MALIGNANT PERITONEAL MESOTHELIOMA – REPORT OF A RARE AND CHALLENGING SURGICAL CASE

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Abstract

Malignant peritoneal mesothelioma is a rare tumour of mesothelial origin arising from the peritoneal linings and its incidence is second to pleural mesothelioma. Clinical presentation is often vague and non-specific posing great difficulty and delay in diagnosis. Thankfully, the biological behaviour and spread of the tumour makes local treatment with combine cytoreductive surgery and chemotherapy the standard first line treatment. We report a challenging case in a 50 year-old woman who presented with symptoms of 9 months duration and had cytoreductive surgery and adjuvant chemotherapy following histological confirmation of malignant peritoneal mesothelioma.

Introduction

Malignant peritoneal mesothelioma (MPM) is a rare tumour arising from the mesothelial cell lining of the peritoneum. Diagnosis is hampered by its vague clinical presentation, non-specific radiological findings and difficulties with obtaining and analysing tumour specimens. Instituting local treatment (cytoreductive surgery and intraperitoneal chemotherapy) earlier before the patient or the tumour becomes inoperable, can delay or halt aggressive local tumour spread.[1-8] In this report, we narrate our experiences and challenges with a case of malignant peritoneal mesothelioma encountered in Irrua Specialist Hospital, Nigeria.

Case Report

A 50 year old woman, who resides and sells fabrics in Abuja, was brought to our facility by family members with a 9 month history of diffuse abdominal pain and abdominal swelling. The swelling started in the left lower half of the abdomen and progressively increased in size towards the upper abdomen, associated with anorexia, weight loss, easy satiety and fullness. There was no vomiting, constipation or fever. She is not hypertensive or diabetic, unaware of any drug or food allergy and no previous surgery. She is a mother of six children; last child birth was 11 years ago and has had regular cycle prior to its cessation 5 months ago. She doesn't smoke nor take alcohol.

Clinical examination revealed a chronically ill-looking and fatigued middle aged woman who was in painful distress. She was dehydrated with pulse rate 110/min, blood pressure 100/70 mmHg, respiratory rate 22/min, temperature 36 ^{0}C and SPO_2 96% at room air. Cardiac exam

was normal. Her abdomen was unevenly distended with a huge firm, mass extending from the pelvis to the epigastrium, more to the left side (figure 1). The bowel sounds where hyperactive. There was a bulging mass in the posterior fornix and rectum contained normal coloured and well formed stool.

Before she presented to our facility, she had visited several hospitals and had done a CT scan, CXR and CA-125. CT scan showed a huge heterogenous predominantly isodense solid soft tissue mass (26 x 20 x 19.8 cm; LS, AP, TS) with foci of hypodense (likely necrotic) areas, in the left retroperitoneal and mesenteric region with displacement of visualized bowel loops and great vessels to the right side and postero-superior displacement of the left kidney. The left colon, mesentery and omentum could not be delineated from the mass. The liver, spleen, kidneys and uterus appeared normal and no abdominal lymphadenopathy or ascites. CT differentials were mesenchymal gastrointestinal tumour and GIST. Abdominal USS showed a large heterogenous, circumscribed, multi-lobulated intra-abdominal mass (30 x 22.8 x 22.2 cm) extending from pelvis to hypochondrium with mass effect on pelvis, abdominal organs and vessels. Both ovaries were visualized but the superior margin of the left ovary was not well delineated and appeared adjacent to the mass. Its impression was mesenteric fibroma or ovarian fibroma. Apart from CA-125 which was 109 U/mL (three times above reference value of 0-35) and haemoglobin of 8 g/dL, other investigations (electrolytes, urea, creatinine, liver enzymes, CXR, ECG) were normal. Covid-19 PCR test (a protocol for elective surgery during the coronal virus pandemic) was negative.

She was optimized (rehydrated and transfused) and consent was obtained for laparotomy and debulking surgery. She also had bowel preparation prior to surgery. On laparotomy, a large tumour was found with solid components and areas of cystic degenerations and necrosis. The distal half of the transverse colon, descending colon, proximal sigmoid colon, anterior leaf of small bowel mesentery and Gerota's fascia of the left kidney were attached to the tumour. The liver, spleen, internal genital organs were normal. Gross tumour debulking was done including resection of attached bowels and a primary colocolic anastomosis. Operation was complicated by significant blood loss, intraoperative hypotension and cardiac arrest. Massive transfusion protocol was activated during the surgery. When patient had a cardiac arrest intraoperatively, she had a successful CPR and lumbar epidural anaesthesia was converted to GA. Postoperatively, she was transferred to ICU where she was extubated. Postoperative hypotension, hypopoproteinemia (albumin 2.6mg/dL) and congestive cardiac failure were the attendant early complications that were managed before patient was discharged.

Macroscopic specimen revealed a 6.6 kg solid tumour with cystic areas containing gelatinous material and the attached bowel loops were edematous and non-obstructed. Microscopic sections showed malignant neoplastic lesions of mesothelial differentiation composed of diffuse sheets, micropapillary, and vague alveolar configuration of mild-moderately pleomorphic epitheloid cells. There were few foci of biphasic areas composed of mainly sarcomatoid appearance with minimal hyalinization and fibrosis. The overall morphology was suggestive of malignant mesothelioma (epitheloid variant).

Three (3) weeks after surgery, she was commenced on adjuvant chemotherapy (cisplatin and doxorubicin). However, after the first dose of the drug, she requested for a referral to another specialist hospital that is near to her home town and place of work. We intend to follow her treatment subsequently by liaising with the patient and her new doctors.

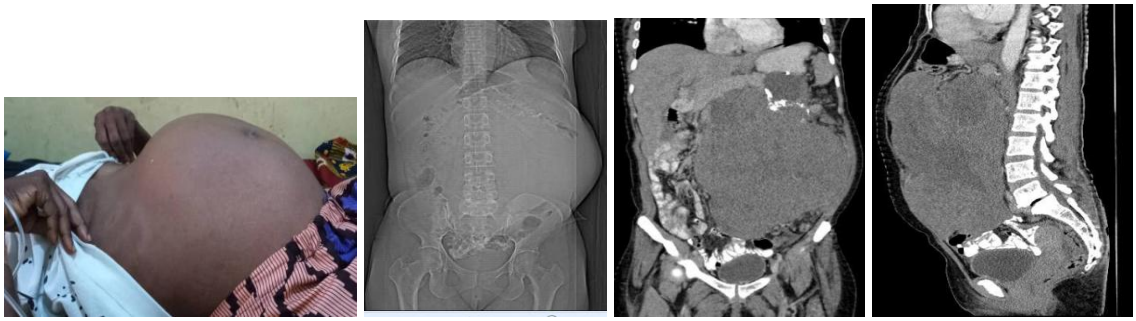

Figure 1. Showing the abdomen of the patient at presentation
Figure 2. Scout thoracoabdominal plain CT view of the patient
Figure 3. Coronal view showing the intraabdominal mass and its push effect on adjacent viscera
Figure 4. Saggital section of the mass

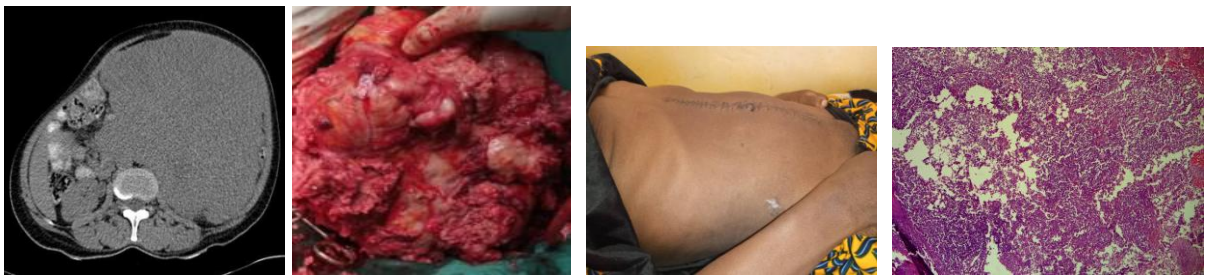

Figure 5. Axial CT view
Figure 6. Specimen removed
Figure 7. Postoperative picture taken 3 weeks after surgery
Figure 8. Photomicrograph showing diffuse sheets of epithelioid cells in a scant fibrocollagenous stroma with areas of haemorrhage (H&E x40)

Discussion

Mesothelioma is tumour of mesothelial surface lining cells of serous cavities (pleural, peritoneal, pericardial and rarely tunica vaginalis of the testes). Pleural mesothelioma is commoner with exposure to asbestos implicated as the most significant risk factor. Malignant mesothelioma of the peritoneum (MMP) is rare accounting for 10-30% of all mesotheliomas.[9-11]

Reported incidence of MPM ranges from 0.5-3 cases per million with a female to male ratio of 0.70. Unlike pleural mesothelioma, its association with asbestos is not well defined. There is some evidence to implicate other industrial pollutants and minerals (eg, mica, talcum, erionite, thorium, thorotrast), therapeutic radiation, chronic peritoneal irritation/inflammation, Hodgkin's disease and infection by simian virus 40 (SV 40) as possible causative agent. 30-45% of cases may be associated with synchronous pleural mesothelioma.[4,12-16] We could not demonstrate a direct causative risk factor in our patient after confirmation of the diagnosis.

The presentation is often nonspecific and vague, delaying diagnosis to more advance stages of the disease. Tumour spread is predominantly expansive or diffuse more than infiltrative. Nodal and metastatic spreads are infrequent and rarely go beyond the peritoneum.[4-7,16-19] The extent of tumour spread within the abdominal cavity determines the clinical presentation. Our patient had abdominal pain, swelling, anorexia, weight loss, fatigue and early satiety. Nausea, vomiting, constipation and/or diarrhea, fever, night sweats and new onset abdominal wall hernia are other common clinical features.[20,21]

More often than not, the diagnosis is suspected by imaging and confirmed by histology and immunochemical staining of specimen obtained either by open, image guided or laparoscopically aided biopsy of peritoneal lesions or rarely from cytologic examination of ascitic fluid. Common radiological (USS, CT or MRI) findings include heterogenous solitary or diffuse peritoneal masses or nodules, thickening or caking of the omentum or mesentery, calcifications, scalloping of adjacent intraabdominal viscera, diaphragmatic and pleural plaques, calcifications, ascites (loculated or diffuse).[4,15,22-24]

Peritoneal mesothelioma is classified into three pathologic subtypes – malignant peritoneal mesothelioma (MPM), cystic mesothelioma (CM) and well-differentiated papillary mesothelioma (WDPM). CM and WDPM are commonly associated with risk factors other than asbestos exposure.[9,16] Other differentials based on presentation and radiological findings include peritoneal carcinomatosis, serous papillary carcinoma, peritoneal lymphomatosis, tuberculous peritonitis, endometriosis, pseudomyxoma peritonei, ovarian neoplasm, mesenteric/omental cysts.[15,22,25] WHO divides MPM into three histologic subtypes – epitheloid (75%), sarcomatoid (rare) and mixed/biphasic (25%). Epitheloid variant as seen in our patient is found commonly in women and associated with a better prognosis. There is no single immunohistochemical marker that is specific for MPM. Positive panel for WT 1, calretinin, CK5/6, EMA, D2-40, HBME-1, CD 10, thrombomodulin, podoplanin and mesothelin maybe helpful.[20,26-28] Immunohistochemical staining was not done in our case as it was not remotely possible in our center. Serum tumour marker eg CA-125 is elevated in some patients as was seen in this case report.[29]

Treatment consist of a combination of cytoreductive/debulking surgery (CRS), hyperthermic intraperitoneal chemotherapy (HIPEC), intraperitoneal instillation of radioactive isotopes, systemic chemotherapy and targeted therapy/immunotherapy. Combined CRS and intraperitoneal chemotherapy is considered the first line treatment for operable patients with good performance status with a longer median survival benefit. Systemic chemotherapy (neoadjuvant or adjuvant) is indicated for high risk patients, those with extensive diseases or in situation where histologic confirmation of diagnosis was made after surgery as seen in this case report. Premetrexed/cisplatin or carboplatin, adriamycin/cisplatin or carboplatin, premetrexed/gemcitabine are reasonable choices.[2,20]

Negative prognostic factors include old age, high Ki-67, presence of lymph node metastasis, non-epitheloid histologic type and poor grade. While the tumour is found more in males possibly because of greater exposure to asbestos, the prognosis is better in females possibly because of greater association with epitheloid variety.[30]

Conclusion

Accurate preoperative diagnosis in the setting of suspected intraabdominal tumour is not always feasible due to limitations posed by clinical presentation, investigations and difficulties in obtaining tissues for examination. Malignant peritoneal mesothelioma should be considered a reasonable differential in patients presenting with abdominal swelling/distension and vague gastrointestinal symptoms with or without a history of exposure to asbestos. Being a locally expanding tumour that rarely spreads extra-peritoneally, intraoperative chemotherapy is considered a major treatment option in combination with cytoreductive surgery. Early and preoperative diagnosis is therefore necessary to plan surgery and maximise the benefits of intraperitoneal chemotherapy.

Acknowledgement

Consent

Consent was obtained from the patient for publication of this case report and accompanying images.

Conflict of Interest

There is no conflict of interest declared

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