Spinal Sarcoidosis Presenting with Epiconus Syndrome

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Abstract

A spinal cord lesion is a rare manifestation of neurosarcoidosis. We herein report a case with dysuria and gradually worsening numbness in both lower extremities. Thoracic magnetic resonance imaging (MRI) revealed a long spinal cord lesion with gadolinium enhancement in the lower part of the lesion. Chest computed tomography demonstrated enlarged hilar lymph nodes, and a biopsy revealed sarcoidosis. Methylprednisolone pulse therapy was started, but a follow-up MRI showed aggravation of the spinal lesion. After the addition of methotrexate to the therapy, the patient’s aggravation of the spinal lesion and clinical symptoms ceased. Early diagnosis and treatment using combined methylprednisolone and methotrexate therapy may improve this devastating spinal cord disease.

Key words: spinal sarcoidosis, magnetic resonance imaging (MRI), immunosuppressive therapy


Introduction

Sarcoidosis is a systemic non-caseating granulomatous disease of unknown etiology resulting in various dysfunctions in multiple organs. However, involvement of the nervous system in the form of neurosarcoidosis is observed in only about 5% of cases, and involvement of the spinal cord is more rare (1, 2). We herein describe a patient with spinal sarcoidosis exhibiting a long edematous spinal cord lesion from the Th1 to L1 level on the magnetic resonance imaging (MRI), which was successfully treated with the combination of methylprednisolone and methotrexate.

Case Report

A 69-year-old man presented to our hospital in December, 2012 with progressive numbness in both of his lower extremities and dysuria. He had been treated for diabetes and hypertension since the age of 40 years. His dysuria had also been treated since April 2012 by an urologist. Lumbar radiography and the MRI showed no abnormalities. However, the patient’s symptoms gradually worsened and he reported numbness in the lower body up to his navel.

On admission, the symmetrical disturbance of vibration sense and numbness without muscle weakness were observed in both lower extremities. Hyper-reflexia and the Chaddock and Babinski signs were also observed in both lower extremities and the patient’s gait was unsteady. The laboratory findings, including the blood analysis and serum biochemistry findings, were normal. The serum concentrations of the angiotensin-converting enzyme and ionized calcium were also normal. A variety of antibodies, such as anti-nuclear, anti-double-stranded DNA, anti-Smith, anticardiolipin, anti-SS-A, anti-SS-B, anti-ribonucleoprotein (RNP), and anti-aquaporin 4, were all negative. The cerebrospinal fluid examination revealed 10 leukocytes/mm³ accompanied by high protein (155 mg/dL) and normal glucose levels (75 mg/dL). Unfortunately, the CD4/CD8 ratio was not measured and bronchoalveolar lavage and fluorodeoxyglucose positron emission tomography (FDG-PET) were not performed. The tuberculin reaction was positive at a diameter of 12 mm.

The T2-weighted MRI performed on admission revealed a long, edematous spinal cord lesion extending from the Th1 to L1 level with signal hyperintensity. Gadolinium enhancement was observed from the Th9 to Th10 level (Fig. 1). Chest computed tomography demonstrated enlargement of the bilateral hilar lymph nodes and diffuse nodules in both lung fields (Fig. 2). Ga-67 scintigraphy findings were nega-
weeks, and the progression of the patient's clinical symptoms ceased (Fig. 5). Prednisolone (20 mg/day) and methotrexate (10 mg/week as a maintenance dose. After initiating this treatment, an endoscopic biopsy of a hilar lymph node. A histological examination revealed a non-caseating epithelioid granuloma (Fig. 4) and sarcoidosis was strongly suspected. A follow-up MRI performed 8 weeks after admission demonstrated further worsening of the spinal cord lesion without symptom aggravation. Methotrexate therapy was therefore increased to 10 mg/week as a maintenance dose. After initiating this treatment, the MRI findings and his clinical symptoms ceased (Fig. 5). Prednisolone (20 mg/day) and methotrexate (10 mg/week) treatment was continued for 12 weeks, and the progression of the patient’s clinical symptoms stopped.

Discussion

Neurosarcoidosis is a term for sarcoidosis involving the nervous system. The incidence of this pathology is very low, seen in 5-6% of cases of sarcoidosis (3, 4). A predominance of female patients was observed in a case series of 166 patients with neurosarcoidosis in Japan. Iizuka et al. (5) classified neurosarcoidosis into five types based on the imaging and clinical features: 1) intramedullary granuloma lesion; 2) meningeal lesion; 3) hydrocephalus; 4) vascular lesion; and (2) encephalopathy. Neurosarcoidosis may present with various neurological symptoms. Because the cranial nerves, the hypothalamus, and the hypophysis are usually involved in neurosarcoidosis, symptoms related to the cranial nerves or a hypophyseal lesion are common (4). Spinal cord lesions are extremely rare, seen in only 6-8% of cases of neurosarcoidosis (2), but this possibility should not be overlooked because it may lead to poor functional outcomes. An isolated spinal cord lesion was observed in only 16% of spinal cord sarcoidosis (1). Several case reports have so far been published, but no case series has yet been reported from Japan. The incidence by location of the sarcoid granuloma has been reported as: intramedullary, 35%; extra-medullary intradural, 35%; a combination of these two compartments, 23%; and extradural, 7% (6). The MRI findings characteristically depict a long, edematous spinal cord lesion with signal hyperintensity on the T2-weighted imaging. The leptomeningeal enhancement can be observed in 40-67% of patients with spinal cord sarcoidosis (7). Although the spinal cord lesion extended from the cervical to lumbar segment, the neurological deficits were limited in both lower extremities. Nerve conduction studies and electromyography also showed no abnormalities. The short-latency somatosensory evoked potentials (SEP) demonstrated the disappearance of peaks after the P24 component, thus suggesting an intramedullary lesion in the epicontus.

An ophthalmological examination revealed no abnormalities in the conjunctiva, uvea, or fundus. Echocardiography yielded normal results. For further examination, we also performed an endoscopic biopsy of a hilar lymph node.

Dysuria, hypoesthesia and paresthesia in the lower extremities gradually worsened. Three weeks after admission, the patient’s thermal nociception dropped to 2/10, the vibration sensation disappeared in both lower extremities, and self-catheterization was required for dysuria. A walker was also necessary for mobility. Although the pathological diagnosis remained unclear, intravenous methylprednisolone pulse therapy followed by oral prednisolone was started due to the aggravation of the patient’s symptoms. After the steroid treatment, the MRI findings improved slightly (Fig. 3) and his clinical symptoms ceased. However, the disappearance of peaks in SEP was unchanged.

A histological examination of the hilar lymph node revealed a non-caseating epithelioid granuloma (Fig. 4) and sarcoidosis was strongly suspected. A follow-up MRI performed 8 weeks after admission demonstrated further worsening of the spinal cord lesion without symptom aggravation. Methotrexate therapy was therefore increased to 10 mg/week as a maintenance dose. After initiating this treatment, the progression of the patient’s clinical symptoms stopped.
Figure 3. The T2-weighted sagittal and axial imagings on admission (A, C) and after 6 weeks (B, D). A consecutive, long segmental and edematous hyperintensity was shortened between the sagittal images (A and B) and was reduced between the axial images (C and D).

Figure 4. The pathological findings of the biopsied hilar lymph node. The pathological findings revealed a non-caseating epithelioid granuloma (Hematoxylin and Eosin staining).

Good prognosis can be expected if treatment is initiated early. Corticosteroids are considered the first-line agent, and oral prednisolone is usually started at a dose of 40-60 mg/day, then gradually tapered (1, 8, 9). However, Lower et al. reported that only 29% of patients with neurosarcoidosis respond to steroids alone (10), and non-responders to steroid therapy or cases that show difficulty in decreasing the steroid dose are advised to receive combination therapy with an immunosuppressant at an early stage (11). In this case, the steroid pulse therapy was followed by oral steroid therapy. Although a slight improvement in the MRI lesion size was seen, the patient's symptoms deteriorated with the gradual decrease in oral steroid use. When we administered additional immunosuppressive therapy with methotrexate, the disease progression stopped.

In an extensive review of the literature, 66% of patients with spinal sarcoidosis improved, 25% deteriorated, and 9% remained stable (1). Spontaneous remission of the clinical symptoms is not seen in spinal sarcoidosis, and patients...
treated before the onset of severe neurological deficits tend to experience better outcomes (8). No guidelines or consensus have yet been reached regarding when additional immunosuppressive therapy should be started. Varron et al. recommend steroid as the first-choice treatment, and methotrexate can be added for patients without any response to steroid therapy or with severe symptoms. Azathioprine or infliximab in conjunction with an immunosuppressant could be used as second-line agents for patients with ineffective therapy (11). Early diagnosis of neurosarcoidosis is important for a good prognosis. However, it is important to note that the present case is not considered typical for neurosarcoidosis (12). In order to diagnose neurosarcoidosis by the diagnostic criteria, a clinical presentation suggestive of neurosarcoidosis must be seen, along with the pathological confirmation of systemic sarcoidosis and positive test results for at least two of the fixed 6 laboratory findings. Although only 1 of the laboratory findings was fulfilled in our case, we initiated treatment for a diagnosis of neurosarcoidosis because we had already excluded all other diseases as the cause of the spinal lesion. If we adhere strictly to the diagnostic criteria, the early treatment of neurosarcoidosis may be delayed; therefore, flexible judgment is required in cases such as ours which cannot be easily examined by an open biopsy of the spinal cord. The suspicion of this rare disease as a differential diagnosis and thorough work-up of other organs for which one can obtain biopsy specimens is warranted.

We herein described a case of spinal sarcoidosis presenting with epiconus syndrome. Spinal lesions are a rare manifestation of sarcoidosis and they are difficult to diagnosis due to non-specific findings. Early diagnosis and treatment initiation can improve the prognosis. However, no standard treatment regimen for spinal sarcoidosis has yet been established and the effects of each medication are not fixed. Therefore, the combination of methylprednisolone and methotrexate represents one choice of treatment to improve this devastating spinal cord disease.

The authors state that they have no Conflict of Interest (COI).

References