

# Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography in the detection of primary pulmonary angiosarcomas

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**ABSTRACT** Angiosarcoma is a malignant vascular tumor that originates from the mesenchymal cells which have undergone angioblastic differentiation. Pulmonary angiosarcomas are invariably (>90%) metastatic tumors form primaries of the skin, bone, liver, breast, or heart. Primary pulmonary angiosarcomas are exceedingly rare, with just about 20 cases being reported in the literature. We report an additional case with a brief review of the literature of a primary pulmonary angiosarcoma in a 26-year-old lady who presented with intractable hemoptysis. In addition, we highlight the potential of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography as an important diagnostic tool in the evaluation of this tumor and thus contribute to the existing sparse literature on this fascinating yet devastating disease.

**Keywords:** Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography, pneumonectomy, primary pulmonary angiosarcoma, prognosis

## INTRODUCTION

Angiosarcomas represent a rare subgroup of soft tissue sarcomas (<2%) which is characterized by an aggressive clinical behavior and is known to occur not only in different anatomical locations, but also in distinct clinical settings (either *de novo* [primary angiosarcoma] or in the postradiation setting or following chronic lymphedema [secondary angiosarcomas]). Pulmonary angiosarcomas are invariably metastatic tumors form primaries of the skin, bone, liver, breast or heart.<sup>[1,2]</sup> Primary pulmonary angiosarcomas are exceedingly rare, with just about 20 cases being reported in the literature.<sup>[1-6]</sup> We report a case of the primary pulmonary angiosarcoma in a 26-year-old lady along with a brief review of the literature.

## CASE REPORT

A 26-year-old lady with no comorbid conditions, presented with a 2 months history of cough and intractable hemoptysis. A bronchoscopic examination performed in another hospital revealed a vascular fleshy growth protruding onto the left main bronchus, and an attempted biopsy resulted in profuse bleeding. The procedure was, therefore, abandoned, and the patient was referred to our center for further management. A repeat bronchoscopy performed at our center confirmed the previous bronchoscopy findings, additionally the tumor was found to completely occlude the left main bronchus. A biopsy from the lesion resulted in profuse bleeding and was managed conservatively. Histology with immunohistochemistry (IHC) correlation suggested a diagnosis of a primary pulmonary angiosarcoma, intermediate grade. The tumor cells were immunopositive for vimentin, smooth muscle actin, CD31 and CD34, negative for keratin, desmin and myoglobin. Thirty percentage of the tumor cells showed nuclear positivity to Ki-67 [Figure 1a-d]. An fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (<sup>18</sup>F-FDG PET/CT) done as a part of the metastatic work up revealed a solitary metabolically active endobronchial lesion measuring 3.5 cm × 1.8 cm (SUV<sub>max</sub> -9.3) in the left main bronchus extending into the left lower bronchus causing complete obstruction and collapse of the entire left lung;

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further corroborating the diagnosis of a primary pulmonary angiosarcoma [Figure 2a-c].

A formal cardiopulmonary evaluation was subsequently done, and the patient was taken up for a definitive surgery. A technetium-99m diethylene triamine pentaacetic acid aerosol and perfusion scan showed a total absence of ventilation and a global hypoperfusion in the left lung, the predicted forced expiratory volume in one after a left pneumonectomy was 1.03 L.

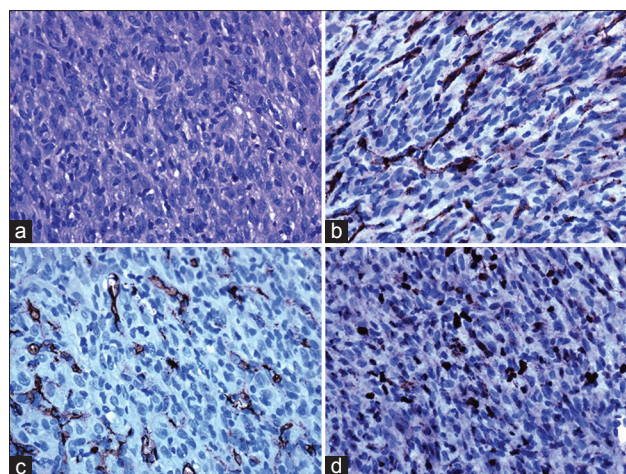
Intraoperatively the tumor was found to originate at the bifurcation of the left main bronchus and a sleeve resection was deemed not possible, the patient, therefore, underwent a left pneumonectomy [Figure 3a and b]. Her postoperative recovery was uneventful; the final histopathology confirmed the diagnosis of a primary pulmonary angiosarcoma. The patient received 50 gray of adjuvant radiotherapy and is on regular follow-up for the past 7 months.

## DISCUSSION

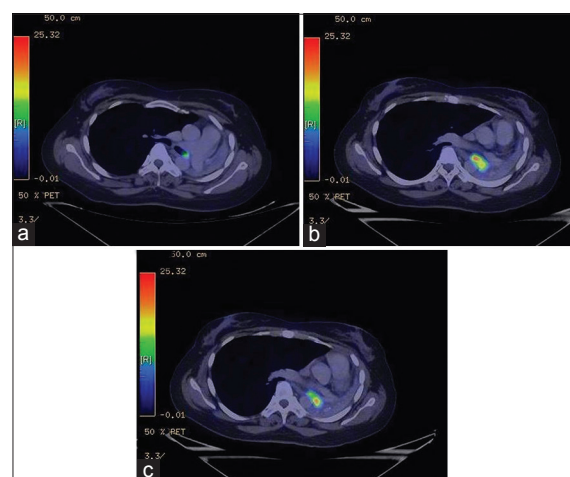
Primary pulmonary angiosarcoma is an exceedingly uncommon condition.<sup>[1-8]</sup> Various predisposing factors have been described including history of prior radiation treatment, exposure to poly-vinyl chloride, thorotrast and copper mining dusts, although history of exposure to these risk factors may not always be forthcoming.

The mean age of the affected patients in the reported series was around 55 years and the majority of them were males (male: Female = 3:1).<sup>[8]</sup> The clinical presentation of angiosarcomas is nonspecific and generally varies, based on site of the tumor, the degree of pulmonary artery involvement and the anatomical structures involved. The presenting symptoms may include hemoptysis, pleuritic chest pain, dyspnea, nonproductive cough, spontaneous hemothorax, cyanosis, syncope or rarely massive pulmonary hemorrhage.<sup>[6-8]</sup>

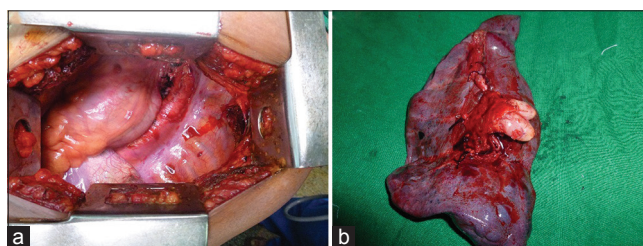
Pulmonary sarcomas of vascular origin, unlike other forms of primary pulmonary sarcomas, usually appear as multiple small nodules between 1 and 2 cm in diameter on imaging with a CT scan.<sup>[9]</sup> An endobronchial presentation of a primary pulmonary angiosarcoma as in our patient is extraordinarily rare. A majority of the endobronchial lesions (>98%) are, in fact, malignant, hamartomas represent the most common benign pulmonary endobronchial lesions. The differential diagnosis of the malignant endobronchial lesions includes bronchogenic carcinomas, bronchial carcinoids, mucoepidermoid carcinomas, adenoid cystic carcinomas and rarely endobronchial metastasis from extrathoracic malignancies. The definitive diagnosis of primary pulmonary angiosarcoma is challenging, it is vitally important to differentiate it from a metastatic carcinoma and an <sup>18</sup>F-FDG PET/CT is an extremely valuable adjunct and possibly the imaging of choice in the evaluation of the same.<sup>[4]</sup> Further, a PET/CT can also reliably differentiate the malignant endobronchial lesions with the distal atelectasis resulting from benign bronchial stenosis.<sup>[10]</sup>



**Figure 1a:** H and E,  $\times 40$  - Tumor showing the characteristic vascular channel formation suggestive of a primary pulmonary angiosarcoma. (b) immunohistochemistry (IHC),  $\times 40$  - Tumor cells showing immunopositivity to CD31. (c) IHC,  $\times 40$  - Tumor cells showing immunopositivity to CD34. (d) IHC,  $\times 40$  - 30% tumor cells showing nuclear positivity to Ki-67



**Figure 2:** (a-c) An fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography revealed a solitary metabolically active endobronchial lesion measuring 3.5 cm  $\times$  1.8 cm (SUVmax-9.3) in the left main bronchus extending into the left lower bronchus causing complete obstruction and collapse of the entire left lung



**Figure 3:** (a) Intraoperative photograph of the tumor bed following a left pneumonectomy. (b) Specimen photograph following the sectioning of the left main bronchus showing the fleshy tumor

The histopathological diagnosis of angiosarcomas is made by the characteristic vascular channel formation. IHC plays an important adjunct role in confirming the endothelial origin of the neoplasm with the expression of at least one of the

vascular markers CD31, CD34, factor VIII-related antigen, FLI1 or ERG.<sup>[11]</sup> The differential diagnoses of primary pulmonary angiosarcomas include myogenic sarcomas and benign conditions such as congenital narrowing of the pulmonary vessels, fibrosing mediastinitis and pulmonary arteritis.

Effective strategies in the management of primary pulmonary angiosarcomas have not been established, the various therapeutic options include surgery, radiotherapy, chemotherapy immunotherapy and steroids.<sup>[3]</sup> Although there are no standard treatment recommendations, radical surgery remains the mainstay in the management of tumors that are locally confined.<sup>[1]</sup> Radical surgery is usually followed with adjuvant radiation therapy in an attempt to reduce the reported high rates of local recurrence. There is currently no data supporting the use of chemotherapy, except in the setting of widespread metastatic disease.

The majority of the reported patients of primary pulmonary angiosarcomas have succumbed between 1 and 9 months of diagnosis, although there have been exceptional survivors who have lived for more than a year.<sup>[8]</sup> Novel therapies using targeted biological agents including inhibition of vascular endothelial growth factor using bevacizumab and tyrosine kinase inhibitors have been attempted but have largely proved to be unsuccessful in improving survival. The study of genetic aberrations has revealed angiosarcomas to be a distinct subgroup of mesenchymal tumors with complex changes in TP53 and PIK3CA/AKT/mTOR pathways that does not depend on the MYC amplification.<sup>[12]</sup> These findings emphasize on the need for further research and possibilities for newer therapeutic options.

## CONCLUSION

Clinicians need to be aware that angiosarcomas found in the pulmonary parenchyma invariably represents a metastasis from a distant primary tumor rather than a primary pulmonary angiosarcoma and an <sup>18</sup>F-FDG PET/CT is an extremely useful adjunct tool and possibly the imaging of choice in aiding this distinction. This distinction is essential for the appropriate and

effective management of primary pulmonary angiosarcomas as was done in our patient.

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