CASE REPORT

# Diffuse malignant epithelioid mesothelioma in a background of benign multicystic peritoneal mesothelioma: a case report and review of the literature

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## SUMMARY

Peritoneal mesotheliomas are unusual entities with diverse origins and outcomes. Both benign and malignant variants exist. Benign multicystic peritoneal mesotheliomas (BMPMs), also known as multiple or multilocular peritoneal inclusion cysts, are extremely rare tumours arising from the peritoneal mesothelium covering the abdominal serous cavity. Even though these entities are considered benign tumours, BMPMs tend to recur after surgical resection, and in two cases have been reported to undergo malignant transformation. In contrast, diffuse malignant peritoneal mesotheliomas, while also quite rare, are the second most common form of malignant mesothelioma after the pleural variety with extremely high mortality and poor response to many treatments to date. We present a rare case of diffuse malignant peritoneal mesothelioma within a large component of a BMPM in a young man admitted to our service.

## BACKGROUND

This case report highlights multiple aspects of the diagnosis and management of a rare disease which presents with atypical characteristics in this particular patient.[1 2]

## CASE PRESENTATION

The patient was a 32-year-old otherwise healthy, Hispanic, construction worker with a 1-year history of vague, diffuse abdominal pain. The patient did not have any history of abdominal distention, changes in bowel habits or weight loss. He had no significant medical history, with the exception of a previous intestinal parasitic infestation. Physical examination revealed a palpable right-sided, non-tender abdominal mass spanning from the lower liver edge to the right anterior superior iliac spine.

## INVESTIGATIONS

Laboratory evaluation was normal. CT scan demonstrated a 14 cm multicystic abdominal mass in the right paracolic gutter beneath the liver, but failed to identify the organ from which the mass originated (figure 1). Invasion could not be ruled out. Upper gastrointestinal (GI) series and colonoscopy were negative. Percutaneous biopsies of the mass revealed only mesothelial hyperplasia.

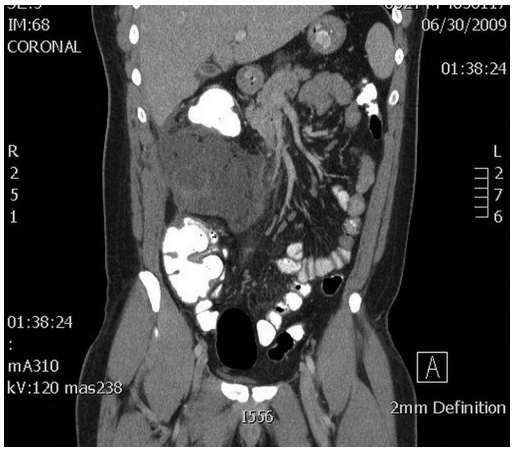


**Figure 1** CT scan demonstrating a large intraperitoneal mass.

## TREATMENT

After discussion at a tumour conference, a decision was made to proceed with abdominal exploration and resection of the tumour. On entering the abdomen, a large mass was noted on the right side of the abdominal cavity, which appeared to be contiguous with the omentum. On initial inspection, the mass was closely adherent to the hepatic flexure, as well as the proximal and transverse colon. No other lesions or suspected implants were noted on the remaining peritoneal surface.

The omentum was divided to grossly uninvolved tissue around the mass and was lifted. The complete specimen was removed en bloc after it was resected from the remaining omentum, the lateral peritoneal attachment to the abdominal wall, the right colon and finally the transverse colon, whose posterior wall was accessed through the lesser sac. The mass was excised without resection of the colon or other intra-abdominal organs. No gross invasion was noted. The abdomen was closed, and the patient was discharged home without immediate complications.

## OUTCOME AND FOLLOW-UP

Pathological examination revealed a large, irregular, multicystic mass, approximately 20 cm in diameter, weighing 640 g. The cysts varied in size and contained serosanguinous and mucoid material (figure 2).

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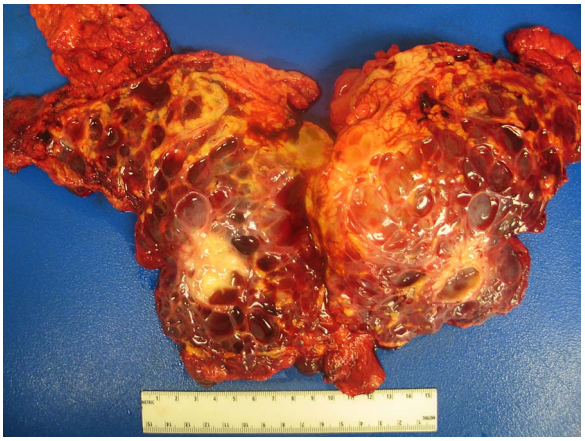

**Figure 2** Gross appearance: irregular multicystic mass with focal solid area.

Microscopic analysis revealed two different components. The majority of the mass consisted of multiple cystic spaces lined by reactive mesothelial cells, with stromal oedema and fibroblastic proliferation, consistent with a benign multicystic mesothelioma (figure 3).

Approximately 1 month following discharge, the patient returned with recurrent abdominal and pelvic pain. A repeated CT scan demonstrated several subcentimetre pulmonary nodules, as well as a pelvic fluid collection, which was percutaneously drained. No malignant cells were noted on cytology.

A third CT scan approximately 4 months following this episode showed the presence of a solid mass measuring about 6 cm in the left lower quadrant, along with two additional pelvic masses which measured 3 and 5 cm in maximum diameter, as well as suspected serosal implants. Given these suspicious findings, pathology of the original specimen was reviewed again, and a small area less than 1% of the specimen was found to have florid mesothelial proliferation associated with a moderate degree of atypia, cytoplasmic vacuolisation and stromal invasion with a cord-like arrangement was noted (figure 4). Immunohistochemical staining was positive for calretinin, CK 8/18 and focally for desmin and progesterone receptor. CD 34, CD 31, factor VIII and CD 68 were negative. This was consistent with a malignant peritoneal mesothelioma. The patient subsequently underwent peritoneal debulking with hyperthermic intraperitoneal chemotherapy (HIPEC) at another institution. He remains disease-free 4 years following his initial presentation.

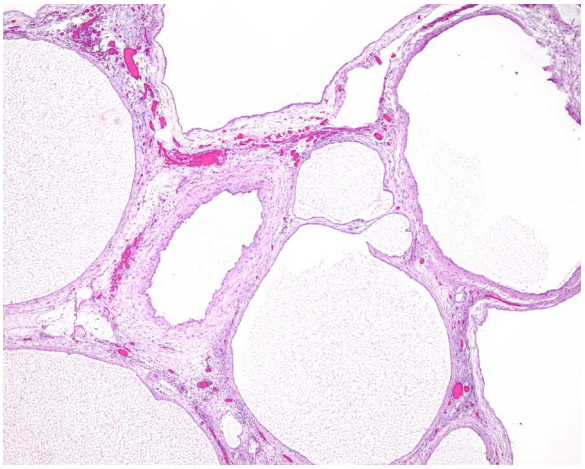

**Figure 3** H&E stain: cystic spaces lined by mesothelial cells (original magnification ×40).

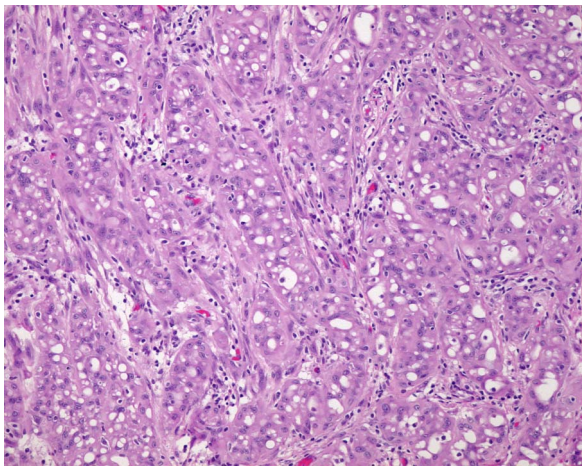

**Figure 4** H&E stain: florid mesothelial proliferation in cord-like pattern (original magnification ×200).

## DISCUSSION

Diffuse malignant peritoneal mesotheliomas (DMPMs) were once exceedingly rare entities, until a dramatic increase in the 1930s, likely due to increased asbestos use.[3] The peritoneum is now the second most common location for malignant mesotheliomas, comprising about 10–25% of patients diagnosed with the disease, the remainder being primarily thoracic. Nonetheless, despite their increased rate of occurrence, they still remain rare, at a rate of 2.2 per million per year in the USA. Despite a variable growth rate, these cancers often present with remarkably florid and rapid progression.

Owing to their association with asbestos, they are predominantly found in middle-aged and elderly men, usually of low socioeconomic status. Given their rarity, no recognised staging system is available, nor are there uniformly accepted/established treatment protocols for these patients.[4–6]

Diagnosis can be very difficult preoperatively, as imaging, cytology and histological findings are usually not specific and overlap with other tumours. Immunohistochemistry is currently the best method of diagnosis. In particular, calretinin, thrombomodulin and keratin 5/6 are the best positive markers for differentiating epithelial malignant mesotheliomas from papillary serous carcinomas of the peritoneum, as well serous carcinoma of the ovary.

Asbestos exposure is the only known risk factor, related to the tumour in as many as 87% of cases in some series. Presentation is typically 30–40 years after exposure with a mean age of 63 at diagnosis.

Initial presenting symptoms include dull abdominal pain, distention or mass, ascites, weight loss, fever, bowel obstruction, thrombocytosis and fatigue. Two hypotheses exist as to how asbestos exposure leads to peritoneal cancer. The first is that the crystals are ingested and over time slowly migrate from the lumen of the GI tract to the peritoneum. The second hypothesis is that the crystals are carried to the peritoneum via the lymphatic system.

DMPMs present in the vast majority of the cases as multiple plaques or nodules over the peritoneum, sometimes associated

with dense adhesions, shortening of the mesentery and almost always associated with ascites. The tumour can very rarely present as a solitary mass.

Prognosis is poor and surgery is often not an option, as the majority of malignant peritoneal mesotheliomas are in their advanced stages at the time of discovery.[7]

This condition has been traditionally regarded as a rapidly lethal disease, with a mean survival of 8 months following diagnosis. Recent multi-institutional trials have attempted to improve the prognosis combining an aggressive surgical cytoreduction with perioperative HIPEC. In particular, Yan *et al* recently published a data registry of over 400 patients treated with surgical debulking and HIPEC at different institutions. The authors report an overall median survival of 53 months (3-year and 5-year survival rates were 60% and 47%, respectively). On multivariate analysis, the epithelial subtype, absence of lymph node metastasis, completeness of cytoreduction and HIPEC were identified as prognostic factors independently associated with improved survival.[8]

This case report highlights multiple aspects of diagnosis and management of a very rare disease which presents with atypical characteristics in this particular patient.

First, the presentation of the disease resembles a benign peritoneal mesothelioma, considering the patient's age, the finding of a single mass lesion with no gross signs of peritoneal dissemination, the fact that the patient was unlikely to have received a significant enough exposure to asbestos to result in a malignant mesothelioma during his relatively short time in construction, and the report of previous chronic abdominal inflammatory condition (parasitic infestation). This diagnosis was supported by the initial pathological examination.

Unfortunately, the extremely aggressive behaviour of the tumour after surgical resection prompted a second review of the specimen with the identification of a small focus of malignant mesothelioma arising in a diffuse background of Benign multicystic peritoneal mesotheliomas (BMPM), which changes the diagnosis to malignancy.

At this point, the interpretation of this information becomes problematic. Spontaneous DMPM is almost universally associated with significant prior asbestos exposure, which our patient likely did not have given his young age and few years of construction work. Malignant mesothelioma almost never presents in less than 20 years from exposure, and is almost exclusively found in men greater than 55 years of age. A less likely explanation could be the simultaneous presence of malignant and benign components of the disease from the beginning, the diagnosis made difficult by the overwhelming presence of BMPM in the background. A more likely explanation, despite only two isolated reports previously, is that the patient initially had a BMPM, which underwent malignant degeneration. This case adds to the growing body of evidence that these two entities are not entirely separate phenomena.

## Learning points

- Diffuse malignant peritoneal mesotheliomas are rare tumours that present with rapid progression, and generally have a poor prognosis with a mean survival of 8 months following diagnosis.
- Immunohistochemistry is the best method of diagnosis with calretinin, thrombomodulin and keratin 5/6 being the best positive markers in differentiating epithelial malignant mesotheliomas from peritoneal papillary serous carcinomas.
- Prognostic factors associated with improved survival include epithelial subtype, absence of lymph node metastases, completeness of cytoreduction and hyperthermic intraperitoneal chemotherapy.

**Contributors** JSM was responsible for drafting the original manuscript and assisting in final revisions. RM was responsible for assisting in critical revision and coordinating the draft between authors. RP was responsible for paring down the article from a literature review into a case report with extensive editing. SV was involved in drafting the pathology sections of the manuscript. LG was responsible for dictation and inclusion of operative findings of the case into the manuscript. CR was responsible for the operative conduct, and ultimately responsible for final revisions.

**Competing interests** None.

**Patient consent** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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