Rare disease

Pseudomyxoma peritonei: disseminated peritoneal adenomucinosis variant

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Summary

Pseudomyxoma peritonei (PMP) is a rare disease and even after advances in its understanding and management it often has a protracted course and multiple recurrences despite aggressive surgery and intraperitoneal chemotherapy. The current preferred treatment of ultraradical surgery and hyperthermic intraperitoneal chemotherapy is associated with considerable morbidity and significant mortality. With better understanding we know that the prognosis of the disease is dependent on the degree of total excision of the disease and type of histology. The authors propose the need to be selective in applying aggressive treatment regimens in all patients with PMP regardless of factors like age, low malignant variants and expected morbidities. Our patient had a good outcome with a conservative approach. However, large studies are needed before reaching a conclusion.

BACKGROUND

Pseudomyxoma peritonei (PMP) was first described by Rokitansky in 1842.¹ Werth in 1884 described the association with ovarian tumours and Franckel in 1901 reported its association with appendiceal cystic tumours.^{2,3} The incidence of PMP, 2/10 000 laparotomies, and its rarity make the study of the disease and its optimal treatment difficult. It is four times more common in women with median age of 54 years.^{4,5} The disease is progressive and is characterised by disseminated intraperitoneal mucinous tumours with peritoneal implants and mucinous ascites. The origin of PMP is controversial but most cases are associated with ruptured cystic adenoma of appendix and ovarian mucinous tumours.⁶ PMP is also used for a diverse group of mucinous tumours in the literature, which have abundant extracellular mucin and may have epithelial cells. Varieties of markers have been studied for establishing the origin of the tumour. Cytokeratin 7 (CK 7) and HAM-56 are positive to ovarian tumours and CK 20 and carcinoembryonic antigen (CEA) are associated with colorectal disease. There

is considerable overlap in the tumours of the appendix and studies suggest that a majority of tumours of the ovary are indeed of appendiceal origin.^{7,8} Classifications have been proposed based on the benign or malignant histology or the degree of malignant potential.⁹ Ronnet *et al* did a clinicopathologic analysis of 109 patients and classified PMP solely on the basis of pathologic features into three groups.¹⁰ Disseminated intraperitoneal adenomucosis (DPAM), peritoneal mucinous carcinomatosis (PMCA) and the intermediate or discordant group (PMCA I/D) are based on histology. The DPAM group had the best 5- and 10-year survival rates in all three groups. The diagnosis of PMP is very difficult to achieve before an operation and is frequently discovered at laparoscopy or laparotomy.¹¹ A progressive increasing abdominal mass is the most frequent presentation.¹² Contrast-enhanced CT (CECT) offers the best modality of evaluation with 'scalloping' of liver and spleen clinching the diagnosis.¹³ Treatment modalities are varied but debulking or cytoreductive surgery is most frequently performed. Ultraradical surgery that includes

Figure 1 (A,B) CECT of abdomen revealing the characteristic scalloping and appendix replaced by a mass.

Figure 2 (A,B) Entire abdomen filled by mucinous material.

polyvisceral resection and hyperthermic intraperitoneal chemotherapy is the treatment of choice and offers best results.^{14 15}

CASE PRESENTATION

We describe a 72-year-old male with type 2 diabetes mellitus having progressive distention of abdomen and loss of appetite over a period of 6 months. There were no associated features of fever, vomiting or pain in the abdomen. His blood sugar was well controlled on oral hypoglycaemics. He is an active person and there was no other significant social or family history.

INVESTIGATIONS

His haematological, biochemical, renal parameters and coagulation profile were normal. Ultrasound abdomen revealed ascites and perigastric thickening. Oesophagogastroduodenoscopy was normal with normal distention of stomach. S CEA and CA 19-9 were also normal. CECT abdomen had features of scalloping around liver surface with ascites (figure 1). Ascitic fluid evaluation had mucinous material and microscopy revealed mucinous tumour of low malignant potential. Preoperative diagnosis of PMP was made and surgery was planned.

TREATMENT

Patient was operated under general anaesthesia in supine position with midline incision. He underwent debulking with right hemicolectomy with ileotransverse anastomosis. Intraoperative chemotherapy was not given as the patient did not agree for it in view of the potential morbidity and low malignant potential on preoperative evaluation. Peroperatively, the entire abdomen was replaced with mucinous material with mucinous deposition in the omentum (figures 2, 3). There was significant solid component in the mucinous material and minimal ascites. Appendix was embedded in a mass and could not be identified individually (figure 4). Liver and spleen were normal and small- and large-bowel mesentery was normal. In total, around 6 l of mucinous material and fluid was removed from the abdomen. The total duration of surgery was 4.5 h and patient did not receive any blood/blood products during surgery. There were three intra-abdominal drains placed in the

right subhepatic, left paracolic and pelvis, respectively. He was extubated on table and had a smooth intraoperative course.

OUTCOME AND FOLLOW-UP

Patient had an uneventful postoperative course and was made ambulatory on the first postoperative day. His left paracolic, right subhepatic and pelvic drains were removed sequentially on days 3, 4 and 6. The nature of the drains was serous throughout. He was allowed liquids on postoperative day 3 and was on full diet on day 5. He was discharged from the hospital on postoperative day 7.

Patient has been on a regular follow-up and is symptomatically relieved. He had a weight loss of 14 kg in the initial postoperative period and now weighs 10 kg less than during preoperative evaluation. He is more than 1.5 years after surgery and has occasional nausea and epigastric discomfort following fatty meals, which are easily controlled with antacids. He was evaluated with ultrasonography of the abdomen 1 year after surgery, which was largely normal apart from perigastric thickening and minimal ascites. Patient is currently doing well and has an active social life.

DISCUSSION

PMP is characterised by disseminated intraperitoneal mucinous tumours, mucinous ascites and a variable poorly predictable prognosis. Appendiceal mucinous adenomas and ovarian mucinous tumours' association with PMP is well documented in the literature. PMP by definition is also applied to a diverse group of mucin-secreting tumours arising from pancreas, colon and rectum, gall bladder and biliary ducts, breast, lung, stomach, urinary bladder and urachus.¹⁶⁻²² The disease has been classified based on the malignant potential and benign or malignant histology. Ronnet *et al* proposed that PMP should be applied to only a category of cases that have homogenous histology and prognosis. The disease was subclassified into three groups. DPAM is composed of uniformly scant low-grade abundant extracellular mucin with fibrosis. PMCA had more abundant mucinous epithelium forming glands or signet ring cells with complex architecture. The third type or the intermediate group (PMCA I) had features predominantly of DPAM with focal areas of well-differentiated mucinous

Figure 3 Omentum infiltrated by mucinous material being removed piecemeal.

carcinoma, whereas the discordant group (PMCA D) had lesions with high-grade dysplasia or intramucosal carcinoma of appendix without features of invasive malignancy. The DPAM group had the best outcomes with 5- and 10-year survival rates of 75% and 68% vis a vis 14% and 3% of PMCA and 50% and 21% of indeterminate group, respectively.¹⁰ The clinical presentation of the disease is variable and is most frequently diagnosed incidentally at laparoscopy or laparotomy. In a series of 217 patients, there was a suspicion of appendicitis in 27%, growing abdominal mass in 23% and exploration for ovarian mass in 39%.¹² New onset inguinal hernia, false hydrocoel or a scrotal mass may be presenting complaints.^{12–23} Non-specific nausea, vomiting, fatigue and urinary symptoms may be present. Extra-abdominal complaints may be present in disease involving pleura or pericardium.^{24–25} PMP does not lead to lymphatic involvement or metastasis.

Routine laboratory studies are not helpful in achieving a diagnosis. CECT reveals the characteristic 'scallop-ing effect' on the surface of the visceral organs resulting from compression by the viscous mucinous secretions and the organising fibrosis.¹³ The role of MRI is unclear.²⁶ The utility of the tumour markers have not been extensively studied although CEA and CA 19-9 may be frequently elevated.¹² Overexpression of gene MUC 2, which is responsible for mucin secretion, is noted in tumours of appendiceal origin.²⁷ Ascitic tap and cytological examination may be

useful but lack of malignant cells on cytology does not exclude malignancy.

Treatment option varies from non-operative radiotherapy to instillation of mucolytic agents and immunotherapy with variable outcomes. Laparoscopic debulking surgery has also been proposed for debulking but the role remains unclear.²⁸ Debulking surgery is the most frequently performed procedure where the peritoneal contents are removed.²⁹ The patient frequently requires repeat surgery for recurrence. Ultraradical surgery proposed by Sugarbaker combined with hyperthermic intraperitoneal chemotherapy is labelled as the procedure of choice.^{30–31} The procedure involves polyvisceral resection of abdominal organs and intraperitoneal chemotherapy with mitomycin C and 5 FU. The 5-year survival is based on the degree of total excision of lesions. However, the above series remains incomparable as it is the only prospective study with a large number of cases in the literature. Studies report a mortality of 3% with considerable morbidity, which is around 40%, and includes prolonged ileus, perforation peritonitis, enteric fistulae, pancreatitis, pulmonary embolism, abdominal pain and intra-abdominal abscess. In a series, 24% patients were re-operated after an ultraradical surgery for complications with a mortality of 9%.^{5–32} The prognosis of the disease is also related to the bulk of the disease as evaluated by the tumour site, preoperative tumour volume and completeness of tumour removal by

Figure 4 Appendix replaced by a mass (pointed by suction tip).

cytoreductive surgery.^{33–36} Patients with elevated CEA and CA 19-9 are at increased risk of developing recurrence and with normal levels of these tumour markers have an overall improved prognosis.^{37 38}

Overall, there is considerable variation in the treatment offered to the patients with PMP and single institution studies have discussed aggressive treatment. The results achieved in these studies have not been replicated probably due to the rarity of the disease. However, as discussed above, there is significant morbidity and mortality associated with aggressive surgery and the outcome is primarily dependent on the degree of total excision of the disease and favourable histology. In our case, in view of the age and the benign nature of the disease, we adopted a conservative approach. No intraoperative chemotherapy was given and postsurgery recovery was largely uneventful. After more than 1.5 years of follow-up, there is no evidence of recurrent disease. The case demonstrates the need to be selective in applying aggressive treatment regimens in all patients with PMP regardless of factors like age, low malignant variants and expected morbidities. However, large studies are needed before reaching a conclusion.

Learning points

- ▶ There is significant morbidity and mortality associated with aggressive surgery.
- ▶ The outcome is primarily dependent on the degree of total excision of the disease and favourable histology.
- ▶ We adopted a conservative approach. No intraoperative chemotherapy was given and postsurgery recovery was largely uneventful.
- ▶ After more than 1.5 years of follow-up, there is no evidence of recurrent disease.
- ▶ Aggressive treatment regimens in all patients of PMP regardless of factors like age, low malignant variants and expected morbidities may not entirely be justified.

Competing interests None.

Patient consent Obtained.

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