Case Report

Utility of Fluorine-18-Labeled Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Diagnosis of Erdheim–Chester Disease with Multisystemic Involvement

Abstract

Erdheim–Chester disease (ECD) is a rare non-Langerhans' cell histiocytic proliferative disorder of unknown origin with multisystemic predilection. It commonly affects adults in the fifth–seventh decades of life, with male preponderance, and has nonspecific clinical manifestations. Presence of characteristic radiological findings and demonstration of CD68 positive xanthogranulomatous infiltrates in histology clinches the diagnosis. Nevertheless, being a nonmalignant condition, it might be fatal due to multiorgan dysfunction. Hence, timely diagnosis and initiation of treatment with corticosteroids, immunosuppressants, or tyrosine kinase inhibitors are of paramount importance. We present a case of ECD with multisystemic involvement, who was initially evaluated for the left lung mass and treated as tuberculosis, where fluorine-18-labeled fluorodeoxyglucose positron emission tomography/computed tomography aided in targeting the metabolically active site for biopsy as well as assessing the multisystemic involvement.

Keywords: *Coated aorta sign, Erdheim–Chester disease, fluorine-18-labeled fluorodeoxyglucose positron emission tomography/computed tomography, hairy kidney sign, multisystemic involvement*

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Introduction

Erdheim–Chester disease (ECD) is a rare type of non-Langerhans' cell histiocytosis characterized by the involvement of multiple organs and systems including bones, central nervous system, skin, heart, kidneys, and vessels. It usually affects adults with male preponderance between the fifth and seventh decades of life.[1] The rarity of this disease and heterogeneity of clinical manifestations makes the understanding and diagnosis of this condition difficult. The survival rates at 1 and 5 years are 96% and 68%, respectively.[2] Although the etiology remains unclear, recent studies demonstrate that an abnormal increase in T-helper-1 immune response, producing several proinflammatory cytokines is responsible for the recruitment and activation of histocytes in the tissues.[1] Multidisciplinary approaches including clinical examination, imaging, and histopathology are required for diagnosis and initiation of treatment, where imaging plays a pivotal role in diagnosis with characteristic radiological findings. We here describe a case of ECD with multisystemic involvement where fluorine-18-labeled fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) helped to arrive at diagnosis as well as assess the extent of disease.

Case Report

A 52-year-old male, known case of type 2 diabetes mellitus, came with complaints of breathlessness on exertion for 1 month. His biochemical inflammatory markers were elevated. Contrast-enhanced CT thorax revealed an enhancing soft-tissue lesion in the left lung upper lobe in the perihilar region causing the left upper lobar bronchus cut off with resultant consolidation of the left lung upper lobe. Few right upper paratracheal, bilateral lower paratracheal, right hilar lymph nodes, and bilateral mild pleural effusion were also seen raising the possibility of primary lung malignancy with metastases. Endobronchial ultrasound-guided transbronchial needle aspiration (TBNA) was done from station 7 and the left lung

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Received: 20-12-2021
Revised: 20-02-2022
Accepted: 23-02-2022
Published: 02-11-2022

Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.ijnm_206_21

Quick Response Code:

How to cite this article: Gauthaman DK, Subramanyam P, Yesodharan J, Palaniswamy SS. Utility of fluorine-18-labeled fluorodeoxyglucose positron emission tomography/computed tomography in diagnosis of erdheim–chester disease with multisystemic involvement. Indian J Nucl Med 2022;37:261-4.

mass, which revealed prominent histiocytic infiltrates with attempted granuloma formation. The patient was started on antitubercular treatment. However, since the patient progressed clinically within a month, he was referred to our department for F-18 FDG PET/CT, which revealed multisystemic lesions. Intense FDG uptake was seen in enhancing left perihilar mass in thorax involving the left upper lobe bronchus (maximum standardized uptake value 17.1), with involvement of pleura, pericardium, supra and infradiaphragmatic lymph nodes, peritoneum, kidneys, arteries, meninges, testis, and bones [Figures 1 and 2].

Possibilities of granulomatous pathology and neoplastic pathology with extensive metastasis were given. Biopsy was done from the intense FDG avid periphery of the left lung mass, which showed ill-defined collections of histiocytes with lymphocytes. On immunohistochemistry, the cells stained positive for CD68 negative for CD1a. In view of the prominence of histiocytes on the TBNA aspirate and lung biopsy as well as the pattern of systemic involvement, the possibility of ECD was suggested [Figure 3].

On retrospectively reviewing the F-18 FDG PET/CT study, hairy kidney sign, coated aorta sign, pleuroparenchymal pulmonary involvement, involvement of pericardium, peritoneum, meninges, and skeletal system directed toward the diagnosis of ECD. Subsequently, bone marrow aspiration showed myeloid preponderance with left shift and increase in histiocytes. Genetic testing for BRAF V600E mutation was negative. The final diagnosis of ECD was made and the patient was started on corticosteroids and interferon. The patient showed partial improvement in symptoms within 2 months of initiation of therapy.

Discussion

Since the first description of ECD by William Chester in 1930, around 550–600 cases have been reported, with tremendous rise in the number of reported cases in the last 10 years due to increased recognition of this disease.[3] ECD is characterized by multisystemic infiltration of histiocytes resulting in heterogeneous clinical presentation depending on the lesions and systems affected. ECD can affect almost every organ, with preponderance toward skeletal system, the pathogenesis could be contributed to abnormal increase in T-helper-1 immune response producing proinflammatory cytokines such as interferon-∝, interleukin-12, and monocyte chemotactic protein-1, which are responsible for the recruitment and activation of histiocytes in tissues.[4] Histological picture is a polymorphic granuloma infiltrated with CD68 positive and CD1a negative foamy histiocytes with fibrosis or xanthogranulomatosis.[1] BRAF-V600E mutations are seen in 50%–100% of cases, thus, identifying the clonal nature of the disorder and its association with the Ras-Raf-MEK-ERK pathway.[5]

Skeletal involvement is more frequent (96%), therefore, bone pain is the most common symptom during the disease course. There is predilection for appendicular skeletal involvement, especially long bones of lower limbs. Classical radiological findings include sclerotic and osteolytic lesions with bilateral symmetrical involvement of

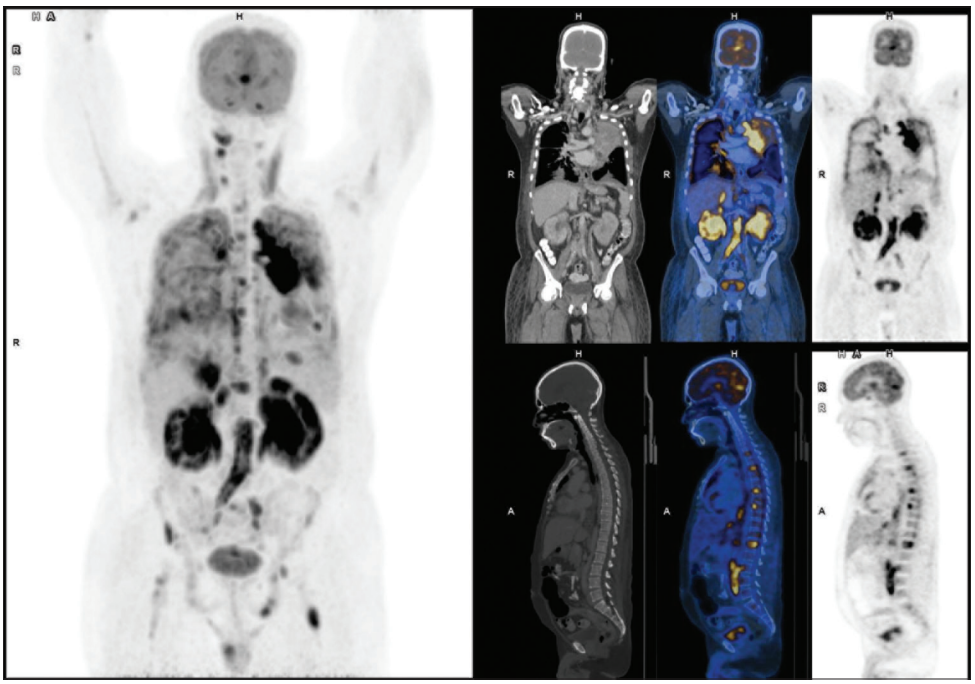

Figure 1: Maximum intensity projection image of fluorine-18-labeled fluorodeoxyglucose positron emission tomography with computed tomography showing left perihilar mass with extensive multisystemic disease involvement. CT, PET/CT fusion, and PET images in coronal (first row) and sagittal (second row) sections showing extensive multisystemic lesions with visualization of hairy kidney sign, coated aorta sign, and multiple FDG avid lytic skeletal and bone marrow lesions

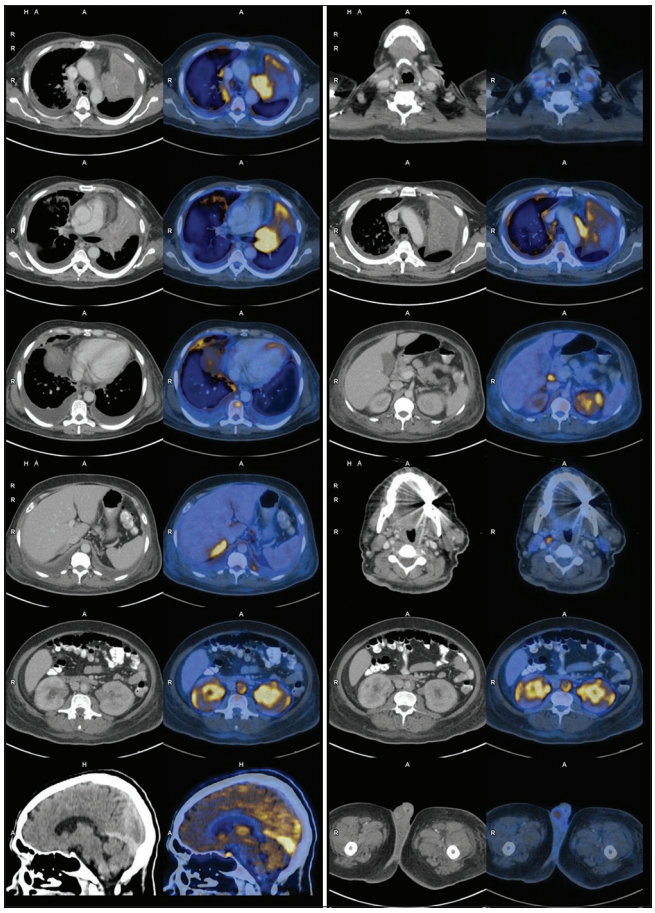

Figure 2: Axial sections of computed tomography and positron emission tomography fusion images illustrating fluorodeoxyglucose (FDG) avid enhancing left perihilar mass in thorax involving left upper lobe bronchus, diffuse bilateral pleural thickening, bilateral pleural effusion, cervical, mediastinal, and abdominal lymph nodes, and peritoneal deposit along segment 7 of the liver, ill-defined hypodense lesions in bilateral renal parenchyma with perinephric soft-tissue thickening and stranding, meningeal deposit, focal wall thickening of the right common carotid artery, symmetrical wall thickening of infrarenal abdominal aorta, and FDG uptake in the right testis

metaphysis and diaphysis, sparing the epiphysis, and axial skeleton.[4] Conventional F-18 FDG PET/CT imaging from head to mid-thigh tends to miss the skeletal involvement. Hence head-to-toe imaging of F-18 FDG PET/CT is must when clinical suspicion of ECD is present. In our case, conventional head to mid-thigh acquisition was performed since the working diagnosis was tuberculosis versus malignancy.

Extraskeletal involvement is seen in around 50% of cases, commonly affecting central nervous and cardiovascular systems, lung, aorta, retroperitoneum, and orbit. Unusual sites of involvement including skin, breast, lymph nodes, thyroid gland, testis, and visceral organs have also been reported.[4] The site and extent of extraskeletal involvement determine the prognosis in ECD. Our case had multiple extraosseous sites of disease involvement, among which were "coated aorta sign" (circumferential periaortic plaque-like soft tissue) and "hairy kidney sign" (perirenal

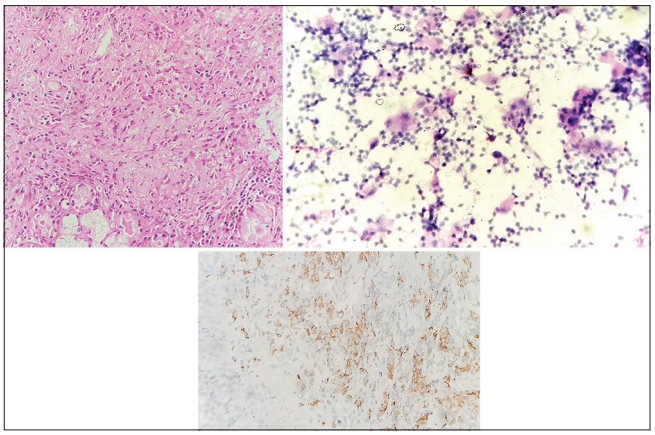

Figure 3: Bronchial biopsy showing histiocytes (H and E stain, ×100), transbronchial needle aspiration smear showing foamy histiocytes (Pap stain, ×100), and immunohistochemistry showing CD68 positivity in histiocytes (×100)

fat infiltration with spiculated appearance) aided toward diagnosis of ECD.[6]

Kirchner *et al*., in a prospective study in 50 patients reported the potential utility of F-18 FDG PET/CT in ECD. They observed that F-18 FDG PET/CT augments the evaluation of disease extent and increases the identification of disease sites.[7] It also aids in selecting appropriate area for biopsy when extraskeletal involvement is prominent.

The treatment includes administration of corticosteroids, immunosuppressants such as interferon- and sirolimus, monoclonal antibodies such as tocilizumab and tyrosine kinase inhibitors like vemurafenib.[8] F-18 FDG PET/CT is useful in therapy response assessment owing to its ability to quantify tracer uptake.

Our case emphasizes the utility of F-18 FDG PET/CT in the assessment of disease extent in ECD including skeletal and extraskeletal involvement and its role in identifying appropriate biopsy site for tissue diagnosis. It also highlights the importance of head-to-toe scan acquisition owing to its predilection to appendicular skeleton, not to miss the involved skeletal sites which assist in diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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