Spontaneous hemothorax: primary pleural epithelioid angiosarcoma

Amit Panjwani[a], Iqbal Singh[b,c], Nagendra Parvataneni[d], Phulkumari Talukdar[e]

[a]Departments of Pulmonary Medicine, [b]Histopathology, [c]Laboratory Medicine, [d]Surgical Oncology, [e]Radiation Oncology, SevenHills Hospital, Mumbai, India

Correspondence to Amit Panjwani, DM, MD, DNB, FCCP, 3203, Type 3 Staff Quarters, SevenHills Hospital, Marol Maroshi Road, Mumbai 400059, India; Tel: 91-9768157947; fax: 91-22-67676767; e-mail: drameetp@gmail.com

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Spontaneous hemothorax is a rare condition seen in coagulation and vascular disorders. Uncommonly, malignant neoplasms may cause spontaneous hemothorax. Primary pleural epithelioid angiosarcomas (excluding the cases with pleuropulmonary or chest wall involvement) are extremely rare pleural tumors, which may be mistaken for mesothelioma or adenocarcinoma, and only 19 cases (one of them from India) have been reported in the English literature, to date. It commonly occurs in older men, has a nonspecific clinicoradiological presentation, and carries a poor prognosis with no survivors beyond a year of establishing the diagnosis. We report a case of primary pleural epithelioid angiosarcoma presenting as a life-threatening spontaneous hemothorax. We also present a brief literature review on pleural angiosarcoma.

Keywords:
angiosarcoma, pleura, spontaneous hemothorax

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Introduction

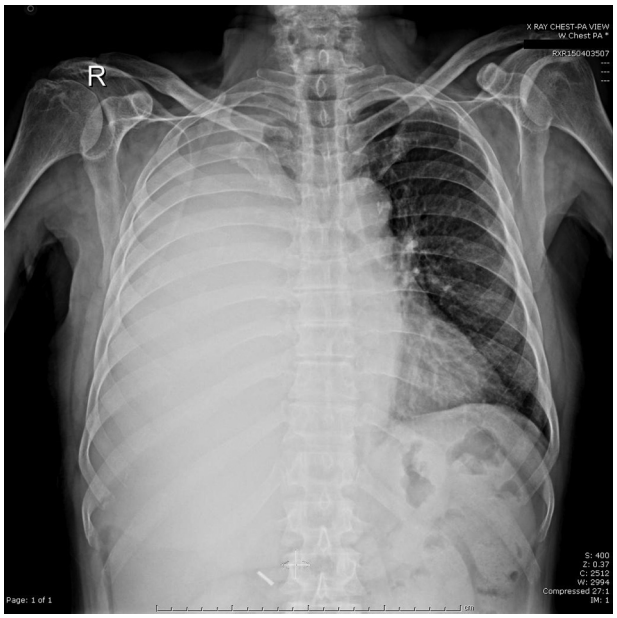
Hemothorax is defined by the presence of hemorrhagic pleural fluid (PF) with a PF hematocrit greater than 50% of the simultaneous blood hematocrit value [1]. If the PF hematocrit is estimated after a few days of the onset of pleural effusion, 25–50% value supports a diagnosis of hemothorax as the erythrocytes in the pleural space may undergo spontaneous lysis. The majority of the cases of hemothorax are related to chest trauma or procedures such as central lines, thoracocentesis, pleural biopsy, and catheterization. Spontaneous hemothorax is an uncommon condition and the causes include malignancies, anticoagulant medications, vascular ruptures such as aortic dissection or arteriovenous malformations (AVMs), endometriosis, pulmonary infarctions, and hemorrhagic diathesis [2]. Angiosarcoma is an exceedingly uncommon malignant neoplasm of vascular origin. It accounts for less than 1% of all soft-tissue sarcomas. Primary pleural angiosarcomas (excluding the cases with pleuropulmonary or chest wall involvement) are very rare aggressive tumors and only 19 cases (one of them from India) have been reported in the English literature, to date. We report the first case of spontaneous hemothorax due to a primary pleural high-grade epithelioid angiosarcoma from India.

Case report

A 76-year-old gentleman, presented with a history of right-sided dull aching chest pain and dry cough of 1-week duration. He had dyspnea Medical Research Council grade (MRC) 2 for 3 days, which progressed to MRC 4 over a period of 12 h. This was associated with orthopnea. He had no wheezing, hemoptysis, fever, weight loss, and anorexia. He had diabetes and was on an oral hypoglycemic drug. He was a former smoker and had smoked 20 pack-years. There were no other comorbidities. He denied a history of trauma. On examination, he was afebrile, pulse was 130/min, blood pressure was 110/70 mmHg, respiratory rate was 30/min, and SpO_2 was 91% on room air. There was an excessive use of accessory muscles. The breath sounds were absent in the right hemithorax. The rest of the physical examination was unremarkable. Chest radiograph (Fig. 1) showed massive right-sided pleural effusion with a mediastinal shift to the left side. Laboratory investigations revealed a hemoglobin of 4.5 g%, hematocrit of 15.5% with normal leukocytes ($4890/mm^3$), and platelets of 330 $000/mm^3$. ECG revealed a sinus tachycardia. Renal function and coagulation profile were within normal limits. Thoracocentesis was performed wherein around 1200 ml grossly hemorrhagic fluid was aspirated. The fluid had a hematocrit of 10.8% (almost 70% of blood hematocrit), which was suggestive of a hemothorax. The proteins were 4.8 g% and glucose was 38 mg% (corresponding serum proteins were 6.79 g% and random glucose was 112 mg%). PF cytology was negative for malignant cells. Contrast-enhanced

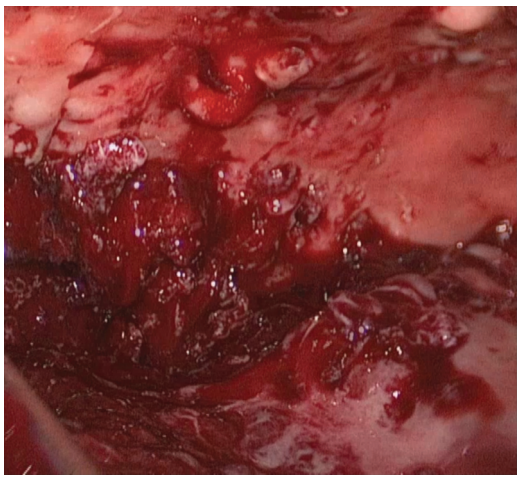
computed tomography of the thorax (Fig. 2a and b) showed nodular heterogeneously enhancing deposits in the parietal pleura on the right side with massive pleural effusion and collapsed right lung. The left lung, pleural space, and mediastinum including the cardia were unremarkable. Ultrasonography of the abdomen and pelvis was unremarkable. In view of advanced age of the patient, massive hemothorax with a significant respiratory distress and hemodynamic compromise, the patient was referred to thoracic surgeon. He was subjected to video-assisted thoracoscopy for surgical management of the hemothorax. The pleural cavity showed hemorrhagic fluid, clots, and multiple nodules along the parietal pleura. There was oozing of blood seen from the nodules along the parietal pleura (Fig. 3). It was difficult to negotiate the thoracoscope easily in the pleural cavity, and hence the patient was subjected to a posterolateral thoracotomy. The hematoma along with hemorrhagic fluid was evacuated and multiple biopsies were taken from the pleural-based nodules. The histopathological examination of the nodules showed a high-grade epithelioid sarcoma with abundant areas of necrosis (Fig. 4a and b). Immunohistochemical studies showed that the tumor was reactive to CD31 and cytokeratin (Fig. 4c and d). It was nonreactive to calretinin, Wilm's tumor gene (*WT1*), thyroid transcription factor-1 (TTF-1), cytokeratin 5/6 (CK5/6), melan-A, and desmin. The overall picture was consistent with a high-grade epithelioid angiosarcoma

Figure 1



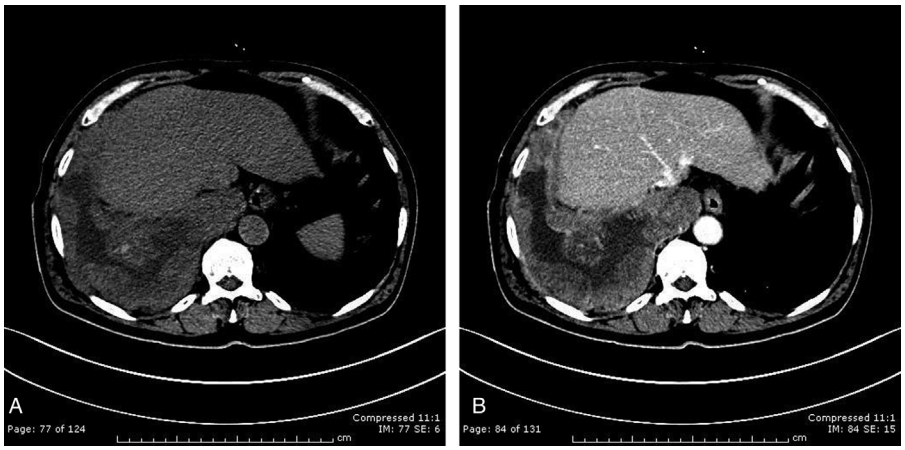
Massive right-sided pleural effusion with mediastinal shift to the opposite side.

Figure 3



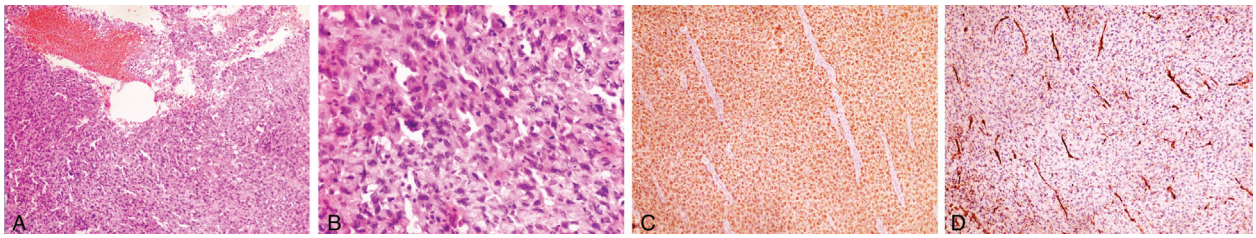
Video-assisted thoracoscopy showing multiple nodules along the parietal pleura. Oozing of blood seen from these pleural-based nodules.

Figure 2



Computed tomography of the thorax: (a) plain study shows nodular heterogeneously enhancing thickening of the parietal pleura on the right side with massive pleural effusion and collapsed right lung, (b) contrast study shows nodular heterogeneously enhancing thickening of the parietal pleura on the right side with massive pleural effusion and collapsed right lung.

Figure 4



The tumor cells express cytokeratin and CD31 (focally). The overall histological features and immunoprofile of the tumor are consistent with a diagnosis of a high-grade epithelioid angiosarcoma of the pleura. Hematoxylin and eosin, (a) ×10; (b) ×40. Immunohistochemical stains, (c) cytokeratin; (d) CD31.

of the pleura. The patient was planned for radiotherapy; however, over the next few days, he developed pneumonia involving the right lung, which progressed to septic shock and multiorgan dysfunction. He deteriorated quickly and succumbed to the illness within 2 weeks.

Discussion

Spontaneous hemothorax is a rare entity. Spontaneous pneumothorax accounts for most of these cases [2]. Diseases such as dissecting aneurysms, AVMs, coagulopathies, vascular tumors, exostoses, endometriosis, and others should be considered as a part of the diagnostic work-up for the evaluation of these cases. The importance of a good history and physical examination cannot be underestimated in the evaluation of spontaneous hemothorax. Besides the coagulation profile, a contrast-enhanced computed tomography of the thorax helps in arriving at a proper diagnosis. An echocardiogram with a bubble study should be considered where AVM is suspected. PF cytology at times may not be sufficient to diagnose vascular neoplasms, and immunochemical markers can be used to save the day. Intercostal tube thoracostomy is the first step in the management of cases with stable spontaneous hemothorax. In a hemodynamically unstable patient, massive hemothorax (>1000 ml), continuous bleeding more than 500 ml in the first hour or more than 200 ml/h for 5 h, and an early surgical intervention is the favored approach, as was performed in our case.

Primary pleural epithelioid angiosarcoma is an extremely rare malignancy. The last literature review by Zhang *et al.* [3] analyzed 19 cases of primary pleural angiosarcoma (excluding the cases with chest wall or pleuroparenchymal involvement) reported in the English literature. Three of these 19 cases had hemothorax as its cardinal clinical manifestation. A few cases of cardiac angiosarcomas with pulmonary involvement have been reported from India in the past [4–6]. Interestingly, only one case each of primary pulmonary angiosarcoma [7] and primary pleural angiosarcoma [8] has been reported from India, ours being the first case of primary pleural angiosarcoma presenting with a spontaneous hemothorax. Angiosarcoma is a soft tissue sarcoma that arises from small vessels in the skin, deep soft tissue, breast, spleen, and liver. They are divided into four groups: cutaneous angiosarcoma unassociated with lymphedema, cutaneous angiosarcoma associated with lymphedema, angiosarcoma of the breast, and angiosarcoma of deep soft tissue. The etiology for this tumor is still unknown. There is a strong correlation seen in Japanese patients between the presence of chronic pyothorax caused by pleural or pulmonary tuberculosis and development of pleural angiosarcoma. However, western researchers propose radiation and asbestos exposure as important etiologic factors leading to this condition. Our patient did not have any history of tuberculosis, radiation, or asbestos exposure. When unrelated to these factors, this case may be described as de-novo tumor.

Clinical presentation is nonspecific. Patients may present with chest pain, dyspnea, cough, anemia, and hemothorax [9,10]. Radiologically, the presentation includes pleural nodules or masses [8,11], pleural thickening, and unilateral or bilateral pleural effusion [12]. This condition may be misdiagnosed as tuberculosis [12], hematoma [13], pleural metastasis, or a mesothelioma [14]. Cytological examination of the PF or the pleural tumor is unhelpful in the majority of the situations [8,10,11]. Definitive diagnosis requires adequate specimens, which may be obtained occasionally by means of needle-core biopsy [11] but mostly through surgical methods [8,10,12]. Histologically, in the majority of the patients, pleural angiosarcomas are usually epithelioid and may be mistaken for mesothelioma or adenocarcinoma [15]. Therefore, immunohistochemistry is a useful way of establishing the diagnosis. Epithelioid markers (e.g. cytokeratin) always stain positive in mesotheliomas and adenocarcinomas, whereas they occasionally stain

positive in epithelioid pleural angiosarcomas, as was seen in our case. Endothelial (vascular) markers such as CD31, CD34, and factor VIII-related antigens are required for establishing a definitive diagnosis of angiosarcoma. CD31 is the most sensitive and specific marker for vascular neoplasms [11]. Mesothelial markers such as calretinin, CK5/6, and *WT1* are used for excluding malignant mesothelioma [14]. Pleural angiosarcomas are managed best with a complete surgical resection, debulking with pneumonectomy, and rib resection, wherever possible. Radiation therapy may be considered in postoperative situations in which the disease is localized and there is no evidence of distant metastasis. Chemotherapy has a doubtful role and may be used as palliative therapy.

Conclusion

Primary pleural epithelioid angiosarcoma is a rare aggressive malignant neoplasm with nonspecific clinical and radiological features, which may cause a spontaneous hemothorax with a rapid clinical deterioration. Awareness of this entity is essential for an early diagnosis and instituting appropriate treatment. This condition has an extremely poor prognosis with hardly any survivors beyond a year, despite treating them with the available modalities.

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Conflicts of interest

There are no conflicts of interest.

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