Case Report

Angiosarcoma of the Pleura

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Angiosarcoma is a rare, highly malignant tumor arising from endothelial cells of small blood vessels. They usually occur in the skin, deep soft tissues, breast and liver. Pleural angiosarcomas are extremely rare and are restricted to case reports in medical literature. It is very difficult to distinguish them from malignant mesotheliomas on clinical, radiological and even histopathological features. Immunohistochemistry is valuable in making the diagnosis, showing negative reactivity for mesothelial markers and positivity for vascular markers. Prognosis is generally dismal except in occasional cases where the disease is localized and amenable for surgical resection. We report a 55-year-old man who presented to us with chest pain, cough and hemoptysis and was diagnosed to have a pleural angiosarcoma. (Ann Thorac Cardiovasc Surg 2004; 10: 187–90)

Key words: angiosarcoma, pleura, thorax

Introduction

Pleural membranes are commonly involved by metastatic tumors, especially peripheral lung adenocarcinomas. Though they are usually localized, they sometimes spread diffusely over the pleura and mimic mesotheliomas. Other tumors which mimic mesothelioma include small cell lung cancer, thymoma and angiosarcoma. Angiosarcoma is a rare and highly malignant tumor of vascular origin and accounts for less than 1% of all soft tissue sarcomas.[1,2] It usually occurs in the skin, deep soft tissue, head and neck, breast, spleen and liver.[1,3] They arise from endothelial cells and usually originate from small blood vessels.[1,2] They are extremely rare in the pleura and other serous membranes like the pericardium and peritoneum.[3] We report a 55-year-old man who was diagnosed to have a pleural angiosarcoma and describe the distinguishing features from malignant mesotheliomas.

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Case Report

A 55-year-old man presented to us with a one-year history of cough with expectoration, right-sided chest pain and hemoptysis. He had no fever, hoarseness or weight loss. He had been clinically diagnosed as having tuberculosis for the same symptoms and had been on anti-tuberculous treatment for five months without any benefit. His past medical history was otherwise unremarkable. General clinical examination was normal and he had no cervical lymphadenopathy. Examination of the respiratory system showed reduced air entry over the right hemithorax. A chest radiograph (Fig. 1) revealed homogeneous opacification of the right hemithorax with absent lung markings. A computed tomographic (CT) scan (Fig. 2) showed a circumscribed mass occupying the entire right hemithorax with calcification within. Fiber optic bronchoscopy showed a distorted trachea and narrowed right bronchial tree due to extrinsic compression with no intraluminal pathology. Transthoracic fine needle aspiration cytology (FNAC) showed atypical cells in a necrotic background. His effort tolerance was good (could climb three flights of stairs, breath holding time was 12 seconds) and his pulmonary function tests revealed good reserve. CT scans of the abdomen and brain and

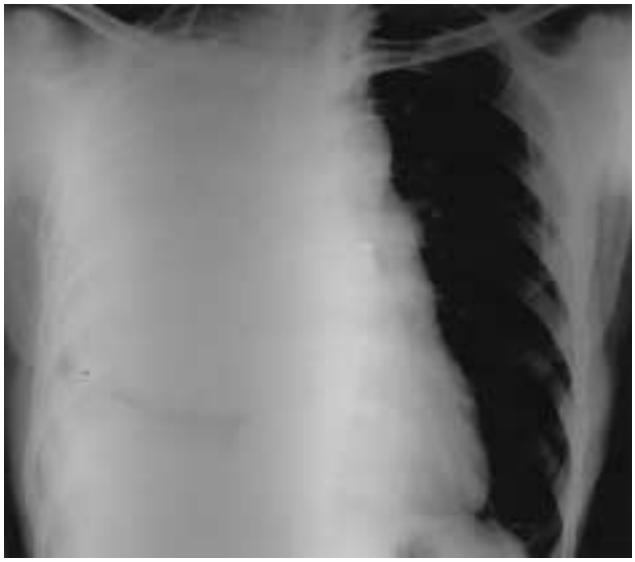

Fig. 1. Chest radiograph showing a homogeneous opacification of the right hemithorax and collapse of right lung.

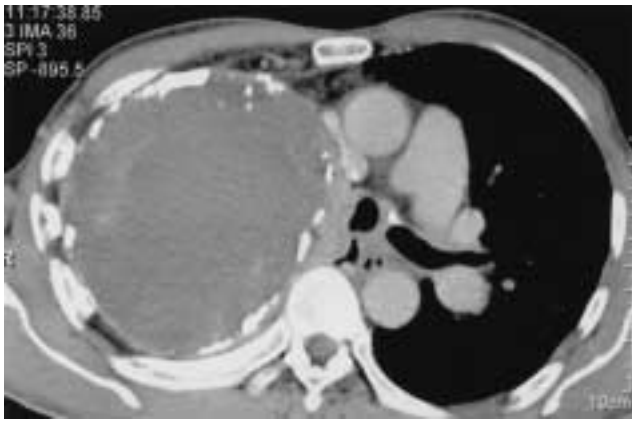

Fig. 2. CT scan showing a large circumscribed mass occupying the entire hemithorax with calcification within, causing lung collapse.

a radionuclide bone scan revealed no evidence of metastatic disease. His hematological and biochemical investigations were within normal limits and he tested negative for the human immunodeficiency virus (HIV). In view of no definitive diagnosis on FNAC, the mass being circumscribed and pulmonary function being good, we planned surgical exploration. We performed a posterolateral thoracotomy through the fifth rib. There was a large, pleural-based mass with extensive necrosis and hemorrhage. The right lung was completely collapsed beneath the mass. The mass had an irregular medial border which was inseparable from the pulmonary hilum and the main vessels. We debulked the mass as a complete resection was not possible. The patient had an uneventful postoperative course and the collapsed right lung expanded partially. On pathology, the gross specimen was seen as multiple bits and pieces aggregating 14×10×8 cm and resembled blood clots. The histopathology of the mass showed extremely scanty viable tumor comprising atypical short spindly cells forming variably sized vascular channels on a background of extensive recent and old hemorrhage (Fig. 3). Immunohistochemical studies showed that the tumor was non-reactive to anti-human mesotherial cell monoclonal mouse antibody (HBME)-1, calretinine, cytokeratin, epithelial membrane antigen (EMA) (mesothelial and epithelial markers) and was reactive to CD31 and CD34 (vascular markers) and vimentin (Fig. 4). The overall pathological features were diagnostic of a pleural angiosarcoma.

Discussion

Angiosarcomas of the pleura are extremely rare malignant neoplasms and are restricted to anecdotal case reports in medical literature.[3-5] The rarity of this condition can be understood by the fact that in a retrospective analysis over 40 years at the Mayo Clinic, no documented case of primary pleuro pulmonary angiosarcoma was found.[1] Similarly, only one case was found in a 15-year review at the Massachusetts General Hospital.[6]

In a review of 31 cases reported till then, Roh et al.[3] reported a mean age of 57 years (range, 22 to 79) and a male-female ratio of 9:1. The pathogenesis and etiology of these tumors is not clear. Etiological factors implicated include trauma, chronic lymphedema, radiation, foreign bodies, thorium, viral infection and chronic pyothorax.[7] Angiosarcomas of the breast have been related to prior radiotherapy for breast cancer and thorotrast has been implicated in the causation of hepatic angiosarcomas. All reported Japanese patients had a history of chronic tuberculous pyothorax preceding the occurrence of pleural angiosarcomas and this seems the strongest association with the disease.[8] However, there are other reports which support a de novo origin.[5]

Some authors[9] hypothesize that serosal angiosarcomas could represent a peculiar differentiation of a malignant mesothelioma along an abnormal angioblastic pathway or alternatively, a lesion arising from the native subserosal

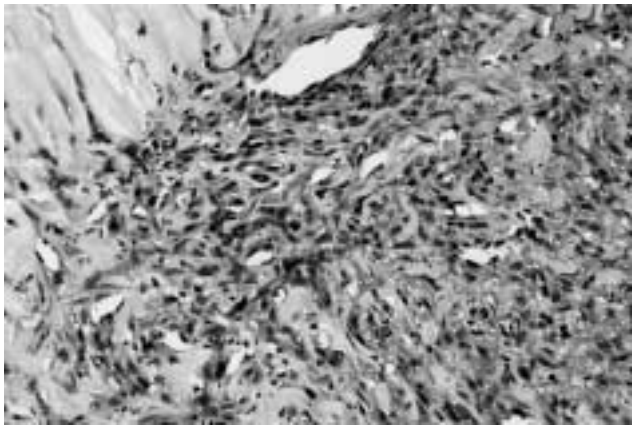

Fig. 3. Photomicrograph showing atypical short spindly cells forming variably sized vascular channels on a background of extensive recent and old hemorrhage (H&E, ×200).

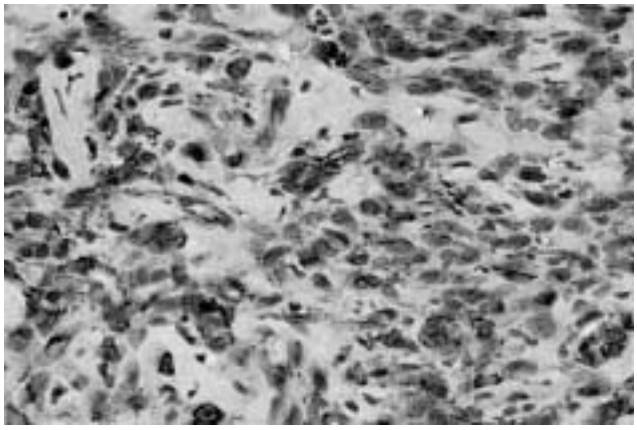

Fig. 4. Photomicrograph showing positive reactivity on immunohistochemical staining with CD 31 (×400).

vessels or a vascular malformation. Most serosal angiosarcomas are located in the pericardium and some are thought to represent tumors extending locally from the heart and great vessels.[10] It is, however, the most common pericardial sarcoma. Metastasis to hilar and mediastinal lymph nodes have also been described.[10] Its biological behavior depends on the histological grade, site of origin and multifocality but generally has a rapidly progressive course.[10] The differential diagnoses are mesothelioma and metastatic carcinoma.[3] Pleural angiosarcomas are often epithelioid[2] (74%) and can be easily mistaken for mesothelioma or carcinoma both clinically and histologically.[4,10] The distinction between angiosarcoma and hemangioendothelioma is only a matter of tumor grade as both lesions arise from the same putative precursor, the endothelial cell.[10]

Immunohistochemistry is useful in differentiating angiosarcomas from the commoner malignant mesothelioma. Mesotheliomas and adenocarcinomas stain strongly positive for cytokeratin. Negative cytokeratin and calretinin and positive vimentin reactivity generally rules out a diagnosis of mesothelioma. These results should also prompt a suspicion of a vascular tumor and vascular markers should be tested. Epithelioid vascular tumors of the pleura show positivity to at least one of the three endothelial markers–CD31, CD34 or factor VIII. Among these, CD31 is a highly specific and sensitive vascular marker which is only rarely and weakly positive in non-vascular tumors.[11] Findings characteristic of angiosarcoma include strong positivity for CD31, CD34 and vimentin, weak positivity for factor VIII and negativity for cytokeratin and calretinin.[3,4]

Presenting symptoms are usually vague and include chest discomfort, cough and dyspnea on exertion.[4] Tumors are usually locoregionally advanced by the time alarming symptoms like chest pain and hemoptysis present. Radiological investigations are usually not specific and there are no specific features characteristic of angiosarcomas. Chest radiographs may only show pleural thickening in early cases or diffuse opacification of the hemithorax in advanced lesions. CT scan findings mimic that of mesothelioma and include a lobulated mass with irregular margins and heterogeneous contrast enhancement.[4] Positron emission tomographic (PET) scan findings, described only in one patient so far, are also non-specific and may show diffuse and homogeneous fluorodeoxyglucose (FDG) uptake indistinguishable from malignant mesothelioma.[4]

Localized angiosarcomas, especially those discovered incidentally may have a relatively good prognosis after resection and occasional long-term survivors have been reported.[5,12,13] Some patients may benefit from postoperative radiotherapy even where the tumor has not been excised completely. In patients with a preoperative diagnosis, angiography with embolization may be performed to reduce blood loss during surgery. However, the overall prognosis is poor and most patients die of disease soon after diagnosis.[3-5] The role of palliative chemotherapy and radiotherapy is not clear given the rarity of the disease and the rapid progression of disease after presentation. As this patient was operated recently, we do not have a long-term follow-up of this patient.

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