An unusual presentation of pulmonary epitheloid hemangioendothelioma

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Abstract
Pulmonary epitheloid hemangioendothelioma (PEHE) is a rare, often incidentally diagnosed, endothelial tumor of the lung. We present a case of a young adult who presented with acute hypoxemic respiratory failure and severe pulmonary hypertension with subsequent imaging and tissue biopsy confirming a diagnosis of PEHE. We briefly highlight the unique clinical, radiographic and histopathologic aspects of this rare disease. We propose that PEHE should be considered in the differential diagnosis for acute hypoxemic respiratory failure associated with bilateral pulmonary cavitary nodules and bronchoscopy should be considered as an initial diagnostic test.

1. Introduction
Pulmonary epitheloid hemangioendothelioma (PEHE) is a rare, often incidentally diagnosed, endothelial tumor of the lung. We present a case of a young adult who presented with acute respiratory failure and hypotension with subsequent imaging and tissue biopsy confirming a diagnosis of PEHE. We briefly highlight the unique clinical, radiographic and histopathologic aspects of this rare disease.

2. Case description
A 20 year old Caucasian male with a one year history of asthma, presented to the hospital with one month history of productive cough, dyspnea, fatigue and unquantified unintentional weight loss. He had failed outpatient therapy with azithromycin and prednisone prescribed one week prior to this admission. On arrival to the ER at an outside facility he was hypotensive and in severely hypoxemic respiratory failure. He was intubated, resuscitated with fluids and vasopressors, and transferred to our hospital for higher level of care. Physical examination was notable for temporal wasting, thin built & low body mass index (BMI of 18 kg/m2). Pulmonary exam revealed bilateral diffuse crackles with wheezing on auscultation. He was started on empirical broad spectrum antibiotic coverage for community acquired pneumonia. His initial Chest radiograph showed bilateral diffuse infiltrates with blunting of bilateral costophrenic angles (Fig. 1).

Subsequent CT chest revealed bilateral ground glass opacities with areas of consolidation, which was most prominent in the right middle lobe. There were multiple bilateral cavitary nodules and an incidental lytic lesion was identified in the T-11 vertebrae (Fig. 2).

His transthoracic echocardiogram revealed enlarged right ventricular cavity size (basal dimension > 4.2 cm RV apical 4 chamber view) with severely reduced systolic function. The estimated pulmonary artery systolic pressure was 80 mm Hg suggestive of severe pulmonary hypertension. The sepal motion was abnormal consistent with right ventricular pressure and volume overload. The left ventricle ejection fraction was 50–54%.

He underwent a bronchoscopy, which showed non-obstructing polypoid lesions in the left lower lobe and a partially obstructing infiltrative lesion in the right middle lobe (Fig. 3).

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His bronchoalveolar lavage was positive for rhinovirus and rest of the cultures including bacterial, mycobacterial and fungal cultures were negative. His endobronchial biopsy showed a high grade epithelial hemangioendothelioma (Fig. 4).

Immunostaining showed the tumor cells were positive for CKA1/3, CAM5.2, EMA, CD31, CD34, ERG, FLI-1, factor 8, and vimentin.

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His condition continued to deteriorate clinically despite aggressive medical management. After multidisciplinary consensus and per family wishes, his goals of care were transitioned to comfort measures.

3. Discussion

Epitheloid hemangioendothelioma is a rare tumor with an incidence of 1:1,000,000 worldwide [1]. It is more common in women with bimodal age distribution [2]. Patients are usually asymptomatic or with minimal nonspecific symptoms such as cough or chest pain at the time of diagnosis. Our patient presented with acute hypoxemic respiratory failure with history of cough, dyspnea and weight loss.

Typical radiographic findings of PEHE include multiple perivascular nodules and pleural effusions [3]. Our patient had multiple cavitory nodules bilaterally with ground glass opacity. The thoracic vertebral lesion seen on CT scan was not sampled but probably related to metastatic disease. The severe pulmonary hypertension estimated on echocardiography likely was a reflection of the vascular involvement and chronic hypoxemia. Release of vascular endothelial growth factor by these tumors may also contribute to the development of pulmonary hypertension in these patients.

Tissue biopsy is needed for a definitive diagnosis. Contrary to other reports, our patient was diagnosed by a bronchoscopic endobronchial biopsy rather than a surgical lung biopsy. The presence of significant weight loss, anemia, pulmonary symptoms, and spindle tumor cell histology with possible metastasis were very poor prognostic factors in our patient. These factors have been shown to be associated with a median survival of less than a year [4]. Given the rarity of the disease, there is no standard therapy and therapeutic options are limited. Observation in milder, asymptomatic patients versus radiotherapy or chemotherapy in severe forms of disease has been used with variable success.

4. Conclusion

PEHE is a rare often incidentally diagnosed tumor. Our patient is a young adult who had an unusual presentation with acute hypoxemic respiratory failure and pulmonary hypertension. He was found to have extensive bilateral pulmonary metastatic disease with possible metastasis to bone. Diagnosis was made on biopsy of the endobronchial lesions. We propose that PEHE should be kept in the differential for acute hypoxemic respiratory failure with bilateral cavitory nodules and bronchoscopy should be considered as an initial diagnostic test.
References

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Fig. 3. Bronchoscopic findings showing: (a) medium-sized partially obstructing fungating infiltrative lesion in the right middle lobe; (b) two non-obstructing polypoid lesions in the left lower lobe.

Fig. 4. (a) Histological evaluation with hematoxylin and eosin stain showing spindle and epithelioid tumor cells in myxohyaline stroma with necrosis and tumor cells with pleomorphic hyperchromatic nuclei and prominent nucleoli. Immunohistochemical analysis was positive for: (b) cytokeratin AE1/AE3; (c) CD31; (d) ETS-related gene (ERG).