Alveolar haemorrhage revealing epitheloid haemangioendothelioma

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Introduction

First reported in 1975 by Hall and Liebow (1) as a bronchoalveolar intravascular tumour, epithelioid haemangioendothelioma (EH) is a rare pulmonary vascular malignancy. Most cases have been described as pulmonary nodular syndromes of minimal clinical expression and slow course in young women. The present authors observed an unusual EH case in a man with inaugural alveolar haemorrhage which rapidly led to a fatal outcome.

Case Report

A 72-year-old man was admitted with a 1-month history of recurrent haemoptysis. His past medical history was remarkable for chronic alcohol abuse and 40 pack-year cigarette smoking. In 1981, he had undergone surgery for atheromatous stenosis of the left renal artery and he was currently taking fluindione. In addition, he had major pleural sequelae resulting from untreated tuberculosis in childhood.

On admission, the patient was in good general health. He was pale but without haemodynamic shock. His temperature was 38°C and his respiratory rate was 24 breaths min⁻¹. Physical examination revealed a left pleural effusion and bilateral diffuse crackles. The liver was enlarged without clinical evidence of liver failure or portal hypertension.

Laboratory data included serum chemistry, liver function tests and urinalysis, all of which were normal except for a haemoglobin of 9 g dl⁻¹ and an increase in the erythrocyte sedimentation rate (77 mm h⁻¹), C reactive protein (15 mg dl⁻¹) and serum lactate dehydrogenase (3000 UI⁻¹). Prothrombin time was 25% with normal factor V.

Chest X-ray film showed major right pleural calcification, bilateral diffuse ground glass pattern and a nodular opacity of the left upper lobe (Plate 1). Chest computed tomography demonstrated multiple bilateral nodules (1–4 cm in diameter), especially in the subpleural areas, a left pleural effusion and few mediastinal lymph nodes (Plate 2).

Left thoracocentesis yielded 250 ml of sterile serohaemorrhagic fluid. Bronchoscopic examination only revealed blood oozing from all bronchopulmonary segments. No biopsy was attempted due to the patient’s coagulation status. Cytological studies of the bronchoalveolar lavage showed haemosiderin-laden macrophages (Golde score >100) without tumour cells. Search for a microbial agent in
PLATE 1. Chest radiograph demonstrating right pleural calcification, diffuse ground glass haziness and left nodular opacity.

PLATE 2. Chest computed tomographic scan showing diffuse alveolar opacities and bilateral pulmonary nodules.

PLATE 3. Diffuse intra-alveolar haemorrhage with vascular proliferation surrounding a pulmonary vessel (Haematcin Eosin Safran stain, final magnification × 175).

Large spectrum antibiotics were administered with high-dose corticosteroids (1 mg kg⁻¹ prednisone) and three-drug anti-tuberculosis therapy. Daily haemoptysis persisted and the patient died from acute respiratory failure 3 weeks after admission.

Autopsy was performed 12 h after death. When the chest was opened, multiple pleural and diaphragmatic adhesions and a voluminous right pleural calcification were observed. The lungs were haemorrhagic and dense without evidence of nodules. Some mediastinal lymph nodes were seen. Abdominal examination only revealed an hypertrophic liver with micronodular cirrhosis, confirmed histologically without tumour.

Histology of the lungs showed numerous vascular neoplastic growths arising from the major vessels, especially from the veins of the septa and involving visceral pleura and vascular walls (Plate 3). The vascular channels were small and recapitulated the appearance of vessels during early angiogenesis. Some neoplastic vascular lumens were lined by spindled cells with irregular and reniform nuclei, prominent nucleolus and eosinophilic cytoplasm (Plate 4). Erythrocytes were frequently observed in these lumens. In some areas, tumoural vascular channels were larger and filled with globular cells of high mitotic index and atypical mitotic figures. One of the regional lymph nodes showed the same tumoural infiltration. Tumour cells were positive for vimentin, factor VIII and CD34. Immuno- stainings were negative for cytokeratin and epithelial membrane antigen.
Discussion

Epithelioid haemangioendothelioma is a very rare pulmonary neoplasm deriving from multipotential endothelial reserve cells (2,3). About three-quarters of cases occur in women with a mean age of 40 years (range 7-76 years) (4,5). This predominance of young female cases might be explained by hormonal factors involved in the abnormal endothelial proliferation. Nevertheless, Ohori et al. (6) could not confirm this hypothesis since they only found one to five cases of EH with oestrogen but no progesterone cell receptors.

Symptomatology is usually sparse and non-specific, including progressively worsening dyspnoea, persistent cough and weight loss (4,5). Physical examination is otherwise normal, although finger clubbing or peripheral adenopathies have been observed (4). In half the reported cases, the tumour is discovered on a routine chest X-ray with widespread bilateral pulmonary nodules. Pleural effusion or enlarged mediastinal lymph nodes have rarely been observed (2,4,5).

The present patient's clinical manifestation was especially unusual. Haemoptysis is exceptional in the clinical course of EH. One patient reported in the literature had a mild haemoptysis which subsided after surgical excision (5). In two other patients, as in the present case, alveolar haemorrhage was the inaugural event (7,8). Both were men with mild recurrent haemoptysis leading to anaemia. Roentgenographic features showed a diffuse ground glass haziness, bilateral alveolar densities and multiple pulmonary nodules. In both cases, as in the present case, the clinical outcome led to death with acute respiratory failure within a few weeks.

Positive diagnosis is based on the analysis of an open lung biopsy. Epithelioid haemangioendothelioma is generally suggested on the basis of light microscopy evidence. In more atypical cases, diagnosis can be confirmed after positive search for specific antibodies directed against endothelium (factor VIII, CD34-related antigen) and mesenchyme (vimetin antigen) (3,9).

The clinical course deteriorates slowly and patients die from restrictive respiratory insufficiency with extensive lung infiltration (4). Regional lymphogenous spread, as reported in the present case, is rare and seems to be a poor prognostic feature (10). The histological features which appear to be useful in predicting metastatic potential include a high mitotic index and numerous atypical cells (11). In about 20% of cases, liver metastasis can occur (4). Some cases of more aggressive tumours with multiple systemic spread have been described (12,13).

Treatment is based on complete surgical resection. No complementary chemotherapy or radiotherapy seems to be effective.

Conclusion

Epithelioid haemangioendothelioma should be considered in the differential diagnosis of alveolar haemorrhage syndrome. Short-term prognosis of the aggressive form with high mitotic index and cellular atypia is poor.

References

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