CASE REPORTS

Pseudomyxoma peritonei

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Pseudomyxoma peritonei is a relatively rare and poorly understood condition in which mucus accumulates within the peritoneal cavity. The presence of cells in the mucin, either inflammatory or neoplastic, distinguishes it from simple acellular mucus ascites caused by mucinous spillage. There is widespread seeding of the peritoneal and omental surfaces with a heavy cancerous glaze. This is principally a complication of borderline or malignant neoplasm of the ovary and/or appendix.

This paper describes two cases of previously healthy women who both presented with an acute abdomen, and were diagnosed postoperatively with pseudomyxoma peritonei. In addition, literature on the clinical presentation, diagnostic procedures, and treatment options has been briefly reviewed.

Pseudomyxoma peritonei characteristically arises from ruptured, primary ovarian, and appendiceal adenomas or (mucinous cyst) adenocarcinomas, but can have an indeterminate site.[1 2] Despite the abdominal viscera being thickly coated with the mucus-secreting tumour cells, invasion into the substance or extraperitoneal sites does not occur. Instead, the abdominopelvic cavities become filled with tenacious, semisolid, neoplastic mucus, rich in glycoproteins. This often forms large loculated cystic masses. Fox and Langley in 1976 proposed the development of pseudomyxoma peritonei to be due to a foreign body reaction following spillage of mucus from ruptured cysts into the peritoneal cavity.[3] This has now been disproved, as the presence of mucus-secreting tumour has been shown to be responsible for the development of this condition.

In the past there has been much discussion regarding the definition and pathology of pseudomyxoma peritonei.[4] A recent paper by Sugarbaker *et al* defined pseudomyxoma peritonei as an intestinal grade 1 mucinous adenocarcinoma that arises from a primary adenoma.[5] They describe a redistribution phenomenon in which cancer cells from appendix tumours are found localised at predetermined sites within the abdomen and pelvis, although in some cases the primary tumour may be small and inconspicuous.

We present two cases of pseudomyxoma peritonei arising from appendiceal tumours in women of different ages. Both underwent emergency surgery and had entirely different long term postoperative outcomes.

CASE REPORTS

Case 1

A 54 year old woman was admitted with a 24 hour history of severe right iliac fossa pain associated with nausea, sweating, and hot and cold flushes. Over a period of a few hours, the niggling pain had moved from the central abdominal region to the right iliac fossa. The patient also gave a history of four previous, 30 minute episodes of central niggly abdominal pain, which had occurred a week before this. She had no other abdominal, gynaecological, or urinary symptoms. At presentation, she was in considerable pain, apyrexial with right iliac fossa tenderness, guarding, and rebound. No masses were palpable. Laboratory investigations including full blood count, amylase, liver function tests, urea and electrolytes were all within normal limits. Urinary microbiology and β-human chorionic gonadotrophin were both negative. On clinical grounds, a diagnosis of local peritonitis secondary to acute appendicitis was made. The patient was taken immediately to theatre. On opening the peritoneal cavity, through a Lanz incision, large volumes of a jelly-like substance were seen. A right paramedian incision was subsequently made for better access. The gelatinous material found covering the walls of both the small and large bowels was removed. A right hemicolectomy was performed. On exploration, the uterus and ovaries were found to be normal. The abdominal cavity was washed out with noxythiolin (Noxyflex, Schering Plough), closed in layers, and a corrugated drain left in situ. Postoperative recovery was uneventful. The histology of resected tissue revealed a ruptured mucin-secreting villous adenoma of the appendix leading to pseudomyxoma peritonei. The proximal part of the appendix was histologically benign. However, distally the appendix was replaced by a less well differentiated, more atypical tumour that disappeared into a mass of extravasated mucin. Despite the atypia, no evidence of invasion or seeding of the tumour onto the serosal surface of the bowel was found. A cytological preparation of the mucin showed numerous histocytes but no tumour cells. On interpretation of this report, a diagnosis of appendiceal mucin-secreting villous adenoma resulting in pseudomyxoma peritonei was made.

This patient has been reviewed regularly in the outpatient clinic and she remains asymptomatic.

Case 2

An urgent referral was made to the surgical department by a general practitioner regarding one of his patients. He explained that the patient, a 52 year old woman, had presented to him with a 72 hour history of severe cramp-like lower abdominal pain associated with malaise and nausea. The frequency of bowel action and consistency of the stool remained unaltered. There were no other symptoms of note. The only other history of relevance was the presence of a paraumbilical hernia, which was first noticed three years previously. Two days earlier, she had attended a surgical outpatient clinic regarding the hernia, which over the last two months had become more prominent, tender, and irreducible on examination. The patient was therefore placed on a list for hernia repair. In view of the history and the obvious concern of a possible strangulating hernia, she was immediately admitted for further investigation and treatment.

On admission, she appeared to be extremely unwell. A mildly tender irreducible swelling of 4 cm in diameter was palpated to the right of the umbilicus. The overlying skin appeared to be smooth but cyanosed a cough impulse was absent. There was also widespread tenderness, rebound, and guarding in the lower abdominal region. Bowel sounds were quiet and the rectum loaded with soft faeces. The remainder of the physical examination was normal. Both the chest and

abdominal plain radiographs were normal, as were all laboratory studies. An ultrasound scan showed free fluid in the abdomen, pouch of Douglas, and within the rest of the pelvic cavity. Soft tissue elements and debris were seen floating in the fluid. No other abdominal or ovarian abnormalities were noted. In view of the scan report, the lack of a firm diagnosis and worsening condition of the patient, an explorative laparotomy was performed. On opening the abdomen, generalised peritonitis and copious amounts of myxomatous tissue were found throughout the abdominal cavity, emanating from the appendix.

A limited right hemicolectomy with end-to-end anastomosis was performed. The abdomen was closed in layers after noxythiolin washouts. Postoperatively she made an uneventful recovery. Histopathological examination revealed fibrinous and mucoid exudate on the ileal, appendiceal, and caecal surfaces. Sections of the appendix showed replacement of normal epithelium by severely dysplastic mucinous epithelium with prominent papillary configuration and moderate nuclear atypia. A diagnosis of well differentiated cystadenocarcinoma of the appendix was confirmed, and therefore she was referred to the oncologists for further treatment. After a course of cisplatin she went into remission. Twelve months postoperatively she began to complain of abdominal pain and diarrhoea. Investigations including a barium enema showed no evidence of recurrence and her symptoms resolved spontaneously. She was seen regularly as an outpatient and remained asymptomatic. Unfortunately, a further two years later she was readmitted as an emergency with generalised abdominal pain and distension, three years after her initial surgery. Non-shifting ascites and faecal loading was found on examination. An ultrasound scan revealed free fluid within the abdomen and in both subphrenic spaces. Computed tomography confirmed this and also showed the presence of omental thickening with prominent mesenteric nodes. After a peritoneal tap, the ascitic fluid was sent for cytology. Malignant cells were found to be present in clusters and papillary groups within the aspirate. Due to the widespread nature of the disease, she was offered surgical treatment. She declined this and was therefore referred to both the Macmillan nurses and the oncology department for further treatment, but she died soon thereafter.

DISCUSSION

Pseudomyxoma peritonei is an indolent disease and is most prevalent in women aged between 50 and 70.[6] Until now, it has always been thought that cases of ovarian origin outnumber those of appendiceal origin. This theory has been put into question due to a recent report by Ronnett *et at* which suggests that women actually have synchronous appendiceal and ovarian tumours.[7] Moreover, a large proportion of these ovarian tumours have been shown immunohistochemically to be secondary to the appendiceal tumours. Either way, the fact remains that more women then men appear to suffer from this condition.

Clinically, although painless, deterioration of general health begins long before diagnosis. Acute presentation during advanced stages of the disease is common and along with a host of non-specific symptoms, the main complaints are those of abdominal pain and distension. Inflammatory changes associated with peritoneal tumour implants can lead to fistula formation and adhesions, which in turn can cause intermittent or chronic partial bowel obstruction. Localised masses are frequently present in pseudomyxoma peritonei of appendiceal origin. Surprisingly, signs and symptoms of cancer such as cachexia are rare.

Diagnosis is seldom absolute until laparotomy is performed. This is despite the presence of a distended abdomen with non-shifting ascites on physical examination. Laboratory studies are also of little help but fortunately, over the past few years, there have been many reports based on radiological imaging techniques, which are proving to be extremely useful in reaching a correct preoperative diagnosis. For example, in later stages of the disease, plain films used when the abdomen is distended with mucus show central displacement of the bowels with obliteration of the psoas muscle border.[8] Occasionally, small calcific lesions can be seen widely disseminated throughout the abdomen. As the disease progresses, plain films become invaluable in following inevitable bowel obstruction and assessing the need for emergency debulking.[9] Furthermore, when used in conjunction with barium studies, the proximal extent of the disease can be assessed and a possible extrinsic tumour causing large bowel obstruction can be ruled out.

Conversely, ultrasonography is more useful and generally has similar features to computed tomography images showing abdominal echogenic masses with ascites, multiple septations, and scalloping of the liver.[10–13]

Computed tomography shows four basic patterns: (1) posterior displacement of the intestines with numerous low density masses and calcifications; (2) diffuse peritoneal infiltration appearing similar to ascites with septated fluid pockets filling the peritoneal cavity; (3) intrahepatic low density attenuated lesions[10]; and (4) scalloping of intra-abdominal organs due to extrinsic pressure of adjacent peritoneal implants. Scalloping of the liver has been widely described but in 1987, Parikh *et al* reported the first case of splenic scalloping in pseudomyxoma peritonei.[14 15]

Finally, magnetic resonance imaging, which is still being investigated, may prove more helpful than computed tomography especially in assessing the rare visceral invasion by mucinous tumours.[16] This is based on the limited number of patients reported. One major disadvantage is the poor cost effectiveness compared with computed tomography.

In summary, preoperative diagnosis could therefore be made with careful physical examination in conjunction with ultrasound and computed tomography. However, explorative laparotomy still remains the main diagnostic tool of choice. A positive finding is indicated by the presence of litres of yellowish-grey mucoid material involving both the omental and peritoneal surfaces.[7 16]

The pathological features of appendiceal mucinous cystadenocarcinomas closely mimic their ovarian counterparts. Histologically these neoplasms contain solid growths with conspicuous epithelial cell atypia and stratification, loss of gland architecture and necrosis, and are similar to colonic cancer in appearance.[17] The pertinent cytological features of pseudomyxoma peritonei include a mucinous background with mesothelial cells and histiocytes.[18] The well differentiated columnar epithelial cells producing mucin usually display

Learning/summary points

- Pseudomyxoma peritonei is an unusual condition in which there is copious mucinous ascites with mucinous peritoneal and omental implants.
- Pseudomyxoma peritonei arises from primary ovarian or appendiceal adenomas and (cyst) adenocarcinomas.
- It is more common in females.
- Radiological investigations can be helpful but are not diagnostic.
- Diagnosis is usually made at operation.
- Treatment involves appendicectomy, oopherectomy, and thorough peritoneal debulking and toilet.
- Multiple laparotomies and peritoneal washouts may be necessary.
- Postoperative radiotherapy and intraperitoneal chemotherapy can be used with limited success.

minimal nuclear features of malignancy.[19] Even though the origins and nature of the parent neoplasms may be variable, this is not reflected in the cytological features of pseudomyxoma peritonei.[20]

Prompt and aggressive treatment, including drainage of the mucus, surgical debulking of the primary and secondary tumour implants, and resection of the omentum should be instituted in all patients. Commonly, at laparotomy a right hemicolectomy is performed. In order to prevent recurrence, resection of both ovaries and the appendix must be carried out in all female patients where the primary site is not found. Unfortunately, recurrences are usual but less frequent when appendiceal mucoceles give rise to pseudomyxoma peritonei.

Beller *et al* reported in 1986 that the instillation of intraperitoneal mucolytics such as dextran sulphate, in concentrations of up to 5%, and plasminogen activators such as urokinase might be useful in preventing and treating recurrences.[6] Postoperative intraperitoneal chemotherapy is also reasonably effective, particularly for ovarian carcinomas.[21] 5-Fluorouracil is especially recommended for this purpose. Intraperitoneal cisplatin and other chemotherapeutic agents have been used but with only minimal benefit. Many patients usually tend to undergo either second look laparotomies or repeated operations to debulk residual or symptomatic recurrent tumours. Radiotherapy of the abdomen with pelvic boost can be given in cases unresponsive to chemotherapy.

In 1996, Sugarbaker *et al* stated in their paper that clinical features, which correlate significantly with therapy failure, are tumour site, histopathological grade, preoperative cancer volume, and completeness of cancer removal by cytoreductive surgery. They therefore concluded that improvements in surgical technologies, to increase total clearance of tumour from the abdominal cavity, and chemotherapy are required to sustain control of small volume residual disease on all peritoneal surfaces.[18]

Advancing abdominal disease caused by intestinal obstruction accounts for the majority of patient morbidity and mortality. Approximately two thirds of patients eventually succumb to local or regional disease, but the slow progression of metastatic disease and the advent of modern therapeutic regimens have lead to prolonged survival in pseudomyxoma peritonei. Generally, five and 10 year survival rates are thought to be around 50% and 20% respectively. Peritomectomy, omentectomy, and combination intraperitoneal chemotherapy with mitomycin C and 5-fluorouracil has been reported to achieve 10 year survival rates of up to 80%.[5] Although these figures are very encouraging, it may take some time before this treatment regimen is more widely used.

CONCLUSION

We have described two patients who developed pseudomyxoma peritonei as a result of appendiceal tumours. In both cases, presentation was acute, with the earliest symptoms being abdominal pain and nausea. In keeping with other reports, diagnosis was made after surgical treatment and histological analysis of resected tissues.

These patients demonstrate the difficulties in diagnosing pseudomyxoma peritonei preoperatively, and the spectrum of possible postoperative outcomes. Awareness of this rare condition allows appropriate primary debulking surgery to be performed when faced with a "belly full of jelly".

There are advantages and disadvantages of available investigation techniques and treatment regimens but their use continues to be invaluable in patients with pseudomyxoma peritonei. This seems to be particularly true for postoperative use of chemotherapy, which has been shown to improve prognosis in some patients.

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