Ambiguous presentations of pulmonary epithelioid hemangioendothelioma: Two case reports of a rare pulmonary malignancy

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Abstract
Pulmonary epithelioid hemangioendothelioma is an uncommon lung malignancy of endothelial origin. Besides demonstrating unpredictable presentation features and prognosis, the paucity of established treatment guidelines remains a challenge in managing these patients. We present two patients. The first patient presented with chronic productive cough over 1-year duration. He was initially diagnosed and showed partial response to treatment for cardiac failure. A persistent right upper zone consolidation on chest radiograph prompted further investigations which revealed the diagnosis of pulmonary epithelioid hemangioendothelioma. The second patient presented with right-sided hemiparesis for 1-month duration. Initial computer tomography scan of the brain showed findings of distant metastatic foci. Subsequent investigations revealed pulmonary epithelioid hemangioendothelioma as the primary lesion. Both patients succumbed without any treatment due to rapid progression of the disease. We believe that pulmonary epithelioid hemangioendothelioma is undoubtedly rarely reported in south-east Asia region. In these two case reports, the patients were diagnosed in west and east Malaysia, respectively, in the same year (2015). Both cases highlight the increasing prevalence of pulmonary epithelioid hemangioendothelioma. We postulate that this could possibly be secondary to the advancement in diagnostic capabilities and improved healthcare facilities available in this region. Late presentation of pulmonary epithelioid hemangioendothelioma generally results in grave prognosis. Further investigations are required to elucidate the nature of progression and therapeutic options for patients with pulmonary epithelioid hemangioendothelioma.

Keywords
Pulmonary epithelioid hemangioendothelioma, lung cancer

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Introduction
Pulmonary epithelioid hemangioendothelioma (PEH) is a rare lung tumour of endothelial origin. It was described previously as an intravascular bronchoalveolar tumour. A literature review found only handful of case reports published worldwide that generally described unpredictable presentations and unestablished standardized treatment options. We present two case reports on this unusual disease. The first case was diagnosed in west Malaysia and the latter was diagnosed in east Malaysia; both managed in the same year (2015). We believe that these are the first two case reports on PEH to be reported in this region.

Case 1
A 59-year-old man with a 30-pack-year smoking history presented with a complaint of progressive breathlessness and productive cough over 1-year duration. On evaluation, he had signs and symptoms of cardiac failure. Hence, he was treated for decompensated cardiac failure. Echocardiography
showed isolated dilatation of the left atrium (LA diameter 4.3 cm) and left ventricle (LV end diastolic diameter 5.5 cm), respectively, preserved ejection fraction of 51% with normal valve morphology. The patient responded to diuretic therapy, oxygenation support and intravenous antibiotics.

On review of his chest radiograph (Figure 1(a)), an area of suspicious homogeneous opacity over the right upper zone lead to a computed tomography (CT) scan of the thorax which showed a heterogeneous enhancing mass within a collapsed right upper lobe and multiple mediastinal and axillary lymphadenopathy. Bronchoscopy showed an endobronchial mass occluding the right upper lobe bronchus with abnormal vascularity of the surrounding mucosa. Histopathological results of the CT-guided biopsy showed fragments of endobronchial tissue with underlying stroma harbouring tumour cells forming small intracellular lumen and vascular spaces lined by atypical endothelial cells. The neoplastic cells were positive for immunohistochemical staining for endothelial markers CD31 and CD34 (Figure 1(b)) and factor VIII, consistent with PEH.

Surgical resection (depending on disease severity) or chemotherapy were among options explored. Unfortunately, upon his readmission 2 weeks later, the patient succumbed to respiratory failure.

**Case 2**

A 67-year-old man (non-smoker) was referred for progressive right-sided body weakness over 1-month duration. He had no other symptoms and no previously known medical illness. On presentation, he had right-sided hemiplegia with power of 3/5 for involving all muscle groups. Cranial nerves were normal. His baseline blood results (blood counts, coagulation, renal and liver profile) were all unremarkable. A contrasted CT scan of the brain showed multiple hyperdense lesions at the right internal capsule and bilateral occipital region associated with marked peri-lesional oedema and midline shift. These findings were suggestive of distant metastatic foci. Subsequent chest radiograph and a full-body CT revealed a homogeneous mass with spiculated margins situated at the anterior segment of the right upper lobe (Figure 2(a)).

Histopathological examination of the biopsy samples obtained via CT-guided biopsy showed presence of atypical epithelioid-like tumour cells (Figure 2(b)). Immunohistochemical studies were positive for CD31, CD34 and factor VIII. These results were consistent with the diagnosis of PEH. However, the patient opted for traditional treatment and defaulted a scheduled oncology visit. He succumbed to his condition 1 month later.

**Discussion**

PEH is a multicentric tumour that originates from endothelial cells. The prevalence of PEH is less than one in 1 million. The mean age of onset of PEH is reported 40.1 ± 17.5 years and majority are females (73%). We believe that apart from the investigation studies reported by Kitachi et al., there are no further reported cases of PEH from this region.

Interestingly, both of our patients were male and they were diagnosed in the same year.

PEH has a low grade to intermediate malignant potential with variable clinical course. PEH predominantly involves the lungs, liver and soft tissues. Majority of patients present with non-specific symptoms such as weight loss, dyspnoea and dry cough. Both our patients presented with symptoms suggestive of non-respiratory diagnosis. Radiologically, pulmonary nodules are a common finding; predominantly in the lower zones, involves small- and medium-sized vessels and bronchi. In our case reports, both patients had pulmonary masses in the upper lobes.

Histopathological samples are mainly obtained from open-lung or thoracoscopic biopsy. Diagnosis obtained via histopathological examination of transbronchial biopsies is uncommon. Chest CT–guided lung biopsy was preferred due to possible increased risk of bleeding associated with vascular-like tumour, whereas the second patient had a peripheral lesion. Diagnosis of PEH lies upon biopsy samples demonstrating atypical epithelioid cells, along with
immunoreactivity of the cytoplasm of tumour cells towards endothelial cell marker, factor VIII–related antigen and antibodies against CD31 and CD34.

Due to its rarity and borderline malignancy features, established data or consensus for therapeutic regimens are lacking. Previous reports have demonstrated patients undergone surgery resection by either wedge resection or lobectomy or partial resection with mixed results. Therefore, surgical resection may possibly benefit some patients with solitary or limited number of pulmonary lesions. Meanwhile, some patients also had received antineoplastic chemotherapy without beneficial effects albeit Pinet et al. demonstrated good partial response with chemotherapy using carboplatin, paclitaxel, bevacizumab, thalidomide or α-interferon. Pazopanib, a second-generation tyrosine kinase inhibitor has demonstrated positive outcome in small number of reported cases. Survival rate for PEH ranges from 6 months to 24 years with a mean survival recorded at 4.6 years. Poor clinical prognostic factors mentioned include symptoms of vascular aggressiveness including haemorrhagic pleural effusion and haemoptysis, anaemia, loss of weight and respiratory symptoms such as dyspnoea, cough and chest pain as a sequelae. Presence of fibrinofibrous pleuritis and spindle tumour cells on histology examination signifies poor outcome. In retrospective, both patients had features consistent with unfavourable outcome which lead to rapid progression of disease and death.

Conclusion

Both cases highlight the increasing prevalence of PEH. We postulate that this could possibly be secondary to the advancement in diagnostic capabilities and improved healthcare facilities available in this region. Further investigations are required to elucidate the nature progression and therapeutic options for patients with PEH.

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References

1. Lau K, Massad M, Pollak C, et al. Clinical patterns and outcome in epithelioid hemangioendothelioma with or without pulmonary involvement: insights from an internet registry in the study of a rare cancer. Chest 2011; 140(5): 1312–1318.
2. Amin R, Hiroshima K, Kokubo T, et al. Risk factors and independent predictors of survival in patients with pulmonary epithelioid haemangioendothelioma. Review of the literature and a case report. Respirology 2006; 11(6): 818–825.
3. Kitaichi M, Nagai S, Nishimura K, et al. Pulmonary epithelioid haemangioendothelioma in 21 patients, including three with partial spontaneous regression. Eur Respir J 1998; 12(1): 89–96.
4. Dail DH, Liebow AA, Gmelich JT, et al. Intravascular, bronchiolar, and alveolar tumor of the lung (IVBAT). An analysis of twenty cases of a peculiar sclerosing endothelial tumor. Cancer 1983; 51(3): 452–464.
5. Cronin P and Arenberg D. Pulmonary epithelioid hemangiendothelioma: an unusual case and a review of the literature. Chest 2004; 125(2): 789–793.
6. Sardaro A, Bardoscia L, Petrizzelli MF, et al. Epithelioid hemangiendothelioma: an overview and update on a rare vascular tumor. Oncol Rev 2014; 8(2): 259.
7. Shang A and Wang X. Pulmonary epithelioid haemangiendothelioma mimicking central lung cancer. Respirology 2009; 14: 452–455.
8. Pinet C, Magnan A, Garbe L, et al. Aggressive form of pleural epithelioid haemangioendothelioma: complete response after chemotherapy. Eur Respir J 1999; 14(1): 237–238.
9. Semenisty V, Naroditsky I, Keidar Z, et al. Pazopanib for metastatic pulmonary epithelioid hemangioendothelioma – a suitable treatment option: case report and review of anti-angiogenic treatment options. BMC Cancer 2015; 15(1): 402.
10. Bagan P, Hassan M, Barthes FLP, et al. Prognostic factors and surgical indications of pulmonary epithelioid hemangiendothelioma: a review of the literature. Ann Thorac Surg 2006; 82(6): 2010–2013.