Case Series

Splenic and lymph nodal involvement in sarcoidosis mimicking lymphoma on fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography

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ABSTRACT

Sarcoidosis is a multisystemic disease presenting with well-defined, bilateral, symmetric hilar and right paratracheal lymph node enlargement. Recently, fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) has been used to stage and detect occult site of active inflammation in sarcoidosis. F-18 FDG PET/CT has become a cornerstone imaging modality in the modern lymphoma management, which can present with generalized lymphadenopathy including mediastinal. We present a case series, which shows how sarcoidosis can be a "great mimic of lymphoma" on F-18 FDG PET/CT and how histopathology is essential in diagnosing sarcoidosis and ruling out lymphoma.

Keywords: Fluorine-18 fluorodeoxyglucose, lymphadenopathy, lymphoma, positron emission tomography/computed tomography, sarcoidosis

INTRODUCTION

Sarcoidosis is a multisystem chronic inflammatory condition of unknown etiology characterized by noncaseous epithelioid cell granulomas. Sarcoidosis can involve any organ but, bilateral well-defined, symmetric hilar and right paratracheal lymph nodes enlargement is the most common finding. Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) is now established as a valuable tool for staging, prognostication, radiotherapy planning and response evaluation in several subtypes of lymphoma. F-18 FDG PET/CT has an accuracy of almost 100% in diagnosing primary splenic involvement during initial staging which can either present as diffusely increased FDG uptake greater than that in the liver and bone marrow or as multiple focal areas of intense FDG accumulation with or without corresponding CT lesions. Liver involvement secondary to the lymphoma presents as patchy foci of FDG uptake originating in the portal areas, with higher standardized uptake values (SUV) than those of the surrounding parenchyma. In most cases of secondary hepatic involvement, the spleen is also infiltrated by lymphoma. In the present study, we present four cases of sarcoidosis with spleen and/or hepatic FDG positivity suggesting lymphomatous involvement in the PET/CT.

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CASE REPORTS

Four adults, three females and one male with an age range of 45–58 years are described in the study. Characteristics of these patients are given in Table 1.

Case 1

A 58-year-old male presented with dry cough, generalized weakness, and maculopapular rashes on the extremities for 3 months. General physical and systemic examination did not yield any abnormalities. Complete hemogram and erythrocyte sedimentation rate (ESR) were within normal limits. Serum angiotensinogen converting enzyme (ACE) level was elevated.

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Table 1: Demographic and clinical features of all patients

Case number	Clinical presentation	Age	Sex	Serum ACE levels	PET/CT: Lymph nodal sites	Organ effected	SUVmax of the lymph node	TST test
1	Dry cough, generalized weakness and maculopapular rash since 3 months	58	Male	Raised	Cervical and mediastinal	Spleen	Right lower paratracheal 4.7	Negative
2	Fever, anorexia and dry cough since 1-month	46	Female	Raised	Cervical, mediastinal and abdominal and pelvic lymphadenopathy	Spleen	Left hilar 17.1	Negative
3	Dry cough and shortness of breath since 1-month	45	Female	Not available	Cervical, mediastinal and abdominal and pelvic lymphadenopathy	Spleen	Subcarinal 7.1	Negative
4	Dry cough, significant weight loss and fever on and off since 3 months	56	Female	Raised	Cervical, mediastinal, abdominal and pelvic lymphadenopathy	Liver and spleen	Right hilar 4.2	Negative

PET/CT: Positron emission tomography/computed tomography, TST: Tuberculin skin test, ACE: Angiotensinogen converting enzyme, SUV: Standardized uptake values

Tuberculin skin test (TST) was negative. A chest radiograph revealed mediastinal lymphadenopathy. F-18 FDG PET/CT showed FDG avid cervical and mediastinal lymphadenopathy. Maximum standardized uptake values (SUVmax) of the spleen, liver and right lower paratracheal lymph node were 7.6, 4.0 and 4.7 respectively [Figre 1a - maximum-intensity-projection (MIP) image]. Diffusely increased FDG uptake was noted in the normal sized spleen which showed no morphological changes in the CT [Figure 1b - transaxial fused, 1c - transaxial CT]. Based on the clinical and imaging findings on PET/CT a provisional diagnosis of lymphoma was made. Skin biopsy showed noncaseating compact epithelioid cell granulomas in the dermis [Figure 1d - photomicrograph, H and E, ×200] and stain for acid fast bacilli was negative. A diagnosis of sarcoidosis was made, and oral prednisolone (0.7 mg/kg/day) was started and after 1-month of therapy patient showed a significant decrease in the cough frequency.

Case 2

A 46-year-old female presented with dry cough for 1-month, low-grade fever, and anorexia. General physical did not yield any abnormalities, and systemic examination revealed splenomegaly. Complete hemogram and ESR were within normal limits. Serum ACE level was elevated. TST test was negative. A chest radiograph revealed mediastinal lymphadenopathy. F-18 FDG PET/CT showed FDG avid cervical, mediastinal, abdominal and pelvic lymphadenopathy. SUVmax of spleen, liver and left hilar lymph node were 16.1, 3.1 and 17.1 respectively [Figure 2a - MIP image]. Diffusely increased FDG uptake was noted in the enlarged spleen [Figure 2b - transaxial fused, 2c - transaxial CT] suggesting that splenic uptake might be lymphomatous in view of the FDG avid lymphadenopathy. Provisional diagnosis of lymphoma was made. Subsequently the patient underwent endobronchial ultrasound-transbronchial needle aspiration from the paratracheal lymph nodes as well as endobronchial and transbronchial lung biopsies, all of which showed noncaseating compact epithelioid cell granulomas with foreign body giant cells in the peribronchial interstitium [Figure 2d - photomicrograph, H and E, ×200] and stain for acid fast bacilli was negative. A diagnosis of sarcoidosis was made and oral prednisolone was started (0.7 mg/kg/day) and after 2 months the patient symptomatically improved now with no fever, improvement in appetite and decrease in cough frequency.

Case 3

A 45-year-old female presented with dry cough and shortness of breath for 1-month. Complete hemogram was normal, and ESR was raised. General physical and systemic examination did not yield any abnormalities. TST test was negative. A chest radiograph revealed mediastinal lymphadenopathy and subsequent F-18 FDG PET/CT showed FDG avid cervical, mediastinal and abdominal and pelvic lymphadenopathy. SUVmax of spleen, liver, and subcarinal lymph node were 5.7, 2.5 and 7.1 respectively [Figure 3a - MIP image]. Moderate FDG uptake was noted in the entire spleen [Figure 3b - coronal fused, 3c - coronal CT]. Excision biopsy from the cervical lymph node showed noncaseating compact epithelioid cell granulomas in the lymph node [Figure 3d - photomicrograph, H and E, ×200] and stain for acid fast bacilli was negative. A diagnosis of sarcoidosis was made, and the patient was started with oral prednisolone (0.7 mg/kg/day) and is symptomatically improving after 1-month of therapy.

Case 4

A 56-year-old female presented with low-grade on and off fever, dry cough and unintentional significant weight loss for 3 months. Complete hemogram and ESR were within normal limits. Serum ACE level was raised. TST test was negative. F-18 FDG PET/CT showed faintly FDG avid cervical, mediastinal and abdominal lymphadenopathy [Figure 4a - MIP image] and intense FDG uptake was noted in ill-defined hypodense lesions in both the lobes of the liver in the periportal region and spleen. SUVmax spleen, liver, and right hilar lymph nodes were 13.3, 7.5 and 4.2, respectively [Figure 4b - transaxial fused, 4c - transaxial CT]. She underwent endobronchial and transbronchial lung biopsies which showed noncaseating compact epithelioid cell granulomas in the peribronchial interstitium [Figure 4d - photomicrograph,

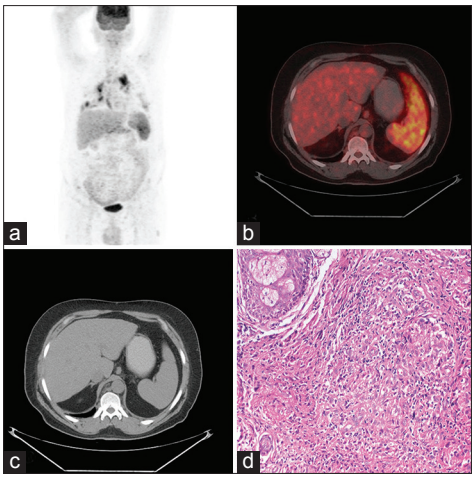

Figure 1: Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (CT) images (a) maximum-intensity-projection showing FDG avid cervical and mediastinal lymph nodes. Transaxial fused and (b) Transaxial CT (c) Increased FDG uptake in the normal sized spleen with no morphological changes in the CT. Photomicrograph (H and E, ×200) of skin biopsy (d) Noncaseating compact epithelioid cell granulomas in the dermis suggesting a diagnosis of sarcoidosis

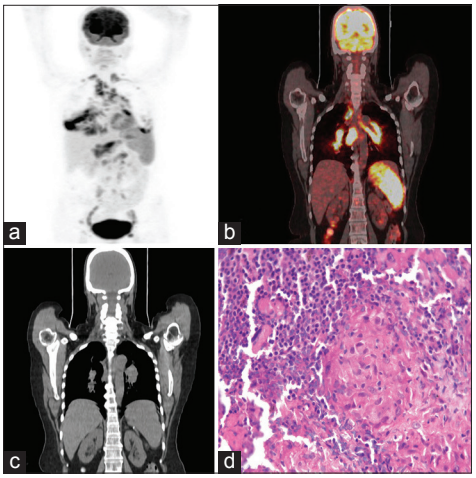

Figure 3: Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (CT) images showing FDG avid cervical, mediastinal and abdominal and pelvic lymphadenopathy on the maximum-intensity-projection image (a) with moderate FDG uptake in the entire spleen (b) coronal fused, (c) coronal CT. Photomicrograph (H and E, ×200) of the excision biopsy from the cervical lymph node shows noncaseating compact epithelioid cell granulomas in the lymph node (d)

H and E, ×200] and stain for acid fast bacilli was negative. A diagnosis of sarcoidosis was made and oral prednisolone (0.7 mg/kg/day) was started and after 4 months patient has shown improvement in symptomatology with increase in weight and complete resolution of cough and fever.

DISCUSSION

The spleen is considered an extra nodal site in NHL and appears to be affected in 20% of patients.[1] Spleen is taken as a nodal organ in Hodgkin's lymphoma and literature shows involvement in 30–40% of cases at presentation.[1]

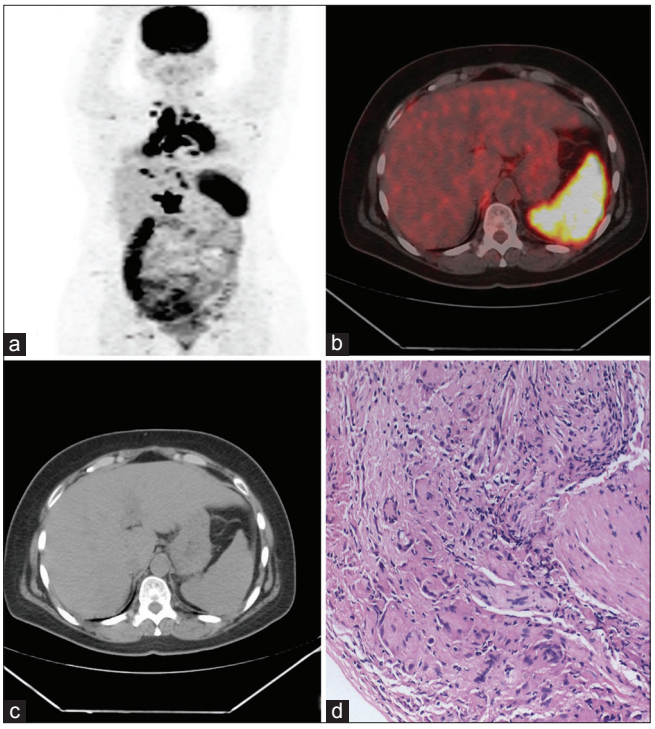

Figure 2: Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (CT) images showing FDG avid cervical, mediastinal, abdominal and pelvic lymphadenopathy on the maximum-intensity-projection image. (a) Transaxial fused (b) and transaxial CT (c) images shows increased FDG uptake in the enlarged spleen. Photomicrograph (H and E, ×200) of the endobronchial ultrasound-transbronchial needle aspiration from the paratracheal lymph nodes (d) show noncaseating compact epithelioid cell granulomas with foreign body giant cells in the peribronchial interstitium

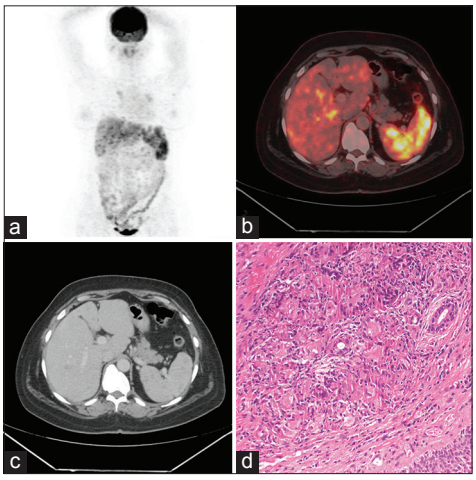

Figure 4: Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (CT) images showing faintly FDG avid cervical, mediastinal and abdominal lymphadenopathy on maximum-intensity-projection image (a) with intense FDG uptake in ill-defined hypodense lesions in both the lobes of the liver in the periportal region and spleen (b) transaxial fused, (c) transaxial CT. Photomicrograph (H and E, ×200) of the lung biopsy shows noncaseating compact epithelioid cell granulomas in the peribronchial interstitium (d)

Lymphomatous involvement of the spleen is considered if the uptake of FDG is more than the liver uptake on F-18 FDG PET scan. Secondary lymphomatous liver involvement

in lymphoma is more common than primary lymphomatous involvement and is said to manifest as small lesions rather than large masses, along with conglomerates of lymph nodes around the porta hepatis and retroperitoneum.[1] Sarcoidosis is a multisystemic granulomatous disease that can involve any organ. Extrapulmonary sarcoidosis occurs in fewer than 5% of cases.[2] Lymphadenopathy is the most common finding in sarcoidosis. Bilateral hilar lymph node enlargement, alone or in combination with mediastinal lymph node enlargement, occurs in an estimated 95% of patients affected with sarcoidosis.[3-5] Histopathology shows noncaseating granulomas although its presence is not definitive[6] of sarcoidosis. Sarcoidosis is known to exhibit lymph nodal SUVs ranging from 2.0 to 15.8. Hence, there might be elevations of SUVs into the "malignant" range in patients with sarcoidosis[7-10] as seen in our cases. This might be attributed to activated macrophages, and lymphocytes that cause increased F-18 FDG uptake. Reported cases of increased splenic FDG uptake include human immunodeficiency virus infection, malaria, infectious mononucleosis, primary splenic lymphoma, congestive splenomegally and therapy with granulocyte colony stimulating factor.[10] Our cases show how lymph nodes, spleen, and liver can be involved in sarcoidosis in patterns similar to lymphoma.

CONCLUSION

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography in sarcoidosis may show increased FDG uptake in the liver and spleen in a pattern which can be mistaken for lymphomatous involvement in lymphoma. These cases highlight the fact that FDG positivity in the spleen or liver in view of generalized lymphadenopathy does not always represents lymphoma.

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