Spinal Neurosarcoidosis

Bao-Luen Chang, Hung-Chuo Kuo, Chun-Che Chu, Chin-Chang Huang

Abstract-

Purpose: Neurosarcoidosis is a multisystemic disorder and is rare in Taiwan. Diagnosis of neurosarcoidosis depends on the clinical features, neuroimage studies and the pathological findings of non-caseous granuloma in various tissues.

Case Report: A 62-year-old woman had diabetic mellitus and an old lacunar stroke in 1996. In 2003, she received steroid therapy for one year for the mediastinal mass lesion with a good response. In June 2006, she suffered from band-like numbness and muscle weakness descending from the abdomen to bilateral lower extremities and urinary difficulty. Spinal magnetic resonance imaging showed an intramedullary lesion in C6~C7 region. The chest computed tomography (CT) scan revealed multiple small and enlarged nodes over the mediastinal regions compared with the previous chest CT in 2005. The pathological changes of the mediastinal mass demonstrated non-caseous granulomatous changes. Therefore, probable cervical neurosarcoidosis was impressed. After an intravenous dexamethasone followed by oral steroid treatment, her symptoms and signs had gradually improved. A follow-up spinal magnetic resonance imaging showed an improvement of the cervical cord lesion.

Conclusion: Spinal neurosarcoidosis can mimic a spinal tumor, an inflammatory lesion, or even a demyelinating lesion in both clinical and neuroimaging studies. A high index of suspicion of sarcoidosis is required for an early diagnosis, and steroid therapy is usually associated with a favorable outcome.

Key Words: sarcoidosis, neurosarcoidosis, spine, myelitis, magnetic resonance image

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INTRODUCTION

Sarcoidosis is an inflammatory multisystem, non-caseous granulomatous disease of unknown cause[1-3]. Sarcoidosis occurs worldwide affecting white women between 20 to 40 years old and is most common in North American African and North European women[4-6]. In North Europe and Japan there is a second peak incidence in women with age more than 50 years. It is rare in Taiwan with a prevalence less than 5 per 100,000 people[7]. Neurosarcoidosis is involved in 5%~15% of patients with sarcoidosis[8,9]. All parts of the nervous sys-

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tem can be attacked, but cranial nerves, hypothalamus and pituitary gland are commonly involved[1]. Spinal intramedullay neurosarcoidosis occurs in less than 1% of sarcoidosis cases[6,7,10,11]. In this report, we describe a patient who had neurosarcoidosis presented as cervical myelopathy.

CASE REPORT

This 62-year-old woman had diabetic mellitus, hypertension without regular medical control and an old stroke in 1996 with left limbs clumsiness. She had intractable vomiting, swallowing difficulty, and cough then multiple nodules were found in the mediastinum in 2003. Biopsy revealed non-caseous granulomatous changes with negative acid fast stain and Periodic acid Schiff reaction (PAS) (Fig. 1). Thus sarcoidosis was diagnosed. She received prednisolone therapy for one year and had totally improved at that time. In June 2006, she suffered from band-like numbness descending from the abdomen to bilateral lower extremities. In the following 2 months, an insidious onset of muscle weakness in bilateral upper extremities was developed and then progressed to the lower extremities. She also had constipation, urine retention and frequency. She denied back pain, insect bite, skin rashes or cervical/lumbar traumatic history. She was afebrile and physical examinations revealed an 2×2cm nodule over lower neck and an 4 cm nodule in the right arm. Muscle strength was 4-/5 in bilateral proximal arms, 4/5 for distal hands, 3/5 for bilateral proximal lower extremities and 4/5 for bilateral lower legs according to the Medical Research Council of the Great Britain (MRCGB). Deep tendon reflex was generally increased over the four extremities without Hoffmann sign or Babinski's sign. Objective sensory tests including pinprick sensation and light tough were impaired below the T10 level; temperature was impaired below the T5 level; vibration sensation was decreased in the bilateral lower extremities but joint position sense was intact. Therefore cervical myelopathy was impressed clinically.

The spinal magnetic resonance imaging (MRI) showed an intramedullary enhanced lesion in the C6~C7 region and multiple ring enhanced vertebral lesions at the thoracic and lumbar spines (Fig. 2). Laboratory studies including complete blood counts, biochemistries and level of Vitamin B12, folate were all within normal ranges. Cerebrospinal fluid (CSF) study showed mild pleocytosis with lymphocyte predominance (WBC: 8 cells/μL), slightly low glucose level (CSF sugar/Blood sugar: 101/269 mg/dL) and mild protein level elevation (52.3 mg/dL). The Gram's stain, acid fast stain, india Ink, cryptococcus antigen, tuberculosis polymerase chain reaction (PCR) and subsequent culture were all

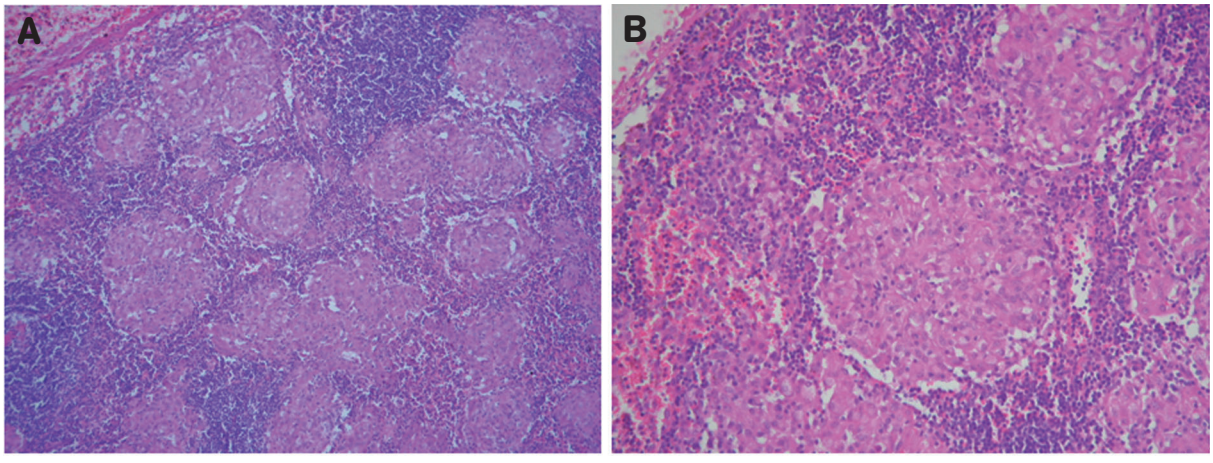

Figure 1. Biopsy from this patient's mediastinal nodules and the pathological findings showed non-caseous granulomatous inflammatory changes (A. H & E stain, 100×) with negative results with Periodic Acid Schiff reaction (PAS) stain (B. PAS stain 200×).

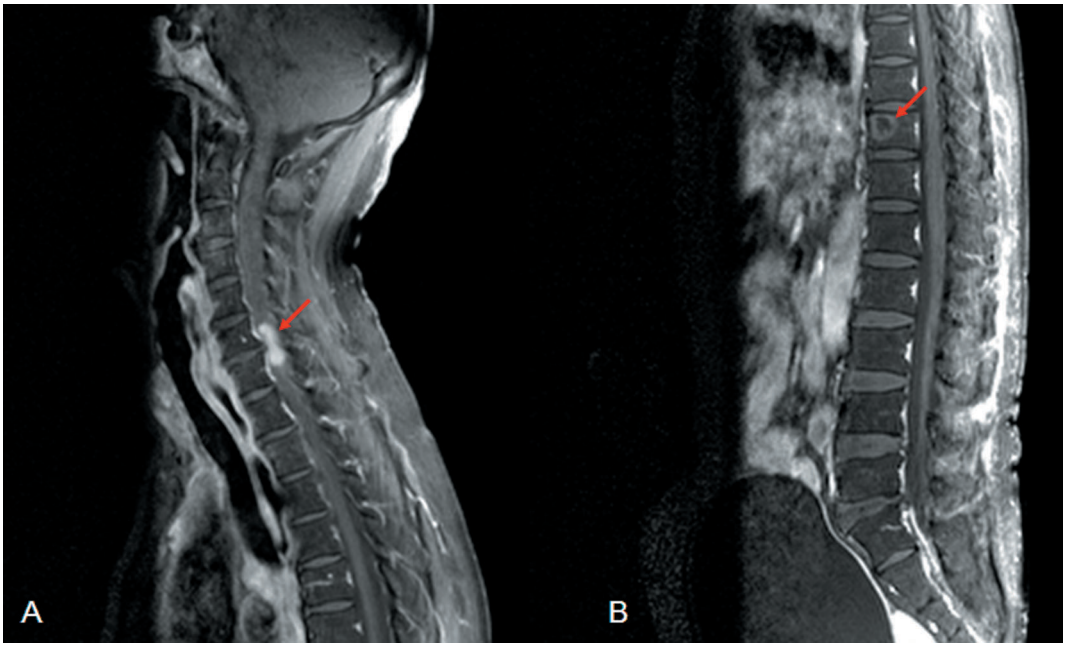

Figure 2. The spinal MRI in Gadolinium-enhanced T1 weighted image showed an intramedullary enhanced lesion (arrow) in the C6~C7 region (A) and multiple well-defined lytic lesions with sclerotic margins and ring form enhanced vertebral lesions at the lumbar spines (B), indicating vertebral sarcoidosis.

negative. The IgG index was 0.55 but neither monoclonal protein nor oligoclonal bands were identified. No significant abnormalities were found in the serologic tests including syphilis and Lyme serologies, tumor markers such as squamous cell carcinoma antigen, carcinoembryonic antigen, carbohydrate-related tumor antigen-125 (CA-125), CA19-9, CA15-2, alpha-fetoprotien and autoimmune profile including perinuclear anti-neutrophil cytoplasmic antibody and cytoplasmic anti-neutrophil cytoplasmic antibody. A follow-up chest computed tomography scan demonstrated progressive multiple small and enlarged nodes over the mediastinal regions after comparsion with the previous chest CT in 2005. Abdominal CT revealed lymphadenopathy in the para-aortic region. Bone scan showed no definite evidence of malignant bony metastasis.

Thus probable cervical neurosarcoidosis was diagnosed and she received intravenous dexamethasone treatment for one week and the medication was shifted to oral prednisolone 1mg/kg/day for about 6 weeks. Then we tapered prednisolone very slowly and kept very low dose oral prednisolone (5mg every other day) till now in the 4 years follow-up. Her muscle power, sensory impairment and sphincter function had improved gradually and a follow-up spinal magnetic resonance imaging two weeks later showed a mild improvement of the cervical cord lesion but 3 years later the cervical cord lesion had disappeared (Fig. 3). Her clinical neurological defects were also almost totally recovery 4 years later.

DISCUSSION

This report describes an unusual patient who had chronic cervical myelopathy caused by neurosarcoidosis in Taiwan. In Taiwan, sarcoidosis is still considered a rare multisystemic disorder and sarcoidosis can be self-limited and chronic in course with remissions and relapses[4,5]. Sarcoidosis commonly presents with bilateral hilar lymphadenopathy, pulmonary infiltration, ocular and skin lesions but the nervous system can also be involved[12-14]. Most patients may present with intrathoracic lesions initially. Two thirds of patients with neu-

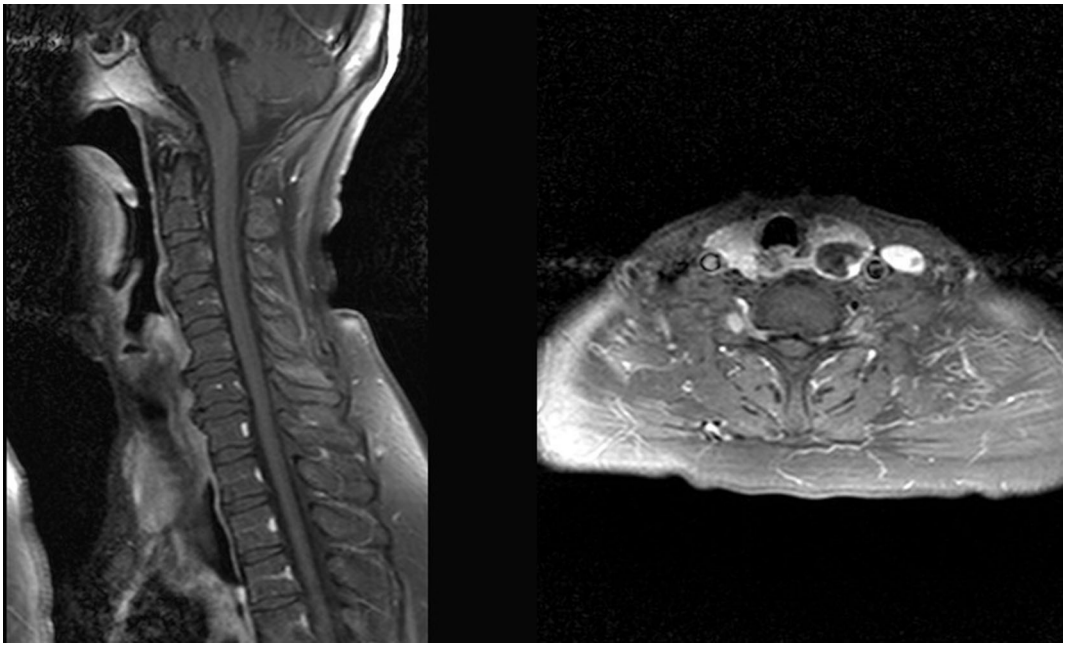

Figure 3. The follow-up spinal MRI 3 years later after steroid therapy showed a complete disappearance of the cervical and vertebral lesions.

rosarcoidosis have a self-limiting monophasic illness[15]. The most common clinical manifestation of neurosarcoidosis is singular or multiple cranial nerves palsy especially the facial nerve[1,16-20]. In addition, neurosarcoidosis can also present as intramedullary spinal lesions similar to transverse myelopathy[3,16-17].

The spinal intramedullay neurosarcoidosis is rare and may mimic malignancy or an inflammatory demyelinating disease. Thus the spinal cord lesions in neurosarcoidosis should be differentiated with spinal cord tumor, inflammatory myelitis such as neuro Behcet's, SLE, Sjogren's disease, mixed connective tissue disease, antiphospholipid syndrome, Lyme's disease, lymphoma or tuberculosis and multiple sclerosis[3]. Among these, multiple sclerosis is one of the most important disease that should be excluded in this patient. According to the history of pulmonary sarcoidosis combined with her chronic progressive course、mild inflammatory change in her CSF study、negative visual evoked potential examination、no other significant central neurvous lesions in her neuroimaging survey and 4 years clinical follow-up with repeated neuroimaging studies, no evidence of time and space dissemination lesions. She doesn't fullfill the revisions of the McDonald diagnostic criteria for MS in 2005 and MS also should not have multiple ring enhancement lesions in the vertebral bodies, so MS had been excluded in this patient.

The diagnosis of neurosarcoidosis is usually difficult, especially when the histological tissue is difficult to approach. Some criteria may support the diagnosis of neurosarcoidosis including clinical presentation compatible with neurosarcoidosis, exclusion of other possible causes, laboratory support of CNS inflammation and evidence of systemic sarcoidosis as in our patient[3,9,14]. However, definite diagnosis of neurosarcoidosis is ultimately depended upon pathological confirmation of noncaseating granulomas in nervous system[27-29]. Our patient showed transverse myelopathy which was compatible with the clinical manifestation of neurosarcoidosis, although it was relatively uncommon; The CSF study showed mild lymphocytic pleocytosis with mild total protein elevation and lower sugar which support of CNS infammation; The extensive laboratory studies included

hematology, biochemistry, serology, CSF culture and cytology, tumor screen, bone scan and whole body CT which were available to exclude CNS infection, malignant diseases and connective tissue diseases. Several nodules over left neck and right arm were noted in PE and progressive multiple small and enlarged nodes over mediastium were found in the follow-up chest CT; We also reviewed the pathohistologic findings of her mediastinum nodules which revealed the evidence of systemic sarcoidosis. However, biopsy in the cervical cord lesion did not perform due to it was too risky and difficult to approach. Thus based on the diagnostic criteria, probable neurosarcoidosis was diagnosed in our patient.

Similar to most patients with sarcoidosis in the literatures, our patient had sarcoidosis with initial intrathoracic lesion and a relapsing spinal cord lesion developed three years later without continuous steriod treatment. The progressive intramedullary cervical lesion and multiple lesions with ring enhencement in the vertebral bodies were occurring in less than 1% of systemic sarcoidosis cases[6,7,11]. Spinal intramedullary neurosarcoidosis frequently affects cervical cord (56%), followed by thoracic cord (37%) and lumbar and sacral cord (7%)[10]. MRI may reveal fusiform enlargement of the spinal cord with high signal on T2-weighted image and low signal on T1-weighted image, and patchy/nodular contrast enhancement or even only abnormal enhancement with normal cord appearance on T1- and T2-weighted image[12,21,22]. Asymptomatic osseous involvement is reported in 1~13% of sarcoidosis patients[23-25] and vertebral lesions usually occur in the lower thoracic and upper lumbar spine[23,26]. In our patient, the MRI findings are multiple well-defined osteolytic lesions with sclerotic margins and inhomogeneous enhancement in the vertebral bodies.

The major treatment for neurosarcoidosis includes steroid, immunosuppresive agents and immunomodulators such as antimalarial agents[3,9,28-36]. However, steroid is the first line of treatment for sarcoidosis and the dosage in treatment of neurosarcoidosis is usually higher than those advised for the treatment of other localizations of sarcoidosis and a relatively long term therapy for at least 6 months is needed[3,9]. Our patient had a good response to a initial high dose steroid therapy followed by a low maintenance dosage of prednisolone treatment. After a 4-year follow up, her neurological deficits improved and the follow-up spinal MRI lesions revealed almost totally subsided. Therefore, we suggest intravenous high potency steroid loading for 1 week then shift to high dose oral prednisolone (0.5~1 mg/kg/day) for 6~8 weeks follow by tapering steroid very slowly and keep low maintenance dosage as patient could tolerate to decrease their relapsing rate. In addition, in refractory neurosarcoidosis, radiation therapy may be a choice of treatment[37-39] and neurosurgical intervention with resection of intracranial and spinal granulomas is warranted only in life-threatening situations or when medical treatment is insufficient[3]. The prognosis of neurosarcoidosis depends on the location and extent of involvement and the mortality from sarcoidosis is usually caused by respiratory failure[22].

In conclusion, neurosarcoidosis presenting as myelitis is rare and can mimic a spinal tumor, an inflammatory lesion, or even a demyelinating lesion. Early diagnosis and prolonged high potency steroid therapy for 6~8 weeks follow by lifelong low maintenance dosage of prednisolone may have a better outcome.

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