

# F-18 Fluorodeoxyglucose and F-18 Fluorothymidine Positron Emission Tomography/Computed Tomography Imaging in a Case of Neurosarcoidosis

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**Purpose:** F-18 fluorothymidine (FLT) PET/CT is considered more specific for malignancy than F-18 fluorodeoxyglucose (FDG) PET/CT. This case report presents F-18 FLT and F-18 FDG scans of a patient with neurosarcoidosis.

**Materials and Methods:** We describe a 34-year-old man who presented with myelopathic symptoms and signs. The patient's evaluation included serological tests for systemic autoimmunity, CSF analysis, magnetic resonance imaging of the spinal cord and brain, abdominal CT, whole-body F-18 FDG and F-18 FLT PET/CT, and high-resolution chest CT. The patient finally underwent transbronchial mediastinal lymph node biopsy for definite diagnosis.

**Results:** The neurologic symptoms were relapsing and remitting. Magnetic resonance imaging demonstrated corresponding abnormal lesions in the spinal cord. Under a tentative diagnosis of multiple sclerosis, the patient was treated with beta-interferon, which showed no beneficial effect. Abdominal CT for evaluation of unexplained abdominal discomfort revealed abdominal lymphadenopathies. F-18 FDG PET/CT showed multiple symmetrical intense accumulations of F-18 FDG on mediastinal and abdominal lymph nodes, whereas only faint to mild F-18 FLT accumulations were observed. Biopsy of mediastinal lymph nodes indicated nontuberculous granulomatous disease. A final diagnosis of neurosarcoidosis was made, and his clinical symptoms and signs were markedly improved by immunosuppressive treatment.

**Conclusions:** Multiple F-18 FDG-avid lymphadenopathies with mild F-18 FLT uptake can be characteristic findings of sarcoidosis. The combination of F-18 FDG and F-18 FLT PET/CT can be helpful in differentiating granulomatous inflammatory diseases such as neurosarcoidosis from malignancy and in localizing the most appropriate biopsy site of active sarcoidosis.

**Key Words:** F-18 FDG, F-18 FLT, PET/CT, neurosarcoidosis, mediastinum

(*Clin Nucl Med* 2010;35: 67–70)

Sarcoidosis is a condition of unknown cause characterized by granulomas in various tissues and can involve the central nervous system. Neurosarcoidosis accounts for approximately 5% to 16% of systemic sarcoidosis cases.<sup>1</sup> The most common symptoms are attributed to cranial nerve involvement. Involvement of the spinal cord, while recognized, is rare and can lead to abnormal sensation or weakness in one or more limbs, or cauda equina symptoms.<sup>2</sup>

Here, we report a 34-year-old man with recurrent myelopathy. The initial workup was interpreted as multiple sclerosis. However, mediastinal and abdominal lymphadenopathies were detected on CT. Subsequent F-18 fluorodeoxyglucose (FDG) and F-18 fluo-

rothymidine (FLT) PET/CT provided supplementary information for the diagnosis of neurosarcoidosis. We describe the F-18 FLT and F-18 FDG scans in this case of neurosarcoidosis.

## CASE REPORT

A 34-year-old white man was evaluated for paresthesia, hyperalgesia, and band-like chest tightness at the T3–T4 dermatome. Magnetic resonance imaging (MRI) of the spine showed a subtle linear T2 hyperintense lesion at the T1–T3 level of the spinal cord (Fig. 1A). Serological studies for systemic autoimmunity, including rheumatoid factor and antinuclear, anti-dsDNA, anti-SSA/SSB, and antiphospholipid antibodies, showed no abnormalities. The cerebrospinal fluid (CSF) analysis was within the normal range. The IgG index was 0.46, and oligoclonal bands were absent. Under a diagnosis of inflammatory myelitis, high-dose intravenous methylprednisolone (1 g/d) was administered for 5 days, after which his symptoms were relieved.

Seven months later, he developed numbness and weakness in both legs, followed by difficulty in urination. He also complained of facial numbness, diplopia, buzzing in the ears, and abdominal bloating. Spinal cord MRI showed a newly developed lesion at C7–T1 (Fig. 1B), which was later extended from C2 to T4 with spotty enhancement at T1 and T3 on a follow-up scan (Figs. 1C, D). Brain MRI showed a few tiny T2 hyperintense lesions in the deep white matter. A CSF study revealed mild lymphocytosis (17/mm<sup>3</sup>). A second round of steroid pulse therapy was performed, and his symptoms were partially alleviated. Based on the clinical, serological, CSF, and MRI findings, multiple sclerosis was suspected, and disease modifying therapy using beta-interferon was started. However, the weakness in both lower extremities slowly progressed for 7 months, with continued relapse and remission.

In addition to his neurologic problems, the patient complained of unexplainable abdominal discomfort for 5 months. We performed abdominal CT, which revealed multiple abdominal lymphadenopathies. He had a family history of malignant lymphoma. F-18 FDG PET/CT was performed to differentiate between malignant and nonmalignant lymphadenopathies. It showed multiple intense F-18 FDG accumulations in both supraclavicular lymph nodes; the paratracheal, mediastinal, bilateral hilar, internal mammary, cardiophrenic, porta hepatis, paraaortic, and aortocaval lymph nodes; both pelvic lymph nodes; and both inguinal lymph nodes (Figs. 2A, B). There was no abnormal FDG accumulation on the spinal cord and the brain. Non-enhanced CT images showed multiple disseminated micronodular lesions in the lung parenchyma with faint FDG accumulation. Systemic diseases, involving the lymphatic system, such as lymphoma, diffuse metastatic, or granulomatous diseases, and mycobacterial infection, were suspected. Aspiration biopsy of the supraclavicular lymph nodes with intense FDG uptake was not diagnostic. Before deciding the next biopsy site, we performed F-18 FLT PET/CT 10 days after FDG PET/CT to assess the proliferative activity of the lesions and also performed high resolution chest CT (HRCT) for further evaluation of pulmonary parenchyma and medias-

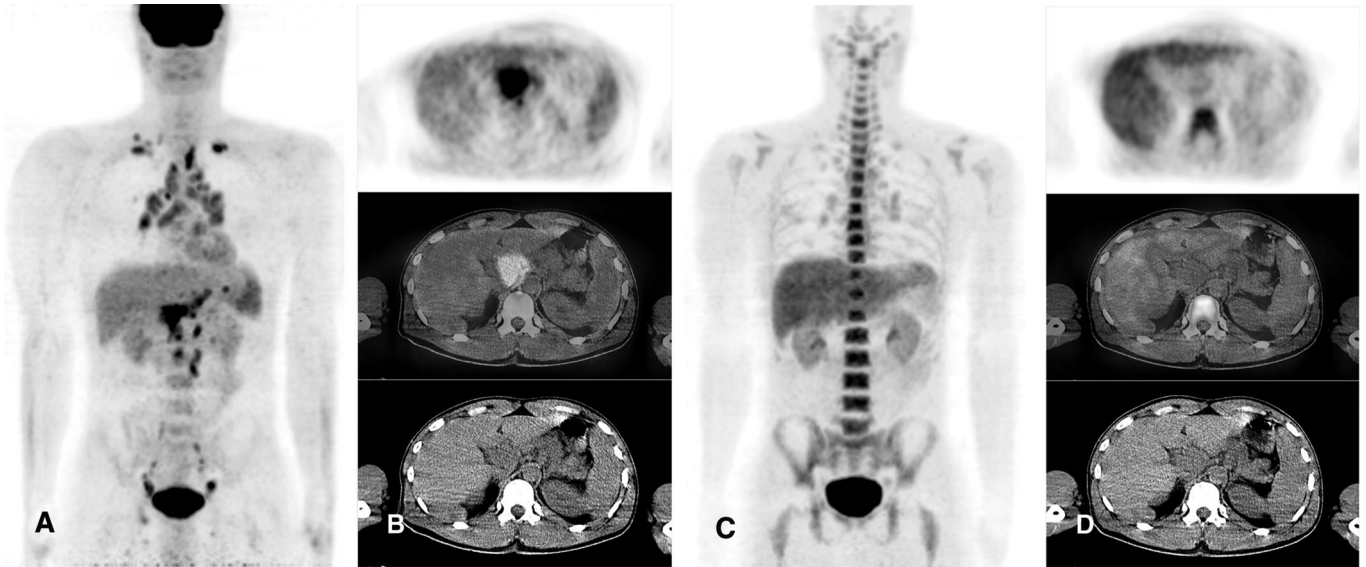
Received for publication May 12, 2009; revision accepted October 8, 2009.  
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ISSN: 0363-9762/10/3502-0067



**FIGURE 1.** MRI of the spinal cord. Sagittal T2-weighted image showed a subtle linear T2-hyperintense lesion at the T1–T3 level of the spinal cord (A). Follow-up MRI performed 3 months later showed another T2-hyperintense lesion at C7–T1 (B). The lesion extended from C2 to T4 on a follow-up scan performed 5-months later (C). A spotty enhancement was noted at T1 and T3 on sagittal gadolinium-enhanced T1-weighted image (D).



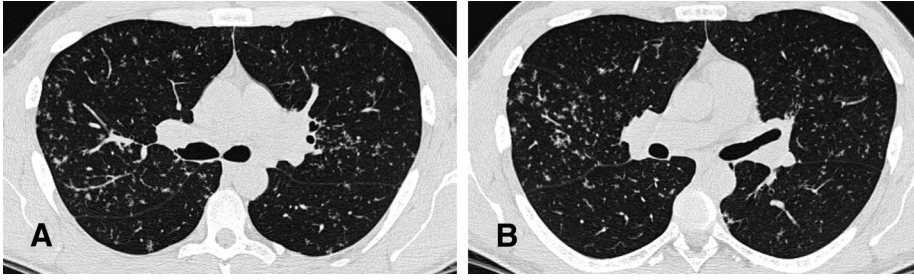
**FIGURE 2.** F-18 FDG and F-18 FLT PET/CT at the active stage of sarcoidosis. F-18 FDG PET/CT demonstrated multiple intense accumulations in both supraclavicular lymph nodes; the paratracheal, mediastinal, bilateral hilar, internal mammary, cardiophrenic, porta hepatis, paraaortic, and aortocaval lymph nodes; both pelvic lymph nodes; and both inguinal lymph nodes (A, B). Maximum standardized uptake value of lymph nodes in F-18 FDG PET ranged from 4 g/mL to 13 g/mL. The F-18 FLT uptake was much lower than that of F-18 FDG in the F-18 FDG-avid lesions (C, D).

tinal lymph nodes. The uptake of F-18 FLT was much lower than that of F-18 FDG (Figs. 2C, D). Neither spinal cord nor brain showed abnormal FLT uptake. HRCT showed parenchymal lesions of multiple disseminated micronodules along the peribronchovascular bundle and in the subpleural area around the fissure in both lungs (Fig. 3).

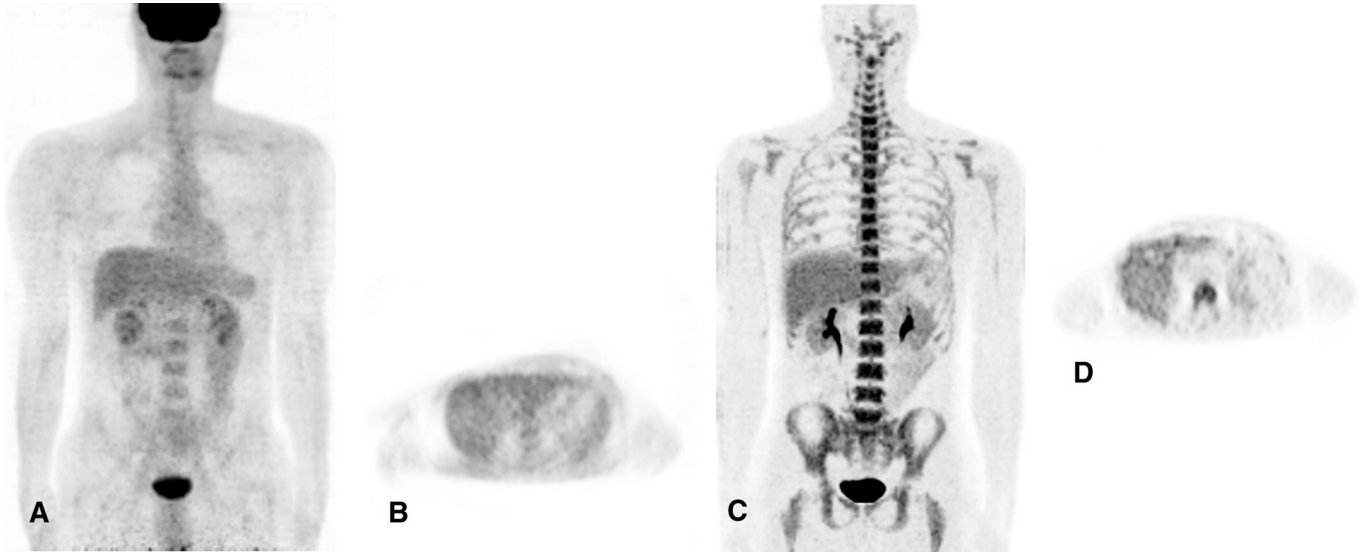
Based on the combination of the F-18 FDG PET/CT, F-18 FLT PET/CT, and HRCT findings along with the clinical history, sarcoidosis, or miliary tuberculosis was suspected. The serum an-

giotension converting enzyme level was elevated (79 U/L). Sputum AFB was negative. A transbronchial lymph node biopsy of a mediastinal lymph node, which showed intense F-18 FDG uptake and mild F-18 FLT uptake, revealed chronic non-necrotizing granulomatous inflammation compatible with sarcoidosis.

The diagnosis was changed from multiple sclerosis to neurosarcoidosis. The patient was treated with high-dose steroid followed by a combination of mycophenolate mofetil and low-dose pred-



**FIGURE 3.** High-resolution chest CT. HRCT showed multiple small centrilobular pulmonary nodules along the peribronchovascular bundle and subpleural area (A, B).



**FIGURE 4.** F-18 FDG and F-18 FLT PET/CT at the resolved stage of sarcoidosis. F-18 FDG (A, B) and F-18 FLT PET/CT (C, D) showed no abnormal accumulations.

nisolone, and his symptoms showed marked improvement. Over the 22 months of follow-up, there was no disease activity on brain or spinal cord MRI or on chest CT. Follow-up F-18 FDG and F-18 FLT PET/CT also showed no abnormal F-18 FDG or F-18 FLT accumulation, which indicated that there was no evidence of active sarcoidosis and that the treatment was effective (Fig. 4).

## DISCUSSION

The diagnosis of neurosarcoidosis is often difficult, as there are no pathognomic diagnostic tests for neurosarcoidosis. In general, this disease has been diagnosed clinically using MRI and lumbar puncture.<sup>3</sup> Only a positive biopsy of suspicious lesions in the brain or elsewhere is considered to be definitive confirmation of the diagnosis of neurosarcoidosis. However, biopsy should be avoided if possible because of the risk involved in approaching the brain or the spinal cord.

Our patient was thought to have multiple sclerosis based on neurologic symptoms and MRI results. However, the disease continued to worsen despite disease-modifying therapy for multiple sclerosis. Unexplainable abdominal lymphadenopathies were found on abdominal CT. Subsequent F-18 FDG PET/CT identified multiple F-18 FDG-avid mediastinal as well as abdominal lymphadenopathies. HRCT showed micronodules compatible with sarcoidosis.<sup>4</sup>

Although F-18 FDG is established and used as an oncological agent,<sup>5</sup> it is also readily taken up in various infectious and inflammatory conditions.<sup>6</sup> Recently, F-18 FDG PET/CT has been used to

aid in the diagnosis and management of sarcoidosis.<sup>7,8</sup> Increased F-18 FDG uptake is well known in active sarcoidosis,<sup>9</sup> and there is a report showing increased F-18 FDG uptake in lymph nodes as well as the spinal cord where there was intense gadolinium enhancement on MRI in a case of neurosarcoidosis.<sup>8</sup> Our patient showed no abnormal uptake in the spinal cord, probably because the scan was performed during a remission period. However, F-18 FDG uptake in sarcoidosis is nonspecific in both intensity and pattern and is not generally useful in making an initial diagnosis. In addition, intense F-18 FDG uptake in lymph nodes and the parenchyma of other organs can be an important mimic of malignancy, specifically of aggressive lymphoma, diffuse metastatic disease, as well as of other active inflammatory lesions.<sup>10</sup> Therefore, there are limitations in differentiating malignancies from active inflammatory or granulomatous disease based solely on F-18 FDG uptake.<sup>11</sup>

F-18 FLT, which is a thymidine analog, has been reported to accumulate stably in proliferating tissues, such as malignant tumors.<sup>12</sup> It has been shown to be useful for the noninvasive assessment of proliferation rates in several types of human cancer, such as lymphoma, colorectal, esophageal, and lung cancers.<sup>13–17</sup> In a rat model, F-18 FLT successfully differentiated tumor from inflammation.<sup>18</sup>

Sarcoidosis has been suggested to be a granulomatous disease with high-turnover characteristics. Specimens from neurosarcoidosis have shown a granuloma rich in epithelioid cells and surrounded by other immune cells (eg, plasma cells and mast cells).<sup>2</sup> Theoretically, F-18 FLT could accumulate in the inflammatory area owing to proliferating inflammatory cells, such as epithelioid cells. However,

in contrast to these speculations, F-18 FLT accumulation was much less than that of F-18 FDG in involved lymphadenopathies. A recent study using H-3 thymidine found mostly low-turnover reactions, and incidentally granulomas with high-turnover characteristics, within the lymph node of a patient with sarcoidosis.<sup>19</sup> Although further studies are required to confirm the beneficial role of F-18 FLT in the differential diagnosis between inflammatory and malignant conditions, low F-18 FLT uptake may exclude aggressive malignant lymphoma, and F-18 FLT PET provides additional diagnostic insights.

## CONCLUSIONS

Multiple F-18 FDG-avid lymphadenopathies with mild F-18 FLT uptake can be characteristic findings of sarcoidosis. The combination of F-18 FDG and F-18 FLT PET/CT can be helpful in differentiating granulomatous inflammatory diseases such as neurosarcoidosis from malignancy and in localizing the most appropriate biopsy site.

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