PSEUDOMESOTHELIOMATOUS ADENOCARCINOMA RELATED PLEURAL EFFUSION- CONTEMPLATE THE DIFFERENTIAL!

Abhishek Gupta1, Ketaki Utpat2, Unnati Desai3, Jyotsna M. Joshi4

1 Junior Resident, Department of Pulmonary Medicine, Topiwala National Medical College and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India.
2 Assistant Professor, Department of Pulmonary Medicine, Topiwala National Medical College and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India.
3 Associate Professor, Department of Pulmonary Medicine, Topiwala National Medical College and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India.
4 Professor and Head, Department of Pulmonary Medicine, Topiwala National Medical College and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India.


PRESENTATION OF THE CASE

Pseudomesotheliomatous adenocarcinoma is a variant of peripheral lung carcinoma that is characterized by extensive invasion of pleura which closely resembles malignant pleural mesothelioma clinically and anatomically. Radiologically, it is distinguished by Leung’s criteria. It most commonly emanates from an adenocarcinoma; however other types of lung carcinomas may also precipitate it. Its elucidation in the literature is very limited. Although the distinct clinical and histopathological features of this entity have been described since a long time, its recognition as a distinct variety of lung carcinoma has remained small fry. Little is known of its incidence and only sporadic cases have been reported until now. We present an intriguing case of this rarefied entity. This middle-aged woman was initially speculated to have Rheumatoid arthritis associated pleural effusion which later on turned out to be metastatic adenocarcinoma, positive for both Thyroid Transcription Factor-1 (TTF-1) and Napsin A. The diagnosis could be consummated with a blind closed needle biopsy of the pleura.

CLINICAL DIAGNOSIS

Adenocarcinoma is the histopathological terminology given to malignancy arising from endocrine or exocrine glands or ducts. They are notorious for their tendency to metastasize widely at an early stage.1 Adenocarcinoma metastasizing to pleura is commonly called as pseudomesotheliomatous adenocarcinoma. The radiological manifestations include consolidation, fibrosis, cavity, ground glass opacities, interstitial, pleural or lung nodules.2 When it metastasizes to the pleura, its radiological presentation as diffuse pleural nodularity is paradigmatic. Pathological, immunohistochemical, and ultrastructural features of this neoplasm closely resemble mesothelioma.3 The name “Pseudomesotheliomatous adenocarcinoma” stems from this close resemblance. Most cases of pseudomesotheliomatous lung cancer are prima facie suspected clinically and radiologically to be mesotheliomas. But when the tissue is further evaluated by immunohistochemistry (IHC) or electron microscopy, the pathologic findings indicate that these tumours are not mesotheliomas but are, in fact, primary lung cancers or metastatic cancers growing in a distribution that macroscopically resembles a mesothelioma.

DISCUSSION OF CASE

A forty-year-old non-addict lady presented to our outpatient department with symptoms of three months’ duration of dry cough, left sided chest pain and progressive breathlessness. She was previously evaluated with chest radiograph (CXR) which showed a left sided large effusion (Figure 1) and was empirically treated with anti-tuberculosis therapy (ATT) with no relief of her symptoms. The patient was then referred for detailed evaluation and management. She was a diagnosed case of Idiopathic Thrombocytopenic Purpura; managed with splenectomy 20 years back and Rheumatoid arthritis (RA) since 15 years managed with methotrexate and chloroquine. On examination, she was afebrile with a pulse of 92 beats per minute, blood pressure of 110/70 mmHg, respiratory rate of 18 cycles per minute and pulse oximetry saturation of 97% on room air.

Respiratory system examination showed signs of volume gain on left side in form of fullness, elevated shoulder, increased spinouspinal distance with dull note, shifting dullness, decreased breath sounds and vocal resonance throughout left hemithorax. Other systemic examination was normal. Contrast enhanced computed tomography (CECT) of thorax showed left pleural effusion with thickening, nodularity and mediastinal lymphadenopathy (Figure 2). RA, tuberculosis, malignancy were considered as the etiological differential diagnoses. We performed a diagnostic thoracocentesis. The pleural fluid was hemorrhagic, exudates with lymphocyte predominant. The adenosine deaminase (ADA) levels were normal. The pleural fluid glucose was markedly low (15 mg/dl). Pleural fluid analysis for cartridge based nucleic acid amplification
test (CBNAAT) was mycobacterium tuberculosis (MTB) not detected. On oral glucose challenge testing, there was no increase in the pleural fluid glucose when compared to the plasma glucose. Hence, the pleural fluid glucose challenge test was positive. In view of her exudative effusion of undetermined etiology she underwent a closed needle pleural biopsy (CNPB) followed by intercostal drain (pig-tail catheter) insertion. Pleural fluid for malignant cytology was suggestive of atypical cells. And the pleural biopsy histopathology revealed metastatic adenocarcinoma with positivity for IHC markers of Thyroid Transcription Factor-1 (TTF-1) and Napsin A. A final diagnosis of pseudomesotheliomatous adenocarcinoma stage IV disease was made. The patient was referred for palliative chemotherapy.

Pleural involvement secondary to a carcinoma at a farther site is known however there is paucity of literature pertaining to its pathogenesis and presentations. The three most frequent tumours to involve the pleura secondarily include lung cancer (35%-45%), metastatic breast cancer (25%), and malignant lymphoma (10%).

Pseudomesotheliomatous carcinoma is a rare variant of peripheral adenocarcinoma of the lung that can manifest with clinical, radiological and pathologic features resembling that of a malignant mesothelioma. Most “pseudomesotheliomas” arise in the peripheral lung tissue although some can metastasize to the pleura from another site. Radiologically they follow Leung’s criteria,5 of pleural nodularity, circumferential pleural thickening, and thickening of parietal pleura like that of mesothelioma. Besides adenocarcinoma, which accounts for 70% of pseudomesotheliomatous carcinomas, other primary lung cancers, including squamous cell carcinoma, small cell carcinoma, large cell carcinoma, and carcinosarcoma may also present as a pseudomesotheliomatous tumor. Hence rather than an autonomous neoplasm, pseudomesotheliomas can be said to be a terminology given to a group of malignancies with the common feature of resemblance to mesothelioma, adenocarcinoma is one of them. Differentials to pseudomesotheliomas are epithelial mesothelioma, sarcomatoid mesothelioma and biphasic sarcomatoid mesothelioma. Previous investigators including Hammar6 and Dodson, Koss et al, Attanoos and Gibbs, have noted that a high proportion of patients with pseudomesotheliomatous adenocarcinoma have a background of occupational exposure to asbestos. However, this still needs better validation and elaboration.7 Pseudomesotheliomatous lung cancers usually present with the same signs and symptoms as diffuse pleural mesotheliomas. The most frequent symptoms are chest pain, dyspnoea, cough, and weight loss. Our patient also presented similar symptoms of a subacute onset and progression.

Pleural effusions are common in both pseudomesotheliomatous lung cancers and pleural mesotheliomas. Pleural fluid in these cases needs to be evaluated further for malignant cells using cytologic, histochemical, immunohistochemical and ultrastructural techniques. Our patient was a young lady and she had never smoked. Hence a consideration of malignancy was low on the cards. We evaluated her keeping into consideration RA versus tuberculosis as aetiology. Tuberculous pleural effusion was less likely owing to absence of fever. RA associated pleural effusions typically show a very low pleural fluid glucose content and also exhibit a positive glucose challenge test.8 Our patient too showed had a markedly low pleural fluid glucose levels and a positive oral glucose challenge test. This gave an inkling of a RA associated pleural effusion, however the pleural fluid cytology showed atypical cells which strongly aroused a suspicion of malignancy. There are studies demonstrating a low pleural fluid glucose and a positive glucose challenge test in malignant pleural effusions.9 The yield of pleural fluid
cytology in the diagnosis of pleural malignancies has been variably reported to be 7 to 12 % in literature.\textsuperscript{10}

**FINAL DIAGNOSIS**

The diagnosis was subsequently confirmed on pleural biopsy histopathology and IHC. The role of a CNPB in undiagnosed exudative pleural effusions is established, however literature focuses on its major utility in the diagnosis of tuberculosis and its value in the diagnosis of malignant involvement of pleura has been sceptical.\textsuperscript{11} In our patient, this simple inexpensive bedside investigation played a pivotal role in clinching the bulls-eye diagnosis. Grossly, pseudomesotheliomatous carcinoma presents as a rend of thick, white to tan, firm tissue encasing the lung in a pattern resembling mesothelioma or fibrothorax. IHC markers for pseudomesotheliomatous adenocarcinoma commonly found to be positive are Thyroid Transcription Factor-1(TTF-1), Napsin A, Carcinomembryonic Antigen (CEA), LeuM1 (CD15), B72.3, Epithelial membrane antigen (EMA) and BerEP.\textsuperscript{12} Pseudomesotheliomatous adenocarcinoma spreads within the pleural space and presents at a primary tumour classification stage of T3 or with malignant pleural effusion. Patients usually present with advanced disease of stage IIB or IV and has a poor prognosis, with a mean survival of approximately 7 months. The prognosis of pseudomesotheliomatous lung adenocarcinoma is similar to that of diffuse epitheloid malignant mesothelioma. Extrapleural pneumonectomy or therapeutic regimens of chemotherapy and/or radiation therapy have been used but are generally ineffective for this advanced form of lung adenocarcinoma.\textsuperscript{13-16} Our patient opted for a palliative chemotherapy.

Hence, we emphasise that pseudomesotheliomatous carcinoma should be considered as a differential diagnosis of a haemorrhagic pleural effusion in any age group and a simple day care procedure of a pleural biopsy should be resorted to arrive at the diagnosis

**REFERENCES**


