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Malignant Pleural Mesothelioma: Case Report of fatal hemorrhagic pleural effusion

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ABSTRACT

Malignant pleural mesothelioma is a rare, invasive and often fatal neoplasm that develops in the pleura. This is a case report of 48 year old men who had dyspnea, cough, right-sided pleuritic chest pain, and weight loss. Physical examination showed a right pleural effusion and chest roentgenograms revealed a homogenous opacity on lower right hemithorax. Biochemical analysis of pleural fluid showed hemorrhagic effusion compatible with exudate. Pleural fluid analysis was negative for tuberculosis. During the pleural biopsy, thickened pleura and multiple nodules in the lung were observed. The histopathological report was compatible with malignant pleural mesothelioma.

Keywords: asbestos, hemothorax, malignant mesothelioma, massive pleural effusion.

INTRODUCTION

Malignant pleural mesothelioma (MPM) is a rare and fatal malignant neoplasm that commonly develops in pleura and peritoneum. Approximately 80% of MPM patients have a history of exposure to asbestos. As it can take decades to develop and, as a result, is usually thought of as a disease of middle age and elder people. [1] Diagnosis requires recognition of patients at risk and knowledge of the typical clinical features of the disease. Patients in whom the disease is detected early have a survival benefit from a multimodality therapeutic approach. [2] This article describes a fatal case of mesothelioma where patient presented with massive hemothorax.

CASE REPORT:

48 years old married gentleman, resident of Bihar, came to the emergency with complaints of right sided chest pain & weight loss for 30 days, cough with minimal expectoration for 20 days and breathlessness on exertion for last 7days. One month before admission, he developed right sided chest pain. Pain was more in lower part, dull aching, non-radiating, not increased with cough, respiration or postural changes. It was associated with cough which was dry. He also developed breathlessness which was increasing from Modified Medical Research Council dyspnea (MMRC) grade 1 to grade 4 over a period of 10 days. There was no history of fever, hemoptysis, or hoarseness of voice. There was no history of tuberculosis, contact with tuberculosis, diabetes, hypertension, heart disease or surgical illness. He was a security guard in an aluminum manufacturing company and was unaware of having been exposed to asbestos. He was cigarette smoker with exposure of 4 pack years but was nonalcoholic. Patient visited private hospitals for his illness was treated with anti-tubercular drugs and NSAIDS.

On general physical examination, patient was conscious and oriented but dyspneic. His pulse rate was 102/min, blood pressure-110/78 mm Hg, and

respiratory rate 36/min (abdomino-thoracic type). Pallor and bilateral pedal edema were present. Icterus, cyanosis, clubbing, and lymphadenopathy were absent. On respiratory system examination, trachea was deviated to left side; right hemithorax was bulged with restricted movement. Vocal fremitus was reduced on right side. Stony dullness was felt over 3rd intercostal space downwards on right side. On auscultation, right sided breath sound was absent, except infraclavicular area where bronchial breath sound was present. Left side chest examinations showed no any abnormality. Examination of other systems was normal. On investigations, chest X-ray revealed right sided massive pleural effusion with mediastinal shifting to left. (Figure-1) Routine investigations showed Hb-10.4gm%, TLC-17,700/mm^3, DLC-$P_{85\%}$, $L_{15\%}$, PCV-30.2%, Platelet count-4.6lakh/mm^3, amylase-30 u/l. Prothrombin time- test-14.9sec, control-12.0(INR-1.28) APTT test-27.4sec, control 29. Liver function test and kidney functions test were normal. HIV, HBsAg, anti HCV, ANA, CRP, and RA factor was non-reactive. Diagnostic thoracocentesis showed hemorrhagic pleural effusion. Cytology of pleural fluid was not possible as field was full of RBC. Pleural fluid protein was 4.8 gms% with glucose 24mg%. Hematocrit of pleural fluid was 10%. LDH-220 U/L (serum LDH of same day-540 U/l), ADA-28 U/L. Pleural fluid culture, TB PCR, and AFB staining was negative. Malignant cells were absent in three samples. As there was massive hemorrhagic pleural effusion, chest tube was put with closed water sealed drainage. Repeat pleural fluid analysis was done which showed similar results. CECT chest showed irregular, nodular pleural thickening (2.5-3 cm) of costal, mediastinal and diaphragmatic pleura with gross right sided pleural effusion with mediastinal shift. (Figure-2) With a possibility of malignant pleural mesothelioma pleural biopsy and FDG-PET was planned.

During hospital stay, initially after tapping of fluid patient symptomatically improved. But repeat chest x ray shows same changes. (Figure-3) Daily fluid collection from pleural fluid remains about 1 litre for 3-4 days. Symptoms gradually increased & patient became increasingly breathless. Then with the help of respiratory physician, pleural biopsy was done. And pleural biopsy report showed fragments of fibrocollagenous tissue with infiltrating sheets of loosely cohesive highly pleomorphic cells with few mitoses. The cells show irregular hyperchromatic nuclei, inconspicuous nucleoli and well defined eosinophillic vacuolated cytoplasm. (Figure-4) Pleural biopsy culture was negative for mycobacterium. Tumor was positive for cytokeratin-5 immunohistochemical stain. And it was negative for other immunohistochemical stain like PAS, mucicarmine, vimetin, calretinin, CEA and S100 stain. The patient was referred to the thoracic surgical and oncology division for further management. Diagnosis of malignant pleural mesothelioma was confirmed and patient was planned for chemotherapy. Unfortunately we lost the patient on 12th day of hospitalization.

DISCUSSION:

Malignant mesothelioma is a cancer of the mesothelium which lines the pleural, peritoneal, pericardial cavities and the tunica vaginalis. Approximately 90% of cases occur in the pleura and are associated with poor prognosis due to delay in diagnosis. Most cases of the cancer are caused by asbestos exposure. [3] Approximately 80% of these cases have history of direct exposure to asbestos. [4] The incidence of malignant mesothelioma is increasing because of the long latency period (≥30 years) from asbestos use. [5]

Asbestos is the commercial name for a hydrated magnesium silicate fiber. There are two main families of asbestos fiber, the serpentine (chrysotile) and the amphibole (eg, crocidolite, amosite, and tremolite) forms. Considerable debate exists about differences in fibrogenicity and carcinogenic properties. [6]

The clinical presentation and manifestations of malignant mesothelioma can be insidious. Despite the varying clinical presentations, the disease process is usually advanced at the time of diagnosis. Most patients have pleuritic chest pain, dyspnea, cough, fatigue, and weight loss. About 25% of patients have symptoms for 6 months or more before seeking medical attention. The ratio of men to women is 5:1. [7]

The findings of the laboratory workup of patients with mesothelioma usually are nonspecific and include hypogammaglobinemia, eosinophilia, and

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anemia. The most common abnormality is thrombocytosis. [1]

The findings of the chest x-ray film at presentation are usually abnormal in most patients with malignant mesothelioma. Seventy- five percent of initial chest x-ray films of patients with malignant mesothelioma reveal pleural effusion, with 60% of the effusions on the right side. Effusions usually are large and occupy more than 50% of the hemithorax. Pleural plaques with varied radiographic features may be evident in both the affected and the contralateral lung. [8] Chest contrast enhanced Computed tomography (CT) is useful in increasing the clinical suspicion of a malignant pleural process. In study by Patz EF et al. CT scans of 50 patients with malignant mesothelioma revealed pleural thickening in 46 (92%), thickening of the pleural surfaces of the interlobar fissures in 86%, pleural effusion in 74%, pleural calcifications in 20%, and invasion of the chest wall in only 18%. [9] Fluorodeoxyglucose positron emission tomography (FDG PET) is an important tool for differentiating benign from malignant disease, as well as being an adjunct for staging. [10] Pleural biopsy aid in the diagnosis and improves the patient's chance of a timely diagnosis. Patients with negative diagnostic studies often undergo an open pleural biopsy. Video-assisted thoracoscopy is becoming the diagnostic method of choice. [11] The varied histologic appearance of malignant mesothelioma, which includes the epithelial, sarcomatoid (fibrous), and biphasic (mixed) patterns, provides a diagnostic challenge. Because a large proportion of these tumors arise within the pleura, it is often difficult to differentiate between a sarcomatoid component and reactive pleural fibrosis. Similarly, distinguishing metastatic adenocarcinoma to the pleura from the epithelial pattern of malignant mesothelioma can be challenging. The cytological smears of needle biopsies and sections from cell blocks of pleural fluid can establish the diagnosis of malignancy, but they usually cannot distinguish between a metastatic adenocarcinoma and a mesothelioma. Combined histochemical and immunohistochemical staining techniques are often needed to confirm diagnosis. Currently, the two most sensitive markers for mesothelioma in our laboratory are used concurrently: calretinin, a calcium binding protein, and cytokeratin 5/6. In addition to these two markers, thrombomodulin and mesothelin are useful. The nuclear antigen TTF-1 (thyroid transcription factor) may be used to identify lung adenocarcinoma in immunohistochemistry studies. [12]

Patients with this malignancy generally do not have a complete response; malignant mesotheliomas pose a treatment challenge. Most patients with pleural mesothelioma, whether treated or untreated, will die of complications of local disease. Respiratory failure is the major cause of mortality despite the fact that as many as 82% of patients have distant metastases at the time of autopsy. Frequent sites of metastases are the liver, adrenal gland, kidney, and contralateral lung. Intracranial metastases have been reported but are rare. [13]

CONCLUSION:

Malignant mesothelioma is difficult to diagnose and is nearly untreatable. Asbestos exposure remains a major factor in the pathogenesis of this malignancy. This case report is a revision to chest physicians and general practitioners to call attention of this rare condition, and require history-taking, complete physical examination and performing adequate tissues specimen analysis for definite diagnosis. An experienced multi-disciplinary team approach is essential and should include physicians, surgeons and pathologists.

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FIGURES:

Figure -1 Chest X-ray showing massive pleural effusion (trachea & mediastinal shift- yellow arrow and blunt costo- phrenic angle-red arrow)

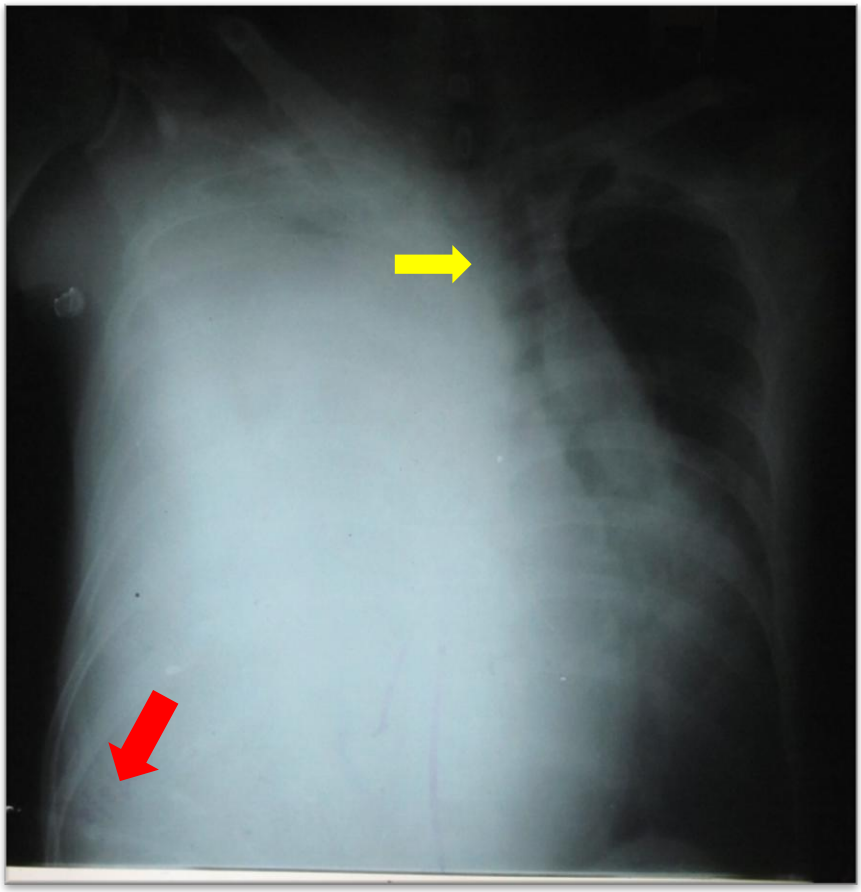

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Figure-2 CECT CHEST showing irregular nodular thickening of pleura (yellow arrow) and massive effusion (red star)

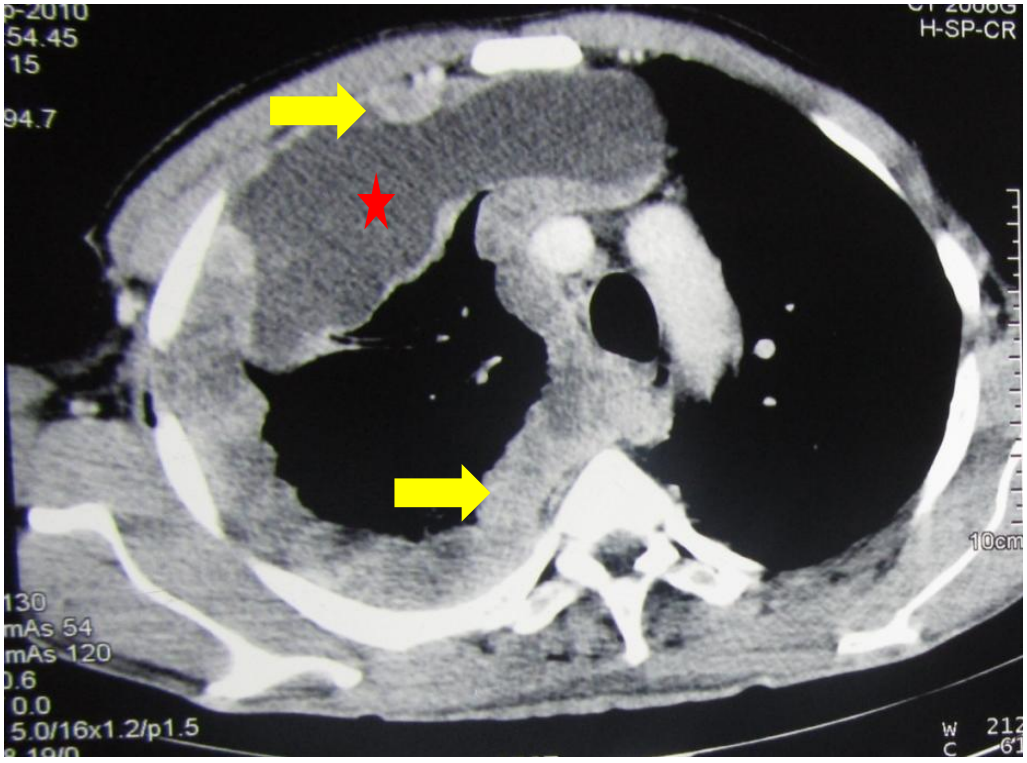

Figure-3 chest X-ray after insertion of chest tube

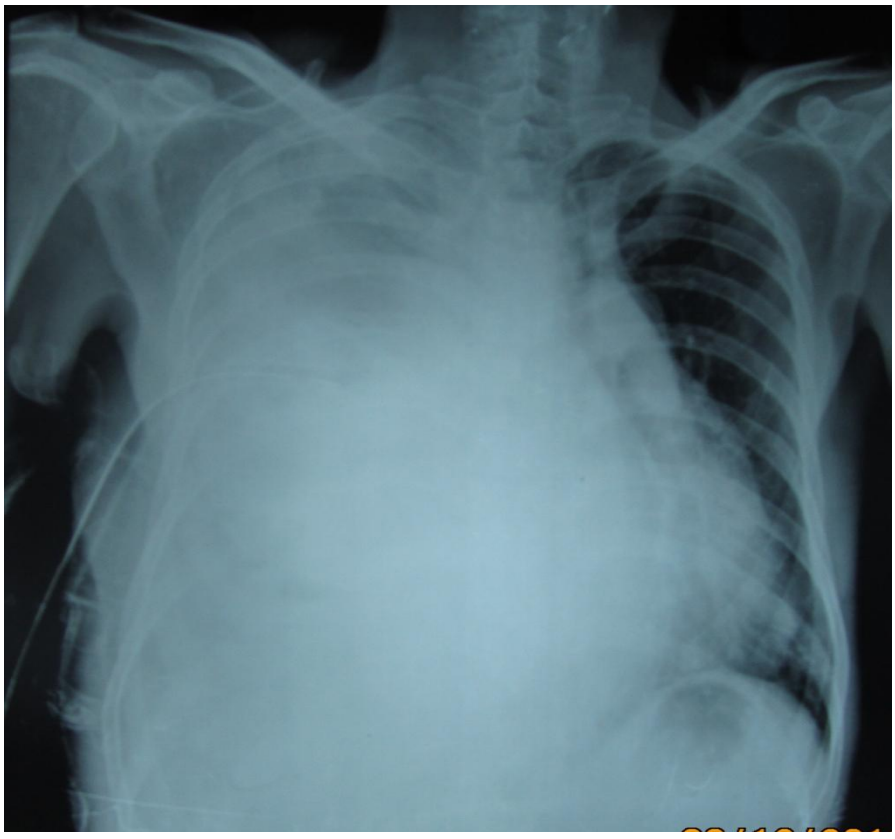

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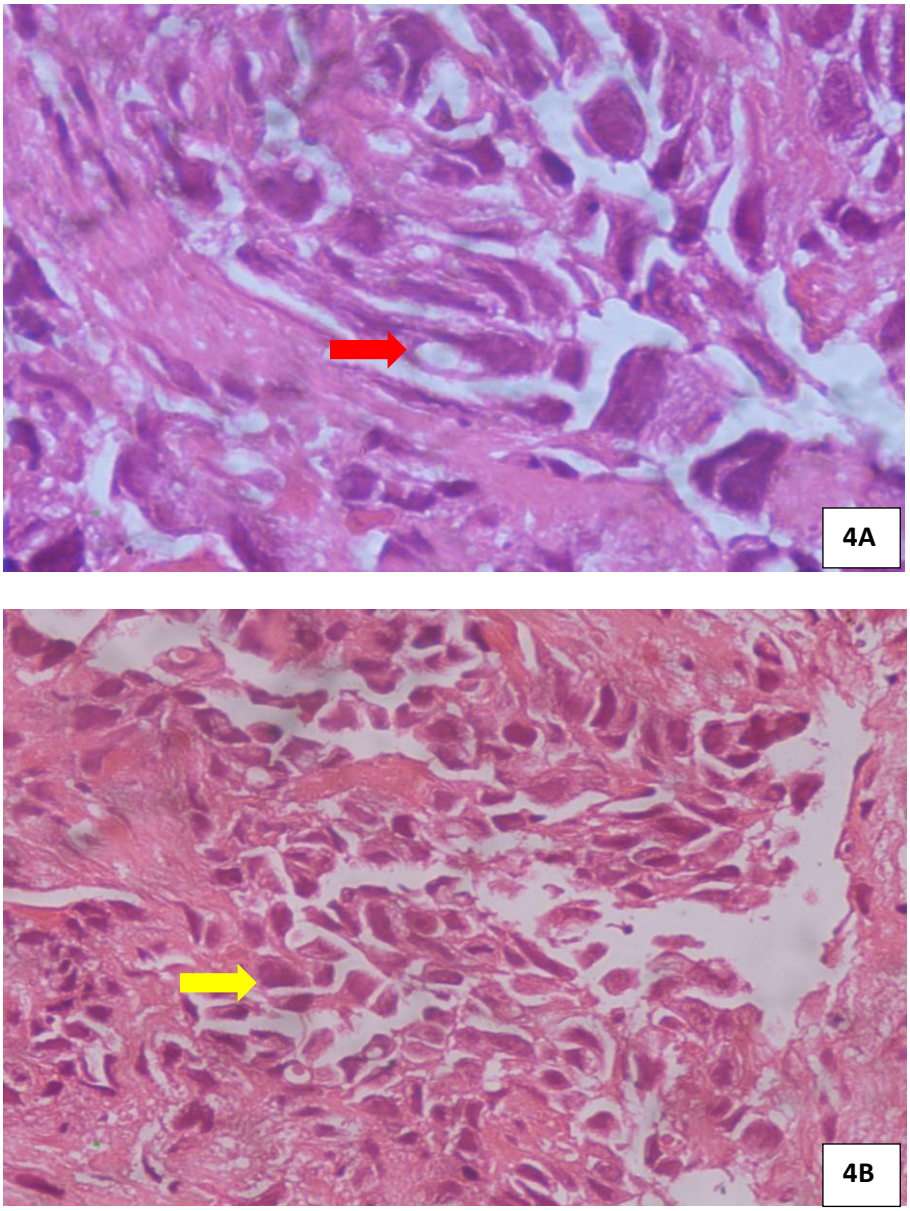
Figure -4A-The pleural tumor shows eosinophillic vacuolated cytoplasm (red arrow) in eosinophillic collagenized background and 4B- Hyperchromatic nuclei (yellow arrow)



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