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Authors

Jimenez, Daniel
Antaki, James
Kamangar, Nader

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Metastatic Pulmonary Angiosarcoma Presenting With Bilateral Secondary Spontaneous Pneumothoraces

Daniel Jimenez, MD¹, James Antaki, BS²,
and Nader Kamangar, MD, FACP, FCCP, FCCM²

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Abstract

Background: Spontaneous pneumothorax (SP) is uncommon and can present as a primary disease process or as a result of underlying lung pathology. Several parenchymal lung diseases, such as malignancy, are known to cause SP. One such malignancy, angiosarcoma, has a high propensity to metastasize to the lung and present as cavitory and cystic lesions. **Case:** We present a case of a 76-year-old male diagnosed with angiosarcoma of the scalp that was found to have extensive cystic pulmonary metastatic lesions. Soon after his initial diagnosis, he presented with severe respiratory distress secondary to a spontaneous left-sided pneumothorax. After intubation and left-sided chest tube placement, the patient developed a right-sided tension pneumothorax requiring emergent chest tube placement. **Conclusion:** Cutaneous angiosarcoma is a rare malignancy that frequently metastasizes the lung. Spontaneous pneumothorax can be the presenting manifestation of the disease and often results in respiratory failure.

Keywords

spontaneous pneumothorax, cutaneous angiosarcoma, respiratory failure, positive pressure ventilation

Introduction

The incidence of spontaneous pneumothorax (SP) is 5 to 10 per 10 000 patients per year. Secondary SP (SSP) occurs in the setting of parenchymal lung diseases such as bullous emphysema, tuberculosis, and malignancy.¹ Angiosarcoma is a rare vascular malignancy that accounts for 2% of all sarcomas and typically originates in the face or scalp. The metastatic potential of angiosarcoma is high, and up to 20% of patients diagnosed with angiosarcoma develop pulmonary metastases.^{1,2} The characteristics of these pulmonary metastases vary but often present as multiple solid, cavitory and cystic lesions.³ Secondary SP is known to develop from spontaneous rupture of cystic lung lesions in angiosarcoma. Although SSP caused by malignancy only accounts for approximately 0.05% of all SSPs, given the high rate of metastatic pulmonary lesions in angiosarcoma, as well as their particular morphological characteristics, it is important to recognize the potential for respiratory compromise in this group of patients.⁴

Case Presentation

A 76-year-old man with a history of hypertension presented to our institution with a growing lesion on the left parietal region of his scalp that was first noticed several months earlier after bumping his head on a car door. Initial biopsy specimens were

inconclusive, but given the high suspicion for malignancy, he underwent a surgical deep tissue biopsy, which revealed high-grade angiosarcoma. He underwent full-body imaging for staging, including computed tomography (CT) scan of the chest, which revealed diffuse thin-walled cystic parenchymal lesions with surrounding ground-glass opacities (Figure 1A-D). After an extensive negative infectious workup, these findings were determined to be consistent with metastatic angiosarcoma. Despite the extent of malignant disease, the patient remained asymptomatic with no signs of respiratory compromise. For these reasons and the fact that treatment with chemotherapy

¹ Department of Medicine, Olive View-UCLA Medical Center, UCLA David Geffen School of Medicine, Sylmar, CA, USA

² Division of Pulmonary and Critical Care Medicine, Department of Medicine, Olive View-UCLA Medical Center, UCLA David Geffen School of Medicine, Sylmar, CA, USA

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Corresponding Author:

Nader Kamangar, Division of Pulmonary and Critical Care Medicine, Department of Medicine, Olive View-UCLA Medical Center, UCLA David Geffen School of Medicine, Room 6B-111, 14445 Olive View Drive, Sylmar, CA 91342, USA.

Email: kamangar@ucla.edu

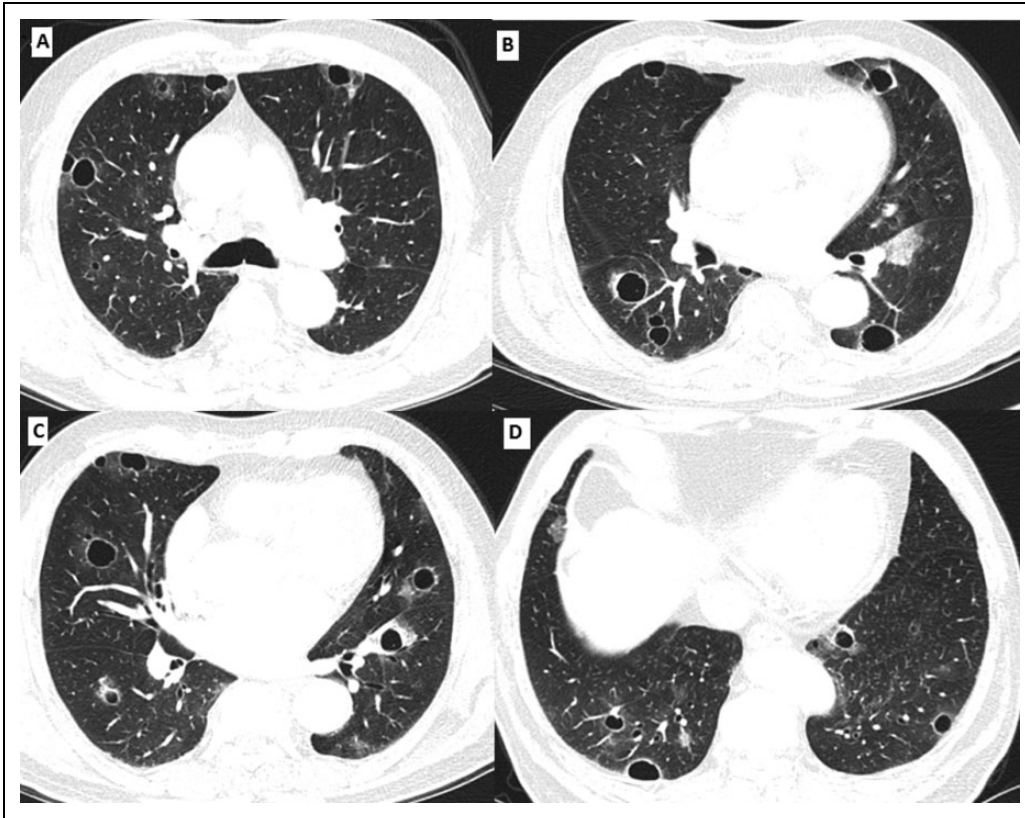


Figure 1. A-D, Chest computed tomography (CT) revealing diffuse cystic parenchymal lesions with surrounding ground-glass opacities.

predisposed him to pulmonary hemorrhage (PH), the patient decided to forgo palliative interventions.

One month later, the patient presented to the emergency department in acute respiratory distress. He was afebrile, with heart rate of 129 beats per minute, blood pressure of 256/153 mm Hg, respiratory rate of 28, and arterial oxygen saturating of 93% on 15-L nonrebreather facemask. He was unable to speak due to respiratory distress, had intercostal retractions with accessory muscle use, and displayed paradoxical diaphragmatic movements. Pulmonary auscultation was notable for coarse bilateral breath sounds throughout the right anterior lung and decreased breath sounds throughout the left lung field. Lactate was elevated to 6.1 mmol/L. Arterial blood gas on 15-L nonrebreather facemask revealed pH 7.22, P_{aCO_2} 49 mm Hg, P_{aO_2} 81, and HCO_3^- 20 mmol/L. Initial portable chest radiograph (CXR) showed a moderate- to large-sized left pneumothorax (Figure 2). Prior to the review of the radiograph, the patient's respiratory status deteriorated, requiring emergent intubation. Immediately after placement on mechanical ventilation, peak and plateau pressures were noted to be greater than 60 cm H_2O . Postintubation CXR revealed a large-sized left pneumothorax with a deep sulcus and contralateral mediastinal shift, requiring emergent chest tube placement (Figure 3). The airway pressures immediately normalized following chest tube thoracostomy.

Approximately 1 hour later, the patient deteriorated and was noted to be acutely hypotensive with a sudden change in



Figure 2. Portable chest radiograph showing a moderate to large-sized left pneumothorax.

ventilator mechanics as manifested by a rise in peak and plateau pressures. Repeat CXR revealed complete resolution of the left pneumothorax; however, it was notable for the development of a new moderate to large-sized right-sided pneumothorax (Figure 4). Emergent placement of a right chest tube resulted in normalization of his hemodynamics and airway

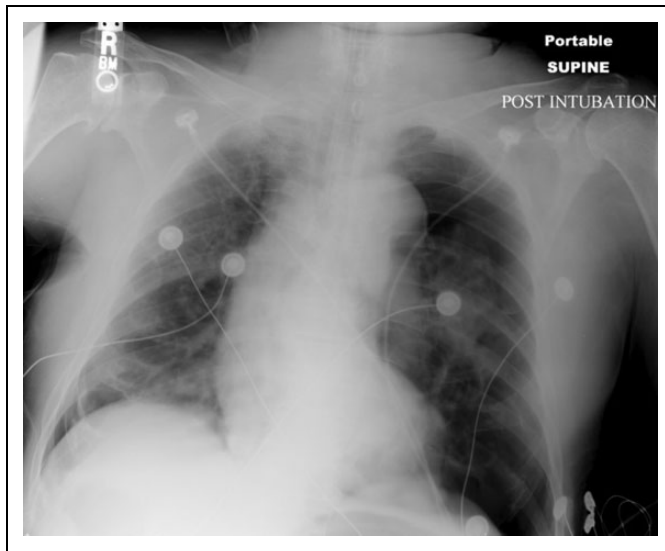


Figure 3. Portable chest radiograph showing a large-sized left pneumothorax with contralateral mediastinal shift and associated deep sulcus sign.

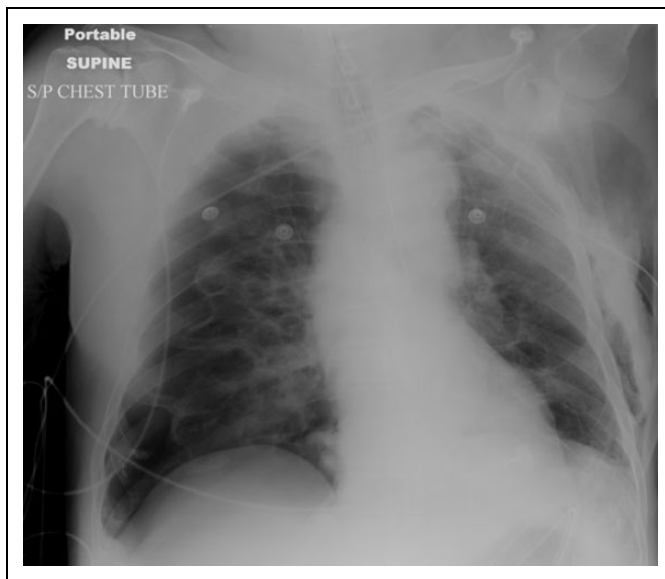


Figure 4. Portable chest radiograph demonstrating a moderate to large-sized right pneumothorax and resolution of the left pneumothorax with chest tube in place, as well as associated left chest wall subcutaneous emphysema.

pressures. The patient remained hemodynamically stable and was soon weaned off mechanical ventilation.

The chest tubes were removed 5 days later, initially with no sequelae. His hospital course was further complicated by recurrence of small bi-apical pneumothoraces requiring placement of small-bore chest tubes. Due to persistent air leaks and the likely presence of bronchopleural fistulae, autologous blood patch, as well as chemical pleurodesis with talc, was performed on both sides, unfortunately to no avail. The chest tubes were ultimately connected to Heimlich valves in order to facilitate

outpatient management. The patient was subsequently discharged home with hospice.

Discussion

Cutaneous angiosarcoma is a rare but highly malignant sarcoma of endothelial origin. It occurs more frequently in men, and the most common primary site is the skin of the head and neck.^{2,5} Angiosarcoma is an aggressive tumor with high rates of metastases and recurrence, despite initiation of therapy.⁶ Multiple factors have been associated with the development of cutaneous angiosarcoma; these include exposure to polyvinyl chloride, thorium dioxide, trauma, foreign bodies, and radiation.^{5,7} Although cutaneous angiosarcoma can metastasize to cervical lymph nodes, liver, spleen, bone, heart, and brain, the most common site of metastatic spread is the lung.^{5,6} Notably, angiosarcoma of the scalp has a high predilection to metastasize to the lung, which has been supported by a review of autopsy data by Kitagawa et al, as well as numerous case reports.⁸⁻¹⁰

The most common presenting symptom of pulmonary metastasis in angiosarcoma is hemoptysis; however, cough, chest pain, dyspnea, or fever may also occur.⁵ Although uncommon, patients may present with other complications such as SSP, pneumomediastinum (PM), and overt PH.^{6,8} Secondary SP, PM, and PH have been shown to occur at significantly higher rates in patients with angiosarcoma of the scalp, with bilateral SSP occurring in 0.9% to 4.0% of such patients.^{7,8,10} In a comprehensive review of SSP complicating all forms of sarcoma by Hoag et al, 153 cases were examined with results revealing unilateral SSP in 58.4% and bilateral SSP in 41.6% of patients. Additionally, up to 45.7% had recurrence of SSP, and 7% of patients had persistent SSP and bronchopleural fistulae, despite appropriate therapy.¹

The most prevalent radiographic findings in patients with metastatic pulmonary involvement are multiple random pulmonary nodules, which can become cavitory or cystic in morphology. In a systematic review of 24 patients with metastatic angiosarcoma of the lung, Tateishi et al concluded that multiple pulmonary nodules were the most common finding on thoracic CT, accounting for 63% of metastatic pulmonary disease. The second most common finding were multiple thin-walled cystic lesions, which was seen in 21% of patients—all of which ultimately resulted in SSPs or hemothoraces.³ Other characteristic imaging findings included air–fluid levels in cystic lesions (13%), likely representing rapid enlargement of the lesions with resultant hemorrhage and ground-glass opacities (32%), which are often indicative of PH.³

Although the exact mechanism by which these cavitory and cystic lesions develop is unclear, 4 major theories have been proposed; these include the following: (1) excavation of a solid nodular lesion through discharge of necrotic material; (2) infiltration of tumor cells into the walls of preexisting bullous lung tissue; (3) circumferential growth of tumor around bronchioles leading to infiltration of malignant cells into the walls of air sacs with resultant cystic distension through the ball-valve

effect of the tumor; and (4) tumor cell proliferation resulting in blood-filled cystic spaces, which is a histopathologic characteristic of angiosarcoma.^{3,9} Although likely multifactorial in etiology, the presence of both nodular and cystic lesions seen in 8% of patients with metastatic angiosarcoma to the lung is suggestive of progressive stages in tumor evolution.^{3,6} The development of SSP in patients with cystic pulmonary lesions typically occurs when lesions that extend to the subpleural space spontaneously rupture, resulting in a pneumothorax. This happens to be a characteristic finding in metastatic angiosarcoma.^{1,4}

Diagnosis of pulmonary metastasis in angiosarcoma is dependent on imaging, with chest CT providing the most detailed assessment of involvement. Although CXR often reveals features indicative of metastatic disease—such as nodules, cavitory and cystic lesions, large masses, and pleural involvement—up to 5.5% can be normal in such patients who present with a SSP.¹ Therefore, chest CT is recommended for evaluating patients with suspected pulmonary involvement. Although 18-fluorodeoxyglucose positron emission tomography (FDG-PET) is typically used for staging of various malignancies, there is no compelling data supporting its use in pulmonary angiosarcoma. In fact, a negative FDG-PET in the presence of suspicious CT findings does not exclude pulmonary metastasis from both osseous and soft tissue sarcomas, including angiosarcoma.⁵ Biopsy is an alternative method of reliably diagnosing pulmonary metastasis, with both transbronchial and transthoracic needle biopsy capable of providing pathologic specimens.⁸ However, transthoracic needle biopsy is often difficult, with a diagnostic yield of 50% and complication rate of up to 50%, notably due to the development of pneumothoraces, particularly in the presence of cavitory and cystic disease.¹¹

The treatment of angiosarcoma is variable and dependent on the extent of disease. Surgical management may consist of excision alone, although in those with metastatic disease can include adjuvant radiation and chemotherapy.⁶ Previously utilized chemotherapy regimens include various combinations of doxorubicin, ifosfamide, dacarbazine, cyclophosphamide, methotrexate, and vincristine. However, in most patients over 50, doxorubicin is often used as a single agent as it has been reported to result in objective, albeit temporary, improvement of disease in up to 70% of patients.^{1,4} In patients with pulmonary metastasis, initiation of a doxorubicin-based chemotherapy regimen has been associated with the development of SSP. Possible mechanisms accounting for this complication include rapid tumor lysis, necrosis of large pulmonary lesions, chemotherapy-induced impairment of the normal repair processes, and possible coinfection of lesions.⁴ Secondary SP is also seen in patients receiving radiation therapy and is thought to be secondary to radiation-induced fibrosis of both the pleura and lung parenchyma. Differentiating the cause of treatment-induced SSP is determined by comparing the time of treatment initiation to the development of SSP. In patients with SSP secondary to chemotherapy, pneumothorax typically develops within 1 to 8 days of induction.

In contrast, radiation-induced SSP is seen 3 to 65 months after initiation of therapy.⁴

Despite multiple treatment options, there is no well-established regimen for patients with metastatic pulmonary angiosarcoma and overall survival is exceedingly low. Patients presenting with SSP generally have a particularly poor prognosis with survival no more than several months despite aggressive therapy.^{5,7} Consequently, pulmonary complications such as SSP are treated in order to ameliorate symptoms. Therapeutic chest tube placement is commonly performed, and in some patients, chemical pleurodesis can be considered.⁷

In this case, our patient with cutaneous angiosarcoma and metastatic pulmonary lesions presented with acute respiratory failure. Given the severity of his clinical presentation, he was emergently intubated prior to the review of the initial CXR, which demonstrated a significant left pneumothorax. The large left-sided SSP was the etiology of his severe dyspnea and ensuing respiratory failure; it likely occurred as a result of the spontaneous rupture of a subpleural cystic metastatic lesion. Although the patient transiently stabilized after intubation, the initial left-sided SSP enlarged as a result of positive pressure ventilation (PPV), requiring chest tube placement. Maintenance on PPV likely led to the development of a new right-sided pneumothorax—in a patient who was at high risk given the subpleural cystic nature of the metastatic pulmonary disease—which rapidly progressed and led to tension physiology, requiring emergent chest tube placement. This patient exhibited rapid progression of metastatic pulmonary disease after the initial diagnosis of primary cutaneous angiosarcoma. Although he had not received chemotherapy prior to the development of respiratory complications, it is unclear whether earlier initiation of treatment would have prevented his rapid and progressive demise.

The finding of simultaneous bilateral SSPs may suggest a serious underlying parenchymal lung disorder such as metastatic angiosarcoma. Angiosarcoma should be considered in the differential diagnosis of older patients presenting with pneumothoraces in the setting of underlying cystic lung disease. Although thin-walled cystic lung lesions are often considered benign, metastatic angiosarcoma appears to be an exception to that rule.

Authors' Note

Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

Declaration of Conflicting Interests

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