Erdheim-Chester Disease on [18F]FDG PET/CT: A Case Report

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AUTHORS' CONTRIBUTIONS

Chunyan Wu collected this case. Li Zhou and Liming Xiao drafted the manuscript. Yixiao He and Ziyi Zhao made the figures. Chuandong He revised the manuscript. All authors contributed to the manuscript and approved the submitted version.

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DISCLOSURES

None.

CONSENT

Yes.

HUMAN AND ANIMAL RIGHTS

Yes.

CONFLICTS OF INTEREST

There are no conflicts of interest to declare.

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ABSTRACT

Erdheim-Chester disease (ECD) is a rare form of systemic non-Langerhans cell histiocytosis with characteristic bone involvement. Extraskeletal involvement sites were found in central nervous system (CNS), cardiovascular system, lungs, kidneys, and so on. The most common site of CNS involvement is the hypothalamic-pituitary axis, but here we report a rare case of ECD with the frontal lobe involvement.

CASE REPORT

BACKGROUND

Histiocytosis are classified into LH cell origin and NLH cell origin. LCH is defined by the clonal proliferation of Langerhans-positive cells. In contrast, ECD, a rare form of non-LCH, is characterized by foamy histiocytes infiltrating tissues or organs [1]. ECD was first reported in 1930 by William Chester and his mentor, the Viennese pathologist Jakob Erdheim [2]. In 1972, Jaffe reported a similar case and named this disease after Erdheim and Chester [3]. The most common site of involvement of ECD is the skeleton, with a prevalence of 74–92% in affected individuals [4]. Extraskeletal involvement sites exist in CNS, cardiovascular system, lungs, kidneys, and skin [5]. There are different clinical manifestations depending on the site of involvement. For example, CNS involvement may present clinically as cerebellar or brainstem syndrome or as a neuroinflammatory disorder, which can result in functional handicaps [6]. In addition, cardiovascular involvement is present in an estimated 36-45% of ECD patients, with approximately 50-75% of those patients experiencing heart involvement [7]. When it comes to kidneys, the “coated aorta” and “hairy kidneys” can be found by CT, which is caused by the infiltration of perirenal fat [8]. With involvement of Orbital, which can occur in 25%–37% of patients, presents with retrobulbar masses that can cause visual impairment, motility disturbance, proptosis, and optic nerve edema [9]. Although imaging techniques such as CT, MRI, radiography, ultrasonography, and nuclear imaging can

detect and identify different manifestations of ECD, the IHC is one of the key tests for diagnosing ECD. Tissue biopsies from ECD lesions are CD68(+), CD133(+), CD1a(-), and CD207(-), while S100 expression is rarely seen [10]. Here we report a rare case of ECD manifested by recurrent involuntary limb tremors, with the frontal lobe and bone involvement.

CASE PRESENTATION

A 50-year-old woman presented with an over five-month history of recurrent involuntary limb tremors. The patient had never smoked or consumed alcohol, had no history of diabetes or hypertension, denied substance abuse, and had no relevant family history of hereditary diseases. Her medical history was otherwise unremarkable and she was not taking any medication. The physical examination revealed involuntary movement of the limbs, the presence of physiological reflexes, and the absence of pathologic reflexs. Furthermore, the muscle strength and tone of the limbs were found to be within normal limits. Laboratory tests yielded no evidence of abnormalities. Only the MRI showed a low TI-weighted signal nodule in the right frontal lobe with surrounding edema (Figure 1A), and a malignant tumor was suspected. So the enhanced MRI scan was performed and the nodule in the right frontal lobe was obvious enhanced (Figure1B). The radiologist diagnosed the tumor as metastatic. The patient underwent [^{18}F]FDG PET/CT on the advice of the clinician. The MIP images demonstrated a clearly bilateral and symmetric increase in uptake at the diaphysis and metaphysis of the femur and tibia(Figure 1C). The nodule, which was shown on MRI, also demonstrated avid [^{18}F]FDG uptake (Figure1D-1F). CT and transaxial fused PET/CT images showed osteosclerosis of the femurs(Figure 1G-1I) and the 5th lumbar(Figure1J-L). The orbit and other soft tissues were not involved.

The microscopic analysis of the distal femoris biopsy revealed the presence of numerous foamy histiocytes. IHC confirmed the diagnosis of ECD as these histiocytes were found to be positive for CD68 and negative for S-100 protein(Figure 2). The patient did not receive treatment at our hospital due to her scheduling issues, but instead, opted for traditional Chinese herbal medicine to manage the nervous system symptoms. After a period of treatment, the patient's condition has stabilized.

DISCUSSION

ECD is a rare non-LCH histologically characterised by the multi-systemic proliferation of mature histiocytes in a background of inflammatory stroma [11], This disease was first described by William Chester in 1930 following collaboration with the Austrian pathologist Jakob Erdheim [2]. Due to the rarity of this disease, multi-organ involvement, and the diverse presentation, diagnosis is often delayed [12]. Skeletal system is the most common involvement site [13,14]. Extraskeletal involvement sites were found in various regions of the body, including the CNS, cardiovascular system, lungs, kidneys, and skin [5]. The most frequent location of CNS involvement in ECD is the hypothalamic-pituitary axis, additional CNS lesions include meningeal, intra-axial, and perivascular lesions [15,16]. But in this case of ECD, only the brain and skeletal system were involved, as evidenced by the [^{18}F]FDG PET/CT scan. The cardiovascular, orbital system, kidneys were not affected. CNS involvement occurs in up to 50% of patients with ECD [17]. The imaging appearance of neurologic ECD is dependent on distribution and extent. The most common findings are multifocal FLAIR hyperintensities of the dentate nuclei and brainstem, with variable enhancement, as in pituitary lesions[18]. PET/CT demonstrates intensely [^{18}F]FDG with ECD lesions [19]. CNS involvements are independent predictors of poor prognoses [18].

Both [^{18}F]FDG PET/CT and ^{99m}Tc-MDP scan are capable of depicting the most relevant lesions of ECD and are valuable modalities for diagnosis of the ECD. In particular, [^{18}F]FDG PET/CT is highly recommended for the initial evaluation, due to its accuracy in detecting extraskeletal involvementand selecting biopsy targets[20, 21]. Overall, ECD is generally considered an indolent disease, with a median survival of over 10 years [22]. Due to the complexity and rarity of the cases, a standardized therapeutic approach has not been established yet. While corticosteroids may reduce oedema acutely, such as in severe exophthalmos, they are not considered an effective monotherapy, and lack the ability to control the disease in the long term [23]. IFN-alpha may be a valuable first-line therapy for long-term treatment of ECD. However, the efficacy of IFN-alpha varies among patients and depend on the site of disease involvement. Symptoms may not respond to treatment, particularly for patients with severe multisystemic forms of ECD involving the CNS and cardiovascular [24]. In 2017, the U.S.FDA has approved vemurafenib for the treatment of adult ECD patients with the BRAF-V600 mutation [25]. These drugs have been proven effective in the treatment of BRAF-V600E-positive multisystem ECD [26], and the prevalence of BRAF-V600E mutations on molecular analysis of ECD samples is as high as 54% [27]. Besides these drugs, cytotoxic chemotherapies, radiotherapy, and surgery have been reported as treatments for ECD patients [23]. As there is no standardised treatment for ECD, the doctor needs to choose the appropriate drug according to the specific situation of the patient, such as the location of the lesion, whether BRAF-V600 is mutated, and so on. However, in this case, due to the lack of money and time, the patient did not receive treatments aforementioned, but instead,tried traditional Chinese medicine to manage the nervous system symptoms. No further examination has been conducted by the patient.

TEACHING POINT

Although skeletal involvement is more common, neurological manifestations may be the only presenting symptoms in a patient with ECD. ECD should be considered in a differential diagnosis scenario, when bone involvement is associated with cardiovascular or orbital system involvement. [^{18}F]FDG PET/CT is highly recommended in the initial evaluation technique, not only for its accuracy in detecting extraskeletal involvement, but also for selecting biopsy targets, which can avoid unnecessary

investigation and treatment.

QUESTIONS

Question 1: ECD belongs to which of the following disease categories?

A. Infectious disease

B. Metabolic disorder

C. Non-Langerhans cell histiocytosis

D. Primary malignant tumor

Answer: C

Explanation: ECD is a rare non-Langerhans cell histiocytosis and characterized by foamy histiocytes infiltrating tissues or organs.

Question 2: Common clinical manifestations of ECD include?

A. Symmetric long bone pain

B. Exophthalmos (orbital involvement)

C. Diabetes insipidus (hypothalamic-pituitary involvement)

D. Retroperitoneal fibrosis

E. Eczema-like skin lesions

Answer: A, B, C, D

Explanation: ECD is a multisystem disease, typically involving bones (long bone pain), orbits (exophthalmos), CNS (diabetes insipidus), and retroperitoneal fibrosis. However, the skin involved in ECD often manifests as nodules or sclerosing lesions.

Question 3: What is the gold standard for diagnosing ECD?

A. Serological antibody testing

B. Tissue biopsy showing CD68+/CD1a- histiocytic infiltration

C. Bone marrow aspiration

D. PET-CT showing abnormal bone metabolism

Answer: B

Explanation: Definitive diagnosis requires tissue biopsy, demonstrating foamy histiocytes (CD68+, CD163+) with CD1a negativity (distinguishing it from Langerhans cell histiocytosis).

Question 4: Which of the following are correct regarding the molecular genetic features of ECD?

A. ~50% of patients carry the BRAF V600E mutation

B. MAPK/ERK pathway activation is a key mechanism

C. All ECD patients should undergo BRAF mutation testing to guide therapy

D. NRAS mutations are common

Answer: A, B, C

Explanation: Approximately 50% of ECD patients have BRAF V600E mutations, and MAPK pathway dysregulation drives the disease. NRAS mutations are rare. BRAF testing is critical for targeted therapy.

Question 5: What is the first-line treatment for ECD?

A. Surgical resection of lesions

B. Interferon-α

C. BRAF inhibitors

D. Glucocorticoid monotherapy

Answer: B

Explanation: Interferon-α remains the traditional first-line therapy. BRAF inhibitors (e.g., vemurafenib) are reserved for BRAF V600E-positive patients. Surgery is rarely curative due to multisystem involvement.

REFERENCES

[1] J. Haroche, F. Cohen-Aubart, Z. Amoura. Erdheim-Chester disease. Blood. 2020; 135(16) :1311–1318,

[2] Chester W. Uber lipoid granulomatose. Virchows Arch Pathol Anat. 1930; 279: 561-602.

[3] Starkebaum G, Hendrie P. Erdheim-Chester disease. Best Pract Res Clin Rheumatol. 2020; 34(4): 101510.

[4] Cives M, Simone V, Rizzo FM, et al. Erdheim-Chester disease: a systematic review. Crit Rev Oncol Hematol. 2015; 95(1): 1-11. PMID: 25744785.

[5] Diamond EL, Dagna L, Hyman DM, et al. Consensus guidelines for the diagnosis and clinical management of Erdheim–Chester disease. Blood. 2014; 124(4): 483–492. PMID: 24850756.

[6] Garg N, Lavi ES. Clinical and Neuroimaging Manifestations of Erdheim-Chester Disease: A Review. J Neuroimaging. 2021; 31(1): 35-44. PMID: 32920940.

[7] Alharthi MS, Calleja A, Panse P, et al. Multimodality imaging showing complete cardiovascular involvement by Erdheim-Chester disease. Eur J Echocardiogr. 2010; 11(7): E25. PMID: 20406735.

[8] Guo G, Zheng D, Wang X, Wang X. Erdheim-Chester Disease presenting with constrictive pericarditis: A case report and review of the literature. Radiol Case Rep. 2024;19(7): 2590-2595. PMID: 38645964.

[9] Huang LC, Topping KL, Gratzinger D, et al. Orbital and chorioretinal manifestations of Erdheim–Chester disease treated with vemurafenib. Am J Ophthalmol Case Rep. 2018; 11: 158-163. PMID: 30094395.

[10] Goyal G, Heaney ML, Collin M, et al. Erdheim-Chester disease: consensus recommendations for evaluation, diagnosis, and treatment in the molecular era. Blood. 2020; 135(22): 1929–1945. PMID: 32187362.

[11] Ozkaya N, Rosenblum MK, Durham BH, et al. The histopathology of Erdheim-Chester disease: a comprehensive review of a molecularly characterized cohort. Mod Pathol. 2018; 31(4): 581-597. PMID: 29192649.

[12] Sioka C, Estrada-Veras J, Maric I, Gahl WA, Chen CC. FDG PET images in a patient with Erdheim–Chester disease. Clin Nucl Med. 2014; 39(2): 170-177. PMID: 23640213.

[13] Della Torre E, Dagna L, Mapelli P, Mellone R, Grazia Sabbadini M. Erdheim-Chester disease: imaging-guided therapeutic approach. Clin Nucl Med. 2011; 36(8): 704-706. PMID: 21716027.

[14]Ding H, Li Y, Ruan C, et al. Chinese Erdheim-Chester disease: clinical-pathology-PET/CT updates. Endocrinol Diabetes Metab Case Rep. 2015; 2015:150055. PMID: 26527559.

[15]Tan AHS, Dhanda S, Jagmohan P, et al. Erdheim-Chester disease: Imaging spectrum of multisystemic manifestations. Ann Acad Med Singap. 2022; 51(11): 742-744. PMID: 36453223.

[16]Filizoglu N, Ozguven S, Ones T, Turoglu HT, Erdil TY. Central Nervous System Complications of Erdheim-Chester Disease: FDG PET/CT Findings. Clin Nucl Med. 2021; 46(7): e387-e388. PMID: 33577201.

[17]Garg N, Lavi ES. Clinical and neuroimaging manifestations of Erdheim-Chester disease: a review. J Neuroimaging. 2021; 31(1): 35–44. PMID: 32920940.

[18]Benson JC, Vaubel R, Ebne BA,et al. Erdheim-Chester Disease. AJNR Am J Neuroradiol. 2023; 44(5): 505-510.

[19]Stuebe CM, Jenson AV, Lines TW, et al. Recurrent petit mal seizures in Erdheim-Chester disease mimicking an intra-axial brain tumor: illustrative case. J Neurosurg Case Lessons. 2023; 6(16): CASE23248. PMID: 37870750.

[20]Kanakis M, Petrou P, Lourida G, Georgalas I. Erdheim-Chester disease: a comprehensive review from the ophthalmologic perspective. Surv Ophthalmol. 2022; 67(2): 388-410. PMID: 34081930.

[21]Lin E. FDG PET/CT for biopsy guidance in Erdheim-Chester disease. Clin Nucl Med. 2007; 32(11): 860-861. PMID: 18075421.

[22]Papo M, Cohen-Aubart F, Trefond L, et al. Systemic histiocytosis (Langerhans cell histiocytosis, Erdheim-Chester disease, Destombes-Rosai-Dorfman Disease): from oncogenic mutations to inflammatory disorders. Curr Oncol Rep. 2019; 21(7): 62. PMID: 31115724.

[23]Diamond EL, Dagna L, Hyman DM, et al. Consensus guidelines for the diagnosis and clinical management of Erdheim-Chester disease. Blood. 2014; 124(4): 483-492. PMID: 24850756.

[24]Haroche J, Amoura Z, Trad SG, et al. Variability in the efficacy of interferon-alpha in Erdheim-Chester disease by patient and site of involvement: results in eight patients. Arthritis Rheum. 2006; 54(10): 3330-3336. PMID: 17009306.

[25]Oneal PA, Kwitkowski V, Luo L, et al. FDA Approval Summary: Vemurafenib for the Treatment of Patients with Erdheim-Chester Disease with the BRAFV600 Mutation. oncologist. 2018; 23(12): 1520-1524. PMID: 30120160.

[26]Estrada-Veras JI, O'Brien KJ, Boyd LC, et al. The clinical spectrum of Erdheim-Chester disease: an observational cohort study. Blood Adv.2017; 1(6): 357-366. PMID: 28553668.

[27]Haroche J, Charlotte F, Arnaud L, et al. High prevalence of BRAF V600E mutations in Erdheim-Chester disease but not in other non-Langerhans cell histiocytoses. Blood. 2012; 120(13): 2700-2703. PMID: 22879539.

FIGURES

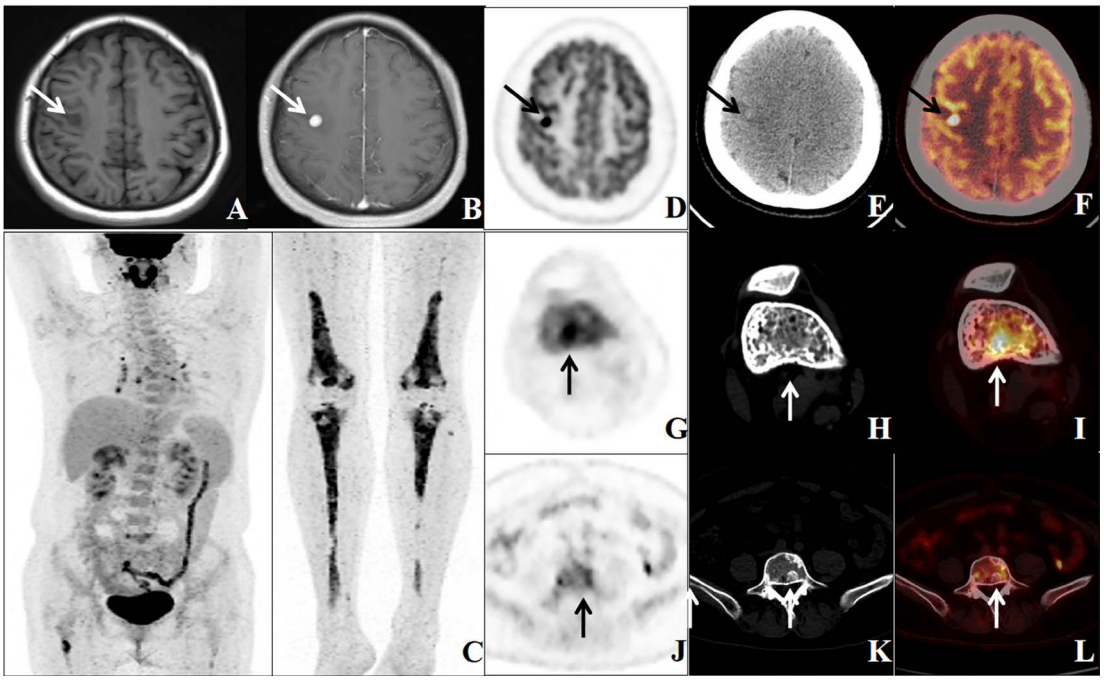

Figure 1: MRI and PET/CT image. (A-B, arrow): The signal nodule in the right frontal lobe showed low TI-weighted signal and obvious enhancement. (C): The MIP showed bilateral and symmetrical increased uptake in the diaphysis of the femur and tibia. (D, PET image; E, CT image; F, fused PET/CT image): The axial views of the brain showed the known brain nodule with a size of 1.0cm×0.8cm and increased activity (SUVmax 41.3). (G, PET image; H, CT image; I, fused PET/CT image): Axial views of the right femur showed increased FDG uptake (SUVmax 11.9). (J, PET image; K, CT image; L, fused PET/CT image): Transaxial images showed the involvement of the fifth lumbar vertebra with intense FDG uptake (SUVmax 5.5).

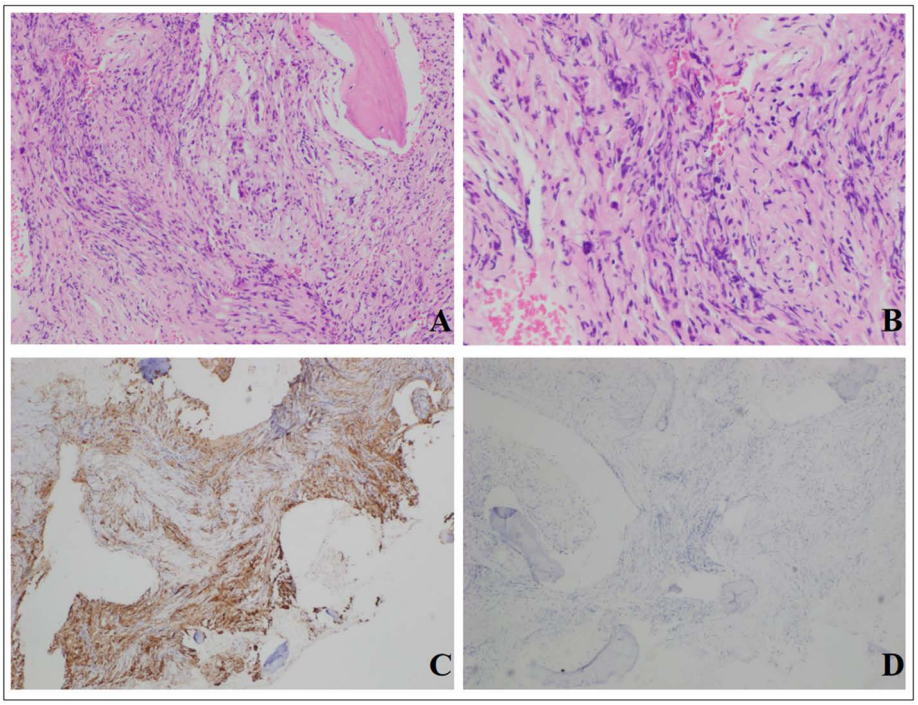

Figure 2: Then biopsy was then taken from right femur. Histological examination revealed fibrous tissue hyperplasia and foamy histiocytes distributed in nests between bone trabeculae (A, HE × 40; B, HE × 200). Immunohistochemistry (C-D) demonstrated CD68 (+), CD1a (−). P-CK (−), MP0 (scattered and focal +), CD21 (−), CD23 (−), Langerin (−), Ki-67 (+, approximately 3%).

KEYWORDS

Erdheim-Chester Disease, ECD, [18F]FDG, PET/CT, CNS

ABBREVIATIONS

ECD = Erdheim-Chester Disease
LH = Langerhans
NLH = Non-Langerhans
LCH = Langerhans Cell Histiocytosis
CNS = Central Nervous System
CT = Computed Tomography
MRI = Magnetic Resonance Imaging
IHC = Immunohistochemistry
[^{18}F]FDG = 2-deoxy-2-[^{18}F]fluoro-D-glucose
PET/CT = Positron Emission Tomography/ Computed Tomography
MIP = Maximal Intensity Projection

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