Case Number 6
Mucinous Cystadenocarcinoma of the Appendix

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Case summary:

Demographic details:
Ms. GM, female, 67 years.
Referred from hospital.

GM, a 67-year-old female, was referred after an appendiceal mucocoele which had been noted and removed during a total abdominal hysterectomy with bilateral oophorectomy (TAH-BSO) was diagnosed on histopathology as being a mucinous cystadenocarcinoma. The patient presented with no signs or symptoms. The patient subsequently underwent a laparoscopic right hemicolectomy and is being followed up at surgical outpatients yearly to exclude recurrence of the malignancy.

Presenting complaint:

The patient was admitted for laparoscopic right hemicolectomy after an appendiceal mass removed during a TAH-BSO procedure was diagnosed as being a mucinous cystadenocarcinoma on histopathology.

History of presenting complaint:

The patient had been admitted for a TAH-BSO procedure after a 7 x 7.8cm complex mass was seen on ultrasound in the right adnexa, which was subsequently confirmed on CT scan as being a cystic mass arising from the right ovary. During surgery however, while the ovaries and the uterus looked normal, a large appendiceal mucocoele was noted and removed via appendectomy. This was then sent to histology where it was diagnosed as being mucinous cystadenocarcinoma.

Past medical and surgical history:

Past medical history:

Depression

Past drug history

Total abdominal hysterectomy with bilateral salpingo-oophorectomy on 6/4/2010

Drug history:

Drug Name	Dosage	Route	Frequency	Reason
Paroxetine	20mg	PO	BD	Anti-depressant
Flupentixol	0.5mg	PO	BD	Anti-psychotic
Lorazepam	1mg	PO	BD	Anti-anxiety

No known drug allergies or anaesthetic problems.

Family history:

No relevant family history.

Social history:

The patient lives with her daughter. She is now retired and used to work as a cleaner. The patient is a non-smoker and does not drink alcohol.

Systemic inquiry:

- General Health: Good and active. Patient looked comfortable after operation
- Cardiovascular System: Nil to note
- Respiratory System: Nil to note
- Gastrointestinal System: Some tenderness close to the operation site for the TAH-BSO procedure
- Genitourinary System: Nil to note
- Central Nervous System: Nil to note
- Musculoskeletal System: Nil to note
- Endocrine System: Nil to note

Discussion of results of general and specific examinations

General examination of the patient was unremarkable. The patient appeared healthy, with no physical signs and symptoms of mucinous cystadenocarcinoma. 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 and respiratory examinations were also unremarkable. These revealed normal heart sounds S1+S2+0, with equal air entry in both lungs and normal vesicular breath sounds. A Pfannenstiel incision was observed on the abdomen due to the TAH-BSO. The abdominal examination did not reveal any masses or organomegaly. There was no guarding or rebound tenderness. There was some slight suprapubic tenderness close to the TAH-BSO operation site. Normal bowel sounds were auscultated and stools were normal.

Differential diagnosis:

- Mucinous cystadenocarcinoma
- Carcinoid tumour of the appendix
- Mucosal hyperplasia
- Adjacent caecal tumour
- Inspissated mucous causing obstruction
- Appendiceal mucinous cystadenoma
- Appendiceal mucinous adenoma
- Appendiceal adenoma
- Appendiceal ganglioneuroma
- Appendiceal paraganglioma
- Appendiceal lymphoma
- Appendiceal mucinous adenocarcinoma
- Appendiceal adenocarcinoma

Diagnostic procedures:

Laboratory exams:

Test: Appendix specimen taken during TAH-BSO surgery for histology.
Justification for test: Appendiceal mucocoele noted and removed during surgery.
Results: The specimen was that of a previously opened appendix measuring 110 x 55 x 17mm. Examination of its mucosal surface showed numerous papillary projections into the lumen and extensive mucoid clots. Also submitted was a yellowish, mucoid mass measuring 180 x 100 x 15mm.
On microscopy, sections from appendix showed malignant cells with vesicular nuclei and prominent nucleoli and frequent mitotic figures invading the full thickness of the appendiceal wall with a desmoplastic stromal reaction.
Conclusion: Mucinous cystadenocarcinoma was diagnosed.

Test: Colon and ileum removed during right hemicolectomy for pathology.
Justification of test: To confirm that there was no residual malignancy and for adequate clearance of the drainage lymph nodes.
Results: Terminal ileum measuring 48mm in length as well as attached colon measuring 160mm were submitted. Obviously no appendix was present. On opening, no mass was present.
On microscopy, both the ileal and colonic resection margins were free of tumour. There was no residual tumour although there were a number of diverticula present.
Conclusion: No residual malignancy was present.

Therapy:

Surgical therapy:

Pre-operative: The patient had been advised to take Dulcolax 5mg two days prior to admission as well as another 5mg a day before admission. The patient was admitted to the surgical wards from admission lounge a day before the surgery for bowel preparation. Two sachets of Klean-Prep were given. A chest X-Ray and an ECG were carried out. Blood tests were taken and cross-match was carried out for two units of blood. Stool charting was done. Informed consent was obtained.

Operation: Laparoscopic right hemicolectomy.
Insufflation was used at 12mmHg. 4 ports were used. Dense adhesions from the previous surgery were noted. Routine lateral to medial right hemicolectomy was carried out. Specimens were obtained in a bag for histology. The ileal and the colonic margins were anastomosed together via a GIA stapler.

A drain to remove blood or potential anastomotic leakage, a nasogastric tube for gastric decompression and a urinary catheter were inserted.

Post-operative: The patient removed the nasogastric tube a day after surgery. The urinary catheter was removed two days after surgery. The patient passed flatus two days after surgery and opened bowels three days after surgery. The drain was removed four days after surgery. The patient was kept nil by mouth for five days after surgery.

The post-operative medications were as follows:

Drugs:

Drug	Dosage	Route	Frequency	Reason
Paracetamol	1g	PO	6hrly / PRN	Pain relief
Cefuroxime (Zinacef)	750mg	PO	BD	Prophylactic broad-spectrum antibiotic
Metronidazole (Flagyl)	400mg	PO	TDS	Prophylaxis against anaerobic organisms and protozoa
Minihep	5000 IU	SC	Daily	Prophylactic anticoagulant to prevent thromboembolism
Metoclopramide (Maxolon)	10mg	IV	6hrly/PRN	To control nausea and vomiting post-operatively
Pethidine	75mg	IM	PRN	Pain relief
Paroxetine	20mg	PO	BD	Anti-depressant
Flupentixol	0.5mg	PO	BD	Anti-psychotic
Lorazepam	1mg	PO	BD	Anti-anxiety

Diagnosis:

The diagnosis was made by histological examination of the appendix and the mucocoele removed during the TAH-BSO. Mucinous cystadenocarcinoma is a low grade malignancy [1] and one type of appendicular mucocoele. The other types, in order of increasing severity, are: retention cyst, mucosal hyperplasia and mucinous cystadenoma. Mucinous cystadenocarcinoma is however the most severe form of them all.

This classification[2], created by the World Health Organization[3], is based primarily on epithelial structure. Neoplastic epithelium and a severe distention of the appendicular lumen are required to diagnose mucinous cystadenocarcinoma histologically[2]. There is also invasion of the glandular stroma, desmoplastic reaction and presence of epithelial cells in peritoneal implants[4]. The massive growth of the appendix lumen is caused by these cancer cells producing vast amounts of mucin and these cells may spread within the peritoneum causing pseudomyxoma peritonei[1]. In fact, the latter syndrome is found in 50% of cases[5] and involves mucinous ascites and is more informally known as "jelly belly"[4]. The appendicular mucocoeles make up only 0.2-0.4% of appendectomy surgical specimens and mucinous cystadenoma forms 11-20% of these cases[2]. It also forms less than 0.5% of intestinal tumours[5]. Therefore, this condition is quite rare[2]. Patients who develop mucinous cystadenocarcinoma are usually younger than patients with adenocarcinoma of the appendix[4].

It is difficult to ascertain a mucocoele's presence preoperatively even if a meticulous physical examination is carried out[4]. Most mucocoeles are asymptomatic so are only found incidentally. However, when symptoms are present they depend on how complicated the disease is. There is a range of symptoms and signs from a palpable mass in slim patients, right lower quadrant pain, signs of intussusception and bowel obstruction including colicky pain, gastrointestinal bleeding and therefore anaemia to acute abdomen with sepsis[3].

Carcinoembryonic antigen may be elevated[5]. Conventional imaging techniques make it difficult to distinguish mucinous cystadenocarcinoma from adenoma. However, ultrasound and computed tomography (CT) scan are effective at detecting mucocoeles[6]. CT scan is the best imaging modality for preoperative planning of tumour resection as it has an overall sensitivity of 93% for detection of mucocoele rupture, peritoneal mucinous carcinomatosis or pseudomyxoma peritonei and wall calcification[5]. Furthermore,

contrast enhanced ultrasonography was used along with CT scan and ultrasound to pre-operatively diagnose mucinous cystadenocarcinoma[6]. Generally, endoscopy cannot access the appendix for investigation however it may detect other tumours growing simultaneously with the mucinous cystadenocarcinoma in the colon of 13% of patients with mucocoeles. Even though sometimes the mucosal biopsies taken are normal, colonoscopy is useful in distinguishing benign from malignant lesions[3]. Examination of frozen sections taken during surgery and histopathological examination of the specimen after surgery can be carried out for diagnosis[5].

Removing the tumour early may cure the patient. An acceptable form of definitive therapy is right hemicolectomy[5, 1] and is preferable to appendectomy alone as its 10-year survival rate is 65% while that after appendectomy is 37%. However, if there is no pre-operative evidence of other tumours and no evidence at surgery of the tumour having spread to the peritoneum (the peritoneum surrounding not just the appendix but also of the liver and pelvis must be checked for tumour deposits and/or mucus and if these are present samples are taken for histopathological and cytological examination) or invaded the lymph nodes, appendectomy is sufficient to treat the mucocoele.

One surgical treatment suggested, based on the fact that usually mucinous appendicular tumours spread through the wall and rarely to the lymph nodes, is resection of the tumour along with retrocaecal appendiceal lymph nodes and these are sent for frozen section. If these sections are negative appendectomy only is enough. This is not the case if the lymph nodes are positive in that case right hemicolectomy is performed. Open surgery to remove the appendix is preferable to laparoscopy as it lessens the chance of perforation and hence pseudomyxoma peritonei however, if the surgeon sees that the chance of perforation is not that high laparoscopy may be done. If the tumour disseminated, then along with right hemicolectomy, aggressive debulking; oophorectomy and omentectomy are beneficial. Bowel obstruction and/or fistulation often occur so the patient would need to undergo repeated operations. Radiotherapy and chemotherapy are not effective in disseminated disease. Mucinous cystadenocarcinoma tumours grow slower than appendiceal adenocarcinomas which means they have a better prognosis[5].

Prognosis in the long term is affected adversely by perforation of the tumour and leakage of mucus into the peritoneal cavity. In fact, patients with spread beyond the appendix only have a 45% survival after 5 years as compared with 100% survival after 5 years in patients with low grade mucinous tumours confined to the appendix. No follow up is needed in the latter cases[3].

Final treatment and follow ups:

The patient was discharged ten days after surgery. The patient was seen 6 weeks later in surgical outpatients. The patient will be followed up yearly at surgical outpatients to exclude recurrence of malignancy. The patient has already survived for four years since the surgery.

Fact Box 6:

Title: Mucinous Cystadenocarcinoma

Mucinous cystadenocarcinoma is the fourth type of appendicular mucocoele in a grouping system chiefly based on the structure of the epithelium. This forms 11-20% of appendicular mucocoeles. The epithelium is neoplastic[1]; desmoplastic reaction and glandular stromal invasion are present and (but not necessarily) epithelial cells can be found in the peritoneal implants[2]. The lumen of the appendix is also severely distended[1]. This may result in rupture which results in mucinous dissemination into the peritoneum which causes mucinous ascites that is named pseudomyxoma peritonei. This syndrome is more informally known as "jelly belly". There is also a high chance of metastasis to the liver and lymph nodes. Patients suffering from this condition have a poor prognosis[2].

Risk factors:

Females of middle and older age are mostly affected by appendicular mucocoeles therefore of mucinous cystadenocarcinoma[6]. Kalmon and Winningingham[7] identified three factors which may lead to mucocoele formation in the appendix: aseptic content, continuous mucus production and narrowing of the valvular opening of the appendix. Obstruction of the appendix may be caused by bending, torsion, inflammation and ileocaecal tumour[6].

Signs and Symptoms:[2]

How the patient presents depends on whether the mucocoele ruptures or not. If it does not rupture, the majority of patients are asymptomatic and it is difficult to ascertain the mucocoele's presence preoperatively even if a meticulous physical examination is done[2]. That is, the symptoms are non-specific. However, some patients may suffer from pain or even just discomfort and have a palpable mass in the right lower quadrant[3]. The condition is an incidental finding during or after an operation via histological testing[2].

Investigations and diagnosis: [2]

Conventional imaging techniques make it difficult to distinguish mucinous cystadenocarcinoma from adenoma. Furthermore, surgery immediately ensues after diagnosis so as to avoid rupture. However, ultrasound and computed tomography scan are effective at detecting mucocoeles[3].

Prevention:

Treatment depends on the extent of the condition. Ileocaecal resection is performed[3].Sodium oxybate for nighttime use.

Prognosis:

Prognosis in the long term is affected adversely by perforation of the tumour and leakage of mucus into the peritoneal cavity. In fact, patients with spread beyond the appendix only have a 45% survival after 5 years as compared with 100% survival after 5 years in patients with low grade mucinous tumours confined to the appendix[4].

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