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Case report

Pleural epithelioid hemangioendothelioma mimicking pleural empyema: A case report

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ABSTRACT

Malignant pleural effusion is an important and difficult differential diagnosis to pleural empyema. Epithelioid hemangioendothelioma is an uncommon vascular tumor, which typically occurs in liver, lung or bone. We present an extremely rare case of primary pleural epithelioid hemangioendothelioma mimicking pleural empyema. We conclude, that pleural epithelioid hemangioendothelioma should be kept in mind as a differential diagnosis in patients suspected of empyema.

1. Introduction

Pleural empyema is an frequent clinical condition with an annual incidence of 10–12 per 100,000 inhabitants(1). The mortality is approximately 10% [1]. Malignant pleural effusion (MPE) has an incidence of ~70 per 100,000 [1] mostly due to pleural dissemination from extrapleural malignancy, and can present as pleural empyema due to early translocation of bacteria via the damaged pleural lining.

We describe a case of primary pleural malignancy presenting as pleural empyema.

2. Case report

A 71-year-old man, presented with dyspnea, cough and no effect of oral antibiotics. He was a current smoker with 80 pack-years, stable COPD and metabolic syndrome, and no known exposure to asbestos. Four years earlier, he had been diagnosed with a right-sided, hemorrhagic, exudative pleural effusion presumably caused by a thoracic trauma. The effusion was found to be culture negative and contained no malignant cells. Low-dose chest computed tomography (CT)-scan four weeks later showed complete remission of the pleural effusion.

At the current admission, chest x-ray showed moderate left sided pleural effusion and blood tests showed elevated leukocyte count ($14.7x10^9$/L) and C-reactive protein (CRP) level (170mg/L). The effusion was drained, revealing hemorrhagic pleural fluid. Pleural empyema was suspected, and the patient was treated with intravenous antibiotics followed by clinical improvement, but no effect on CRP level. Repeated pleural fluid analysis showed exudative effusion (pleural fluid LDH/plasma LDH-ratio > 0,60, normal leukocyte differential count, no malignant cells (analysed twice, 28mL and 40mL respectively) and no bacterial growth (cultured four times). Throat swab for *mycoplasma pneumonia*, *Chlamydophila pneumonia*, *Chlamydophila psittaci*, *Respiratory Syncytial virus*, *Influenza A* and *B* and *Covid-19* and investigations for *Legionella* and *pneumococcus antigen* in the urine were all negative. Chest ultrasound confirmed a septated left-sided pleural fluid. Treatment with intrapleural fibrinolytics was started via a 14 Fr drain.

Contrast enhanced CT showed left-sided pleural thickening without contrast-enhancement, moderate left-sided loculated pleural effusion, an enlarged 12mm mediastinal lymph node at station 8 and an osteolytic process in Th10 (shown in Fig. 1). Magnetic Resonance Imaging (MRI) of the spine revealed multiple lesions compatible with metastases without spinal cord affection. A Fluorine-18-labeled fluorodeoxyglucose (^{18}F-

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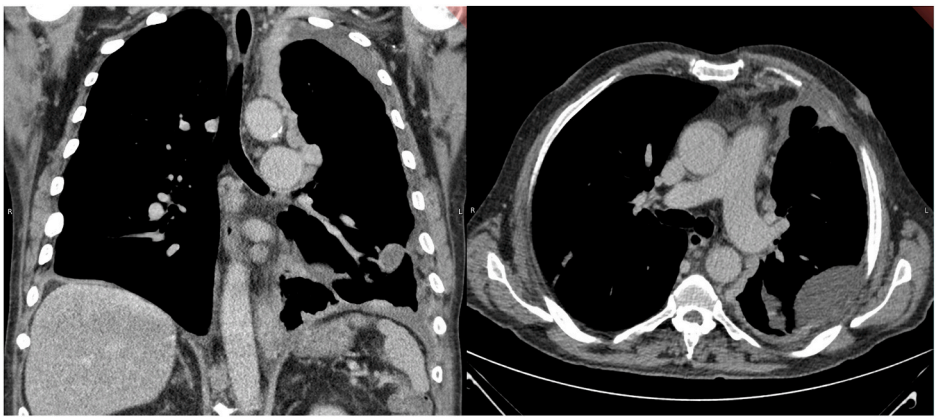

Fig. 1. Contrast enhanced chest CT showing left-sided pleural thickening without contrast-enhancement and left-sided pleural effusion in pockets.

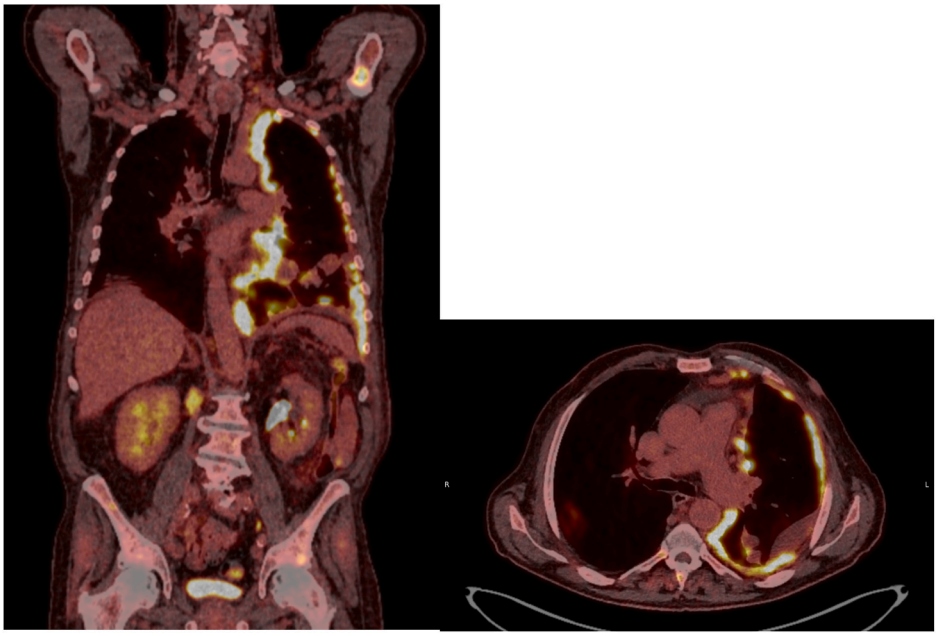

Fig. 2. PET-CT showing increased uptake in the left pleura, in multiple pathological lymph nodes over and under the diaphragm and in the skeleton.

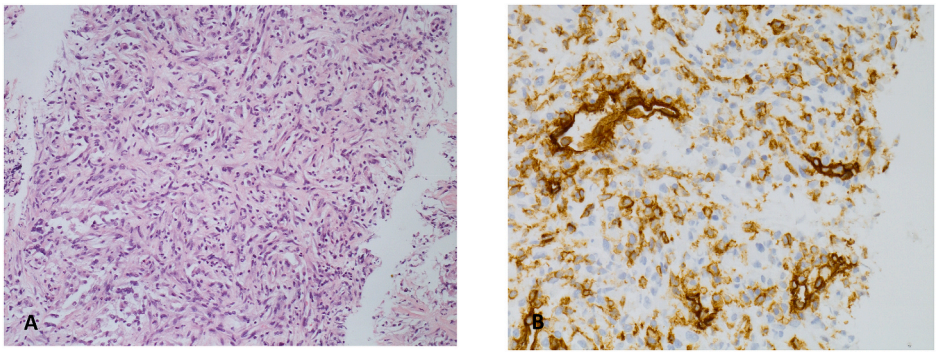

Fig. 3. Histopathologic findings showing epithelioid hemangioendothelioma. A: Hematoxylin and eosin stain showing malignant cells with intra-cytoplasmic vacuoles. B: Positive immunostaining for CD 31.

FDG)-positron emission tomography (PET)-CT showed increased FDG uptake in the left pleura, multiple metabolic active lymph nodes in the cervical and mediastinal region and under the diaphragm and increased FDG uptake in the skeleton (shown in Fig. 2). Disseminated malignant mesothelioma was suspected.

Ultrasound-guided closed pleural biopsy, 18G, from the PET-positive, left dorsal parietal pleura showed malignant cells, some with intra-cytoplasmic vacuoles, and immunohistochemistry positive reaction to CD31 and CD34, suggesting pleural epithelioid hemangioendothelioma (shown in Fig. 3). The patient was referred for oncological

treatment, but his clinical condition worsened rapidly, and he died before treatment could be started.

3. Discussion

Epithelioid hemangioendothelioma is a rare vascular tumor (estimated global prevalence is < 1:1,000,000 [2]), which typically arises in liver(21%), both liver and lung (14%), lung exclusively (12%) or bone exclusively (14%) [3,4], whereas pleural effusion only has been described in ~4% of the patients [5]. Histological characteristics include epithelioid cells with intra-cytoplasmic vacuoles and a prominent myxoid and hyalinised or condroid stroma (shown in Fig. 3) [6]. Immunohistochemistry is often positive for the endothelial markers CD31 (shown in Fig. 3) and CD34 [7]. Generally, epithelioid hemangioendothelioma is more prevalent in females (around 60% [5,8]) and in young adults, but can occur over abroad age range from 2 to 82 years [5,8]. The 5-year survival rate is 60–73% [5,9]. In contrast, pleural epithelioid hemangioendothelioma (PEH) is most frequently seen in elderly men [10], and is associated with a 5-year survival rate of 2% (median survival <1 year) [9]. Symptoms include chest pain, dyspnea, productive cough and fever, thus symptoms of pleural inflammation or infection [5,9,10]. Typical CT findings are small-moderate, unilateral pleural effusions and pleural thickening [10]. The diagnostic yield of pleural cytology has only been considered in two case reports involving three patients: one with negative cytology, one with atypical cells and one with undifferentiated malignancy [10,11]. We found no malignant cells in repeated cytological analysis of the pleural fluid. Treatment options of PEH are casuistically reported, and include pleural decortication, chemotherapy, immune therapy and best supportive care [10,12–14].

In our case story the episode of a contralateral pleural effusion four years earlier made us consider the possibility of a connection between the episodes, but we ended up concluding that they were independent of each other. Pleural effusions are not uncommon [15] and a contralateral PEH four years earlier is contradicted by the dismal prognosis of this disease and pleural malignancy in general [1,16].

4. Conclusion

PEH should be remembered as a differential diagnosis in patients with pleural thickening and signs of empyema.

Statement of ethics

Written informed consent was obtained from the patient.

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No funding has been received for the study.

Author contributions

All authors contributed to the manuscript writing and approved the submission of the final manuscript. KF stood for drafting. All authors undertook critical revision. Correspondence should be addressed to KF. All authors read and approved the final manuscript.

Declaration of competing interest

The Authors have no conflicts of interest to declare.

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