CASE REPORT

Challenging and uncommon diagnosis of long-evolution ascites

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SUMMARY

This is a case report of a 45-year-old Caucasian man with chronic alcoholism. No history of liver disease or asbestos exposure. He complained of ascites during the last 3 years with worsening in the last year with severe ascites development. Diagnostic paracentesis showed SAAG 1.1 and high cellularity with neutrophil count >250 cells/μL. Ascitic fluid cytology revealed reactive mesothelial hyperplasia. Thoracoabdominopelvic ultrasonography/CT/MRI and fludeoxyglucose positron emission tomography/CT showed 'omental cake' pattern suggesting peritoneal carcinomatosis. An exploratory laparoscopy revealed moderate interloop adhesions and necrosis with whitish exudate in the right pelvic excavation. Biochemical/cytological/histological/microbiological study only revealed reactive mesothelial cells, necrosis and lymphohistiocytic inflammatory infiltrate. A second exploratory laparoscopy with liver and peritoneal biopsies and appendectomy/mesoappendix excision showed a well-differentiated tubulopapillary mesothelioma. The patient was referred for intraperitoneal chemotherapy and is undergoing monthly therapeutic paracentesis.

BACKGROUND

The aetiological diagnosis of ascites can be challenging. Well-differentiated papillary mesothelioma of the peritoneum (WDPMP) is a rare and distinct subtype of peritoneal mesothelioma, being more common in young women with no previous exposure to asbestos.^{1,2} This type of tumour often presents as an incidental finding with indolent course, making preoperative diagnosis challenging.^{1,3} The lack of atypical mitosis/organ invasion in cytological specimens and the difficult differentiation from reactive papillary hyperplasia, other mesothelial lesions and serous neoplasms by cytology and routine H&E-staining histology determine an extensive diagnostic work-up.¹⁻⁴

We present a case of long-evolution ascites by a rare subtype of mesothelioma with challenging preoperative diagnosis. Additionally, given its rarity, WDPMP features in male patients were reviewed.

CASE PRESENTATION

A 45-year-old Caucasian man with chronic alcoholism (120g/day) worked as a garbage collector for several years. There was no medical history of liver disease or previous exposure to asbestos. He complained of abdominal pain, postprandial

fullness and severe ascites during the last year. Physical examination was unremarkable, except for the presence of overweight (body mass index 27 kg/m²) and non-tense severe ascites. There were no constitutional symptoms. Three years ago, an extensive study for mild ascites was performed with no conclusive diagnosis.

INVESTIGATIONS AND DIFFERENTIAL DIAGNOSIS

The laboratorial study only showed a slight elevation of lactate dehydrogenase (339; N:125–220 IU/L). Chest and abdominal X-rays were normal. Abdominal ultrasonography showed a voluminous ascites with no other abnormalities. A diagnostic paracentesis was performed revealing high cellularity (3900 cells) with high neutrophil count (1800 cells/μL) and 55% of other cells, elevated total protein (4 g/dL) and serum-ascites albumin gradient (SAAG) of 1.1. Further ascitic fluid study was non-diagnostic, including amylase, ACE, adenosine deaminase, triglycerides, conventional cultures, PCR-based rapid test and culture for *Mycobacterium tuberculosis*. Ascitic fluid cytology showed reactive mesothelial hyperplasia negative for malignancy (calretinin+, EMA+, Ber-Ep4-, CEA-, WT-, h-caldesmon- and Ki67-). Initial misdiagnosis of decompensated cirrhosis with spontaneous bacterial peritonitis was considered and cefotaxime 2 g intravenous once daily 8 hours and human albumin (1.5 g/kg day 1, 1.0 g/kg day 3) were started. However, 48-hour revision paracentesis continued to show the same findings, including high cellularity. A thoracoabdominopelvic CT (figure 1A) revealed massive free peritoneal effusion and large omental densification like 'omental cake' pattern, suggesting peritoneal carcinomatosis of unknown primary tumour. Abdominopelvic MRI (figure 1-B) and fludeoxyglucose positron emission tomography (figure 2) were then performed without additional findings. Esophagogastroduodenoscopy with biopsies revealed hiatal hernia and Barrett's oesophagus C3M3.5. Ileocolonoscopy with biopsies showed hyperplasia and pseudolipomatosis of the peripendicular mucosa. Other infections or autoimmune conditions were ruled out. It was decided to perform an exploratory laparoscopy which revealed multiple and diffuse greyish white 5–10 mm milary nodules, isolated or cluster forming, throughout the parietal peritoneum, interloop adhesions and necrosis with whitish exudate in the right pelvic

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Figure 1 Thoracoabdominopelvic CT (A) and MRI (B) showing massive free peritoneal effusion and large omental densification like 'omental cake' pattern.

excavation (see online supplementary video 1). Biochemical, cytological, microbiological and histological study (figure 3A,B) of surgical biopsies specimens and ascitic fluid were inconclusive showing reactive mesothelium with no atypia and necrosis with lymphohistiocytic inflammatory infiltrate (CD68+) in the right pelvic excavation.

TREATMENT, OUTCOME AND FOLLOW-UP

During the first year, the patient lost follow-up given ascites controlled under diuretic therapy (furosemide 40 mg/day and spironolactone 100 mg/day) and ethylic cessation. Subsequently, he developed a refractory ascites requiring regular monthly therapeutic paracentesis. Repeated ascitic fluid analysis remained inconclusive. Because of clinical worsening, a second exploratory laparoscopy was performed showing multiple diffuse micronodules in the peritoneum, epiploon, appendix surface and mesoappendix (see online supplementary video 2). Liver and peritoneal nodules biopsies and appendectomy with mesoappendix excision revealed papillary structures lined by cuboidal mesothelial cells and fibrovascular stroma. Few cells showed atypia or mitotic figures. Necrosis, histiocytic reaction and lymphoplasmocitary inflammatory process were also identified. On immunohistochemical study, the tumour cells were calretinin+, desmin+, CK 5/6+, EMA+ (focally), WT1-, CEA- and Ber-Ep4- (figure 4A–C). A diagnosis of WDPMP was made, based on a long-evolution ascites, histomorphology and immunohistochemistry. In a multidisciplinary therapeutic consensus meeting, the patient was proposed for intraperitoneal chemotherapy since the presence of symptomatology and tumour distribution considered too extensive to allow a complete surgical excision. He presents a general well-being

Figure 2 Positron emission tomography with diffuse epiploic thickening and nodular areas with mild diffuse fludeoxyglucose uptake, suggesting peritoneal carcinomatosis.

Figure 3 Histopathological study showed reactive mesothelium with no malignancy features and necrosis with lymphohistiocytic inflammatory infiltrate (CD68 positivity) in the right pelvic excavation. (A) Peritoneum, H&E 100x; (B) Pelvic excavation, H&E 100x.

under monthly therapeutic paracentesis while awaiting intra-peritoneal chemotherapy.

DISCUSSION

Mesothelioma is a relatively rare tumour arising from serous membranes. Peritoneal origin occurs in 20%–40% of cases. WDPMP is a very rare subtype of epithelioid mesothelioma, with distinct presentation, pathology and prognosis. Usually, it presents in women in the third and fourth decade, without history of asbestos exposure, indolent course and a better prognosis than diffuse malignant peritoneal mesothelioma (DMPM).^{3 5} The histological features include a thin fibrovascular papillae lined by uniform cuboidal mesothelial cells⁴ and occasionally psammoma bodies with absence/rare mitotic figures or atypia.⁶ WDPMP differential diagnosis is challenging, including multiple conditions such as reactive mesothelial hyperplasia, metastatic peritoneal adenocarcinoma, serous papillary adenocarcinoma and DMPM.² The presence of inflammation and well-differentiated papillary elements with no cytological atypia favours reactive

Figure 4 Histopathology of surgical biopsy specimens showed papillary structures with uniform cuboidal mesothelial cells and fibrovascular stroma. Few cells showed atypia or mitotic figures. Necrosis, histiocytic reaction and lymphoplasmocitary inflammatory process were also present. On immunohistochemical study, the tumour cells were calretinin+, desmin+, CK 5/6+, EMA+ (focally), WT1-, CEA- and Ber-Ep4-. Histopathological features were compatible with well-differentiated papillary mesothelioma of the peritoneum without lymphovascular embolisation or lymph node metastasis. (A) Ileocecal appendix, H&E 100x; (B) Omentum, H&E 40x; (C) Peritoneum, H&E 40x.

mesothelial hyperplasia diagnosis. However, for WDPMP diagnosis to be made, the demonstration of reactive changes/invasion signs in adjacent serosal tissue and scarce atypical cells is crucial.^{3 7 8} WDPMP has a low malignant potential, but cases of tumour recurrence following surgery or malignant transformation in a long-term follow-up have been reported.^{1 9}

WDPMP management is not well established and involves complete tumour debulking surgery, intraperitoneal or intravenous chemotherapy, radiotherapy, immunotherapy, sclerotherapy or a combination of some of them.^{5 10} Follow-up is necessary to avoid misdiagnosis and given the possibility of recurrence or malignant transformation.^{2 3 5}

Although its rarity, WDPMP is much more common and subsequently well-characterised in female patients. However, the diagnosis in male gender is extremely rare and poorly described. As far as we know, only five cases of WDPMP have been described in men. Patients ranged in age from 36 to 70 years (mean, 54.2 years). There was no history of asbestos exposure in any case. Four patients were symptomatic at presentation, mainly abdominal pain/mass (60%) and ascites (40%). In four patients, the WDPMP was multifocal. One patient had previous surgery (hydrocele surgical repair) and one patient presented a concomitant bladder cancer. All cases presented typical histopathological features described for WDPMP, such as individual or nests of cells with glandular/tubular pattern, bland mesothelial cells and absent/rare mitotic figures. Three patients underwent surgery with no tumour recurrence for an average follow-up of 15.5 months and one patient undergone chemotherapy with cisplatin/pemetrexed with 9 months follow-up. The remaining case did not receive any treatment, being under surveillance.^{5 11 12}

In conclusion, we present a case of a challenging diagnosis of long-evolution ascites in a middle-age man. It represents one of

the few reported cases of extensive and symptomatic WDPMP in men. Given its rarity, the differential diagnosis with reactive mesothelial hyperplasia by imaging, cytology, histopathology and immunohistochemistry is very difficult. An exhaustive aetiological study is often required with diagnostic laparoscopy being crucial for the definitive diagnosis.

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Learning points

- ▶ Long-evolution ascites can be a challenging diagnosis.
- ▶ Well-differentiated papillary mesothelioma of the peritoneum is an uncommon cause of ascites and a rare subtype of epithelioid mesothelioma, more common in female patients and typically associated with a long survival.
- ▶ Differential diagnosis with reactive mesothelial hyperplasia by imaging, cytology, histopathology and immunohistochemistry is difficult.
- ▶ Diagnostic laparoscopy remains crucial for the definitive diagnosis, with the possibility of a second intervention in case of inconclusive first laparoscopy.

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