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CLINICAL CASE SERIES

Dual Time-Point ^{18}F-FDG PET/CT in Spinal Sarcoidosis

A Single Institution Case Series

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Study Design. A case series of dual time-point ^{18}F-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) for the diagnosis of spinal cord sarcoidosis.

Objective. The aim of this study was to illustrate three cases of spinal sarcoidosis with occult presentation and subsequent identification with the use of dual time-point ^{18}F-FDG PET/CT.

Summary of Background Data. Sarcoidosis of the spinal cord is very rare and when it occurs without systemic manifestations of disease can be a challenging diagnostic dilemma frequently resulting in the need for spinal cord biopsy in order to establish a diagnosis.

Methods. Case series presentation and report.

Results. This manuscript presents a case series experience of dual time-point ^{18}F-FDG PET/CT for the diagnosis of spinal cord sarcoidosis. We review the cases of three patients who presented with myelopathy and underwent ^{18}F-FDG DTPI as part of the evaluation for enhancing spinal cord lesions of unknown etiology for 2 years at a university-based cancer hospital. ^{18}F-FDG DTPI was vital in making the diagnosis of sarcoidosis, and in two of the cases, the patients were able to avoid biopsy, thereby avoiding potential morbidity from an invasive procedure.

Conclusion. ^{18}F-FDG PET/CT imaging is a noninvasive imaging technique that can be crucial in the diagnosis of sarcoidosis of the spinal cord and help avoid unnecessary procedures.

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Level of Evidence: 4

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Sarcoidosis is a systemic inflammatory disease characterized by noncaseating granulomatous infiltrates, most commonly involving the lungs and intrathoracic lymph nodes (90%); however, it can affect any organ, with a wide range of clinical and radiological manifestations.[1,2] Spinal cord involvement of sarcoidosis is very uncommon, with an estimated incidence of 0.43% and it is typically a late manifestation of the disease. Very little literature exists addressing spinal cord involvement as a presenting symptom.[3–5] The radiographic and clinical features of spinal neurosarcoidosis are nonspecific and have considerable overlap with those seen in malignancy, infection, and other inflammatory and demyelinating conditions. Given the rarity, isolated spinal neurosarcoidosis is a diagnosis of exclusion, frequently requiring a spinal cord biopsy for confirmation.[6,7]

Dual time-point ^{18}F-fluoro-2-deoxy-D-glucose (^{18}F-FDG) positron emission tomography (PET) imaging (DTPI) is a technique where a second delayed PET/computed tomography (CT) acquisition 5 hours after tracer administration in addition to the standard 1-hour acquisition is acquired. In our case series, we utilize DTPI to demonstrate that increased uptake of ^{18}F-FDG tracer on delayed imaging represents a distinct uptake profile seen in granulomatous disease that can assist in the differentiation from other benign etiologies.[8] The presence of extraspinal sites of uptake, reflecting subclinical sites of disease, can further assist with the diagnosis of sarcoidosis and exclude a primary spinal cord neoplasm.

CLINICAL PRESENTATION

We describe three patients who presented with myelopathy and nonspecific enhancing cord lesions who after evaluation were determined to have spinal sarcoidosis. Due to the retrospective nature of this small case series, informed consent is not required.

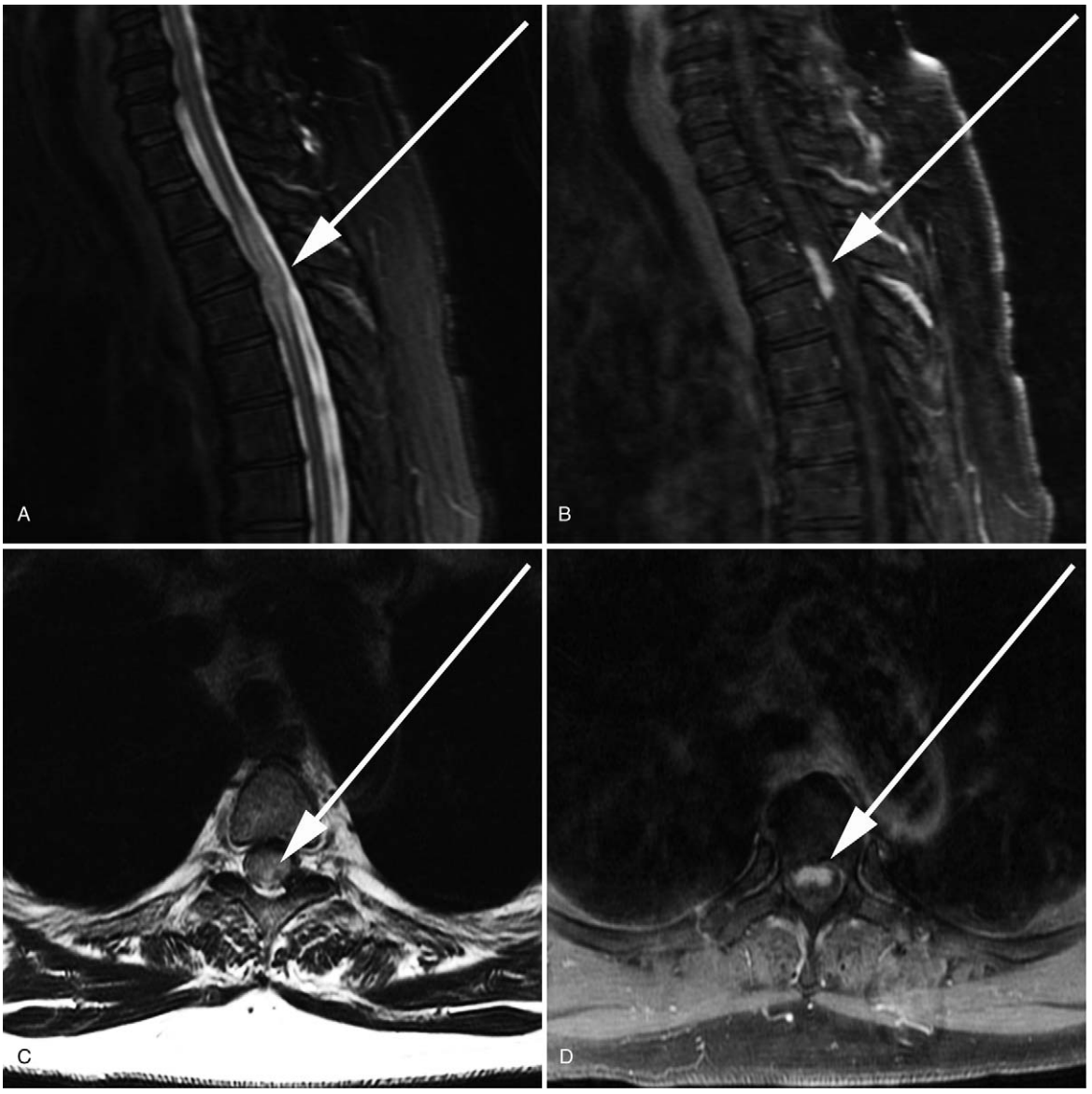

Figure 1. A 69-year-old woman with spinal sarcoidosis who initially presented with lower extremity weakness. MRI of the spine revealed a slightly distended T2 hyperintense abnormality predominantly affecting the ventral aspect of the mid-thoracic spinal cord (**A** and **C**). Postcontrast imaging (**B** and **D**) revealed corresponding irregularly bordered enhancement involving the bilateral ventral aspects of the cord. FDG PET CT anterior projection MIP image of the chest (**E**) displays bilateral hilar and paratracheal hypermetabolic lymph nodes. One-hour post-FDG injection (**F**) PET imaging displays hypermetabolism corresponding to the area of abnormal cord enhancement with a maximum SUV of 4.7. The degree of hypermetabolism significantly increases on 5-hour postinjection imaging with a maximum SUV of 14.0 (**G**).

Case 1

A 69-year-old female came to medical attention with a 5-month history of progressive lower extremities weakness and changes in lower extremities sensation. She was having subjective difficulty standing up and walking, with more than three reported falls. At the time of presentation, the patient was experiencing progressive decline in her functional capacity.

Magnetic resonance imaging (MRI) of the thoracic spine was performed revealing irregularly marginated intramedullary T2 hyperintensity. There was corresponding enhancement along the anterior two-thirds of the spinal cord with involvement of the right greater than left hemicord (Figure 1). The patient underwent a lumbar puncture for cerebrospinal fluid (CSF) testing for oligoclonal bands, culture, viral cultures, and antigens, which were all negative. The leading differential considerations at this time included a high-grade spinal cord tumor or an inflammatory process.

^{18}F-FDG DTPI was performed, which revealed hypermetabolism along the region of abnormal cord enhancement that increased between the initial and delayed time points with maximum standardized uptake value (SUV) of 4.7 and 14.0, respectively. Hypermetabolism was also noted within nonenlarged hilar and paratracheal lymph nodes reflecting subclinical sites of disease (Figure 1). The lungs on the CT portion of the examination were normal.

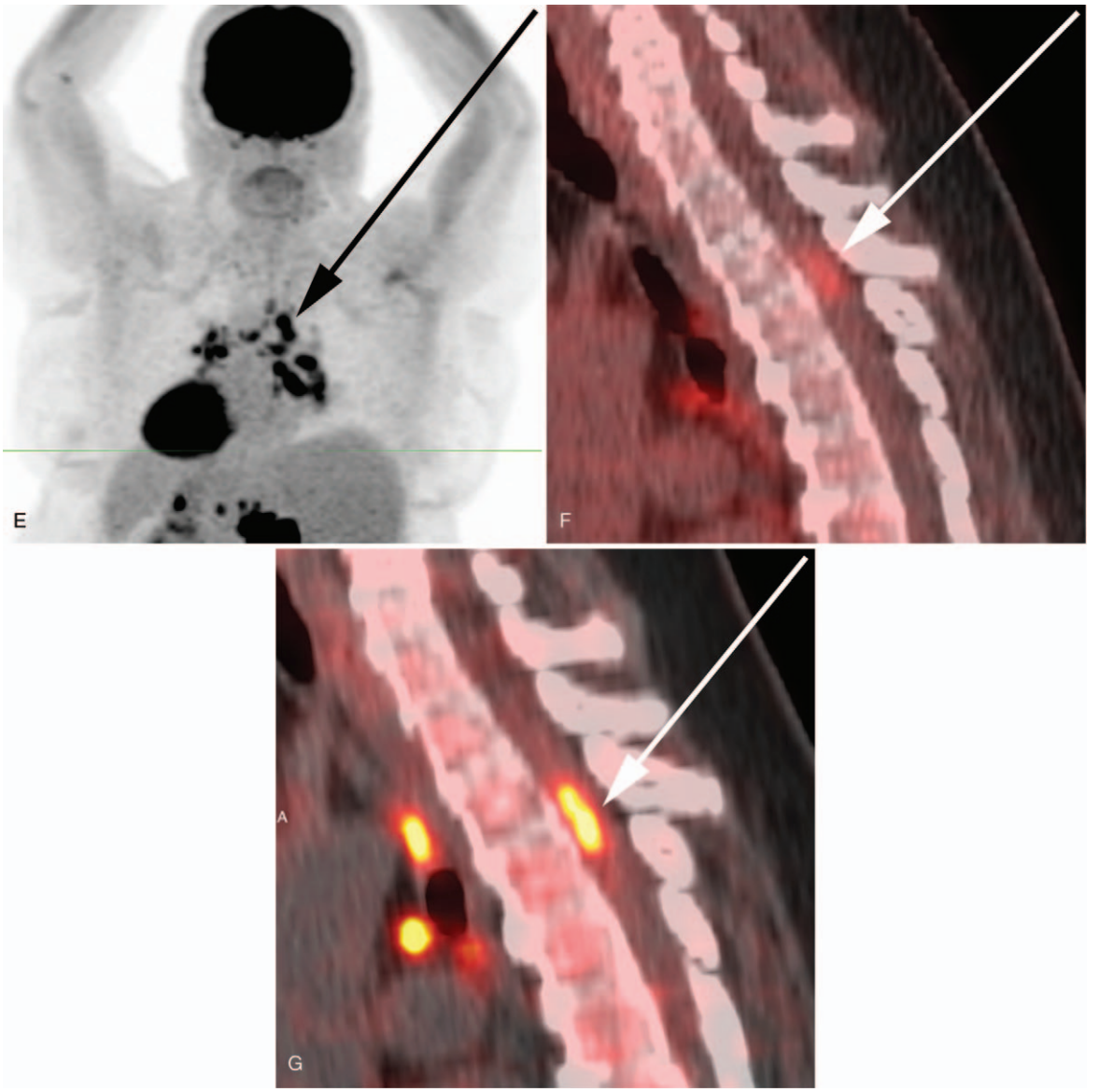

Figure 1. Continued

Case 2

A 52-year-old man presented with a history of numbness and tingling in the hands and feet. An MRI of the spine was performed demonstrating an ill-defined intramedullary cervical cord lesion at C2-C5 with areas of enhancement involving the dorsal cord (Figure 2). The MRI of the brain was normal. The patient was started on oral Decadron. His sensory symptoms improved, but never fully resolved. To make a definitive diagnosis, the patient underwent further evaluation, including two lumbar punctures and blood tests for vitamin B12 deficiency, autoimmune-induced diseases such as vasculitis, syphilis, and a HIV test. CSF analysis showed oligoclonal bands, very mild elevation of protein, and a normal white blood cell count. CSF cytology examination was negative for malignancy. The other tests were noncontributory toward a diagnosis.

A cervical cord biopsy was performed with pathology demonstrating a mixed chronic inflammatory process and gliosis. After the biopsy, the patient was left with right lateral chest, and right lower extremity numbness and tingling, and the patient was again placed on steroids.

^{18}F-FDG DTPI was performed that revealed hypermetabolism along the region of abnormal cord enhancement, which increased between the initial and delayed time points with maximum SUV of 8.0 and 11.1, respectively (Figure 2). Hypermetabolism was identified within nonenlarged hilar and paratracheal lymph nodes, representing subclinical sites of disease involvement. Hypermetabolic areas of pleural thickening were also noted on the DTPI examination, which is a finding that can be seen associated with sarcoidosis.[9] The lung parenchyma was unremarkable.

Case 3

A 46-year-old Caucasian male presented with a history of tingling and numbness of the fourth and fifth finger of bilateral hands and the anterolateral surface of the right

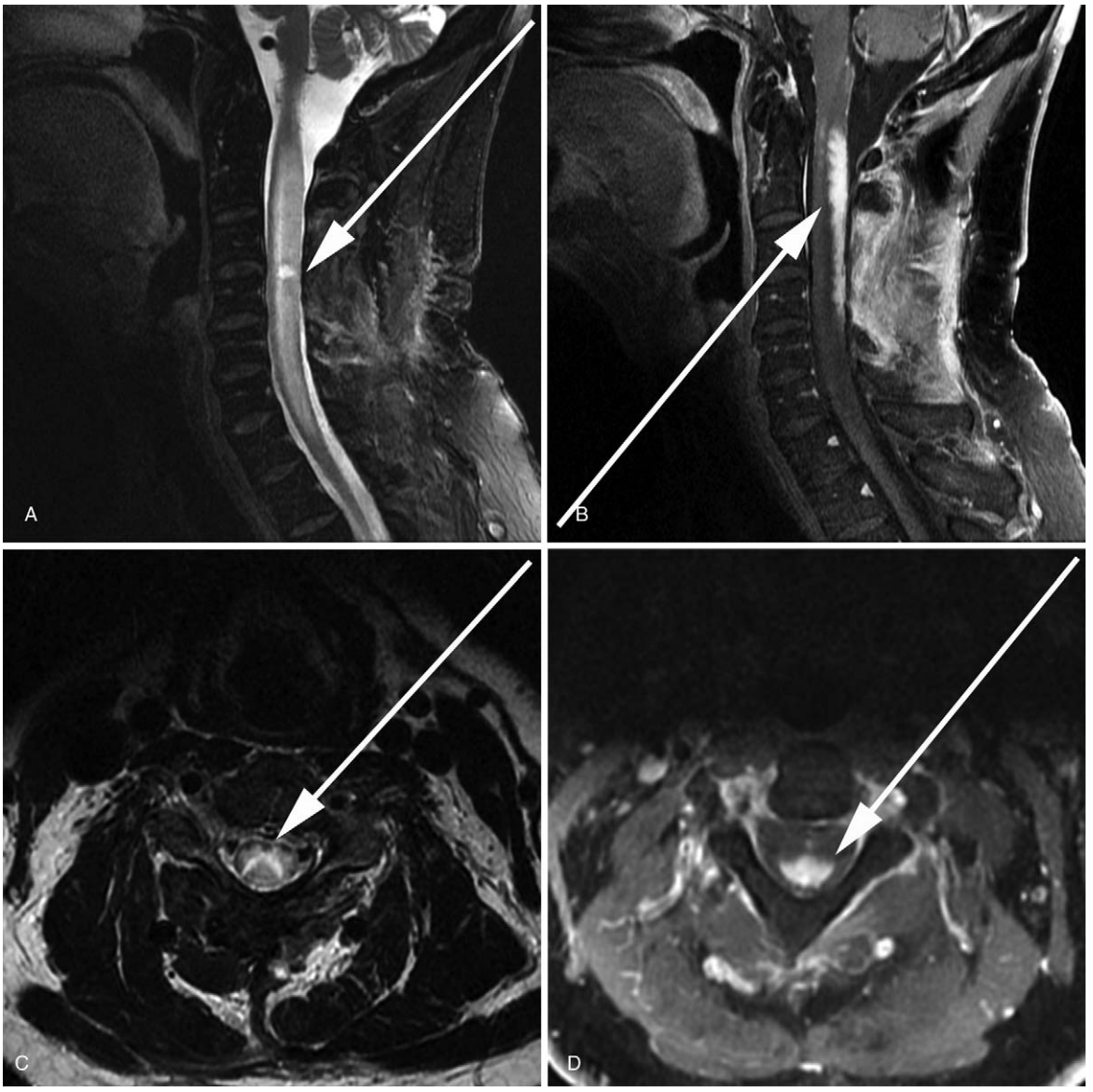

Figure 2. A 52-year-old man with spinal sarcoidosis who initially presented with numbness and tingling of the hands and feet. MRI of the spine revealed a long segment T2 hyperintense abnormality associated with cord dilatation along the entire cervical cord (**A** and **C**). The biopsy site is seen at the C3-4 level (**A**, white arrow). Postcontrast imaging (**B** and **D**) revealed an extended area of irregular bordered contrast enhancement affecting the dorsal aspect of the cord. FDG PET CT anterior projection maximal intensity projection (MIP) image of the chest (**E**) displays bilateral hypermetabolic hilar lymph nodes. One-hour post-FDG injection (**F**) PET imaging displays hypermetabolism corresponding to the area of abnormal cord enhancement with a maximum SUV of 8.0. The degree of hypermetabolism significantly increases on 5-hour postinjection imaging with a maximum SUV of 11.1 (**G**).

leg and left knee. An MRI of the cervical spine was performed. The imaging showed cord expansion associated with an enhancing intramedullary lesion. The lesion was ill-defined, without a sharp margin to the surrounding normal spinal cord and was located dorsally, extending from C5 to C7 (Figure 3). Differential at this time included primary spinal cord neoplasm, inflammatory myelitis, and multiple sclerosis.

^{18}F-FDG DTPI was performed that revealed hypermetabolism along the region of abnormal cord enhancement, which mildly increased between the initial and delayed time points with maximum SUV of 6.1 and 6.4, respectively. Hypermetabolism was also noted within nonenlarged hilar and paratracheal lymph nodes (Figure 3). The lungs on the CT portion of the examination were normal.

DISCUSSION

Sarcoidosis involving the central nervous system (CNS) is rare, but a devastating manifestation of the disease that affects approximately 5% of patients with systemic sarcoidosis[10] and with less than 1% presenting with isolated involvement of the (CNS). Neurosarcoidosis has a wide range of presentations, but it commonly is seen as infiltration and thickening of the leptomeninges with a basilar predilection (40%). The cervical spine is the most common site of involvement in the spine.[7,10] Spinal neurosarcoidosis

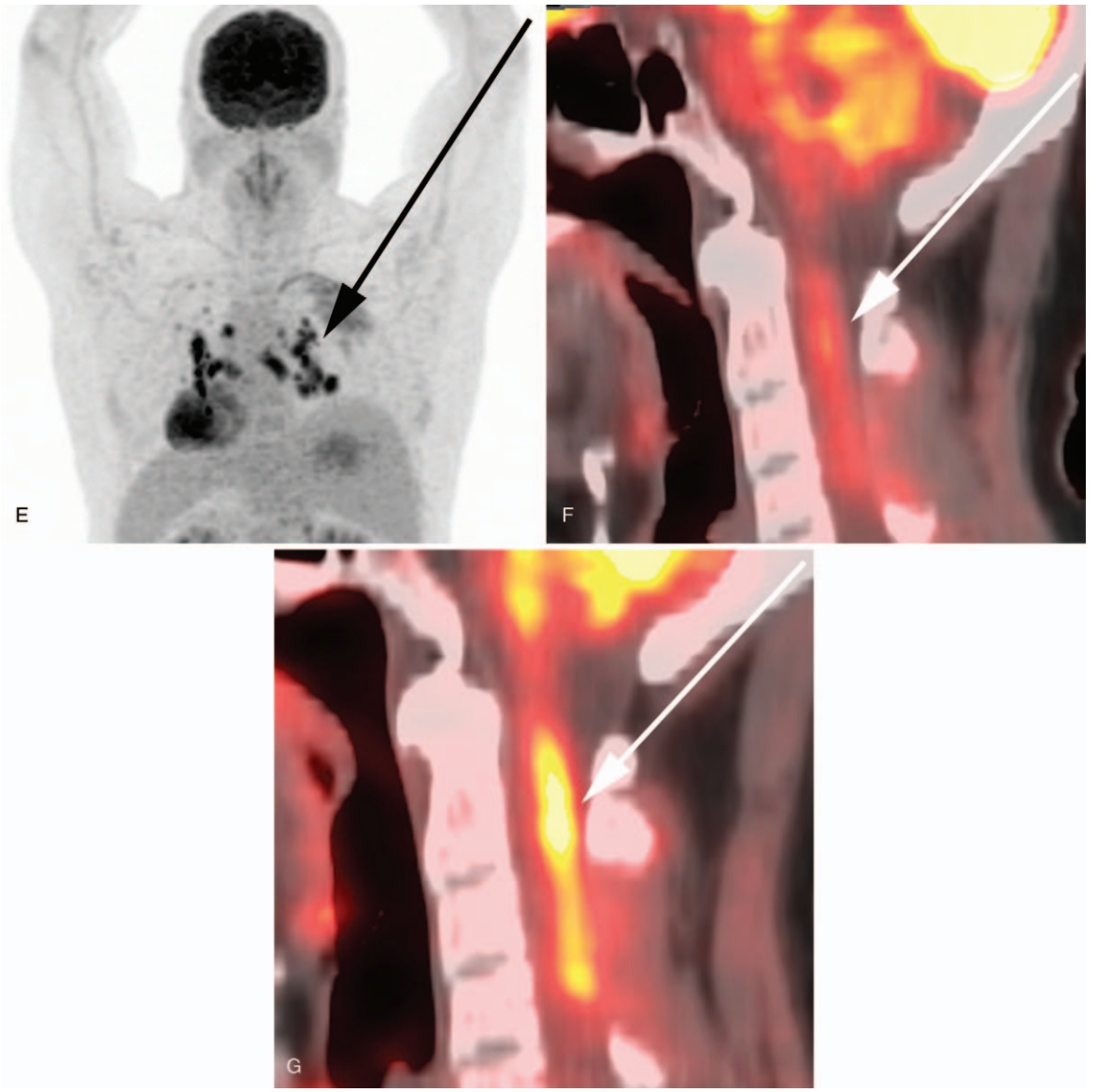

Figure 2. Continued

can present with intramedullary disease involvement (35%) or as leptomeningeal infiltration (60%) or as combinations between the two.[6,10] Symptoms can be very nonspecific with patients presenting with muscle weakness, paresthesias, and hypoesthesia.[6,7,11] The imaging findings reflect the patterns of disease involvement and can range from leptomeningeal enhancement to focal or diffuse spinal cord enlargement with enhancement or even atrophy.[7,12]

Unfortunately, the imaging and clinical presentation of spinal neurosarcoidosis are nonspecific. In addition to MRI of the spine, work-up often includes CT imaging of the chest and abdomen and MRI of the brain to evaluate for systemic disease. Blood and CSF analysis are frequently necessary.[13] Despite exhaustive imaging and laboratory work-up, a subset of patients requires a spinal cord biopsy for definitive diagnosis.[6,7]

[18]F-FDG demonstrates high uptake in inflammatory conditions such as sarcoidosis and is a very sensitive noninvasive method used both for the diagnosis of sarcoidosis, frequently identifying subclinical sites of disease and for follow-up and treatment guidance.[14–17] Despite this, little literature exists about the specific use of [18]F-FDG PET/CT for the evaluation of sarcoidosis affecting the spinal cord.[18]

The differential increase in tracer uptake of lesions on DTPI has previously been described in sarcoidosis and has been used as a surrogate for prognosis with greater differential uptake at a delayed time point associated with a worse prognosis.[19] In the brain tumor literature, increasing uptake on DTPI was seen when imaging primary brain tumors,[20] and it has been used to distinguish viable brain metastases from post-treatment necrosis.[21]

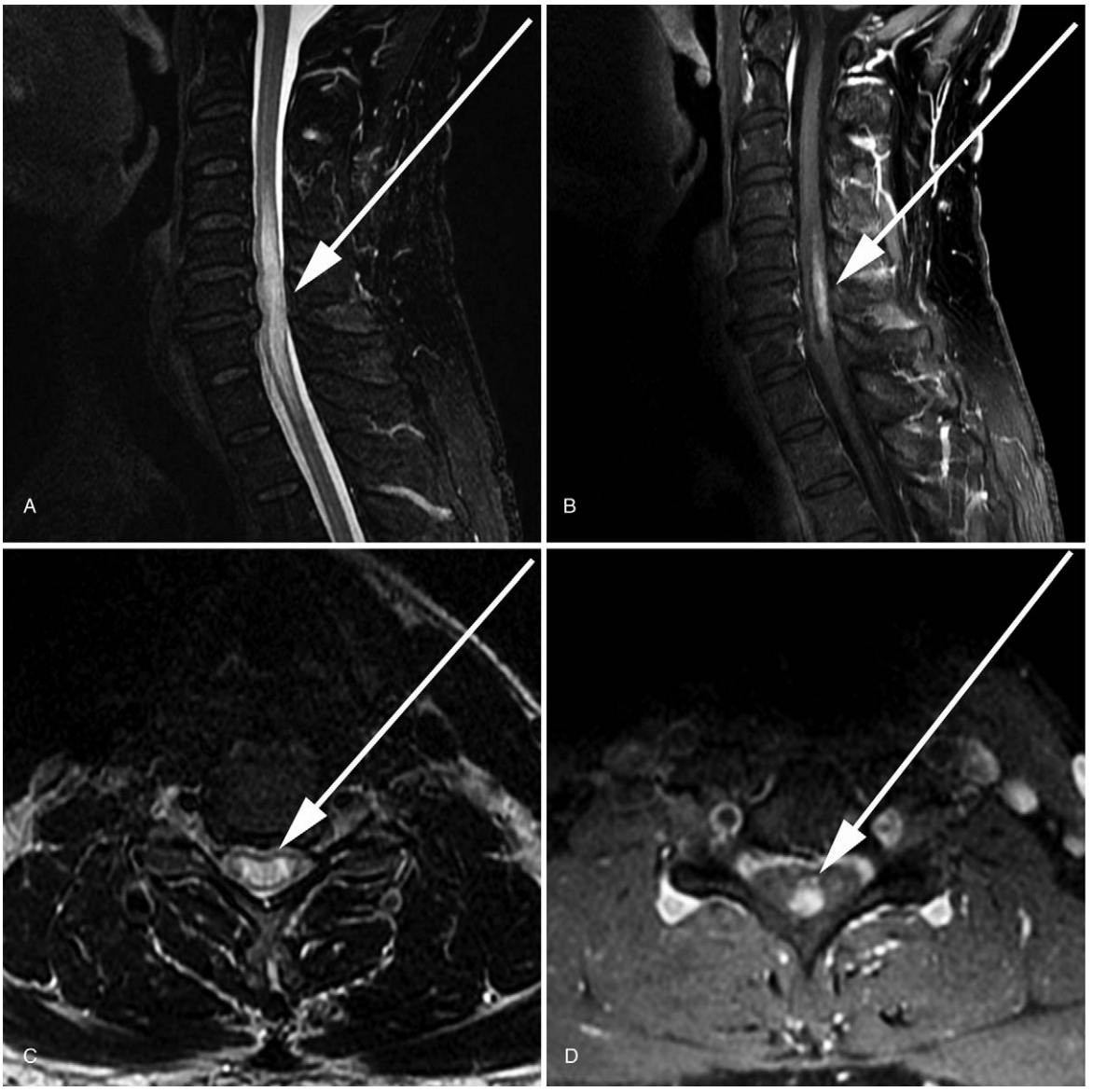

Figure 3. A 46-year-old man who presented with numbness and tingling of the bilateral fourth and fifth fingers. MRI of the spine revealed a T2 hyperintense abnormality with cord distension centered at the C6 vertebral body level (**A** and **C**). A disc protrusion at the C6-7 disc level (**A**, white arrow) was not felt an adequate explanation for the findings. Postcontrast imaging (**B** and **D**) revealed a relatively well-defined area of enhancement involving the central cord. FDG PET CT right posterior oblique projection MIP image of the chest (**E**) displays bilateral hypermetabolic hilar lymph nodes. (**F**) One-hour post-FDG injection PET imaging displays hypermetabolism corresponding to the area of abnormal cord enhancement with a maximum SUV of 6.1. The degree of hypermetabolism increases on 5-hour postinjection imaging compared with the normal appearing spinal cord. The maximum SUV at this time was 6.4 (**G**).

The upregulation of glucose metabolism seen as an increased uptake of ^{18}F-FDG is a nonspecific finding that can be seen in a range of benign infectious and inflammatory conditions.[22] However, increasing uptake of ^{18}F-FDG on DTPI is not a well-described phenomenon in non-neoplastic disease and in particular, not previously described in neurosarcoidosis. In our case series, the presence of concomitant hypermetabolic thoracic sites of systemic involvement in conjunction with the increasing ^{18}F-FDG uptake on DTPI was crucial in suggesting the diagnosis of sarcoidosis. The pattern of a nonspecific FDG avid cord lesions in conjunction with the characteristic FDG avid systemic involvement was decisive in turning the primary diagnostic consideration away from cord neoplasm. Although the distribution of disease outside of the neuroaxis was typical for sarcoidosis, the increasing FDG metabolism between the early and delayed time points for both the cord lesion and the systemic disease has not been previously described. This pattern is important to recognize, as systemic disease in sarcoidosis may be variable and a less stereotypic presentation of systemic disease could be misinterpreted as malignancy based on the increasing metabolism between early and delayed time points.

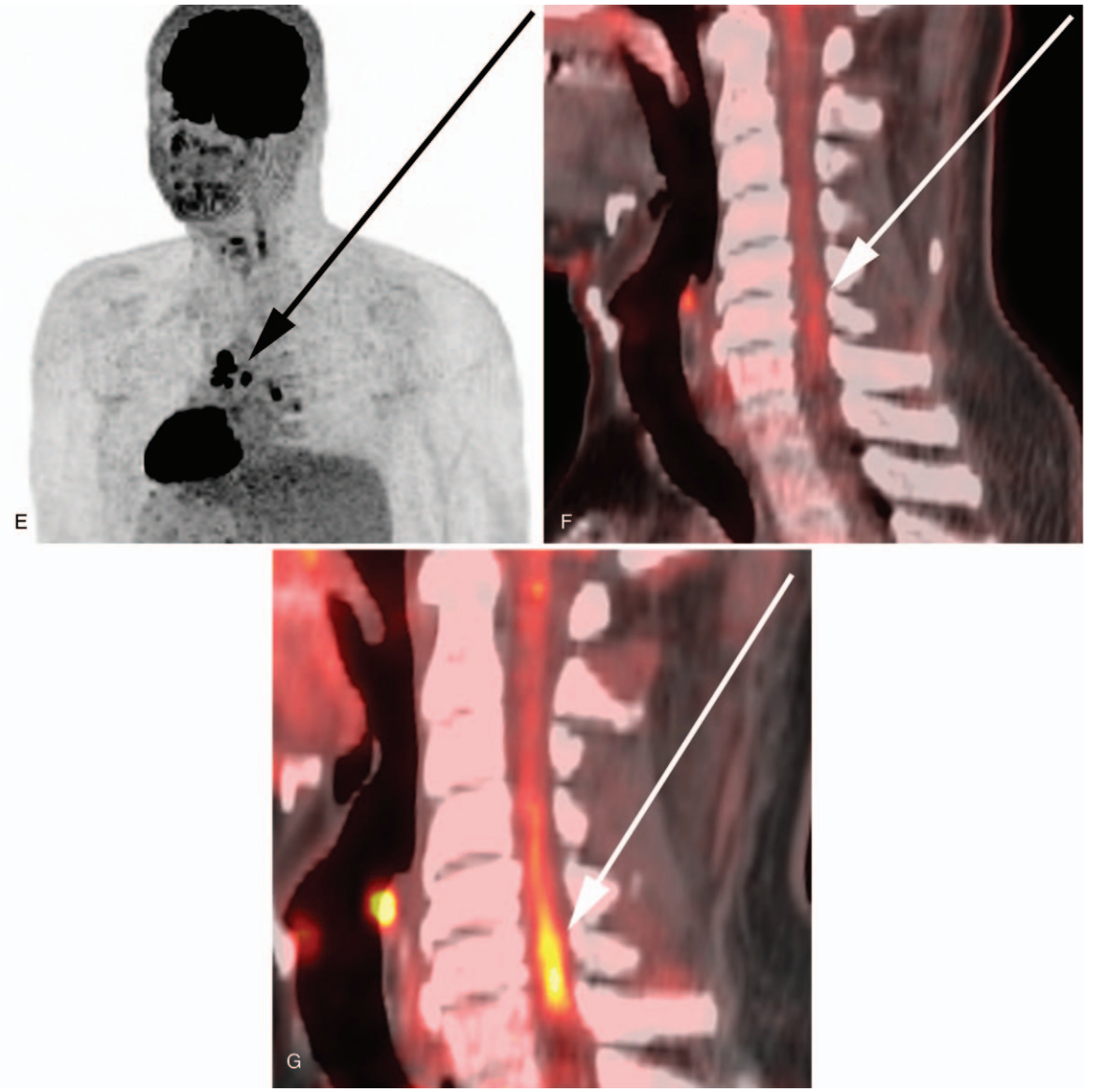

Figure 3. continued.

Applications of DTPI in inflammatory diseases may vary. DTPI has been used for assessment of lung involvement in patients with sarcoidosis[19] and in the prediction of disease progression in patients with idiopathic interstitial pneumonitis.[23] The use of DTPI is limited in the differentiation of tuberculosis (TB) and neoplasm due to the significant overlap between SUV values of active TB lesions and malignant lesions, especially in immunocompromised patients.[24] However, DTPI is useful in the assessment of treatment response in patients with known TB given that metabolism changes precede structural changes with a positive response to therapy.[24,25]

It is important to keep in mind the limitations of FDG, as the presence of active infection or inflammation may result in false positives. The use of DTPI technique may be helpful in situations wherein acute infection is suspected, as FDG uptake of acute inflammatory cells peaks at approximately 60 minutes.[24] Conversely, some low-grade tumors, for example, low-grade sarcomas, may result in false-negative findings. Other well-known limitation of FDG is the effect of elevated serum glucose or muscular activity on the uptake of FDG in target lesions, significantly decreasing the sensitivity of the test. There are reports in the literature cautioning against using the known response to steroids in inflammatory conditions as a way to differentiate from neoplasm as it has been demonstrated that tumors may show decrease in FDG uptake following short-term treatment with steroids. Further research into the potential applications and limitations of DTPI in inflammatory diseases is needed. [26]

Our case series reflects a single-center experience with DPTI for spinal sarcoidosis diagnosis and needs to be validated further with higher case numbers. The use of delayed time point ^{18}F-FDG PET/MR can potentially further enhance this imaging technique.

CONCLUSION

Noninvasive diagnosis of patients who present with myelopathy and are found to have intramedullary spinal cord lesions remains a diagnostic dilemma. Our case series demonstrates how DTPI can be helpful in narrowing the differential and possibly make the diagnosis of sarcoidosis, thereby preventing potential morbidity from spinal cord biopsy.

➢ Key Points

- ❑ New enhancing lesions of the spine are often a diagnostic dilemma and the additional of FDG PET CT can be beneficial in determining the diagnosis noninvasively.
- ❑ Dual time-point FDG PET CT has been used to differentiate inflammatory from neoplastic lesions, but DTP FDG PET CT in the setting of spinal sarcoidosis overlaps with findings of high-grade malignancy.
- ❑ Imaging findings outside of the central nervous system, in this case the chest, allowed for highly suspicious findings for the spinal lesion etiology without invasive testing.

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