CASE REPORT

Lung lobar collapse as the first manifestation of pulmonary epithelioid haemangioendothelioma diagnosed with fiberoptic bronchoscopy

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Accepted 7 October 2016

SUMMARY

Pulmonary epithelioid haemangioendothelioma (PEH) is a rare tumour of endothelial origin that usually occurs in the lung and liver. It usually presents as bilateral multiple nodular lesions. We report a middle-aged woman with a unique presentation of PEH with lung lobar collapse. The diagnosis was made with fiberoptic bronchoscopy rather than video-assisted thoracoscopy. Clinicians and pathologists should be aware of rare conditions that can present as lung lobar collapse.

BACKGROUND

Pulmonary epithelioid haemangioendothelioma (PEH) is a rare vascular neoplasm that arises in a variety of sites, not only the lung but also the liver, soft tissue, bone and pleura.¹ PEH of the lung classically presents as bilateral multiple pulmonary nodules, although unusual presentation has been described in patients with solitary pulmonary lesions. Lung collapse due to bronchial obstruction is an extraordinarily rare presentation.² The diagnosis usually requires histopathological identification of neoplastic cells with immunostaining positive for CD31.³ A biopsy is always taken by video-assisted thoracoscopy, except a few reported cases that had biopsies taken by fiberoptic bronchoscopy.^{4 5} Treatment depends on the number and site of the nodules, with surgery preferred for solitary unilateral nodules and chemotherapy for multiple bilateral lesions.^{1 6 7} Patients have a variable life expectancy ranging from 1 to 15 years.⁸

In this case, a Caucasian woman presented with left lower lobe lung collapse due to external compression of the left lower lobe bronchus by the tumour, which is an extremely uncommon presentation of PEH of the lung. The diagnosis was made by a biopsy taken through bronchoscopy, whereas the definitive diagnosis in the literature was usually confirmed by a biopsy taken through video-assisted thoracoscopy.⁵

She denied shortness of breath, wheezing, sputum production, fever, chills or sweating, weight loss and haemoptysis. Her past medical, surgical and family history were unremarkable. She was not taking any medicines and did not report any allergies. She reported that she has never smoked or used any illicit drugs but drinks alcohol occasionally. There was no recent travel.

On physical examination, she was not in acute distress. She was slightly tachycardiac, but the rest of her vitals were within normal levels. The trachea was central. There was no tenderness on palpitation or dullness on percussion, but she had decreased breath sounds in the left lower lung with no crackles. There were no enlarged lymph nodes.

Her chest X-ray showed atelectatic changes in the left lower lobe (figure 1). A CT scan of the chest with contrast ruled out pulmonary embolism but showed left lower lobe medial collapse of the lung with calcification (figures 2 and 3).

The patient was admitted to the hospital for bronchoscopy, which showed 75% stenosis of the left lower lobe bronchus due to extrinsic compression. There were no endobronchial lesions or masses. The superior segment of the lower lobe was completely collapsed, and the basilar segment was 95% stenosed. Bronchial washing, brushing and endobronchial biopsies were obtained and sent for the histopathological examination.

Sections of the bronchial biopsy showed expansions of peribronchial interstitium by a population of relatively bland epithelioid cells arranged individually and in small nests within a pale-staining

Figure 1 Anteroposterior chest X-ray showing left lower lobe atelectasis.

To cite: Abdalla A, Seedahmed E, Bachuwa G, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-216411

CASE PRESENTATION

A Caucasian woman aged 42 years non-smoker with no significant medical history presented with 6 months history of chronic non-productive cough. She received two courses of antibiotics with no improvement. A bronchodilator inhaler and steroids failed to relieve her symptoms. Two months later, she started reporting of left-sided back pain as well as left shoulder pain for which she went to physical therapy. The patient still had a dry cough.

Figure 2 CT of the chest coronal view showing atelectasis of the superior and basilar of the left lower lobe.

basophilic myxoid stroma. On closer inspection, individual cells showed variably abundant pale-staining eosinophilic cytoplasm with occasional coarse cytoplasmic vacuoles. Occasional cells demonstrated intranuclear cytoplasmic pseudoinclusion (figures 4 and 5). These findings raised two main possibilities, including not only epithelioid haemangioendothelioma but also adenocarcinoma. For that reason, immunostains were used and were strongly positive for CD31, with negative staining for pan-cytokeratin (figure 6).

INVESTIGATIONS

An MRI of the brain was normal. The PET/CT showed subtotal left lower lobe collapse with extensive left pleural involvement. There were no enlarged lymph nodes or evidence of distant metastasis.

Figure 3 CT of the chest axial view showing collapse of the superior segment of the left lung.

Figure 4 Expansion of peribronchiolar interstitium by a population of relatively bland epithelioid cells arranged individually and in small nests within a pale staining basophilic myxoid stroma (H&E, original magnification $\times 100$).

TREATMENT

The patient was referred to a tertiary centre for a second opinion and possible surgical resection. But because of PET scan's extensive pleural involvement, which indicate worse prognosis, systemic treatment rather than surgery was considered. The patient was started on bevacizumab and palliative radiotherapy. Her pain was treated appropriately with narcotics.

OUTCOME AND FOLLOW-UP

Shortly after starting bevacizumab and palliative radiotherapy, she developed a large, loculated pleural effusion in the left thoracic cavity, causing a complete collapse of the left lung and mediastinal shift to the right side. She had chest tube placement. The pleural fluid showed malignant cells. Then, she underwent video-assisted thoracoscopy with multiple pleura and chest wall biopsies, which were positive for PEH.

Her course was complicated with vancomycin-resistant enterococci urinary tract infection and healthcare-associated pneumonia, and she was hospitalised for a few days. Her chest tube continued to drain.

She continued to follow-up with her oncologist for pain control and chemotherapy. But due to lack of response to the

Figure 5 Individual cells show variably abundant pale staining eosinophilic cytoplasm with occasional coarse cytoplasmic vacuoles (H&E, original magnification $\times 400$).

Figure 6 Positive staining by CD31 immunohistochemical stain (original magnification $\times 400$).

therapy, she was referred to home hospice after 8 months from initial diagnosis. She died at home 3 weeks later.

DISCUSSION

Epithelioid haemangioendothelioma was first reported by Dail and Leibow in 1975 and was named intravascular bronchioalveolar tumour. It was regarded as an invasive type of bronchioalveolar cancer invading the blood vessels.^{9–11} It was then correctly named PEH in 1982 after Enzinger and Weiss discovered its nature is angiogenic rather than bronchogenic.^{11–13}

According to a December 2008 literature review of 221 reported cases, the median age at the time of diagnosis is 41 years, and 66% are females.¹⁴ Recently, there was an increase in the prevalence of PEH, likely due to improvement in diagnostic competencies.¹⁵

Most cases are discovered incidentally on chest imaging in asymptomatic patients or those with minor symptoms.¹⁶ The usual radiological findings in chest CT are bilateral nodular shadows about 2 cm in diameter.¹⁷

PET/CT can be used as a prognostic tool. Despite the fact that data are limited, high metabolic activity determined by larger FDG intake by the tumour corresponds to the malignant activity of PEH, which has worse prognosis.⁸

Gross pathology, PEH presents as single or multiple lung nodules ranging from millimetres up to a few centimetres and rarely with calcification. They are described in the literature as having a rubbery or cartilage-like consistency and a grey–white to the yellow–brown cut surface.^{17 18} Endobronchial nodules have been reported in few cases.⁵

Histopathology, PEH has a hypocellular sclerotic core and hypercellular peripheral zone. The cytoplasm is abundant and eosinophilic. Intracellular vacuoles are common, sometimes showing a signet-ring appearance.^{6 13} A recent case report described a young man with endobronchial mass as well as multiple lung nodules and lytic lesions in the ninth rib. The biopsy, which was taken through fiberoptic bronchoscopy, revealed a histopathological feature of osteoclast-like giant cells in PEH.¹⁹

Histoimmunostaining usually lead to the definitive diagnosis.^{17 20} CD31 has been used to confirm the diagnosis of vascular tumours, as it is found in neoplasms developed from endothelial cells.^{3 14} Biopsies are usually obtained through thoracoscopy. However, about 2% of the cases reported were diagnosed with bronchoscopy biopsies.^{1 5}

There is no standard treatment for PEH. Some asymptomatic patients with diffuse lesions have conservative therapy with regular surveillance without active treatment.¹³ Surgical resection is advised when the lesions are small and limited in number.^{1 6} For metastatic disease including pleural involvement, various chemotherapeutic agents have been used, and results are variable. Thus, there is no clear recommendation for standard chemotherapy.^{7 20} Radiotherapy is ineffective but has been used for symptomatic palliative treatment.^{18 20} Stabilisation of PEH has been observed in cases managed with interferon 2- α .²¹ Antiangiogenic therapy against vascular endothelium growth factor might be a promising treatment option for PEH.^{20 21}

Prognosis is uncertain because of the small number of cases reported. As shown by a review of the literature that was performed in 2006 and included 80 patients of PEH, there is a 5-year survival rate of 60% (range 47–71%).¹ Cases with long-term survival spanning at least 10 years have been reported only rarely.¹³ A small retrospective study was performed in 2016 in South Korea trying to identify prognostic factors of epithelioid haemangioendothelioma with and without thoracic involvement. The study included 42 total patients and 19 of them were with thoracic involvement. Age above 55 was the only significant prognostic factor.²²

The most common cause of death is respiratory failure resulting from the growing and multiplying tumour nodules. Weight loss, anaemia, pulmonary symptoms and haemorrhagic pleural effusion have been found to increase the likelihood of a poor prognosis.^{1 13}

To the best of our knowledge, only two other cases have been reported of PEH presenting with lung lobe collapse. Shang and Wang's 2009 report describes a woman aged 40 years who had a left hilar mass and partial atelectasis in the apical segment of the left lower lobe on a CT scan of the chest. One month after undergoing whole lung resection, she died of respiratory failure.² Another case was reported in Malaysia 2016, a man aged 59 years found to have a heterogenous enhancing mass within a collapsed right upper lung lobe. CT-guided biopsy of the mass diagnosed PEH.¹⁵

In conclusion, we are reporting a patient with PEH presenting as lobar lung collapse. The patient was diagnosed with fiberoptic bronchoscopy rather than video-assisted thoracoscopy.

Learning points

- ▶ Clinicians and pathologists should be aware of rare conditions that can present with lung lobe collapse.
- ▶ Immunostaining of biopsy specimens should be performed to rule out pulmonary epithelioid haemangioendothelioma (PEH) in suspected cases.
- ▶ Surgical biopsies through video-assisted thoracoscopy is usually the diagnostic tool for the common PEH presentation with multiple bilateral nodules. In few cases presenting with lung collapse or endobronchial nodules, a less invasive fiberoptic bronchoscopy can be used for diagnosis.

Acknowledgements The authors thank Dr Jeffrey L Myers MD, Department of Pathology, the University of Michigan, for his valuable help with the histological findings.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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