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Case Report

Pathology Section

Case of Peritoneal Malignant Mesothelioma in a 60-year-old Lady Presenting Clinically with Huge Abdominopelvic Mass: A Diagnostic Challenge

USHA SARMA[1], RITUPARNA DAS[2], MAYURPANKHI SAIKIA[3]

ABSTRACT

Peritoneal malignant mesothelioma is a rare tumour that poses diagnostic challenges due to vague clinical symptoms, a variable histologic picture and being a common site for metastasis from GI organ, ovary, kidney and several other organs. We presented a case of peritoneal malignant mesothelioma in a 60-year-old lady who presented clinical symptoms of abdominal obstruction due to an omental cyst on a Computed Tomography (CT) scan. The case has been diagnosed as peritoneal malignant mesothelioma on histology along with a panel of immunohistochemical stains like calretinin (diffuse nuclear and cytoplasmic positivity), WT1 (diffuse nuclear positivity), CK 7 (focal positivity), PAX8 (focal positivity), CK20 (negative). At least two positive immunohistochemical markers and one negative marker help to distinguish mesothelioma from other entities. There was no history of active or passive asbestos exposure. She has been referred to a nearby regional cancer centre and managed accordingly. During her first postoperative check-up, she was asked about the history of asbestos exposure either in active or in passive form, which she denied. The present case report discusses the diagnostic dilemma in routine Haematoxylin and Eosin (H&E) stained tissue sections with a list of differential diagnoses as: 1) Primary tumour (peritoneal malignant mesothelioma versus primary serous carcinoma); 2) Sex cord-stromal tumour of ovarian origin; 3) Metastatic adenocarcinoma from neighbouring organ.

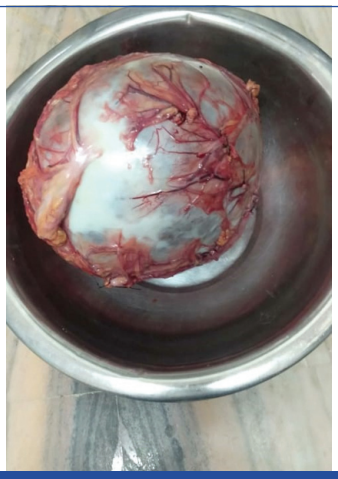
Keywords: Calretinin, Cytokeratin 20, Epithelioid mesothelioma

CASE REPORT

A 60-year-old lady was admitted to the Emergency Department (ED) of our hospital with signs and symptoms of acute abdomen with abdominal swelling and obstipation for the last five days. She complained of abdominal discomfort and distension for the last 6 months along with gradual weight loss. There was no recent or past clinical history that suggested ovarian pathology. Physical examination revealed a huge abdominopelvic swelling involving all quadrants of the abdomen, 30×30×20 cm approximately cystic in nature, not adhered to the skin, mobile, no discolouration seen, non-tender, non-pulsatile, no fluid thrill perceived. Bowel sounds were absent. She was diagnosed with bowel obstruction based on clinical examination. She carried a report of a Computed Tomography (CT) scan of her abdomen which was done a few days back in a private centre, which stated a large abdominopelvic predominantly cystic mass with enhancing solid mural nodules measuring 40×25 mm size likely to be mesenteric/ovarian origin. The image of her CT scan could not be shown as the patient did her CT scan in outside lab and brought the report only. In the present hospital, she underwent an emergency laparotomy as she was diagnosed of bowel obstruction without much delay.

Clinically mesenteric/ovarian cyst was thought of and emergency laparotomy was planned. Routine investigation as complete blood profile was within normal limit except for haemoglobin (7.1 g/dL). Biochemical tests like random blood sugar, serum creatinine, serum electrolytes, Liver Function Test (LFT), Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), and International Normalised Ratio (INR) were within normal range. Clinically, mesenteric/ovarian cyst was suspected and an emergency laparotomy was done. A large cystic mass was resected out. Other intra-abdominal organs were unremarkable. About 50 mL of fluid collection (minimal ascites) was seen within the abdominal cavity. Intraoperative ascitic fluid was sent to the cytology section which showed reactive mesothelial cells and cyst fluid showed necrotic debris and degenerated cells on cytological study.

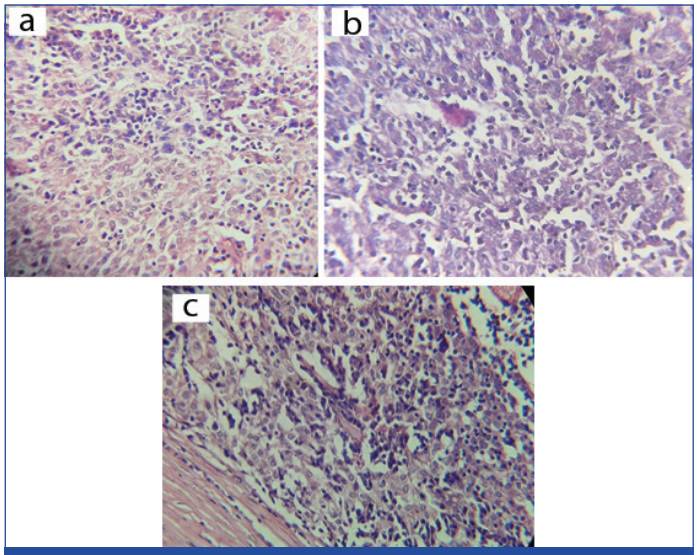
A cystectomy was carried out. The cyst was around 5 kg in weight [Table/Fig-1]. Intraoperative ascitic fluid and cyst fluid were sent for cytological study, the report of which showed reactive mesothelial cells. The specimen was fixed in 10% buffered formalin and sent for histopathological evaluation. The postoperative follow-up showed improvement in her symptoms and recovery was speedy. Ovaries and uterus were unremarkable.



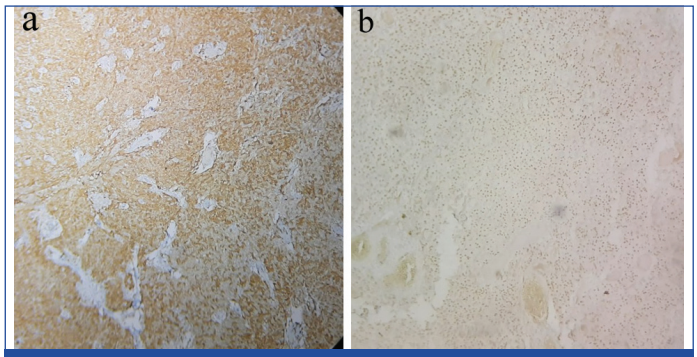
[Table/Fig-1]: Cystectomy specimen weighing 5 kg.

The specimen was unilocular measuring 11.5×10.0×6.0 cm in size. The cyst wall showed irregular thickening with one solid nodular friable growth measuring 4.0×2.0×1.0 cm in size. The cyst contained greyish brown thick material. Four lymph nodes were also dissected out. Histological examination showed the epithelioid tumour cells arranged in a mostly solid, tubulo-papillary and microfollicular pattern. The cells were mostly polygonal to cuboidal with abundant

eosinophilic cytoplasm. Nuclear atypia was mild to moderate, and there were areas of necrosis [Table/Fig-2a-c]. Mitosis was 1-2/10 high power field. Some of the tumour cells showed nuclear grooves. Grossly uninvolved cyst wall showed complete replacement of epithelium by fibrosis with large numbers of diffuse lymphocytic cellular infiltration. The lymph nodes were free from tumour deposits. Considering the gross finding and microscopic features, three differential diagnoses came to our mind: 1) Primary tumour (peritoneal malignant mesothelioma versus primary serous carcinoma); 2) Sex cord stromal tumour of ovarian origin. 3) Metastatic adenocarcinoma from neighbouring organ. A panel of Immunohistochemistry (IHC) stains were used, which showed diffuse membranous positivity of tumour cells by calretinin, and nuclear positivity by WT1 [Table/Fig-3a,b]. Focal positivity by Paired Box Gene 8 (PAX8) and both Cytokeratin 7 (CK7) and Cytokeratin 20 (CK20) negativity were noted. Correlating all the clinico radiological and pathological findings, a final diagnosis of peritoneal malignant mesothelioma has been considered. She has been referred to a nearby regional cancer centre and managed accordingly. Initially, the possibility of mesothelioma was not suspected of as a differential diagnosis, so the history of asbestos exposure was not asked. After the biopsy report, she was asked if there was any history of asbestos exposure during her first postoperative check-up, either in active or passive form, which she denied.



[Table/Fig-2]: H&E stain, (400x): The epithelioid tumour cells are arranged microfollicular (a), and tubule-papillary pattern (b) with a thick cyst wall (c).



[Table/Fig-3]: IHC stain (100x): Diffuse membranous positivity of tumour cells by calretinin (a), and nuclear positivity by WT1 (b).

DISCUSSION

Malignant mesothelioma is a rare neoplasm of mesenchymal cells of the serous membranes, with an incidence of about one to two cases in every million inhabitants per year [1]. Approximately 85% of malignant mesotheliomas develop in the pleural cavity, with most of the remainder arising in the peritoneum [1]. Primary peritoneal mesothelioma is rare and accounts for only 7-10% of all types of mesotheliomas [2]. This tumour is common in older age groups. The present case was also in the older age group (60 years). Due to vague clinical symptoms of abdominal distension and discomfort, being common sites for secondaries and rarity, accurate diagnosis of peritoneal mesothelioma is always challenging. Several times, patients have chronic non-specific abdominal discomfort and pain but the present patient developed huge abdominopelvic swelling, occupying all quadrants of the abdomen. Radiology also provides a diagnosis of ascites. The present case was diagnosed with a cystic mass on CT scan. It needs a combination of extensive clinical evaluation, CT imaging and histologic evaluation. Furthermore, the morphologic overlap between benign mesothelial proliferations and malignant mesothelioma complicates reliable distinction by histomorphology alone, mostly in small biopsy and cytopathology specimens. Hence, ancillary diagnostic techniques, particularly IHC stains have become essential for accurate diagnosis of mesothelioma. A multimodal approach to the diagnosis of malignant mesothelioma is described by several authors [Table/Fig-4] [3-6]. The analysis of ascitic fluid might not be helpful [7]. The present case also gave no clue to ascitic fluid analysis. Though CT scan may play an important role in preoperative diagnosis, it could not provide a specific diagnosis in the present case. In this case, the CT scan only revealed the presence of a cystic mass. On histology, the presence of nuclear groove and microfollicular patterns of some of the tumour cells on evaluation makes it challenging to consider granulosa cell tumour in the list of differential diagnoses. The epithelioid morphology of tumour cells could be due to poorly differentiated carcinoma, either primary or secondary. IHC markers helped to finalise a diagnosis of Primary Mitochondrial Myopathies (PMM). In a study of 24 cases of mesothelioma by Hui M et al., IHC

Author	Age (Years)	Sex	History of asbestos exposure	Clinical presentation	Radiological findings (CT/MRI/USG)	Histology	IHC marker	
							Positive	Negative
Reddy P et al., 2022 [3]	55	Female	Not available	Abdominal mass	PET-CT reports of the patient were inconclusive	Epitheloid pleural mesothelioma d/d angiosarcoma	Calretinin CK 5/6 Vimentin	CK20 HMB45 CD34
Lin LC et al., 2022 [4]	42	Male	N/A	Lower abdominal pain	USG - Ascites CT - Peritoneal thickening	Epithelioid mesothelioma	Calretinin WT1	TTF CDX2
Singh H et al., 2018 [5]	54	Female	No	Chronic non-specific upper abdominal discomfort	Mild nodularity with pelvic ascites	Epithelioid pleural mesothelioma d/d metastatic adenocarcinoma	Calretinin Anti D240Ab	CEA MOC31
Kulkarni PS et al., 2017 [6]	45	Male	No	Lower abdominal pain and ascites	USG - Ascites	Monomorphic epithelioid pleural mesothelioma	Calretinin CK 5/6	CD15 BerP4
Present study	60	Female	No	Huge abdominopelvic swelling and bowel obstruction	CT - Abdomino pelvic cystic mass	Epithelioid mesothelioma d/d 1) Sex cord-stromal tumour of ovary 2) Metastatic adenocarcinoma	Calretinin WT1 PAX 8	CK7 CD20

[Table/Fig-4]: Review of peritoneal malignant mesothelioma cases reported based on clinical, radiological and histological features with Immunohistochemistry (IHC) markers.
CD: Cluster of differentiation; CDX2: Caudal-type homeobox 2; CEA: Carcinoembryonic antigen; CK: Cytokeratin; HMB: Human melanoma black; TTF: Thyroid transcription factor; WT1: Wilms tumour 1

markers like calretinin and Wilms Tumour gene 1 (WT1) helped to confirm the diagnosis [8].

A combination of two "positive" mesothelial and two "negative" carcinoma markers has been advocated by the International Mesothelioma Panel for the diagnosis of mesothelioma [9]. While selecting the IHC panel, one should consider judiciously and rationally the site of the tumour, histologic type, and the list of differential diagnoses considered in each case [7]. Depending on the morphology, IHC panels should be chosen and they must contain both positive and negative markers for mesothelial differentiation and lesions considered in the differential diagnosis [10]. IHC markers should have either sensitivity or specificity greater than 80% for the lesions in question. Interpretation of positivity generally should take into account the localisation of the stain (e.g., nuclear versus cytoplasmic) and the percentage of cell staining (>10% is suggested for cytoplasmic and membranous markers) [9]. The availability of IHC markers in the laboratory is also an important issue. In resource-constraint conditions, a minimum of two positive mesothelioma markers and two negative carcinoma/sarcoma markers help in confirmation of malignant mesothelioma [9]. The presence of a history of asbestos exposure should not dictate the diagnosis of mesothelioma; rather, it should be based on histological findings and IHC that the diagnosis of mesothelioma be confirmed or excluded [9]. This patient did not give a history of asbestos. Several studies detected mesothelioma cases without a history of asbestos exposure [11,12].

CONCLUSION(S)

Diagnosis of mesothelioma creates a huge challenge for the pathologist because of its rarity, several other entities of tumours including metastatic tumours, and vague clinical presentation. Hence, ancillary diagnostic techniques, particularly IHC stains, have become essential for accurate diagnosis of mesothelioma. Tissue biopsy along with a panel of IHC markers is extremely helpful in final diagnosis. Two positive IHC markers calretinine and WT1 and negative markers like CK20 aided the authors in overcoming the challenge of diagnosis of PMM. As the patient did not give a history of asbestos exposure, it highlights the scope for searching for other risk factors related to the development of mesothelioma in this region.

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PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Pathology, Gauhati Medical College, Guwahati, Assam, India.
2. Registrar, Department of General Surgery, Gauhati Medical College, Guwahati, Assam, India.
3. Assistant Professor, Department of Pathology, Gauhati Medical College, Guwahati, Assam, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Usha Sarma,
Professor, Department of Pathology, Gauhati Medical College, Hilltop,
Guwahati-781032, Assam, India.
E-mail: ushajunu@gmail.com

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