

Malignant Epithelioid Peritoneal Mesothelioma in a middle-aged lady with extensive travel history and longstanding abdominal symptoms

James J*; Aziegbe W; Bebb J

¹Royal cornwall hospital, Truro, cornwall UK.

Received Date : Aug 02, 2022
Accepted Date : Sep 17, 2022
Published Date : Sep 24, 2022
Archived : www.jcmimagescasereports.org
Copyright : © James J 2022

***Corresponding Author:** James J, Royal cornwall hospital, Truro, cornwall UK.
Email: j.james3@doctors.org.uk

Abstract

Malignant peritoneal mesothelioma (MPM) is a rare type of mesothelioma, the most common site of mesothelioma being the pleura. It is a malignancy of the peritoneal linings and is sometimes associated with exposure to asbestos. Clinical presentation is usually vague and Imaging (Magnetic resonance imaging (MRI), computed tomography (CT) and positron-emission tomography (PET) is key in evaluation of these patients. Definitive diagnosis is by histopathology/immunohistochemistry and first line treatment is cytoreductive surgery and intraperitoneal chemotherapy.

A middle aged lady with extensive travel history by virtue of her job and 20-year history of recurrent unspecific abdominal symptoms for which no aetiology had been found despite recurrent admissions, extensive investigation, and surgical intervention. She was admitted to our centre with recurrent abdominal pain, distension, and poor oral intake. There was no known exposure to asbestos and initial impression was symptoms were likely due to a chronic infection acquired during her travels. Extensive testing to identify an infectious or auto-immune cause of her symptoms was unremarkable. Repeat imaging (CT scan and PET-CT), diagnostic laparoscopy (including ascitic drainage, adhesiolysis, left salphingoophorectomy and peritoneal biopsies) and histology revealed a Malignant epithelioid mesothelioma with small bowel involvement.

Clinical presentation is usually vague and non-specific; this throws up diagnostic dilemmas and the diagnosis is usually clinched late as in this case as other diagnostic options may be pursued. Although, this diagnosis is a very rare entity, it should be considered in patients with long-standing abdominal symptoms for which no other cause has been found, especially in the context of raised inflammatory markers and change in symptomatology.

Background

Malignant peritoneal mesothelioma (MPM) is a malignancy of the peritoneum, the lining which covers the internal organs of the abdomen. It is a rare cancer, with a worldwide incidence of approximately one case per four to five million people with a higher incidence in developed and industrialised nations [1].

Case Presentation

A middle aged logistics manager was admitted to hospital with deterioration after a recent admission for constant abdominal pain, distension, and weight loss. Prior to this, she had an extensive history of abdominal problems and interventions spanning twenty years, and a very extensive travel history for work including visits to at least 20 countries. She was not sexually active, did not smoke and drank alcohol occasionally.

Chronology

Her abdominal problems were first noticed approximate-

ly twenty years prior (2000) to her first presentation to us (2021). It started as severe generalised abdominal pain without any other symptoms which would last for twenty to thirty minutes. Symptoms progressed over the years, to involve mild abdominal distension, severe abdominal pain which required admission for pain control and on one occasion was associated with syncope (2004). Her C-reactive protein was usually found to be elevated. A colonoscopy done at that point did not reveal any cause of symptoms. She subsequently had a laparoscopic appendectomy in 2005, which did not result in much improvement. A colonoscopy done around this time showed a mildly inflamed colon only. We were unable to determine if biopsies were taken at this time.

Seven years later in 2012, while abroad, she was treated for a Peritoneal abscess likely due to Stump appendicitis. She was also treated for pneumonia and parapneumonic effusion with intravenous antibiotics and ultrasound drainage in a tertiary hospital in 2018. CT chest then showed a left-sided consoli-

Citation: James J. Malignant Epithelioid Peritoneal Mesothelioma in a middle-aged lady with extensive travel history and long-standing abdominal symptoms. J Clin Med Img Case Rep. 2022; 2(5): 1250.

dation with parapneumonic effusion and no pleural plaques were seen. The pleural fluid was negative for Tuberculosis (TB), other infections and malignant cells.

In the year she presented to us in 2021, which was twenty years from symptom onset, she had a flare up of abdominal pain and was admitted to a hospital in Januray 2021 and underwent ultrasound and CT of the abdomen and pelvis as well as an Oesophago-gastro-duodenoscopy (OGD) which were all reported as normal. It was concluded that the cause of her symptoms was less likely to be malignant given the reassuring nature of the investigations and duration of symptoms. There was a thought of testing for Familial Mediterranean fever (FMF) and to rule out porphyria should the symptoms persist.

Unfortunately she presented again in march of the same year with similar symptoms, where a barrage of tests including auto-immune screening tests (antinuclear antibodies, anti-neutrophil cytoplasmic antibodies, Rheumatoid factor, complement and immunoglobulins), viral screening (Hepatitis B, C and HIV), fungal markers (Aspergillus serology and β -d-glucan (BDG), QuantiFERON and Lyme test which performed which were all negative. She had a positive IgG EBV indicating a past infection and a mildly raised cancer antigen 125 (CA 125). A repeat CT Thorax abdomen and pelvis (CTTAP) however now showed a diffuse mural oedema involving the colon and stomach, with associated stranding, nodularity of the mesentery and minor free fluid pooling within the pelvis. No stricturing or obstructing lesion was seen (see Figure 1). The appearance was reported as favouring a widespread inflammatory-type process.

A CT angiogram of the abdomen done during this admission showed no obvious clots or ischaemia. She was treated empirically with Colchicine for FMF and genetic testing to confirm this was also sent but was subsequently found to be negative. Urine porphobilinogen to test for porphyria during this admission was also negative.

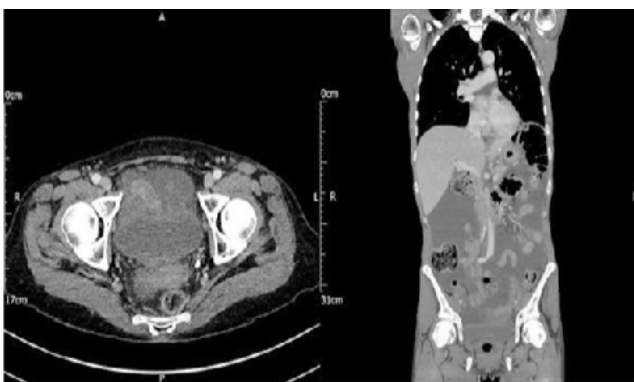


Figure 1: IMAGING Report after multidisciplinary team (MDT) review of scans: Low volume ascites in the subphrenic spaces, tracking down the paracolic gutters into the iliac 1 / 3 fossae and cul-de-sac. Diffuse parietal peritoneal thickening, most evident on the pelvic sidewalls and lateroconal fascia. Low-attenuation material around the stomach extending into the root of the small mesentery with a number of small nodes. Minor Nodularity of the mesentery but no definite serosal involvement.

Case Presentation

A middle aged logistics manager was admitted to hospital with deterioration after a recent admission for constant abdominal pain, distension, and weight loss. Prior to this, she had an extensive history of abdominal problems and interventions spanning twenty years, and a very extensive travel history for work including visits to at least 20 countries. She was not sexually active, did not smoke and drank alcohol occasionally.

She was admitted to our hospital later that year for the first time, with a three-week history of severe abdominal pain. Her inflammatory markers were once again elevated (C-reactive protein (CRP)-227 mg/l), with mildly raised CA-125 (46 u/ml) and normal liver function test. Investigation mentioned above as well as tumour markers were unremarkable as before. CTAP done this admission however showed large volume ascites with concerns for malignancy with no obvious primary noted and no site for biopsy (see Figure 2). No malignant cells were seen on ascitic fluid and no organisms, including tuberculosis or Actinomycosis were isolated from this. Her serum albumin ascitic gradient was less than 11 g/L (exudative). On Flexible sigmoidoscopy, limited views of the colon was visualised due to inadequate bowel preparation, but this did not show features of inflammatory bowel disease. Rectal biopsy was negative for amyloid or any other pathology. She had a diagnostic Laparoscopy which showed a very inflamed looking abdomen, friable bowel matted to walls, with mildly bile-stained fluid in pockets, no pus or fibrin seen. Fluids were aspirated from this and the culture was negative even for TB. The ascetic fluid culture and blood culture were also negative.

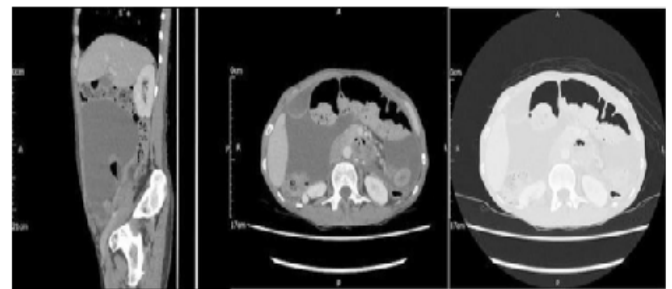


Figure 2: Progression of ascites particularly left upper quadrant and both flanks. Compartmentalisation of small bowel loops with low-attenuation material in the small bowel mesentery with 2 cm deposit indenting the jejunum. Nodular thickening on the pelvic sidewalls and parietal peritoneum has increased.

She received parenteral nutrition and broad spectrum antibiotics and as her pain improved she was discharged with outpatient follow up with the gastroenterology team. On outpatient follow up, an OGD was performed and duodenal biopsy taken to look for features of Whipple's disease, which was negative. Her case was discussed with the Infectious disease team, who were concerned about an infectious cause as she had extensive travel history, but investigations did not reveal any findings to support this. No serological evidence of Brucellosis was found and investigations for parasitic infections including Strongyloidiasis, Schistosoma and Trypanosoma were also negative.

Her abdominal pain continued to worsen necessitating re-ad-

mission to hospital from the out-patient clinic for nutritional support and further investigations two months after her initial presentation to us. On examination, she looked cachectic (body mass index of 17kg/m²) with evidence of muscle loss and generally tender in the upper half of the abdomen. She also had a left-sided pea sized inguinal node. She was admitted for nutritional support, further imaging and a gynaecology review. CTTAP on admission showed large volume complex ascites with progression of peritoneal nodularity, but no evidence of bowel obstruction or primary thoracic or abdominopelvic malignancy was identified (see **figure 3**). A PET scan showed abnormal peritoneal uptake with a large volume of ascites, which was thought to be due to diffuse peritoneal malignancy (see **figure 4**). She subsequently had a repeat diagnostic laparoscopy which revealed multiple small bowel adhesions, with bowel adherent to anterior abdominal wall in the upper abdomen, atrophic ovary and fallopian tube seen with evidence of disease infiltration. The sigmoid mesentery was also infiltrated, and disease had involved the small bowel, anterior abdominal wall, pelvis and omentum. Adhesiolysis, left salpingoophorectomy and peritoneal biopsy with drainage of two litres of ascitic fluid was carried out.

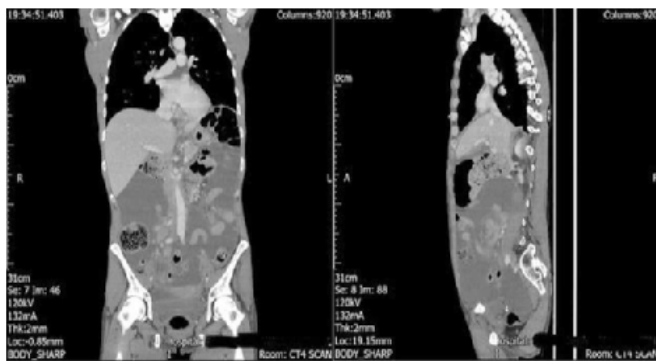


Figure 3: Persisting large volume ascites with diffuse nodular parietal peritoneal thickening. Progression of disease around the stomach and within the gastrocolic ligament. Loculated ascites measuring 4 cm scalloping the left lateral aspect of the liver and 2.3 cm below the left rectus sheath. Diffuse nodularity throughout the mesentery leaves with some areas concerning for mesenteric retraction. Apparent irregularity of the surface of loops of small bowel is suspicious for serosal disease but no oral contrast.

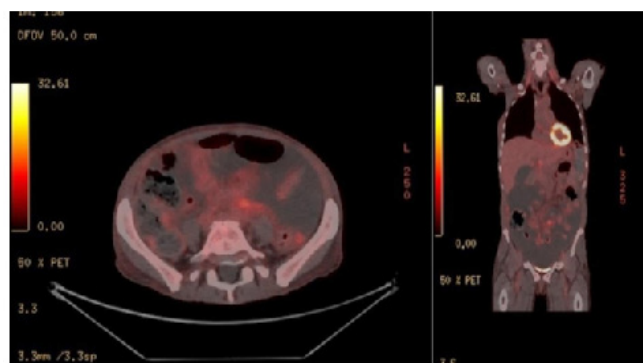


Figure 4: Diffuse nodular uptake throughout the entire parietal peritoneal, predominantly in both flanks, extending down into the pelvis. Some concern for areas of uptake within the small mesentery and possibly even on the small bowel serosa. Impression: Progression of diffuse peritoneal disease with increasing ascites, diffuse global parietal peritoneal thickening and concern for mesenteric and serosal small bowel involvement.

Histology of peritoneal tissue revealed an Epithelioid Peritoneal mesothelioma with immunohistochemistry showing clusters of atypical cells expressing Wilms' tumour-1 protein (WT-1) (focal), Calretinin and D2-40 (**Figure 5, 6A and 6B**). Her nutrition was supported parenterally, and she was subse-

quently discharged when she was able to tolerate oral feeds. She was referred to the peritoneal malignancy specialist team for specialist opinion. They advised her disease would not benefit from Cytoreductive surgery (CRS) and Hyperthermic intraperitoneal chemotherapy (HIPEC) at this point, as it involved the small bowel and recommended systemic chemotherapy. Her care was transferred to a tertiary hospital in another city as she wished to move base to be closer to her family.

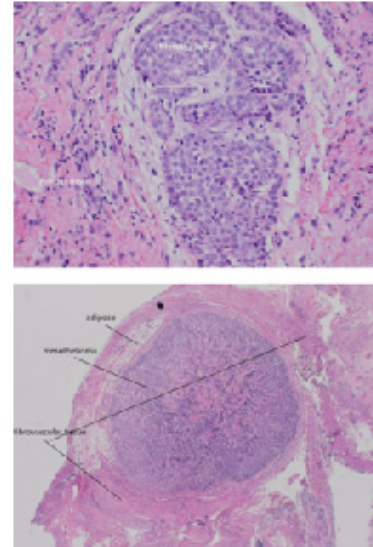


Figure 5: Abdominal wall biopsy Histology report: Epithelioid malignant mesothelioma. Epithelioid malignant mesothelioma involves the biopsies from the anterior abdominal wall, right pelvic sidewall, sigmoid mesentery, right upper quadrant peritoneum and the serosa of the left ovary and fallopian tube.

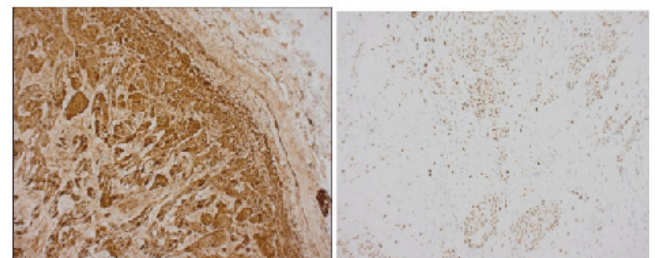


Figure 6: Figure 6A and 6B: immunohistochemistry stains
Figure 6A: Calretinin stain - strong staining of the whole of the tumour cell (nuclear and cytoplasmic staining) whilst not staining the background. The cells show a tubulopapillary growth pattern. They express calretinin, D2-40 and WT-1. They are negative for CK20, ER, PAX-8 and MOC31. There is loss of BAP1 expression. The ki67 proliferation index is 11%.

Figure 6B: WT1 stain: This is a nuclear stain. It is positive in mesothelium and in some epithelial tumours.

Differential Diagnosis

The main diagnosis initially was of tropical infection like Whipple's or an infection that was difficult to culture like Actinomycosis. FMF and porphyria was also considered given the chronicity of symptoms but rule out. Given progression in CT scan malignancy was considered especially Pseudomyxoma peritonei and peritoneal Carcinomatosis but there was no evidence of this on diagnostic laparoscopy and biopsy showed MPM.

Outcome and Follow-Up

This lady moved back to be closer to family one month after the diagnosis and underwent four cycles of systemic chemotherapy. Her health deteriorated despite this and was admitted into hospice care currently, seven months from the time of diagnosis.

Discussion

MPM is a very uncommon malignancy of the peritoneal lining. It has always been considered a very aggressive neoplastic disease.

In the United Kingdom, 7,210 new cases of Mesothelioma were diagnosed between 2016 and 2018. Peritoneal mesothelioma accounted for 260 cases, 64% were male and 36% were female and the median age was 71 [2]. Approximately 3000 new cases of Mesothelioma are diagnosed every year in the United States [3]. Peritoneal mesothelioma accounts for about 15-20% of all Mesothelioma diagnoses [4]. MPM is not usually linked with asbestos exposure and it affects men and women equally. Patients with peritoneal mesothelioma usually have a history of previous intra-abdominal surgeries and age at presentation usually ranges between 40 to 65 years [5]. In this case, there was no history of asbestos exposure and the long-standing abdominal history and the extensive travel history made an infectious aetiology more likely. She also had previous abdominal surgery abroad, it is not known if her previous abdominal surgeries are related with developing intraperitoneal mesothelioma as she had experienced abdominal symptoms prior to the surgeries.

MPM usually presents with progressive features including bloating, intermittent abdominal pain, ascites, weight loss and reduced energy. Sometimes, a palpable abdominal mass is described on examination. Initial imaging is usually CT with intravenous contrast with findings of diffuse omental masses, mesenteric nodules or nodularity, or parietal peritoneal thickening, sometimes ascites might be present. Other imaging modalities used in investigation include MRI and PET-CT for staging. Definitive diagnosis is from histology and immunohistochemical staining (calretin, vimentin, cytokeratin 5/6, epithelial membrane antigen (EMA), WT1) of samples obtained by CT guided biopsy or diagnostic laparoscopy. There are three histologic subtypes of MPM, epithelioid, sarcoïd and mixed, with the epithelioid type having the best prognosis [6].

The current standard of care for MPM is CRS and subsequently intraperitoneal chemotherapy which could be HIPEC or early post-operative chemotherapy (EPIC). This is the first-line treatment for patients with epithelioid subtype, good performance status and no metastatic disease. 5-year survival is 74% with this treatment compared with a median survival of 5-12 months without treatment. Patients not eligible for CRS-HIPEC are offered systemic chemotherapy (pemetrexed with either carboplatin or cisplatin). An alternative second line treatment could be the molecular agent Tremelimumab [6,7]. Prognosis is variable depending on the histologic type of disease with epithelioid subtypes having better prognosis than sarcoïd and biphasic subtypes. Other factors used to predict survival include, age, involvement of lymph nodes and presence of biomarkers [8].

Peritoneal mesothelioma, although uncommon should be considered as a differential diagnosis in patients presenting with long-standing abdominal symptoms for which no aetiology has been isolated. This case highlights the importance of tissue diagnosis when faced with a diagnostic dilemma. Tissue sampling should have been obtained during the first laparoscopy as this might have aided in securing a diagnosis earlier. It is also worthy to mention that in cases of peritoneal meso-

thelioma a history of asbestos exposure is not needed. It is important to approach diagnostic dilemmas such as this with a wide diagnostic net and perform thorough clinical assessments so as not to miss the diagnosis. Repeat CT Scans and reviewing previous results and imaging from other hospitals helped identify disease progression and help understand the diagnostic thought process of other clinicians previous looking after the patient. This helps to reach the correct diagnosis in a timely manner and improve patient outcome.

Finally, it is important to pay attention to the change in symptoms of a patient with chronic abdominal pain as this may alert you to a progression of disease or a new diagnosis altogether. It was unclear if the chronic pain for this patient was due to the peritoneal mesothelioma from the very beginning.

Learning Points/Take Home Messages 3-5 bullet points

- “Tissue is the issue” -Important to acquire tissue samples early on for complex cases like this when a diagnosis is not clear to help guide management
- Always crucial to review previous images and investigations conducted elsewhere to understand other clinicians thought processes and help prevent duplication of work
- It is Important to understand the chronology of symptoms to reach the right diagnosis and to repeat investigations when symptoms have changed

References

1. Boffetta P. Epidemiology of peritoneal mesothelioma: a review. *Annals of Oncology*. 2007 Jun 1; 18(6): 985–90.
2. National Mesothelioma Audit report 2020 [Internet]. 2020.
3. Baumann F, Carbone M. Environmental risk of mesothelioma in the United States: An emerging concern-epidemiological issues. *Journal of toxicology and environmental health Part B, Critical reviews* [Internet]. 2016; 19(5–6): 231–49.
4. Mazurek JM, Syamlal G, Wood JM, Hendricks SA, Weston A. Malignant Mesothelioma Mortality-United States, 1999–2015. *MMWR Morbidity and Mortality Weekly Report* [Internet]. 2017; 66(8): 214.
5. Lee M, Alexander HR, Burke A. Diffuse mesothelioma of the peritoneum: a pathological study of 64 tumours treated with cytoreductive therapy. *Pathology*. 2013 Aug 1; 45(5): 464-73.
6. Alexander HR, Burk AP. Diagnosis and management of patients with malignant peritoneal mesothelioma. Vol. 7, *Journal of Gastrointestinal Oncology*. Pioneer Bioscience Publishing; 2016; 79-86.
7. Sugarbaker PH. Update on the management of malignant peritoneal mesothelioma. Vol. 7, *Translational Lung Cancer Research*. AME Publishing Company; 2018; 599-608.
8. Boussios S, Moschetta M, Karathanasi A, Tsiouris AK, Kanellos FS, Tatsi K, et al. Malignant peritoneal mesothelioma: clinical aspects, and therapeutic perspectives. *Annals of Gastroenterology* [Internet]. 2018; 31(6): 659.