



An unusual thoracic localizations of Erdheim- Chester disease: A case report



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ABSTRACT

Erdheim- Chester disease is a rare non- Langerhans cell histiocytosis that usually involves the bones, heart, central nervous system, retroperitoneum, eyes, kidneys, skin and adrenals. Lungs are affected in up to one-half cases; at CT scan various patterns are described: interstitial disease, consolidations, micronodules and microcysts, with or without pleural involvement.

We presented a case of a 59 year-old man with unusual intrathoracic manifestation of Erdheim-Chester disease. Singularities of our report are the lonely thoracic involvement at the onset of the disease and a histiocytic lesion in the posterior mediastinum.

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1. Introduction

ECD is a rare syndrome, with around 650 cases described worldwide [1], characterized by xanthomatous or xanthogranulomatous infiltration of tissues by foamy histiocytes, "lipid-laden" macrophages, surrounded by fibrosis [2]. It affects organs like bones, skin, heart, lungs, central nervous system, retroperitoneum, kidneys and lymph nodes.

Lung involvement is described in up to one-half of cases and its clinical course depends on the extent and the distribution of the disease [3]. Pulmonary function tests could be normal or reveal a restrictive pattern with a reduction in DLCO and hypoxemia [3]. Characteristics HRCT features are smooth interlobular septal thickening, centrilobularmicronodules, ground glass opacities, parenchymal consolidations, microcystic lesions, with or without pleural effusion or pleural thickening [3,4]. However, it has to be mentioned that microcystic lesions could be found more frequently in LCH rather than non-LCH, and in the association of these two disorders, so called "mixed" histiocytosis [5].

We present a case of a patient with unusual intrathoracic lesions

from ECD.

2. Case report

A 59 year-old man presented to our observation with cough and dyspnoea. He was a former smoker (25 pack/years) and did not report previous toxic exposures.

A chest HRCT showed microcystic lesions, bilateral smooth interlobular and intralobular thickening with centrilobular and subpleuralmicronodules, (Fig. 1). Lung function tests pointed up a moderate reduction of total lung volume, vital capacity and residual volume, with severely reduced DLCO. Laboratory examinations were not diagnostic and BAL showed an increase of neutrophils and lymphocytes (macrophages 14%, lymphocytes 25%, neutrophils 60%, eosinophils 1%); the transbronchial lung forceps biopsy demonstrated the presence of fibrosis and intra-alveolar histiocytes. Immunohistochemistry utilizing S-100 and CD1a monoclonal antibodies did not reveal specific features. The pathologic features were considered not diagnostic. Unfortunately the patient refused further investigations but a cycle of therapy with prednisone led to a stabilization of disease.

Three years later, the patient showed up with increased cough, dyspnoea and hypoxemia at rest. The HRCT showed multiple bilateral pseudonodular consolidations, subpleural, perilobular and pleural thickening and microcystic lesions (Fig. 2), with no

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Abbreviations list

ECD	Erdheim- Chester Disease
HRCT	High Resolution Computer Tomography
DLCO	Diffusing Capacity of the Lung for Carbon Monoxide
LCH	Langerhans cell histiocytosis
BAL	Broncho Alveolar Lavage
BRAF	proto-oncogene B-Raf
CT	Computer Tomography
MRI	Magnetic Resonance Imaging
PEG-IFN α	α 2a-pegylated interferon- α
18 FDG- PET	18 Fluoro- Deoxy- Glucose Position Emission Tomography
SUV	Standardized Uptake Value
WT	Wild Type

response to steroid and antimicrobial therapy. A surgical lung biopsy demonstrated a diffuse infiltrated of histiocytes, located along the pleura and in the interlobular bundle, with no abnormalities, characterized by abundant clear cytoplasm, not foamy, and a vesiculous nucleus with a small nucleolus. There were not Touton cells, but only mononuclear histiocytes. The proliferation was associated with a fibrotic stroma and few lymphocytes. Immunohistochemical analyses were positive for CD68, S100 (focal) and negative for CD1a markers (Fig. 3). This picture was compatible with ECD. BRAF v600E mutation was not detected.

No abnormalities were seen in X-ray of long bones (femurs and chins), 99m Tc bone scintigraphy, abdomen CT scan and brain MRI.

Therapy with PEG-IFN α was started at the doses of 135 mcg weekly with a stabilization of the disease after 3 months. Six months later, a 18 FDG- PET- CT was carried out: a symmetric diaphyseal uptake in the long bones of the legs was noted along with a pathological uptake in the prevertebral space, beyond the already known pulmonary lesions (Fig. 4). A chest enhanced CT scan confirmed the presence of a vascularised prevertebral tissue in

the posterior mediastinum on the right (2.4 × 7 cm), displacing the oesophagus.

The needle aspiration biopsy of such lesion highlighted the presence of histiocytes.

Therapy with PEG-IFN α was then raised to 180 mcg weekly but despite this a progression in the number and in the PET activity of the pulmonary nodules was seen after 12 and 18 months, whilst the prevertebral lesion and the bone involvement remained unchanged.

3. Discussion

In our case the clinical, functional and radiological features are similar to other cases of lung involvement by ECD already described, but some peculiarities are present. Lung lesions were the only detectable abnormalities at the presentation of the disease: in only 4% of ECD cases bone lesions are absent and the diagnosis is based on the specific organ involvement [3]. Our case is peculiar because of the thoracic involvement (without any other sign of organ involvement) at the onset. Furthermore, the prevertebral lesion is an unusual mediastinal localization of ECD. Various mediastinal localizations have been previously described: the most common is a periaortic fibrotic infiltration [6], with a “coated” aspect of the aorta, but also a large mediastinal soft tissue that compressed the patient's left anterior descending coronary artery [7] and abnormal areas of PET positivity in the mediastinum and hila [8] were reported. The needle biopsy of the prevertebral lesion revealed the presence of histiocytes, suggesting the possible correlation with ECD. This lesion could be considered similar to the circumferential soft-tissue sheathing of the thoracic and abdominal aorta or to the retroperitoneal infiltration already reported. Indeed, around the 30% of ECD patients present with imaging features suggestive of retroperitoneal fibrosis, which is a fibrous reaction that takes place in the periaortic retroperitoneum and often entraps the ureters causing obstructive uropathy.

About therapeutic options, we decided to treat the patient with PEG-IFN α , because at that time it had the largest amount of evidences. However, in case of WT BRAF, currently other therapeutic options are available, like cladribine, anakinra and cobimetinib.

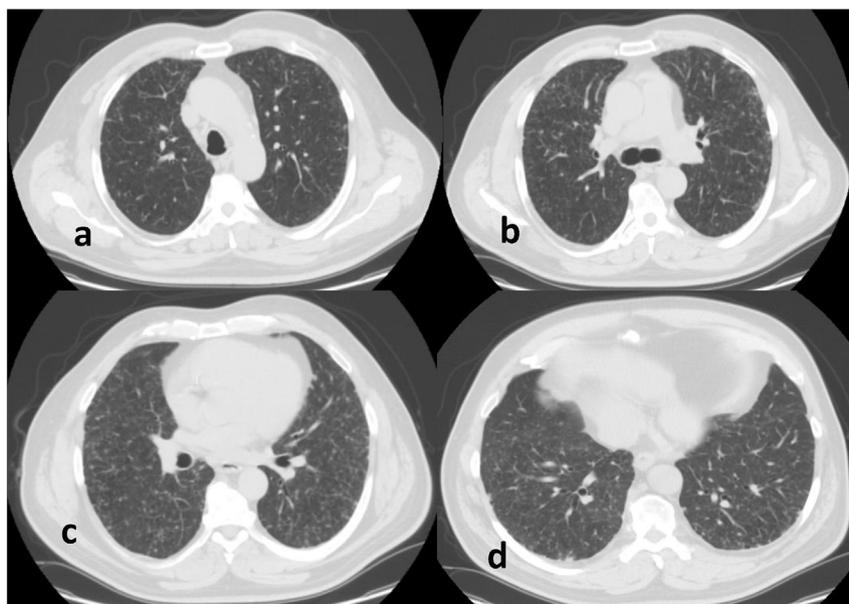


Fig. 1. a) microcystic lesions; b) c) and d) multiple smooth interlobular and intralobular thickening with centrilobular and subpleural micronodules.

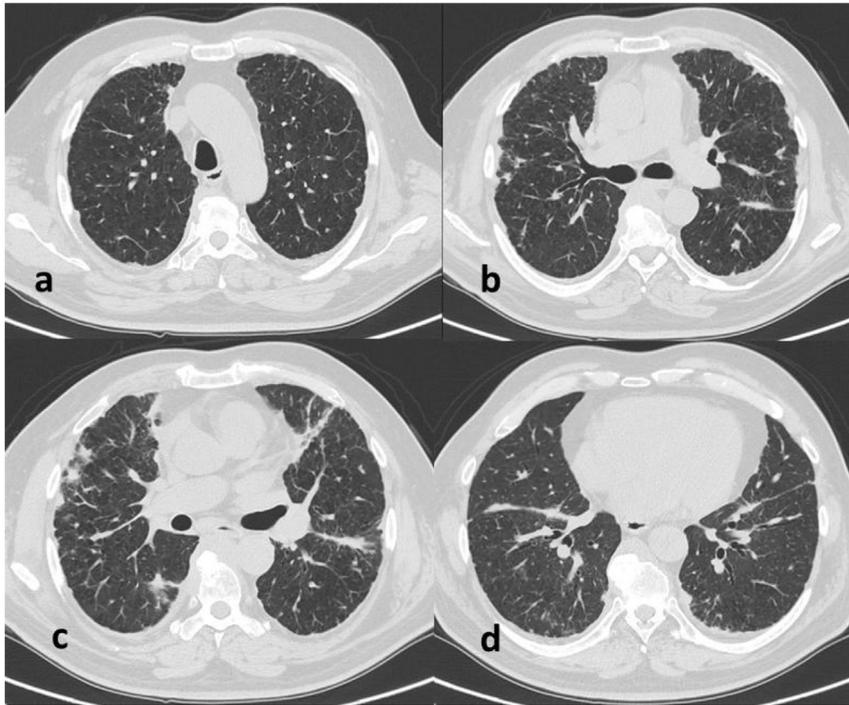


Fig. 2. a) microcystic lesions; b) and c) multiple pseudonodular consolidations; d) pleural thickening.

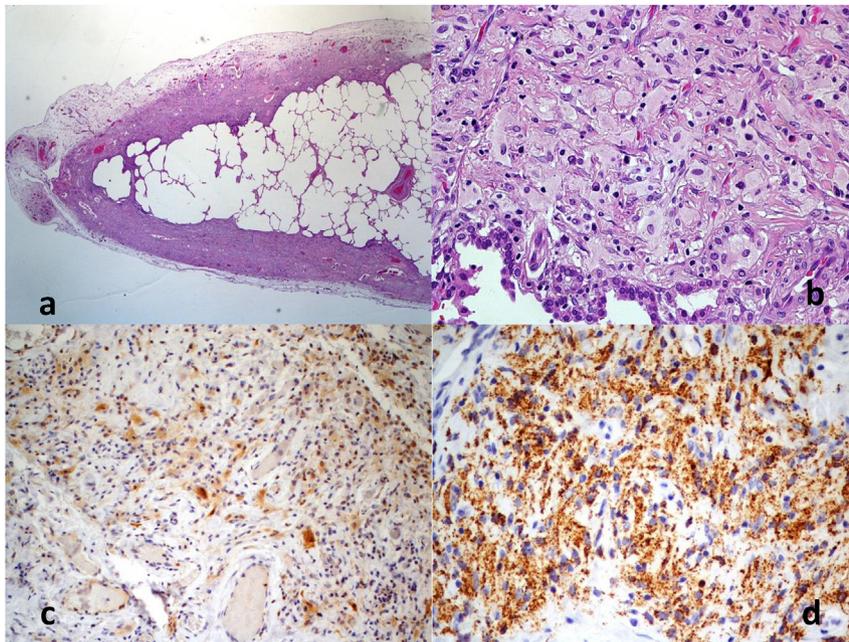


Fig. 3. a) fibrous pleural and subpleural thickening, along the interlobular septal; b) diffuse infiltrated of histiocytes with abundant cytoplasm and vesiculous nuclei, accompanied by lymphocytes and plasma cells with abundant fibrosis with no granulomas; c) positivity for CD68; d) positivity for S100.

Cohen AubartF et al. [9] reported a good efficacy and safety profile of cobimetinib in three WT BRAF ECD patients refractory to conventional therapy. Moreover, mutations in the MAPK and PIK3 pathway were found in patients with ECD and LCH suggesting that both disorders could be classified as an inflammatory myeloid neoplasia [10,11].

In conclusion, this is a report of unusual intrathoracic

localizations of ECD due to their lonely presence at the presentation of the disease and due to the atypical prevertebral lesion.

Conflict of interest

The authors declare that they have no competing interests.

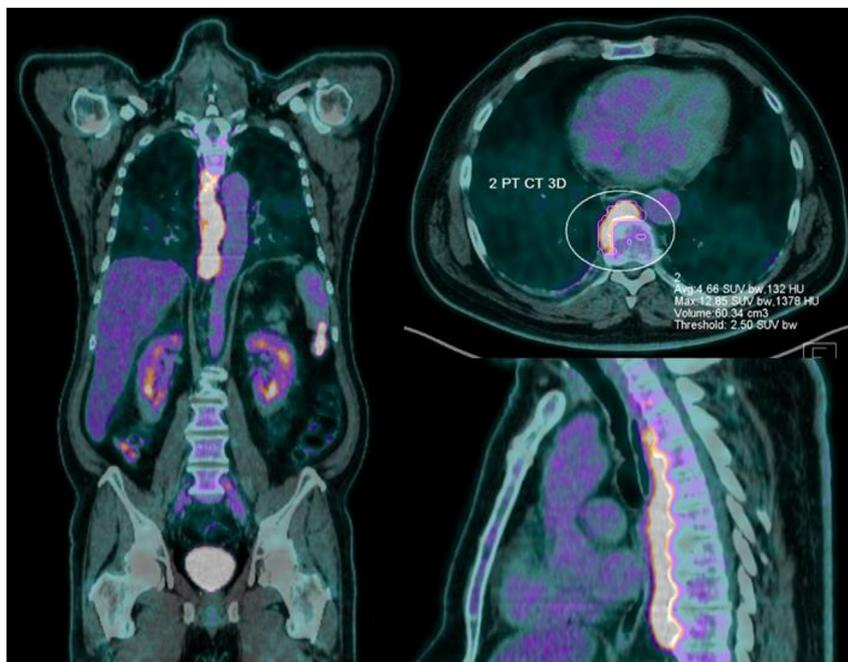


Fig. 4. Legend- ^{18}F FDG- PET- CT showing the prevertebral tissue.

Authorship statement

All authors are responsible for the conception of this case report and participated in its draft. All authors read and approved the final manuscript.

As this is a case report without patient identifiers, approval from Ethical Committee is not required at our Institution.

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