Erdheim-Chester Disease Presenting as an Anterior Mediastinal Tumor without Skeletal Involvement

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Erdheim-Chester disease (ECD) is a form of non-Langerhans cell histiocytosis that most commonly involves the skeletal system. We report an unusual case of ECD presenting as an anterior mediastinal tumor without skeletal involvement. A 60-year-old man with no remarkable medical history was referred for evaluation of a mediastinal mass. The patient underwent surgical excision of the tumor via video-assisted thoracoscopic surgery. Histologic examination revealed marked proliferation of atypical histiocytes with sclerosis, and the results of immunohistochemical staining were suggestive of ECD.

Key words: 1. Erdheim-Chester disease 2. Histiocytosis 3. Non-Langerhans cell 4. Mediastinum 5. Video-assisted thoracic surgery

Case report

1) Introduction

Erdheim-Chester disease (ECD), a rare form of non-Langerhans cell histiocytosis with an unknown cause, was first described by Chester [1] in 1930. Histopathologically, ECD is characterized by xanthogranulomatous infiltration of numerous “lipid-laden” macrophages surrounded by fibrosis. Immunohistochemically, ECD histiocytes are typically positive for CD68, CD163, and factor XIIa, and negative for CD1a [2-4]. Although ECD is regarded as a multisystemic and heterogeneous disease, skeletal involvement is present in 96% of cases [3]. Herein, we report an unusual case of ECD presenting as an anterior mediastinal tumor without skeletal involvement that was treated surgically.

2) Case description

A 60-year-old man with no remarkable medical history was referred to Asan Medical Center in Seoul for the evaluation of an anterior mediastinal mass. He had presented to a local hospital with a 4-month history of moderate cough. His laboratory findings were nonsignificant, but computed tomography showed a 4.0-×6.5-cm irregular anterior mediastinal mass with heterogeneous enhancement (Fig. 1A). A percutaneous needle biopsy was nondiagnostic, but was suggestive of an inflammatory myofibroblastic tumor. Positron emission tomography–computed to-
Fig. 1. (A) Contrast-enhanced chest computed tomography scan, showing a 2.6-cm mass in the right anterior mediastinum. (B) Contrast-enhanced chest computed tomography scan, showing enlarged intrathoracic lymph nodes presumed to indicate recurrence.

mography demonstrated increased fluorodeoxyglucose uptake without any other hypermetabolism suggestive of metastasis. Brain magnetic resonance imaging and technetium-99m bone scintigraphy revealed no significant abnormal findings.

Under suspicion of a thymic neoplasm, the patient underwent surgical excision of the tumor via video-assisted thoracoscopic surgery (VATS). Two 11.5-mm ports and one 5-mm port were created, with the patient in the left semilateral decubitus position. An approximately 5.5-cm firm irregular mass was observed in the anterior mediastinum, and was excised completely via VATS. Because it was strongly suspected that the mass had invaded the right upper lobe of the lung and pericardium, pulmonary wedge resection and partial pericardiectomy were also performed. One of the 11.5-mm ports was extended, and the tumor was pulled out using an endoretrieval pouch. On frozen biopsy, an inflammatory lesion with lymphoplasmacytic infiltration and fibrosis was observed, with no residual tumor on the resection margins. Because there was no clinical finding suggesting malignancy, no further resection was attempted. As the operation was primarily performed to obtain a biopsy sample, the pericardial resection was very small (<2 cm); this rarely results in cardiac herniation, so the pericardial resection space was left open. After hemostasis, a Jackson-Pratt drain was inserted into the mediastinal side of the pleural cavity, and the patient was transferred to the postanesthetic care unit.

The specimen included a well-demarcated, lobulated, firm mass (5.5×4.2×4 cm) in the mediastinal soft tissue. The cut surface showed pinkish-white fibrosis with multifocal necrosis, and extension to the lung parenchyma was observed (Fig. 2). Histologic examination revealed marked proliferation of atypical histiocytes with sclerosis, and the results of immunohistochemical staining were positive for CD68 and factor XIIIa, and negative for CD1a. Although a BRAF V600E mutation test was negative, the overall findings were suggestive of ECD. The mass was densely adherent to the pericardium with microscopic invasion, and extension to the visceral pleura of the lung was also observed. These histologic findings were confirmed by 2 expert pathologists through an intradepartmental consultation.

The patient’s postoperative course was uneventful, and he was discharged on postoperative day 3 without any complications. Three months after discharge, follow-up computed tomography revealed enlarged internal thoracic lymph nodes in the right first and second intercostal spaces (Fig. 1B). The patient underwent repeated VATS for excisional biopsy using the previous incisions. The lymph nodes were excised en bloc with adjacent soft tissue, and pathology
confirmed recurrence of ECD. The patient showed no further disease recurrence during the following 22 months.

**Discussion**

Although the total number of reported cases of ECD has increased in the most recent decade, only 500–550 cases have been reported worldwide [2]. The mean age at diagnosis is 53–55 years [3], and most published data show a male predominance [3]. The pathogenesis of ECD is uncertain, but it has been reported that more than half of cases are associated with the BRAF V600E mutation [5].

ECD is diagnosed based on clinical, radiologic, and histopathologic findings. Although ECD is a multisystemic disease, the most commonly affected organ is the skeletal system. Symmetric diaphyseal and metaphyseal osteosclerosis of the long bones of the lower extremities is present on technetium-99m bone scintigraphy in nearly all patients [2-4]. According to a report by Arnaud et al. [3], only 4% of patients with ECD lack radiographic findings of skeletal involvement. Central nervous system involvement usually is asymptomatic; it is relatively common (25%–50%), and has been reported to be a crucial prognostic factor [2,3].

The most important diagnostic hallmark of ECD is its histopathologic characteristics, because xanthomatous or xanthogranulomatous infiltration of tissue by foamy histiocytes is a typical finding. Furthermore, ECD has a unique inflammatory cytokine signature consisting of elevated levels of interferon alpha, interleukin (IL)-12, and monocyte chemotactic protein-1 and decreased levels of IL-4 and IL-7 [2]. Furthermore, immunohistochemical staining of ECD histiocytes is positive for CD68, CD163, and factor XIIIa, and negative for CD1a, whereas staining of Langerhans cell histiocytosis is positive for CD1a and negative for CD68 [2-4].

The patient in this report presented with an anterior mediastinal tumor that mimicked a locally invasive thymic neoplasm without distant metastasis. Although intrathoracic manifestations of ECD are rather common, no previous case has been published of ECD presenting as a mediastinal tumor without skeletal involvement. Most intrathoracic manifestations of ECD include skeletal lesions, and may have cardiovascular involvement or nonspecific patterns of pulmonary disease. Only a few cases of ECD have
presented as a mass, usually as an infiltrative lesion in the right atrium [4].

The prognosis of ECD has been reported to be poor; in one study, fewer than half of patients (43%) were alive after a mean follow-up of 32 months [2]. The initial treatment is based on interferon alpha therapy, with a recent report demonstrating an improved 5-year survival rate of 68% [3]. In patients with the BRAF V600E mutation, treatment also may include a mutant BRAF inhibitor (vemurafenib).

In conclusion, ECD without skeletal involvement is rare, and can be diagnosed only by a histopathologic examination. Therefore, awareness of this disorder and expert pathologic review are important for managing patients with ECD. Although surgical excision may help to confirm the diagnosis, its role in treatment is uncertain. More observational data are needed to clarify the prognosis of patients who undergo surgical treatment of ECD.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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