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Title:

FDG-PET SUV can distinguish between spinal sarcoidosis and myelopathy with canal stenosis

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Abstract

Spinal cord sarcoidosis is a rare manifestation of sarcoidosis. Magnetic resonance imaging (MRI) of spinal cord sarcoidosis sometimes resembles that of the non-inflammatory spinal cord lesion. ^{18}F -fluorodeoxyglucose positron emission tomography (FDG-PET) is an effective method to detect both systemic and central nervous system lesions in sarcoidosis. This study compared the standard uptake value (SUV) of FDG-PET between spinal cord sarcoidosis and non-inflammatory spinal cord lesion. We retrospectively reviewed the records of patients who underwent both spinal MRI and FDG-PET scans. We used SUV to evaluate the FDG-PET uptake of the lesion. The region of interest was the center of high-intensity areas on T2-weighted MR images. We included three patients with spinal cord sarcoidosis, five with myelomalacia caused by cervical spondylosis or ossification of the posterior longitudinal ligament, one with spinal cord edema associated with cervical spondylosis, and one with spinal cord edema associated with dural arteriovenous fistula. The spinal cord sarcoidosis group had a significantly higher SUV (mean = 4.38, range: 3.30 – 4.93) than patients with the other diseases (mean = 1.87, range 1.42 – 2.74). The SUV of FDG-PET thus may be able to distinguish spinal cord sarcoidosis from other non-inflammatory lesion. FDG-PET can play an important role in the diagnosis of spinal cord sarcoidosis because the

gadolinium enhancement in MRI is sometimes seen in spondylotic myelopathy or vascular malformation. FDG-PET is informative for the accurate diagnosis of spinal cord sarcoidosis and may enable clinicians to start treatment at an earlier stage.

Introduction

Neurosarcoidosis has traditionally been considered a rare complication of systemic sarcoidosis, but recent progress in diagnostic imaging has found that subclinical neurosarcoidosis may not be as uncommon in patients with sarcoidosis as previously thought [1]. Nevertheless, spinal sarcoidosis is a particularly rare manifestation of neurosarcoidosis [2].

A diagnosis of spinal cord sarcoidosis is difficult due to the invasive nature of central nervous system biopsies and primarily depends on first certifying systemic sarcoidosis. In addition, the appearance of spinal cord sarcoidosis in cervical magnetic resonance imaging (MRI) sometimes resembles that of spondylotic myelopathy or other non-inflammatory spinal cord lesions [3]. In cases of cervical spondylosis associated with spinal cord sarcoidosis, extensive cervical laminoplasty has been shown to be ineffective [3]. Furthermore, treatment of spinal cord sarcoidosis with, for example, corticosteroids is quite different from these other diseases. To choose an effective therapeutic strategy, it is important to differentiate spinal cord sarcoidosis lesions from other non-inflammatory spinal cord lesions.

Recently, ^{18}F -fluorodeoxyglucose positron emission tomography (FDG-PET) was reported to be useful in detecting neurosarcoidosis and spinal cord sarcoidosis [4,5].

However, no study thus far has compared neurosarcoidosis and other non-inflammatory, non-neoplastic lesions from the standpoint of intramedullary spinal cord lesions with canal stenosis. FDG-PET has the potential to improve the accuracy of diagnosing spinal cord sarcoidosis and expand the diagnostic criteria of neurosarcoidosis. The purpose of this study was to evaluate the usefulness of FDG-PET in differentiating between spinal cord sarcoidosis and other non-inflammatory, non-neoplastic spinal cord lesions.

Methods

We retrospectively reviewed the records of patients who underwent both spinal MRI and FDG-PET scans in Hokkaido University Hospital from April 2004 to March 2010. Patients with spinal cord sarcoidosis were diagnosed with neurosarcoidosis using the criteria proposed by Zajicek et al [6]. According to these criteria, a diagnosis of “definite” is defined as a clinical presentation suggestive of neurosarcoidosis and the presence of positive nervous system histology. A diagnosis of “probable” is defined as a clinical syndrome suggestive of neurosarcoidosis, with laboratory support for CNS inflammation and evidence for systemic sarcoidosis. A diagnosis of “possible” is defined as a clinical presentation suggestive of neurosarcoidosis in which the above criteria are not met.

Non-inflammatory lesions were diagnosed by radiologists based on MRI and clinical records. Exclusion of sarcoidosis was based on clinical records and without abnormal uptake in lymph nodes as visualized by FDG-PET. We excluded patients with primary or metastatic spinal cord tumors. We used the standard uptake value (SUV) for the evaluation of FDG-PET uptake by the lesion. The region of interest was the center of high-intensity regions on T2-weighted images. Data were expressed as SUV of each patient and the mean of each group. In all patients, FDG-PET was performed before the start of steroid therapy. Statistical analysis by Mann-Whitney U test was performed to compare the SUV between patients with spinal cord sarcoidosis and those with non-inflammatory spinal cord lesions. PET-CT imaging was performed using an ECAT EXACT 47 scanner (Siemens, Knoxville, TN). This study was approved by the Institutional Review Board of Hokkaido University.

Result

Patient demographics and SUV data are summarized in Table 1. There were two patients with non-inflammatory spinal cord lesions that had gadolinium enhancement in MRI. Additional characteristics of patients with spinal cord sarcoidosis are shown in Table 2. A total of three patients with spinal cord sarcoidosis with canal stenosis (cases 1

– 3) and seven with non-inflammatory spinal cord lesions with canal stenosis (cases 4 – 10) were included in the analysis. Examples of patients with sarcoidosis, dural arteriovenous fistula (AVF) and canal stenosis with spondylotic change, and myelomalacia are shown in Figure 1. All of the patients with spinal cord sarcoidosis responded to treatment with steroids. The mean SUV was 4.38 (range: 3.30 – 4.93) in patients with spinal cord sarcoidosis and 1.87 (range: 1.42 – 2.74) in patients with myelomalacia, a significant difference ($p = 0.02$).

Discussion

This comparative study demonstrated the potential usefulness of FDG-PET in distinguishing spinal cord sarcoidosis from other non-inflammatory spinal cord lesions. Previous reports have focused on cerebrospinal fluid and showed that measurement of angiotensin-converting enzyme was a reliable method to detect neurosarcoidosis [7], however, this method may not be sensitive enough to rule out other diagnoses. Similarly, gadolinium enhancement of MRI has been used to diagnose neurosarcoidosis, but spondylotic myelopathy sometimes shows gadolinium enhancement that resembles spinal cord sarcoidosis [8]. Furthermore, cervical spondylosis occasionally causes spinal cord edema resembling an intramedullary tumor or inflammatory lesion [9]. Another

study of systemic sarcoidosis demonstrated that the uptake seen in FDG-PET is associated with hypermetabolism of lesions [10]. Uptake by spinal cord lesions in this study was consistent with the systemic lesions of sarcoidosis. Myelomalacia did not show uptake using FDG-PET, perhaps due to reduced metabolic activity caused by mechanical compression [10]. However, spondylotic edematous myelopathy and dural AVF with gadolinium enhancement in MRI did show a slightly increased SUV. Gadolinium enhancement might be caused by a breakdown of the blood-cord barrier, indicating that a slightly higher SUV cannot exclude non-inflammatory spinal cord lesions.

In the present study, this qualitative difference was detected as a difference of SUV in FDG-PET scans. Since the invasiveness of spinal cord biopsies makes diagnosing spinal cord sarcoidosis difficult, FDG-PET can play an important role in the differential diagnosis. In particular, the evaluation of metabolic activity by FDG-PET provides information about lesions that is crucial in the diagnosis of solitary spinal cord sarcoidosis.

There are several limitations in this study. First, we did not compare spinal cord sarcoidosis with other forms of myelitis including multiple sclerosis, neuromyelitis optica, or infectious myelitis. Therefore, a difference of SUV in FDG-PET in those

diseases could not be examined. Second, this study consisted of a small number of subjects collected retrospectively, which didn't allow us to evaluate the diversity of SUV in spinal cord sarcoidosis. Taken together, these limitations indicate that a larger prospective study that includes inflammatory disorders such as multiple sclerosis and that evaluates the difference in SUV before and after treatment for spinal cord sarcoidosis is necessary.

In conclusion, the use of FDG-PET is a novel approach for detecting spinal cord sarcoidosis and can distinguish it from non-inflammatory, non-neoplastic spinal cord lesions in clinical practice. Further investigations to evaluate the reliability of SUV in FDG-PET for the diagnosis of spinal cord sarcoidosis will be needed.

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Table 1. Patient demographics and maximum standard uptake values (SUV)

Case	Age	Sex	Diagnosis	MRI Level	gadolinium enhancement	PET Level	max SUV
1	76	F	spinal cord sarcoidosis with canal stenosis	C4-C7	+	C5	4.93
2	63	F	spinal cord sarcoidosis with canal stenosis	C5-T1	+	C6	3.30
3	67	M	spinal cord sarcoidosis with cervical spondylosis*	C3-T1	+	C6	4.90
4	62	M	spinal cord edema with dural AVF and canal stenosis	C1-T2	+	C6/7	2.74
5	67	F	spinal cord edema with cervical spondylosis	C5-C7	+	C5/6	2.70
6	65	M	myelomalacia with cervical spondylosis*	C6/7	ND	C6	1.42
7	79	M	myelomalacia with cervical spondylosis	C4/5	ND	C4/5	1.48
8	74	F	myelomalacia with OPLL	C5/6	ND	C5/6	1.59
9	67	F	myelomalacia with OPLL	C4/5	ND	C4/5	1.63
10	62	M	myelomalacia with cervical spondylosis	C6/7	ND	C6/7	1.52

● *post-operative

OPLL: ossification of the posterior longitudinal ligament

● ND: gadolinium enhancement not done

Table 2. Characteristics of spinal cord sarcoidosis patients

Case	Diagnosis	First symptom of sarcoidosis	Onset of neurological symptoms	Systemic lesion	The site of positive histology with sarcoidosis	Serum ACE* (U/l)	CSF cells (/mm ³)	CSF protein (mg/dl)	CSF ACE** (U/l)	Responsiveness to steroid therapy
1	Probable	Uveitis	Dysesthesia of UE	Mediastinal lymph nodes; Orbit	Mediastinal adenopathy	19.5	2	33	1.8	Yes
2	Probable	Uveitis	Dysesthesia of LE	Mediastinal lymph nodes; Orbit	ND	23.0	4	58	1.3	Yes
3	Probable	Myelopathy	Dysesthesia of UE	Thyroid; Mediastinal lymph nodes; Orbit	Mediastinal adenopathy	23.0	4	60	1.9	Yes

UE: upper extremity, LE: lower extremity, ND: pathological study not done

**Normal range of serum ACE: 8.3-21.5 U/l*

***Normal range of CSF ACE has not yet been established*

FIGURE LEGEND

Figure 1. (A) Sagittal T2WI of case 1 showing spinal cord sarcoidosis with cervical spondylosis from C4 to C6. (B) PET-CT image of case 1 revealing abnormal uptake in C5 spinal cord. (C) Sagittal T2WI of case 4 showing long spinal cord lesion with edema from C1 to T2. (D) PET-CT image of case 4 showing slight uptake in C6 spinal cord. (E) Sagittal T2WI of case 9 showing myelomalacia caused by ossification of the posterior longitudinal ligament from C3 to C5. (F) PET-CT image of case 7 did not detect abnormal uptake in C4/5 spinal cord.

Figure 1.

