MINIMA MEDICAMENTA - 2014 EDITION

Minima Medicamenta

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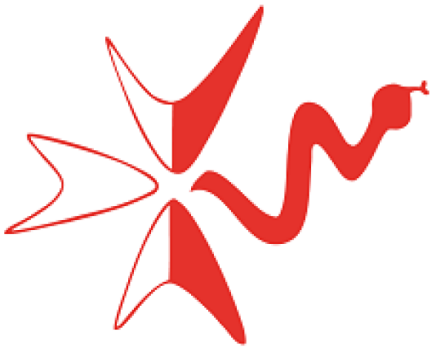

MMSA

Malta Medical Students' Association

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

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Message from the Dean of Medicine and Surgery

Minima Medicamenta, the Malta Medical Students' Association (MMSA) compilation of unusual clinical cases, is now in its third year of publication.

This commendable task, undertaken by our medical students through their association, has the recognition of the International Federation of Medical Students' Associations.

For the third year running, our students have put together unusual clinical cases they have come across their ward rounds. This exercise, in turn, benefits all the contributors as it extends their clinical knowledge and enhances their skills at presenting the case studies from a wide-ranging medical area.

Apart from congratulating MMSA and the contributing students for once again taking on this initiative, I must also extend a thank you to the colleagues who are annually supporting this publication.

Professor G. LaFerla
Dean, Faculty of Medicine and Surgery

Message from the President of the Malta Medical Students' Association

Dear MMSA members and friends,

Minima Medicamenta, now in its 3rd Edition, is probably one of the most relevant projects to medical students, giving each one of us a unique opportunity. Often during clinical attachments we encounter patients suffering from rare conditions which are interesting to medical society. It is Minima Medicamenta that then gives a chance to all MMSA members to publish these cases within a student-run publication. Being a project very close to my heart, since it was begun as one of my own initiatives as the Medical Education Officer three years ago, I am even more satisfied to see how far it has progressed.

This project is a tangible sign of how our association works tirelessly to contribute to a holistic educative experience for all our members. Such projects targeted directly at the medical student encompass the very essence of why our association was created over 60 years ago … to represent the students and give them opportunities which would enhance their experience in the medical field.

I would therefore like to commend this project, offer my sincerest thanks to all its contributors and wholeheartedly recommend that the great work done so far is continued by our successors. I hope that you will work to continuously broaden the opportunities our association offers in order to improve the medical education offered to all students studying medicine at the University of Malta. With that I encourage you all to make the most of all opportunities that come your way in order to broaden your medical experience as well as that of fellow colleagues.

I sincerely hope that you all enjoy this edition of Minima Medicamenta.

Robert Cachia.

Robert Cachia
MMSA President 2013-2014
Malta Medical Students' Association

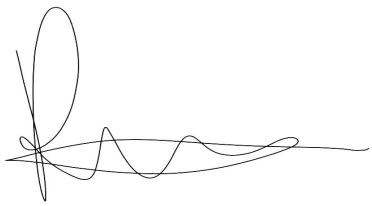
Message from the Malta Medical Students' Association Medical Education Officer

The Standing Committee on Medical Education (SCOME) within the MMSA aims at offering students the opportunity to participate and continue exploring different areas of their medical education. By encouraging students to actively contribute to their own learning process and broadening their interests, by means of various seminars, workshops and publications, SCOME aims to make their education as well rounded as possible.

Minima Medicamenta is SCOME's main publication, which came about by the hard work and efforts of everyone involved in the publication. Not only is this project useful to readers of these cases, it has also allowed numerous students to take a more active interest in certain clinical rotations and cases, and given them an opportunity to try their hand at writing and publication, with impressive results.

My appreciation and admiration goes towards the coordinators, as well as everyone involved in the Minima Medicamenta team, who were extremely dedicated and motivated towards this publication, which is evident from the end result. With this being the third edition of Minima Medicamenta, I would especially like to thank the coordinators of this project, Isaac Bertuello and Maria Grazia Grech, for their constant efforts in continuing upon the great work already done.

I hope readers fully enjoy and benefit from this publication!



Rebecca Stoner
MMSA Medical Education Officer 2013-14
Malta Medical Students' Association

Message from the Editors

Minima Medicamenta is now its third year of publication after last year's success following dramatic changes to the format. This year we focused on quality rather than quantity of cases however they still cover a wide variety of rare, unusual and interesting diseases in various specialties including surgery, cardiology, oncology and neurology.

As in previous editions, the aim of this publication is two fold. It is a journal which provides a medium through which students can be published which in turn will help them become more proficient at scientific writing. We also aim to be a source of information for medical students regarding how different illnesses present and the management of the patients.

We would like to extend our appreciation to all those who helped make this publication possible. Firstly we would like to thank Robert Cachia, the President of the Malta Medical Students' Association (MMSA) and Rebecca Stoner, the Medical Education Officer. We would also like to thank the MMSA PRO team, the proofreader Stephanie Vella, and Valentina Fenech for obtaining sponsorships and funding for this publication. Last but not least, we would like to thank all the students who participated and wrote the cases and the doctors who supported them throughout.

We hope you find this publication instructive and useful.

Isaac Bertuello
Minima Medicamenta Editor 2014
Malta Medical Students' Association

Maria Grazia Grech
Minima Medicamenta Editor 2014
Malta Medical Students' Association

Case Number 1
Familial Adenomatous Polyposis

John Xuereb and Yana Marie Dimech
Reviewed by: Mr. Dennis T. Gatt L.R.C.P.(Lond.), F.R.C.S.(Eng.), F.R.C.S.(Edin.)

Case summary:

Demographic details:
Ms. OC, female, 17 years.
Referred from: home due to strong family history.

OC, a 17-year-old female, was referred due to a strong family history of Familial Adenomatous Polyposis. Multiple relatives (mother, two uncles, several cousins and others) have had Familial Adenomatous Polyposis and had undergone proctocolectomy to prevent the benign polyps from undergoing malignant transformation. The patient presented with no signs and symptoms. On colonoscopy, multiple polyps were found at 10 cm, 15 cm, 40 cm, 80 cm, 110 cm and even in the caecum. The patient subsequently underwent elective Restorative Proctocolectomy with an Ileal Pouch Reservoir. No defunctioning ileostomy was created but the patient was instead managed on TPN (Total Parenteral Nutrition) post-operatively for 2 weeks until a gastrografin small bowel study confirmed the integrity of the pouch and the anastomosis. The patient will be followed up by means of yearly pouchoscopy to exclude the possibility of malignant change at the Transitional Zone between the anal canal and the pouch.

Presenting complaint:

The patient was admitted for elective restorative proctocolectomy with an ileal pouch, after being diagnosed with Familial Adenomatous Polyposis on colonoscopy.

History of presenting complaint:

The patient has a strong family history of Familial Adenomatous Polyposis. She presented with no signs and symptoms. She complains of no bleeding per rectum, no nausea, no abdominal pain, no pyrexia and no change in bowel habits. Despite the presence of so many polyps in her colon she passed stools regularly with no changes in frequency, colour and consistency.

Past medical and surgical history:

Past medical history:

- Sinusitis
- Allergic Rhinitis

Past surgical history:

- Tonsillectomy and Adenoidectomy (16/02/2001)

Drug history:

Nil to note. No known drug allergies.

Family history:

OC has a strong family history of Familial Adenomatous Polyposis. Multiple relatives; including her mother, two uncles, several cousins and other distant relatives have had Familial Adenomatous Polyposis and were operated upon, on confirmation of the diagnosis.

Social history:

Patient still lives with her parents. She has stopped attending school after her O-levels and is currently working at Methode Electronics Malta Ltd.

The patient is a social drinker and does not smoke or make use of recreational drugs.

Systemic inquiry:

- General Health: Good and active. Patient looked comfortable after operation
- Cardiovascular System: Nil to note
- Respiratory System: Allergic Rhinitis and Sinusitis
- Gastrointestinal Tract: Nil to note
- Genitourinary System: Nil to note
- Central Nervous System: Headaches associated with sinusitis
- Musculoskeletal System: Nil to note
- Endocrine System: Nil to note

Discussion of results of general and specific examination:

General examination of the patient was unremarkable. The patient appeared healthy, with no physical signs and symptoms of Familial Adenomatous Polyposis. The patient was not pale, jaundiced or cyanosed. There were no evident signs of recent weight loss and the patient denied recent rapid weight loss. She was afebrile.

Cardiovascular, respiratory and abdominal examinations were also unremarkable. These revealed normal heart sounds S1+S2+0, with equal air entry in both lungs and normal vesicular breath sounds. On the abdomen no swelling or scars were observed. The abdominal examination did not reveal any masses or organomegaly. There was no guarding or rebound tenderness. Normal bowel sounds were auscultated and stools were normal.

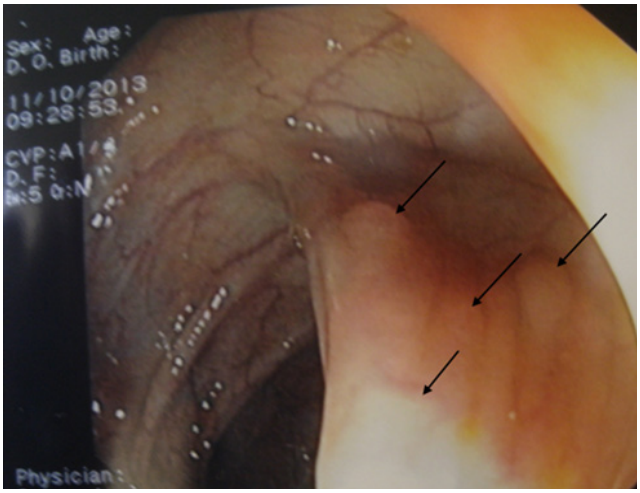
Differential diagnosis:

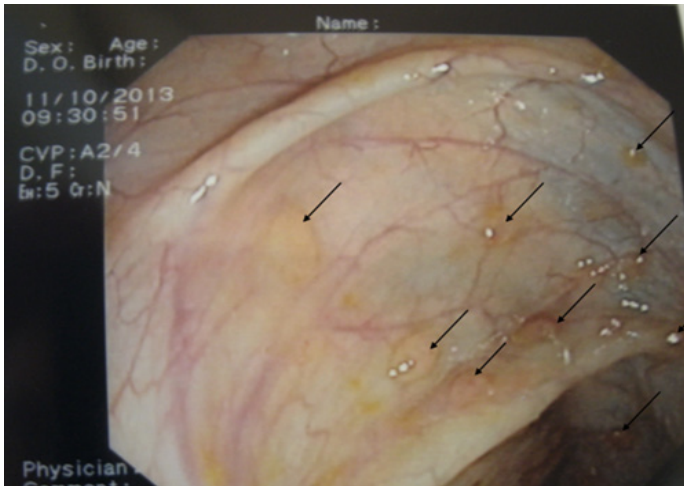
- MUTYH associated polyposis (MAP)
- Juvenile polyposis
- Peutz-Jeghers Syndrome
- Mixed Adenomatous hyperplastic Polyposis
- Hyperplastic Polyposis syndrome
- Colonic lymphoid hyperplasia

Diagnostic procedures:

Instrumental exams:

Test: Colonoscopy .
Justification for test: Strong family history of Familial Adenomatous Polyposis.
Results: Multiple polyps at 10 cm, 15 cm, 40 cm, 80 cm, 110 cm and the caecum. More than 30 polyps were present at 80 cm.
Conclusion: Morphology suggestive of Familial Adenomatous Polyposis.





Figures 1 and 2: Colonoscopy showing multiple polyps.

Laboratory exams:

Test: Biopsy for histology from colonoscopy.
Justification for test: Multiple polyps on colonoscopy.
Results: Biopsies from colon at 100 cm show portion of normal colonic mucosa with a single small area of crypt epithelial hyperplasia resembling edge of hyperplastic polyp.
Biopsies from colon at 90 cm, 40 cm, 15 cm and 10 cm all show portions of colonic mucosa with areas of mild crypt epithelial dysplasia, resembling low grade tubular adenoma. There is no evidence of severe dysplasia or other abnormal feature of note.
Conclusion: The colon at 100 cm shows hyperplastic polyp while the colon at 90 cm, 40 cm, 15 cm and 10 cm shows low grade tubular adenoma.

Test: Proctocolectomy bowel specimen sections for histology.
Justification of test: To confirm diagnosis and exclude high grade dysplasia or invasive adenocarcinoma after restorative proctocolectomy with ileal pouch-anal anastomosis.
Results: Sections from proctocolectomy specimen showed multiple small tubular adenomas with low grade dysplasia. Numerous prominent lymphoid follicles were also present. There was no evidence of high grade dysplasia or invasive adenocarcinoma. Sections from small bowel were unremarkable. Both surgical margins were unremarkable. All of the twenty retrieved lymph nodes show sinus histiocytosis and reactive follicular hyperplasia.
Conclusion: Multiple tubular adenomas with low grade dysplasia, typical of Familial Adenomatous Polyposis and reactive lymph nodes, typical of inflammatory and immune reactions, were diagnosed.

Therapy:

Surgical therapy:

Pre-operative: The patient was admitted to the surgical wards from admission lounge a day before the surgery. The patient was started on Klean prep, for bowel cleansing. Four sachets were taken in total, one sachet with one litre of water every two hours. The patient was allowed fluids for that day but then nil by mouth from midnight. TED stockings were applied. An ECG and cross-match were carried out. Stool charting was started. Informed consent was obtained.

Operation: Restorative proctocolectomy with ileal pouch-anal anastomosis.
Total mobilisation of the colon including; the caecum, ascending colon, transverse colon, splenic flexure, descending colon, sigmoid colon and the rectum was performed. The dissection at the pelvic brim was carried out, very close to the colon to preserve the Nervi Erigentes. The rectum was dissected by a combination of blunt and sharp dissection, all the way down to the pelvic floor and transected with a Contour Stapler. The terminal ileum was also divided at this stage, with a GIA stapler. A 35 cm Ileal Pouch Reservoir was created from the terminal ileum in a J shape using 3 firings of the GIA stapler. The lower end of the J was then anastomosed to the anal canal using a CEA 28 stapler and the doughnuts were inspected to make sure they were not broken. The abdomen was closed with drainage to the pelvis and no defunctioning ileostomy was used.

A central venous catheter was also inserted during the operation for Total Parenteral Nutrition (TPN). The right jugular vein was used.

Post-operative: A naso-gastric tube was inserted. Total Parenteral Nutrition was started three days after surgery; when serum potassium, calcium, magnesium and phosphates were all in normal ranges. The abdominal drainage was minimal on the fourth day following surgery. The patient was also passing flatus and greenish liquid stools on the fourth day following surgery.

The post-operative medications were as follows:

Drug Name (Generic)	Dosage	Route	Frequency	Reason
Paracetamol	1 g	IV/PO/PR	4-6 hrly / PRN	Pain relief
Ciprofloxacin	200 mg	IV	BD	Broad spectrum antibiotic (prophylaxis)
Metronidazole (Flagyl)	500 mg	IV	TDS	Prophylaxis against anaerobic organisms and protozoa
Diclofenac (Voltaren)	500 mg	PO	PRN	Pain relief
Magnesium sulphate 50%	2 mls in 100 mls normal saline	IV	BD	Acts as a supplementary analgesic therapy to suppress the acute post-operative pain
Clexane	4000 units	SC	QD	Prophylaxis for deep vein thrombosis and pulmonary embolism
Prochlorperazine (Stemetil)	12.5 mg	IM	PRN	To control nausea and vomiting post-operatively
Pethidine	50 mg	IM	PRN	Pain relief

Diagnosis:

Familial Adenomatous Polyposis was diagnosed by means of colonoscopy and histological examination of the biopsies taken from the various polyps found. The colonoscopy was indicated because of the strong family history. The diagnosis was then confirmed after restorative proctocolectomy by more detailed histological evaluation of the entire colonic specimen. In this case, high grade dysplasia and invasive adenocarcinoma were also excluded.

Familial Adenomatous Polyposis (FAP) is classically characterised by the development of numerous polyps (polyposis) in the colon and rectum at atypical early ages, usually during the second decade of life[1-2]. This condition carries a 100% lifetime risk of malignant transformation of adenomas into colorectal carcinoma[3]. FAP is inherited as an autosomal dominant disease caused by the germ-line mutation of the APC (Adenomatous Polyposis Coli) gene[4].

FAP is typically asymptomatic, especially in children and adolescents, until the polyps are large and numerous sufficiently to start causing rectal bleeding, constipation, diarrhoea, change in bowel habits or abdominal pains. Some patients also evolve palpable abdominal masses and weight loss. Many patients remain asymptomatic until they develop colorectal carcinoma (CRC)[2].

On colonoscopy, classic FAP presents with hundreds and thousands of colorectal adenomatous polyps. These typically start to develop in early childhood, predominately at the rectosigmoid and later on, in adolescence, these are typically established throughout the colon[2]. It is shown that at 15 years of age 50% of the patients have established adenomas while at 35 years of age up to 95% have developed adenomas[5]. Though colorectal carcinoma in the majority of cases develops by the age 40-50 years it can still develop in children[2].

FAP patients also commonly present with extra-colonic gastrointestinal features. These include fundic gland polyps in the stomach, adenomatous polyps in the duodenum and periampullary region and small bowel adenoma[2]. Fundic gland polyps have the potential to progress to carcinoma but rarely do so[6]. About 5% of adenomatous polyps in the duodenum and periampullary region progress to malignancy in a 10-year period[7]. Small bowel polyps also carry a risk for malignant transformation though this is lower than the risk in duodenal and ampullary neoplasm[2].

FAP may also present with any of its extraintestinal manifestations. These include congenital hypertrophy of the retinal pigment epithelium, dental abnormalities (including supenumerary teeth, congenital absence of one or more teeth and unerupted teeth), osteomas, desmoid tumours and extracolonic cancers (including thyroid, liver, bile ducts and central nervous system tumours). Gardner's syndrome is a clinical variant of FAP where the extra-colonic features are prominent[2].

A milder form of FAP can present, Attenuated FAP, is a less aggressive variant where one develops fewer adenomas and the adenomas and colorectal carcinoma both develop at a later age[2].

Nearly every patient with FAP will develop colorectal carcinoma if they are undiagnosed or untreated. However, at present it is very atypical to find patients presenting with symptoms of the colorectal carcinoma since most of the patients today are diagnosed and treated surgically before there is malignant transformation[2].

A high clinical index of suspicion is needed as patients are usually asymptomatic but may present with a strong family history. Questions such as; whether anyone in the family ever had cancer, what type of cancer and at what age it presented are vital in this case. One may also identify extra-colonic manifestations of FAP, on which grounds a physician should perform a flexible sigmoidoscopy or a colonoscopy. Genetic testing is also of use in FAP. Its main role is in screening and in the early asymptomatic stages of the

disease in patients with a strong family history. Numerous types of genetic tests are currently available to investigate for APC germline mutations. Direct sequencing of the APC gene is the preferred and most commonly used method at present[2].

The aim of management in FAP patients is tumour prevention while maintaining a good quality of life. This is usually obtained, after their genetic diagnosis and endoscopic procedures, by prophylactic colorectal surgery. Since colorectal carcinoma is rare in asymptomatic children and adolescents, these should be followed up and then at around 16 -18 years of age an elective procedure is planned[8]. Multiple surgical options are available. These include; subtotal colectomy with ileorectal anastomosis (IRA), total proctocolectomy with ileostomy and proctocolectomy with or without mucosectomy and ileal pouch anal anastomosis (IPAA).The latter procedure is preferred for classical FAP, especially if numerous rectal adenomas are present [9,10].

Post-operatively it is crucial to follow-up these patients. Initially, one should deal with the physical and psychological adjustments to surgery and identifying desmoid tumour formation which is associated with FAP[2]. In IRA, due to the risk of rectal adenomas and carcinomas, life-long rectal endoscopic investigations should be carried out annually. Also, studies have shown that after restorative proctocolectomy, adenomas and even adenocarcinomas can evolve in the ileo-anal pouch and the transitional anal zone. Therefore it is vital to undertake endoscopic surveillance of both the pouch[11] and the transitional anal zone[12].

Final treatment and follow ups:

The patient was kept nil by mouth until a small bowel gastrografin enema was carried out and this confirmed that the pouch and the anastomosis were intact. At this stage she was started on a light diet and the total parenteral nutrition was stopped 17 days post-operatively.
The patient will be followed up by means of yearly pouchoscopy, to exclude the possibility of malignant change at the Transitional Zone between the anal canal and the pouch.

Fact Box 1

Title: Familial Adenomatous Polyposis

Familial Adenomatous Polyposis (FAP) is an inherited autosomal dominant disease[4]. It classically characterised by the development of numerous polyps (polyposis) in the colon and rectum at atypical early ages, usually during the second decade of life[1-2]. FAP is caused by the germ-line mutation of the APC (Adenomatous Polyposis Coli) gene[4]. This condition carries a 100% lifetime risk of malignant transformation of adenomas into colorectal carcinoma[3].

Signs and symptoms: FAP is typically asymptomatic until patients develop colorectal carcinoma (CRC). In some cases, especially after adolescence, when polyps are large and numerous sufficiently, symptoms and sings can be elicited. These include:

- Rectal bleeding
- Constipation
- Diarrhoea
- Change in bowel habits
- Abdominal pains
- Palpable abdominal masses
- Weight loss

Risk factors: Family history

Investigations to confirm diagnosis:[2]

- Flexible sigmoidoscopy or colonoscopy
- Biopsy for histology
- Genetic testing

Prevention of Colorectal carcinoma:[9,10]

- Subtotal colectomy with ileorectal anastomosis (IRA)
- Total proctocolectomy with ileostomy
- Proctocolectomy with or without mucosectomy and ileal pouch anal anastomosis (IPAA)

The latter procedure is preferred for classical FAP, especially if numerous rectal adenomas are present.

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Case Number 2
Infective Endocarditis in a patient with Tetralogy of Fallot

Gabriella Grech
Reviewed by: Dr. Herbert Felice

Case summary:

Demographic details:
Patient: FG, Male.
Resident in Fgura.
Age: 29 years.
Referred by: Presented at Accident and Emergency.

Mr. FG is a 29-year-old man from Fgura. He is a known case of Tetralogy of Fallot and mitral valve replacement (double-disc prosthetic valve), and presented at Accident and Emergency with a headache and fever. Following history, examination and investigations it was found that the patient was suffering from Subacute Bacterial Endocarditis. He was given antibiotics to treat the infection and due to his high risk of recurrence he continued the antibiotics.

Presenting complaint:

Headache
Fever of 103 degrees
Palpitations
Nausea

These symptoms were of recent onset.

History of presenting complaint:

Three previous episodes of infective endocarditis, the last one being 2 years ago.

Past medical and surgical history:

Past medical history:

- Mild asthma
- Obstructive sleep apnoea

Past surgical history:

- Blalock-Taussig shunt at the age of 9 months
- Mitral valve replacement with a mechanical prosthesis at the age of 7
- Replacement of the prosthetic valve with double-disc prosthesis at the age of 12
- Angiogram – 4 months ago

Drug history:

Drug	Dosage	Frequency	Type	Reason
Amiodarone	200mg	Daily	Anti-arrhythmic	To decrease the risk of developing atrial fibrillation due to multiple heart surgeries.
Warfarin	According to INR	Daily	Anti-coagulant	Due to risk of emboli developing on the mechanical mitral valve.
Fluticasone	100 micrograms	Prn	Inhaled glucocorticoid	Due to mild asthma.

Family history:

The patient has a history of cyanotic heart disease in his family with his uncle suffering from the same condition. His father died of lung cancer at the age of 52.

Social history:

He used to work as a minibus driver but had to stop 4 months ago due to complications of an angiogram. He is a non-smoker and binge drinks heavily - 1 bottle of vodka every weekend. He is active and exercises regularly by playing football and walking.

Systemic inquiry:

- General Health: Looks well in general
- Cardiovascular System: Recent palpitations
- Respiratory System: Some shortness of breath during extreme exercise and sleep apnoea
- Gastrointestinal System: Few vomiting episodes, dysphagia
- Genitourinary System: Nil to note
- Central Nervous System: Sudden headache and fever
- Musculoskeletal System: Nil to note
- Endocrine System: Nil to note

Discussion of results of general and specific examinations:

On examination, the patient had symmetrically warm hands and a pulse of around 60 beats per minute. The JVP was not elevated. There was no sign of anaemia and there was no sign of central cyanosis on examination of the mouth.

On palpation of the precordium a thrill was felt on the left sternal edge.

On auscultation, a pan-systolic murmur (best heard at the apex), high-pitched decrescendo early diastolic murmur (best heard at the upper sternal border) and mid-diastolic murmur (heard best at the apex) were auscultated and the prosthetic click of the valve was heard. Auscultation of the lung bases was normal and there was no sign of sacral oedema.

Differential diagnosis:

- Subacute bacterial endocarditis
- Systemic lupus erythematosus
- Atrial myxoma and other cardiac neoplasms
- Lyme disease
- Antiphospholipid syndrome
- Polymyalgia rheumatica
- Reactive arthritis[1]

Diagnostic procedures:

Laboratory exams:

Test: Complete blood count.
Justification for test: To check for sign of infection or anaemia.
Result: Elevated white cell count with an increase in neutrophils.
Conclusion: This supports the idea of subacute bacterial endocarditis.

Test: Urea and Electrolytes.
Justification for test: To assess state of hydration, renal function and electrolyte imbalances.
Result: Normal.
Conclusion: This excludes any renal disease.

Test: Liver Function Tests.
Justification for test: To assess liver function.
Result: Normal.
Conclusion: This excludes any liver disease.

Test: C-Reactive Protein.
Justification for test: Acute phase reactant.
Result: Elevated.
Conclusion: This is an indication of an invasive bacterial condition.

Test: Blood culture.
Justification for test: To detect the presence of actively multiplying bacteria or fungi in the bloodstream, to identify the microorganism present and to guide antimicrobial treatment.
Result: Positive for *Streptococcus mitis.*
Conclusion: This further supports the diagnosis of infective endocarditis.

Instrumental exams:

Test: Electrocardiogram.
Justification for test: To detect any conduction defects.
Result: Right bundle branch block.
Conclusion: This could be a normal variant or due to history of heart defects.

Test: Trans-thoracic Examination.
Justification for test: To check for vegetations or infected tissue.
Result: There is moderate right ventricular outflow tract stenosis with moderate pulmonary regurgitation. There is severe right ventricular dilatation with mildly impaired systolic function. The left ventricle is of

normal size and good systolic function. There is evidence of significant mitral prosthetic stenosis with an estimated valve area of 1.96 cm^2. There is patient-prosthesis mismatch, however the left atrium is of normal size. The right ventricle is severely dilated with mild right ventricular hypertrophy. There is a left hand sided aortic arch.
Conclusion: The mitral stenosis explains the diastolic murmur, best heard on auscultation at the apex with the patient in the left lateral position. Pulmonary regurgitation explains the high-pitched decrescendo diastolic murmur secondary to pulmonary regurgitation at the upper sternal border and the pansystolic murmur of tricuspid regurgitation was audible in the 4^{th} left intercostal space in the patient as a result of right ventricular dilatation.

Test: Trans-oesophageal Echocardiogram.
Justification for test: To assess for the presence of vegetations or infected tissue.
Result: No vegetations were detected on aortic, tricuspid or mitral valves. The pulmonary valve was not well seen. A shelf-like structure was observed in the left ventricular outflow tract.
Conclusion: This did not confirm the diagnosis of infective endocarditis.

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Benzyl penicillin	1.2g	Every 4hrs	Antibiotics	Due to streptococcal infection
Gentamycin	1mg/kg	Every 8hrs	Antibiotics	Due to streptococcal infection

Diagnosis:

Infective endocarditis (IE) is defined as an infection of the endocardial surface of the heart, which may include one or more heart valves, the mural endocardium or a septal defect. Its intracardiac effects include severe valvular insufficiency, which may lead to intractable congestive heart failure and myocardial abscesses. If left untreated, IE is always fatal.

The Duke diagnostic criteria are generally used to make a definitive diagnosis of infective endocarditis. The criteria combine the clinical, microbiologic, pathologic, and echocardiographic characteristics of a specific case[2]:
Major blood culture criteria for IE include:

- two blood cultures positive for organisms typically found in patients with infective endocarditis,
- blood cultures persistently positive for one of these organisms, from cultures drawn more than 12 hours apart, or
- three or more separate blood cultures drawn at least 1 hour apart.

Major echocardiographic criteria include echocardiogram positive for infective endocarditis, documented by:

- an oscillating intracardiac mass on a valve or on supporting structures, in the path of regurgitant jets, or on implanted material, in the absence of an alternative anatomic explanation,
- myocardial abscess,
- development of partial dehiscence of a prosthetic valve, and
- new-onset valvular regurgitation.

Minor criteria for IE include:

- predisposing heart condition (in this particular case: Tetralogy of Fallot),
- intravenous drug use, fever of 38°C (100.4°F) or higher,
- vascular phenomenon, including major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhage, or Janeway lesions,
- immunologic phenomena such as glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor,
- positive blood culture results not meeting major criteria or serologic evidence of active infection with an organism consistent with infective endocarditis, and
- echocardiogram results consistent with IE but not meeting major echocardiographic criteria.

A definitive clinical diagnosis can be made based on the presence of:

- 2 major criteria;
- 1 major criterion and 3 minor criteria or;
- 5 minor criteria[3].

Congenital heart disease is one of the risk factors of IE. Tetralogy of Fallot represents the largest proportion of IE cases. Repaired Tetralogy of Fallot often has residual aortic regurgitation - a substrate for aortic valve IE. Moreover in this case there was prosthetic valve replacement increasing the predisposition to infection[4].

Final treatment and follow up:

He was given a 2 week course of intravenous benzyl penicillin and gentamicin and was advised to continue benzyl penicillin for 2 weeks prophylaxis. The patient was given an appointment to be followed up at 'Grown-ups with congenital heart defects' clinic.

Fact Box 2:

Alexia Grech

Name of Condition: Tetralogy of Fallot

Tetralogy of Fallot is a congenital heart defect[5] which involves four abnormalities of the heart. These include ventricular septal defect (VSD), pulmonary stenosis, misplaced aorta (often described as an aorta over riding the septum) and right ventricular hypertrophy. They usually result in an insufficient amount of oxygenated blood reaching the body[6].

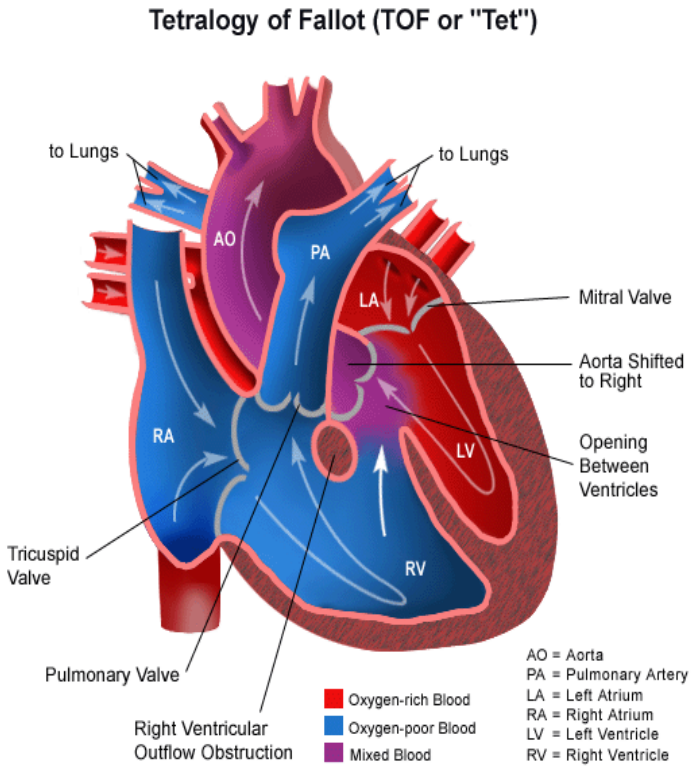

Figure 1: The Heart in Tetralogy of Fallot[7]

Risk factors:

The exact cause of Tetralogy of Fallot is not yet known but there are several factors and conditions that may increase the risk of having a child with this heart defect, which are associated with the mother carrying the child during pregnancy. These include: viral illness, alcoholism, poor nutrition and age (older than 40)[8]. The condition is also seen more in babies with Down syndrome and DiGeorge syndrome[9].

Symptoms and Signs:

- Peripheral & central cyanosis.
- Shortness of breath and difficulty in breathing especially during exertion.
- Fainting[10].
- Clubbing of fingers and toes[11].
- Growth and development in children are slower[10].
- Cervical lymphadenopathy (> 15 mm diameter, usually unilateral, single, non-purulent and painful).

Investigation to confirm diagnosis:

- Heart murmurs upon auscultation.
- Electrocardiogram: shows the four abnormalities of the heart which are ventricular septal defect (VSD), pulmonary stenosis and misplaced aorta (often described as an aorta over riding the septum) and right ventricular hypertrophy.
- Chest X Ray: shows cardiomegaly and pulmonary oedema[12].
- Treatment: Tetralogy of Fallot is repaired with open-heart surgery, either soon after birth or later in infancy. The surgery aims to repair the defects: the ventricular septal defect, pulmonary stenosis, and misplaced aorta so the heart can work as normally as possible[13].

Long term complications:

- Incompetent heart valves
- Arrhythmias
- Pulmonary artery branch stenosis
- Right ventricular aneurysms
- Residual ventricular septal defects
- Coronary artery disease

Prognosis:

The outlook for a child born with Tetralogy of Fallot is much better today than it was in the past. Advances in testing and treatment mean that most children who have this congenital heart defect survive into adulthood. However, they require long-term care provided by specialists in order to remain as healthy as possible[14].

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Case Number 3
Creutzfeldt-Jakob Disease

Thelma Xerri & Daniela Zammit
Reviewed by: Norbert R. Vella, MD

Case summary:

A 62-year-old man was admitted in October 2013 due to worsening involuntary movements of his arms and legs. This was confirmed on examination which revealed persistent jerky movements in his left upper limb associated with generalised stiffness and hyperreflexia in his lower limbs. His dystaxia had developed in August 2013 whilst visiting Argentina. An MRI and EEG were consistent with a diagnosis of Creutzfeldt-Jakob Disease (CJD). Over the following weeks, he developed rapidly progressive cognitive decline and myoclonus. The patient was eventually placed on palliative care.

History of presenting complaint:

A 62-year-old man presented in October 2013 with worsening involuntary movements of the left upper limb and dystaxia. These problems developed in August 2013 whilst visiting his daughter in Argentina where he was hospitalised for a few days and eventually discharged on anti-platelet agents for a presumed diagnosis of a posterior circulation cerebrovascular event.

The patient was falling frequently but there was no history of loss of consciousness. He had also lost an appreciable amount of weight possibly due to loss of appetite. He exhibited no psychiatric symptoms and had not been administered any new medications.

His clinical examination on admission revealed bilateral dystaxia, worse on the left, as well as a left alien hand syndrome. He had increased tone, particularly on the left side. Motor strength was normal on the right but difficult to assess on the left. The deep tendon reflexes were increased in both lower limbs but the plantar responses were flexor. Sensory exam seemed grossly intact.

Past medical and surgical history:

Hyperlipidaemia
Bilateral inguinal hernia

Drug history in hospital:

Drug	Dosage	Frequency	Type	Reason
Aspirin	100mg	Daily 0-1-0	Anti-platelet agent	Inhibits the production of thromboxane A2 by irreversibly inhibiting COX-1 enzyme – secondary prophylaxis for ischemic strokes
Lipitor (atorvastatin)	40mg	Daily 0-0-1	Statin	Lowers blood cholesterol by inhibiting HMG-CoA reductase – hyperlipidaemia treatment

Family history:

Strong history of diabetes mellitus.
One sibling succumbed to ischemic heart disease, another suffers from colonic cancer, and another sustained a cerebrovascular event.

Social history:

Retired green grocer, married with two grown children.

Systemic inquiry on admission:

- General Health: Looked cachectic
- Cardiovascular System: Blood pressure: 135/88 mmHg. Pulse: 81 bpm. Heart sounds: S1 + S2+S0
- Respiratory System: Trachea was central. Breathing rate = 16/min. SpO_2 was 96%. Decreased air entry in apices due to poor compliance.
- Gastrointestinal System: Vomiting during vigorous exercise
- Genitourinary System: Nil to note
- Central Nervous System: Nil to note
- Musculoskeletal System: No calf tenderness and no dependant oedema
- Endocrine System: Nil to note
- Mental State: Normal
- Temperature: 36.7 °C

Differential diagnosis of CJD

- Infectious: viral encephalitis, HIV dementia, progressive multifocal leukoencephalopathy, aspergillosis, syphilis, lyme disease, balamuthia, Whipple's disease.
- Toxic-metabolic: hepatic encephalopathy, porphyria, bismuth toxicity, heavy metal toxicity, uraemia.
- Autoimmune: Hashimoto's encephalopathy, paraneoplastic limbic encephalopathy, non-paraneoplastic autoimmune encephalopathy, lupus cerebritis, sarcoidosis.
- Metastases/neoplasm: non-autoimmune paraneoplastic conditions, metastasis to CNS, primary CNS lymphoma, lymphomatoid granulomatosis, gliomatosis cerebri.
- Iatrogenic: toxic exposure history or medication use.
- Neurodegenerative: Alzheimer's disease, dementia with Lewy bodies, frontotemporal dementia, corticobasal degeneration, progressive supranuclear palsy.
- Systemic: sarcoid, mitochondrial disease

Diagnostic procedures:

Blood work: Within normal limits.
Brain MRI: The diffusion-weighted sequence revealed increased signal along the fronto-parietal cortical ribbon, especially on the right side, as well as the right lentiform nucleus and head of the caudate (Figure 1).
EEG: Abnormal record showing generalised theta activity and periodic sharp wave complexes compatible with a diagnosis of Creutzfeldt-Jakob disease (Figure 2).

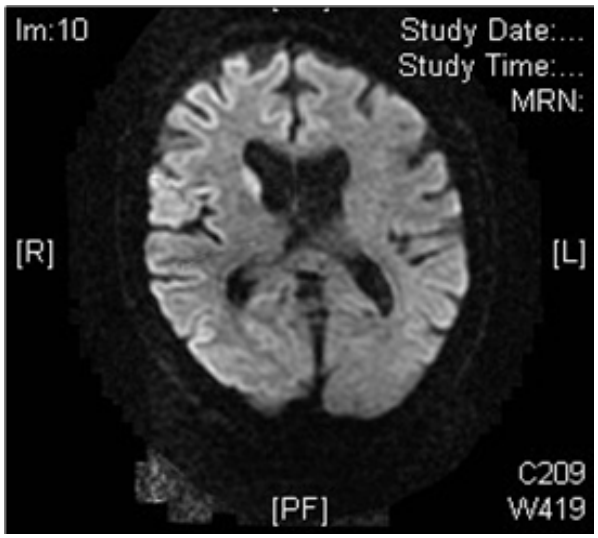

Figure 1: The brain MRI

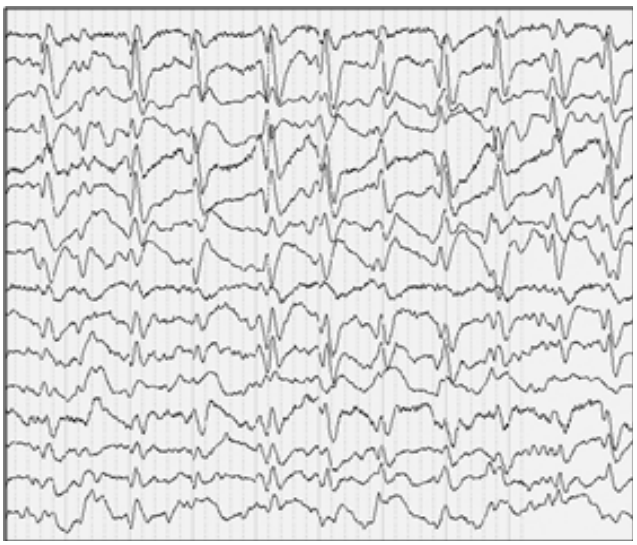

Figure 2: The EEG

Diagnosis:

During his hospital stay, the patient's cognitive function declined rapidly and the myoclonic jerks increased significantly. This together with the MRI and EEG findings confirmed the diagnosis of Creutzfeld-Jakob Disease (CJD) (refer to Fact Box for CDC Criteria).
This diagnosis was discussed with the wife and relatives, who were made aware of the grim prognosis. The Public Health Department was also notified.

Final treatment and follow ups:

Towards late October 2013, the patient was placed on palliative care and it was agreed with his relatives to strive for comfort measures only. The physical therapists helped with bedside therapy and upon the recommendation of the speech-language pathologists a nasogastric tube was inserted for feeding purposes. The medical treatment during his hospital stay comprised sodium valproate and clonazepam to control the myoclonic jerks as well as lorazepam, hydroxyzine and haloperidol to help calm him down. Pain was controlled with paracetamol which was eventually changed to codeine and ultimately he was put on a morphine infusion until he succumbed to his illness.

Fact Box 3:

Name of Condition: Creutzfeldt-Jakob Disease (CJD)

TCJD is a rare transmissible encephalopathy with prominent cerebral and cerebellar cortical spongiform degeneration and the presence of prions. It is mostly prevalent between the ages of 50 and 70 years.

Classification:

- Sporadic CJD, which occurs for no known reason.
- Familial CJD, which is hereditary.
- Iatrogenic CJD, which occurs from contact with infected tissue, possibly following a medical procedure.
- Variant CJD, which is transmitted via meat contaminated by CNS tissue affected by bovine spongiform encephalopathy (BSE) ('mad cow disease').

Clinical Features: CJD results in rapidly progressive cognitive decline with memory and/or personality changes, focal neurological signs, myoclonus, ataxia, akinetic mutism, visual disturbances, depression, and coma and death within one year of disease onset.

Diagnosis and Management: CJD can be diagnosed in patients with rapidly progressive dementia and at least two out of the four signs: myoclonus, visual/cerebellar signs, pyramidal/extrapyramidal signs, akinetic mutism and a positive result on at least one of the following laboratory tests:

- typical EEG findings with periodic sharp wave complexes;
- presence of protein 14-3-3 in the cerebrospinal fluid;
- characteristic MRI changes in the caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR).

Treatment: There is as yet no effective cure or treatment for CJD. Preventive measures are in place in cases of bovine spongiform encephalopathy and iatrogenic CJD.

Prognosis: CJD is a rapidly progressive neurodegenerative condition often resulting in death within 6 months.

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Case Number 4
Chronic Granulomatous Disease (CGD)

Mark Anthony Sammut & Abigail Magro
Reviewed by: Dr. Tonio Piscopo MD, FRCP (Lond), DTM&H (Lond)

Case summary:

Demographic details:

Ms. CC, female, Rabat.
Referred from: Hospital.

An 8-year old girl presented with a 2-year history of recurrent nasal skin infections. In this context of a prolonged history of facial and nasal infections, multiple perianal abscesses and a non-specific chronic colitis, an underlying immunodeficiency was suspected. She was referred for further immunological assessment and after ruling out other haematological disorders, the diagnosis of Chronic Granulomatous Disease (CGD) was made following an abnormal Nitroblue Tetrazolium (NBT) test. The patient was started on long-term prophylactic antibiotics and genetic testing is currently being carried out on her family. Bone marrow transplantation is the optimum treatment but will only be considered when the benefits outweigh the risks.

Presenting complaint:

Repeated nasal skin infections – 2 years.

History of presenting complaint:

The patient has been suffering from recurrent nasal skin infections for the past two years which, despite response to co-amoxiclav, merited referral to hospital. She complains of nasal congestion and purulent discharge. She also has associated excoriation and crusting of the nose. On one occasion, chronic herpes simplex virus infection was suspected but there was no improvement on treatment with acyclovir. Similar episodes occurred before the age of four some of which were associated with aphthous ulceration of the mouth.

Past medical and surgical history:

Past medical history:

Nasal furunculosis – 6 months of age
Maxillary sinusitis and facial cellulitis treated with intravenous antibiotics – 4 years of age
Nasal vestibulitis treated with intravenous antibiotics – 6 years of age
Pustule on left palm – 7 years of age

Past surgical history:

Incision and drainage of several perianal abscesses – 6 years of age
Sigmoidoscopy + rectal biopsy – 6 years of age
Colonoscopy + multiple biopsies suggesting mild chronic non-specific colitis without Crohn's abscesses – 7 years of age

Drug history:

Co-amoxiclav

No known drug allergies.

Family history:

The parents are unrelated and currently well.
Her father has suffered from a chronic skin ulceration over both knees but has no other major illnesses.
Her 9-year-old brother is well and there are no significant illnesses in any other family member.

Social history:

The patient lives with her parents and older brother. She goes to school and interacts well with her peers.

Systemic inquiry:

- General Health: Feeling well in general. Afebrile.
- Cardiovascular System: Nil to note.
- Respiratory System: Nil to note.
- Gastrointestinal System: Nil to note.
- Genitourinary System: Nil to note.
- Central Nervous System: Nil to note.
- Musculoskeletal System: Nil to note.
- Endocrine System: Nil to note.
- Others: Nil to note.

Current therapy:

Ciprofloxacin 250mg bd – to treat nasal infection due to staphylococcus and streptococcus.
Rifampicin 300mg bd – to treat nasal infection due to staphylococcus and streptococcus.

Discussion of results of general and specific examinations:

General examination:

Admission weight: 27.3kg (60th centile)
Admission height: 133cm (80th centile)
Blood pressure: 100/60 mmHg

There is moderate submandibular lymphadenopathy.

Specific examinations:

Examination of the cardiovascular and respiratory systems was unremarkable. Heart sounds were normal and the chest was clear. Abdominal examination showed a soft non-tender abdomen and no hepatosplenomegaly. Neurological examination was normal as were the ears and throat. The patient has a markedly inflamed nose with crusting and occlusion of the nares.

The lymphadenopathy and nasal inflammation point towards an upper respiratory tract infection. The rest

of the examination was unremarkable indicating that the infection has remained localised and no other system has been affected.

Differential diagnosis:[1,2]

- Common variable immunodeficiency
- Inflammatory bowel disease
- Myeloperoxidase deficiency
- Severe combined immunodeficiency
- Autoimmune neutropenia
- Hyperimmunoglobulinaemia E syndrome
- Infection with Mycobacterium tuberculosis
- Primary immunodeficiency
- Impetigo
- Sarcoidosis
- Seborrhoeic dermatitis
- Glucose-6-phosphate dehydrogenase deficiency (G6PD)
- Childhood HIV disease
- Eosinophilic pustular folliculitis
- Leukocyte adhesion deficiency type I
- Wiskott-Aldrich syndrome

Diagnostic procedures:

Laboratory exams:

Test: Full blood count.
Justification for test: Screening for anaemia, acute or chronic infection, thrombocytopenia and any haematological disease.
Result: Hb – 12.7g/L
WCC – 5.9 x 109/L
Platelet count – 139 x 109/L
Conclusion: No anaemia present. WCC within normal values suggesting a more chronic course of infection and no neutropaenic cause. Mild thrombocytopenia non-specific.

Test: Urea and electrolytes.
Justification for test: Baseline values.
Result: Normal.
Conclusion: No electrolyte disturbance or acute renal dysfunction.

Test: LFTs.
Justification for test: Liver has a tendency to become infected in immunodeficiency and form abscesses.
Result: Normal bilirubin, alkaline phosphatase and alanine transaminase.
Conclusion: No hepatic dysfunction.

Test: Nasal culture and sensitivity.
Justification for test: Isolation of causal micro-organism.
Result: Presence of Staphylococcus aureus and group G beta-haemolytic streptococci sensitive to flucloxacillin and ampicillin.
Conclusion: Staphylococcus cultured but no other opportunistic pathogens present.

Test: Nitroblue tetrazolium (NBT).
Justification for test: Screening for chronic granulomatous disease.
Result: Zero reduction of the dye.
Conclusion: Result is consistent with chronic granulomatous disease.

Test: G6PD screen.
Justification for test: Screening for possible homozygous G6PD giving CGD phenotype.
Result: Normal.
Conclusion: Exclusion of G6PD.

Test: Autoimmune screen.
Justification for test: Screening for systemic lupus erythematosus.
Result: Anti-nuclear factor, rheumatoid factor and anti-neutrophil cytoplasmic antibodies were all negative. Anti-cardiolipin antibodies were mildly elevated.
Conclusion: No autoimmune diseases suggested.

Test: Miscellaneous.
Justification for test: To rule out specific haematological diseases.
Result: Immunoglobulins, neutrophil chemotaxis and CD18 expression were all normal.
Conclusion: There is no hypogammaglobulinaemia, neutropaenic disorders and leukocyte adhesion deficiency respectively.

Instrumental exams:

Test: Chest X-ray.
Justification for test: Screening for lung infections, abscesses and especially TB.
Result: Normal.
Conclusion: No lower respiratory chest infections or abscesses detected.

Test: Sinus X-ray.
Justification for test: Surveying the extent of infection.
Result: Moderate mucosal thickening in both antra.
Conclusion: Presence of chronic infection.

Therapy:[3]

Drugs:

Drug	Dosage	Frequency	Type	Reason
Ciprofloxacin	250mg	BD	Fluoroquinolone antibiotic	Treatment of infection
Rifampicin	300mg	BD	Rifamycin antibiotic	Treatment of infection

Diagnosis:

The history of recurrent infections coupled with an abnormal NBT test confirms the diagnosis of chronic granulomatous disease (CGD). Although full genetic analysis has not yet been carried out, CC is probably suffering from the autosomal recessive form of the disease due to an unremarkable family history to date.

Chronic granulomatous disease (CGD), also known as Bridges-Good syndrome, consists of a heterogenous group of disorders characterised by mutations in genes coding for different subunits of phagocyte NADPH oxidase. In normal individuals, this enzyme catalyses the transfer of electrons from NADPH

to oxygen resulting in formation of the superoxide anion, the first step in the production of reactive oxygen species (ROS) necessary for physiological phagocytic killing of bacteria and fungi. The failure to produce the superoxide anion and downstream antimicrobial oxidant metabolites makes the CGD patient susceptible to severe, life-threatening bacterial and fungal infections and excessive inflammation leading to granuloma formation[4]. Mutations can occur in one of at least 5 different genes involved in the assembly and activation of NADPH oxidase. The gene coding for the enzymatic centre, gp91phox is found on the X-chromosome and accounts for about two-thirds of cases. Autosomal forms occur, in descending order of frequency, from mutations in p47phox, p67phox, p22phox and p40phox, all subunits of the enzyme. X-linked CGD patients (gp91phox deficient) are most severely affected. CGD affects 1 in 200,000 persons worldwide[5].

CGD typically presents in early childhood with sinopulmonary infections, skin and organ abscesses, lymphadenitis or a general failure to thrive. In the absence of a known immunodeficiency, specific opportunistic infections caused by organisms such as Staphylococcus aureus, Burkholderia cepacia, Serratia marcescens, Nocardia species and Aspergillus species should increase the suspicion of CGD[6]. Inflammatory disorders such as inflammatory bowel disease at an early age and granulomatous cystitis can also be manifestations of CGD[4]. A family history of males with severe or recurrent infections could point towards the diagnosis of X-linked CGD whereas consanguineous parents increase the risk for the autosomal recessive form. In this young patient, severe infection of the face, recurrent sinus infection and perianal abscesses point towards an immunodeficiency of possible genetic origin such as CGD. The colonoscopy and biopsy findings of a Crohn's-like colitis further reinforce the diagnosis. An unremarkable family history and her female gender suggest against X-linked CGD in favour of the autosomal recessive type.

Being a rare disease, other primary immunodeficiency disorders were excluded before a diagnosis of CGD was strongly suspected. Hypogammaglobulinaemia, neutropaenic disorders and leukocyte adhesion deficiency were all tested for and excluded. The diagnosis of CGD requires demonstration of defective NADPH oxidase activity in neutrophils. The two most common diagnostic assays are the nitroblue tetrazolium (NBT) test and the dihydrorhodamine (DHR) test, the former being the easier to perform. It depends upon direct reduction of NBT to insoluble blue formazan by NADPH oxidase. Lack of NADPH activity, as happens in CGD, gives a negative result (no blue colour change). The DHR test involves staining whole blood with dihydrorhodamine and stimulating it to produce superoxide radicals which oxidize DHR to the fluorescent dye rhodamine in cells with normal function. A negative result seen in flow cytometry indicates a defect in PHOX enzymes[7] (Figure 1). Females who are homozygous for the genetic mutation causing glucose-6-phosphate dehydrogenase deficiency (G6PD) have reduced NADPH levels and therefore, can present phenotypically with CGD. This was excluded in the patient by means of a G6PD screen[8]. Zero reduction of the nitroblue tetrazolium in this case therefore confirmed the diagnosis of chronic granulomatous disease.

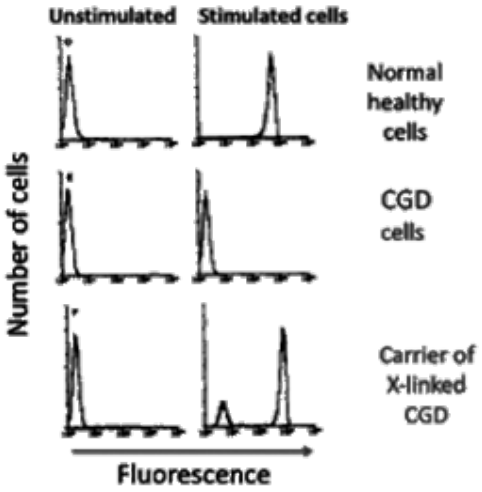

Figure 1:The DHR test for diagnosis of chronic granulomatous disease[9].

Final treatment and follow ups:

Ciprofloxacin and rifampicin were continued for 2 weeks, after which rifampicin was stopped and ciprofloxacin was changed to flucloxacillin 250mg qds together with co-trimoxazole 480mg bd. These were continued for a further 2 months for complete eradication of the current infection.

Long-term prophylactic co-trimoxazole and itraconazole were also initiated to prevent bacterial and aspergillus infections respectively. Itraconazole should only be taken if the frequency of infections starts to increase as the benefits of continual anti-fungal therapy are outweighed by the risks. In view of the fact that she has largely suffered from staphylococcal infections, measures to reduce staphylococcal carriage with application of mupirocin to her anterior nares and regular dusting with hexachlorophene powder should be used. An antiseptic shower wash should also be used for bathing.

Should the patient suffer from new infections or have a recurrence of her current problem, early and aggressive antibiotic treatment should be administered utilising an intravenous antibiotic if necessary. Some studies have shown that treatment with gamma interferon decreases the risks of invasive bacterial infections in patients with CGD.

The patient and her mother are currently undergoing full phenotypic and genotypic analysis to establish the form of inheritance of the disorder. The parents will then receive genetic counselling. Genetic testing for the patient's brother is also being taken into account.

The optimum treatment for a patient with CGD is a bone marrow transplant which will be considered as an option if the disease increases significantly in severity.

Fact Box 4:

Title: Chronic Granulomatous Disease

Chronic granulomatous disease (CGD) is an inherited immunodeficiency caused by defects in the NADPH oxidase complex responsible for producing the superoxide anion necessary for physiological killing of bacteria and fungi. This predisposes the individual to severe, life-threatening infections, excessive granulomatous inflammation and autoimmune diseases.

Risk factors

- Parents carrying the recessive trait
- Male sex in the X-linked type
- Female sex in the recessive type[10]

Symptoms

- Frequent skin infections that are difficult to treat
- Persistent diarrhoea
- Failure to thrive
- Bone pain
- Joint pain[10]

Signs

- Pyrexia
- Lymphadenopathy
- Hepatomegaly
- Splenomegaly
- Signs of pneumonia
- Furuncles
- Signs of cellulitis and impetigo[10]
- Atypical childhood infections eg. osteomyelitis, hepatic abscesses, especially if recurrent

Prevention

CGD cannot be prevented but prophylactic antibiotics and antifungals can be given to minimise the number and severity of infectious complications. Genetic counselling may also have a role in affected families[10].

Complications

- Sinopulmonary: pneumonia, upper respiratory tract infections, lung abscesses
- Dermatological: abscesses, furunculosis, impetigo, eczema
- Lymphadenitis
- Gastrointestinal: gastroenteritis, perianal abscesses and fistulae, gingivitis, granulomatous ileocolitis, stomatitis, gastric outlet obstruction
- Hepatobiliary: liver abscesses or granuloma
- Musculoskeletal: osteomyelitis, septic arthritis
- Neurological: meningitis, brain abscesses
- Urinary: lower urinary tract infections, pyelonephritis
- Haematological: septicaemia, anaemia[5, 11]

Prognosis:

There are currently no studies reviewing the long-term prognosis of CGD with modern treatment. Children without treatment die in the first decade of life, the commonest causes being bacterial or Aspergillus pneumonia and septicaemia. The X-linked type carries a worse prognosis than the autosomal recessive type with median survival time being 37.8 and 49.6 years respectively[11].

Treatment:

The mainstay of treatment is antibiotic prophylaxis with trimethoprim/sulfamethoxazole (co-trimoxazole), ciprofloxacin, clindamycin or rifampicin. Fungal prophylaxis with itraconazole is also recommended. Interferon gamma delivered by subcutaneous injection up to 3 times a week is useful in a few patients. Granulocyte infusions are increasingly given to CGD patients when traditional therapies fail to resolve severe, life-threatening infections, especially with *Aspergillus spp*. Stem-cell transplantation is associated with a significant risk of morbidity and mortality but is curative[12].

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Case Number 5
Systemic Lupus Erythematosus (SLE)

Rebecca Borg & Marika Borg
Reviewed by: Dr Bernard Coleiro

Case Summary:

Demographic details:

Ms. YM, female, Attard.
Referred from: Home.

Ms. YM, a 16-year-old girl, presented to A&E with a 1 week history of progressive, bilateral, and symmetrical lower limb weakness and lethargy. She was also complaining of decreased sensation in her lower limbs and an itchy erythematous rash on the palms of her hands. A couple of weeks prior to this she had been admitted to hospital and treated for pericarditis and chest infection. Neurological examination revealed inconsistency in all muscle groups, and giveaway weakness. The patient was also noted to have abnormal behaviour. Bilateral palmar erythema and multiple splinter haemorrhages were observed. With these clinical features and the investigations carried out systemic lupus erythematosus could be diagnosed and the appropriate treatment was started. The patient will be followed up at Rheumatology, Neurology, and Ophthalmology Outpatients, with physiotherapy for rehabilitation.

Presenting complaint:

Progressive weakness in the lower limbs – 1 week
Lethargy – 1 week

History of presenting complaint:

Ms. YM presented to A&E with a one-week history of progressive weakness in her lower limbs and lethargy. She could not walk into Casualty unaided although she does not have a clear memory of these times. Four days prior to admission she also found it very difficult to get out of bed and needed to be helped to get to the bathroom. She was not able to wash herself either. Ms. YM described equal weakness in both limbs and also decreased sensation. She had no neurological symptoms in her upper limbs on admission, however developed weakness and tingling in her upper limbs 5 days after admission.

A few days after admission, she developed an itchy erythematous rash on both hands. She did not have a butterfly rash over her face and did not complain of headache. She did not experience any rigors or hot flushes. This was her first episode.

Past medical and surgical history:

Past medical history:

She was hospitalised about a month previously and treated for pericarditis and chest infection.

Past surgical history:

Nil to note.

Drug history:

Nil to note.
No known drug allergies.

Family history:

Nil to note.

Social history:

Ms. YM lives with her parents and her two sisters, in a first floor apartment. She did not finish her last year at secondary school last year because of anxiety problems and she has not been working. She enjoys horse-riding and swimming. For the past two years, she had been smoking about 5 cigarettes per day; she has not smoked since she was ill with the chest infection.

Systemic inquiry:

- General Health: Lethargic
- Cardiovascular System: No chest pain on this admission
- Respiratory System: No dyspnoea on this admission
- Gastrointestinal System: Nil to note
- Genitourinary System: Nil to note
- Central Nervous System: Possible personality change noted by relatives
- Musculoskeletal System: Lower limb weakness, arthralgia
- Endocrine System: Nil to note
- Others: Relatives also noted repetitive oro-facial movements; itchy palmar rash

Discussion of results of general and specific examination:

On examination body temperature was 37.8ºC, blood pressure was 160/104 mmHg, SpO_2 was 96%, and the respiratory rate was 17 breaths per minute.
Heart sounds were normal (S1 + S2 + 0).
Chest was clear and there was good air entry on both sides.
The abdomen was soft and non-tender.
Bilateral palmar erythema and multiple splinter haemorrhages were noted.

On neurological examination, neck flexion and extension was 5/5, there was inconsistency on examining power in all muscle groups, with giveaway weakness (4/5 in both upper and lower limbs, except left ankle dorsi-flexion 3/5 and plantar-flexion 2/5). There was normal sensation. Biceps and triceps jerks were decreased bilaterally. Glasgow Coma Scale 15. She was demonstrating abnormal behaviour (smiling inappropriately and showing “la belle indifference”, a naive and inappropriate lack of emotion and concern toward her physical symptoms).

Differential diagnosis:

- Systemic lupus erythematosus
- Antiphospholipid antibody syndrome
- Infective endocarditis
- Pulmonary embolism
- Multiple sclerosis

- Guillain-Barré syndrome
- Conversion disorder

Diagnostic procedures:

Laboratory Exams:

Test: Complete blood count (on admission).
Justification for test: As a baseline to get an idea of haematological parameters. Patient had a variety of symptoms; she was weak, with a possibility of having anaemia. Ms. YM had a chest infection few days before so white blood cell count and differential had to be assessed.
It was repeated on several days afterwards to monitor progression.
Result:
Haemoglobin: 11.0g/dL (low)
Haematocrit: 31.6% (low)
Mean Cell Volume: 75.4fL (low)
Mean Cell Hb: 26.3pg (low)
Platelets: 58 x 109/L (low)
White blood cell count: 7.80 x 109/L (normal on admission but increased to abnormal high levels from day 5 post-admission, reaching a peak of 42.60 x 109/L on day 15 post-admission to decrease gradually afterwards).
The other parameters were within normal ranges.
Conclusion: Microcytic anaemia and thrombocytopenia. Although both occur in SLE, they could be due to several other pathologies and further investigation was necessary. The high white blood cell count indicates either an inflammatory or infective process.
Characteristic haematological disorders in SLE include haemolytic anaemia, leucopaenia, lymphopenia or thrombocytopaenia, all in the absence of a drug effect.

Test: C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (taken from day of admission to day 14 post-admission).
Justification for test: To assess if there is an inflammatory process in a multi-system disorder.
Result: On admission CRP was 49mg/L (high) and went down to 6mg/L on day 5 post-admission.
ESR on admission was 108mm/hr (high), and gradually went down to 18mm/hr on day 14 post admission.
Conclusion: High ESR and CRP confirm inflammation is present. The classical picture in SLE is a high ESR with normal CRP levels. When both ESR and CRP are high the indication is more towards infection, arthritis, or serositis.

Test: Urea (serum) and creatinine (serum) (taken regularly from the day of admission to the day of discharge).
Justification for test: As a baseline and also because urea and creatinine rise in lupus nephritis.
Result: Creatinine was always within the normal range. Urea increased from 6.60mmol/L on admission, reaching a peak of 12.40mmol/L (high) on day 8 after admission, and decreased gradually to 10.30mmol/L on the day of discharge.
Conclusion: Urea and creatinine derangements are not specific to SLE but occur in several conditions. Urea and creatinine are high only in advanced lupus nephritis so in this case, kidney involvement cannot be excluded.

Test: 3 sets of blood cultures (day 3 post-admission).
Justification for test: Suspicion of infective endocarditis after Ms. YM developed multiple splinter haemorrhages.
Result: No bacteria grown.

Conclusion: This, together with a normal echocardiogram (see below), made the diagnosis of bacterial endocarditis unlikely.

Test: Viral screen, toxoplasma and mycoplasma (done between day 2 and day 5 after admission).
Justification for test: To exclude a viral infection, toxoplasma and mycoplasma in view of lethargy and the possibility of infective endocarditis.
Result: Rubella virus IgM antibodies: negative
Syphilis serology: negative
Cytomegalovirus IgM and IgG antibodies: negative
Epstein-Barr virus IgG antibodies: positive
Epstein-Barr virus IgM antibodies: negative
Hepatitis A IgM antibody: negative
Hepatitis B surface antigen: negative
Hepatitis C antibody: negative
Herpes simplex virus IgM I/II: negative
Toxoplasma IgM antibodies: negative
Mycoplasma IgM antibody: negative
Conclusion: Ms. YM does not have a current viral, mycoplasma or toxoplasma infection. EBV results indicate that the patient does not have a recent infection, but IgG antibodies are present from an old infection.

Test: Serum antibody tests (done between day 3 and day 8 after admission)
Justification for test: Disease involving several body organs, suspecting an autoimmune rheumatic disease.
Result: Anti-Nuclear antibody (ANA): positive 1/640
Anti-ds DNA antibody: positive 82.9 U/ml (high)
ANF pattern: speckled
ANCA: negative
Anticardiolipin antibodies: positive ACA IgG >120.0 GPL U/ml (high).
ACA IgM 12.3MPL U/ml (high).
Lupus anticoagulant: positive
Conclusion: Diagnosis of Systemic Lupus Erythematosus (SLE) was made. Anti-ds DNA antibody is highly specific of SLE although it is only positive in about 60% of cases. ANA is positive in more than 95% of patients with SLE. Total antinuclear antibody (ANF) is positive in 99% of SLE patients but occurs in other diseases such as Mixed Connective Tissue Disease, Scleroderma, Sjögren's syndrome and Raynaud's disease. Anticardiolipin antibodies and lupus anticoagulant antibodies are associated with an increased thrombotic risk.

Test: Serum complement C3 and C4 (day 3 post-admission; repeated on day 6 post-admission)
Justification for test: SLE is associated with a decrease in C3 and C4 complements due to their consumption.
Result: C3 complement decreased from 1820mg/L on day 3 (high) to 1172mg/L (normal);
C4 complement decreased from 159mg/L on day 3 (normal) to 61mg/L (low).
Conclusion: The decrease in C3 and C4 compliments is consistent with SLE.

Test: Lumbar puncture (day 5)
Justification for test: CSF examination to investigate biochemistry, possibility of infection, Multiple Sclerosis (MS) or Guillain-Barré Syndrome (GBS).
Result: Normal. Nothing was cultured and biochemistry was normal.
Conclusion: CNS infection is excluded, with no evidence of MS or GBS.

Test: Arterial Blood Gases (day 8; repeated on day 9).
Justification for test: Patient had episodes of shortness of breath with pleuritic chest pain. SpO_2 on air was 93%.
Result: pO2 63.1 mmHg (low) and improved to normal range the following day.
Conclusion: Hypoxia due to temporary reduced lung efficiency.

Test: D-dimer quantitative (day 8 post-admission).
Justification for test: To assess for pulmonary embolism (PE) after the patient developed sudden onset of shortness of breath, with a recent diagnosis of pro-thrombotic antibodies.
Result: 3300
Conclusion: Although D-dimers are high, the test is not specific to PE but is also positive in other conditions such as deep vein thrombosis and disseminated intravascular coagulation. A CT pulmonary angiogram is necessary to exclude PE.

Test: Microscopy cellular casts (day 10 post-admission).
Justification for test: SLE can involve the kidneys (lupus nephritis) giving rise to cellular casts.
Result: Absent.
Conclusion: Lupus nephritis is highly unlikely.

Test: Albumin creatinine ratio (2nd morning urine) (day 16 post-admission).
Justification for test: A high ratio is an early indicator of lupus nephritis.
Result: 83.44mg/g (high)
Conclusion: A high ratio is associated with kidney involvement in SLE however it can be due to other kidney disease and hence lupus nephritis cannot be confirmed with this test alone.

Test: Serum folate, serum vitamin B12 and serum iron levels (day 2 post-admission).
Justification for test: To assess for folate, vitamin B12 and iron deficiency that may be associated with fatigue, anaemia and neurological signs of muscle weakness.
Result: Folate: 13.50nmol/L (normal)
Vitamin B12: 435.00pmol/L (normal)
Iron: 5.03umol/L (normal)
Conclusion: Excluded the possibility of folate, vitamin B12 or iron deficiency.

Instrumental investigations:

Test: Chest X-ray (CXR) (on admission) (Figures 1 and 2).
Justification for test: To assess progression from recent chest infection and pleural effusion, opacity at both bases, and local pleural thickening of lower interlobar pleura seen on CXR in the previous admission.
SLE can cause a pleural effusion.
Result: No pulmonary lesion seen. Heart not enlarged. Costo-phrenic sinuses blunted bilaterally.
Conclusion: Clearing of previous opacities at bases. No evident lung pathology from CXR.

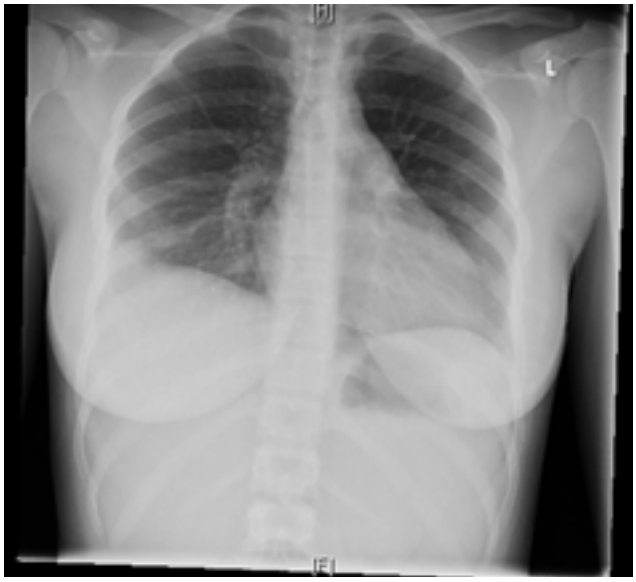

Figure 1: Chest X-ray from the previous admission, about a month before, showing right pleural effusion.

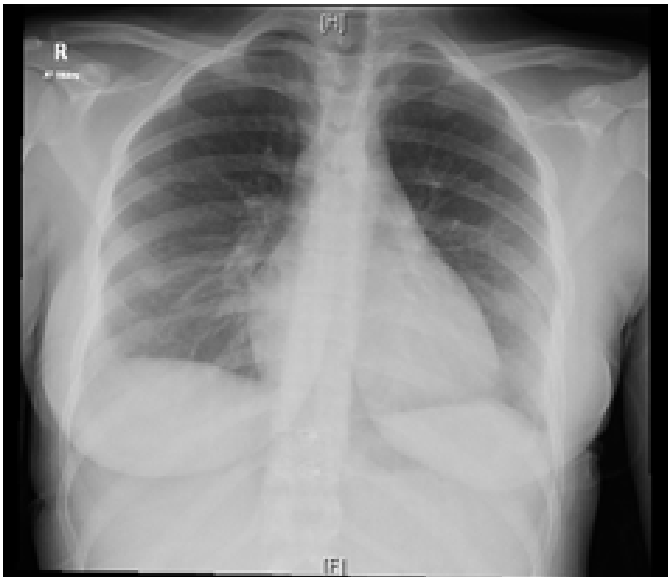

Figure 2: Chest X-ray on the day of admission, showing no pulmonary lesions and costo-phrenic sinuses blunted bilaterally.

Test: ECG (on admission).
Justification for test: Ms. YM had pericarditis a few days ago. She also had tenderness over the 6th to 8th ribs that extended posteriorly to the right scapula. SLE may cause pericarditis.
Result: Non-specific T wave inversions in anterior leads, otherwise normal sinus rhythm.
Conclusion: In acute pericarditis, ECG classically demonstrates saddle-shaped (concave) ST segment elevations throughout, however ECG may be normal.

Test: CT brain (on admission).
Justification for test: To look for brain pathology causing lower limb weakness and abnormal behaviour.
Result: Normal. No haemorrhage or fresh ischaemic changes seen.
Conclusion: No evidence of haemorrhagic or ischaemic stroke.

Test: Transthoracic echocardiogram (ECHO) on day 2 followed by a repeat ECHO and Transoesophageal echocardiogram (TOE) on day 3.
Justification for test: Ms. YM had pericarditis few days ago, and had a mild troponin rise. SLE is known to cause pericarditis. Repeat ECHO was done due to suspicion of infective endocarditis after the patient developed multiple splinter haemorrhages.
Result: No pericardial effusion. Good global left ventricular function. Aorta and left atrium had normal dimensions and the right ventricle was not dilated. Aortic valve appeared to prolapsed into the left ventricular outflow tract.
Conclusion: Possibility of pericarditis or myocarditis was excluded. Diagnosis of infective endocarditis unlikely.

Test: MR spine thoracic, lumbar/sacral (on day of admission) (Figure 3).
Justification for test: To assess for the possibility of Guillain-Barré Syndrome (GBS) or organic spinal pathology. Patient was admitted with ascending bilateral lower limb weakness and flaccid paralysis.
Result: No abnormality detected.
Conclusion: No organic spinal pathology present and GBS unlikely.

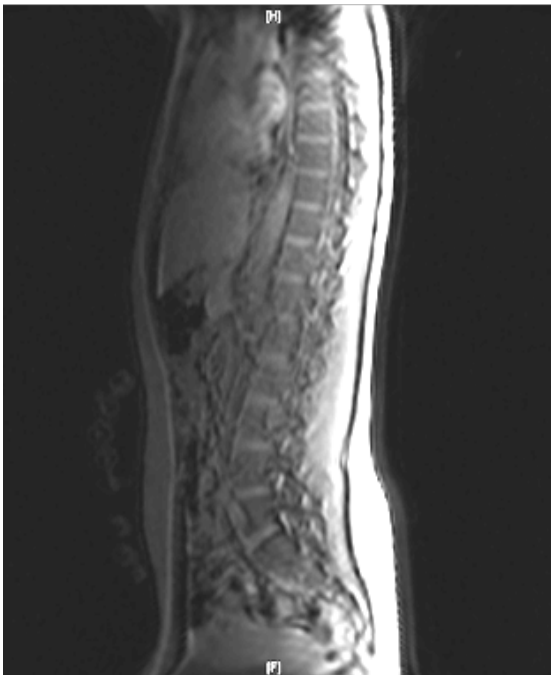

Figure 3: MR spine on the day of admission, showing no pathological finding.

Test: MR head (done on day 3; repeated on day 6 and day 20) (Figure 4).
Justification for test: To assess for any pathology causing muscle weakness or accounting for the behavioural changes.
Result: In the first MR head, multiple oval lesions of high signal intensity were noted in both periventricular regions and posterior fossa on both sides.
The repeat MR on day 6 showed a mild increase in the number of lesions in the cerebellum and right posterior cerebral cortex and subcortical white matter.
The repeat MR on day 20 showed an improvement in the lesions, but there were new areas of cortical high signal intensity in the right parietal and right frontal lobes, best seen on FLAIR sequence.
Conclusion: The first MR head results suggested a demyelinating disease.
Several micro-infarcts in the MR head suggest the possibility of emboli.

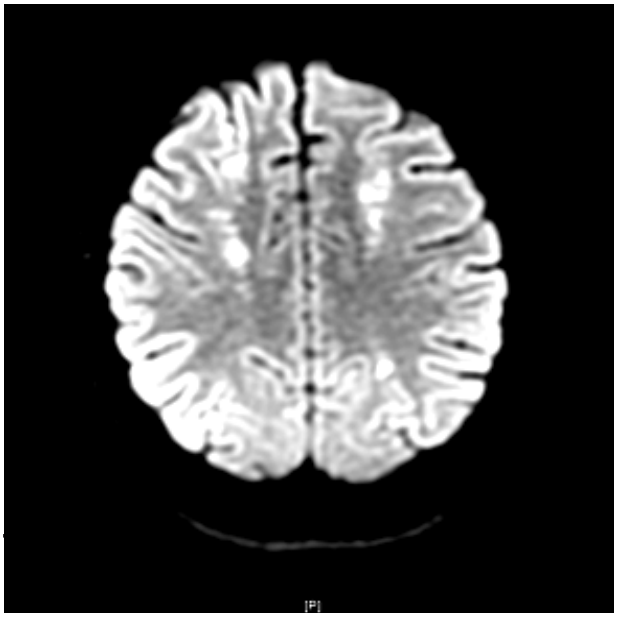

Figure 4: MR head on day 20 post-admission, showing multiple areas of cortical enhancement in both cerebral hemispheres. New changes of cortical high signal intensity in the right frontal and right parietal lobes.

Test: Electromyography (EMG) (day 3).
Justification for test: Weakness in several muscle groups in both upper and lower limbs.
Result: Asymmetrical sensory responses.
Conclusion: No specific conclusion.

Test: Electroencephalography (EEG) (day 4; repeated on day 13).
Justification for test: Behavioural changes (such as smiling inappropriately).
Result: Bihemispheric slowing.
Conclusion: Presence of encephalopathy.

Test: CT pulmonary angiogram (day 8).
Justification for test: To exclude pulmonary embolism after the patient experienced sudden onset shortness of breath, in view of having antibodies predisposing her to thrombotic events. SLE increases the risk of both arterial and venous thrombosis.
Result: Bilateral ground glass appearance.
Conclusion: Pulmonary embolus excluded. Changes likely to be due to congestion. However they could also be due to other pathology.

Test: Lung function tests (day 16).
Justification for test: SLE may affect the lungs rarely, giving rise to a restrictive lung defect. Patient had shortness of breath.
Result: Restrictive pattern found but quality was poor.
Conclusion: Possible lung involvement.

Test: Bone Mineral Density scan.
Justification for test: SLE carries an increased risk for osteoporosis.
Result: No T-score or Z-score values were recorded.
Conclusion: No osteoporosis as yet.

Therapy:

Drugs:

Drug Name	Dosage	Frequency	Type	Reason
Omeprazole	20mg	Bd	Proton pump inhibitor	Heartburn
OStrong	1 tab	Daily	Calcium and Vitamin D supplements	Osteoporosis prevention
Warfarin	4mg	Daily; for 3 days	Anticoagulant	Prevention of further thrombosis in cerebral vessels
Prednisolone	25mg	Daily; for 21 days	Corticosteroid	Immunosuppression (high dose used during an acute phase)
Prednisolone	20mg	Daily; for 14 days after the 21 days of 25mg	Corticosteroid	Immunosuppression
Prednisolone	15mg	Daily; for 7 days after the 14 days of 20 mg	Corticosteroid	Immunosuppression
Hydroxychloroquine sulfate	200mg	Bd	Antimalarial	For joint and skin symptoms of SLE

Diagnosis:

Ms. YM's previous admission with pericarditis and chest infection, her splinter haemorrhages, and the

presence of multiple lesions of high signal intensity on MR Head might point towards the diagnosis of infective endocarditis with embolic phenomena. However, she was not septic clinically, and apart from involvement of the heart, lung, and nervous system, there was also involvement of the musculoskeletal system (arthralgia) and skin (palmar erythema). This indicates the presence of a systemic disease, such as systemic lupus erythematous. Ms. YM is also of the appropriate age and gender for the onset of this disease[1, 2, 3]. Thus the antinuclear antibodies were tested and found to be strongly positive.

When a patient fits 4 or more of the below 11 criteria (serially or simultaneously), systemic lupus erythematosus can be diagnosed: [4, 5]

- Malar rash: fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds.
- Discoid rash: erythematous raised patches with adherent keratotic scales and follicular plugging, with or without atrophic scarring.
- Photosensitivity: unusual reaction to light on exposed skin.
- Oral ulcers: oral or nasopharyngeal ulceration, usually painless.
- Non-erosive arthritis: involving 2 or more joints with tenderness, swelling, or effusion
- Serositis: pleuritis or pericarditis.
- Renal disorder: persistent proteinuria or cellular casts.
- CNS disorder: seizures or psychosis.
- Haematological disorder – haemolytic anaemia or leucopenia or lymphopenia or thrombocytopenia.
- Immunological disorder – anti-dsDNA, anti-Sm, or antiphospholipid antibody.
- Positive antinuclear antibody (ANA).

Apart from the positive antinuclear antibody, Ms. YM also had a haematological disorder (thrombocytopenia and microcytic anaemia), positive ds-DNA, a history of pericarditis and a positive lupus inhibitor screen and abnormal serum levels of IgG and IgM anticardiolipin antibodies, indicating the presence of antiphospholipid antibodies. The diagnosis of infective endocarditis was also made more unlikely by the absence of bacterial growth from blood cultures and by the result of the echocardiogram. Thus the diagnosis of systemic lupus erythematosus could be made. The micro-infarcts seen on the MR head are most probably due to thromboembolic events as a result of antiphospholipid antibody syndrome, that is secondary to SLE.

Final Treatment and Follow ups:

After discharge she will be followed at Neurology Outpatients and Rheumatology Outpatients in 6 weeks. She also has a follow-up appointment at Ophthalmology Outpatients in 6 months' time, because of possible ocular toxicity associated with hydroxychloroquine therapy.

Ms. YM will continue physiotherapy as an outpatient.

In view of her warfarin therapy she needs to be followed at ACC and Phlebotomy for regular monitoring of INR.

Fact Box 5:

Title: Systemic Lupus Erythematosus (SLE)

Overview:

SLE is an inflammatory, autoimmune rheumatic disease that affects several systems in the body, with clinical features ranging from arthralgia and rashes to serious cerebral and renal effects.

Risk Factors: The exact cause of SLE is not known, but predisposing factors include:

- Heredity: higher concordance rate in monozygotic twins.
- Genetics: around 20 genes have been linked to SLE, such as homozygous deficiencies of complement genes C1q, C2, or C4.
- Sex hormone status: premenopausal females are most commonly affected.
- Drugs: a mild form of SLE can be induced by hydralazine, isoniazid, procainamide, and penicillamine.
- UV light: this can trigger flare-ups, especially in the skin.
- Exposure to Epstein-Barr virus (EBV): EBV can possibly be a trigger for SLE.

Signs and Symptoms:

Clinical features vary between different patients, but the most common are fatigue, arthralgia, and skin problems. Figure 5 below shows the various systemic clinical features.

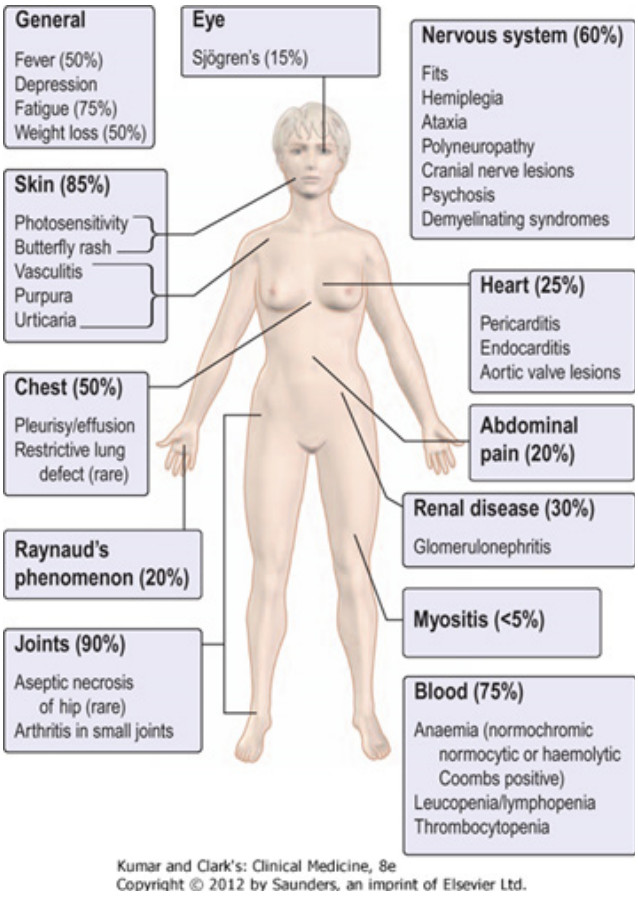

Figure 5: Clinical Features of SLE

Investigations

- Blood:
  -Complete blood count: anaemia of chronic disease/autoimmune haemolytic anaemia, leucopenia, lymphopenia, thrombocytopenia.
  -Erythrocyte sedimentation rate (ESR): raised.
  -Urea and creatinine: raised when there is renal involvement.
  -Autoantibodies: anti-nuclear antibody (ANA), anti-dsDNA, anti-Ro, anti-Sm and anti-La most significant; antiphospholipid antibodies present in 25-40% of cases.
  -Serum complement: C3 and C4 reduced during active disease.
- Histology: immunofluorescent abnormalities with deposition of IgG and complement on kidney and skin biopsies.
- Imaging: CT scans may show infarcts or haemorrhages and cerebral atrophy; MRI can detect white matter lesions.

Treatment:

- General management measures: discussion with the patient regarding the effect of the disease on lifestyle, advice such as avoidance of excessive sun exposure and cardiovascular risk factors.
- Symptomatic treatment with NSAIDs for arthralgia, fever, etc.
- Topical corticosteroids for cutaneous lupus; also use of sun protection cream and avoidance of excessive sun exposure.
- Antimalarials, such as hydroxychloroquine, for skin disease, fatigue, and arthralgias not responsive to NSAIDs. However care must be taken because of the risk of retinal toxicity with such drugs.
- Severe, acute flares of haemolytic anaemia, thrombocytopenia, nephritis, arthritis, pleuritis, pericarditis, and cerebral disease require high-dose corticosteroids.
- Renal and cerebral disease would also require immunosuppressive drugs, such as cyclophosphamide, mycophenolate mofetil, azathioprine, and rituximab.

Prognosis and Complications:

SLE is a chronic condition, with a relapsing and remitting course. 10-year survival rate is around 90%, but it may be decreased if major organs are involved. Early on, death may be due to renal or cerebral disease or infections, while later cardiovascular disease would be more common. Patients with SLE have increased risk of developing certain cancers, especially lymphoma, as well as of cardiovascular disease and osteoporosis. Although fertility is usually normal, pregnancy in SLE patients carries risk for complications, such as thrombosis, pre-eclampsia, infection, and patients may have recurrent miscarriages, especially if positive for antiphospholipid antibodies. If an SLE patient becomes pregnant, she would require a review of her medications. Exacerbations may be more frequent post-partum.

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Case Number 6
Narcolepsy & Cataplexy

Paula Gauci & Tara Giacchino
Reviewed by: Dr. Malcolm Vella

Case summary:

Demographic details:
Mrs AT, Female, Serbian, Self-employed.

A 35-year-old woman from Serbia presented to the neurology department with a 20 year history of excessive daytime sleepiness and recurrent episodes of dropping to the floor whilst still retaining consciousness. These episodes were brought on by laughing or strong emotions.

Presenting complaint:

Daily excessive daytime somnolence – 20 years
Occasional loss of facial tone brought on by strong emotions – 20 years
Occasional drop attacks brought on by strong emotions – 20 years

History of presenting complaint:

The patient dates her symptoms of excessive daytime sleepiness back to when she was 15 years old and would find it difficult to remain awake during lessons at school. She describes the symptoms as an intense feeling of needing to sleep that would almost always result in her napping for approximately 5 to 20 minutes, after which she would wake up feeling refreshed. This sleepiness occurs daily and is not related to the quantity or quality of her sleep the night before. The fact that it occurs without warning has a negative impact on her life; sometimes she would be driving and would have to stop the car at the side of the road as she would not be able to resist the urge to sleep. This is very worrying to the patient considering she has two young children. The patient also complains of sudden loss of muscle tone during moments of heightened emotion, especially when she is laughing with friends. This symptom also dates back to when she was 15 years old, however is much less frequent lately. When it does occur, it usually affects her facial muscles only, she feels her face begin to droop and she is told that she suddenly becomes expressionless. Rarely, it has affected her whole body tone resulting in her dropping to the floor. These episodes usually last for approximately 30 seconds and are never associated with loss of consciousness. The impact of these symptoms on her life is not as great as those of excessive daytime sleepiness, as she can usually tell when it is going to happen and can warn others around her. The patient has never experienced any hypnagogic or hypnopompic hallucinations and does not recall any episode of sleep paralysis.

Past medical and surgical history:

No significant medical or surgical history of note.

Drug history:

Patient is on no current treatment.

A Serbian doctor had prescribed amphetamines but the patient never actually took them because of fear of dependency.

Family history:

The patient recalls her maternal grandfather having similar symptoms of excessive daytime sleepiness – he was a bus driver and would often need to park his bus at the side of the road to take a nap. However, he was never formally investigated and/or diagnosed.

Social history:

The patient is married with 2 children; a 5-year-old son and an 11-month-old daughter. She smokes and drinks alcohol only occasionally during the weekends. She is self-employed.

Systemic inquiry:

- General Health: Patient is well in general with no remarkable findings on systemic enquiry
- Cardiovascular System: Nil to note
- Respiratory System: Nil to note
- Gastrointestinal System: Nil to note
- Genitourinary System: Nil to note
- Central Nervous System: Nil to note
- Musculoskeletal System: Nil to note
- Endocrine System: Nil to note

Differential diagnosis:[1]

- Narcolepsy with associated cataplexy
- Epilepsy
- Insomnia and other sleep disorders
- Psychiatric illnesses: major depressive disorder, bipolar disorder, psychotic disorder
- Idiopathic hypersomnia
- Conversion disorder
- Malingering

Diagnostic procedures:

The following investigations were carried out in the past:

Test: CT Brain.
Justification for test: To exclude a space occupying lesion or any pathology in the region of the hypothalamus.
Result: Normal CT Scan.
Conclusion: No brain pathology present.

Test: MRI.
Justification for the test: To exclude any neurological pathology in the region of the hypothalamus.
Result: Normal MRI.
Conclusion: No neurological pathology present.

Test: EEG.
Justification for the test: To exclude any abnormal electrical activity in the brain.
Result: Normal EEG.
Conclusion: Normal brain electricity.

Test: Polysomnography.
Justification for the test: To exclude SOREMPs (sleep-onset rapid eye movement periods) and a mean sleep latency of less than 8 minutes which would strongly suggest narcolepsy.
Result: Normal parameters measured.
Conclusion: Normal sleep patterns.

Test: ECG.
Justification for the test: To exclude any arrhythmias.
Result: No abnormalities detected.
Conclusion: Normal heart rhythm.

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Modafinil	200 mg	1 - 0 - 0	Psychoanaleptic, centrally acting sympathomimetic[2]	Promotes wakefulness[2]
Methylphenidate Hydrochloride	10 mg	1 - 0 - 1	Psychostimulant	Effective for treatment of daytime sleepiness due to narcolepsy[3]
Selegiline	5 mg	1 - 1 - 0	MAO Inhibitor	Effective treatment for all narcoleptic symptoms[3]
Fluoxetine	20 mg	0 - 0 - 1	SSRI	Effective treatment for cataplexy, sleep paralysis and hypangogic hallucinations[3]

Non-pharmacological treatment[3]

- Scheduled naps to overcome daytime sleepiness.
- Following a diet including light or vegetarian meals throughout the day and avoidance of heavy meals before important activities.
- Making family, friends and colleagues aware of the condition to avoid being labeled as lazy or not interested.

Diagnosis:

The patient's diagnosis is that of narcolepsy with associated cataplexy. Narcolepsy (also known as Gélineau's syndrome) is a rare sleep disorder that affects 0.02% of the population. Patients present in their teenage years or young adulthood with excessive daytime sleepiness that cannot be resisted and that may occur under inappropriate circumstances[4]. Narcolepsy often forms part of a tetrad of clinical features[5]:

- Excessive day time sleepiness with sleep attacks that usually last approximately 15 to 20 minutes, from which the patient wakes up feeling refreshed.
- Cataplexy: sudden loss of muscle tone with retained consciousness that is provoked by heightened emotions.
- Sleep-onset and/or sleep-offset paralysis: an inability to move or speak when falling asleep or waking up respectively.
- Hypnagogic and/or hypnopompic hallucinations: hallucinations occurring whilst falling asleep or waking up respectively. The hallucinations are typically visual or auditory.

However, the most common clinical feature associated with narcolepsy is cataplexy. In fact, the patient reported symptoms of the latter disorder but denied any symptoms of sleep paralysis and hallucinations. The performed tests ruled out other causes of the patient's symptoms.

There is a genetic basis behind the disorder and an apparent association with the HLA DQB1*0602 allele that predisposes individuals to the disorder[4], therefore the fact that the patient's grandfather very likely suffered from the same condition further strengthens the diagnosis.

Final treatment and follow ups:

The patient was started on Modafinil with excellent outcome. She was advised to regularly attend follow-up appointments at Neurology Outpatients in order to monitor her condition and identify potential drug side effects.

She was given precautions as regards dangerous activities and driving.

Fact Box 6:

Gianluca Fava

Title: Narcolepsy
Also known as: Hypnolepsy, Gelineau syndrome

Narcolepsy is a neurological disorder that affects the ability to control and regulate sleep-wake cycles. It is characterised by a disturbance in nocturnal sleep, particularly chronic intense sleepiness and recurrent daytime sleep attacks[6,7]. The exact cause of narcolepsy is not fully understood, but a reduction in the levels of hypocretin has been linked to this disorder. The precise mechanism leading to a decreased production of this protein in the brain is yet unknown but may have several contributing factors[8].

Risk factors:[8,9,10]

- Age: Narcolepsy may appear at any age. Usually symptoms appear during adolescence or young adulthood and are rare before age 5.
- Sex: Narcolepsy affects both men and women.
- Heredity: Low hypocretin levels may be linked to certain genes.
- Autoimmune disorders: Low hypocretin levels may be linked to an autoimmune disorder involving the hypothalamic neurons that produce it.
- Brain injuries: Low hypocretin levels may be a result of brain tumours, strokes or trauma.
- Infections.
- Heavy metals.
- Pesticides and herbicides.
- Smoking and secondhand smoke.

Signs and Symptoms:[7,8,11]

- Excessive daytime sleepiness (EDS): Periods of extreme drowsiness during the day which consist of a strong urge to sleep and are often followed by a sleep attack. These usually last less than 30 minutes can be brought about suddenly by strong emotions, periods of inactivity and meals. Such patients complain of mental cloudiness, lack of energy and extreme exhaustion, problems in focusing and concentration, memory lapses and depression.
- Cataplexy: Sudden loss of muscle tone leading to feelings of weakness and a loss of voluntary muscle control. May range from slurred speech to weakening and buckling of the knees and total body collapse. Most attacks last no longer than 30 seconds and may be missed but may last for several minutes during which time the person is paralysed. Cataplexy may be triggered by strong emotions.
- Hallucinations: Vivid dreams which may occur while dozing, falling asleep or waking up. All senses may be involved.
- Sleep paralysis: Temporary inability to move or speak while falling asleep or waking up. These episodes are usually brief lasting a few seconds or minutes but may be frightening experiences.

Testing and diagnosis: [7,8,12]

- Physical examination.
- Exhaustive medical history.
- ECG: Measuring electrical activity of the heart.
- EEG: Measuring electrical activity of the brain.
- Polysomnography (PSG): This overnight sleep study records brain activity, eye movements, heart

rate and blood pressure. It helps to determine how quickly the patient falls asleep, how often the patient wakes up during the night and how long it takes for the patient to go into rapid eye movement (REM) sleep after falling asleep.

- Multiple sleep latency test (MSLT): This daytime sleep study measures how sleepy a patient is. The patient is required to nap for 20 minutes every 2 hours throughout the day for a total of four or five times during which brain activity is monitored. This test measures how long it takes for the patient to reach various stages of sleep and how quickly the patient falls asleep during the day after a night's sleep.
- Hypocretin test: A lumbar puncture is done to measure the hypocretin levels in the cerebrospinal fluid surrounding the spinal cord.

Treatment:[8,13]

There is no known cure for narcolepsy as of yet and thus treatment aims to control symptoms. This involves:

- Emotional counseling and lifestyle changes: This includes planning naps to decrease the frequency of sudden sleep attacks, possibly after meals. Patients should also eat light during the day and avoid heavy meals before important activities. Bosses and supervisors should be informed about the condition. Patients may also not be allowed to drive and operate certain machinery.
- Stimulant drugs: These may help the patient to stay awake. Armodafinil is usually used but other stimulants may be used, namely dextroamphetamine and methylphenidate.
- Antidepressant medication: This may help to reduce the frequency of hallucinations and episodes of sleep paralysis and cataplexy. Such medication includes selective norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine; selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, paroxetine and citalopram; and tricyclic antidepressants such as protriptyline and imipramine.
- Sodium oxybate for nighttime use.

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Case Number 7
Status Epilepticus

Martha Dimech & Giulia Magro
Reviewed by: Dr. Nicola Dingli

Case summary:

Demographic details:

AC, Male, 67, St. Julian's.

67-year-old gentleman presented to the A&E department with new-onset generalised tonic-clonic seizures lasting about 30 minutes. A nasopharyngeal airway was inserted on arrival, intravenous access obtained and he was given intravenous diazepam to stop the seizures, followed by intravenous phenytoin under cardiac monitoring. Arterial blood gases revealed a type II respiratory failure and he needed intubation and transfer to ITU. He was also given ceftriaxone and acyclovir in A+E in view of his new onset *status epilepticus*. Once in ITU, no further seizures were recorded and he did not require any inotropic support. Further investigations including routine blood tests, toxicology as well as a lumbar puncture were normal. MRI head done the following day showed a high-intensity signal in the right temporal lobe region suggestive of Herpes Simplex Encephalitis.

After a 3 day stay in ITU, he was transferred to the ward and acyclovir continued for a total of 21 days. He remained well and was eventually discharged home.

Presenting complaint:

New-onset generalised tonic-clonic seizures.

History of presenting complaint:

This was the first time the patient experienced such seizures. He had his first seizure at home and then had a subsequent attack in the ambulance, which resolved spontaneously. These recurred in A+E, where he was noted to have eye-rolling and generalised tonic-clonic seizures with incontinence of urine. No fever, associated neck stiffness or other signs of meningism were present.

Past medical history:

Hernia repair.
Tonsillectomy.
Past history of suicidal thoughts related to anxiety.

Drug history:

The patient was previously well and on no regular medication.
Noted to have been on Deanxit in the past.
He has no known drug allergies.

Family history:

Brother suffers from epilepsy.

Social history:

The patient has a history of heavy alcohol intake until 1994.
He is also a heavy smoker, smoking 40 cigarettes daily. Pensioner.
He lives with his wife and is independent in all activities of daily living.

Systemic inquiry:

Nil to note

Discussion of results of general and specific examinations:

On examination (on admission to A+E):
Cardiovascular system: Normal heart sounds.
Respiratory system: Clear chest with mild crepitations on expiration.
Widespread decreased air entry which eventually improved.
Gastrointestinal system: Abdomen soft and non-tender.
Pupils: Equal and reactive to light.
Lower limbs: normal, no signs of oedema or any other abnormality.
Upper limbs: Flaccid left upper limb; tone normal in right upper limb- withdraws more to pain than left.
Unable to elicit upper limb reflexes; lower limb reflexes are normal; no plantar response.
Skin: No rashes observed.

Parameters:
Glasgow Coma Scale: 6
Temperature: 36.5 ^{0}C
Blood Pressure: 130/85 mmHg
HGT: 8.1 mmol/L
Heart Rate: 94 bpm
SpO_2: 95%.

Other Investigations:
CXR - nil of note .
CT brain - no midline shift or hemorrhage.
ECG - normal sinus rhythm, 118 bpm, isolated ventricular ectopic beats.
ABG - CO_2 retention; oxygen switched to 24% via Venturi mask.
CT Thorax/Abdomen/Pelvis – normal.
Anti-voltage gated potassium antibodies & Anti-neuronal antibodies – negative.

Differential diagnosis:

- Herpes Simplex Encephalitis
- Limbic encephalitis
- Paraneoplastic
- Auto-immune
- Low-grade glioma of the right frontal lobe region

Diagnostic procedures:

Laboratory Exams:

Test: Lumbar puncture.
Justification for test: In order to obtain CSF composition.
Result: Lab results showed mildly raised glucose and protein levels. No pleocytosis was evident.
Conclusion: A normal CSF does not rule out a viral encephalitis.

Test: Toxicology Screen.
Justification for test: To exclude intoxicants as cause for the seizures as well as to exclude sudden withdrawal from a seizure medication (patient in this case was not on any previous anti-epileptics).
Result: Negative lab results.
Conclusion: Seizures were not precipitated by an exogenous agent, an adverse drug reaction or increased/ decreased levels of medication.

Instrumental Exam:

Test: CT thorax/abdomen/pelvis.
Justification for test: In view of possible paraneoplastic encephalitis.
Result: Small focal fibrotic changes seen in bases of lungs. Hepatic steatosis; no other abnormalities seen.
Conclusion: No paraneoplastic syndrome/ limbic encephalitis present.

Test: MRI head.
Justification for test: To exclude any structural brain lesion that could have precipitated the seizures.
Result: The right temporal lobe was shown to be oedematous with no apparent enhancement or restricted diffusion. Oedema of the right frontal lobe with a suggestion of mild enhancement, mass effect and possible mild restricted diffusion was also noted.
Conclusion: This is likely to represent herpes encephalitis.

Current Drug Therapy:

Patient was given 3 doses of 2.5mg diazepam IV in the acute scenario.

In ITU he was on the following medication:

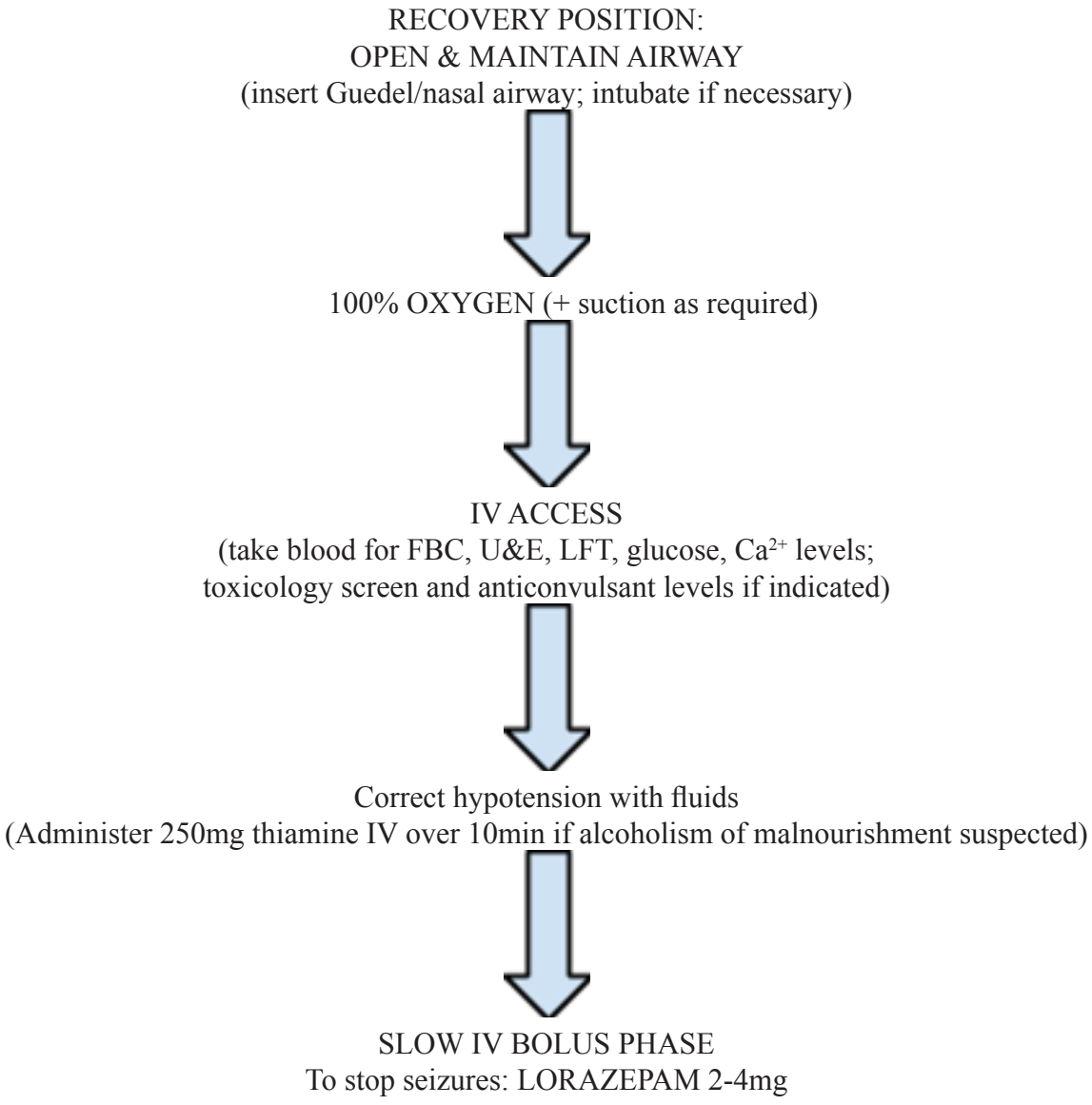
Drug	Dosage	Frequency	Type	Reason
Aciclovir	750mg	TDS	Anti-viral	To treat suspected viral herpes encephalitis
Co-amoxiclav	1.2g	TDS	Antibiotic	Broad spectrum antibiotic in view of possible aspiration
Phenytoin	100mg	TDS	Anti-epileptic	As prophylaxis for subsequent seizures
Perindopril	4mg	Daily	ACE-Inhibitor	To lower blood pressure
Clexane	40mg	Daily	LMWH (low-molecular weight heparin)	Anticoagulant, to act as prophylaxis for DVT

Paracetamol	1g	6-hourly/ PRN	Analgesic	To provide pain relief
Morphine	1mg/mL		Analgesic/Sedative	To provide sedation
Lactulose	15mL	BD	Laxative	Relief of constipation which is a side-effect of morphine
Propofol	10mg/ mL	1 injectable dose	Hypnotic	To provide sedation

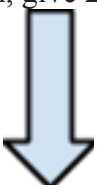
Diagnosis:

Status Epilepticus is an acute life-threatening neurological emergency defined as seizures lasting more than 30 minutes or repeated seizures without intervening episodes of consciousness. It generally occurs in known epileptics, thus first presentation should raise a high index of suspicion of the patient having a structural brain lesion. The longer the length of the attack the higher the risk of permanent brain damage as well as an increased chance of mortality. In this case the *status epilepticus* was triggered by a viral infection caused by herpes simplex.

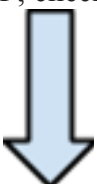
The following is an algorithm illustrating the management of *Status Epilepticus* adapted from 'Oxford Handbook of Clinical Medicine - 8th Ed.'



(If no response within 2min, give 2nd dose of LORAZEPAM)



IV INFUSION PHASE: START PHENYTOIN
18mg/kg IVI, at a rate equal to/less than 50mg/min
ALTERNATIVE: DIAZEPAM INFUSION: 100mg in 500mL of 5% dextrose
(Monitor ECG and BP; check maintenance doses)



GENERAL ANAESTHESIA PHASE:
If seizures continue, call expert help.
Paralysis and ventilation with continuous EEG monitoring in ITU is required.

Final treatment and follow ups:

No surgical interventions were performed. Treatment on discharge included phenytoin (100mg tds) and perindopril (4mg daily). A repeat MRI head to be done 6 weeks following discharge was booked and an outpatient follow-up arranged.

Fact Box 7:

Abigail Mula

Title: Status Epilepticus (SE)

Short description of condition:

Status Epilepticus is a neurological disorder involving an acute, prolonged epileptic crisis characterised by multiple seizures. It is commonly a result of an exacerbation of a seizure disorder. In this case however this condition is secondary to Herpes Simplex Encephalitis. The virus affects the epileptic-prone regions of the brain, particularly the frontal and temporal lobes, hence the epileptic episodes. Unfortunately SE is a life-threatening condition.

Risk factors:

General:

- Young age
- Acquired brain insults e.g. Herpes Simplex Encephalitis
- Genetic predisposition

Children:

- Fever
- Pre-existing epilepsy
- Cerebral palsy
- Hypoxic-ischemic encephalopathy

Adults:

- History of epilepsy
- Cerebrovascular disease
- Drug intoxication
- Alcohol intoxication
- Head Trauma

Symptoms:

- Imbalance and poor motor control
- Drowsiness
- Unresponsiveness (in severe cases)

Investigation(s) to confirm diagnosis

- CT scan (which would show a high intensity signal in the region of the temporal lobe)
- Electroencephalogram (EEG)
- Lumbar puncture (if aetiology is unknown or patient is immunocompromised)

Prevention

This condition can be prevented by prompt treatment of the seizures. Individuals already suffering from epilepsy, including those on medication must inform the physician if any changes in perception or mood are noted. Moreover, such individuals should limit their alcohol intake. Finally, persons on anti-epileptic medication should undergo regular blood testing.

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Case Number 8
Hailey- Hailey Disease

Maria Bonnici and Amy Chircop
Reviewed by: Dr. Liam Mercieca and Dr. Michael Boffa

Case summary:

Demographic details:
Mr. J.M., Male, Fgura, 73 years of age.

Mr. J.M. is a 73-year old gentleman who was diagnosed with Hailey-Hailey disease at the age of 28 and is being followed up at Dermatology out-patients. He has suffered since early adult life from recurrent maceration of the skin especially at the groin, inner thighs, axillae and neck folds. These areas are accompanied by erythema, itching, pain and oozing of a malodorous fluid and are waxing and waning in nature. Currently the patient has 2 areas of skin maceration over both inner thighs, worse on the left side with involvement of the left scrotum.

Presenting Complaint:

Pain and irritation of the skin of the left inner thigh and scrotum with maceration.

History of Presenting Complaint:

A 73-year old gentleman with a 45 year history of Hailey-Hailey disease seen as an out-patient at Sir Paul Boffa Hospital. When the patient was in his late twenties, he noticed several areas of itching followed by redness and pain in varying locations such as inner thighs, groin, axillae and neck folds. The condition was waxing and waning in nature. At this point it was not severe enough to warrant medical attention. During the following 5-6 years, the development of new affected areas was becoming more severe with resulting fissuring, severe pain and oozing of a malodorous fluid. This prompted the patient to seek medical attention and a clinical diagnosis of Hailey- Hailey disease was made which was subsequently confirmed with a skin biopsy.

The patient describes a phase of itching 2 days prior to development of redness, fissuring and oozing of fluid which is occasionally accompanied by pus. The resulting pain interferes with walking especially when the inner thighs and inguino-scrotal folds are affected. The condition is worse in summer, during periods of stress, when wearing nylon clothing and following laborious work. Relieving factors include swimming, increased frequency of bathing and application of a mild topical steroid cream.

Currently the patient has an affected area over the left inner thigh and scrotum. This episode was described by the patient as being mild when compared to previous episodes, but the patient would like to start treatment to prevent further maceration of the skin.

Past medical and surgical history:

Past medical history

Hypertension
Diabetes Mellitus Type 2
Asthma
Ischaemic heart disease with previous episodes of Angina (Angiogram and PCI done)

Past surgical history

Endoscopy for epigastric pain done 30 years and 20 years ago; both were negative.
Angiogram and PCI done 7 years ago.

Drug history:

Drug	Dosage	Frequency	Type	Reason
Metformin	500mg	TDS	Biguanide	Type 2 Diabetes Mellitus
Perindopril	8mg	BD	ACE Inhibitor	Hypertension
Amlodipine	5mg	Once daily	Calcium Channel Blocker	Hypertension
Aspirin	75mg	Once daily	Anti-platelet	Ischaemic Heart disease
Simvastatin	40mg	Nocte	Statins	Ischaemic Heart disease
Salbutamol	-	PRN	Bronchodilator	Asthma

Allergies:

Betamethasone Cream

Family history:

J.M.'s mother suffered from sub-mammary fold fissuring, Hailey-Hailey disease, however no histological diagnosis was made.
J.M.'s sister was diagnosed with Hailey-Hailey disease a few years after his diagnosis.
J.M. has 2 sons and a daughter. One of the sons suffers from eczema and Hailey-Hailey was excluded following investigations. The youngest son is suspected to be suffering from the same condition but has not yet sought medical attention.

Social History:

Occupation: The patient is a retired civil servant.
Status: J.M. is a widower, since 10 years ago. The condition did not affect the relationship with his wife, since a physician had put their mind at rest that it was not contagious.
Habits: The patient is an ex-smoker since the age of 15 years but stopped 25 years ago. He smoked 2 packets daily. He consumes alcohol socially.
Lifestyle: The patient led a very busy lifestyle especially due to his occupation. The condition affected him both physically and psychologically, due to the pain, odour, and persistent fear of having a sexually transmitted disease prior to the correct diagnosis.

Systemic inquiry:

- General Health: Patient looks well in general. No loss of appetite or weight
- Cardiovascular System: None
- Respiratory System: Recent onset of shortness of breath on activity especially when climbing stairs and slopes. No accompanying chest pain, cough or lower limb oedema.
- Gastrointestinal System: None
- Genitourinary System: None
- Central Nervous System: None
- Musculoskeletal System: None
- Endocrine System: None

Discussion of results of general and specific examinations:

On general inspection the patient appeared well and not distressed. On examination of the affected areas, areas of hyperpigmentation were noted over both axillae, with the left axilla being more prominent, and both inner thighs. There was erythema, maceration and fissuring over the left inner thigh extending to the left scrotum (Figure 1). There were no vesicles or discharge however a slight malodour was noted.

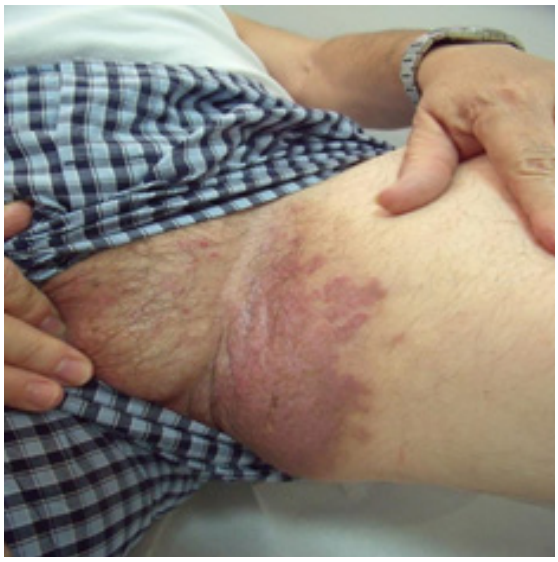

Figure 1: The affected area at presentation over the left inner thigh/scrotum.

Areas of hyperpigmentation and dryness were also noted over both shins, likely due to venous insufficiency. Mild lower limb pitting oedema was also present.

Differential diagnosis of intertrigo:

- Seborrhoeic Eczema
- Flexural Psoriasis
- Candidiasis
- Tinea Corporis
- Erythrasma
- Acanthosis Nigricans
- Pemphigus Vegetans

Diagnostic procedures:

Laboratory Exams:

Skin Biopsy: Date: 20/5/2000

Test: 5mm punch biopsy from right axilla.
Justification for test: To confirm diagnosis.
Result: Sections from the skin show epidermal hyperplasia with suprabasal acantholysis that involves the spinous layer giving a 'dilapidated brick wall' appearance. Corps ronds and grains are infrequent.
Conclusion: Hailey-Hailey disease.

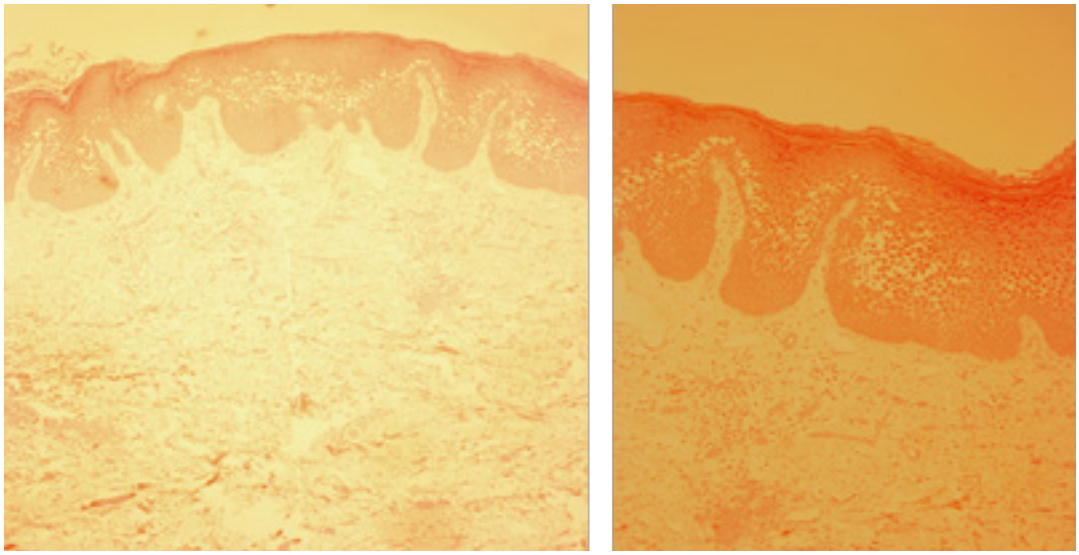

Figure 2: Histology photos of Mr. J.M. showing characteristic features of Hailey-Hailey disease, including epidermal hyperplasia with suprabasal acantholysis.

Diagnosis:

Hailey-Hailey disease is a rare autosomal dominant blistering disorder of the skin which results in defective adhesion of keratinocytes resulting in breakdown of affected skin layers[1]. First signs of the condition usually appear between ages of 15 to 40, 28 years in the case of Mr. J.M. Affected individuals complain of red, scaly areas or small blisters at areas of friction such as inner thighs and axillae, as in this patient. These areas may become secondarily infected by bacteria, fungi or viruses explaining the malodorous discharge the patient describes[2]. The clinical presentation and strong family history pertaining to Mr. J.M. give a strong indication of Hailey-Hailey disease, however a biopsy was still done to confirm diagnosis[3]. The skin biopsy showed suprabasal acantholysis involving the spinous layer giving a 'dilapidated brick wall' appearance, which is typical of Hailey-Hailey disease[6].

Final treatment and follow ups:

Patient was advised to apply a 1:1 mixture of Hydrocortisone butyrate 0.1% cream and Clotrimazole Cream to affected areas until resolution.

In addition, he was prescribed Ciprofloxacin 500mg BD PO x 2weeks.

Fact Box 8:

Title: Hailey-Hailey disease

General overview: Hailey-Hailey disease is a rare autosomal dominant blistering condition which was first described by the Hailey brothers in 1939. It is sometimes called 'familial benign chronic pemphigus', but this creates confusion in the medical literature. Pemphigus is a general term for a group of autoimmune blistering skin disorders, whilst Hailey-Hailey is not an autoimmune disorder but a distinct genetic disorder[4]. It can occur at any age, but usually appears in the third or fourth decade. Clinically the condition has a fluctuating course and both the activity and the affected areas may vary[5].

The defect responsible has been identified on ATP2C1 gene found on chromosome 3q21-24. This gene codes for the protein Secretory Pathway Calcium/manganese-ATPase (SPCA1), which is a calcium and manganese pump. The keratinocytes normally stick together via desmosomes and due to this defect leading to insufficient calcium, the desmosomes do not assemble properly[2,6-7]. Normally the cells are packed together tightly like bricks and mortar. Patients with this Hailey-Hailey disease have defective 'mortar' leading to the cells falling apart, reminiscent of a dilapidated brick wall[6].

Signs and Symptoms:

Clinically it typically presents with a painful erosive rash in the intertriginous areas namely the axillary (Figure 3), inguinal, perineal (Figure 1) and neck folds. At first they come and go leaving no scars. They can become thickened if present for some time. The skin often breaks down leaving painful fissures. Secondary bacterial infection gives rise to a malodour[2,6]. Mucous membranes are less affected. Longitudinal white lines on the nails may be found.

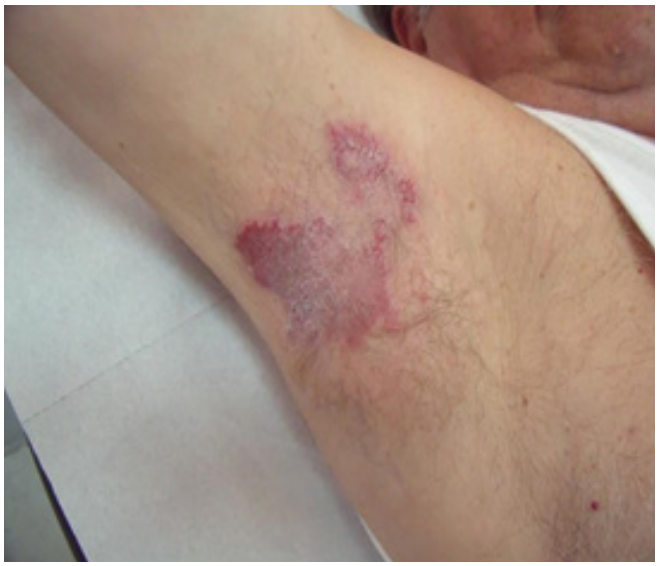

Figure 3: An affected area at the axilla during a previous flare up.

Epidemiology: No precise data is available on the incidence of Hailey-Hailey disease. Many patients lack an accurate diagnosis or do not seek treatment. It causes discomfort but is not a life threatening condition and does not affect life expectancy. Both sexes are affected equally and there is no apparent difference in prevalence among different ethnic groups[7].

Aggravating factors: Mechanical irritation, hyperhydrosis, bacterial, fungal and viral super infection and maceration of the skin are considered important aggravating factors[8]. Most patients find that their condition worsens during the summer months[6].
Prognosis: Many patients have long remissions and may improve with age.

Management: There is no cure for the disease and treatment aims at reducing symptoms and preventing flare ups. The mainstay of treatment includes topical steroids and appropriate use of topical or systemic antimicrobials. It is important to educate patients to avoid aggravating factors such as sweating, synthetic and tight clothing and being overweight. Emphasis should be made on strict glycaemic control in diabetics. Retinoids, ciclosporin, dapsone, methotrexate, botulinum toxin to reduce sweating and laser therapy have been used with variable results[6].

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Case Number 9
Superior Mesenteric Venous Thrombosis

Ramona Camilleri
Reviewed by: Mr. Ernest Ellul

Case summary:

Demographic details:
Mr. G.B., male, Birkirkara.
Referred from: GP.

Mr. G.B., a 69-year-old gentleman, was admitted with severe periumbilical pain radiating to the left lower quadrant. A diagnostic CT scan revealed superior mesenteric vein thrombosis as the underlying cause for the pain. In view of the fact that there were no contraindications to thrombolysis, it was possible to manage this patient with medical treatment using recombinant tissue plasminogen activator (rt-PA; Alteplase). The patient's condition improved and he was deemed fit for discharge on long-term warfarin ten days after admission.

The aetiology of thrombus formation in this gentleman is not as yet known. Further investigations will need to be carried out in order to find the underlying cause.

Presenting complaint:

Gentleman presented with a three week history of episodic worsening lower abdominal pain, associated with nausea and one episode of vomiting.

History of presenting complaint:

The pain was severe in nature, worse in the periumbilical area and in the left lower quadrant. It was associated with nausea and one episode of vomiting. It was not relieved by rest, paracetamol or by opening bowels.

The patient complained of reduced appetite and reduced frequency of bowel opening. Patient last opened his bowels on the morning of admission. He denies any blood with stools, malaena, haematemesis or coffee-ground vomitus.

There was no associated weight loss, fever, chills, rigors or lower urinary tract symptoms.

Past medical and surgical history:

Past medical history:

Chronic obstructive pulmonary disease
Hypertension
Hypercholesterolemia
Depression

Past surgical history:

Stabilization of T12 and L1 fracture (2009)
Movement under anaesthesia and external fixation of fractured tibia and fibula (2009)

Drug history:

Drug	Dosage	Frequency	Type	Reason
Ipratropium	2 puffs	BD	Anticholinergic	Shortness of breath
Budesonide	2 puffs	BD	Inhaled corticosteroid	Shortness of breath
Quetiapine	50mg	Nocte	Atypical antipsychotic	Depression
Lorazepam	2mg	Nocte	Short-acting benzodiazepine	Depression
Paroxetine	20mg	Daily	SSRI antidepressant	Depression
Simvastatin	40mg	Nocte	Statin	Hypercholesterolaemia

The patient suffers from no known drug allergies.

Family history:

Father died of a myocardial infarction at 50 years of age.
Mother had hypercholesterolaemia.

Social history:

Mr. G.B. smokes four cigars daily and does not drink alcohol. He lives with his wife and has good social support. He is fully mobile and copes well with activities of daily living. He is currently a pensioner and used to work as a teacher.

Systemic inquiry:

Systemic enquiry revealed episodic headaches but was otherwise unremarkable.

Discussion of results of general and specific examinations:

General examination:
Patient was alert, not distressed and afebrile. Glasgow Coma scale 15/15.

Respiratory examination:
Respiratory rate: 26 breaths/min
Oxygen saturations: 100% on air.
Chest was clear and there was good air entry bilaterally

Cardiovascular examination:
Capillary refill time: <2seconds
Pulse: 100bpm
Blood pressure: 185/95mmHg
Heart sounds: HS1+ S2+0

Abdominal examination:
Soft abdomen, no distension, tender in epigastrium and left lower quadrant. No rebound tenderness and

no guarding. Percussion tenderness present on left side of the abdomen. No masses were palpable.

Direct rectal examination: brown stools, enlarged prostate, no blood or malaena present.

Differential diagnosis:

- Superior mesenteric vein thrombosis
- Superior mesenteric artery occlusion
- Abdominal malignancy
- Diverticulitis
- Inflammatory bowel disease
- Pancreatitis
- Submucosal haemorrhage or haematoma

Diagnostic procedures:

Laboratory exams:

Test: Bloods: Complete blood count.
Justification for test: Infection, anaemia, thrombocytopaenia.
Result: White cell count raised, raised neutrophils.
Conclusion: Leukocytosis present. No anaemia or thrombocytopaenia.

Test: Bloods: Urea and electrolytes, creatinine.
Justification for test: Renal function, electrolyte balance.
Result: Potassium raised (5.92).
Conclusion: Hyperkalaemia present.

Test: Bloods: Amylase.
Justification for test: Query pancreatitis.
Result: Normal.
Conclusion: Pancreatitis unlikely.

Test: Bloods: Arterial blood gases.
Justification for test: Acid-base status, query sepsis.
Result: pH 7.65, pCO2 15.6, Base Excess -6.1, HCO3: 13.6, Lactate 1.9.
Conclusion: Compensated respiratory alkalosis, no sepsis.

Test: APTT, INR.
Justification for test: Baseline, query need for thrombolysis.
Result: INR: 1.13, APTTr: 0.90.
Conclusion: No contra indication to thrombolysis.

Instrumental exams:

Test: Chest X-ray.
Justification for test: Active lung lesions, hypertension, air under diaphragm.
Result: No active lung lesion was noted. No cardiomegaly present and no perforation suspected.
Conclusion: Normal chest X-ray.

Test: Abdominal X-ray.
Justification for test: Acute abdomen, bowel perforation, impacted faeces, bowel obstruction.
Result: No air or fluid levels were noted. Metallic fixation of the vertebral bodies was seen.
Conclusion: No signs of bowel perforation, obstruction or impacted faeces.

Test: CT scan (Figure 1).
Justification for test: To find aetiology of pain, exclude malignancy.
Result: Superior mesenteric vein thrombosis extending to the portal confluence with correspondent jejunum and proximal ileum. Mesenteric panniculitis. Small ascites. Diverticular disease of the large bowel.
Conclusion: Superior mesenteric vein thrombosis diagnosed.

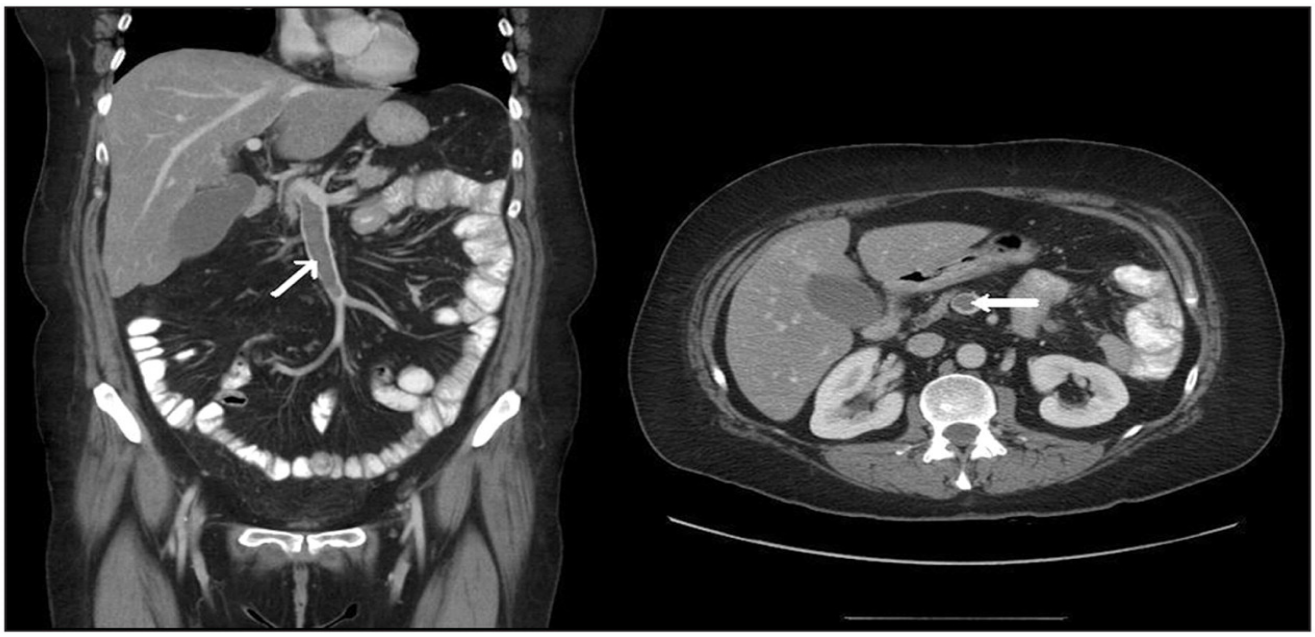

Figure 1: CT scan showing thrombosis of superior mesenteric vein.

Management and therapy:

1. Patient was reviewed and admitted to intensive therapy unit (in view of his condition).
2. He was kept nil by mouth.
3. Nasogastric tube was inserted and stomach contents aspirated.
4. Urinary catheter was inserted with urinometer – input and output charting was monitored hourly.
5. Fluids were administered – 1L normal saline alternating with 5% dextrose I L 6 hourly.
6. Parameters were monitored hourly (including: pulse, blood pressure, temperature, oxygen saturations).
7. Medications were started as shown below.

Drugs:

Drug	Dosage	Frequency	Type	Reason
Cefuroxime	750mg IV	TDS	Antibiotic	Empirical
Metronidazole	500mg IV	TDS	Antibiotic	Empirical
Omeprazole	40mg IV	Daily	Protein pump inhibitor	Reduces risk of bleeding
Paracetamol	1g IV	QDS	Analgesic	Pain relief
Pethidine	75mg IM	TDS/PRN	Analgesic	Pain relief

Prochlorperazine (Stemetil)	12.5mg IM	TD/PRN	Dopamine antagonist	Anti-emetic
Alteplase	See below	See below	Tissue plasminogen activator	To dissolve thrombus in SMV

Thrombolysis: In view of the fact that there was probably prolonged onset and there were no contraindications to thrombolysis, it was decided to thrombolyse the patient using alteplase 0.9mg/kg. Patient weighed 82kg and therefore a total of 73mg alteplase was administered as follows:
-10mg as IV bolus
-50mg over 1 hour
-15mg over the next hour
Following thrombolysis, an unfractionated heparin infusion 6000U IV 6-hourly was started. APTT was checked after 6 hours of starting heparin and an APTTr of 2.5 - 3 was aimed for.

Diagnosis:

Superior mesenteric vein thrombosis is a relatively uncommon condition which carries significantly high morbidity and mortality rates. It causes 5-15% of cases of acute mesenteric ischaemia and its prognostic outcome depends on early diagnosis and adequate treatment. A high level of clinical suspicion is therefore required to ensure prompt and effective treatment administration.

Relevant Anatomy (Figure 2):

The superior mesenteric vein is formed by the jejunal, ileal, ileocolic, right colic and middle colic veins. The inferior mesenteric vein joins the splenic vein which in turn join the superior mesenteric vein to form the portal vein. The superior mesenteric vein drains the small intestine, caecum, ascending colon and transverse colon.

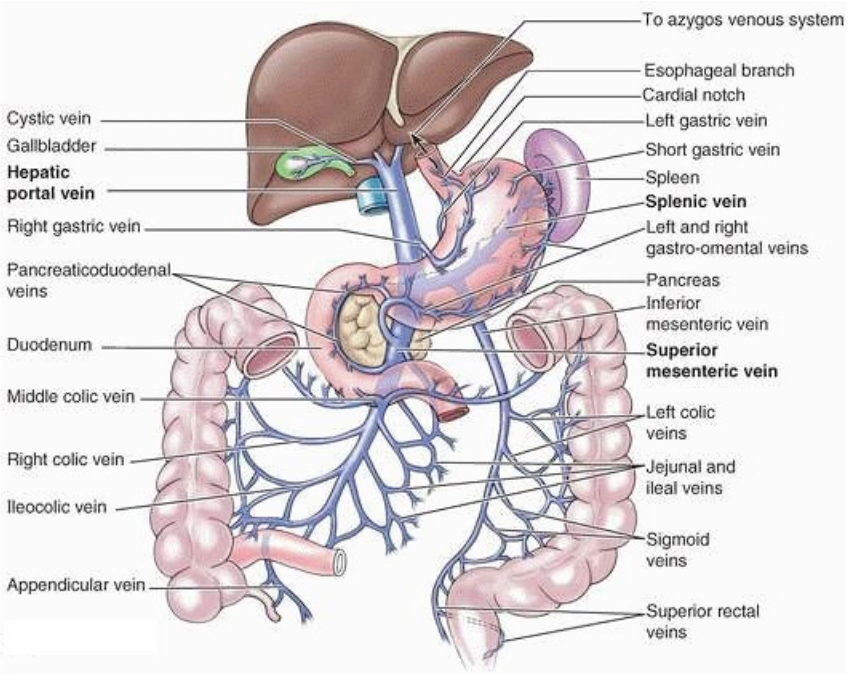

Figure 2: Anatomy of superior mesenteric vein.

Aetiology:

- Patients at increased risk of thrombus formation include those having:
- Hypercoaguable states – polycythaemia vera, protein C deficiency, protein S deficiency, anti-

thrombin III deficiency.
- Visceral infection and inflammation – diverticulitis, pancreatitis, perforated viscus.
- Malignancy (by direct invasion and by hypercoaguable state).
- Abdominal trauma.
- Post-abdominal surgery – including, but not limited to, post-splenectomy, Roux-en-Y gastric bypass, colectomy.
- Portal hypertension.
- Drugs – oral contraceptive pill.

The most common cause is intra-abdominal sepsis and up to 20% of cases are idiopathic (Medscape, 2012).

Pathophysiology:

The underlying pathophysiology of acute mesenteric ischaemia is due to an increased fluid volume in the bowel wall and lumen which results in systemic hypovolaemia and haemoconcentration. Thrombus formation in the superior mesenteric vein occludes the outflow of blood. This together with resulting bowel wall oedema, impede inflow of arterial blood leading to bowel ischaemia.

Presentation:

Patient typically complains of generalised severe periumbilical pain which gradually worsens over a few days and is associated with fever, nausea and vomiting. On examination, the abdomen is usually distended and tender.

Relevant Investigations:

Haematological investigations mainly help to exclude other possible causes. They may reveal leucocytosis and haemoconcentration. Other useful haematological investigations which would aid in diagnosing the cause, include protein C and S deficiencies, anti-thrombin III antibodies, abnormalities in lupus anticoagulant, cardiolipin antibody, platelet aggregation studies.

Imaging should include:

-Abdominal X-ray - may reveal dilated loops of bowel, air under diaphragm
-CT scan or angiography – diagnostic
-ECG – especially in this case in view of hyperkalaemia

Treatment:

It is crucial to determine the underlying cause of the patient's hypercoaguable state and treat it appropriately.

Supportive:

1. Ensure patent airway, breathing present, circulation stable
2. NG decompression by nasogastric tube insertion and suction
3. Fluid resuscitation
4. Bowel rest
5. Fluid input-output charting

Pharmacological:

- Lytic therapy: Thrombolysis using recombinant tissue plasminogen activator (rt-PA) administered according to local protocols.
- Anticoagulation: Heparin administered initially until the desired APTT range was achieved. Once an APTT of 2.5-3 was achieved, the patient was converted to warfarin.

Surgical:

- Thrombectomy with thrombolysis
- Intravenous catheterisation with thrombolytic infusion
- Excision of infarcted non-viable bowel

Indications for surgery include:

- Peritonitis
- Bowel infarction
- Haemodynamic instability
- Inadqeuate response to medical treatment

Prognosis:

This is highly dependent on the time taken to diagnose this condition and treat it appropriately. It is associated with 30% mortality rate and 25% recurrence rate in patients not given anticoagulant therapy. Anticoagulant therapy combined with surgery is associated with the lowest recurrence rate (3-5%). Superior mesenteric vein thrombosis is associated with the best prognosis from all aetiologies of mesenteric ischaemia.

Final treatment and follow ups:

The patient's parameters and progression of general condition were monitored. He was discharged from the intensive therapy unit two days after admission to hospital and was admitted to a surgical ward.

His APTTr was monitored and the dose of heparin was increased or decreased by 500U accordingly. Once the target APTTr range (2.5-3) was achieved, the patient was started on warfarin. He was started on 10mg warfarin for two days and on the second day his International Normalised Ratio (INR) was taken. On the third day since warfarin was started, his warfarin dose was reduced to 5mg (as per protocol). Heparin was stopped once his INR was more than 2. Antibiotics were also stopped.

Mr. G.B's condition got progressively better. He opened his bowels, was started on light feeds and was mobilised. He was deemed fit for discharge ten days after admission, on 5mg warfarin. He was informed that he will need lifelong warfarin and was informed regarding the associated side-effects and interactions. He will be followed up at the ACCX clinic daily for two weeks and then accordingly.

A repeat CT chest thorax and abdomen was performed in order to exclude any underlying pathology responsible for the thrombosis. The CT showed clear lungs with scattered bronchiectasiae, no lymph node enlargement, no organ pathology or free fluid. Thrombosis of the superior mesenteric vein was seen to have completely resolved.

The patient will be followed up at surgical outpatients clinic in three months and was referred for a haematological consultation for coagulation studies.

Fact Box 9:

Title: Superior Mesenteric Vein Thrombosis

Incidence: 10-15% of cases of mesenteric ischaemia.

Risk Factors: Hypercoaguable states, abdominal sepsis and inflammation, malignancy, trauma and post-abdominal surgery.

Presentation: Insidious onset, abdominal pain, abdominal distension and tenderness.

Diagnostic Investigation: CT scan, MRI

Treatment: Resuscitation,
Pharmacological – thrombolysis, anticoagulation
Surgical – thombectomy with infusion of thrombolysis, excision of non-viable bowel

Prognosis: High mortality attributed to long delay in diagnosis. If treated promptly and adequately, mortality is significantly reduced and recurrence is reduced to 3-5%.

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Case Number 10
Dandy-Walker Syndrome

Gianluca Gonzi and Gilbert Gravino
Reviewed by: Dr. Stephen Attard

Case summary:

Demographic details:
SA, female.
Aged 8.
Resident in Pembroke.

Ms. SA is an 8-year-old known case of Dandy-Walker syndrome managed through supraventricular and infraventricular peritoneal shunts. Having acquired normal developmental milestones till seven years of age, she currently has cognitive impairment, gait abnormality and speech defects following shunt complications.

Presenting complaint:

Cognitive Impairment
Speech Deficit
Locomotor Disturbance

History of presenting complaint:

Ms. SA is a known case of Dandy-Walker syndrome diagnosed at two years of age on the 8th January 2007 following investigation of supposed meningitis. MRI studies revealed the presence Dandy-Walker cyst malformation which was responsible for raised intra-cranial pressure. A supraventriculo-peritoneal shunt was inserted via a right occipital bore-hole.

Ms. SA had reached developmental milestones besides delayed speech development and a clumsy gait. She was described as an intelligent girl and was coping with the educational activities encountered in primary school.

The patient progressed to suffer multiple episodes of shunt failure typically following an upper respiratory tract infection. She frequently presented with fronto-occipital headaches that would wake her up during the night, being exacerbated when lying down and associated with multiple episodes of vomiting and irritability. The first such episode was on 28th February 2008, and a second episode took place on 2nd February 2012. In each case the cause was due to secondary raised intracranial pressure following shunt obstruction and required surgical revision.

On the 6th April 2012 Ms. SA at 7 years of age presented to casualty with a presentation similar to previous episodes of shunt failure but also had an episode of a generalised tonic-clonic seizure. On examination the patient was neurologically intact and had a negative Kernig's sign and no neck stiffness. On fundoscopy bilateral papilloedema was found, being greater on the left side. The shunt was also tense and indicated failure of drainage, dilated ventricular systems were subsequently revealed through CT scanning. A new shunt was inserted to drain the Dandy-Walker cyst through a right parietal borehole which was connected with the supra-ventricular shunt through a Y-connector.

Following the procedure Ms. SA suffered cardiac arrest a total of three times requiring cardiopulmonary resuscitation and developed acute respiratory distress syndrome requiring ITU admission. Following this she went into a coma lasting six weeks, where upon returning to consciousness she was found to have cognitive impairment, loss of speech ability and an impaired gait.

Ms. SA was seen on Wednesday 26th March 2014 at specialist neurosurgical review wherein her gait and speech was assessed. She had a fourth shunt failure in December 2013 with no complications which resulted in revision of the ventriculo-peritoneal shunts. Her speech and gait have greatly improved and she is now capable of conversation but has significant cognitive impairments. She is not able to stand independently but is able to walk with assistance of devices.

Past medical and surgical history:

Past Medical History

- Diagnosed Pulmonary Stenosis at birth with several cyanotic spells requiring admission to SCBU
- Coarctation of the Aorta
- Dandy-Walker Syndrome
- Double kidney on the right diagnosed on 10/01/07
- Missing left little toe and aplasia of her left little finger noted at birth
- 30% bilateral sensorineural hearing loss treated with hearing aids
- Cleft soft palate

Past Surgical History

- Ventriculo-peritoneal shunt first done on the 8/01/07. Revisions of the shunt carried out on 6/14/12 and 28/02/12, 13/12/13
- Adenoidectomy plus grommet insertion February 2008

Drug history:

Patient is currently on no regular therapy and does not suffer from any known drug allergies.

Family history:

No known family history of Dandy-Walker syndrome or any other congenital malformations.

Social history:

Ms. SA is an only child currently residing with her mother and grandfather in Pembroke. She currently attends primary school with the aid of a Learning Support Assistant.

Systemic inquiry:

- General Health: Patient looks well with no recent weight loss.
- Cardiovascular System: No chest pain or palpitations.
- Respiratory System: No cough, wheeze or shortness of breath. The child complains of early morning drowsiness and tiredness through the day with episodes of gasping during sleep indicative of sleep apnoea.
- Gastrointestinal System: No dysphagia, no abdominal pain, slight constipation, no diarrhoea.
- Genitourinary System: No urinary frequency or dysuria.

- Central Nervous System: Suffers from occasional frontal headaches responding to paracetamol.
- Musculoskeletal System: Nil of note.
- Endocrine System: Nil of note.

Current therapy:

The patient currently has multiple ventriculo-peritoneal shunts for the management of Dandy-Walker Syndrome. She also regularly attends physiotherapy and speech therapy.

Discussion of results of general and specific examinations:

The patient has visible facial dysmorphic features with close set eyes, low lying ears and a beaked nose; a missing left little finger was also noted, bilateral hearing aids were also present. On cardiorespiratory examination a loud S2 was noted with no systolic or diastolic murmurs, slight radiofemoral delay was also found.

Ms. SA showed excellent neurological progress from previous examinations with good cognition and improved speech. Her gait is slightly ataxic and she is able to walk with assistance, otherwise being neurologically intact.

Differential diagnosis:

Differentiation from other posterior fossa cystic lesions such as mega cisterna magna and retrocerebellar arachnoid cyst is straightforward through the use of standard neuroimaging. The position of the choroid plexus in the fourth ventricle helps in differential since this is normal with an arachnoid cyst, displaced into the superior cyst wall with a Blake pouch, and absent in Dandy-Walker malformation.

Diagnostic procedures:

Laboratory exams:

Karyotype done on 21/2/2012 showing 46 XX – normal female karyotype

Imaging:

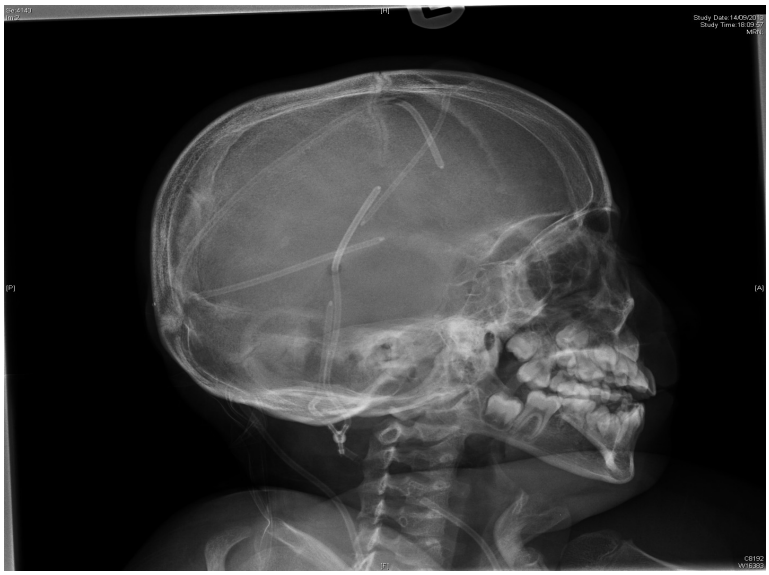

Figure 1: Lateral View Shuntogram

Description of Image

This is a lateral skull X-ray indicating a total of four shunts. Note the Y-connector and valve positioned inferior to skull base and posterior to the vertebral column on the radiograph.

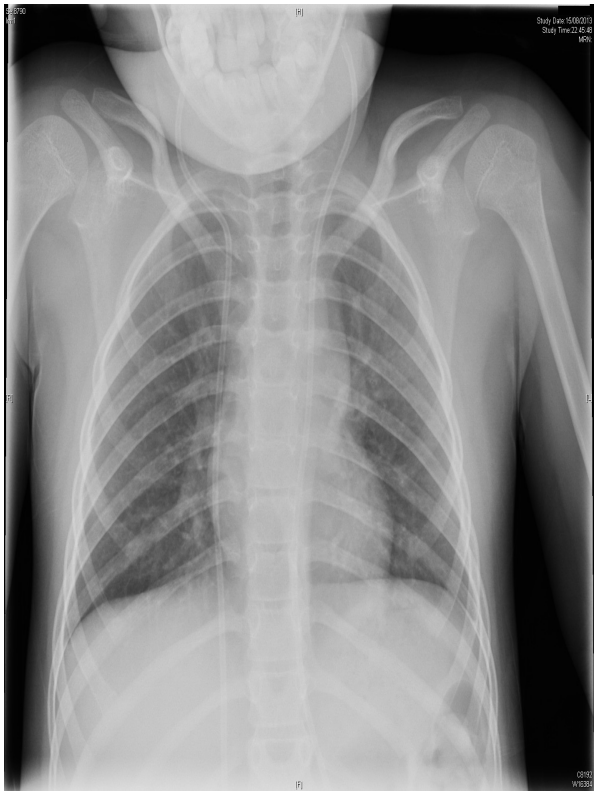

Figure 2: PA Chest X-ray

Description of Image

The above is a posteroanterior chest X-ray of the patient exhibiting the ventriculo-peritoneal shunts.

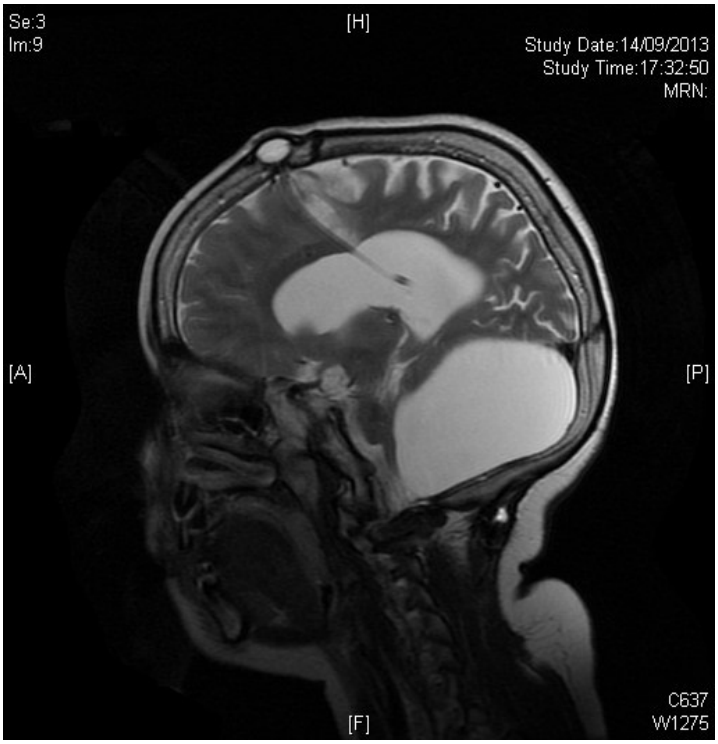

Figure 3: Sagittal T2 weight MRI study

Description of Image

This is a sagittal T2-weighted image. A fluid filled cyst is present in the posterior cranial fossa with superior displacement of the tentorium cerebelli and hypoplasia of the cerebellar vermis consistent with Dandy-Walker syndrome. There is also ventriculomegaly and visible supratentorial shunt.

Diagnosis:

Dandy-Walker Malformation with multiple ventriculoperitoneal shunts.

Final treatment and follow-ups:

To be reviewed at Child Outpatients in six months' time.

Fact Box 10:

Title: Dandy-Walker Syndrome

Brief Overview: The Dandy-Walker syndrome refers to a rare congenital malformation characterised by agenesis or hypoplasia of the cerebellar vermis, cystic dilatation of the fourth ventricle and an enlarged posterior fossa[1]. The newborn infant may be symptomatic or asymptomatic with the majority of cases presenting with a macrocephaly and raised intracranial pressure[2-3]. Around 80% are diagnosed at infancy, whereas others are identified in adulthood[2-5]. The aetiology is not well understood but is probably multifactorial. In most cases the syndrome is isolated but it may also be associated with defined Mendelian disorders, chromosomal abnormalities, and other syndromes such as Ritscher-Schinzel, Hydrolethalus, and Marden-Walker[6-12].

Epidemiology: Osenbach and Menezes, estimated that isolated Dandy-Walker Syndrome has a prevalence of about 1 per 30,000 live births and a study by Hirsch revealed that it accounts for about 2-4% of infantile hydrocephalus[4,13]. A study by Long et al., involving a population based survey of the foetal posterior fossa anomalies found an incidence of about 1 per 11,000[14].

Symptoms and signs:[2-3,15]

- macrocephaly
- symptoms of raised intracranial pressure such as lethargy, vomiting, and irritability
- occipital encephalocoele (unusual presentation)
- apneoa (unusual presentation)
- nystagmus
- motor deficits
- intellectual impairment

Investigations:[12, 16-17]

- Magnetic Resonance Imaging (MRI) is the preferred investigation for detailed imaging.
- Ultrasound is useful in prenatal diagnosis which may reveal an enlarged fourth ventricle at 14-16 weeks gestation as a transient phenomenon and therefore allows diagnosis close to 20 weeks gestation.

Treatment: If progressive hydrocephalus is evident, the current treatment of choice involves various techniques of shunt placement. Some specialists prefer an initial attempt with a standard ventriculo-peritoneal shunt, others prefer a cystoperitoneal derivations, and other recommend combined shunting of the cyst and the lateral ventricles[4,13,18]. Physiotherapy is also an important component of management to ensure optimal psychomotor development.

Prognosis: Survival and outcome are largely dependent on other associated findings, such as cardiac anomalies and other central nervous system malformations. Also, preservation of vermian lobulation and the absence of supratentorial anomalies favour a better intellectual prognosis[19-20]. Shunt dysfunction is a source of complication but sudden unexpected deaths unrelated to shunt problems have also been reported[21].

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Case number 11
The Complex Heart

Isaac Bertuello & Matthew Baldacchino
Reviewed by: Professor Simon Attard Montaldo

Case summary:

WB, a four-month-old Caucasian baby boy from Mosta was admitted to the paediatric ward in Mater Dei following an incidental finding of dextrocardia, failure to thrive and developing signs of respiratory distress, all indicating possible chronic heart failure.

Following examination and testing, baby WB was found to have a double outlet right ventricle, transposition of the great vessels, a VSD with blood mixing, and an element of heart failure. WB is termed to be having a complex heart. The patient is currently not fit for operation and is being managed on feeds to facilitate his growth.

Presenting complaint:

WB had incidental findings of dextrocardia, failure to thrive and signs of respiratory distress, raising concerns about chronic heart failure.

History of presenting complaint:

WB appeared well at home, with no obvious symptoms of chronic heart failure, no cyanosis, no chest infections, afebrile and seemingly feeling well. His referral was following an incidental finding during routine immunisation and was not prompted by any obvious signs noted by the parents.

Past medical and surgical history:

Past medical history:

Gestation & Birth:

- Normal gestation
- Twelve-hour labour
- Delivered by emergency caesarean section
- No perinatal complications
- No referrals to NPICU
- Birthweight: 3.89 kg
- Other: nil of note

Past surgical history:

Nil of note

Drug history:

Nil of note

Family history:

WB is the second child of a 38-year-old mother, and a 36-year-old father, who also have an 8-year-old son.

WB's mother is allergic to penicillin, but other than this, there is no history of ill family members.

Social history:

WB is the second child in the family, and lives in a supporting household.

Systemic inquiry:

- General Health: Generally looks well and alert but is pale and mildly cyanosed.
- Cardiovascular System: Tachycardic (heart rate of 120 bpm), well perfused, capillary refill under 2 seconds, cyanotic tinge around the mouth, apex beat felt on the right with heart sounds loudest in the right side of the chest, heaves felt in right 4-5 intercostal space veering to the right anterior axillary line and also felt along the right parasternum, and no murmurs, loud S2 with some splitting.
- Respiratory System: Tachypnoeic (respiratory rate 40/min), SpO_2 75% on air, significant subcostal recessions, indrawing of intercostal muscles, tracheal tug, clear chest sounds.
- Gastrointestinal System: Currently feeding, liver edge palpable on the left side extending 1.5 cm, abdomen is soft and non-tender.
- Genitourinary System: Nil of note.
- Central Nervous System: Nil of note.
- Musculoskeletal System: Reduced subcutaneous fat.
- Endocrine System: Nil of note.
- Others: Nil of note.

Current Therapy:

Cannula for venous access inserted and a CXR and echocardiogram ordered.

Discussion of results of general and specific examinations:

During the general examination it was evident that the baby was in distress and cyanosed. The apex beat was remarkably strong on palpation and the second heart sound was very loud because the aortic valve lies very superficial and close to the chest wall.

Diagnostic procedures:

Laboratory exams:

Test: Complete Blood Count.
Justification for test: Check haemoglobin level because of cyanosis.
Result: Patient had an increased red cell count, increased haemoglobin, a high haematocrit and increased red cell distribution width (RDW).
Conclusion: Shows attempted compensation for hypoxia by increasing the oxygen carrying capacity of the blood.

Test: Renal Profile (Serum).
Justification for test: Check that there is adequate renal function due to new cyanosis and heart failure.

Result: Patient had a low Creatinine and a high potassium.
Conclusion: Low Creatinine indicates that the kidneys are functioning normally while the high potassium is due to the potassium sparing diuretics.

Test: Calcium and Phosphate (Serum).
Justification for test: Check to see if electrolytes are normal because $CaPO_4$ tends to get reduced in children in heart failure and on diuretics.
Result: Patient had high calcium and a high phosphate.
Conclusion: Patient not having $CaPO_4$ lowering side effects from treatment.

Instrumental exams:

Test: Chest X-ray.
Justification for test: To confirm dextrocardia and check for situs inversus or radiological signs of heart failure.
Result: There is dextrocardia and total viscerus inversus. The liver is left-sided and the spleen is right-sided.
Conclusion: Diagnosis confirmed and mild signs of heart failure seen.

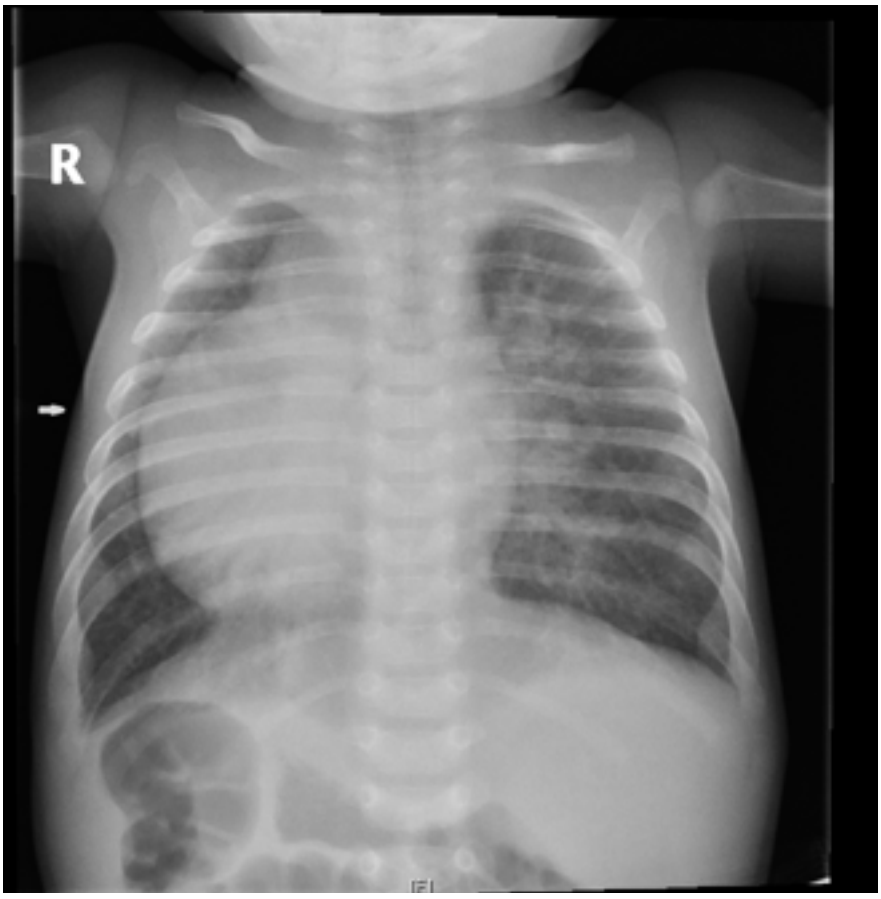

Figure 1 Chest X-ray showing dextrocardia.

Test: Abdominal Ultrasound.
Justification for test: To visualise all abdominal organs and their anatomy since situs inversus was found on chest X-ray.
Result: There is total viscerus inversus. The liver is left-sided. The spleen is right-sided. The liver, spleen, pancreas and kidneys are of normal size and structure. The gall bladder is contracted. The bladder is empty. No ascites or pleural effusions.

Conclusion: Situs inversus is present but all abdominal organs are still normal in size and structure although they are mirror images.

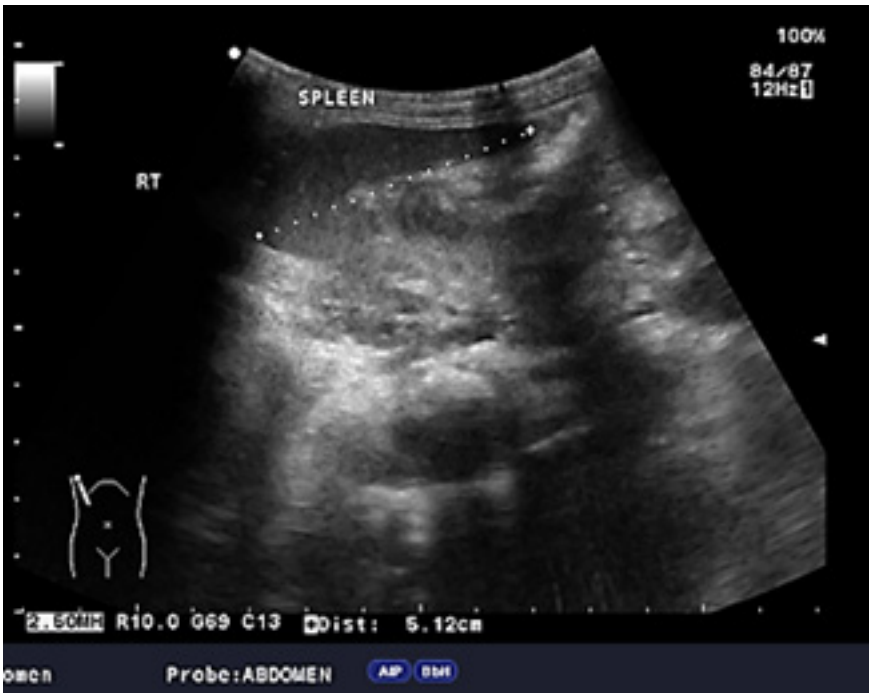

Figure 2: Ultrasound scan showing spleen on the right side.

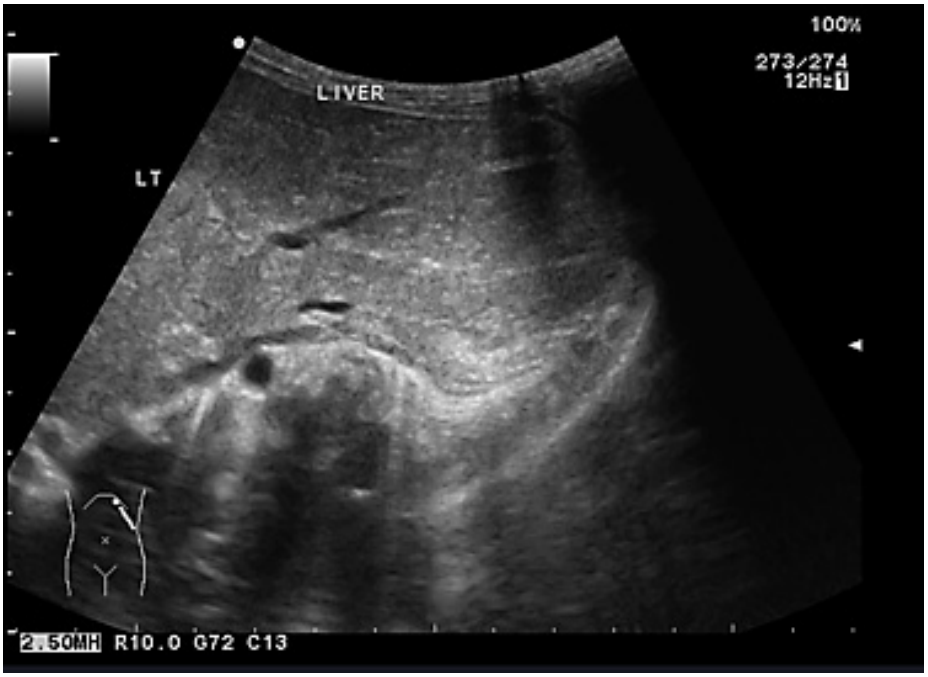

Figure 3: Ultrasound scan showing liver located on the left

Test: Echocardiogram.
Justification for test: To screen for congenital cardiac defects since patient has situs inversus and has a cyanotic tinge.
Result: There is dextrocardia and abdominal situs inversus. Inferior vena cava on the left and ductus arterious on the right. There is a very large right atrium and a smaller left atrium, inter-atrial septum is intact except for a small patent foramen ovale.
The right ventricle is enlarged and hypertrophied with multiple muscle bands and gives off both great arteries. The aorta is smaller and is centrally placed overriding a ventricular septal defect (VSD). The

pulmonary artery is much larger and is anterior and to the right of the aorta and can be seen to bifurcate. The aorta turns directly backwards and narrows down a bit where it joints the ductus arteriosus but there was no turbulence on Doppler.

The VSD extends from the inlet septum where it is relatively small to the outlet septum where it is 1.3cms across. There is another small VSD closer to the apex. There is moderate atrioventricular valve regurgitation. The pulmonary blood flow is unrestricted.
Conclusion: There is Dextrocardia, DORV (double-outlet right ventricle), a large VSD and unrestricted pulmonary blood flow present.

Therapy:

Drugs:

Drug	Dosage	Frequency	Type	Reason
Spirinolactone	4.5mg	BD	Aldosterone antagonist Diuretic	Reduce fluid load and prevent congestive heart failure
Furosemide	4.5mg	BD	Loop Diuretic	Reduce fluid load and prevent congestive heart failure
Duocal			Feeds	Increase calorie intake for weight gain as the patient is currently failing to thrive due to the excess energy consumption from his abnormal circulation

Diagnosis:

Dextrocardia, Double-outlet right ventricle, Ventricular septal defects and Transposition of the great vessels.

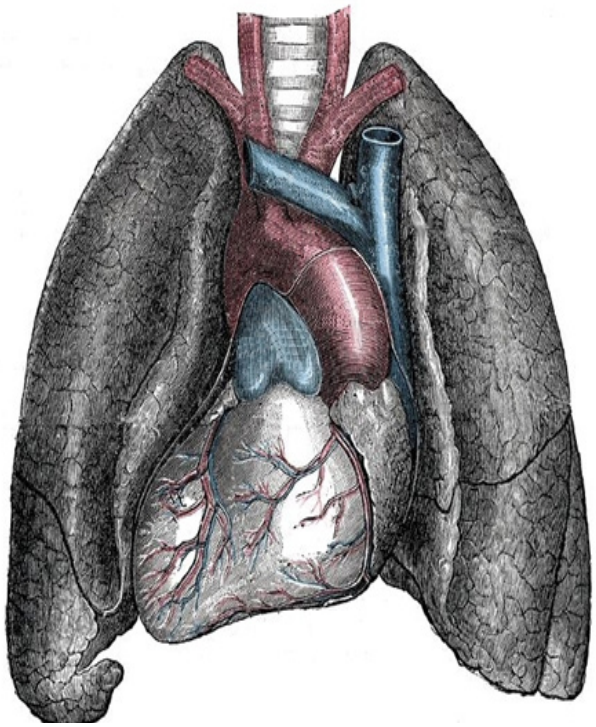

Figure 4: Diagram showing dextrocardia and transposition of the great vessels.

Final treatment and follow-ups:

The aim of treatment is to correct his cardiac defect by closing the VSD and exchanging the arteries with each other so as to make the heart function efficiently. However the patient cannot undergo this surgery as of yet because his weight is still too low at 3.8kgs. He needs to be at least 5kgs.

When the necessary weight is achieved he will be sent abroad to a specialised hospital where he will undergo a corrective procedure. However, prior to this the patient may need pulmonary artery banding to reduce excessive pulmonary blood flow and improve his heart failure whilst decreasing his failure to thrive.

Fact Box 11- Part 1

Title: Situs Inversus

Definition: Situs inversus (also called situs transversus or oppositus) is a congenital condition in which the major visceral organs are mirrored from their normal positions. The normal arrangement being known as situs solitus.

Effect on Anatomy: The condition affects all major structures within the thorax and abdomen. Generally, the organs are simply transposed through the sagittal plane. The heart is located on the right side of the thorax, the stomach and spleen on the right side of the abdomen and the liver and gall bladder on the left side. The left lung is trilobed and the right lung bilobed and blood vessels, nerves, lymphatics and the intestines are also transposed.

If the heart is swapped to the right side of the thorax, it is known as situs inversus with dextrocardia or situs inversus totalis. If the heart remains on the normal left side of the thorax, a much rarer condition (1 in 22,000 of the general population), it is known as situs inversus with levocardia or situs inversus incompletus. This case is thus a situs inversus with dextrocardia.

Prevalence: Situs inversus is thought to be present in 0.01% of the population.

Genetics: It is an autosomal recessive condition but is also X- linked in some cases.

Significance:

- In the absence of congenital heart defects, individuals with situs inversus are phenotypically normal, and can lead normal healthy lives, without any complications related to their medical condition.
- But there is a 5 –10% prevalence of congenital heart disease in individuals with situs inversus totalis, most commonly transposition of the great vessels, as in this case.
- The incidence of congenital heart disease is 95% in situs inversus with levocardia.

Diagnosis:

- Many people with situs inversus totalis are unaware of their unusual anatomy until they seek medical attention for an unrelated condition. The reversal of the organs may then lead to some confusion, as many signs and symptoms will be on the atypical side.
- For example, if an individual with situs inversus develops appendicitis, they will present to the physician with lower left abdominal pain, since that is where their appendix is located. Thus, in the event of a medical problem, the knowledge that the individual has situs inversus can expedite diagnosis especially if the person is unable to communicate.

Advice: Patients with this rare condition may inform their physicians before an examination, so the physician can redirect their search for heart sounds and other signs. Wearing a medical identification tag can help to inform health care providers in the event of the person being unable to communicate.

It is advisable to screen for Kartagener's Syndrome since about 25% of individuals with situs inversus have an underlying condition known as primary ciliary dyskinesia (PCD). PCD is a dysfunction of the cilia that manifests itself during the embryologic phase of development. Normally functioning cilia determine the position of the internal organs during early embryological development, and so individuals with PCD have a 50% chance of developing situs inversus. If they do, they are said to have Kartagener syndrome, characterised by the triad of situs inversus, chronic sinusitis and bronchiectasis. Cilia are also

responsible for clearing mucus from the lung and thus the dysfunction causes increased susceptibility to lung infections.

Other complications: Situs inversus also complicates organ transplantation operations as donor organs will more likely come from situs solitus (normal) donors. As hearts and livers are chiral, geometric problems arise when placing an organ into a cavity shaped in the mirror image. For example, a person with situs inversus who requires a heart transplant needs all the vessels from the transplant donor heart reattached to their existing ones. However, the orientation of these vessels in a person with situs inversus is reversed, thus alterations have to be made.

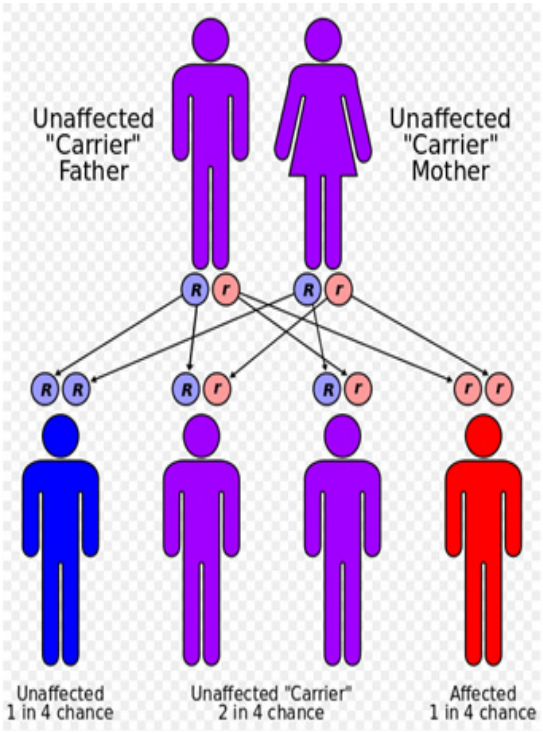

Figure 5: Diagram showing the autosomal pattern of transmission of dextrocardia.

Fact Box 11 - Part 2

Title: Transposition of the great vessels (TGV)

Definition: TGV is a group of congenital heart defects involving an abnormal spatial arrangement of any of the great vessels: superior and/or inferior venae cavae, pulmonary artery, pulmonary veins and aorta. Transposed vessels can present a large variety of atriovenous, ventriculoarterial and/or arteriovenous discordance. The effects may range from a change in blood pressure to an interruption in circulation, depending on the nature and degree of the misplacement and which vessels are involved. Although "transposed" literally means "swapped", many types of TGV involve vessels that are in abnormal positions, while not actually being swapped with each other.

Variants:

- Transposition of the great arteries, a condition where the congenital heart defect involves only the primary arteries, that is the pulmonary artery and aorta.
- Dextro-Transposition of the great arteries.
- In dextro-transposition of the great arteries (dextro-TGA) deoxygenated blood from the right heart is pumped immediately through the aorta and circulated to the body and the heart itself, bypassing the lungs altogether, while the left heart pumps oxygenated blood continuously back into the lungs

through the pulmonary artery. In effect, two separate "circular" (parallel) circulatory systems are created. It is called a cyanotic congenital heart defect (CHD) because the newborn infant turns blue from lack of oxygen.

- Levo-Transposition of the great arteries.
- Levo-Transposition of the great arteries is an acyanotic heart defect in which the primary arteries are transposed, with the aorta anterior and to the left of the pulmonary artery, and the morphological left and right ventricles are also transposed.

Difference between simple and complex TGV: In many cases, TGV is accompanied by other heart defects, the most common type being intracardiac shunts such as atrial septal defects including patent foramen ovale, ventricular septal defect, and patent ductus arteriosus. Stenosis or other defects of valves and/or vessels may also be present.
When no other heart defects are present it is called 'simple' TGV; when other defects are present it is called 'complex' TGV.

Treatment: For newborns with transposition, prostaglandins can be given to keep the ductus arteriosus open which allows mixing of the otherwise isolated pulmonary and systemic circuits. Thus oxygenated blood that recirculates back to the lungs can mix with blood that circulates throughout the body. This was not needed in this case because blood was mixing due to the VSDs present. Surgical correction is the definitive treatment for a transposition.

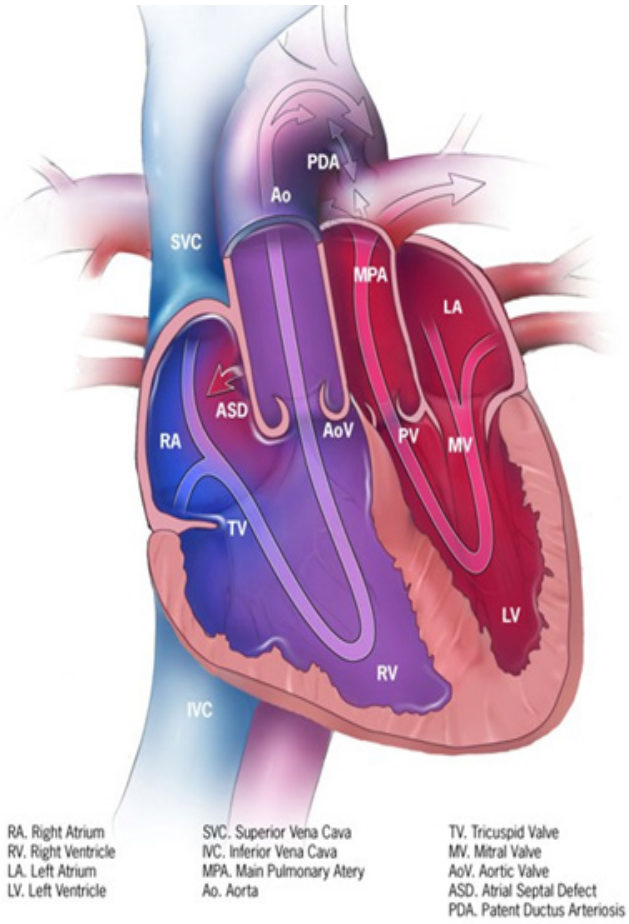

Figure 6: Diagram showing transposition of the great vessels.

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