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Pseudomyxoma peritonei induced by a well-differentiated appendicular mucinous adenocarcinoma: An uncommon cause of isolated ascites in a young man patient

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Abstract

Pseudomyxoma peritonei (PMP) remains difficult to diagnose and has a guarded prognosis. Pseudomyxoma peritonei is a rare entity, of appendicular origin in the majority of cases. Its clinical symptomatology is not specific, the diagnosis is evoked by imaging and surgery, and confirmed by histology.

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Abstract

Pseudomyxoma peritonei (PMP) remains difficult to diagnose and has a guarded prognosis. Pseudomyxoma peritonei is a rare entity, of appendicular origin in the majority of cases. Its clinical symptomatology is not specific, the diagnosis is evoked by imaging and surgery, and confirmed by histology.

Keywords: Pseudomyxoma peritonei, Appendicular mucinous adenocarcinoma, Diagnosis, Treatment

Key clinical message

Pseudomyxoma peritonei is a rare entity, of appendicular origin in the majority of cases. Its clinical symptomatology is not specific, the diagnosis is evoked by imaging and surgery, and confirmed by histology.

INTRODUCTION

Peritoneal pseudomyxoma (PMP) or gelatinous disease of the peritoneum is a rare clinico-pathological entity, characterized by a diffuse peritoneal involvement, composed of a mucinous ascites, associated or not with neoplastic epithelial cells.[1,2] However, the origin, pathology, treatment, prognosis and even the definition of this condition remain controversial.[2] The incidence is 1 to 2 cases per year and per million inhabitants with a female predominance. Appendicular origin remains the most frequent and represents 90% of the causes.[1-3] As PMP has no specific clinical manifestations, it is difficult to diagnose before surgery.[2] Nevertheless, the diagnosis can be established by ultrasonography, computed tomography (CT scan), magnetic resonance imaging (MRI) and diagnostic laparoscopy followed by histopathological verification.[4] Well-differentiated mucinous appendicular adenocarcinomas are more likely to cause PMP than to act as typical colorectal adenocarcinomas and to cause distant metastasis.[5] In Madagascar, no description of this condition has been reported. We report a case of PMP secondary to a well-differentiated appendiceal mucinous adenocarcinoma in a 48-year-old Malagasy man.

CASE REPORT

A 48-year-old man was hospitalized for a large volume ascites. He had a history of arterial hypertension under angiotensin II receptor antagonist treatment and an appendectomy. All information regarding the procedure, macroscopic and histological appearance of the anterior appendectomy was not available at the time of patient interview. The patient did not report a family history of cancer. He had been presenting for 6 months with a progressive increase in abdominal volume, sometimes associated with transit disorders such as constipation and vague abdominal pain. Physical examination on admission revealed significant abdominal distension. He had no fever, no signs of liver failure, no signs of cardiac failure and no signs of occlusion. Abdominal and pelvic ultrasound was objectified a large, multicompartmental, viscous intraperitoneal effusion with peritoneal nodules and deep adenopathy. There was no evidence of portal hypertension. Chest, abdominal and pelvic CT scan visualized a large volume ascites with liver scalloping, without intra-abdominal tumor syndrome (Figure 1A) and small nodules of the lungs of secondary appearance (Figure 1B). Several failed attempts to puncture the peritoneal effusion led to a median laparotomy under the umbilical vein, which was extended upwards. A gelatinous disease of the peritoneum was discovered, disseminated throughout the abdomen, essentially in sub-mesocolic region with infiltration of omentum. A gelatin evacuation and a biopsy of the greater omentum in infiltrated areas were performed. Histopathological examination of the biopsy specimen and intraperitoneal gelatin had revealed an fibroadipose structures dilacerated by mucus puddles accompanied or containing isolated mucinous cells or epithelial streaks sometimes cystic glandular, sometimes papillary, and minimal cyto-nuclear atypia suggesting a histological appearance of well-differentiated adenocarcinoma with peritoneal pseudomyxoma probably of appendicular origin (Figure 2 A, B). Tumor marker assay reported carcinoembryonic antigen (CEA) at 34.62 ng/mL (N: $<$ 5 ng/mL), carbohydrate antigen (CA) 19-9 at 385.2 U/mL (N: $<$ 37 U/mL), CA 125 at 54.7 U/mL (N: $<$ 36 U/mL), prostate-specific antigen (PSA) at 0.40 ng/mL (N: $<$4ng/mL) and α-foetoprotein at 2.02 ng/mL (N: $<$ 10 ng/mL). The other biological examinations are reported in Table 1. Lower gastrointestinal endoscopy showed an absence of a colorectal tumor. We ultimately retained the diagnosis of pseudomyxoma peritonei induced by a well-differentiated appendicular mucinous adenocarcinoma. The evolution was marked by the rapid

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recurrence of gelatinous ascites despite surgery. A chemotherapy of FOLFOX-6 (4 cycles) with a second surgery was proposed after a multidisciplinary consultation meeting. The patient refused this proposal and was subsequently lost to follow-up.

DISCUSSION

PMP or formerly called "gelatinous disease of the peritoneum" remains a rare disease. The true incidence of PMP in the population is not known, as few data are available. Historical data from autopsy studies have estimated the incidence of mucocele of the appendix to be approximately 0.2%.[6] The incidence of PMP was initially proposed to be approximately 1 per million population per year, but this estimate was not based on strong evidence.[1-6] Recent Dutch data from Smeenk et al estimated the incidence of mucinous epithelial neoplasms of the appendix to be approximately 0.3% and progression to PMP in approximately 20% of these patients.[1]Extrapolating the data, this places the incidence of PMP at approximately 2 per million per year. However, experience from high-volume centers suggests that the true incidence may be higher, at 3-4 operable cases per million per year.[7] Our case was the first reported case of PMP in Madagascar. Although our case was male, PMP affects women 2 to 3 times more frequently than men.[1-5] Most tumors (90%) are of appendicular origin from low or high grade mucinous appendicular neoplasm and appendicular adenocarcinoma, associated with a mucocele, as in our patient's case.[1-7] Other tumors are mucinous adenocarcinomas of colonic, gastric, pancreatic, urachal, pulmonary, endocervical or mammary origin, or more rarely mucinous ovarian tumors, cystadenomas or cystadenocarcinomas.[2,8] Some authors have reported non-neoplastic intraperitoneal mucinous deposits caused by alternative processes such as mucin retention due to a stercolith or diverticulum, or mucinous metaplasia of the fallopian tubes, but such situations are very rare and debatable.[2,9]

Its pathophysiology is explained by the obstruction of the appendicular lumen due to a hypersecretion of mucus by the appendix leading to its progressive distension, called appendicular mucocele. The rupture of the appendix is responsible for the dissemination of mucus into the peritoneal cavity which is the origin of the pseudomyxoma of the peritoneum.[1-7] Mucin deposits in the peritoneal cavity, more or less associated with tumor cells, are due to the redistribution phenomenon and the epithelial-mesenchymal transition.[2,10] Hematogenous and lymphatic dissemination routes seem to be infrequent in this complex pathology, which is still partially understood. However, due to its clinical course, PMP is considered a neoplastic condition with variable behavior, either indolent or aggressive.[2,10]

The clinical presentation is aspecific and poor. PMP is often asymptomatic, discovered incidentally on imaging (ultrasound, abdominal CT scan, abdominal MRI) or during laparotomy.[1-7] It may be manifested by abdominal pain, increased abdominal volume, nausea, vomiting, altered general condition, signs related to the impact of the disease on the digestive tract and/or urinary tract.[2]Our patient had presented with increased abdominal volume with vague abdominal symptoms.

Radiologically, abdominal CT scan has become the first examination of choice for diagnosis and follow-up of the patient, as the scan appearance of PMP is well known.[10] The most common appearance was the presence of deformation of the contours of the solid organs (liver and spleen) by extrinsic compression of the gelatinous masses. This typical aspect of PMP, called "scalloping", is considered a pathognomonic scan sign of PMP. A hypodense, sometimes multicompartmental peritoneal effusion associated with curvilinear calcifications may also be seen. The peritoneal implants present as hypodense, heterogeneous nodular lesions that are enhanced after injection of contrast medium, often located in areas of declining stasis, notably the cul-de-sac of Douglas and the parietocolic gutters, and may coalesce at the level of the greater omentum to form the "omental cake".[11,12] In our case, the CT scan objectified a scalloping change around the liver.

PMP has no specific tumor markers. CEA, CA19-9 and CA125 are used to reflect the severity and prognosis of the disease.[2,13,14] The postoperative survival time of CEA, CA19-9- and CA125-negative patients was 2.6 times longer than that of patients positive for the three tumor markers.[2,15-18]

Therapeutically, cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPC) was the standard treatment for PMP. This surgical procedure may include localized peritonectomies, right

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hemi-colectomy, omentectomy with splenectomy, cholecystectomy. In the absence or impossibility of CRS, a "debulking surgery" can be adopted, consisting in removing the maximum of gelatinous and tumor formations.[6,19] In our case, he underwent a simple evacuation of the gelatin and a biopsy of the greater omentum in infiltrated areas due to the presence of pulmonary nodules of secondary appearance. HIPC is not yet available in Madagascar. Regarding the outcome of patients undergoing treatment, Chua TC et al, had confirmed that PMP patients treated with CRS combined with HIPC have good long-term therapeutic results and a guarded prognosis with a median overall survival time of 196 months (16.3 years) and a median progression-free survival time of 98 months (8.2 years). The survival rate at 3 years, 5 years, 10 years, and 15 years was 80%, 74%, 63%, and 59%, respectively. While patients treated by CRS without HIPC, the 5-year and 10-year survival rate was 40% and 10%, respectively.[20] In our case, a multidisciplinary consultation meeting had opted for systemic chemotherapy such as FOLFOX-4 in view of the absence of HIPC in Madagascar. Moreover, Chen CF et al. had already reported a case of PMP with excellent response under this systemic chemotherapy.[21]

CONCLUSION

PMP is a rare entity, of appendicular origin in the majority of cases. Its clinical symptomatology is not specific, the diagnosis is evoked by imaging and confirmed by histology. The treatment of choice is a combination of complete CRS and HIPC. Prognosis is related to early management of the disease, histological grade, and quality of the surgical procedure.

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None.

CONFLICT OF INTERESTS

The authors have no conflicts of interests to declare.

AUTHORS CONTRIBUTIONS

NHR, MACR, ALR, CIR, and VFR were major contributors in drafting the manuscript and revised the content. NHR, MACR, CIR, DHHL, MR, HR, AFR, ASR, ALRR, THR, FR, and RMR were the gastroenterologists and oncologists responsible for treating the patient and revised the manuscript for important content. SHR revised the manuscript for important content.

ETHICS APPROVAL AND CONSENT PARTICIPATE

The authors declare that the involved patient gave informed consent for participation in research. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A signed consent form authorizing the publication is available and included in the patient's chart. The study was done according to the declaration of Helsinki.

DATA AVAILABILITY STATEMENT

Data are available on request from the corresponding author.

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FIGURE 1 Chest, abdominal and pelvic CT scan of a 48-year-old man, showing a large volume ascites with liver scalloping (Fig. 1A) and small nodule of the lung of secondary appearance (Fig. 1B).

FIGURE 2 (A, B) Histopathological appearance of epiploic biopsy of a 48-year-old man, showing a well-differentiated adenocarcinoma with pseudomyxoma peritonei (Legend: 01: tumor glands; 02: fibrous epiploic tissue; 03: mucus puddles; 04: cavity lined with atypical, muco-secreting cells); Staining: Hematoxylin and

eosin; Magnifications: A x100; B x40.

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Figure 1. PMP.pptx available at https://authorea.com/users/344475/articles/571879-pseudomyxoma-peritonei-induced-by-a-well-differentiated-appendicular-mucinous-adenocarcinoma-an-uncommon-cause-of-isolated-ascites-in-a-young-man-patient

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Figure 2. PMP (1).pptx available at https://authorea.com/users/344475/articles/571879-pseudomyxoma-peritonei-induced-by-a-well-differentiated-appendicular-mucinous-adenocarcinoma-an-uncommon-cause-of-isolated-ascites-in-a-young-man-patient

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Table 1. PMP. docx (1).docx available at https://authorea.com/users/344475/articles/571879-pseudomyxoma-peritonei-induced-by-a-well-differentiated-appendicular-mucinous-adenocarcinoma-an-uncommon-cause-of-isolated-ascites-in-a-young-man-patient

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