

A 58-year-old Woman with Dry Cough and Pulmonary Nodules

Dear Editor,

Pulmonary epithelioid haemangioendothelioma is a rare vascular neoplasm of endothelial origin. We describe a case which involved solely the lungs and a novel therapeutic strategy using pegylated liposomal doxorubicin was attempted.

Case report

A 58-year-old food-handler and life-long non-smoker presented with dry cough and exertional dyspnoea for 2 weeks duration. She had no haemoptysis, chest pain, fever, weight loss or other constitutional symptoms. Her only significant past medical history was hysterectomy with bilateral salpingoopherectomy for cervical intraepithelial neoplasia (CIN) III and endocervical adenocarcinoma-in-situ 6 years ago. Physical examination was normal.

Complete blood count, renal, hepatic panels and calcium level were all within normal ranges. Electrocardiogram and N-terminal pro brain natriuretic peptide were normal. Sputum for acid fast bacillus was negative. Her chest radiograph (CXR) and computed tomography (CT) of thorax are shown in Figure 1.

CXR showed bilateral diffuse nodular opacities (3 mm to 5 mm) and a small right pleural effusion (Fig. 1a). CT of thorax showed innumerable pulmonary nodules which appeared randomly distributed throughout both lungs (Figs. 1b and 1c). They were adjacent to bronchovascular bundles (yellow arrow 1b) and perivenular nodules (yellow arrow in Fig. 1c). They demonstrated an irregular outline and mostly measured at least 5 mm in diameter with no evidence of cavitation. Irregular thickening of bronchovascular bundles and small pleural effusions were noted bilaterally (Fig. 1d). No ground-glass change or consolidation was seen.

Bronchoscopy, bronchoalveolar lavage and transbronchial lung biopsy (TBLB) from the left lower lobe were performed. Initial hematoxylin and eosin (H&E) sections of the TBLB showed only tiny abnormal nodules of epithelioid cells in the parenchyma. Deeper sections revealed larger tumour nodules comprising epithelioid tumour cells with small nuclei/ tiny nucleoli and a small amount of eosinophilic cytoplasm; no mitotic activity was observed. They were surrounded by strands of hyaline connective tissue as highlighted by the periodic acid-Schiff diastase (PAS-D) stain. The cells did not contain mucin vacuoles. Positive immunohistochemical stains were vimentin, CD31, CD34

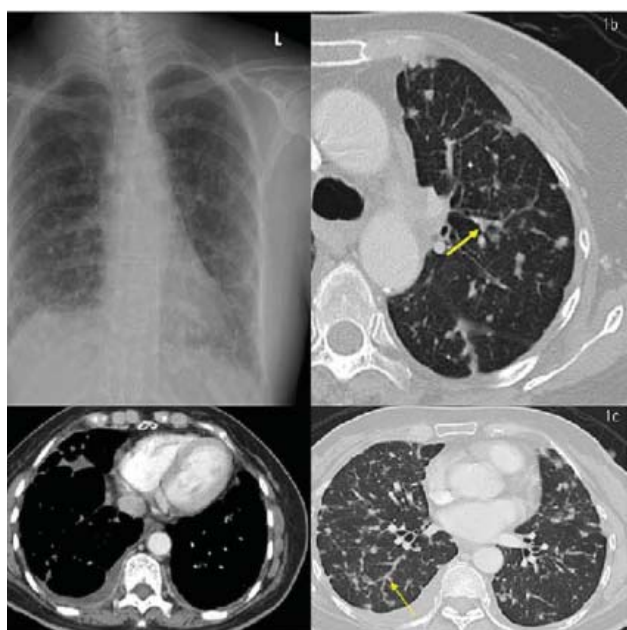


Fig. 1. Chest radiograph and computed tomography of a 58-year-old woman with dry cough and exertional dyspnoea for 2 weeks.

and Factor VIII (Von Willebrand Factor) confirming the endothelial origin of these tumour cells. The proliferation marker MIB-1 showed a low proliferative rate. Based on the biopsy and immunohistochemistry findings mentioned above, the diagnosis of pulmonary epithelioid haemangioendothelioma (PEH) was made.¹

Our patient was started on pegylated liposomal doxorubicin. She received 2 cycles of treatment and experienced clinical progression with worsening of her pleural effusion. She was then switched to sunitinib. However, she did not respond and passed away 4 months later.

Discussion

Our initial differential diagnoses based on clinical and radiological presentation were narrowed down to metastatic cancer, mycobacterial infection, sarcoidosis and less commonly diffuse pulmonary lymphangiomatosis.

Mycobacterial infection was considered but unlikely as there was no fever or other constitutional symptoms, transbronchial lung biopsy did not reveal any granulomatous inflammation and mycobacterial cultures were negative from sputum and bronchoalveolar lavage. Sarcoidosis was also deemed unlikely due to lack of hilar/mediastinal lymph node enlargement, presence of effusion (which is rare in sarcoidosis) and distribution of lung nodules (which is usually upper lobe in sarcoidosis). Diffuse pulmonary lymphangiomatosis was not considered based on age (as it is usually reported in children) and lack of lymphatic distribution of pulmonary lesions and mediastinal soft tissue infiltration.

Transbronchial lung biopsy clinched the diagnosis of pulmonary epithelioid haemangioendothelioma (PEH). It is a rare vascular neoplasm of endothelial origin with clinical behaviour intermediate between haemangioma and angiosarcoma.² It is 4 times more common in women, usually presenting between 12 and 60 years,³ as in our patient. From an internet registry,² 28% of patients were asymptomatic at presentation, and 74% of the symptomatic patients presented with chest pain. Other common symptoms are cough, haemoptysis, dyspnoea and weight loss.^{3,4} Although epithelioid haemangioendothelioma commonly involved other organs, such as liver and bone, it was not the case in our patient (Abdomen and pelvis CT did not reveal any mass, lymph node enlargement, peritoneal thickening or masses). Most cases require open lung biopsy for diagnosis but TBLB alone can diagnose PEH as supported by a previous paper.³

Adverse prognostic factors reported are male gender, age >55 years, pleural effusion or ascites,² respiratory symptoms at presentation, extensive lymphangitic spread, pleural

invasion, hepatic metastases, peripheral lymphadenopathy, fibrous pleuritis with extrapleural proliferation of tumour cells and spindle tumour cells at histology.⁴

Anthracyclines and/or ifosfamide are generally recommended in the first line treatment of patients with advanced soft tissue sarcomas (STS). Although doxorubicin is the most commonly used anthracycline in STS, treatment with this agent may be toxic at doses typically used in STS management. Hence, our patient was started on pegylated liposomal doxorubicin.⁵ She received 2 cycles of treatment and experienced clinical progression with worsening of her pleural effusion. She was then switched to sunitinib. However, she did not respond and passed away 4 months later.

In summary, this was a case of pulmonary epithelioid haemangioendothelioma that was solely diagnosed with transbronchial lung biopsy. The patient had several adverse prognostic factors and a novel therapeutic strategy was attempted but did not succeed in reversing the prognosis.

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