



Case Report

A sarcomatoid malignant mesothelioma diagnostic challenge even on immunohistochemistry

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ABSTRACT

Sarcomatoid mesothelioma a rare variant accounts for 10-15% of malignant mesothelioma having a fatal outcome. Therefore it becomes essential to differentiate sarcomatoid mesothelioma from other variants. Morphologically it mimics malignant spindle cell tumor. Immunohistochemistry therefore becomes mandatory to offer definitive diagnosis. However IHC markers also show overlapping expression, making its interpretation difficult. In such challenging situations, clinicoradiological features, morphology together with panel of IHC markers help to solve the riddle/dilemma. Here we report a case of sarcomatoid mesothelioma with its varied IHC profile posing diagnostic challenge.

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1. Introduction

Malignant Mesothelioma (MM) is the most common primary malignant tumour of pleura. It represents less than 1% of all cancers. Histologically malignant pleural mesotheliomas are classified as epithelial (50%), sarcomatoid (15%) & biphasic (35%).¹ The Sarcomatoid type of MM is most difficult to diagnose on histology as it can easily be confused with various types of spindle cell sarcomas like synovial sarcoma, both primary and metastatic sarcoma, and carcinosarcoma.^{2,3} Immunohistochemical profile at times is less amenable to diagnosis and may even show calretinin and cytokeratin negativity causing diagnostic dilemma.⁴ We report a case of Sarcomatoid variant of Malignant Mesothelioma posing diagnostic difficulty even on IHC.

2. Case Report

A 45 year female, attended OPD with complaint of breathlessness and cough of 2 months duration. Her general examination findings were within normal limit except

for presence of pallor. On auscultation, she had reduced breath sounds on left hemithorax along with dullness on percussion. Her chest Xray revealed left sided moderate pleural effusion with contralateral mediastinal shift. The CT scan showed left sided extensive nodular pleural thickening with collapse of underlying lung parenchyma. It was interpreted as a neoplastic etiology with pleural effusion by radiologist. Thoracoscopic decortication of pleura was performed and we received multiple soft to firm greyish brown tissue pieces aggregating 20×12×2cm in size (Figure 1).

Sections from pleura lesion revealed tumour cells arranged in fascicles and bundles, predominantly spindle shaped separated by fibrous septa. Focally the areas with highly pleomorphic cells with moderate eosinophilic cytoplasm and enlarged nuclei with coarse chromatin were seen. Brisk mitotic activity around 4-5 mitotic figures per high power field were present. Areas of necrosis and haemorrhage were also seen (Figures 2 and 3).

Based on histomorphological features the provisional diagnosis of malignant spindle cell tumour with various differentials 1) Leiomyosarcoma 2) Rhabdomyosarcoma, 3) Metaplastic carcinoma 4) Malignant Mesothelioma

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Fig. 1: Gross- multiple, greyish white, firm tissue bits

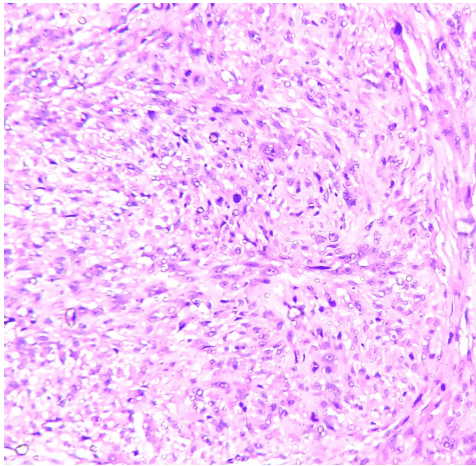


Fig. 2: Tumour cells arranged in fascicles and bundles with brisk mitosis (H&E, 20X)

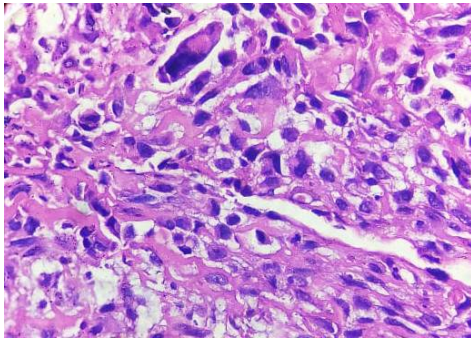


Fig. 3: Spindle shaped tumour cells with pleomorphism and bizarre cells (H&E; 40X)

were offered. To arrive at a definitive diagnosis panel of IHC markers were studied. Desmin and Caldesmon was immunonegative so Rhabdomyosarcoma and Leiomyosarcoma were least likely. CK7, CK20, Pancytokeratin and EMA were negative so possibility of metaplastic carcinoma was ruled out. As most suspected diagnosis was Malignant Mesothelioma - the primarily applied marker such as Calretinin and WT-1, CK5/6 were done and unfortunately were negative. Therefore more specific marker Podoplanin was applied which showed diffuse cytoplasmic expression along with Vimentin positivity (Figures 4 and 5).

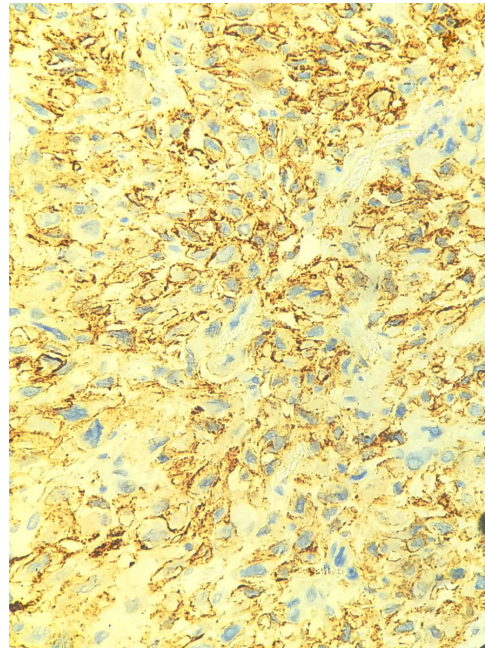


Fig. 4: Podoplanin - membrane positivity (IHC; 40X)

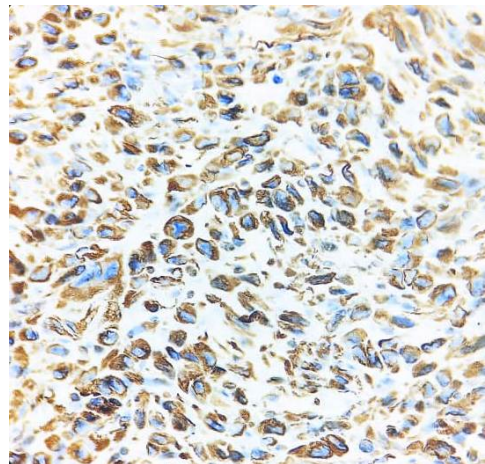


Fig. 5: Vimentin - strong cytoplasmic positivity (IHC; 40X)

Considering all these features, the final diagnosis of Malignant Mesothelioma-Sarcomatoid variant was made. The Patient was thereafter referred to higher centre for further management.

3. Discussion

Sarcomatoid Mesothelioma constitutes the least common form which constitutes about 10% of Malignant Mesothelioma.⁵ Diagnosis requires a multimodal approach including clinical findings, imaging studies, and tissue sampling for routine histology and immunohistochemistry (IHC).⁶ Clinically patient present with breathlessness in early stages due to pleural effusion, dull and heaviness in chest. The nonspecific symptoms include fatigue, anorexia, weight loss, sweats and malaise. Cough, haemoptysis and lymphadenopathy are less common as compared with bronchogenic carcinoma. Some patients are asymptomatic, and have an abnormality detected on imaging undertaken for a different reason.⁷ The Computed tomography scan reveals pleural thickening, thickening of the interlobar fissures, pleural calcifications, effusion and invasion of chest wall.²

Histopathological examination of the biopsy sample showed spindle shaped cells arranged in a haphazard pattern with plump and enlarged, elongated nuclei with hyperchromatic chromatin with moderate amount of eosinophilic cytoplasm. Multinucleation with atypia and mitotic figures were present. These features suggest the diagnosis of Sarcomatoid (fibrous) type Malignant Mesothelioma.].

On IHC CK 7, CK20, CK5/6 negativity was seen along with Calretinine negativity which is the most commonly used marker for Mesothelioma. Diffuse Vimentin positivity was noted along with Podoplanin which is considered as a novel marker for Mesothelioma.

The tumour cells lost Keratin and Calretinin production in the process of de-differentiation. The negative staining for CD31 and CD34 ruled out a vascular tumour or a malignant fibrous tumour. The tumour cells expressed Vimentin thus confirming the mesenchymal origin of the tumour cells. These immunohistochemical and histological findings, along with the clinical findings and the age of the patient, support the diagnosis of Malignant Mesothelioma of the Sarcomatoid type.^{4,8,9}

The sarcomatoid variant of malignant mesothelioma is less amenable to diagnosis using immunohistochemistry than the epithelial variant. In the present case, tumour was immunonegative for Calretinin and cytokeratin 5/6. It has been suggested that some malignant mesotheliomas become undifferentiated and lose keratin and calretinin expression.²

Prognosis of Malignant Pleural mesothelioma is poor and median survival ranges from 8 to 14 months from diagnosis. In contrast to epithelial type which has the

most favourable prognosis of 13.1 months. The sarcomatoid variant is associated with the worst outcomes, with a median survival of just 4 months.¹⁰

Even though IHC is an ancillary technique its interpretation can be confusing especially in dealing with rare variant Sarcomatoid Mesothelioma. In such cases correlation of clinical details, radiological findings and histomorphological features forms the basis to arrive at a definite diagnosis and it should be given importance along with IHC findings.

4. Source of Funding

None.

5. Conflict of Interest

None.

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