

# Granulomatous Lymphangitis Masquerading as Relapsed Hodgkin Disease on FDG PET/CT

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**Abbreviations:** Fludeoxyglucose (<sup>18</sup>F) positron emission tomography/computed tomography (FDG PET/CT), computed tomography (CT), maximum intensity projection (MIP)

## ABSTRACT

A 38-year-old woman with Hodgkin lymphoma was referred for staging fludeoxyglucose (<sup>18</sup>F) positron emission tomography/computed tomography (FDG PET/CT) that showed widespread intensely FDG-avid disease in multiple nodal stations above the diaphragm and spleen and extranodal involvement in the lungs and vertebral bodies. She underwent chemotherapy and radiotherapy. Progress FDG PET/CT 5 months later showed significant metabolic and anatomic response. Repeat FDG PET/CT 1 month later was highly suspicious of recurrent disseminated FDG-avid lymphoma in multiple nodal stations above and below the diaphragm, spleen, multiple bones, and lungs. Subsequent bone marrow biopsy showed sarcoid-like granulomatous inflammation with no evidence of lymphoma. The patient was clinically well and no active treatment was instituted. Subsequent FDG PET/CT 2 months later showed complete resolution of metabolic activity.

## INTRODUCTION

Fludeoxyglucose (<sup>18</sup>F) (FDG) uptake in positron emission tomography/computed tomography (FDG PET/CT) is based on identifying increased glycolytic activity in malignant cells. Lymphoma is a malignancy that originates in the lymphocytes. FDG-PET/CT has high sensitivity in detecting nodal disease and extranodal in lymphoma (Hodgkin and non-Hodgkin) and is currently the preferred method of staging, assessment of treatment response, restaging, and surveillance. FDG PET/CT has supplanted conventional imaging techniques such as gallium scintigraphy, computed tomography (CT) or magnetic resonance imaging (1).

Nonmalignant processes such as infection, inflammation, and granulomatous disease (such as sarcoidosis or sarcoid-like reaction) can also show high FDG uptake and can mimic a malignant process on FDG PET/CT. Nonmalignant conditions causing FDG uptake in lymph nodes (enlarged or nonenlarged) such as infection and granulomatous disease are not infrequent; however, the coexistence of a malignant disease increases the possibility of lymphadenopathy being malignant in nature (2). The differentiation between malignant and nonmalignant FDG uptake may require histopathological confirmation.

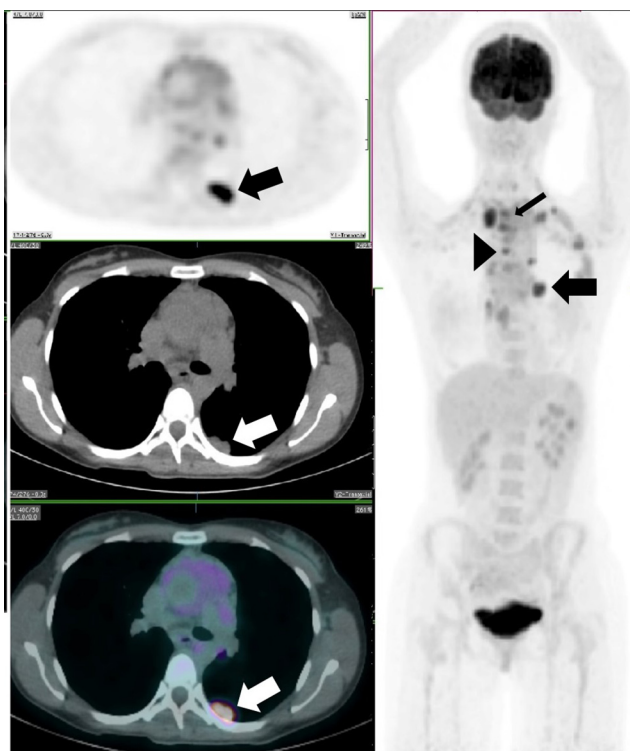
Sarcoid-like reaction has been reported to be associated with malignancy and/or therapy (3). This case highlights the importance of confirming unexpected FDG PET/CT findings with histopathology to avoid unnecessary treatment in nonneoplastic conditions.

## METHODS

A 38-year-old woman presented with lymphadenopathy. Lymph node biopsy confirmed nodular sclerosing Hodgkin lymphoma, and she was referred for staging FDG PET/CT. Intense FDG uptake was seen in multiple nodal stations above the diaphragm and spleen and extranodal involvement in the left lung and in T1, T2, and T5 vertebral bodies (Figure 1).

The patient underwent radiotherapy and 6 cycles of chemotherapy (escalated BEACOP). End-of-treatment FDG PET/CT (5 months following diagnosis) showed significant metabolic and anatomic response in the previously FDG-avid multiple nodal stations above the diaphragm and spleen, but it revealed uptake in the periportal region (Figure 2).

A progress FDG PET/CT 6 months following diagnosis (with no interim treatment) showed widespread FDG-avid uptake in nonenlarged lymph nodes in multiple nodal stations above (hilar lymph nodes, arrowheads) and below the diaphragm, spleen, and multiple bones was highly suspicious of recurrent disseminated FDG-avid lymphoma (Figure 3). The patient was clinically well; the concern about early relapse resulted in bone marrow biopsy that demonstrated sarcoid-like granulomatous inflammation without evidence of Hodgkin disease. Other laboratory tests showed normal corrected calcium level, 2.40 mmol/L (NR, 2.20–2.55); normal angiotensin-converting enzyme, 35 µg/L (NR < 40); autoimmune serology, negative; blood cultures, negative; and blood culture for mycobacteria, negative.



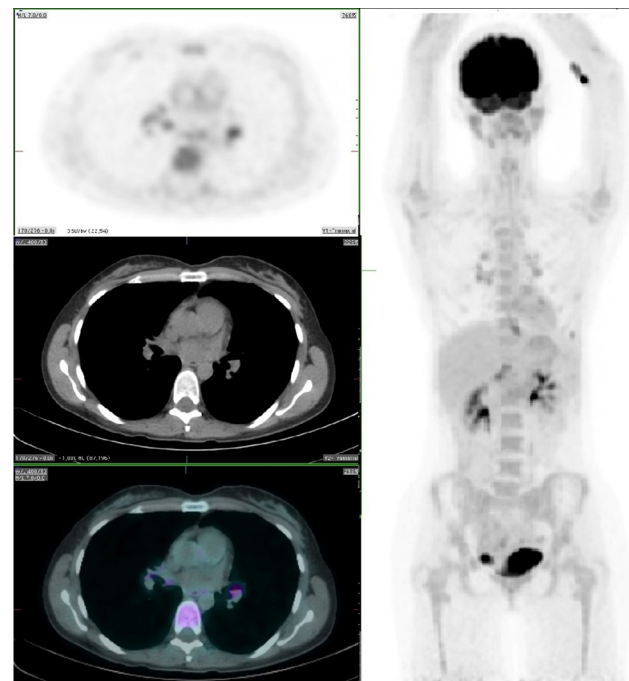
**Figure 1.** The maximum intensity projection (MIP) image showed intense fludeoxyglucose ( $^{18}\text{F}$ ) (FDG) uptake in multiple nodal stations above the diaphragm (arrowhead) and in the spleen and extranodal involvement (thick arrows) in the left lung (axial positron emission tomography [PET], computed tomography [CT] and fused PET/CT images) and in T1, T2, and T5 vertebral bodies (thin arrow).

The patient did not receive any treatment. A further FDG PET/CT 8 months following diagnosis confirmed resolution of uptake in lymph nodes, spleen, and bone (Figure 4).

## DISCUSSION

Granulomatous lymphadenitis is a rare condition and is classified into 2 different groups: noninfectious and infectious. The noninfectious type includes berylliosis, Hodgkin lymphoma, non-Hodgkin lymphoma, lymph node-draining neoplasms (sarcoid-like granuloma), and sarcoidosis. The infectious type can be categorized into suppurative lymphadenitis and nonsuppurative lymphadenitis. Suppurative lymphadenitis occurs in tularemia, cat scratch disease, *Yersinia* lymphadenitis and lymphogranuloma venereum. Nonsuppurative lymphadenitis includes tuberculosis and Bacille Calmette-Guerin (BCG)-lymphadenitis (4, 5).

Sarcoidosis is a disease of unknown origin, with a global incidence of cases 8/100 000. It involves multiple organs, including pulmonary hilar lymph nodes, lungs, eyes, and skin (4). Useful diagnostic tests include demonstration of bilateral hilar lymphadenopathy on X-ray or CT, hypercalcemia, elevated an-



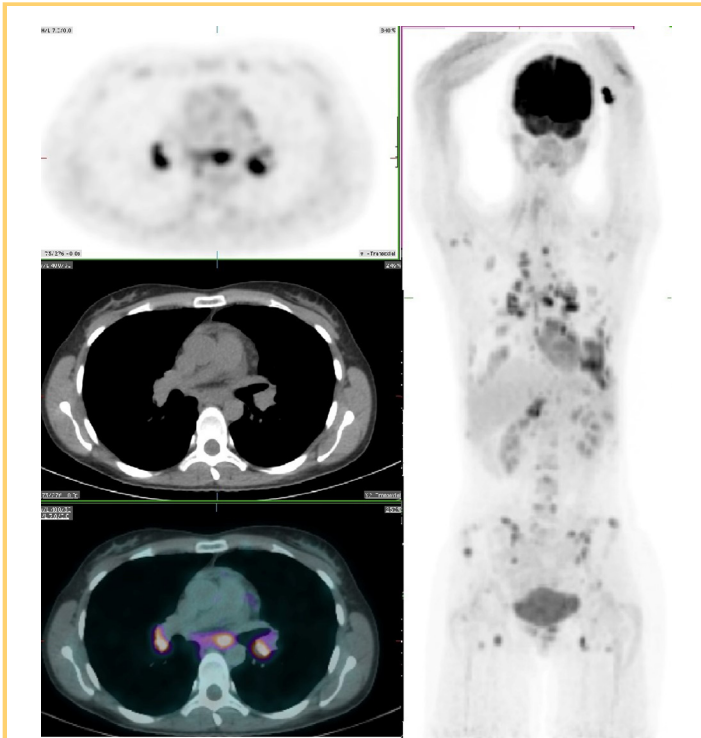
**Figure 2.** MIP and axial PET, CT, and fused PET/CT images of progress PET/CT performed 5 months following diagnosis showed significant metabolic and anatomical response in the previously FDG-avid multiple nodal stations above the diaphragm and in the spleen.

giotensin-converting enzyme level, and negative tuberculin test and histopathology (4).

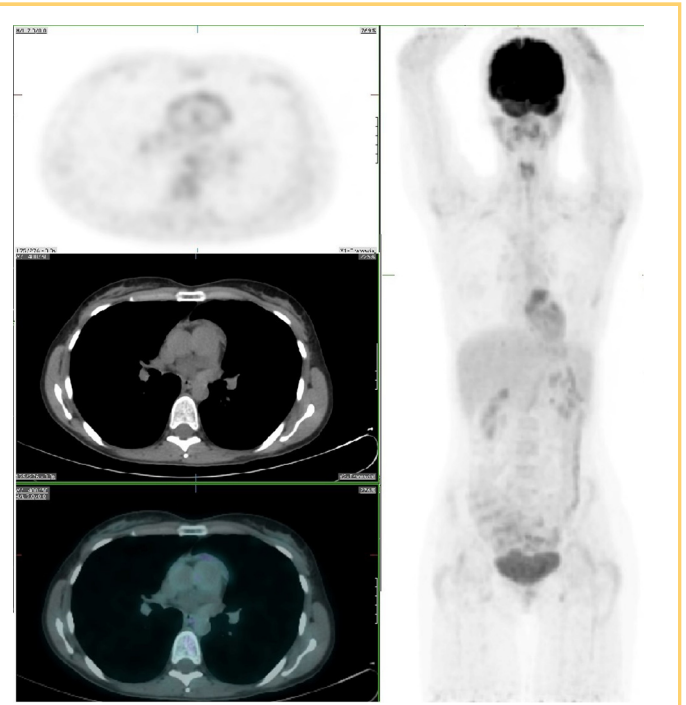
Sarcoid-like reaction refers to the presence of noncaseating granuloma in regional lymph nodes in patients with occult or evident disease without fulfilling the criteria for systemic sarcoidosis (6) and may occur in many solid tumors and draining lymph nodes, such as those draining carcinomas of lung, stomach, uterus, ovaries, and melanoma (7, 8, 9). Sarcoid-like reaction has also been reported in tumors that have been treated with chemotherapy and radiotherapy (10, 11) and in nonregional tissue including bone marrow and spleen (12). The reported incidence is 13.8% of Hodgkin lymphoma and 7.3% of non-Hodgkin lymphomas (12). The clinical symptoms usually depend on the underlying disease. There is no hilar lymphadenopathy on X-ray and the tuberculin test is also negative. A biological defense mechanism in regional lymph nodes against antigens produced by tumor cells is postulated to be the reason for this reaction (13).

Tularemia is a zoonotic infection, a rare, often serious, disease, which affects ~125 people in the USA annually. The average incubation period is 3–5 days. The disease starts with an acute onset of nonspecific symptoms including, fever, anorexia, and general weakness. The diagnosis is confirmed by serology, polymerase chain reaction, and culture (14).

Other infectious types of granulomatous lymphadenitis can be diagnosed with serology, and culture with histopathology of



**Figure 3.** MIP and axial PET, CT, and fused PET/CT images of progress PET/CT 6 months following diagnosis showed widespread FDG-avid uptake in nonenlarged lymph nodes in multiple nodal stations above (hilar lymph nodes arrow-heads) and below the diaphragm, spleen, and multiple bones highly suspicious of recurrent disseminated FDG-avid lymphoma.



**Figure 4.** MIP and axial PET, CT, and fused PET/CT images of the progress PET/CT 8 months following diagnosis confirmed complete resolution of the widespread lymph node uptake with virtual complete metabolic response in all the nodal stations, spleen, and the skeleton.

the lymph node may be helpful (4). The distribution is variable with cat scratch disease and tularemia usually involving the cervical and axillary nodes, while *Yersinia lymphadenitis* in-

volves mesenteric nodes and lymphogranuloma venereum the inguinal nodes (4).

## CONCLUSION

This case illustrates the importance of confirming unexpected PET/CT findings with histopathology in avoiding unnecessary toxic treatment in non-neoplastic conditions.

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