumour is one of the most important factors in choosing treatment. As a general rule, resection alone is sufficient for early low-risk tumours. Chemotherapy is added in intermediate-risk tumours, or it may be used before surgery to reduce the size of the tumour and facilitate resection. High-risk tumours are treated with surgery and chemotherapy and bone marrow transplantation if exceedingly resistant[12].

Dumbbell neuroblastoma with spinal cord compression is, in many cases, unresectable. Decompressive laminectomy is mainly performed in those cases of recent onset neurological dysfunction[10].

With regards to chemotherapy for unresectable disease, the following drugs may be given:

- Akylating agents - cyclophosphamide, ifosfamide
- Platinum compounds - cisplatin, carboplatin
- Topoisomerase II inhibitors – etoposide, doxorubicin
- Vincristine
- Busulfan and melphalan are sometimes used during stem cell transplant[12]

Radiotherapy targeting the primary tumour is used for high-risk patients following chemotherapy. It is also useful as palliative therapy for bone metastases and hepatomegaly[12]. There is a lower recurrence rate associated with radiation therapy given before or after bone marrow transplantation[9]. The most common sites of relapse are bone and bone marrow[11].

In the future, this patient may be given an additional treatment modality which is autologous stem cell transplant for consolidation which helps to re-populate the bone marrow after chemotherapy[13]. Also, immunotherapy and retinoids are used for maintenance[11]. Immunotherapy is the use of a monoclonal antibody ch14.18 which binds to the ganglioside GD2 on the surface of many neuroblastoma cells. This is usually done after a stem cell transplant[13]. Retinoic acid is used as a form of differentiation therapy.

There are several complications associated with treatment for neuroblastoma and for other tumours in general. The kidneys are vulnerable due to toxicity of cisplatin chemotherapy and radiotherapy[9]. In this case, kidney damage due to pressure effects by the paraspinal mass is also possible. If surgery is attempted on this patient, there may be significant spinal damage[8]. Toxic effects of chemotherapy include vomiting, diarrhoea, cardiotoxcitity, infertility, deafness, dry desquamation, secondary malignancies, derangements in liver function tests and skeletal abnormalities. Radiation may cause skin reactions, nausea and vomiting, lethargy, infertility and secondary malignancies. The main complication of stem cell transplant is post-transplant shock[9]. All these complications have to be looked out for during the follow-up period.

Fact Box 8:

Title: Congenital Spinal Neuroblastoma

Short description of condition: Congenital Spinal Neuroblastoma is a solid tumor of the spinal cord which arises in utero. Neuroblastoma has an incidence of 1 in 7000 live births, ranking it as the commonest neoplasm in fetuses and neonates.

Risk factors: As the condition arises in utero, pathogenesis of disease in mainly genetic.

Symptoms:

- Pain
- Parasthesia
- Diarrhoea
- Vomiting
- Loss of appetite

Signs:

- Abdominal / chest mass
- Paraplegia
- Hypertension
- Flushing
- Tachycardia
- Sweating

Prevention: There are no specific preventions that can be made, but a diet rich in folate pre-conception is associated with a decreased incidence of neuroblastoma.

NOTE: As you can appreciate, since the condition develops in utero preventive measure are not really adequate (Folate is given to every obstetric patient for the prevention of various NT defect, not neuroblastoma specifically) and the only signs can be elicted from a newborn is paraplegia and decreased tone. The symptoms above are relevant to those diagnosed at a later stage.

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Case Number 9
Posterior fossa craniectomy and C1/C2 laminectomy for Arnold-Chiari II decompression of syrinx

Daniela Zammit & Kelly Iles
Reviewed by: Mr. Antoine Zrinzo

Case summary:

Demographic details:
Mr. CC, Male.
Referred from: Home.

Presenting complaint:

Patient had a three-week history of gait disturbance, balance problems, paraesthesia in his right arm and pain in his right shoulder, together with urine frequency and urgency.

History of presenting complaint:

This patient was diagnosed shortly after birth with right-sided facial palsy as a result of lower motor neuron facial nerve involvement, together with spinal abnormalities and hearing impairment (patient currently uses hearing aids). He also has 13 ribs on his left side and 11 ribs on the right, hemi-vertebra at T2/T3 and T8/T9 and fused vertebral bodies at C2/C3 and C6/C7. As a result, clinically he has a short neck with restriction of all neck movements, particularly rotation. Patient is also known to have situs inversus.

From the MRI, it showed he had an Arnold-Chiari malformation. Therefore, the cerebellar tonsils herniated through the foramen magnum which resulted in disruption of the CSF flow. This lead to the formation of a syrinx within the spinal cord, the condition being known as Syringomyelia. The syrinx can expand and elongate over time, destroying part of the spinal cord so that the damage will cause the symptoms felt by the patient. Symptoms vary between patients and also depending on the location of the syrinx; in this case, the patient experienced the gait disturbances, balance problems, paraesthesia, pain and bowel control issues. His symptoms suggest a cape-like distribution of paraesthesia and sensory disturbance attributable to syringomyelia.

Past medical and surgical history:

Past medical history:

Sinusitis
Irritable Bowel Syndrome (IBS)
Shortness of breath at times, especially on lying down (Orthopnoea)

Past surgical history:

Inguinal Hernia repair

Drug history:

Drug	Dosage	Frequency	Type	Reason
Desloratadine (NeoClarityn)	1 tablet	BD	Anti-histamine	Relief for nasal congestion
Triamcinolone (Nasacort)			Nasal spray containing adrenocortical steroid	To treat nasal allergies
Alfuzosin (Xatral)	5mg	BD	α1- Receptor antagonist	Relaxes bladder and prostate neck to ease urination
Ambroxol (Muciclar)	10ml	TDS	Mucolytic agent	Reduces the viscosity of the mucus by stimulating production of surfactant

Family history:

The patient's mother is diabetic but no similar congenital malformations were observed in his family.

Social history:

Patient lives with his parents. He is a university student in his final year. Does not smoke and drinks alcohol socially.

Systemic inquiry:

- General Health: the patient appeared well and afebrile. He was not suffering from headaches or visual disturbances. However, he requires bilateral hearing aids.
- Cardiovascular System: no chest pain or palpitations.
- Respiratory System: complained of shortness of breath on lying down (orthopnoea) and gross sinusitis. Patient was producing yellowish-green sputum up to a week before the surgery. However, both right and left lungs were clear on chest examination.
- Gastrointestinal System: no abdominal pain, bleeding or melaena. Opens bowels around three times per day (small bouts). Abdomen is soft but not tender.
- Genitourinary System: one month history of urinary frequency and urgency. No dysuria.
- Central Nervous System: right sided facial palsy; Bilateral hearing impairment; Horizontal Nystagmus.
- Musculoskeletal System: marked restriction of neck movements.
- Endocrine System: nil to note.

Current therapy:

Patient was undergoing physiotherapy before being admitted.

Discussion of results of general and specific examinations:

Physical examination: Blood pressure recorded 141/51. Chest auscultation is clear both on the right and left sides.

Neurological examination: Patient has right sided facial palsy, bilateral hearing aids and horizontal nystagmus.

Musculoskeletal examination:

UPPER LIMBS:

		Right	Left
Tone		Normal	Normal
Power:	Shoulder Flexion	5/5	5/5
	Extension	5/5	5/5
	Elbow Flexion	5/5	5/5
	Extension	5/5	5/5
	Finger Flexion	5/5	5/5
	Extension	5/5	5/5
	Abduction	5/5	5/5
	Adduction	5/5	5/5
	Thumb Flexion	5/5	5/5
	Extension	5/5	5/5
Sensation		Normal	Normal
Reflexes:	Biceps	++	++
	Triceps	++	++
	Hoffmann's	-ve	-ve

LOWER LIMB:

		Right	Left
Tone:		Normal	Normal
Power:	Straight Leg Raising	5/5	5/5
	Knee Flexion	4/5	4/5
	Extension	4/5	4/5
	Ankle Flexion	5/5	5/5
	Extension	5/5	5/5
	Toe flexion	5/5	5/5
Sensation:		Reduced at lower outer leg	Normal
Reflexes:	Knee	++	++
	Ankle	++	++
Gait:	Ataxic	++	
	Cannot walk on tiptoes		
	Cannot walk on heels		

Diagnostic procedures:

Instrumental exams:

Test: MR Head
Justification for test: To assess for spinal pathology.
Result: The cerebellar tonsils are herniated 1.8 cm below the Foramen of Magnum secondary to a shallow posterior fossa. No vermian agenesis is demonstrated. There are no midline anomalies or space occupying lesions. Ventricles are not dilated.
Conclusion: Malformations compatible with Arnold-Chiari were present.

Test: MR Whole spine - Cervical Spine, Lumbar/sacral and Thoracic
Justification for test: To assess the presence of syrinx.
Result: Tonsillar herniation and large syrinx within the spinal cord of cervical spine extending till cervico-thoracic junction. There is bone abnormality in which the C5 - C6 and C7-Th1 vertebral bodies are fused. The thoraco-lumbar spine shows normal alignment. The disk spaces are maintained

and no cord or thecal compression seen.

Conclusion: Presence of syrinx and cerebellar tonsillar herniation confirmed. X-ray of cervical spine recommended for better evaluation of the bones.

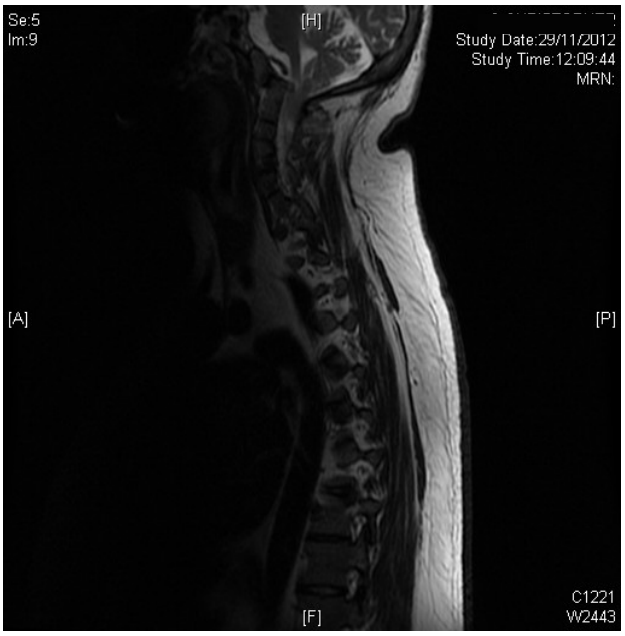

Figure 1: MRI scan showing the cerebellar herniation through the foramen magnum and vertebral fusion.

Test: Chest X-Ray

Justification for test: X-ray of cervical spine for better evaluation of the bones.

Result: There is probably situs inversus (known) together with scoliosis which is probably a consequence of congenital abnormality of Th7-Th8 vertebrae. No pulmonary lesions observed. No cardiomegaly.

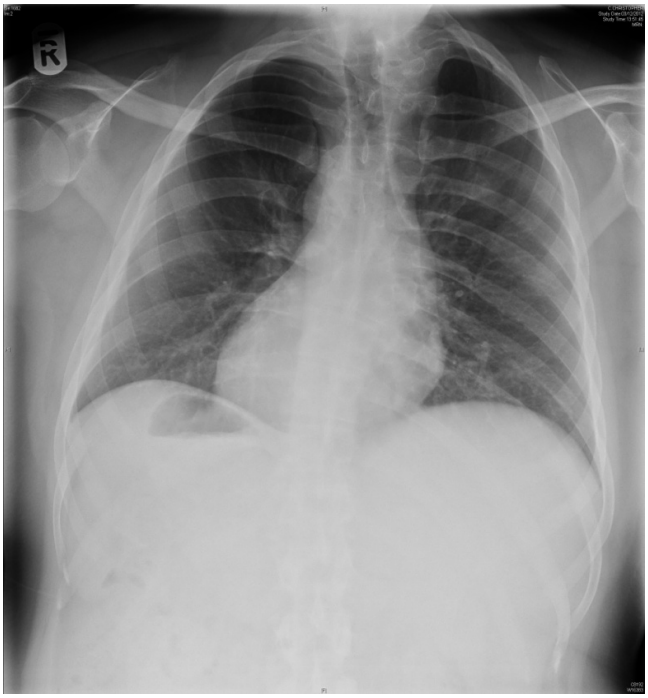

Figure 2: Chest X-Ray showing Situs Inversus in the patient.

Test: US Bladder and Kidneys.

Justification for test: Urinary urgency and frequency was one of the presenting complaints.
Result: Kidneys appeared normal in both size and shape. No stones or hydronephrotic changes seen.
Residual volume of the rest urine is ca. 157mls.
Conclusion: Source of pathology is not of nephrotic or genitourinary origin.

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Paracetamol	1g	QDS	Analgesic & Antipyretic	To treat pyrexia
Enoxaparin (Clexane)	20mg	DLY	Anticoagulant (LMW Heparin)	To prevent formation of blood clots post-op
Rocephin (Ceftriaxone)	2mg	DLY	3rd generation Cephalosporin antibiotic	Wide-spectrum activity against Gram negative and Gram positive bacteria
Metoclopramide (Maxolon)	10mg	TDS	Antiemetic	To treat or prevent nausea and vomiting
Pethidine	75mg	QDS	Opioid analgesic	To diminish pain
Codeine	30mg	TDS	Opiate	To treat mild/moderate pain and/ or IBS
Xylometazoline (Otrivin)	2 drops	TDS	Decongestant	Used as a topical nasal decongestant
Oxybutynin (Ditropan)	2.5mg	TDS	Anti-cholinergic	Relieves his urinary frequency and urgency

Surgical therapy:

Pre-operative: The patient was admitted on 3rd December 2012 and prepared for the operation to take place the following day on the 4th of December. The pre-op plan consisted of taking a cross-match and an ECG, undergoing an ENT review, consent form signed, to take CXR and blood samples for the following tests:

- Thyroid Function Test
- Full Blood Count
- Renal Profile (serum)
- Erythrocyte Sedimentation Rate
- Lipid Profile (Serum)
- Calcium and Phosphate (Serum)
- Glucose – Random (Plasma)
- C-Reactive Protein (Serum)
- Liver Profile (Serum)
- Estimated GFR
- Urine Mid Stream Specimen for MCS
- Urinalysis
- Nose and Throat Swab for MRSA
- Coagulation Screen
- Blood type and Screen
- Antibody Screen

Operation: Patient is in a prone position on frame with head fixed in a Mayfield. 2gm ceftriaxone were

given I.V. pre-operatively. Following disinfection of the skin with alcoholic betadine and subsequently with alcoholic solution, the skin was marked and infiltrated with xylocaine 2% with adrenaline.
A 12cm incision extending caudally from the external occipital protuberance was made. The scalp was elevated off the periosteum. Subcutaneous tissue and paraspinal muscles were dissected off the first 2 spinous processes. 3 burr holes were created using a craniotome. Double-action and Kerrison's upcut were used to extend the burrholes into a posterior fossa craniectomy (about 7x5cm) and a laminectomy of the first 2 vertebrae. The dura was marsupialised to expose cerebellum and tonsils thus relieving any pressure. Dura was sutured to fascia and Spongistan was applied over the cerebellum.

The wound was closed in layers (Vicryl 1/0 to muscle and fascia and dermal Vicryl 2/0 and Monocryl 3/0 to subcutis).

Post-operative: The patient returned back to the ward at 4pm, conscious but drowsy. He was moving all 4 limbs without difficulty and both hand grips were present and equal. I.V.I was in progress, administering N/Saline alternating 2x5% Dextrose 500cc 6-hourly. Catheter in-situ draining well into bag. PCA pump was in progress as well with the treatment being given as prescribed. Neurological and vital signs were checked and charted as per post-op regime.

The patient had a good first night's sleep post-operatively. Neurologically stable, oriented, moving all limbs well and his grip was present in upper limbs too. All the neurological signs and parameters were checked and charted and treatment continued as per chart. Sips were started and well-tolerated.

Post-operative, the patient developed recurrent spikes of fever. Three sets of blood cultures showed no growth and the fever subsided. The patient was passing large volumes of urine post-op as well. He was seen by Mr. K German who started him on Ditropol 2.5mg tds. He will be reviewed in two months' time from the urology point of view.

Diagnosis:

Syringomyelia refers to a fluid-filled cavity within the spinal cord. In this patient, the syrinx was a result of Arnold-Chiari malformation, meaning that the cerebellar tonsils herniate through the foramen magnum into the cervical spinal canal and cause the disruption of CSF flow; resulting in the formation of a syrinx. Infantile hydrocephalus is sometimes also associated with the Chiari malformations, as well as Spina Bifida[2]. The onset of Chiari syndrome symptoms usually occur in the second or third decade, as exemplified in this patient during his adolescence[1].

There is high clinical variability among patients, ranging from asymptomatic patients to patients with severe neurological deficits[1]. The pain the patient experienced in his right arm can be merited to syringomyelia, since such patients often suffer from upper limb pain exacerbated by exertion or coughing, together with spastic lower limb partial paralysis. Cerebellar lesions as a result of Chiari malformations were clinically demonstrated as nystagmus[2]. Urine frequency and urgency were the result of compression of the cervical spinal cord by the syrinx[3].

The diagnosis of Chiari malformation in patients with or without symptoms is established with neuro-imaging techniques, preferably with Magnetic Resonance Imaging (MRI). The most effective therapy is surgical decompression of the foramen magnum. Other methods include non-surgical therapy, used to relieve the symptoms caused by neuropathic pain. Next, rehabilitation therapy is commonly prescribed, including medical, such as the use of analgesics or anti-inflammatory agents to reduce the pain and occupational therapy, to continue relieving the pain and optimise articular movements in order to continue improving the patient's quality of life and work activities[1].

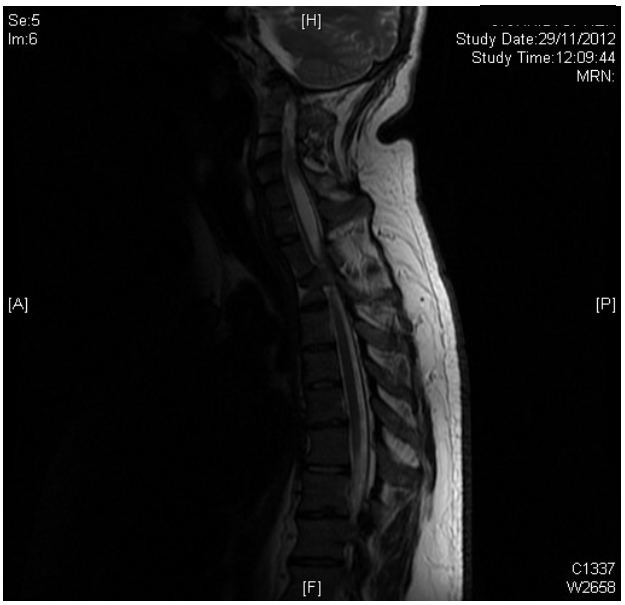

Figure 3: MRI scan showing the syrinx within the cervical spinal canal and vertebral fusion

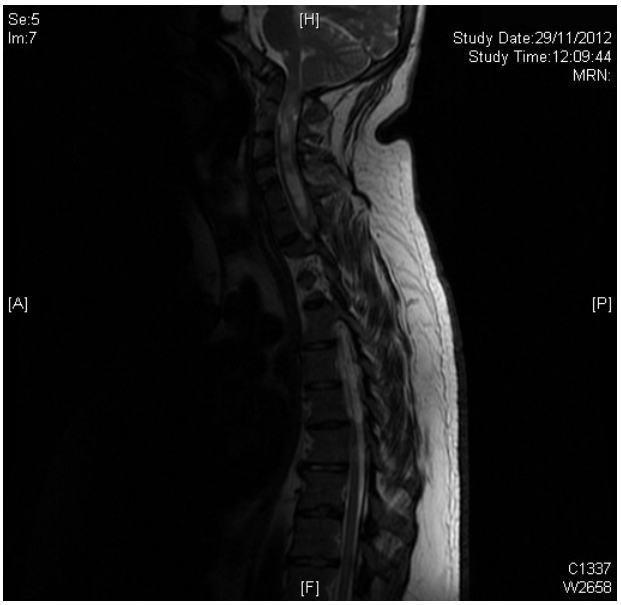

Figure 4: MRI scan showing the syrinx within the cervical spinal canal and vertebral fusion

Final treatment and follow ups:

He was discharged home on 19th December 2012 and will be reviewed at Surgical Out-Patients (SOP) in four weeks' time.

Treatment on Discharge:

Drug	Dosage	Frequency	Type	Period
Oxybutynin (Ditropan)	2.5mg	TDS	anticholinergic	Indefinite
Alfuzosin HCl (Xatral SR)	5mg	BD	α1- Receptor antagonist	Indefinite

Fact Box 9:

Title: Syringomyelia (Syrinx)

Short description of condition: Syringmyelia refers to the formation of a cyst in the spinal cord which progressively expands and elongates destroying nerve fibers which conduct information from the brain to the extremities as it does so.

Symptoms and signs:

- Progressive weakness in the arms and legs
- Back stiffness as well as stiffness in the shoulders arms or legs and chronic severe pain
- 'Cape sign' which is a loss of sensation that spreads over the shoulders and back is evident in some but not all patients

Symptoms may also include:

- Headache and a loss of ability to feel extremes of hot and cold most notably in the hands,
- Difficulty articulating words
- Dizziness
- Hoarseness
- Impaired unilateral or bilateral sensation in the face
- Rapid involuntary rolling of the eyeballs
- Loss of or deficiency in the power to use or understand language
- Loss of bladder and bowel function may also occur

Symptoms vary amongst individuals depending on the location and size of the syrinx.

Causes and Risk Factors:

- Abnormalities of the spine or skull base that are present from birth account for up to 50% of cases.
- Expansion of the syrinx during teen and young adult years is observed for unknown reasons.
- Syrinx may also develop with tumors or after a spinal injury.

Prevention: There is no way of predicting who will develop syringomyelia, however, certain injuries and infections are known to contribute to the condition. Avoiding such injuries and infections may prevent syringomyelia from developing. Rather than preventing the development of the disease, prevention of disease complications such as irreversible damage to the spinal cord and life-long neurological sequelae is more effective. In this case report, the surgeon opted for a craniotomy in an attempt to avoid further neurological deficit by the syrinx.

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Case Number 10
Hirschsprung's Disease

Sarah Ellul & Kay Vanhear
Reviewed by: Prof. Simon Attard Montalto

Case summary:

Demographic details:
Mr. ST, male, B'Kara
Admitted to NPICU from Obstetric Ward, 48 hours after delivery.

A 28-year-old, primagravida woman, gave birth to a boy at 40 gestational weeks. On delivery, the baby was found to have blood stained liquor. This was followed by non-bilious vomiting after feeds and a distended abdomen. He was transferred to NPICU at 36 hours of age due to persistent vomiting and failure to open his bowels.

An initial diagnosis of septic shock necessitated the following management plan: nurse in an incubator, establish intravenous access and perform a septic screen. Nevertheless, at 50 hours of age, persistent bilious vomiting and abdominal distension persisted.

An upper GI contrast study excluded a malrotation. Hirschsprung's Disease was then suspected and confirmed on punch rectal biopsies. A surgical operation was carried out, which included a mapping laparotomy and a colostomy. Three days after the operation was performed, he developed wound dehiscence and required re-repair in theatre. The small and large intestine were cleaned and replaced in the abdomen and the stoma site secured. Swabs taken from the wound grew *Enterococcus faecalis* and *Pseudomonas aueriginosa*.

Presenting complaint:

Persistent non-bilious vomiting after feeds: within the first 48 hours after delivery
No bowel opening: within the first 48 hours of delivery
Distended abdomen: within the first 48 hours of delivery
Vomiting altered to bilious vomiting: 2 days later once transferred to NPICU

History of presenting complaint:

A 28-year-old primagravida woman had a normal uncomplicated pregnancy, where no medications or drugs were needed. On abdominal examination, the foetus had a cephalic presentation. After 40 weeks of gestation, there was a spontaneous rupture of membranes and a baby boy was born via normal vaginal delivery. He weighed 3.7kg and was not noted to have any dysmorphic features. The placenta seemed normal.

No meconium was passed in the first 48 hours after birth and the newborn started to pass non-bilious, non-bloody vomitus soon after birth. Due to the persistent vomiting, he was transferred to NPICU, but both the vomiting and abdominal distension persisted at 50 hours from birth.

Past medical and surgical history:

Nil to note

Drug history:

The drugs listed below were administered to the mother during labour:

Drug	Dosage	Frequency	Type	Reason
Nitrous oxide + Oxygen (Entonox)		TDS	Analgesic	Pain relief during contractions
Pethidine	25mg/ml	once	Analgesic	Pain relief during contractions
Metoclopromide Hydrochloride (Maxalon)	10mg	TDS	Antiemetic	To decrease symptoms of nausea and vomiting

Family history:

No relevant family history from either maternal or paternal side.

Social history:

The mother was a 28-year-old and did not smoke or drink.

Systemic inquiry:

- General Health: persisting bilious vomiting with peri-umbilical erythema and a distended abdomen.
- Cardiovascular System: nil to note.
- Respiratory System: tachypnoeic (60 breaths per minute).
- Gastrointestinal System: persisting bilious vomiting, distended abdomen, did not pass meconium in the first 48 hours.
- Genitourinary System: nil to note.
- Central Nervous System: normal.
- Musculoskeletal System: nil to note.
- Endocrine System: nil to note.

Initial Management:

Closed incubator care: The infant needed close observation because of an increased risk of abnormal heat loss. He was also at risk to develop sepsis, and close monitoring with further tests needed to be done so as to exclude this possibility.

Given intravenous fluids (120ml/kg/day): As the infant had been persistently vomiting, he needed continuous monitoring and adequate hydration so as to prevent dehydration and electrolyte imbalance.

Nil orally: Total parental nutrition was administered as the infant was not getting any form of oral nutrition since there was a strong indication that part of his digestive system was not functioning.

Given antibiotics: amoxicillin and clavulanic acid (Augmentin) and ciprofloxacin hydrochloride (Cifran) as prophylaxis against infection.

Frequent surgical review (to monitor progress).

Cross-matched blood prepared in reserve.

Discussion of results of general and specific examinations:

On general examination, he was found to be tachypnoeic with a capillary refill time of 2-3 seconds. He was found to have a normal positive tone and movement of his upper and lower limbs. His fontanelles were soft. His anus was patent.

On abdominal examination, the infant was found to be slightly jaundiced and had a distended abdomen. He also had an erythematous rash peri-umbilically.

The main presenting feature of concern was the delayed passage of meconium in the newborn period and bilious vomiting, both potentially indicative of intestinal obstruction due to (very uncommon at this age), atresia, malrotation and a strangulated inguinal hernia. Assessment and exclusion of dehydration and shock were also important at this stage.

Differential diagnosis:

- Constipation
- Hypothyroidism
- Intestinal obstruction e.g. malrotation, atresia
- Hirschsprung's Disease

Diagnostic procedures:

Laboratory exams:

Test: Complete Blood Count.
Justification for test: To check for any signs of infection (high white blood cell count) or anaemia (low haemoglobin levels).
Result: Normal.
Conclusion: No underlying blood disorders or signs of infection.

Test: Thyroid Function Tests.
Justification for test: To exclude hypothyroidism.
Result: Normal.
Conclusion: Hypothyroidism was not present.

Test: Urea and Electrolytes.
Justification for test: To check for any electrolyte imbalance and aim for appropriate fluid management.
Result: Normal.
Conclusion: No underlying dehydration.

Test: Clotting Screen.
Justification for test: To ensure that clotting disorders are corrected before surgery.
Result: Normal.
Conclusion: No underlying clotting disorder was present.

Test: Blood Culture and an MRSA swab.
Justification for test: To exclude septicaemia and MRSA.
Result: Negative.
Conclusion: No underlying MRSA infection.

Test: CRP/ESR.
Justification for test: To check for any underlying inflammation from an infection.
Result: Raised.
Conclusion: Possibility of an ongoing inflammatory process.

Test: Septic Screen.
Justification for test: To exclude a bacterial bloodstream infection, meningitis, pneumonia etc.
Result: Normal.
Conclusion: No underlying infection.

Test: Swab from the post-operative wound.
Justification for test: To detect the causative organisms for the wound dehiscence and treat appropriately.
Result: Positive for *Enterococcus faecalis* and *Pseudomonas spp*.
Conclusion: Treat appropriately with antibiotics to cover for these organisms.

Imaging:

Test: Plain Abdominal X-Ray.
Justification for test: Routine test for abdominal distension and its possible causes.
Result: Distended bowel loops.
Conclusion: Abdominal distension was confirmed.

Test: Upper Gastrointestinal Contrast Study.
Justification for test: To exclude malrotation.
Result: Normal.
Conclusion: Malrotation was not present.

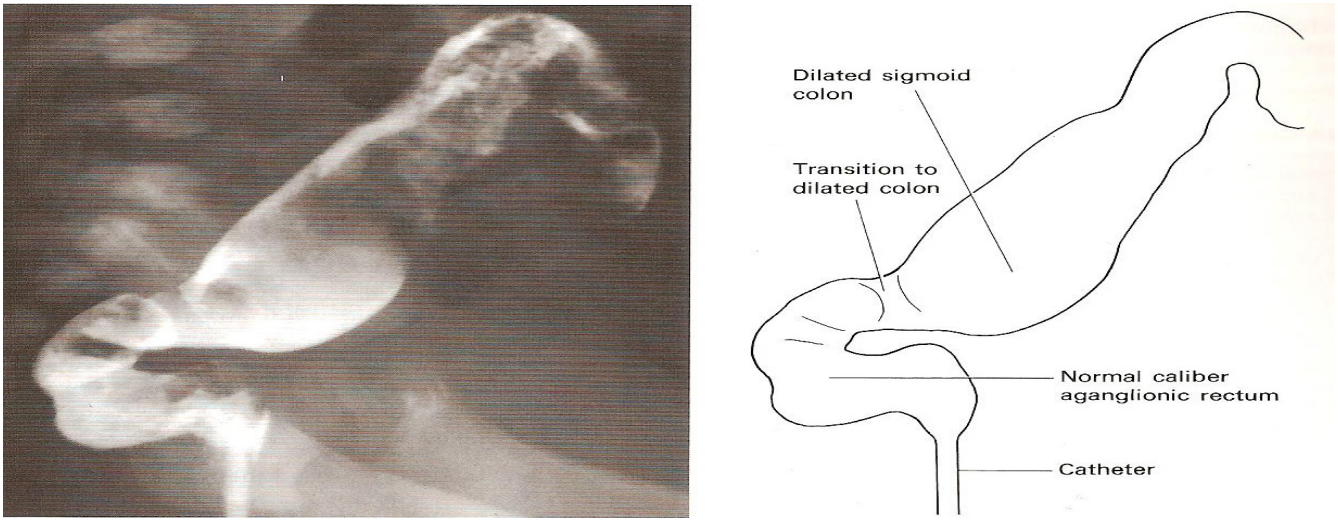

Figure 1. Hirschsprung's Disease on barium enema. Note the transition between the normal caliber aganglionic rectum and the dilated sigmoid colon[1].

Test: Rectal Biopsy.
Result: Ganglionic Cells were found in the transverse and in the Sigmoid Colon but an aganglionic segment was noted distally, starting from the rectum.
Conclusion: Hirschsprung's Disease.

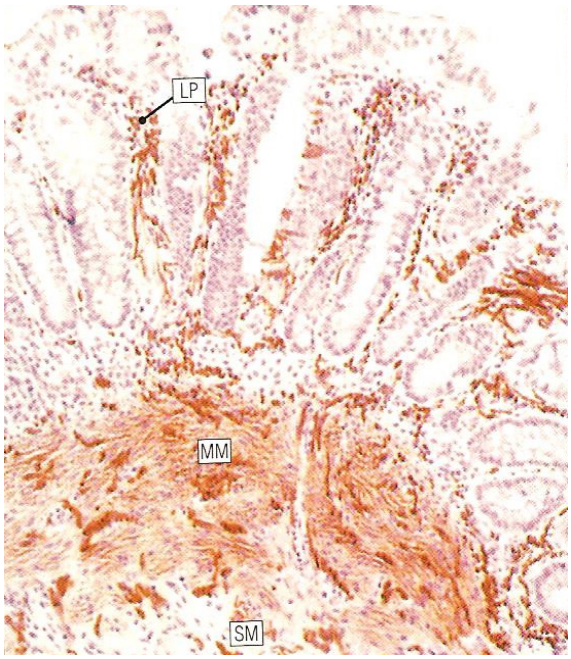

Figure 2. Hirschsprung's Disease. Rectal Biopsy. Micrograph showing prominent nerve twigs in the lamina propria (LP), muscularis mucosae (MM) and submucosa (SM)[2].

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Meropenem	10mg/kg	8 hourly	I.V.	Broad-spectrum antibiotic to cover gram-positive and gram-negative (including *Pseudomonas*) organisms
Teicoplanin	10mg/kg/12hours	Daily	I.V.	Antibiotic which covers gram-positive organisms such as MRSA and *Enterococcus faecalis*
Ranitidine	1-2mg/kg/dose	2-3 times daily	Suspension	To prevent gastro-oesophageal reflux and erosive oesophagitis
Morphine	0.05mg/kg	Every 4-8 hours	I.V.	Pain relief
Amoxicillin and clavulanic acid (Augmentin)	20mg/5mg/kg/day	Given in 3 doses	Suspension	Prophylactic broad-spectrum antibiotic

Surgical therapy:

Pre-operatively abdomen was found to be distended but the anus was patent.
Operation: Mapping laparotomy and colostomy.
Post-operatively: Wound dehiscence developed a few days later and the infant was returned to theatre to repair the stoma and clean the bowel whilst reconstructing the wound. The wound layers were closed using individual stitches and not with continuous stitching.

Diagnosis:

The rectal biopsies confirmed that the infant had Hirschsprung's Disease.

On full thickness rectal biopsy, pathophysiology shows absence of both the myenteric (Auerbach) plexus and the submucosal (Meissner) plexus which are responsible in the reduced bowel peristalsis and function[3].

The treatment of this condition is by surgical management. However, initial medical management is needed in order to stabilise the patient before any surgical treatment is undertaken. Medical management includes the correction of any fluid or electrolyte imbalances, antibiotic therapy if enterocolitis is found and rectal decompression using rectal irrigations and tubes till the surgery is undertaken.

The basic aim for the definitive surgical treatment of this disease is the resection of any aganglionic segment, which is followed by a pull-through of any ganglionic bowel down to the anus.

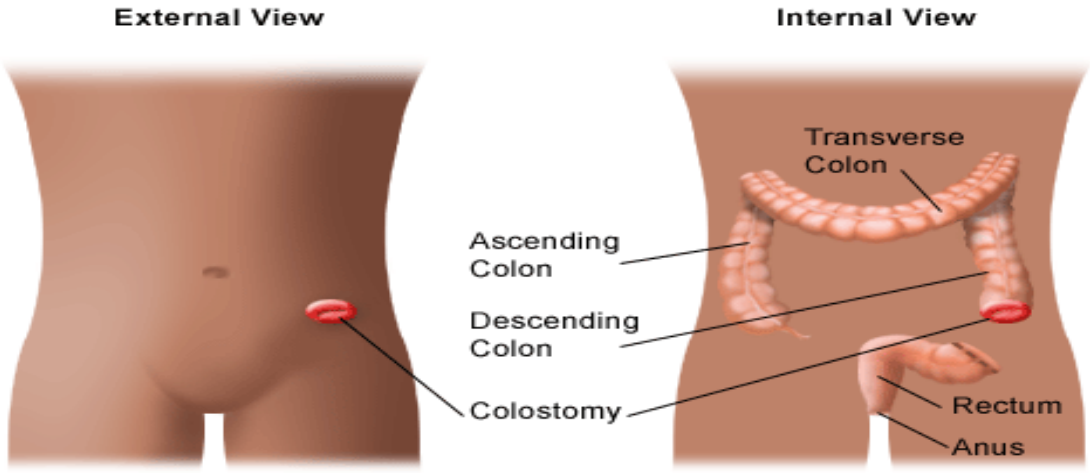

Figure 3. Bowel resection and colostomy in Hirschsprung's disease[4]

There are quite a variety of procedures which have been used, but the most commonly used are the following: Swenson pull-through (rectosigmoidectomy), Duhamel pull-through (retrorectal transanal pull-through) and Soave pull-through (endorectal pull-through)[5].

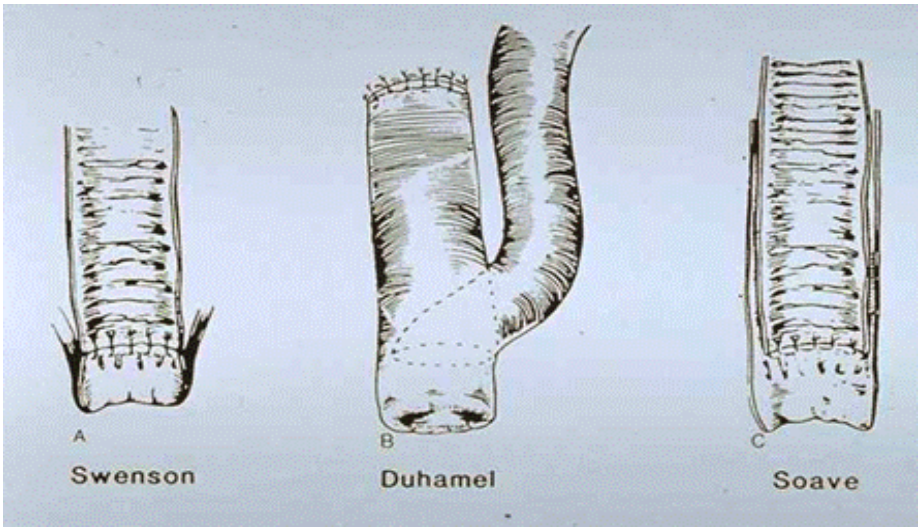

Figure 4. Types of surgical procedures for the pull-through of the ganglionic bowel down to the anus in Hirschsprung's disease[6]

Final treatment and follow-up:

On performing a microscopy and culture of the wound swabs, *Enterococcus faecalis* and *Pseudomonas aueriginosa* were cultivated. Therefore it was advised to stop Augmentin and start the infant on Teicoplanin and Metronidazole.

He was managed nil by mouth, given morphine and started on the above-mentioned antibiotics. He was also put on total parenteral nutrition at 160mls/kg/day at 26ml/hour.

After three days following the operation, he was stabilised although still intubated. All his parameters were noted to be improving and the wound had started to heal.

After six days his condition was significantly better and he was allowed to start feeding, whilst still continuing on the prescribed antibiotics.

Fact Box 10:

Title: Hirschsprung's Disease

Description: Hirschsprung's disease (HSCR) is a congenital disorder arising in 1 per 5000 newborns worldwide. It is characterised by an absence of enteric ganglia along a variable part of the intestine giving a functional obstruction where the aganglionic zone remains tonically constricted, preventing the passage of faecal material[1]. The HSCR phenotype is highly variable with respect to:

- Gender, with a 4:1 male-to-female incidence ratio.
- Length of agangliosis, where HSCR is subdivided into short-segment (S-HSCR: aganglionosis up to the upper sigmoid colon), long-segment (L-HSCR: aganglionosis up to the splenic flexure and beyond) and total colonic aganglionosis (TCA) forms.
- Familiality
- The presence of additional anomalies, such as Down's syndrome, multiple endocrine neoplasia type II, neurocristopathy syndromes and many more[3].

Currently, research is mainly focused on RET proto-oncogene on 10q11.2. This makes up 50% of familial and 20% of all the sporadic cases regarding this disease. It is especially noted in those patients presenting with long segment disease. This proto-oncogene is linked with multiple endocrine neoplasia, type IIA[4]. Eight genomes are associated with this disorder and Down's syndrome is the most common chromosomal abnormality linked with the Hirschsprung's disease[5].

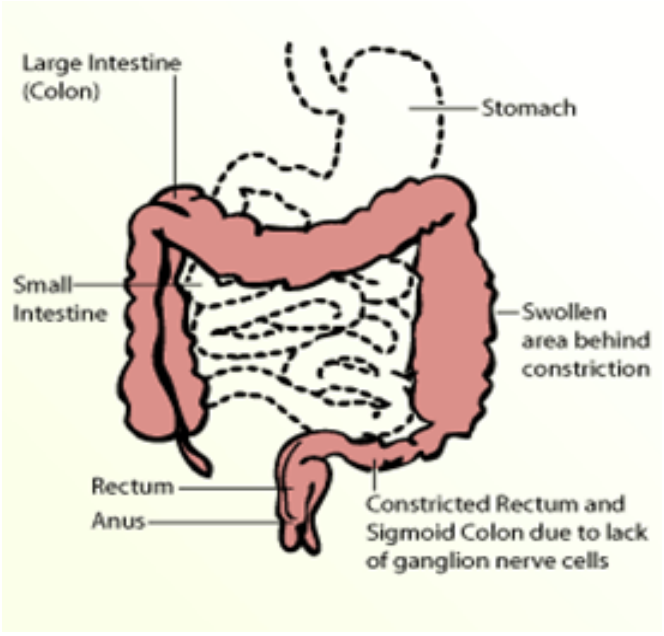

Figure 1: Functional obstruction in Hirschsprung's disease[2]

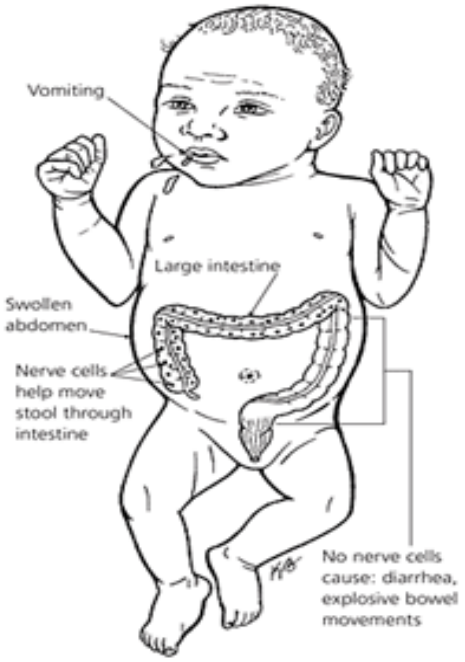

Figure 2: Signs and symptoms in an infant with Hirschsprung's disease[6]

Symptoms:

- Inability to pass meconium in the first 24 hours after birth.
- Poor feeding, generally associated with failure to thrive.
- Bilious vomiting.
- Progressive abdominal distension, with significant constipation[5].

Signs:

- Anemia
- The abdomen can be distended due to retention of faeces
- Rectal examination will demonstrate tight anal sphincter which is usually followed by an explosive discharge of foul-smelling faeces and gas[5]

The main presenting feature which should raise a red flag for the possibility of Hirschsprung's disease is delayed passage of meconium in any newborn, or a history of chronic constipation in any child since birth. Although a study shows that if the age at onset of constipation is after the neonatal period, a rectal biopsy is unnecessary as the child would be unlikely to have HRSC[7].

Treatment: The treatment of this condition is by surgical management. However, initial medical management is needed in order to stabilize the patient before any surgical treatment is undertaken.

Medical management includes the correction of any fluid or electrolyte imbalances, antibiotic therapy if enterocolitis is found, and rectal decompression using rectal irrigations and tubes till the surgery is undertaken.

The basic aim for the definitive surgical treatment of this disease is the resection of any aganglionic segment, which is followed by a pull-through of any ganglionic bowel down to the anus.

There are quite a variety of procedures which have been used, but the most commonly used are: Swenson pull-through[5] (rectosigmoidectomy), Duhamel pull-through (retrorectal transanal pullthrough) and Soave pullthrough (endorectal pull-through)[8].

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Case Number 11
Hypertrophic Pyloric Stenosis

Andrea Vella Baldacchino & Trevor Tabone
Reviewed by: Dr. Raymond Parascandalo

Case summary:

Demographic details:
Ms. KP, female,
Referred from: clinic

A 6-week old baby was brought to A&E by her parents, after a 3 week history of frequent vomiting, not tolerating feeds, and weight loss. She was well for the first 3 weeks of life, before she stopped tolerating any feeds. Despite several changes with the feeds given, the baby's symptoms did not improve. Moreover, she started losing weight, while she became increasingly irritable and inconsolable. Her consultant paediatrician decided to admit her for a trial of other formula feeds, and further investigations. In hospital, examination was unremarkable, except for an intermittently palpable mass in the RUQ. An ultrasound of the abdomen confirmed the diagnosis of pyloric stenosis. She was kept nil by mouth, an NG tube inserted for drainage, and intravenous fluids administered, with close monitoring of fluid input and output. Pyloromyotomy was performed and the patient was discharged after ensuring that she was tolerating feeds.

Presenting complaint:

Vomiting, not tolerating feeds: 3 weeks
Recent weight loss

History of presenting complaint:

KP was well for the first 3 weeks, during which she was growing adequately, reaching a weight of 3.78kg. She was initially fed on breast milk and formula milk (Aptamil). At 3 weeks, she started vomiting frequently with excessive, inconsolable crying. The vomiting was non-bilious, and at variable times after feeds, sometimes right after feeds or 1-2 hours later. At this time, she was seen by a paediatrician and feeds were changed, first to Novalac AC (anti-colic) and then to Novalac AR (anti-reflux), but with minimal improvement. Consequently, she was started on ranitidine and since she was failing to thrive, having lost weight down to 3.56kg, she was admitted for trial of HA formula and additional investigations. By the time of admission, she had visibly lost weight, and was becoming increasingly irritable and inconsolable.

Past medical and surgical history:

Born: 39^{+2}/40 weeks
Birth weight: 2.86kg
Occipitofrontal circumference: 33cm
Mode of Delivery: Normal vaginal delivery; no complications
No vaccinations yet

Drug history:

Drug	Dosage	Frequency	Type	Reason
Ranitidine	1mL (15mg)	BD	H2-receptor antagonist	To reduce acidity of gastric contents in gastro-oesophageal reflux
Simethicone		PRN	Anti-foaming agent	Reduces colic caused by gas in GIT

NKDA

Family history:

No family history of note

Systemic inquiry:

- General Health: Lost weight since stopped tolerating feeds
- Gastrointestinal System: Passes stools twice daily, parents claim it has been looser than usual
- Afebrile

Discussion of results of general and specific examinations:

General examination and vital signs: Patient appeared alert, not cyanosed (pink in air). A papular erythematous rash on the face and trunk was noted, and she had little subcutaneous fat stores. The following parameters were taken:

Admission weight: 3.56kg (3rd centile)
Capillary refill time: <2seconds
Heart rate: 140bpm
Blood pressure: 116/80 mmHg
O2 saturations: 98% in air
Temperature: 36.7ºC

General examination:
It was established that the patient was haemodynamically stable on admission, especially given her history of recurrent vomiting. Her alertness, normal capillary refill time, heart rate and blood pressure indicate that there is no clinical dehydration. Absence of fever suggests that there is no significant inflammatory process or infection contributing to the presenting symptoms. The poor subcutaneous adipose tissue is consistent with the history of weight loss and failure to thrive.

Respiratory examination:
Clear chest with good air entry. These findings are relevant given the history of frequent vomiting, since pulmonary aspiration of gastric contents can cause recurrent pneumonia, cough and wheezing.

Abdominal examination:
Abdomen was soft on palpation, and a mass was intermittently palpable in the right upper quadrant. Bowel sounds and hernial orifices were normal, and there was no organomegaly. The ‘olive’ mass in the RUQ is characteristic of pyloric stenosis, felt on gentle, deep palpation halfway between the midpoint of the anterior border of the right ribcage, and the umbilicus. It must be differentiated from other abdominal masses in infants, such as the ‘sausage shaped’ mass found in intussusception (although this condition is typically found in older age groups). Normal bowel sounds confirm that there is no bowel obstruction and normal bowel motility.

Differential diagnosis:

- Pyloric stenosis
- Cow's milk protein allergy
- Gastro-oesophageal reflux
- Infant colic
- Infection (urinary tract, otitis media)

Diagnostic procedures:

Laboratory exams:

Test: Complete blood count
Justification: Anaemia e.g. deficiency anaemias secondary to repeated vomiting or due to oesophagitis complicating reflux; neutropenia could indicate sepsis; neutrophilia and thrombocytosis could indicate an inflammatory process; baseline blood counts to monitor disease process or as part of preoperative assessment if surgery needed.
Result: Normal values

Test: Urea, electrolytes and creatinine; venous blood gases
Justification: Since history of recurrent vomiting, essential to determine if there is significant dehydration (high urea), and electrolyte disturbances such as hypokalaemia, hypochloraemia and alkalosis. eGFR values can help in excluding pre-renal acute kidney injury due to hypovolaemia.
Result: Normal values
Conclusion: No metabolic derangement

Test: Blood glucose
Justification: Hypo- or hyperglycaemia in neonatal sepsis; increased susceptibility to develop hypoglycaemia due to poor fat depots; Hyperglycaemia with DKA (diabetic ketoacidosis) consistent with vomiting and weight loss.
Result: 4.3mmol/dL (normal range)
Conclusion: Normoglycaemic

Test: IgE & RAST (radioallergosorbent test)
Justification: Cow's milk allergy
Result: Negative
Conclusion: Cow's milk allergy unlikely to be the underlying cause for the presenting symptoms.

Instrumental investigations:

Test: Abdomen Ultrasonography
Justification: To confirm of refute the diagnosis of hypertrophic pyloric stenosis
Result: - Thickened and elongated pylorus (Pyloric width: 17mm; Length: 18mm - both exceed normal values)
- Hyperechoic gastric content, stomach distended despite having had last feed more than 3hours before.
- Pylorus not seen to open

Conclusion: All measurements and observations are in keeping with a diagnosis of pyloric stenosis.

Therapy:

Resuscitation and hydration	Dosage	Frequency	Type	Reason
Dextrose and KCl in saline.	5% dextrose in 0.45 saline and 2.7mLs of 20% KCl in each 500mL	19mL/hr IV	Crystalloid	Fluid resuscitation as a pre-operative measurement.

Surgical therapy:

Pre-operative: Following diagnosis of pyloric stenosis on ultrasound, the paediatric surgeon was informed. KP was subsequently kept on a nil by mouth regimen, and an intravenous infusion at 19mL/hr of 5% dextrose in 0.45 saline and 2.7mLs of 20% KCl in each 500mL saline was started. Strict input/output charting and daily weight measurements were recorded. A nasogastric tube was left on open drainage.

Operation: An open pyloromyotomy was performed (Ramstedt's procedure). Two control trials of passing air through pylorus were carried out – no leaking was reported. After ensuring adequate haemostasis, the wound was closed in layers with vicryl 4/0 and 6/0.

Post-operative: Day 1: Early morning occasional retching with posseting of small amounts of clear fluid was noted. KP slept comfortably and did not appear in pain according to mother. The patient was also afebrile, with a slightly elevated serum K+ level of 5.65.
Day 2: The nasogastric tube was removed and half-strength feeds were started, which were tolerated. On examination, the abdomen was found to be soft and non-tender whilst the wound was noted to be healing well.
Day 3: Full strength feeds started at 60mL/3hr.
Day 4: All feeds were now being tolerated, hence it was decided that KP is deemed fit for discharge, after all post-operative parameters were found to be normal. Paracetamol 60mg 8 hourly per rectum was prescribed.

Diagnosis:

A definitive diagnosis of hypertrophic pyloric stenosis (HPS) was made. HPS is characterized by diffuse hypertrophy and hyperplasia of the muscular layers at the gastric antrum and pylorus, leading to a narrowing of the pyloric channel and a functional gastric outlet obstruction[1,2]. This rather common condition has an incidence of 2-4 per 1,000 births in white populations, being slightly less prevalent among Black, and rare in Asian populations. It is far more common in males than in in females, with a ratio of approximately 4:1. Curiously, there appears to be a greater risk for offspring of mothers who had HPS, than of fathers who had the condition, and HPS has been associated with B and O blood groups, as well as certain congenital anomalies, namely tracheo-oesophageal fistula and hypoplasia/agenesis of the inferior labial frenulum[3].

The aetiology of HPS remains unknown. However, immunocytochemistry techniques have determined a number of abnormal features within the muscular layers including a deficiency in nerve terminals, markers for nerve supporting cells, peptide-containing nerve fibres, nitric oxide synthase (NOS) activity (and mRNA for NOS) as well as interstitial cells of Cajal. Moreover, increased expression of insulin-like growth factor (IGF-1) mRNA and platelet-derived growth factors (PDGF) have been found. One hypothesis postulates that this abnormal innervation of the muscular layers leads to reduced muscular relaxation, with increased growth factor production, which promote muscular hyperplasia, hypertrophy and obstruction[2].

This case presented with symptoms which began at three weeks of life, and this is typical of HPS (average age of presentation 3/4 weeks). Almost all cases are diagnosed within the range of 1 to 12 weeks of life, and is exceedingly rare in stillbirths and preterms, hence the belief that HPS develops after birth[1,4]. The 'hypergastrinaemic hypothesis' attempts to justify this belief by proposing that an inherited increase in the parietal cell mass causes hyperacidity and decreased gastrin control, which in turn leads to repeated contractions of the pylorus and secondary work hypertrophy. This could explain why pyloric stenosis develops after initiation of feedings. In a study by Krogh et al.[6], a strong correlation of pyloric stenosis with bottle-feeding was recorded, with bottle-fed infants experiencing a 4.6-fold higher risk of developing PS than those who were exclusively breast-fed. In our case, we note that the baby was both breast and bottle-fed for the first 3 weeks before initiation of symptoms.

Pyloric stenosis usually presents with either intermittent or regular non-bilious vomiting after each feeding, with symptoms typically starting at 3 weeks of age. The vomitus may be blood stained with protracted vomiting, presumably due to underlying gastritis. The classical clinical picture described for pyloric stenosis is that of progressively projectile vomiting, hypochloraemic metabolic alkalosis, a hard "olive-shaped" mass palpated in the mid-epigastrium and visible gastric peristaltic waves, more pronounced after feeding. This traditional description of the clinical presentation of HPS has become increasingly uncommon. Glatstein et al.[6] reported drastic reductions in the frequencies of HPS cases in which an "olive" was palpated (from more than 50% in previous studies down to 13.4%) and also cases with electrolyte disturbances at presentation. The same trends were recently echoed in a study by Taylor et al.[8] in which frequencies of palpation of an "olive", hypochloraemia, visible peristalsis and haematemsis were all shown to be reduced when compared to a study evaluating patients treated between 1984 and 1995. These studies point to the fact that pyloric stenosis is being diagnosed earlier due to the increase reliance on ultrasound rather than clinical examination. This earlier diagnosis accounts for the decreasing number of patients presenting with metabolic derangements and the classical signs and symptoms. Imaging by ultrasound is now firmly established as the chief diagnostic method as is reflected in the vast majority of cases being diagnosed by sonography, given its accuracy with a specificity of 100% and sensitivity of 98%, ease of repeating the test and non-invasiveness[9].

Our case is consistent with these current trends of presentation and diagnosis. At the time of diagnosis, the patient did not demonstrate any strongly suggestive symptoms. Palpation of an 'olive' mass was not consistently reported by all medical professionals, and was only first noted after several previous examinations had failed to pick up the sign, which shows the unreliability of clinical examination.

The definitive treatment for pyloric stenosis is by pyloromyotomy, in which the hypertrophied muscle, but not the mucosa, is divided. Nowadays, the major treatment modalities available are either as an open procedure, also known as Ramstedt's procedure, which was done in our case (see below), or laparoscopically. Since its introduction, laparoscopic pyloromyotomy (LP) has gained popularity with the advances being made in laparoscopic technology. Current controversy exists about which approach is the more superior and most effective. A study by Oomen et al.[10] revealed that the time needed postoperatively to start full feeds and later hospital stay were both statistically significantly shorter when compared to patients that had undergone an open pyloromyotomy. Moreover, the major postoperative complication rate (such as incomplete pyloromyotomy and perforation – needing reoperation) after LP was found to be no different from that following an open procedure. While this might point towards the laparoscopic approach as being superior to the traditional open one, there is still no unanimous agreement. Some studies have even reported more complications following LP, particularly with regards to mucosal perforation and incomplete pyloromyotomy (Hall et al.[11], Adibe et al.[12]). Furthermore, while most studies agree that LP is associated with shorter times to full feeds and hospital stays postoperatively, these improvements only amount to a few hours at most. Therefore, it must be acknowledged that LP is associated with a steep learning curve, with the implication that this approach should only be considered as a standard of care and as a safe alternative to the open approach if done by experienced professionals with specific expertise in LP.

Final treatment and follow ups:

The definitive treatment was by pyloromyotomy, which resulted in complete resolution of signs and symptoms. The patient was discharged on the basis of having remained hydrated, tolerating feeds, and on adequate enteral intake.

A follow-up appointment at paediatric surgical outpatients was booked. The main reason for this is to check that the patient is thriving adequately for her age – which is a sign that feeds are being tolerated. Thus it is important that an accurate weight measurement is obtained and plotted on the growth chart.

Fact Box 11:

Title: Hypertrophic Pyloric Stenosis

Epidemiology:

- Prevalence: 2-4 per 1000 live births
- More common in caucasians
- More prevalent in males than in females, ratio 4:1
- Family history, especially maternal history, increases risk
- Associated with O and B blood groups, and congenital anomalies.
- Bottle-fed infants at higher risk

Symptoms:

Frequent vomiting, starting at around 4 weeks, and progressively more forceful, resulting in the pathognomonic projectile vomiting.

Signs:

- Gastric Peristaltic waves visible especially after feeds
- Pyloric mass, palpated as an 'olive' in the right upper quadrant
- Signs of dehydration: tachycardia, low urine output, mucosal dryness, sunken eyes, cold peripheries and, if decompensated dehydration, hypotension

N.B. The classical clinical presentation of projectile vomiting, visible peristalsis and a palpable 'olive' is much less commonly seen, with the advent of ultrasonography which has superseded clinical examination as the chief diagnostic method, allowing diagnosis to be made at a younger age, and institution of treatment before metabolic derangements. Therefore, clinicians should have a high degree of suspicion and consider pyloric stenosis with presentations of recurrent vomiting in infants of the appropriate age, in the absence of the later classical signs.

Treatment:

- Following diagnosis, patient is kept nil by mouth, while intravenous fluids are given, to correct electrolyte disturbances and dehydration.
- Pyloromyotomy (open or laparoscopic) provides an excellent outcome and minimal complications

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Case Number 12
An Unusual Case of Multiple Myeloma

Daniel Farrugia and Julian Delicata
Reviewed by Dr. D .J. Camilleri

Case summary:

The case concerns the unusual presentation of a non-secretory multiple myeloma with diarrhoea secondary to large bowel infiltration.

In December 2009, a 74-year-old lady presented to hospital and complained of a two year history of intermittent diarrhoea which had been worsening over a three month period. She also had sustained a deep vein thrombosis and was investigated for pulmonary embolism. Routine blood investigations showed a raised ESR & CRP and a normochromic normocytic anaemia. Urea and electrolytes, liver function tests, calcium, phosphate and albumin where all normal, creatinine was elevated. Serum protein electrophoresis was normal at presentation. Chest X-ray revealed lytic rib and vertebral lesions which were followed by CT scan and MRI. Colonic biopsy revealed a plasma cell infiltration and rib trucut biopsy revealed plasmacytoma. Bone marrow biopsy confirmed Multiple Myeloma.

Presenting complaint:

December 2009: 74-year-old woman presented with a prolonged history of repeated watery stool motions becoming frequent - up to 12 times a day. She reported no signs of bowel cramping and denied any bleeding PR. There were no other associated features such as hot flushes, nausea and vomiting or dyspnoea. No weight loss. She had low grade pyrexia on admittance.

History of presenting complaint:

The patient reported a prolonged history of watery diarrhoea of up to two years, which she controlled using Imodium. The frequency had become progressively worse over the past several months up to 12 times a day necessitating hospital admission.

Past medical history and surgical history:

Past medical history:

- Hypertension
- Possible chronic renal insufficiency secondary to hypertension
- Hypothyroidism
- Osteoarthritis
- Hypercholesterolaemia

Past surgical history:

- Total abdominal hysterectomy-bilateral salpingo-oopherectomy
- Bladder surgery
- Lower segment Caesarean Section
- Cataract extraction

Systemic inquiry

- Cardiorespiratory System: nothing of note.
- Genitourinary System: nothing of note.
- Central Nervous System: nothing of note.
- Endocrine System: nothing of note; Hypothyroidism well controlled on Levothyroxine.
- Musculoskeletal System: suffers from Osteoarthritis for which she takes NSAIDS intermittently.

Drug history:

Drug	Dosage	Frequency	Type	Reason
Perindopril	4mg	BD	ACE inhibitor	Used as an anti-hypertensive
Catafast	Not Specified	Intermittently	NSAID	Pain relief for Osteoarthritis
Nortrilen	10mg	Nocte	Tricyclic Anti-depressant; Nortriptyline	Anti-depressant
Lexamil	1.5mg	Nocte	SSRI	Anti-depressant
Zopiclone	3.5mg	Nocte	Non-benzodiazepine	Hypnotic
Salazopyrine	500mg	TDS	Aminosalicylate	Osteoarthritis
Folic Acid	5mg	Daily	Vitamin B9	Vitamin supplement due to Salazopyrine treatment
Cholestyramine	4g	BD	Bile Acid Sequestrant	Hypercholesterolaemia
Nexium	20mg	Daily	Proton Pump Inhibitor	Gastro-oesophageal reflux disease
Dioralyte	2 Sachets	Daily	Electrolytes	Electrolyte replenishment in view of chronic diarrhoea
Candesartan	16mg	Daily	Angiotensin Receptor Blocker	Hypertension
Imodium	2mg	Q.I.D	Opioid Agonist; Loperamide	Anti-diarrhoeal
Eltroxine	100mcg	Daily	Levothyroxine	Thyroid medication

Family history:

Nothing of note.

Social history:

Married wife with two children and owns a shop selling textiles. Housewife.

Current therapy:

Irrelevant to the case. All treatment listed in Therapy section later on.

Discussion of results of general and specific examinations:

General examination was unremarkable and revealed nothing useful apart from low-grade pyrexia. Inflammatory Bowel Disease was excluded via colonoscopy and biopsy and histology and the latter

revealed plasma cell infiltration of the colon. Faecal microscopy and culture ruled out parasitic and bacterial causes. Coeliac serology was negative as was 24 hr Urinary 5-HydroxyIndoleAcetic acid testing making both Coeliac disease and Carcinoid syndrome respectively, an unlikely cause of diarrhoea.

Radiology was requested in view of DVT developed one month after presentation. Chest X-ray revealed an incidental 9th right rib lesion, confirmed as a plasmacytoma on trucut biopsy. T2 and T6 lytic lesions were found on CT scan. Serum protein electrophoresis revealed no monoclonal gammopathy, but serum free light chain ratio was elevated at 5.5, as was β2-Microglobulin at 3.8mg/L bone marrow biopsy confirmed Multiple Myeloma diagnosis. Normochromic normocytic anaemia; raised ESR; CRP and creatinine were all supplementary to the diagnosis, but the latter should be considered in light of hypertensive disease and possible chronic renal failure. The disease was staged at II-IIIA by Durie Salmon Staging system using results obtained, and at Stage I by the International Staging System.

Differential Diagnosis:

- Inflammatory Bowel Disease
- Parasitic/ Bacterial Gastroenteritis
- Coeliac Disease
- Carcinoid Tumour

Diagnostic Procedures:

The diagnostic procedures performed in December 2009 will be listed here. Divided into five parts:
1. Blood investigations
2. Microbiology
3. Radiology
4. Instrumental investigations
5. More specific tests

Laboratory Investigations:

Blood investigations:

Test: Full blood count
Justification for test: To check for anaemia for possible malabsorption; chronic disease; to check for infection.
Result: Haemoglobin 9.9g/dL, MCV: 87fL.
Conclusion: Normocytic Normochromic Anaemia.

Test: ESR & CRP
Justification for test: To check for an inflammatory process.
Result: ESR was 80mm/hr; CRP was 30mg/L
Conclusion: Inflammatory process is present.

Test: Urea and Electrolytes; Corrected Calcium Levels:
Justification for test: To check for electrolyte abnormalities in view of chronic diarrhoea.
Results: Urea: 5.7mmol/l; Potassium: 4.3mmol/l; Sodium: 137mmol/l
Creatinine: 135umol/L;
Corrected Calcium: 2.6mmol/L
Conclusion: Creatinine is elevated. Calcium is within normal range.

Test: Liver Function Tests
Justification for test: IBD associated deranged LFTs; Liver involvement in view of carcinoid syndrome-like symptoms.
Result: Within normal ranges
Conclusion: LFT's are normal; does not exclude mentioned disease.

Test: Albumin
Justification for test: Possible Protein losing enteropathies.
Result: Normal: 40g/L
Conclusion: Protein Losing Enteropathy unlikely.

Test: Thyroid Function Tests
Justification for test: Known Hypothyroidism on medication.
Result: Within normal ranges.
Conclusion: Controlled Hypothyroidism.

Microbiology

Test: Stool cultures & microscopy for bacteria; microscopy for ova; cysts for parasites.
Justification for test: Check for possible bacterial and parasitic cause for chronic diarrhoea.
Result: Negative.
Conclusion: Bacterial and parasitic causes excluded.

Radiology

Test: Chest X-ray
Justification for test: Investigation for pulmonary embolism.
Result: 9th rib lesion noted on chest X-ray.
Conclusion: Bone lesion to be biopsied for histology. No signs of PE seen on X-ray.

Test: CT Pulmonary Angiogram
Justification for test: Investigation for pulmonary embolism in view of DVT sustained.
Result: Pulmonary embolism present.
Conclusion: Pulmonary embolism confirmed.

Test: CT chest/abdomen/pelvis
Justification for test: To check for any other bone lesions in view of CXR findings.
Result: Lesion in 9th rib confirmed. Two lytic lesions in T2 & T6 vertebrae were identified.
Conclusion: Rib lesion to be biopsied for histology.

Test: MRI spine
Justification for test: Check for any lesions that could not be identified on CT.
Result: No other significant findings.
Conclusion: No significant findings, other than those identified on CT already.

Instrumental Investigations

Test: Colonoscopy & colonic biopsies
Justification for test: To investigate the presence of Inflammatory Bowel Disease (IBD) and other neoplastic pathology.
Result: Plasma cell infiltration on histology, normal mucosa.
Conclusion: IBD unlikely.

More Specific Tests

Test: 24 hour urine collection for HIAA (5-Hydroxyindoleacetic acid)
Justification for test: Carcinoid tumour.
Result: Negative.
Conclusion: Carcinoid tumour unlikely.

Test: Coeliac serology
Justification for test: In view of symptoms described.
Result: Negative.
Conclusion: Coeliac disease unlikely.

Test: Right 9th Rib lesion Trucut biopsy
Justification for test: In view of CT scan findings.
Result: Plasmacytoma on histological analysis.
Conclusion: Multiple lesions indicate Plasmacytomas.

Test: Serum protein electrophoresis (SPE)
Justification for test: To investigate findings suggestive of multiple myeloma.
Result: No monoclonal spike of note in gamma position.
Conclusion: No monoclonal gammopathy present.

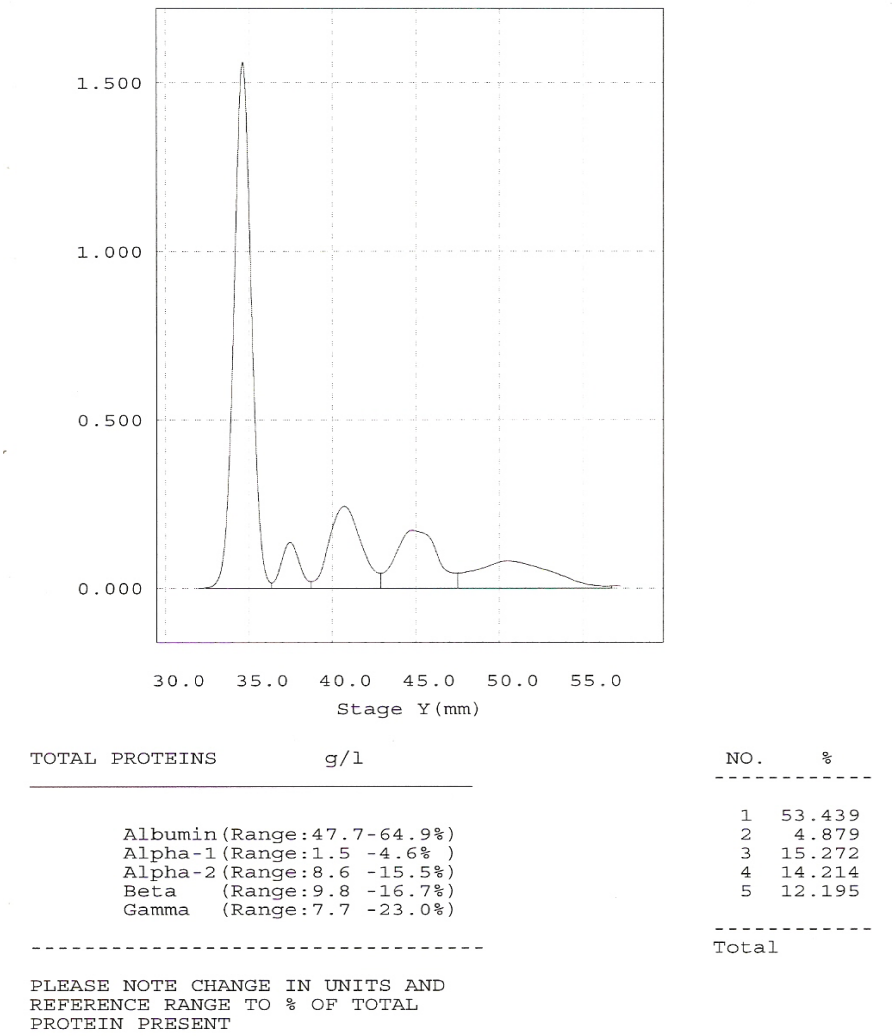

Figure 1: This graph shows the first Serum Protein Electrophoresis (SPE) taken and shows no significant spike in gamma position (the latter being the 5th and last curve of the graph).

Subsequent SPEs taken during therapy show a Hypogammaglobulinaemia as normal immunoglobulin levels decrease secondary to chemotherapeutic regimen.

Test: Serum Free Light Chain Ratio (SFLC)
Justification for test: In view of biopsy findings and normal SPE result.
Result: 5.5
Conclusion: The SFLC ratio is deranged indicating Multiple Myeloma.

Test: Beta-2 Microglobulin
Justification for test: In view of biopsy findings. Useful prognosticator.
Result: 3.8mg/L
Conclusion: Elevated. Normally elevated in Plasma Cell Dyscrasias and Lymphoproliferative Disorders.

Test: Bone Marrow Biopsy
Justification for test: In view of Plasmacytoma.
Result: Plasma cell infiltration of 20%.
Conclusion: Multiple Myeloma confirmed.

Therapy

Drugs:

Cyclophosphamide Thalidomide Dexamethasone (CTD) regimen was initiated for an indefinite period of time as treatment to Multiple Myeloma as according to CDT protocol.

Drug	Dosage	Frequency	Type	Reason
Cyclophosphamide	500mg	Once Weekly	Alkylating Agent	Multiple Myeloma
Dexamethasone	20mg	Daily	Glucocorticoid	Multiple Myeloma
Thalidomide	50mg	Nocte	Immunomodulatory Drug	Multiple Myeloma
Allopurinol	300mg	Daily	Xanthine Oxidase Inhibitor	Hyperuricaemia prophylaxis for MM Chemotherapy
Septrin	960mg	Daily	Co-trimoxazole; Antibacterial	Antibiotic Prophylaxis In view of CDT regimen.
Fluconazole	50mg	Daily	Triazole Antifungal	Antifungal Prophylaxis In view of CDT regimen
Enoxaparin	100U	Daily	Low Molecular Weight Heparin	Anticoagulation therapy due to recent history of DVT and also is advised with Thalidomide and Lenalidomide therapy. No international consensus exists as to choice of anticoagulant.
Zometa	4mg	4 weekly	Zoledronate; Bisphosphonate	Osteoporosis and Hypercalcaemia Secondary to Multiple Myeloma

The patient was reviewed monthly by haematologist. Bone marrow biopsy showed Morphological Remission by 4th cycle of chemotherapy with <5% plasma infiltration. Colonic biopsy and CT scan done after 8th cycle showed regression of older lesions and no plasma cell infiltration at colonic biopsies. MRI showed no other new bony lesions.

Diagnosis:

Multiple Myeloma is a disease of uncontrolled plasma cell proliferation in the bone marrow accounting for 1% of all malignant disease and is incurable except in cases where allogeneic stem cell transplant is possible.[1, 2,3]

It peaks in incidence at the seventh decade, shows a slight predilection for male gender and increased prevalence in people of African ethnicity.[3,12,]

The disease forms part of a spectrum of disorders characterised by a Monoclonal Gammopathy (MG) which are classified according to strict criteria for distinction.[3,11]

Table 1. The following table considers criteria for classification of Myeloma related Monoclonal Gammopathies only: (adapted from reference[11])

Standard name	New name	Definition
MGUS (Monoclonal gammopathy of undetermined significance)	MGUS (Monoclonal gammopathy)	• M-protein <30g/L • Bone marrow plasma cells <10% • No "CRAB"* • No B-cell lymphoproliferative disorder
Smouldering or indolent myeloma	Asymptomatic myeloma	• M-protein ≥30 g/L and/or • Bone marrow plasma cells ≥10% • No "CRAB"*
Myeloma	Symptomatic myeloma	• M-protein in serum or urine • BM (clonal) plasma cells or plasmacytoma • "CRAB"*

*"CRAB" is organ dysfunction characterised by any one of:

C - calcium elevation (>2.75 mmol/L)
R - renal dysfunction (creatinine >173 μmol/L)
A - anaemia (haemoglobin <100 g/L)
B - bone disease (lytic lesions or osteoporosis with compression fractures)
Other: symptomatic hyperviscosity, amyloidosis, recurrent bacterial infections (>2 episodes in 12 months)

The monoclonal spike, when present, is usually of IgG in 60% of cases of MM.[3] The exact causes are still undefined. However, a set of genetic abnormalities such as Hyperploidy; Chromosome 14 translocations and Chromosome 13 deletions, are common to a majority of MM cases. These confer a different prognosis in patient groups with particular genetic abnormalities.[1,3,12]

Monoclonal Gammopathy of Uncertain Significance (MGUS) is a diagnosis present in 3% of the population over 50 years of age and has a 1% risk of MM progression per year.[1,3,12] The proportion of MGUS is much higher in ethnic Africans.[13]

Non-Secretory Multiple Myelomas as this case, constitute 3% of all cases and are characterised by absence or undetectable levels of monoclonal protein in serum by Serum Protein Electrophoresis (SPE) or Immunofixation.[4,11] In such cases Serum Free Light Chain Ratio (SFLC) is a more sensitive alternative to detect any change in the Free Light Chain Ratios of κ:λ which are typically 0.26-1.65.[3,5,7]

Hence in view of the absent monoclonal spike in SPE, SFLC ratio was evaluated and found to be deranged (5.5). The deranged ratio shows altered light chain production by aberrant plasma cells causing high κ

light chain levels in this case[3]. Non-Secretory Multiple Myelomas can be theoretically divided into a "Producer" type in which plasma cells produce immunoglobulin but are unable to secrete it; the "Non-Producer" type does not produce immunoglobulin[6].

There are two possible scenarios in Multiple Myeloma involvement of the bowel, the first is plasmacytoma that is extramedullary which is extremely rare, the second is by plasma cell infiltration of the GI tract which in itself is also rare and usually involves the stomach and small intestine. Very rarely large bowel can be involved as in this case, causing the unusual presentation of diarrhoea prompting in this case colonoscopic examination which was unremarkable except on biopsy and histology[8,9].

This case of multiple myeloma was confirmed on the grounds of radiological evidence of lytic bone lesions together with significant plasma cell infiltration on Bone Marrow Biopsy. The β2 microglobulin levels and albumin levels are useful for prognosis for Multiple Myeloma and are used in the International Staging System[1,10]. The elevated creatinine levels; the normochromic normocytic anaemia and high ESR and CRP are also typical features of Multiple Myeloma[3]. Durie Salmon Staging of the disease depends on Haemoglobin levels (decreased); Calcium levels (raised); Radiological findings (numbers of plasmacytomata) and quantity of Bence Jones Protein levels[10]. Creatinine levels (elevation) are also taken into account[10]. This system gives an indication of the bulk of myeloma cell mass[10].

Final treatment and follow ups:

On further review one year after colonoscopy showing remission, patient was reviewed and reported new onset low back pain radiating to the right side at the level of the 7th-8th rib.
Bone marrow biopsy from posterior iliac spine confirmed a relapsed Multiple Myeloma that showed hypercellularity and suppression of erythropoiesis. A 75% Plasma Cell Heterogeneous population with intracellular Russell Bodies was found with a proportion of plasma cells having a plasmablastic morphology. C-Reactive Protein was elevated as well. New relapse was shown to involve T9; T1; T2; T12; lumbar spine through MRI spinal imaging.

Treatment at this stage was directed at controlling pain through spinal radiotherapy and also at achieving remission through an 8 cycle plan of Velcade (Bortezomib) and Dexamethasone regimen, each cycle lasting 21 days. Zometa monthly was also added in order to control risk of fractures.
The patient sustained a pathological fracture of the right femur requiring orthopaedic intramedullary nail and subsequent rehabilitation.

Blood transfusions were given as needed according to blood haemoglobin levels. Patient also developed hypercalcaemia necessitating urgent treatment. Bone Marrow Morphological Remission after the 8th cycle of chemotherapy was achieved. Patient relapsed a second time shortly after and is due for Lenalidomide and Dexamethasone chemotherapy.

Therapy for fit patients and <65 years is chemotherapy, followed by bone marrow transplantation. This can be allogeneic or autologous stem cell transplant with the former being the ideal as it is potentially curative[4]. In this case, due to comorbidities and age, chemotherapy and maintenance regimen are advocated.

Fact Box 12:

Title: Multiple Myeloma

Short Description: This is a plasma cell disorder that characterised by abnormal proliferation and accumulation in the bone marrow. Typically it is accompanied by monoclonal protein in the serum and/or urine and consequent tissue damage such as kidney failure and pathological fractures due to bone damage.

Risk Factors:

- Age: peaks at 70
- Afro-Carribean ethnicity
- Sex: men
- Obesity
- Monoclonal Gammopathy of Uncertain Significance

Symptoms:

- Classically it presents with bone pain notably back ache
- Fatigue due to anaemia
- Recurrent infections
- Weight loss
- Abnormal bleeding tendency

Other symptoms such as:

- Anorexia
- Vomiting
- Constipation and mental disturbance follow due to hypercalcaemia symptoms
- Uncommonly amyloidosis may be symptomatic e.g. macroglossia

Signs:

- A complete blood count indicating bone marrow suppresion
- A renal profile indicating renal failure
- Lytic lesions on X-ray imaging
- Bone marrow biopsy showing bone marrow infiltration

Prevention: Patients that have Monoclonal Gammopathy of Undetermined Significance may benefit from yearly screening as they have a 1% risk of MM progression. Surveillance in patients having smouldering/asymptomatic myeloma.

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Case Number 13
Transposition of the Great Arteries, Atrial Septal Defect & Ventricular Septal Defect

Ramona Camilleri
Reviewed by: Prof. V. Grech, Dr. R. Farrugia

Case Summary:

Demographic Details:
Ms. BB, 3-day-old female, Żebbug.

Three-day-old baby girl, transferred to NPICU because of low saturations and a development of a murmur. Following a number of rigourous test and the appropriate investigations, she was diagnosed with Transposition of the Great Arteries (TGA), a large Atrial Septal Defect, and a malaligned Ventricular Septal Defect. She was then transferred to Great Ormond Street Hospital (GOSH) for corrective surgey.

Presenting complaint:

39 week gestation baby girl was transferred to NPICU on third day of life because she became increasingly cyanotic and developed a murmur.

History of presenting complaint:

Baby BB was born to a 34-year-old, healthy, primigravida mother, blood group A positive. There were no significant problems during the pregnancy, antenatal scans were normal and birth was uneventful. The time from the rupture of membranes until delivery was 18 hours.

Baby BB was born at 39 weeks of gestation by normal vaginal delivery and weighed 2.97kg. Apgar scores her both 9 at 1 and 5 mins respectively. Examination at NPICU revealed that the baby was tachypnoeic, centrally cyanosed (with dusky lips) and jaundiced.

Past medical and surgical history:

Baby B.B was previously healthy. Her medical and surgical history are unremarkable.

Drug History:

During Pregnancy:

Drug	Dosage	Frequency	Reason
Folic Acid	400mcg	daily	To prevent Neural Tube Defects in the growing embryo
Iron Supplements		daily	To prevent iron deficiency anaemia

During Labour:

Drug	Dosage	Frequency	Reason
Entonox		prn	Pain relief
Pethidine	100mg	once	Pain relief
Maxalon	10mg	once	Anti-emetic

Family history:

Baby BB was born to healthy non-consanguineous parents, who have no relevant family history of medical problems. Maternal grandmother suffers from Diabetes Mellitus and Hypertension. Paternal grandmother died from myocardial infarction at age 64.

Current therapy:

On admission to NPICU, baby BB was on no medication.

Examination:

Baby BB was well perfused, with a capillary-refill time of 2 seconds and warm peripheries. She was slightly jaundiced and had no dysmorphic features.

Weight: 2.73kg
Saturations: 89-90% in air.
Temperature: 36.7^{o}C
Pulse: 100bpm

Respiratory rate: 32 breaths per minute.

Cardiovascular system: S1 + S2 + 2/6 ejection systolic murmur radiating to the back.

Chest: clear, with good air entry bilaterally.

Abdomen: soft, non-tender, no organomegaly and no palpable masses.

Neurological examination: baby was active, had a soft fontanelle and both femorals were palpable.

Blood pressure:
- Right upper limb: 88/41mmHg
- Right lower limb: 85/39mmHg
- Left upper limb: 117/89mmHg
- Left lower limb: 93/78mmHg

Discussion of results and general and systemic examinations:

From the above findings, it can be concluded that the baby had relatively low saturations in air, which explains why she was tachypnoeic, had dusky lips and was therefore centrally cyanosed. The low saturations, which did not respond to oxygenation, were most probably related a cardiac condition, as was the murmur which was heard on auscultation. She does not have signs of organomegaly and therefore she was not in heart failure. Since there are no differences between the blood pressure of her right upper limb and the other blood pressure readings, it is unlikely that she was suffering from coarctation of the aorta.

Differential Diagnosis:

- Congenital Heart Disease (involving mainly right to left shunts)
  -Transposition of the Great Arteries
  -Right Obstruction: Pulmonary Stenosis, Tetralogy of Fallot
  -Left Obstruction: Aortic Stenosis, Coarctation of the aorta, Hypoplastic left heart syndrome

- Sepsis
- Respiratory Distress
- Methaemoglobinaemia

Diagnostic Procedures:

Laboratory exams:

Test: Arterial Blood Gases
Justification for test: Due to cyanosis
Result: pH:7.40, pCO_2: 30mmHg, pO_2: 40mmHg, HCO_3:20.1; Base Excess: -4.6; Saturations: 76%.
Conclusion: Hypoxaemia.

Test: Complete Blood Count
Justification for test: As a baseline and moreover, to assess if patient has polycythaemia (which would also present with cyanosis) or has an infection (to exclude sepsis).
Result: Normal
Conclusion: The patient does not have polycythaemia and does not have increased white cells, which would indicate a possible infection.

Test: CRP, Blood Cultures
Justification for test: To assess if there is an inflammatory or infectious process occuring and therefore exclude sepsis.
Result: Normal
Conclusion: The patient does not have a inflammatory or infectious process and therefore sepsis is unlikely.

Test: Liver Function Tests especially Bilirubin (both total bilirubin and conjugated bilirubin)
Justification for test: Jaundiced patient
Result: Bilirubin: 271 (Normal: <230)
Conclusion: Patient was started on phototherapy.

Other Investigations:

Test: Chest X- Ray
Justification for test: To assess the lung fields for potential pneumonia or other inflammatory process, due to cyanosis.
Result: Clear lung fields, no consolidation or white shadowing.
Conclusion: Pneumonia or other infectious process unlikely.

Test: Echocardiogram
Justification for test: Possible congenital heart disease.
Result:
- Situs Solitus
- Transposition of the Great Arteries (TGA)
- Large Atrial Septal Defect (ASD)
- Malaligned over riding Ventricular septal defect (VSD)
- Turbulence in main pulmonary artery but the valve appears normal with velocities less than 2m/s

Conclusion: The patient was diagnosed with TGA and VSD; there was sufficient mixing of systemic and pulmonary circulations, through the VSD, and therefore did not require a Rashkind procedure (septostomy).

Therapy:

Drug Therapy at NPICU:

Drug	Dosage	Frequency	Type	Reason
Co-amoxiclav	90mg	Bd	Broad spectrum antibiotic	Against Listeria monocytogenes
Cefotaxime	150mg	Bd	Third Generation Cephalosporin	Against Group B streptococcus

Surgical Therapy:

The patient was transferred to Great Ormond Street Hospital – United Kingdom, were she had her TGA repaired and her VSD and ASD patched at 7 weeks of age.

Pre- operative: The patient was transferred to Great Ormond Street Hospital, London.

Operation:

- Median sternotomy, thymectomy, pericardial patch taken, atrio-aortic CPB 28C, left atrial vent.
- Duct ligated, divided and oversewn.
- Pulmonary arteries mobilised and controlled with sialastic loops, AXC, cold blood cardioplegia via isolated aortic root and then via coronary ostia.
- Cavae snared, right atriotomy.
- Ventricular septal defect closed with bovine pericardial patch and continuous 7-0 prolene, with one additional reinforcing pledgetted interrupted suture.
- Aorta transpected and coronary buttons mobilised.
- Autologous pericardial patch reconstruction of neo-pulmonary arterry with continuous 7-0 prolene.
- Coronary buttons relocated to medially hinged trapdoor flaps in neo-aorta with continuous 7-0 prolene.
- Lecompte maneouvre and neo-aortic anastomosis completed with continuous 7-0 prolene.
- Atrial communication closed with 6-0 prolene.
- AXC off following de-airing, heart regaining sinus rhythm.
- Neo-pulmonary artery completed with continuous 7-0 prolene, atriotomy closed in two layers with continuous 7-0 prolene.
- Off cardiopulmonary bypass easily in sinus rhythm on 0.05adr and 0.5 milrinone once warm.
- Modified ultrafiltration, prolonged haemostasis, x2 Right Atrium and x1 right ventricle pacing wires, mediastinal drain, x1 peritoneal dialysis catheter, vicryl to sternum, layered closure.

Post operative: Chest drains were removed on day 2 and the patient was extubated on day 3. Feeds re-established post operation and she was discharged on demand feeds. She was noted to be arching her back after feeds and occasional vomiting and so was started on anti-reflux medications.

Post operative medications were as follows:

Drug	Dosage	Frequency	Reason
Amiloride	0.6mg	BD	Diuretic
Furosemide	3mg	BD	Diuretic
Domperidone	0.9mg	QDS	Stomach/Reflux
Ranitidine	6mg	TDS	Stomach/Reflux

Diagnosis:

Ms. BB, was diagnosed with a congenital heart disease – namely a Transposition of the Great Arteries, a malaligned VSD and a large ASD.

Transposition of the Great artery is typically characterised by atrioventricular concordance and ventriculoarterial discordance (VA). In this type of malformation, the right atrium and the right ventricle are morphologically connected, giving rise to the aorta, whilst the left atrium and left ventricle are also morphologically connected, and these give rise to the pulmonary trunk. As a result, the systemic circulation is separate from the pulmonary circulation and therefore deoxygenated and oxygenated bloods do not mix.

The incidence of transposition of the great arteries is typically 1 in every 3500-5000 births, and it is typically commoner in males, with a male:female ratio of 1.5-3.2:1. Ventriculoarterial discordance is usually an isolated finding. This malformation can also be associated with other cardiac malformations, such as a VSD and left ventricular outflow obstruction. In these patients, the onset and presentation is typically delayed. If TGA is present with a VSD, but not left ventricular obstruction, cyanosis may be present only during exertion of the child; such as during crying or feeding. In such patients, heart failure is the prevalent feature.

Even though the aetiology of this congenital condition has been associated with some risk factors, such as exposure to rodenticides and antiepiletic medication, as well as a number of mutations such as growth differentiation factor-I, the exact aetiology remains unknown.

Diagnosis is made by echocardiography and further treatment and management is based on the findings at echocardiography. Typically, in isolated TGA, palliative therapy with prostaglandins and septostomy is required in order to ensure adequate mixing of blood, before corrective surgery. However, in this particular case, palliative therapy was not necessary, because there was sufficient mixing of blood through the VSD.

The type of corrective surgery performed was an arterial switch operation. In this procedure, the aorta and pulmonary trunks are sectioned, transposed and anastomosed. The coronary arteries, are then translocated to the neo-aorta.

Alternatively, a REV procedure (repair without extracardiac conduit) or its modification, and the Rastelli procedure can be used. Both these procedures involve creating an interventricular tunnel which connects the left ventricle to the aorta. In the Rastelli procedure, a patch is placed to create an interventricular tunnel and an extra cardiac conduit is placed between the right ventricle and the pulmonary arteries, whereas in the REV procedure the muscular outlet septum resected and the Lecompte manoeurve which avoids the use of the extracardiac conduit.

Final Treatment and Follow up:

Once the patient returned back to Malta, she underwent a follow-up echocardiogram. This demonstrated a patched VSD and no ASD. Furthermore, it also showed good function and suitable outflows with no significant obsturction. There were no effusions. Another follow-up echocardiogram was scheduled for a month later.

Fact Box 13:

Title: Transposition of the Great Arteries, Ventricular Septal Defect, Atrial Septal Defect

Description: Transposition of the Great artery is typically characterised by atrioventricular concordance and ventriculoarterial discordance (VA). The right atrium and the right ventricle are morphologically connected, giving rise to the aorta. The left atrium and left ventricle are also morphologically connected, and these give rise to the pulmonary trunk. As a result, the systemic circulation is separate from the pulmonary circulation and therefore deoxygenated and oxygenated bloods do not mix. This malformation can be assosicated with other lesions such as a Ventricular Septal Defect and Atrial Septal Defects (as in this case).

Risk Factors:

- Idiopathic
- Inutero exposure to rodenticides and anti-eplieptic treatment

Signs and Symptoms:

- The typical presentation is cyanosis in a newborn, with low saturations and hypoxaemia. Presentation, depends on the malformation present.
- Typically with an isolated TGA, cyanosis is present soon after birth. If the malformation is a TGA and VSD, the cyanosis is typically delayed until a few days after birth. With a TGA and VSD but no left ventricular obstruction, cyanosis is typically present only after exertion. These patients will develop heart failure earlier on in their life.

Diagnosis: Established by echocardiogram.

Management: According to findings at echocardiogram.

- In isolated TGA: Palliative treatment by septostomy and prostaglandins is required to ensure adequate mixing of blood, until corrective surgery is performed.
- In TGA and VSD: Palliative treatment is not usually required as there is adequate mixing of blood through the Ventricular Septal Defect.

Corrective Surgery: This is typically achieved by an arterial switch operation. Briefly, the aorta and pulmonary trunks are sectioned, transposed and anastomosed. The coronary arteries, are then translocated to the neo-aorta.

Prognosis: Prognosis is very good following corrective surgery, with more than 90% survival after 5 years.

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Case Number 14
Crohn's Disease

Franklin Abela & Anthony Pio Dimech
Reviewed by: Ms. Josephine Psaila FRCS(Edin)

Case summary:

Demographic details:
G.J., married housewife.
Referred from: home and admitted to Surgical Ward 5.

G.J, 44-year-old female known case of Crohn's disease and depression who presented with a few hours' history of severe abdominal pain and multiple episodes of vomiting faeculant matter. An inflamed terminal ileum and ascending colon were found at laparatomy and resection of terminal ileum and caecum (right hemicolectomy) was carried out.

Presenting complaint:

Few hours' history of: Severe abdominal pain
Vomiting faeculent matter

History of presenting complaint:

The pain was initially epigastric and then migrated to the periumbilical region. She reported multiple episodes of vomiting faeculant matter and had passed loose stools. There was also marked abdominal distension.

Past medical and surgical history:

Past medical history:

Crohn's disease (diagnosed 8 years ago in 2004).
Clinical depression.

Past surgical history:

Never had surgery.
Never had anaesthesia.
Drug History: Allergic to penicillin.

Drug	Dosage	Frequency	Type	Reason
Mirtazapine	30mg	nocte	Noradrenergic and specific serotonergic antidepressant (NaSSA)	For treatment of depression[1]
Paroxetine	40mg-20mg-0	BD	SSRI (selective serotonin reuptake inhibitor)	For treatment of depression

Bromazepam	3mg 2-2-2	TDS	Benzodiazepine	For the treatment of anxiety
Esomeprazole	20mg	once daily	Proton pump inhibitor	To treat symptoms of gastroesophageal reflux disease (GORD)
Hydroxocobalamin	1mg	once daily	A synthetic injectable form of vitamin B12	To treat low levels (deficiency) of vitamin B12
Folic acid	5mg	once daily	Water-soluble B vitamin	To treat low levels of folic acid and anaemia
Mesalazine	500mg 2-2-2	TDS	Anti-inflammatory agent	To treat inflammatory bowel disease
Prednisolone	30mg (tailing dose since last admission)	once daily	Corticosteroid	To treat inflammatory disease

Information on type of drug and indications was obtained from BNF, 2011[1]

Family History:

Nil of note.

Social History:

The patient was a non-smoker who lived with her husband and had no relevant history of recreational drug use/abuse.

Systemic enquiry:

- General Health: unwell, afebrile, pale and visibly in pain.
- Cardiovascular System: haemodynamically stable. Heart sounds: S1 + S2 + 0.
- Respiratory System: clear breath sounds heard bilaterally.
- Gastrointestinal System: distended abdomen, soft with tenderness in the epigastrium (which did not radiate to the back), left iliac fossa and infraumbilical region.
- Genitourinary System: nil of note.
- Central nervous System: nil of note.
- Musculoskeletal System: no abnormality detected.
- Endocrine System: no abnormality detected.

Treatment on admission:

Intravenous infusion of Hartmann's solution was set up to prevent dehydration from vomiting since the patient was unable to tolerate oral fluids.

Nasogastric tube – to empty stomach contents in an attempt to reduce the bouts of vomiting.

Urinary catheter – to monitor fluid output and detect dehydration as early as possible.

Discussion of results of general and specific examinations:

Crohn's disease can affect the whole gastrointestinal system. Inflammation may occur at any point in the bowel, from the mouth to the anus. Tenderness over the left iliac fossa and infraumbilical region may have been due to the inflamed bowel, but peritonitis due to perforation of the bowel should be excluded. Since the patient was apyrexic, peritonitis was unlikely; however one must remember that she was on steroids and therefore may not have pyrexia in spite of peritonitis.

Epigastric pain may follow straining due to recurrent vomiting as well as irritation of the lower oesophagus by gastric acid. It can also be caused by gallbladder disease, peptic ulceration and pancreatitis. However, the latter was unlikely because pain did not radiate to the back[2]. Blood tests to detect any hepatic involvement were taken which turned out negative.

Bowel obstruction in Crohn's is mainly caused by strictures due to the inflamed bowel. At times, the inflammation itself can reduce the diameter of the lumen enough to cause obstruction[3]. Bowel obstruction is a major cause of morbidity in patients with Crohn's disease[4]. They often present with faecal vomiting if the stricture is in the lower gastrointestinal tract, as well as marked abdominal distension.

Loose stools and diarrhoea in Crohn's mainly originate due to malabsorption in the large intestine. It may or may not be bloody[7]. At times, it can arise from side effects of the drugs used in Crohn's, for example sulfasalazine and mesalazine[1].

Differential diagnosis:

- Intestinal obstruction[5]
- Peritonitis
- Peptic ulceration[6]
- Appendicitis
- Diverticulitis
- Bowel tuberculosis
- Small bowel cancer
- Coeliac sprue
- Lymphoma
- Behcet's disease
- Ischemic colitis
- Ulcerative colitis
- Infectious enteritis
- Non-steroidal drug enteropathy[7]

Diagnostic procedures:

Laboratory exams:

Test: Blood test.
Justification for test: The reason behind doing a full blood count in Crohn's disease is because of the predisposition towards anaemia due to iron deficiency (malabsorption), anaemia of chronic disease, blood loss from the gastrointestinal tract and drug-induced (e.g. mesalazine). Anaemia may also be due to folate or vitamin B12 deficiency. Thus knowing the levels of these substances in blood is important[8]. A high white cell count may also show signs of infection.

Measurement of the erythrocyte sedimentation rate (ESR) and the C-reactive protein (CRP) is done to determine whether there is inflammation. CRP is known as an acute phase protein. All these tests can be altered by steroids and disease-modifying drugs.

Liver function tests are required whenever a patient complains of epigastric pain, especially if there is associated vomiting. The results can confirm or exclude biliary involvement. Serum albumin tends to be low in Crohn's disease. It was also noted in a study that pre-operative hypoalbuminaemia was one of several factors associated with early postoperative complications in inflammatory bowel diseases[9]. Thus, its measurement is important. Liver function tests help to exclude any liver pathology which can be a cause of low albumin.

The reason for measuring serum magnesium levels is because of the tendency towards malabsorption of the mineral. This may cause additional problems that need to be dealt with separately, including functional hypoparathyroidism, by reducing the synthesis of parathyroid hormone (PTH). Low PTH can affect adversely the kidneys and the skeleton[10].

Results: Hb: 9.35g/dL (11.5-16)
MCV: 90.3fL (79-96)
Platelets: 280 x 10^9/L (150-400)
Reticulocytes: 48.2 x 10^9/L (20-130)
WBC: 4.2 x 109/L (3.5-11)
Neutrophils Abs (Absolute Value): 8.64 x 109/L (2.5-7.5)

Ferritin (serum): 116ng/mL (15-200)
Vitamin B12: >738pmol/L (200-900)16
Folate (serum): >54.4nmol/L (7-30)17

ESR: 81mm/hr (30)
CRP: 78mg/L (<0.8)

Alkaline phosphatase (serum): 33U/l (30-150)
Alanine aminotransferase (serum): 6U/l (5-35)
Gamma glutamyl transferase (Abs): 14U/L (5-36)
Total protein (serum): 53.1g/L (60-80)
Albumin (serum): 32.1g/l (35-50)

Globulin: 21.4g/l
Magnesium (serum/plasma): 0.83mmol/l (0.75-1.2)

Conclusion: Haemoglobin levels were slightly lower than the normal range for a female. However, all other blood cell parameters, as well as ferritin, vitamin B12 and folate, were normal. The cause may be anaemia of chronic disease[11]. The ESR and CRP were high, indicating an inflammatory process. Liver function was normal and there was no indication of biliary pathology. A low serum protein and albumin level is a common finding in long-standing cases of Crohn's disease, mostly due to malabsorption of nutrients from the intestine. Another rare cause is protein-losing enteropathy, which is a severe complication of Crohn's disease. It is a diagnosis of exclusion, done after eliminating malnutrition and liver or kidney failure. The pathogensis of protein-losing enteropathy implies excessive leakage of protein through the injured intestinal mucosa[12].

Instrumental exams:

Test: Chest X-ray
Justification for test: Patient was tachypnoeic.
Result: Poor respiratory effort. No obvious pulmonary lesion is seen. There was cardiomegaly and lung congestion.
Conclusion: This finding had to be taken care of separately. Medications and procedures that could worsen chest signs had to be avoided.

Test: Abdominal X-ray
Justification for test: This non-invasive test is often done to evaluate pathology in the small intestine and colon. Its importance in Crohn's is to detect the presence of ulceration, strictures, cobblestoning, string signs (narrow lumen), fissures and loss of haustrations[7].
Result: The contrast coating of the oesophagus, stomach and duodenal bulb showed no stricture, mass or wall abnormality. There was no hiatus hernia. There was a stricture of a long segment of the terminal ileum, in keeping with Crohn's disease. Faecal loading was visible. A slightly widened loop of the small bowel was noted in the left mesogastric region.
Conclusion: The strictures visible on barium follow-through were causing the obstruction, explaining the faecal vomiting and abdominal distension.

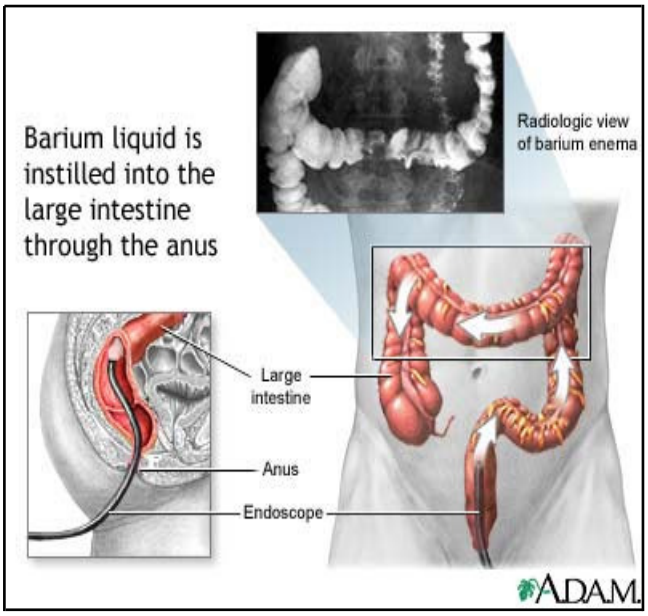

Figure 1

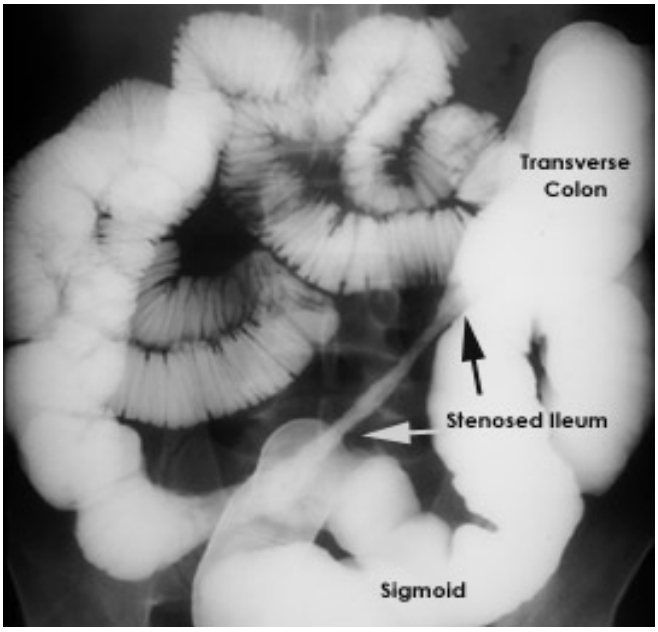

Figure 2

Figures 1,2: Barium Enema

Test: CT abdomen and pelvis
Justification for test: To exclude bowel obstruction and examine the cause of abdominal distension.
Result: Ascites and free fluid in pelvis were noted. Several sections of the small bowel showed contrast-enhancing oedematous walls which also involved the terminal part of the ileum. Some small bowel loops (particularly in the lower abdomen) also showed distension. A radial hyper-dense fluid collection containing small air bubbles was seen near the terminal ileum. This might have possibly been a sign of incipient abscess formation. The colon was collapsed, the intestines in the left abdominal part were moderately distended and fluid filled. No lymphadenopathy was noted. No free gas was identified.
Conclusion: These findings were compatible with Crohn's disease of the small bowel complicated by abscess formation and bowel obstruction.

Test: Colonoscopy

Justification for test: Direct vision of the large bowel and terminal ileal mucosa, with the possibility of taking biopsies[7].

Result: Oedematous colonic mucosa. There was severe inflammation of a large segment of the terminal ileum, caecum and ascending colon up to the hepatic flexure.

Conclusion: These findings match Crohn's disease of the terminal ileum with extension to the proximal colon.

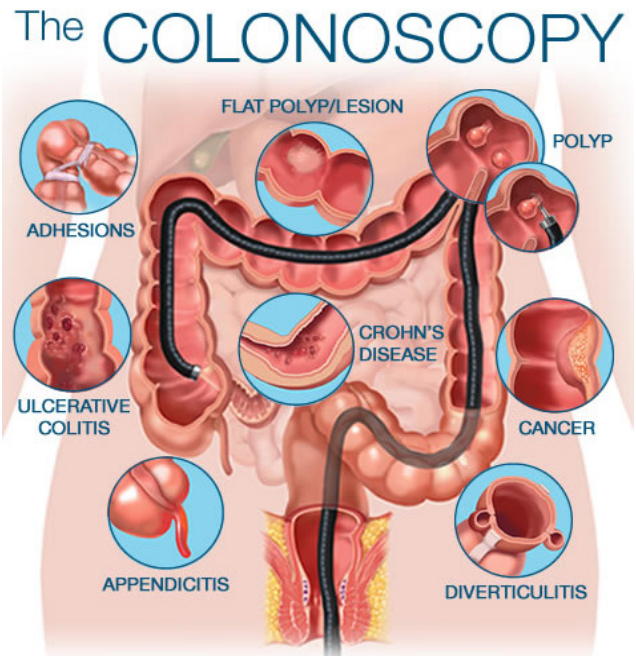

Figure 3: Colonscopy

Therapy:

Drug therapy:

Drug	Dose	Frequency	Type	Reason
Metoclopramide	10mg IV	TDS	Dopamine receptor antagonist	To reduce the nausea and vomiting
Rantidine	50mg IVI	6-8 hourly	H2-receptor antagonist	To inhibit stomach acid production
Paracetamol	1g IVI	4-6 hourly	Non-opioid analgesic	Pain relief
Ciprofloxacin	400mg IV	8-12 hourly	Quinolone antibiotic	Prophylaxis against possible gastrointestinal infection (Gram negative and Gram positive)
Metronidazole	500mg	8 hourly	Antibiotic	Prophylaxis against anaerobic organisms and protozoa which can cause gastroenteritis

Information on type of drug and indications was obtained from BNF, 2011[1]

Surgical therapy:

Pre-operative: The patient was kept nil by mouth in hospital. She was admitted for surgery as soon as all the investigations were carried out.

Operation: The surgical site was disinfected and a median laparotomy incision was made. On gross examination, an inflamed terminal ileum, was identified. A section of colon distal to the ileocaecal valve was collapsed.

The right part of the colon and caecum were mobilised. The mesentery was divided to demarcate the dissection margins. Resection of terminal ileum and caecum with primary bowel anastomosis was carried out. Bowel specimens were sent for histology. The anastomosis was hand sewn using polydioxanone (PDS) absorbable sutures. Haemostasis was confirmed before closing. Lavage of the area was necessary. A Nelaton drain was inserted and secured via a nylon suture. The skin was closed with metal staples.

Post-operative period: The following instructions were given to the nursing staff in the post-operative period:

- Keep nil by mouth with nasogastric tube in situ
- IV fluids
- Analgesia : Paracetamol 1g IV 6 hourly , Pethidine 75mg IM 6 hourly
- DVT prophylaxis: Enoxaparin sodium 40mg SC daily and stockings
- Antibiotics: Ciprofloxacin 250mg IV
- Oxygen must also be given to the patient

On examination, the patient was stable, afebrile and not in pain. Parameters were stable (Sp O_2 was 99% on air, blood pressure 110/80mmHg).

Diagnosis:

The formal diagnosis in this case was that of Crohn's disease with involvement of the terminal ileum, caecum and ascending colon.

Crohn's disease is one of the two forms of chronic inflammatory bowel diseases, the other being ulcerative colitis. Crohn's is relatively common in Western Europe, compared to the rest of the world and its incidence has increased over the past half century. Onset of the disease is early in life (at approximately 20 years of age) with little preference between the two sexes. The aetiology of the disease is unknown, but there is a familial tendency towards inflammatory bowel disease in general, making scientists believe that it must be polygenic and genetically heterogenous. The genes involved in Crohn's include NOD2 and CARD15, but this remains an active area of research[5].

Another, hypothesis suggests that the activation of Crohn's disease is caused by a rapid and severe immunological stimulus in the bowel, such as severe gastroenteritis. The effect of this is a rapid activation of resting macrophages with the release of many cytokines, including interleukin-1 (IL-1). Interleukins bind to cellular receptors and promote an inflammatory reaction in the bowel, with all its consequences of tissue damage. Genetic and environmental predisposition towards the exaggerated activation of the immune system plays a very important role in the pathophysiology of Crohn's. Furthermore, tobacco smoking predisposes to Crohn's, but somehow exhibits a degree of protection against ulcerative colitis[7].

Crohn's disease affects any part of the gastrointestinal tract sparing some areas in between. Thus the disease is patchy, forming skip lesions, unlike ulcerative colitis. The following table shows the relative incidence of Crohn's in different areas of the bowel:

Area of bowel	**Incidence Rate**
Small intestine (mainly terminal ileum)	50%
Large intestine	20%
Both large and small intestine	30%

The mouth, oesophagus, stomach and duodenum are also occasionally involved. The disease can also affect the perianal area, with or without influencing the large bowel[5].

In Crohn's disease, the inflammation of the bowel is transmural, i.e. involving the whole thickness of the bowel wall. The consequences of this include obstruction, fistulation and perforation. Several interspersed fissured ulcers which extend deep into the muscle layer are common, producing a cobblestone appearance. Granulomas (often non-caseating) are also present. They contain multinucleate giant cells. Fibrosis may follow prolonged inflammation, producing bowel strictures which can lead to obstruction[5].

The effects of mucosal inflammation are varied. If the colon is involved, the patient may pass diarrhoea streaked with blood. In small bowel involvement, partial obstruction may occur, which causes colicky abdominal pain. Diarrhoea and malabsorption may predispose to protein-calorie malnutrition, anaemia (reduced iron and folate absorption) and failure to thrive (in children). If the terminal ileum is involved, the patient may suffer from vitamin B12 malabsorption, and if bile salts are not reabsorbed in the ileum, they can irritate the colon, causing more diarrhoea. In addition, lack of bile salts in the circulation predisposes to gallstones[5].

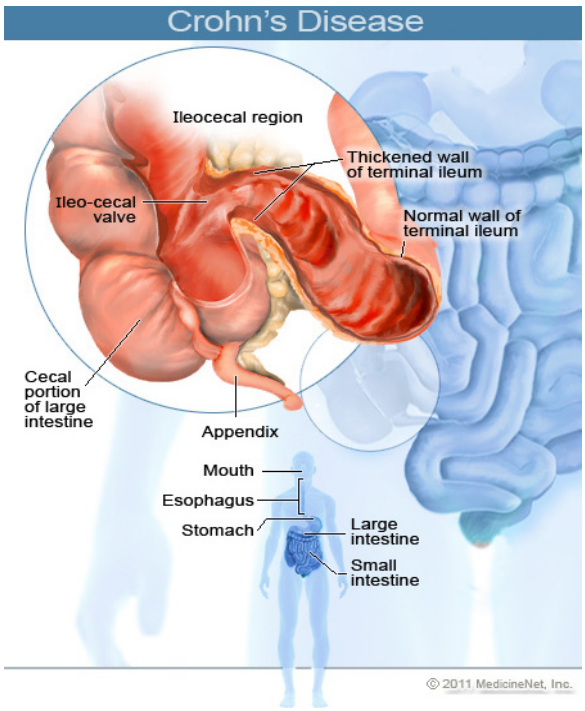

Figure 4: General overview of Crohn's Disease

Transmural inflammation in Crohn's may cause peritonitis, with severe, localised pain. In the terminal ileum, it may mimic appendicitis. Rarely, toxic megacolon may ensue. If the serosa is breached, adhesions may form to adjacent organs. However, these are rarely symptomatic. Bowel perforation may be free (with contents spilling out in the abdominal cavity) or contained (forming localised abscesses). Fistulae between the bowel and nearby hollow viscera may form. Some examples and clinical manifestations of these fistulae are listed in the table below[5].

Type of fistula	**Structures involved**	**Clinical features**
Gastro-colic	Colon and stomach	Faecal vomiting
Ileo-rectal	Ileum and rectum	Exacerbation of diarrhoea
Entero-vesical	Bowel and bladder	Recurrent UTIs and pneumaturia
Entero-vaginal	Bowel and vagina	Passage of faeces through vagina
Entero-cutaneous	Bowel and skin	Passage of soft stools through skin opening

Perianal involvement can occur in patients with Crohn's disease, especially if there is small bowel involvement[5]. This can manifest itself as multiple abscesses, piles, hypertrophied skin tags, anal fissures, numerous fistulae between the rectum and perianal skin (pepper-pot perineum), and perineal scarring[7].

Extraintestinal manifestations of Crohn's disease may be severe and correlate with the intestinal activity of the condition. The joints (e.g. ankylosing spondylitis, sacroilitis), skin (e.g. erythema nodosum, pyoderma gangrenosum), eyes (e.g. uveitis, episcleritis), and hepatobiliary system (primary sclerosing cholangitis) may be implicated[7].

Fact Box 14:

Title: Crohn's Disease

Description: Crohn's is a chronic inflammatory bowel disorder of unknown aetiology which can affect the whole gastrointestinal system (from mouth to anus) and is typified by asymmetric, focal, transmural inflammation and sometimes granuloma formation in the bowel wall. Signs of extraintestinal manifestation can be marked. The life-long disease is punctuated by periods of exacerbation and remission[15]. Genetic and environmental contributors, as well as immunological factors are implicated in the pathogenesis and severity of Crohn's disease.

Risk factors:

- Genetic factors (family history)
- Immune system
- Infection (mycobacteria, paramyxovirus, cytomegalovirus)[7,13]
- Diet (high intake of meat, fats and polyunsaturated fatty acids)[14]
- Smoking
- Perhaps other risk factors not yet identified

Histological features of bowel wall:

- Transmural inflammation of bowel wall
- Thickened, oedematous, fibrotic submucosa
- Lymphoid aggregates (may extend deep to the muscularis propria)
- Non-caesating granulomas (not always present)[7]

Clinical features:[7]

Gastrointestinal involvement:

- Nausea
- Vomiting
- Dysphagia
- Odynophagia
- Aphthous ulcers over the hard palate
- Postprandial fullness
- Abdominal pain
- Weight loss
- Anorexia
- Abdominal mass
- Diarrhoea (may or may not be bloody)

Extraintestinal involvement:

- Fever
- Uveitis
- Episcleritis
- Erythema nodosum
- Pyoderma gangrenosum
- Ankylosing spondylitis
- Sacroiliitis

- Seronegative polyarteritis
- Primary sclerosing cholangitis

Complications:[5]

- Strictures
- Fistulae (intestinal, anal)
- Anal and perianal lesions
- Haemorrhage
- Intestinal obstruction
- Intestinal perforation
- Toxic megacolon (very rare)

Treatment:[15]

- 5-aminosalicylic acid compounds e.g. mesalazine, sulfasalazine (modified for local release)
- Corticosteroids e.g. prednisolone and budesonide (local or systemic)
- Immunomodulators e.g. azathioprine, 6-mercaptopurine, methotrexate, infliximab
- Supportive treatment: antidiarrhoeal drugs, antispasmodics, dietary modification, vitamin and mineral supplements
- Surgery

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Case Number 15
Pleomorphic Sarcoma

Isaac Bertuello & Maria Bonnici
Reviewed by: Mr. Christian Camenzuli

Case summary:

Demographic details:
Ms. AC, female, 67
Referred from home by GP

67-year-old female who was referred from her general practitioner because of uncontrolled right popliteal knee pain which was very severe and continuously deteriorating. She could not bend her knee and sleep because of the pain. She could only walk on tiptoes with increased pain on weight bearing. Originally the popliteal swelling was thought to be a baker's cyst. Arthroscopy showed no changes and MRI showed a large, primarily solid lesion in the popliteal fossa measuring 6x6x9 cms. This was biopsied and histopathology showed a sarcoma and an above knee amputation had to be performed. The patient is now well undergoing physiotherapy and occupational therapy to get back to her life.

Presenting complaint:

Severe pain in the right knee leading to decrease mobility.

History of presenting complaint:

The patient complained that after a fall in April 2011, in which she hit her knee, she felt an ever growing knee pain. She also complained of swelling and was noted that she could not extend her knee. Her pain increased with weight bearing and could only walk on tiptoes.

The pain was very severe and crushing in nature. It did not allow her to sleep at night. She was very desperate and has spent the last two weeks unable to move unless assisted by someone. The patient did not find a way to reduce the pain and not even powerful painkillers prescribed by her general practitioner were working. The patient was also given two cortisol injections in her knee joint but these had no beneficial effect on her.

Past medical and surgical history:

Past medical history:

Hypertension
Hypercholesterolaemia

Past surgical history:

Tonsillectomy as a child
Excision of benign lipoma of right shoulder (2000)

Drug history:

Drug	Dosage	Frequency	Type	Reason
Atenolol	50 mgs	daily	Beta blocker	Hypertension
Bumetanide	1 mgs	BD	Diuretic	Hypertension
Simvastatin	20 mgs	BD	Statin	Hypercholesterolaemia
Enalapril	20 mgs	BD	ACE inhibitor	Hypertension
Glucosamine	1 tablet	BD	Joint care	Arthritis
Amlodipine	10 mgs	daily	Calcium channel blocker	Hypertension
Solpadol	30 mgs	TDS	Analgesic	Pain relief

Family history:

Mother died of a stroke at the age of 65.
Father died of a brain tumour at the age of 83.
There is a history of hypertension and hypercholesterolaemia in the family.

Social history:

Married.
Lives with husband who is independent and helps her when needed. Her children also give her a helping hand.
She has one flight of stairs but does not need to use it as everything is found on the first floor.
No smoking.
No alcohol intake.
No recreational drugs.

Systemic inquiry:

- General Health: good and active. Patient looked comfortable after operation.
- Cardiovascular System: hypertension and hypercholesterolaemia.
- Respiratory System: nil to note.
- Gastrointestinal Tract: nil to note.
- Genitourinary System: nil to note.
- Central Nervous System: nil to note.
- Musculoskeletal System: after amputation she is already standing up and doing exercises with the help of physiotherapy.
- Endocrine System: nil to note.

Current therapy:

Patient was fast-tracked due to the amount of pain she was suffering and given powerful analgesics till the operation.

Discussion of results of general and specific examinations:

On examination: The patient had fixed flexion of the knee and painful ROM. Mass at the popliteal fossa was felt, which was tender on palpation.

Differential diagnosis:

- Baker's cyst
- Popliteal aneurysms

Diagnostic procedures:

Laboratory Investigations:

Test: Biopsy for histology (18/1/13)
Justification for test: Popliteal mass in right knee.
Result: Multiple biopsies show poorly differentiated spindle cell lesion composed of pleomorphic spindle cells with scattered abnormal mitosis and occasional bizarre nuclei which are forming sheets and fascicles. The cells are SMA positive but Desmin, Cytokeratin and HRF-35 negative.
Conclusion: Pleomorphic Sarcoma.

Imaging:

Test: MRI (17/1/13)
Justification for test: Popliteal mass of right knee.
Result: There is a large primarily solid mass lesion within the popliteal fossa measuring 6x6x9 cm. It is of intermediate to high signal intensity on fluid-sensitive sequences and low signal intensity on T1. Its solid component is seen to avidly enhance post contrast administration. A few central cystic components are noted within the mass lesion. The lesion is seen to encase the popliteal neurovascular bundle. It displaces the gastrocnemius muscle belly posteriorly. A small effusion is also noted.
Conclusion: Large mixed solid cystic popliteal mass lesion appearances of which are suspicious for sarcomatous change.

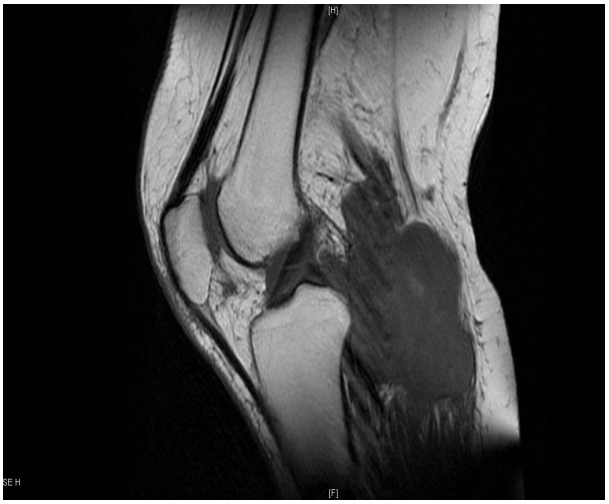

Figure 1: MRI (Coronal Section) of the knee showing clearly the popliteal mass

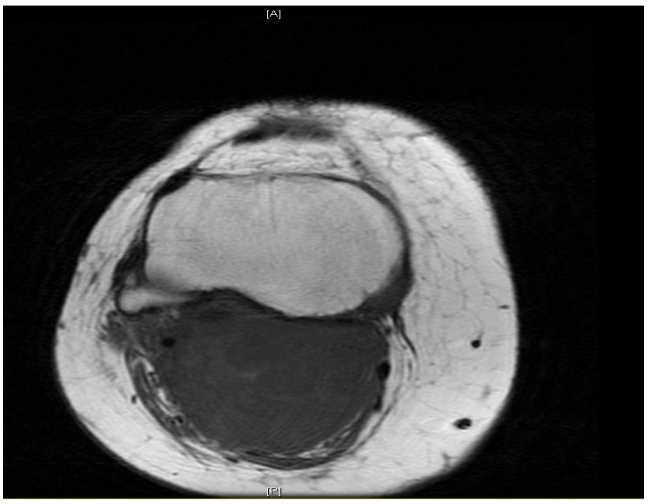

Figure 2: Cross sectional MRI view of the right knee showing the popliteal mass

Test: CT Abdomen, CT pelvis and CT thorax
Justification for test: Staging.
Result: No abnormality seen in the chest. In the abdomen and pelvis, the liver is seen to contain four tiny lesions likely to be simple cysts. Both kidneys are noted to have cortical lumps which probably represent foetal lobulations. The remaining structures are intact. No free fluid or enlarged lymph nodes are observed.

Conclusion: No abnormality in chest but cortical lumps noted in kidney which might need further investigation.

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Atenolol	50mgs	daily	Beta blocker	Hypertension
Bumetanide	1 mgs	BD	Diuretic	Hypertension
Simvastatin	20 mgs	BD	Statin	Hypercholesterolaemia
Enalapril	20 mgs	BD	ACE inhibitor	Hypertension
Glucosamine	1 tablet	BD	Joint care	Arthritis
Amlodipine	10 mgs	daily	Calcium channel blocker	Hypertension
Solpadol	30mgs	TDS	Analgesic	Pain relief
Enoxaparin (SC)		daily	Low molecular weight heparin	Given post-operatively for pain relief
Pethidine (IM)		PRN	Opioid analgesic	Given post-operatively for pain relief

Surgical therapy:

Pre-operative: The tumour in the right popliteal fossa had infiltrated the nerve bundle and thus the limb was unsalvageable. Patient was fit for general anesthetic and prepared the night before. There was discussion with oncologist and radiologist before undergoing surgery and the multidisciplinary team decided that the limb should be operated on because it was invading the neurovascular bundle.

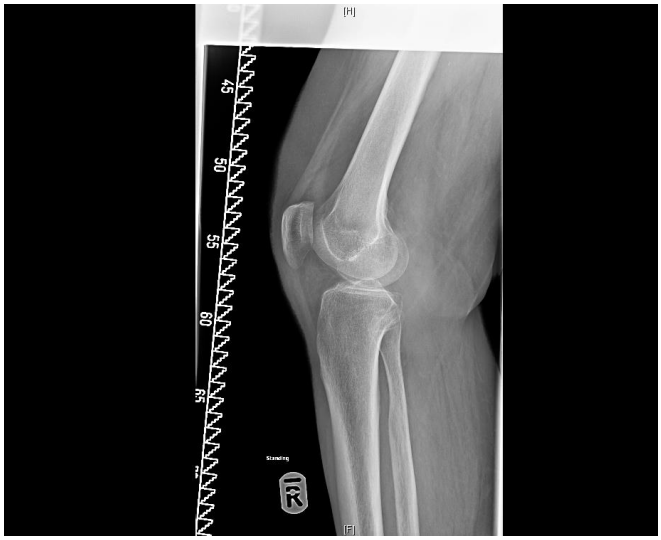

Figure 3: X-ray of right Knee showing a mass in the popliteal fossa

Operation – Above-Knee Amputation: The patient was administered general anesthetic and put in a supine position. Co-amoxiclav was given intravenously and the skin was prepared and draped. Fish-mouth flaps were fashioned. This was followed by sharp dissection down to the bone. The vessels were identified medially and divided between clips and transfixed to the proximal stump with PDS 0. The sciatic nerve was identified and infiltrated with 1% 10 ml of lignocaine. This was done for better analgesia as well as reducing the chances of phantom limb.

Then the periosteum was elevated from the bone and the bone was divided 5cms above the lower border of the stump. The stump was then sanded down to round edges and bone wax was applied to the bone marrow.

After haemostasis was achieved, the bone was covered with muscle using Vicryl 2/0 and the fascia was sutured to the opposite fascia by using Vicryl 0. Finally the skin was stapled and the wound was infiltrated with bupivacaine 0.25% once again for better pain management of the patient.

The leg and fat from the stump were sent to the histology lab for further investigations. The fat from the stump required analysis in order to determine whether the cancer was resected completely or otherwise, as this would change the future treatment regimen.

Post-operative: The patient was watched till awake and was given 1L 8 hourly intravenous infusions of Hartmann's solution. Hartmann's IV Infusion is used to replace body fluid (as it is isotonic to blood) and mineral salts that may be lost for a variety of medical reasons. For the first 6 hours temperature, blood pressure and pulse were taken 2 hourly and then 6 hourly. The patient was allowed to drink and eat when feeling well and was monitored for any bleeding. Also analgesia was continued and clexane was given to prevent deep vein thrombosis.

Diagnosis:

Pleomorphic sarcoma in right popliteal fossa which was compressing her nerve bundle.

Final treatment and follow-ups:

Patient is undergoing physiotherapy and occupational therapy to regain her mobility and independence. Patient looks healthy and strong and it seems that she will recover well.

Cell Pathology report (6/3/13):
Macro: Above-knee amputation measuring 600mm in length. Skin over the knee and popliteal fossa are erythematous. On sectioning there is an ill-defined pale and brown necrotic intravascular mass which measures 440mmx50mmx60mm. This mass appears to be intramuscular and doesn't infiltrate bone.
Micro: Sections show an infiltrative, poorly differentiated sarcoma composed of spindle pleomorphic neoplastic cells which in places show fascicular arrangement. There is prominent focal necrosis. Small residual aggregates of fat cells resembling lipoblasts are also identified suggesting that the tumour is very likely a dedifferentiated liposarcoma with extensive pleomorphic component. It is completely excised. Separate biopsies include fat from stump show no notable abnormalities.

Patient is now being evaluated at Boffa hospital to see if she will require additional treatment such as chemotherapy or radiotherapy, although this seems unlikely since the histology result suggests that the resection was complete and there seems to be no metastasis.

Fact Box 15:

Title: Pleomorphic Sarcoma

Also known as malignant fibrous histiocytoma (MFH), it is one type of sarcoma from about 50 other types of sarcoma. It is a malignant neoplasm of uncertain origin that arises both in soft tissue and bone. No true cell of origin has ever been identified[1]. Most commonly found in thigh.

Types: Pleomorphic sarcoma manifests itself as a broad range of histologic appearances with four sub-types described; Storiform-pleomorphic, Myxoid, Giant cell, Inflammatory [2].

Of these, the storiform-pleomorphic is the most common type, accounting for up to 70% of most cases. The myxoid variant is the second most common accounting for approximately 20% of case.

Risk factors:

- Age (50-70)
- Male

Symptoms:

- Very rare: pain only when a nerve is compressed
- Rarer: weight loss and fatigue
- Signs: a lump might be felt

Treatment:

- Surgery
- Radiation
- Chemotherapy

Prognosis: Prognostic factors that are known to correlate with survival in patients with pleomorphic sarcoma include tumour grade, depth, size, metastatic status, patient's age and histologic subtype [3]. Favourable prognostic factors include age less than 60 years old, tumor size less than 5 cm, superficial location, low grade, the absence of metastatic disease and a myxoid subtype. Older patients with large (> 5cm), deeply seated, high grade tumors do not have as favourable an outcome. For example, patients with a small low grade tumor are likely to be cured completely. Patients with large, deep, high grade tumors (Stage III) have a 5 year survival estimate which ranges from 34 to 70% [4].

Recurrence: Local recurrence (LR), i.e. recurrence of the tumor in the same location, will occur in approximately 20-30% of all patients with soft tissue sarcomas [5]. LR is lowest in extremity sarcomas and highest in retroperitoneal and head and neck sarcomas. This distribution is directly related to the ability to completely resect a tumor at the time of surgery. Higher LR rates are observed in the setting of positive surgical margins, which are more difficult to achieve in anatomic locations outside of the extremity [6]. Whether local control has an impact on overall survival is unclear and remains controversial.

Summary:

MFH is a curable disease.

The term "Malignant Fibrous Histiocytoma" has been changed by the WHO to Undifferentiated Pleomorphic Sarcoma Not Otherwise Specified.

The mainstays of treatment for MFH are complete surgical excision, most often supplemented with adjuvant radiation therapy.

Chemotherapy is reserved for patients with the highest risk of disease recurrence or patients that already have recurrence.

Patients with recurrent MFH can still be cured.

Favorable prognostic factors that correspond to superior survival include small tumor size, low grade, extremity location, superficial location and localised disease.

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Case Number 16
Prader-Willi Syndrome

Lara Maria Zammit & Mikhail Vella Baldacchino
Reviewed by: Dr. J. Torpiano

Case summary:

Demographic details:
Ms. LS, female
Referred from: Children's Out-patients

Ms. LS is a three-year old girl, suffering from Prader-Willi Syndrome, a rare genetic disorder with characteristic, easily recognisable dysmorphic features. She was seen at Children's Out-patients as part of a follow-up regimen, performed every three months. This consultation was held on the 3rd October, 2012 and another one was planned for the 5th of January, 2013.

The clinical picture of developmental signs and symptoms are very characteristic and early diagnosis is beneficial for the anticipation of complications, reduction in unnecessary investigations and improved prognosis.

Presenting complaint:

The main complaint was the insatiable hunger of the child and her unusual food-seeking behaviours, such as binge eating. The mother was aware from beforehand that this might happen. During their discussion, the mother was asking the doctor on how to approach the child and what sort of diet she should provide her with.

History of presenting complaint:

Ms. LS had experienced increased appetite for the past one and a half months. She increased her food portion size and the frequency of meals. Her mother noticed that the child was putting on weight more rapidly than usual and decided to be more stringent with meal times and snacks. A week prior to the consultation, the mother found her daughter eating food from the garbage bag.
On observation and examination, the child weighed 15.1kg and her height was 85.7 cm.

Past antenatal and perinatal history:

Ms. LS was born to a 35-year-old primagravida, blood group O positive mother, at 29 weeks gestation on the 28th of September, 2009. She was delivered via an emergency lower segment caesarean section under general anaesthesia, after a persistent history of intra-uterine growth retardation. The estimated date of delivery was on the 12th of December of the same year. Her birth weight was 870 grams.
The paediatric patient had a cephalic occipito-anterior presentation, the liquor was clear and no abnormalities in the placenta were detected but it was sent for histology.
The baby girl had an Apgar score of 6 in the first minute and on ventilation she improved it to 10, after 5 minutes.

The Apgar Score:

Apgar Score Criteria	After 1 Minute	After 5 Minutes
Heart Rate	2	2
Respiratory effort	1	2
Muscle tone	1	2
Reflex irritability	1	2
Colour of skin	1	2
TOTAL SCORE	6	10

Table 1: The Apgar score during the first minute and first five minutes post-delivery. The child was ventilated between the end of the first minute and the end of the fourth minute

The baby was transferred to the Neonatal and Paediatric Intensive Care Unit for elective intubation with an endotracheal tube and ventilation with surfactant. Neonatal examination showed a patent anus. Thyroid and thallassaemic screens were taken and results were normal.

During her first day, Ms. LS was kept on the ventilator and fluids were pushed in. Urgent blood tests were organised. A complete blood count (CBC), urea and electrolytes (U&E), random blood glucose and arterial blood gases, blood cultures and surveillance swabs and a cross match were taken. These were drawn through an umbilical artery catheter at the level of T7. The young girl was anaemic and was transfused. Her blood group is A positive and she received group O positive blood. Her random blood glucose was 22.6 mmol/L and she was put on an insulin infusion of 0.1mg/hour. Her pH level was 7.3.

A chest X-ray was performed. The lungs had a ground glass appearance and the endotracheal tube and umbilical catheter at the level of T7 were seen.

Soon after, the baby girl, was prescribed and administered cefuroxime (25mg, 12 hourly, intravenously), as prophylactic antibiotics in the light of her vulnerable preterm state and being on the ventilator. B2P (45mg, 12 hourly, intravenously) and Vitamin K (0.3mg, stat, intramuscularly). These two drugs were given as supplements to prevent vitamin deficiency bleeding.

On day 2, the baby had her arterial blood gases rechecked and a decision to extubate her was taken. She was put on nasal continuous positive airway pressure. Naloxone (0.09 mg, one dose, intramuscularly) an opiod inverse agonist, was added to her drug chart.

Up till day 3, the baby girl had never opened her bowels. On examination, the child had depressed fontanelles, her capillary refill time was three seconds and the pubes were palpable. Chest movements were symmetrical with minimal recessions. The abdomen was soft. The plan was to continue on nasal continuous positive airway pressure, keep the intravenous fluids and switch to total parenteral nutrition, have her bloods repeated and maintain the first line antibiotics for 10 days. The child was also given caffeine and exposed to phototherapy for early signs of neonatal jaundice.

On day 4, the child was clinically pink and well perfused. She had no signs of oedema. A decision to restrict her fluid intake was taken in review of a patent ductus arteriosus. The established fluid intake was 120mls/g/day and total parenteral nutrition at 2mls per hour. 20 ml of packed cells were given over 4 hours. Intravenous infusions were stopped. Standard dopamine (1ml/hour) was started and insulin infusion was continued at 0.3ml per hour. In view of her deterioration in blood gases (Ph- 7.18, pO2- 63.6, pCO2- 2.53, HCO3- 17.6.), the patient was intubated via an uncuffed endotracheal tube. Phototherapy was continued.

An atrial septal defect and a patent ductus arteriosus were found.

Past medical and surgical history:

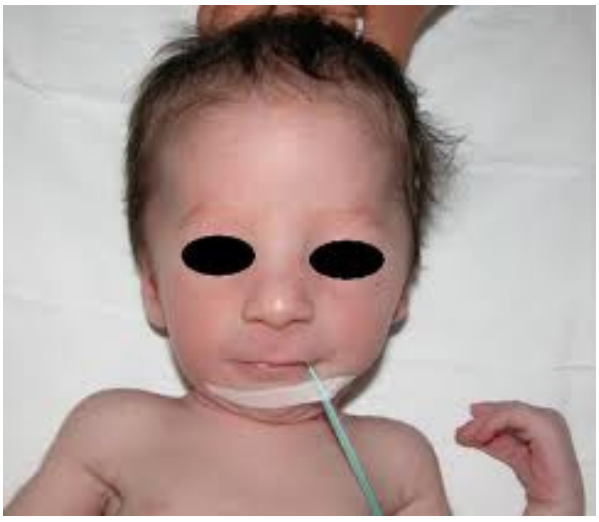
Past medical history:

During the period from 18.11.2009 to 17.12.2009 there was persistent hypotonia complicated by an episode of aspiration pneumonia. The hypotonia was such that there was no:

a) reaction to touching stimuli
b) rooting reflex
c) gaping reflex
d) sucking reflex
e) gagging reflex

The child was provided with a pacifier to stimulate the sucking reflex.

On January 7th, 2010, genetic testing excluded mytonic dystrophy Type 1 and established a karyotype of 46 XX. At the age of 4 months and 22 days, on examination, the child had a box-like face reminiscent of Prader-Willi Syndrome (PWS). The infant had good peripheral/abdominal tone with very good limb reflexes but still decreased central tone. By the age of 7 months, the girl was weaned off on solids and her weight went up to 4 kg. Parents claimed that the child is sleeping for more than usual.



Picture 1: A photograph of a three month old Prader-Willi affected child, already showing some of the characteristic facial features.[4]

Picture 2: A diagrammatic representation of assessing hypotonia in the neonate.[5]

On observation and examination, the child was noticed to spontaneously move all of her four limbs but was still hypotonic. She had not started talking. Ms. LS was noticed to have almond-shaped eyes with thin, down-turned lids, small hands and dolichocephaly in infants with narrow face and bifrontal diameter.

Another genetic consultation was made. Blood was withdrawn and sent for molecular genetic analysis for PWS.

A month later, genetic testing results confirmed Prader-Willi Syndrome. The syndrome was explained to the parents who were offered testing. The diagnosis had raised family dispute between the unmarried couple and eventually separation followed.

A 29-year-old healthy male had a female Prader-Willi affected child from a 35-year-old healthy lady. They were cohabiting together at one point but currently they are not. The daughter is living with her mother, although this is not shown in the pedigree.

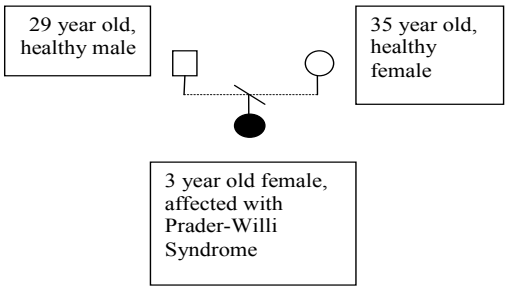
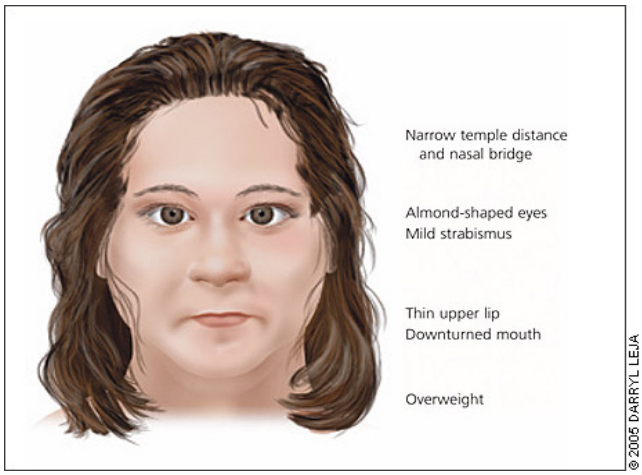


Figure 1: The Pedigree of the family



Picture 3: A diagrammatic representation of a Prader-Willi dysmorphic face[6]

During that visit, the parents reported that the girl had started to babble and make sounds with her mouth. She was passing hard stools with difficulty, on average incidence of once weekly. On observation and examination, there was no shortness of breath. The child was still hypotonic. Heart sounds were recorded as S1 + S2 + 0, with a split S2. The chest was clear.

At the age of 1 year, the head control had improved but was not completely achieved. Truncal support had also improved but she still required support to keep upright. Hence, the child was still unable to sit unaided. The child weighed 6.692kg and her height, measured by a stadiometer, was 69.5cm. An endocrinological referral was made to investigate the child for hormone deficiencies, particularly growth hormone. The doctor opened a discussion with the mother regarding hormonal therapy.

At the age of one year 7 months a detailed assessment of the child was made. Gross motor skills had improved. She was cruising, holding onto furniture, yet she could not walk independently. She was sitting by herself but could not stand. With respect to fine motor skills, the child was transferring objects between hands and developed a good pincer grip. Her speech revolved around mama and papa. She continued to babble and started to understand simple commands. Her social interaction had improved. She was smiling, recognising faces and her play had developed. Her diet consisted of cow`s milk and a balanced mixed diet with some solids. Occasionally, she continued passing hard stools though the frequency had significantly gone down to once every three weeks. On observation and examination, the girl was alert and oriented. She was well perfused with no signs of rashes or oedema. She was sitting by herself and had good head control. The child weighed 8.4kgs and her height measured 73cm. Her head circumference was 43cm. These values were all under the third centile following a steady rate of growth. Her heart sounds were S1+ S2 + 0. Chest was clear. The abdomen was soft and non-tender. No organomegaly was present and femoral pulses were easily palpable, of normal character and rhythm. There was nothing abnormal in the ear, nose and throat. A neurological examination showed that she was grossly intact, slightly hypotonic and moved all four limbs against resistance.

Two months later, at the age of 1 year 9 months the child weighed 9.16kgs and her height was 7.22cm. A hormone profile was taken, particularly for assessment of the level of the growth hormone.

On the 18th of October, 2011, the child was diagnosed with growth hormone insufficiency and was started on treatment. Growth hormone at a dose of 0.3mg per day equivalent to 14.7 units/m^2/week was prescribed.
A month later, on the 24th of November 2011, the mother reported that the child is suffering from nocturnal headaches since the onset of the growth hormone treatment. Hence the dose was decreased to 0.2 mg per day.

During the month of April 2012, at the age of 2 years 7 months, Ms. LS started walking unaided. She had no problems during sleep, such as sleep apnoea and her hormone levels were within their respective normal ranges. In June 2012 her dose of growth hormone was increased, to increase GH, to 0.4mg/day equivalent to 15.6units/m^2/week.

Drug history:

Drug	Dosage	Frequency	Type	Reason
Growth hormone	0.4 mg	daily	Peptide hormone	To support growth in a child with growth hormone insufficiency

Family history:

Mother and father are both healthy. No significant distant family history.

Social history:

Ms. LS was born to an unmarried couple. Since the diagnosis of Prader-Willi syndrome and its association with a paternal defective chromosome, the father left the house to go and live with his friends. Her mother is Maltese. Her father is of African origin. At the time, the daughter was living with her caring mother and they enjoy a very good relationship. Her father was visiting her frequently at her mother`s house, in the presence of the mother.

Systemic enquiry:

- General Health: the child had characteristic dysmorphic features of Prader-Willi Syndrome. She had almond-shaped eyes with thin, down-turned lids, small hands and dolichocephaly with a narrow face and reduced bifrontal diameter, a small mouth with thin upper lip and down-turned corners of mouth. She had a short stature and a weighty appearance.
- Cardiovascular System: heart sounds were S1+S2+0. A physiologically closed patent ductus arteriosus and a stable and silent atrial septal defect.
- Respiratory System: chest was clear. No sleep apnoea.
- Gastrointestinal System: hyperphagia with an insatiable appetite. Once every two weeks, she was finding difficulty in passing hard stools.
- Genitourinary System: nil to note.
- Musculoskeletal System: short stature, small hands and feet for height and age, with tapering of fingers. Her face was long and narrow.
- Central Nervous System: nil to note.
- Endocrine System: growth hormone deficiency was being treated. The child was not on insulin or any other anti-glycaemic agents. The child did not show any sign of pubic hair development.

Current therapy:

Growth hormone at a dose of 0.4 mg daily to treat growth hormone deficiency and support her in her growth. No other drug treatments. The mother ensured that her daughter eats healthy and involved her in physical activity.

Discussion of results of general and specific examinations:

On observation and examination, the three-year-old girl had a syndromic face and general appearance. Her height and weight were constantly under the third centile following a steady increase.
She did not show any signs or precocious puberty such as deposition of pubic hair or breast development. On auscultation her heart sounds were normal (S1+S2+0). Her chest was clear. Her abdomen was soft and non-tender.

Blood investigations showed a euthyroid state (TSH: 2.38 mlU/L), with a normal free T4 level, towards the lower end of the reference range (fT4: 10.6 pmol/L). This result necessitated a repeat of the thyroid function test. A hypothyroid state may predispose toward weight gain. The early morning cortisol level is within reference range (Cortisol: 320 nmol/L) and the insulin-like growth factor is low (IgF-1: 278 mg/mol (SD1- 303). This is needed for growth, height and protein catabolism.

Differential diagnosis:

- Anxiety Disorder: Obsessive-Compulsive Disorder
- Cryptorchidism
- Failure to Thrive
- Fragile X Syndrome
- Growth Hormone Deficiency
- Hypogonadism
- Obesity
- Obesity-Hypoventilation Syndrome and Pulmonary Consequences of Obesity
- Obstructive Sleep Apnoea Syndrome
- Osteoporosis
- Short Stature
- Sleep Apnea[1]

Diagnostic procedure:

Medical examination:

The child had a syndromic face of Prader-Willi Syndrome. She had almond-shaped eyes with thin, down-turned lids, and dolichocephaly with narrow face and bifrontal diameter. She had short stature, small hands and feet for height age, with tapering of the fingers.

Genetic examination:

Genetic studies confirmed Prader-Willi Syndrome. She was diagnosed at the age of 8 months. The clinical features and the genetic study result were consistent with a diagnosis of Prader-Willi Syndrome.

Therapy:

Drug treatment:

Drug	Dosage	Frequency	Type	Reason
Growth hormone	0.4 mg	daily	Peptide hormone	To support growth in a child with growth hormone insufficiency

There is no cure for the insatiable hunger apart from monitoring the child`s diet.

Diagnosis:

The child is suffering from Prader-Willi Syndrome (PWS). PWS is a genetic disorder which gives rise to a collection of signs and symptoms.

The genetics of PWS:

The PWS chromosomal region is found at 15q11-13. The paternal copy of this chromosomal region has to function for normal development; in its absence, a child will develop PWS.

The genetic cause is loss of yet unidentified genes normally contributed by the father[1]. Occurs from three main genetic errors: Approximately 70% of cases have a non-inherited deletion in the paternally contributed chromosome 15; approximately 25% have maternal uniparental disomy (UPD)—two maternal 15s and no paternal chromosome 15; and 2–5 % have an error in the "imprinting" process that renders the paternal contribution non-functional. The prevalence for all sexes and all races varies between, 1:12,000 and 1:15,000[3].

Genetic studies provide the best modality of diagnosing this condition. DNA methylation analysis confirms diagnosis of PWS. FISH and DNA studies can locate the the genetic defect and estimate the risk of recurrence.

The major clinical features:

- Neonatal and infantile central hypotonia, improving with age
- Feeding problems and poor weight gain in infancy
- Excessive or rapid weight gain between 1 and 6 years of age; central obesity in the absence of intervention
- Distinctive facial features—dolichocephaly in infants, narrow face/bifrontal diameter, almond-shaped eyes, small-appearing mouth with thin upper lip and down-turned corners of mouth
- Hypogonadism—genital hypoplasia, including undescended testes and small penis in males; delayed or incomplete gonadal maturation and delayed pubertal signs after age 16, including scant or no menstruations in women
- Global developmental delay before age 6; mild to moderate mental retardation or learning problems in older children
- Hyperphagia/food foraging/obsession with food[3]

The minor clinical features:

- Decreased fetal movement, infantile lethargy, weak cry
- Characteristic behaviour problems—temper tantrums, violent outbursts, obsessive/compulsive behaviour; tendency to be argumentative, oppositional, rigid, manipulative, possessive and stubborn; perseverating, stealing, lying
- Sleep disturbance or sleep apnoea
- Short stature for genetic background by age 15
- Hypo-pigmentation—fair skin and hair compared with family
- Small hands and/or feet for height age
- Narrow hands with straight ulnar border
- Eye abnormalities (esotropia, myopia)
- Thick, viscous saliva with crusting at corners of the mouth
- Speech articulation defects
- Skin picking[3]

Developmental analysis:

Motor skills - Motor milestones in these children are typically delayed. They are born with hypotonia which improves by time. However, other motor skills, such as strength, coordination, balance and motor planning are deficient to different degrees. Occupational therapy and physiotherapy provide these patients with better adaptation to daily living.

Oral motor and speech - Hypotonia may create feeding problems, poor oral-motor skills and delayed speech. A speech and language pathologists can help these children in their communication. Sign language and picture communication are aids that one can make use of, depending on the severity of the case.

Cognition - IQs range from 40 to 105, with an average of 70. Those with normal IQs typically have learning disabilities. Problematic areas may include attention, short-term auditory memory and abstract thinking. Common strengths include long-term memory, reading ability, and receptive language. Early infant stimulation should be encouraged and the need for special education services and supports assessed in preschool and beyond.

Growth - Failure to thrive and short stature are common features in PWS, in spite of their food intake. They tend to have a high BMI and tend to fall under the third centile on the adjusted growth charts. A metabolic component is responsible for this. Growth hormone may be needed since growth hormone deficiency causes short stature, lack of pubertal growth spurt and a high body fat ratio, even in those with normal weight. This may not always be indicated and the drug has its own side effects.

Sexual Development - Sex hormone levels (testosterone and oestrogen) are typically low. Cryptorchidism in male infants may require surgery. Both sexes have good response to treatment for hormone deficiencies, although side-effects have been reported. Early pubic hair is common, but puberty is usually late in onset and incomplete.

Quality of life:

The general health and well-being of an affected individual are not usually compromised if they follow an adequate eating pattern. This constant need for food restriction and the tantrums that these patients might show are often distressing to the families and may be a cause of non-compliance to medical advice. Behavioural and family counselling is often needed.
Their life expectancy can be normal. These patients can lead a normal life and also work under supervision.

Final treatment and follow-ups:

Drug treatment:

Drug	Dosage	Frequency	Type	Reason
Growth hormone	0.4 mg	daily	Peptide hormone	To support growth in a child with growth hormone insufficiency

There is no cure for the insatiable hunger apart from monitoring the child`s diet.

Follow-up:

Blood tests were to be repeated. These include a thyroid function test, including T3 levels, an early morning serum cortisol and the insulin-like growth factor-1 (IgF-1). A sleep study was rebooked.

Fact Box 16:

Title: Prader-Willi Syndrome, (PWS)

Short Description: PWS is a genetically inherited condition.

The PWS chromosomal region is found at 15q11-13. The paternal copy of this chromosomal region has to function for normal development; in its absence, a child will develop PWS.

There are no significant risk factors towards the disease.

Symptoms:

- Narrow temple distance and nasal bridge
- Down-slanting eyes
- Narrow upper lip and down-turned mouth
- Short stature

Signs:

These children tend to:

- Be hypotonic
- Have neonatal feeding difficulty
- Fail to thrive
- Have hypogonadism
- Have developmental delay
- Have learning difficulties

Difficulty in feeding turns into insatiable hunger at the age of around three years. Such a condition cannot be prevented but early diagnosis would allow for better prognosis and anticipation of complications to decrease morbidity and improve the achievement of activities of daily living.

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Patient's Experience: Back to peeing like a man!

Isaac Xuereb

I'm a 20 year old university student diagnosed with Ulcerative Colitis (UC) about two years ago. My father was diagnosed with UC six years before me but was in remission. When I started seeing blood in my stools and experiencing the typical UC symptoms, I immediately knew what was wrong.

My Story:

My colitis experience started with seeing blood in my stools. In a few days, this led to increasing trips to the toilet, diarrhoea and so on. When I saw the blood for the first time, I started to get worried since I had a strong feeling that I had the same disease as my father. I confirmed this when we started comparing the symptoms that I had and we immediately came to the conclusion that I had UC. Before visiting my consultant for the first time, I knew that probably I had to do a colonoscopy. However I was ordered to do a flexible sigmoidoscopy, which was better since I did not have to do any specific preparation beforehand and I was not sedated during the procedure. In addition, I knew what was happening and could see the inflammation, making it easier for me to understand what was wrong with my colon.

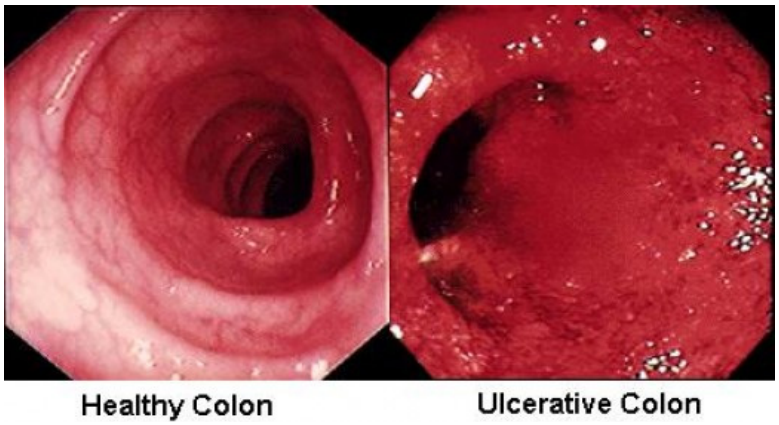

Figure 1: Images taken during colonoscopy showing the differences in appearance between a healthy colon and a colon in a patient suffering from ulcerative colitis.

Upon being diagnosed, I was put on Mesalazine tablets and enemas. I was already told beforehand that I might have to take a large number of medications, but now this had been confirmed. I had to accept the fact that my life would be totally transformed! My father knew exactly what I was going through and he hoped that the medication would work on me as fast as it did on him. However, the Mesalazine only helped to reduce the trips to the toilet (to around 10-15 trips daily from 25+) but the blood and loose stools persisted!

After around two months with little improvement, Mesalazine tablets where out of stock due to a shipping error and with only the enemas, my condition regressed to as it was before I had started the treatment - living more in the bathroom than anywhere else. My GI consultant put me on Prednisolone (starting at 30mg and then tapering off slowly) in order to help my colitis. When the Mesalazine tablets where back in stock and I started taking them again, my symptoms where reduced greatly and I even started to do some sports again. I managed to take part in the Malta Half Marathon for the first time, which was a great achievement since all my family took part.

Fast forward a few weeks, I started feeling very weak and sleepy and my UC symptoms returned, but were not as severe as before I was diagnosed. Whenever I climbed a flight of steps or ran a few metres, I used to get shortness of breath and would have to stop for a few minutes to regain my energy. I informed

my doctor about this and from the blood tests it resulted that I had a very low haemoglobin level (around 7 – when it should be between 13.8 and 17.2) so I had to spend the night in hospital for a blood transfusion. After this I was put on Prednisolone for the second time, starting with 40mg daily. I finally had my energy levels restored and could catch up on studying for my university exams. Thanks to the side effects of steroids (namely insomnia and very big appetite), I only slept around 2 hours every night throughout the 3 week exam period - so I had enough time to study and get good grades!

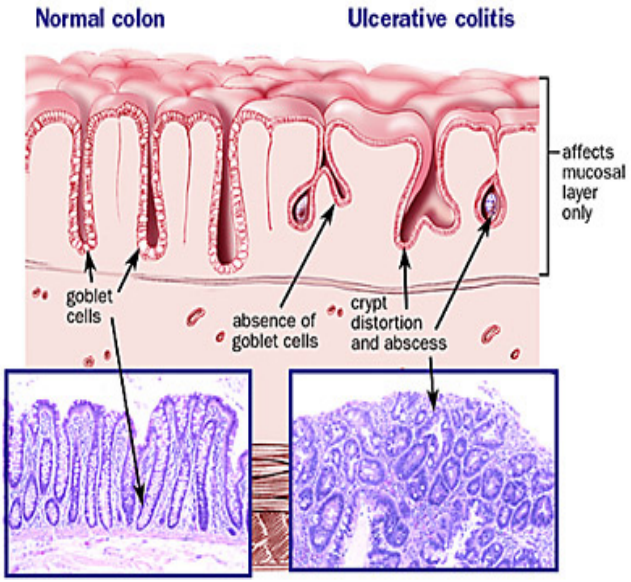

Figure 2: Diagram showing the histological differences between a normal colon and an ulcerative colitis colon.

Since I could not be on Prednisolone all my life, my doctor also put me on Azathioprine in order to stay in remission once the steroids were stopped. After around 2/3 months I was in remission and after a year and half after my symptoms first presented, I regained the ability of going to a toilet just to pee! This was the best feeling ever - I think all the male UC patients will agree!

Research:

Throughout my UC experience, I have done a lot of research about Ulcerative Colitis and the medications I was taking. This is mainly due to the fact that I knew that I had to live with them for the rest of my life! I had to figure out how to shape my lifestyle around this disease, especially with the side effects of my medications. Upon reading a number of articles and real-life stories of other patients, I had a more positive view on things since I knew that a lot of other people where going through the same situation or even worse! My father went into remission after a few weeks of starting the treatment, but now I could relate to other people that spent a large number of years trying different medications with no improvement. I considered myself lucky that I saw some improvement and that I knew that the medications where working on me.

One of the things that I discovered was that Mesalazine enemas have a side effect of the patient having a more loose stool and that the coating on the Mesalazine tablets did not dissolve to release the drug in the right place if there are loose stools in the system. I thought this was a contradiction, so I stopped taking the enemas for a few days. Since I saw an improvement, I told my doctor and he agreed that my reasoning made sense and that I should stop the enemas since the tablets and Azathioprine where doing the job.

When researching about Azathioprine I was a bit shocked when I learnt what exactly it is they do exactly and their side effects. My consultant assured me that he was monitoring everything through the blood tests and that the benefits from the steroids where outnumbering the risk of the side effects of steroids!

To monitor my symptoms, I found an application for my smartphone on which I could list the details of my stools (amount of blood, consistency etc). A graph would then be drawn-up automatically to make the data easier to analyse. This helped my doctors to monitor my situation more accurately and consequently they could give me more personalised help.

Regarding the diet, I researched a lot but nothing was clear as to what exactly works and what doesn't and my doctors always said that diet does not have an effect. Due to university and going out etc, it's tough to follow a strict diet. However I always noticed (especially during a flare-up) that whenever I eat something that is not really healthy such as burgers or other junk food, my symptoms always seem to slow down. This also happens when I take alcohol, milk and other dairy products which a lot of UC patients seem to avoid. I have now even adopted the habit of drinking a glass of milk whenever I see some blood in the toilet! I am now compiling a list of the foods that have caused me to flare up in order to determine my trigger foods. This is not really scientific but I learnt that I have to try out new ways in order to learn what my body is capable of and how to treat my colitis! Patients have to find what is good or bad for them!

Conclusion:

Even though I did a lot of research and had very helpful doctors, I'm very grateful that I had the support of my whole family and that of my friends. All of this helped me keep a positive outlook on things so that I could beat my disease and not let it destroy my life!

Fact Box: Patient's Experience

Isaac Bertuello

Title: Ulcerative Colitis

Ulcerative colitis is a type of inflammatory bowel disease (IBD) that affects the lining of the large intestine (colon) and rectum. The cause of ulcerative colitis is unknown and stress and certain foods can trigger symptoms (but not cause the disease). It may affect any age group, although there are peaks at ages 15 - 30 and then again at ages 50 - 70.

Risk factors:

- Family History

Symptoms and Signs:

- Abdominal pain and cramping
- Abdominal sounds (a gurgling or splashing sound heard over the intestine)
- Blood and pus in the stools
- Diarrhoea, from only a few episodes to very often
- Fever
- Tenesmus (rectal pain)
- Weight loss

Investigation to confirm diagnosis:

- Colonoscopy and biopsy
- Barium enema
- Complete blood count (CBC)
- C-reactive protein (CRP)
- Sedimentation rate (ESR)

Prevention:

Because the cause is unknown, prevention is also unknown. Non-steroidal anti-inflammatory drugs (NSAIDs) may make symptoms worse. Due to the risk of colon cancer associated with ulcerative colitis, screening with colonoscopy is recommended.