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Case Report

# When a Pleural Effusion Becomes an Unexpected Diagnosis

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## Abstract

Mesothelioma is a neoplasm originating from the serous membranes, most often pleura. We present a 72-year-old man with hypoxemic respiratory failure associated with unilateral pleural effusion. The computed tomography (CT) of the chest didn't show other alterations besides the pleural effusion. Thoracoscopy showed a pleural thickening described as reactive mesothelial hyperplasia. Repeated contrast- enhanced chest CT showed a mass in the posterior mediastinum. Bronchoscopy and bronchoalveolar lavage cytology showed atypical inflammatory cells. Finally, mediastinoscopy pleural biopsy revealed an epithelioid mesothelioma with locally invasive disease and distant dissemination later exposed on F18-fluorodeoxyglucose positron emission tomography (F-18FDG PET-CT). He started palliative treatment but suffered disease progression and death in two years. The low cytological and histological sensitivity in the diagnosis of mesothelioma add more complexity and invasiveness to the present clinical case. To overcome these limitations, less invasive immunohistochemistry and molecular techniques have emerged in the definition of mesothelioma.

**Keywords:** Malignant Pleural Mesothelioma; Unilateral Pleural Effusion

## Introduction

Malignant pleural mesothelioma is a rare neoplasm, originating from the serous membranes, associated with a poor prognosis [1]. The incidence is higher in males, after 50 years of age, with an average diagnosis at 70 years of age [2]. It most commonly affects the pleura, although it can also affect another serosa such as the peritoneum and tunica vaginalis. Genetic predisposition and previous exposure to asbestos are the main risk factors for mesothelioma [3].

## Case Report

A 72-year-old man came to the emergency department due to dyspnea for one month. On admission, he was polypneic and had a hypoxemic respiratory failure. He had no relevant occupational history. Chest X-ray showing a large volume pleural effusion on the right (Figure 1). Chest CT without contrast showed a large pleural effusion on the right hemithorax. Diagnostic thoracocentesis with citrine yellow liquid, compatible with exudate (1300 erythrocytes, 1156 leukocytes with 32.4% of polymorphonuclear and 67.6% of mononuclear leukocytes, 388 uncharacterized cells, 5.1g/dL proteins, lactic dehydrogenase 279 IU/L and ADA greater than 100 U/L). The bacteriological and mycobacteriological analysis, as well as the PCR test for Mycobacterium Tuberculosis in the pleural fluid, were negative. Cytological analysis revealed reactive mesothelial cells. A thoracoscopy showed a pleural thickening in the pleura at the level of the costophrenic cul-de-sac and the lower third of the posterior parietal pleura, which was biopsied. Histology documented reactive mesothelial hyperplasia. The patient underwent evacuation thoracentesis and repeated contrast- enhanced CT scan (Figure 2), which revealed an ill-defined tissue lesion in the posterior mediastinum of a probable neoformative nature with an ill-defined origin. With this new result, a bronchofibroscopy with biopsy of the respective mass was performed, but the histology was inconclusive. Cytology of the bronchial aspirate with multiple mesothelial cells of epithelioid morphology with atypia. To better clarify the tissue injury, a PET-CT was requested, identifying a mediastinal and diaphragmatic

pleural thickening with increased F-18-FDG uptake and associated with a large hypermetabolic mass in the retrotracheal position and in the related right internal mammary chain, with malignant infiltration (Figure 3). The patient underwent a mediastinoscopy with mass biopsy with histology compatible with malignant epithelioid mesothelioma. After the diagnosis of unresectable epithelioid mesothelioma, he did pleurodesis 54 days after hospitalization. Patient completed 6 sessions of chemotherapy with carboplatin and pemetrexed followed by radiotherapy. Due to disease progression, he underwent 2 cycles of pembrolizumab, which were suspended due to pulmonary toxicity. He performed rechallenge with 6 sessions of carboplatin and pemetrexed and maintenance with pemetrexed. Despite the treatments carried out, the mesothelioma always presented itself in progression, culminating in the death of the patient two years after the diagnosis.

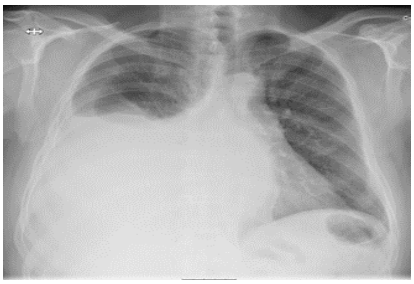

**Figure 1:** Chest x-ray showed right pleural effusion.

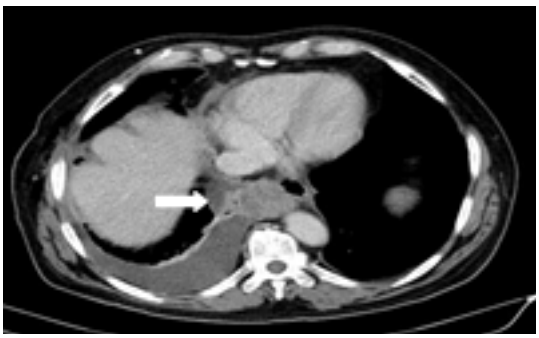

**Figure 2:** Chest computed tomography showed an ill-defined tissue lesion in the posterior mediastinum (white arraow).

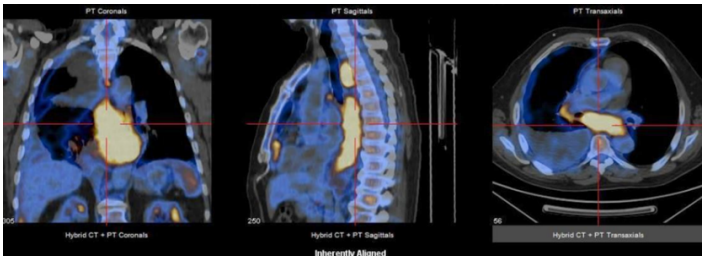


**Figure 3:** F-18FDG PET-CT showed a large hypermetabolic mass in the retrotracheal position.

## Discussion

Unilateral pleural effusion is the most common manifestation of pleural malignant mesothelioma. Exams such as chest X-ray, contrast-enhanced computed tomography, thoracentesis, pleural fluid cytology and pleural biopsy are the first exams to be performed in its etiological study. However, the diagnosis of mesothelioma is usually complex and over the last few years its diagnosis and classification have been revised. Mesothelioma has 3 main histologic types: epithelioid, sarcomatoid, and biphasic. The histological variety and as the pleura are often the site of metastatic and reactive disease, cytological and histological analysis are commonly insufficient in the diagnosis [2]. Cytological characteristics such as the presence of atypical mesothelial cells, mitosis, necrosis, high cellularity index may be present in cases of neoplasia but also in benign reactive mesothelial proliferation. Thus, immunohistochemistry and molecular analysis are used, promoting a less invasive and more sensitive diagnosis. Currently, mesothelioma is defined by loss of the BAP1 gene (more frequent in the epithelioid subtype) or of the MTAP gene (demonstrated by immunohistochemistry). On the other hand, the homozygous deletion of CDKN2A (detected by FISH) is present in more than 90% of the sarcomatoid subtype [1]. As for the histological diagnosis, biopsy in at least 3 different sites and preferably guided by thoracoscopy is recommended to increase the profitability in diagnosis and classification. In this case, there would be two main diagnostic limitations. Firstly, this immunohistochemical and molecular analysis was not accessible and secondly, 3 biopsies were never performed in the same procedure [2]. Thus, biopsy through mediastinoscopy and PET CT have become essential for diagnosis. F-18FDG PET-CT proved to be beneficial in staging with characterization of disease extension, especially in patients who are candidates for surgical resection. More than 10% of preoperatively staged patients had extrathoracic disease on PET CT [4]. Treatment is based on staging, functional status, age, comorbidities, and patient preferences. Surgery is reserved for resectable tumors [2]. After surgery, the average survival varies according to the histological subtype, being 19 months in the epithelioid, 14 in the biphasic and 4 months in the sarcomatoid [1]. In the clinical case presented, despite portraying the subtype with the best prognosis, local invasion and metastatic dissemination excluded surgery and determined a palliative treatment. The case presented shows the complexity associated with the diagnosis of mesothelioma. Despite recent scientific advances with techniques such as immunohistochemistry and FISH, not all laboratories have this capability. In this way, it is important to think about mesothelioma when studying the etiology of pleural effusion, in order to reduce the timing until diagnosis and consecutively until treatment, in the hope of thus improving the prognosis.

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**Conflicts of Interest:** None.

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