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Case Report

A rare case of Erdheim-Chester disease with esophageal involvement: unusual imaging findings

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Abstract: Erdheim-Chester disease (ECD) is an uncommon non-Langerhan cell histiocytosis that affects multiple systems and most commonly involves the bones. A 34-year-old patient with a three-month history of progressive dysphagia, underwent the gastroscopy which revealed esophageal mucosal constriction 34 cm from the incisor and external pressure stenosis. Enhanced computed tomography (CT), magnetic resonance imaging (MRI), and 2-[fluorine-18] fluoro-2-deoxy-d-glucose (^{18}F-FDG) positron emission tomography (PET)/CT findings confirmed diffuse soft-tissue infiltration filled periesophageal space and excluded lesions involving the bone and other organs within the scanning range. The patient was later diagnosed with esophageal involvement of ECD by thoracotomy surgery and paraesophageal soft tissue biopsy. Progressive dysphagia, a rare clinical manifestation of ECD, has been reported in only two cases. It is the first demonstration of MRI and PET/CT imaging findings of ECD esophageal invasion as far as we known. Through the comparison of multiple images, we have a preliminary recognition of characteristic radiological features of gastrointestinal infiltration in ECD.

Keywords: ^{18}F-fluorodeoxyglucose, Erdheim-Chester disease, esophagus, positron emission tomography-computed tomography, thorax

Introduction

Erdheim-Chester disease (ECD) is a rare non-Langerhans cell histiocytosis, characterized by the infiltration of foamy histiocytes and first described by Erdheim and Chester in 1930 as "lipid granulomatois" [1]. It was initially denominated by Jaffe in 1972 [2]. Only approximately 400 cases had been reported in the medical literature before 2011 [3]. Due to the increased recognition of the disease and improved diagnostic technology over the past ten years, the number of diagnosed cases has significantly increased to more than 1,500 cases [4]. In the 2016 revision of the histiocytosis classification of five-group scheme, ECD along with Langerhans cell histiocytosis (LCH) was classified under "L Group" as a malignant disorder, because both diseases have clonal mutations involving genes of the MAPK pathway in >80% of cases [5].

ECD mostly affects patients of 55 to 60 years of age and has a male preponderance (sex ratio, 3:1) [5]. The clinical manifestations in ECD are nonspecific and heterogenous considerably between patients, including bone pain, dyspnea, diabetes insipidus, ataxia and visual disturbance, etc. But, the gastrointestinal involvement is extremely rare. The diagnosis of ECD is based on appropriate histology, which demonstrates diffuse xanthogranulomatous infiltration with the non-Langerhans immunophenotype of $CD68^+$, $CD1a^-$ and $CD207^-$ [4]. Imaging findings play an essential role in assessing the involvement of tissues and organs. Preliminary studies have reported some classical features of ECD by computed tomography (CT) or magnetic resonance imaging (MRI), such as "coated aorta" and "hairy kidneys" which indicated fat infiltration around arteries and kidneys respectively [6, 7]. However, gastrointestinal manifestations have not

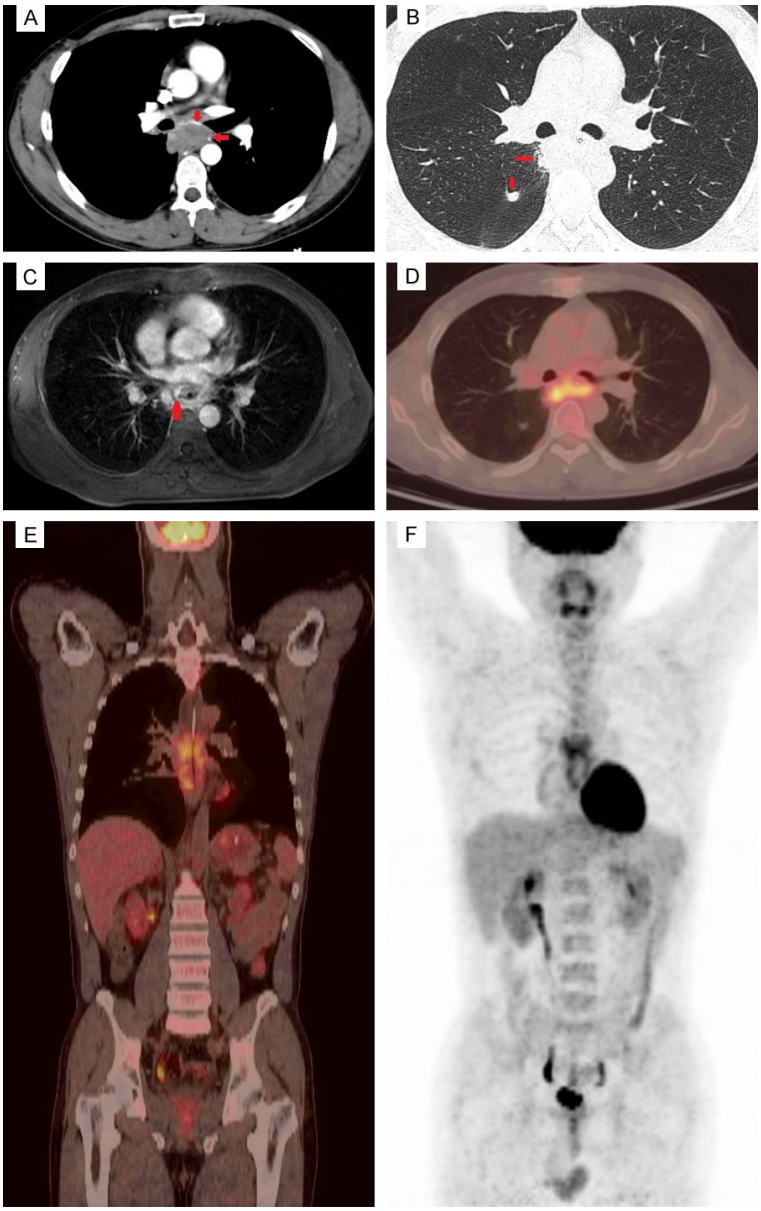

Figure 1. Imaging findings of the patient. A. CT scan confirmed the presence of periesophagus soft tissue, with several bronchial arteries, which was inhomogeneously contrast-enhanced. B. Axial high-resolution CT scan revealed a lesion invading the right mediastinal pleura, and a solid nodule on the oblique fissure pleura. C. The lesion exhibited a widespread slightly high signal and non-enhanced ring line-like low signal on the gadolinium-enhanced LAVA sequence of the MRI scan. D, E. Periesophagus soft tissue (measuring 11.6 cm in length, SUVmax of 4.9) demonstrated avidity on axial and coronal ^{18}F-FDG PET/CT fusion image. Conversely, a solid nodule on the right oblique fissure pleura, exhibited no avidity. F. Maximum intensity projection FDG PET/CT image demonstrated abnormal FDG-avidity in the mediastinal region, but no involvement of the bone or other organs.

been well known. Here, we describe a case of ECD with esophageal involvement, focusing on imaging features of enhanced CT, MRI and positron emission tomography/CT (PET/CT), and discuss the utility of different imaging examinations in the diagnosis of ECD.

Case report

A 34-year-old man, who had previously undergone resection of a mediastinal calcifying fibrous tumor three years ago, was admitted because of a three-month history of progressive dysphagia. Before admission, the gastroscopy revealed esophageal mucosal constriction 34 cm from the incisor and external pressure stenosis. His abnormal prothrombin was 43.00 mAu/ml (normal range: 0-40 mAu/ml), while other cancer indicators were within normal limits. To determine the cause of the esophageal compression, he underwent enhanced CT and MRI of the chest, as well as an ^{18}F-FDG PET/CT scan, ranging from the head to the thigh. The CT scan confirmed the presence of periesophageal soft tissue with inhomogeneous contrast enhancement, filling the entire postmediastinal space and extending toward the tracheal carina (**Figure 1A**) and the right mediastinal pleura (**Figure 1B**). The lesion exhibited a widespread slightly high signal and non-enhanced ring line-like low signal on the gadolinium-enhanced LAVA sequence of the MRI scan (**Figure 1C**), and moderate avidity at ^{18}F-FDG PET/CT (**Figure 1D-F**). PET/CT excluded lesions involving the bone and other organs within the scanning range (**Figure 1F**). The patient underwent thoracotomy surgery, which revealed the mass, surrounding the middle and lower esophagus. It invaded the spine, aorta, and trachea. Since it presented with a frozen state, separation and removal were not feasible. A

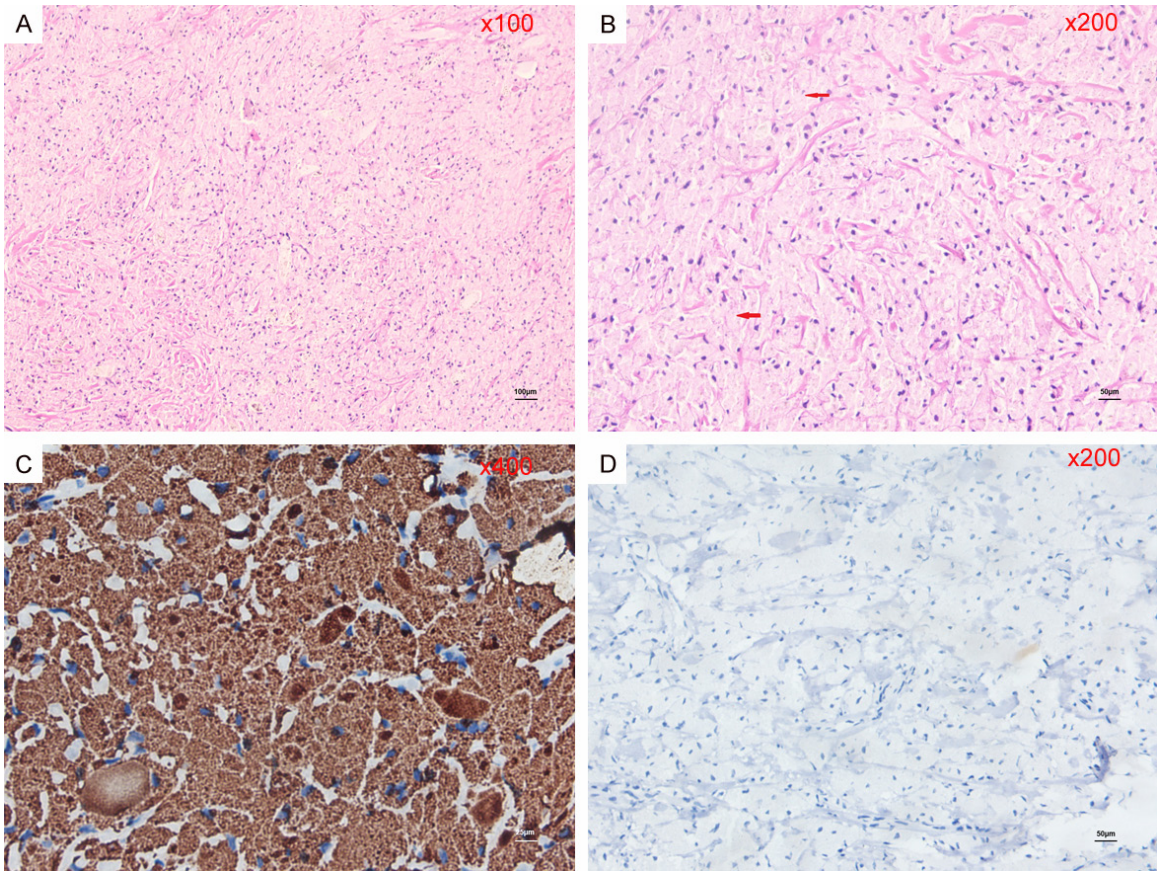

Figure 2. Histopathological findings and immunohistochemical staining. (A, B) Histopathological examination of the paraesophageal soft tissue revealed diffuse histiocytic infiltration in the fibrotic tissues. The majority exhibited foamy cytoplasm (arrows in B) (Hematoxylin-eosin stain); (C, D) Immunohistochemistry staining was positive for CD68 (C) and negative for CD1a (D); (A) Scale bar, 100 μm; (B) Scale bar, 50 μm; (C) Scale bar, 25 μm; (D) Scale bar, 50 μm.

subsequent paraesophageal soft tissue biopsy revealed multiple foamy histiocytes, surrounded by fibrosis (**Figure 2A**, **2B**). The immunohistochemical staining was positive for CD68 and negative for Langerin, CD1a, and S-100 protein (**Figure 2C**, **2D**). These findings confirmed the diagnosis of ECD.

Discussion

ECD is a rare non-Langerhans cell histiocytosis, characterized by the infiltration of foamy $CD68^{+}CD1a^{-}$ histiocytes. Bone involvement, which has been observed in 80-95% of patients, is almost universal in ECD [8, 9]. About 50% of cases affect at least one extra-skeletal site, including the periorbital tissues [10], skin [11], lungs [12, 13], cardiovascular system [14], central nervous system [15], and retroperitoneum [16]. The involvement of liver, pancreas, mesentery and gastrointestinal tract is extremely rare [17-23]. The clinical manifestations in ECD are heterogenous, resulting in varied radiologic findings, which make misdiagnosis common. Although the number of known patients has dramatically increased during the last 15 years because of the better awareness of the disease, the mean time from symptoms onset to diagnosis was still up to 2.7 years according to the latest large sample study [4].

Since gastrointestinal tract involvement is exceedingly rare in ECD, we know little about the characteristics of such lesions. Thus, we searched relevant case reports published in the English literature in the PubMed database. Until now, a total of 5 gastrointestinal ECD has been reported (**Table 1**). The presented patient had no obvious bone involvement but only demonstrated periesophageal infiltration, which

Table 1. Summary of 5 cases with ECD involving the gastrointestinal tract

No. References	Sex/ age	Symptoms	Radiological findings	Endoscopic findings	Biopsy sites	Immunohisto-chemistry	Other organs involved	Treatment	Outcome
Vermeirenetal et al. [19]	F/54 y	Progressive dysphagia	Multiple adenopathies with esophageal compression showed by CT images	An inhomogenous mass of 2 cm thickness in the esophageal wall	LN	CD68 (+) CD1a (-) S100 (-)	Lung, retroperitoneum, kidney	Steroids, cyclosporine	Resolution
Pan et al. [20]	M/69 y	Lethargy, fever, decrease in appetite, vomiting, weight loss, dry cough	Peri-aortic and oesophageal infiltration showed by CT images	Normal	Liver, omentum, LN	CD68 (+) CD1a (-) S100 (-)	Bone, aorta, lung, peri-cardium, liver, kidney, omentum, small bowel mesentery	Steroids	Death
Tevlin R et al. [21]	F/30 y	Dyspepsia, anorexia, abdominal distension, weight loss	A large retroperitoneal mass showed by CT and PET/CT images	Normal	Distal ileum	CD68 (+) CD163 (+) Factor XIII (-) CD1a (-)	NO	Chemotherapy	NA
Christophi GP et al. [22]	F/68 y	Fever, fatigue, dyspnea on exertion, chronic diarrhea	Wall thickening of the descending colon, sigmoid colon, and rectum along with gas and fluid distention of the ascending and transverse colon showed by CT images	Segmental colitis	The hepatic and splenic flexure of colon	CD68 (+) CD163 (+) CD3 (-) CD20 (-) S100 (-)	NO	Steroids	Progression
Ben-Yaakov G et al. [23]	F/36 y	Diarrhea, weight loss, nausea, vomiting, fever, weakness	NA	A cobblestone-like raised nodular gastritis of the entire stomach, numerous small round hyperpigmented lesions with decreased vascularity in the surrounding mucosa extending from the rectum to the cecum	Gastric and colonic mucosa, bone, LN	CD68 (+) CD1a (-) S100 (-)	Bone, LN	Chemotherapy	Resolution

NA = not available; LN = lymph node; ECD = Erdheim-Chester disease.

made diagnosis extremely challenging. Among the 5 cases we searched, there were 2 cases with similar upper gastrointestinal symptoms and imaging findings to our case [19, 20]. Vermeirenetal et al. reported a case of progressive dysphagia due to mediastinal adenopathies, compressing the esophagus [19], and Pan et al. reported a case involving the gastrointestinal, skeletal, retroperitoneal, cardiovascular, and respiratory system simultaneously [20]. Our case is different from previous reports in three aspects. First, the periesophageal infiltration is the first and only affected lesion observed in our patient, while Pan's case demonstrated typical multisystemic involvements of ECD including oesophageal infiltration, and Vermeirenetal's case presented mediastinal esophageal compression several years after lung and retroperitoneal involvement of ECD was diagnosed. Second, in our case, the lesion around the esophagus is diffuse and extensive that almost fill the fatty space of the posterior mediastinum, even invading the right mediastinal pleura. This radiological finding was similar to some of typical ECD manifestations such as diffuse soft-tissue infiltration of the perirenal space ("hairy kidneys") or periaortic space ("coated aorta") [6, 7]. By contrast, the sheathing of esophagus in Pan's case was inapparent and secondary to peri-aortic tissue infiltration, and esophageal involvement in Vermeirenetal's case due to the compression of mediastinal lymph nodes' infiltration caused by ECD. Third, as far as we know, it is the first description of esophageal infiltration seen on MR and ^{18}F-FDG PET/CT imaging and confirmed as ECD by biopsy. We observed a non-enhanced ring line-like low signal on the gadolinium-enhanced LAVA sequence of the MRI scan, which might suggest the presence of fibrosis in the lesion.

The first manifestations and clinical course in ECD are variable depending on the affected organ, being asymptomatic, clinically atypical but sometimes life threatening. A better recognition of its specific imaging features seems to be crucial for early diagnosis and improved prognosis. A whole-body PET/CT scan simultaneously displays skeletal and extra-skeletal lesions that may not be detected by single-site CT or MRI. Thus, it is useful for establishing the diagnosis, guiding biopsies, and evaluating the treatment response in ECD patients. Meanwhile, organ-specific CT or MRI is used to describe the features and location of the lesions in greater anatomic detail. Although gastroenterological tract manifestation of ECD is rare, it should be considered in differential diagnosis in patients exhibiting typical radiological features, especially those suggestive of multi-organ involvement.

Disclosure of conflict of interest

None.

Abbreviations

CT, computed tomography; ECD, Erdheim-Chester disease; ^{18}F-FDG PET, ^{18}F-fluorodeoxyglucose positron emission tomography; MRI, magnetic resonance imaging.

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