Pseudomesotheliomatous Lung Carcinoma of Poorly Differentiated Large Cell Type: A case report and review of the literature

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Abstract:
A 46-year-old female presented with a 20-day history of right pleuritic chest pain and progressive shortness of breath. She was found to have a right pleural based malignancy initially thought to be a malignant mesothelioma but staining with the mesothelioma tumor markers calretinin, HBME-1 and CK5/6, was negative. Some epithelial markers were positive and microscopically it was consistent with a poorly differentiated large-cell carcinoma. The case was diagnosed as a pseudomesotheliomatous lung carcinoma of poorly differentiated large-cell type.

Introduction:
Pseudomesotheliomatous carcinoma is a rare variant of peripheral lung carcinoma that is clinically, radiologically, and macroscopically indistinguishable from malignant pleural mesothelioma and shares with the latter a rapidly fatal course (2). A variety of histochemical and immunohistochemical methods have been proposed to aid the differential diagnosis of pleural malignant mesothelioma and pleural metastases of carcinoma.

Case Presentation:
A 46-year-old Egyptian housewife with three children, resident in Doha for the past 13 years, presented with 20-day history of right-side pleuritic chest pain, dry cough and progressive shortness of breath. There was no history of fever, weight loss, loss of appetite, hemoptysis, asbestos exposure, contact with sick patients or contact with animals. She was not a smoker and was not taking regular medications.

She was dyspneic but not cyanosed, pale or jaundiced. There was no clubbing and no palpable lymph nodes. Vital signs were Temp 36.8, RR 25, B.P 120/80, P 90/min regular, oxygen saturation 95% on 2 L/min oxygen by nasal canula. Chest examination revealed no deformity, a centrally located trachea, stony dullness on percussion of the right mid-lower lung zones, with decreased tactile fremitus, resonance and diminished breathing sounds in the same area. Examination of the left side of the chest was normal. The rest of physical examination including, cardiovascular, breast, abdomen and neurological evaluation was normal.

CBC on admission was WBC 14.2 plate/109/L, (neutrophils 79.6%, lymphocytes 14.8%) Hb 12.3 g/dl, ESR 22 mm/hr, normal kidney function and serum electrolytes. Liver function test: ALT 68 iu/L, AST 59 iu/L, T.Bilirubin 7 umol/L, T.protein 64 g/L, Albumin 37 g/L. Coagulation profile was normal, ABG (on room air): pH 7.41, pCO2 37, p02 69.2 calculated O2 sat 93.8%. ECG was normal.

A chest x-ray showed a moderate right-side pleural effusion with a clear left lung field (Figure 1). Blood and urine cultures showed no growth. She did not provide a sputum sample; the tuberculin PPD test was negative.

Figure 1: Chest x-ray on admission shows evidence of right side pleural effusion. Left lung field is clear.

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She was admitted as a right parapneumonic effusion and started empirically on IV augmentin and zithromycin (?). Bedside pleural tapping was attempted but failed. Ultrasound-guided aspiration of the pleural effusion produced blood-stained fluid containing WBC: 1150 u/L (neutrophils 27%, Lymphocyte 67%, monocyte 6%, mesothelial cells 3%), RBC 76,600 u/L, T.Protein 47 g/L, pH 7.488, Glu 4.8 mmol/L. Stains and cultures of the pleural fluid were negative for AFB and other bacteria. Cytological staining was negative. A CT scan of the chest and abdomen was highly suggestive of pleural-based malignancy with the differential diagnosis of metastasis, mesothelioma or lymphoma. A video-assisted thoracoscopic biopsy was done by a CT surgeon and a chest drain was inserted.

**Pathologic Description:**

Sections showed fragments of a tumor growing in sheets and nests of large polygonal cells with large vesicular nuclei containing prominent nucleoli (Figure 3), and occasional intranuclear inclusions. The cell borders were prominent, the cytoplasm abundant and deeply eosinophilic although in some areas it appeared clear. Numerous mitotic figures were present, some of them abnormal. The stroma was sparse. There was no evidence of squamous or glandular differentiation.

Immunoperoxidase stains showed the tumor cells to be strongly and diffusely positive with antibodies against pan keratin (AE1/AE3) (Figure 4), Vimentin, EMA, and CD10. The tumor cells were negative with Calretin in (Figure 5), HBME-1, CK5/6, TTF-1, CD45RA, HMB-45, CD15, Hepat, Desmin, SMA, CD99, CD31, CD34, Ber-EP4, thyroglobulin, CK7, CK20, CK8, BRST-2 and chromogranin.

**Discussion:**

The World Health Organization (WHO) classification of lung tumors, revised in 1999, remains the foundation for lung carcinoma nomenclature. The entity of pseudomesotheliomatous carcinoma is briefly mentioned in current pulmonary pathology textbooks but it has not been included in the revised classifications of lung tumors by the World Health Organization (WHO) or Lung Cancer Study Group. Although the distinct clinical and histopathologic features of this peripheral lung cancer were described many years ago, its recognition as a...
distinct variety of lung carcinoma has not gained wide acceptance. Little is known of its incidence and only a few cases have been reported. Compared to lung carcinoma which originates from epithelial cells, malignant mesothelioma arises from mesothelial surfaces of the pleura, peritoneal cavities, tunica vaginalis or the pericardium and is an insidious neoplasm with a dismal prognosis.

Pseudomesotheliomatous carcinoma is a rare variant of peripheral lung carcinoma that mimics malignant mesothelioma in its clinical, pathological and radiologic features. Despite these morphologic similarities, pseudomesotheliomatous carcinoma is characterized by extensive invasion of the pleura and a rapidly fatal course. Because of this biologic behavior it deserves recognition as a distinct variant of peripheral lung carcinoma. This disease occurs usually in elderly patients who present with pleuritic chest pain, dyspnea, cough and pleural effusion. In contrast to mesothelioma, there is no apparent causal association with exposure to asbestos or other environmental carcinogens. Macroscopically this tumor appears as thick fleshy pleural plaques and masses that extend along the pleural surface and encase the lung. Microscopically it is a tumor of epithelial nature by its positive immunohistochemical reactions for epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), Leu-M1, B 72.3, and surfactant apoprotein but it is negative to calretinin which is regarded as the most specific and sensitive mesothelial marker for pseudomesotheliomatous lung cancer.

A carcinoma mimicking pleural mesothelioma can be of primary lung origin or metastasis from other sites. Over a 10-year (1990-2000) study period fifty-three carcinomas mimicking diffuse pleural mesothelioma (“pseudomesotheliomatous” carcinoma) were identified in a study group of 50 men and three females, age range 33-77 (median 68) years. In 46 (87%) cases there was a history of smoking and in 40 (76%) cases a history of asbestos exposure. Histologically the pleural “pseudomesotheliomatous” carcinomas could be divided into two broad groups: 47 primary pulmonary carcinomas with florid pleurotropic growth of which 34 (70%) were adenocarcinomas; and six diffuse carcinomatous involvement of the pleura by metastatic tumors. This latter group comprised two transitional cell carcinomas of bladder, one renal (clear) cell carcinoma, one ductal pancreatic adenocarcinoma, one prostatic adenocarcinoma and one squamous cell carcinoma of parotid gland origin. Therefore the term pseudomesotheliomatous neoplasm in some studies is not only used for metastatic lung cancer but is used also for other tumors that mimic mesothelioma clinically, radiologically and pathologically.

Conclusion:

Pleural “pseudomesotheliomatous” carcinomas are uncommon pathologically heterogeneous tumors that resemble pleural mesothelioma in clinical, radiological and pathological features and can be of primary lung origin or metastases from other sites. To distinguish pseudomesotheliomatous carcinoma from malignant pleural mesothelioma in patients with diffuse pleural thickening and effusion requires adequate tissue sampling by thoracotomy or video-assisted thoracoscopic surgery and a panel of immunohistochemical stains. Such a tumor has a poor prognosis and a poor response to treatment.

References:
