

# Biphasic Malignant Mesothelioma with Brain Metastasis

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## ABSTRACT

Malignant pleural mesothelioma is usually associated with asbestos exposure. It rarely metastasizes to brain. We are reporting a case of biphasic malignant pleural mesothelioma confirmed with trucut biopsy of pleura in a 40-year-female with classical costal and mediastinal rim like pleural

thickening on CT scan thorax. The patient also had brain metastasis on presentation. Due to the incurable nature of her disease, the patient was given palliative chemotherapy but she died soon after presentation.

Keywords: Biphasic malignant mesothelioma; brain; metastasis

## INTRODUCTION

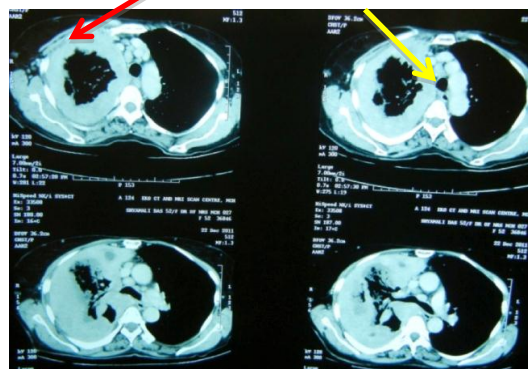
Malignant pleural mesothelioma is a malignant neoplasm of mesodermal origin and arises from multipotent mesothelial or subserosal cells of the pleura, pericardium or peritoneum. On microscopic examination it can be differentiated into three forms: epithelioid (60%), sarcomatoid (10-20%) and biphasic patterns (20-30%) [1]. Metastasis to brain is rare. The most common sites for metastasis in men are the lungs (27%), kidneys (13%) and skin (13%); in women, the common sites include breast (24%) and genital organs (17%), followed by bone (10%) and kidney (10%) [2]. Work-related asbestos exposure has been associated in 70% of all pleural mesothelioma cases [3]. The tumor is commonly seen in patients during their fifth and sixth decades. The latency between exposure and clinical presentation of mesothelioma takes approximately 20 to 40 years. Median survival from the time of presentation is 9 to 12 months [4]

## CASE REPORT

A 40-year-old female patient presented with complaints of chronic dry cough for 4 months without any specific aggravating and relieving factors. She also complained of right sided severe stabbing localized chest pain, consistent with pleuritic chest pain for 3 months prior to her presentation. Her pain was worsened by coughing and deep inspiration. Pain was so

severe that it affected her sleep. Chest pain was associated with progressive persistent shortness of breath with MMRC (Modified Medical Research Council) grade 4, that is, dyspnea during dressing and undressing. Patient also complained of blurry vision without diplopia and sharp occipital headache without any specific aggravating factors for 15 days prior to her presentation. Clinical examination revealed decreased respiratory movement and dull percussion note all over the right side of the chest with decreased vesicular breath sounds consistent with right sided massive pleural effusion. She also had a right sided firm, mobile supraclavicular lymph node. Pleural fluid, obtained during thoracentesis, examination showed lymphocytic exudative (protein 5.33

**Figure 1:** CT scan thorax with contrast irregular rim like thickening of costal (yellow arrow) and Mediastinal pleura (red arrow)



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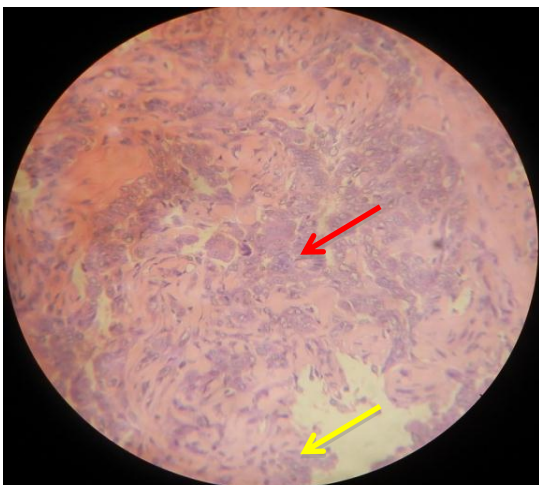
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gm/dl, glucose 90 mg/dl) effusion with adenosine deaminase of 11.3 U/L. Contrast enhanced CT scan of the thorax showed irregular costal and mediastinal pleural thickening, exceeding 10 mm with encasement of the lung in between (Figure 1). There was also evidence of mediastinal lymphadenopathy, peribronchial cuffing of right main bronchus and esophagus along with right sided pleural effusion. Bronchoscopy showed right lower lobe and middle lobe bronchi narrowed by external compression; however, malignant cells were not detected on bronchial brush and bronchoalveolar lavage fluid examination. Ultrasonography guided pleural biopsy revealed a piece of fibrofatty tissue infiltrated by a biphasic tumor containing both epitheloid (due to the presence of round, cube-like cells that have long and slender microvilli) and sarcomatous (due to presence of spindle-shaped cells arranged in a disorganized fashion) properties suggestive of malignant biphasic mesothelioma (Figure 2).

On immunohistochemistry, the tumor cells expressed calretinin, CK-5/6, WT-1, HBME-1 and were immunonegative for Ber ep4. Contrast enhanced CT scan of brain showed an enhancing lesion in the left occipital region. Overall, the data was consistent with biphasic malignant mesothelioma with brain metastasis in occipital lobe without prior history of asbestos exposure (Figure 3).

The patient presented with stage IV disease due to the presence of occipital metastasis, and thus surgery had no role in her case. Palliative

**Figure 2:** Histopathology of pleural biopsy showing fibrofatty tissue infiltrated by biphasic tumor having both epitheloid (yellow arrow) and sarcomatous (red arrow) properties suggestive of malignant biphasic mesothelioma.

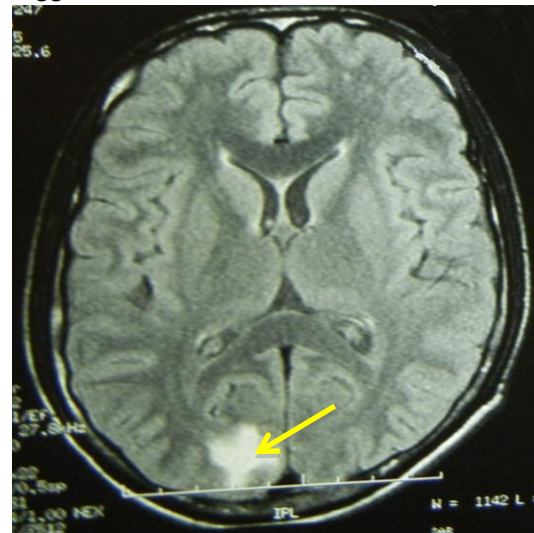


chemotherapy was given with combination regimen of pemetrexed and cisplatin. After 5 days of chemotherapy, she developed severe respiratory distress with vomiting. Supportive management was started with fluid resuscitation and bronchodilators but patient died 7 days after presentation due to sudden cardiac arrest.

## DISCUSSION

The occurrence of mesothelioma is often associated with prior exposure to asbestos, and occasionally due to endemic erionite exposure as in Turkey, ionizing radiation or chest injuries [5]. Pleural effusion, usually with dyspnea and often with chest wall pain, is the most common presentation in mesothelioma patients [6]. A fixed hemithorax on clinical examination, that is, unilateral lack of chest expansion, is usually a late sign. Clubbing is rare. Metastatic deposits of mesothelioma are commonly found during post mortem but are usually not detected before death [7]. The conventional chest X-ray typically shows pleural effusion. An encircling ring of tumor and/or extensive lobulated pleural-based tumor can be seen early but are usually a late feature [8]. Thoracic CT scan usually shows pleural effusion only. Pleural-based masses with or without thickening of interlobular septa can also be seen at presentation. Classical picture of mesothelioma on CT scan thorax is thickening of pleura, with an irregular, often nodular internal margin, most pronounced at the base of the lung [9]. At times, pleural thickening is seen predomi-

**Figure 3:** MRI brain with contrast showing eccentric solid lesion with peripheral rim enhancement at occipital lobe (yellow arrow) suggestive of metastasis



nantly along the mediastinum. Malignant mesothelioma should be suspected on CT scan thorax when there is ring-like pleural involvement, mediastinal pleural involvement, and pleural thickness more than 1 cm, as seen in our patient [10]. If the diagnostic modality of CT scan is not available, mesothelioma can still be suspected on the basis of clinical features and suggestive chest X-ray findings. Prognosis of patients with mesothelioma can be predicted using relatively crude criteria, such as tumor extension and differentiation, rather than on more precise genetic information [11]. Poor prognosis at presentation is associated with poor performance status, high white blood cell (WBC) count, probable/possible histological diagnosis of mesothelioma, male gender and sarcomatoid histological subtype of mesothelioma [12, 13]. Treatment for mesothelioma generally depends more on the stage and location of the tumor than the cell type involved. Because biphasic mesothelioma carries a slightly worse prognosis than epithelioid mesothelioma, patients with the biphasic cell type may not be considered for as aggressive treatment plan as patients with epithelioid subtype. The median survival time of biphasic mesothelioma cancer patients is six months. Treatment in most cases is limited to palliation, since the disease is usually diagnosed too late for curative surgery. Mesothelioma is usually treated with multimodal therapy involving a combination of radiation and chemotherapy; surgical techniques may be used to relieve symptoms. Potentially curative surgery, which is only performed in few centres, involves extrapleural pneumonectomy usually followed by some form of adjuvant therapy. Palliative surgery includes partial pleurectomy with pleurodesis, thoracoscopy with pleurodesis and pleuroperitoneal shunting. Pemetrexed plus cisplatin, a combination of a multitargeted antifolate and a platinum compound, has been shown to improve overall survival by nearly 3 months with an objective response rate of 41 percent [14].

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