Case Report

# Neurosarcoidosis: An under-diagnosed cause of myelopathy

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## Abstract

Sarcoidosis is a granulomatous disorder with multi-organ involvement, and etiology still remains unknown. Neurosarcoidosis is the involvement of the nervous system in sarcoidosis. Spinal cord involvement is usually intra-dural, but extra-dural involvement can also occur. Here, we report a case of 30 years old lady presenting with subacute onset paraparesis with bladder and bowel involvement, which was finally diagnosed as sarcoidosis-associated myelopathy with the longitudinally extensive transverse myelitis (LETM) phenotype.

**Keywords:** LETM, neurosarcoidosis, paraparesis, sarcoidosis, spinal cord

## Introduction

Sarcoidosis is a rare multi-system inflammatory disease characterized by non-caseating granulomas on histology.[1] Neurosarcoidosis (NS) is seen in 10–15% of cases of sarcoidosis.[2] Among them, 70–90% of cases have extra-neural involvement from the onset of the disease. Prognosis is fatal in more than 15% of patients.[3] Both central and peripheral nervous systems can be involved, the most common being the hypothalamus-pituitary axis, brain parenchyma, cranial nerves, meninges, spinal cord, and peripheral nerves. Among cranial nerves, the facial nerve is the most affected, followed by the optic nerve and the trigeminal and vestibulocochlear nerves. Moreover, only 10% cases of neurosarcoidosis involve the spinal cord, affecting mainly the intra-medullary region.[3-6] In a previous study, magnetic radioimaging (MRI) has revealed four groups of spinal cord involvement in NS: longitudinally extensive transverse myelitis (LETM) (45%),[2] meningoradiculitis/meningitis (23%),[3] tumefactive myelitis (23%),[4] and anterior myelitis next to disc generation (10%). Additionally, it was also found in the same study that the most commonly affected area is the cervicothoracic region.[7] Moreover, it is difficult to be diagnosed because of the lack of awareness and feasibility of tissue biopsy. Diagnosis is usually made by MRI and cerebrospinal fluid (CSF) analysis showing inflammatory changes and tissue biopsy showing non-caseating granuloma.[8] Here, we report a case of NS presenting with subacute onset paraparesis.

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## Case Report

A 30 years married female presented with complaints of weakness associated with tingling sensation in bilateral lower limbs and difficulty in passing urine for 14 days.

Weakness was subacute in onset, rapidly progressive, and symmetrical and involved both proximal and distal lower limbs. It was associated with tingling sensation without numbness. There was no history of difficulty in turning on



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bed or band-like sensation. She had difficulty in micturation in the form of painful retention, followed by dribbling with a longer duration of urination. She also had complaints of bowel involvement in the form of constipation. There was no complaint suggestive of autonomic, cerebellar, cranial nerve involvement.

On general examination, mild pallor was present. Respiratory, cardiovascular, and abdominal examination revealed no significant abnormality. On neurological examination, her higher mental functions were normal. Motor examination showed normal bilateral muscle bulk with decreased muscle tone in lower limbs. The muscle power was 3/5 at all joints in bilateral lower limbs. On sensory examination, a sensory level of T5 was demarcated for fine touch, crude touch, pain, and temperature with 50% reduction. Bilateral plantar reflex was extensor with an absent knee and ankle reflex. Motor and sensory examination of bilateral upper limbs was within normal limits.

On investigation, hemoglobin was 10 g/dl, TLC was 11600/mm$^3$ (79% neutrophils), and platelet count was 2 lac/mm$^3$. Renal and liver function tests, lactate dehydrogenase, serum calcium, and phosphate were normal. Urine routine examination was within normal limits. ESR was raised [70 (normal 20 mm)]. Viral markers including HIV, Hepatitis B, and Hepatitis C were negative. Ig M for CMV was negative. Antinuclear antibody, Anti SSA, and Anti SSB were negative. The ANCA profile was negative. CSF routine and microscopy were within normal limits, and oligoclonal bands were absent. The gene expert for MTB was negative. Serum Anti Myelin oligodendrocyte glycoprotein MOG and anti aquaporin 4 IgG were negative. Serum ACE was normal.

Chest x-ray PA view revealed bilateral hilar opacities [Figure 1]. HRCT thorax showed multiple enlarged mediastinal lymph nodes, the largest being 1.7 cm [Figure 2]. CT-guided mediastinal lymph node biopsy was done. HPE showed a markedly distorted lymph node architecture with multiple small non-necrotizing granulomas composed of epitheloid cells with scattered Langerhans giant cells and lymphocytes. No AFB-like organism was seen on ZN stain.

The MRI whole spine showed long segment cord T2 hyperintensity from the C2 vertebral level to conus with braids like ventral subpial enhancement at the anterior aspect of the spinal cord from D5 to the D9 vertebral level, suggestive of neurosarcoidosis [Figure 3(a-c)]. The patient was started on high-dose pulse intravenous methylprednisolone for 5 days, followed by oral prednisolone at the dose of 1 mg/kg. She was discharged on day 8 on oral prednisolone, and the patient was kept on long-term immunosuppression with methotrexate during follow-up with favorable response.

## Discussion

Neurosarcoidosis is uncommon, but isolated spinal sarcoidosis or sarcoidosis-associated myelopathy (SAM) is much rarer. The pathophysiology of NS includes inflammation-mediated destruction of myelin with nerve and muscle biopsy specimens remarkable for epineural granulomas and endoneurial infiltrates.[9] Initial presentation with spinal neurosarcoidosis without any systemic manifestations requires a high index of suspicion and a comprehensive approach. Common clinical manifestations are cranial neuropathies such as unilateral seventh nerve palsy or facial diplegia, encephalopathy, aseptic meningitis, myopathy, myelopathy, radiculopathy, peripheral neuropathy, and neuroendocrine dysfunction.[10]

Diagnosis is made by radiological and histological findings. Various radiological findings in NS include intra-medullary lesions, cord edema, arachnoiditis, and pachymeningitis in case of spinal cord involvement.[11,12] Non-caseating granulomas and the absence of acid-fast or fungal organisms on histopathology is fundamental to diagnose sarcoidosis. CNS biopsy is ideal, but due to its associated risk, another site of involvement may be

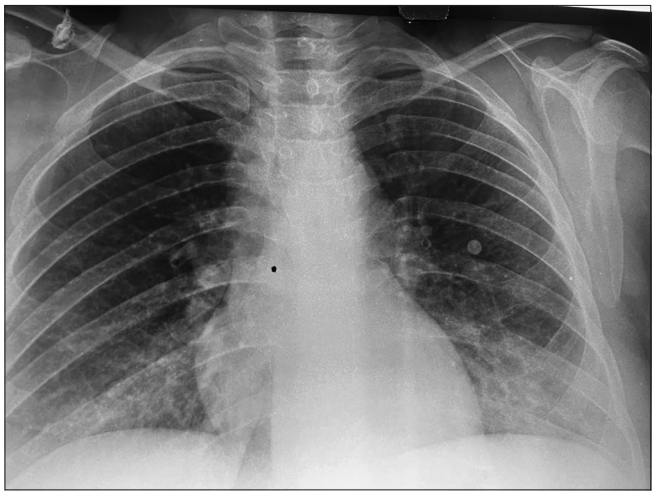

**Figure 1:** Chest X ray PA view showing Bilateral hilar opacities

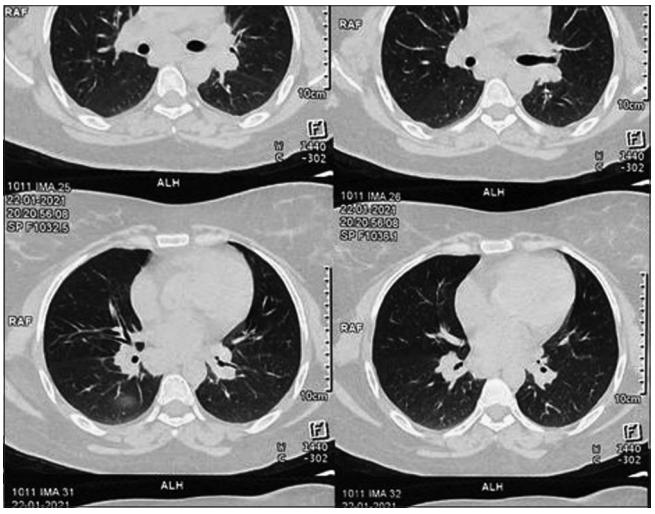


**Figure 2:** HRCT suggestive of multiple enlarged mediastinal lymphnodes

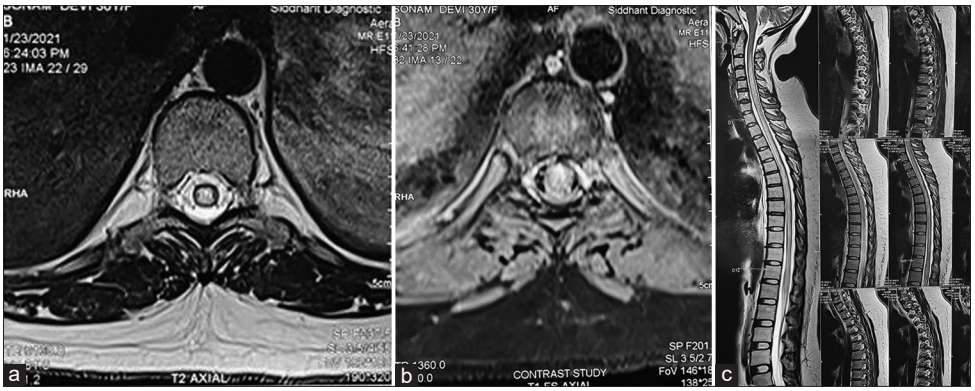


**Figure 3:** (a-c) MRI whole spine showing long segment cord T2 hyperintensity from C2 vertebral level to conus with ventral subpial enhancement at anterior aspect from D5 to D9

identified for tissue diagnosis. CSF findings are mononuclear pleocytosis, elevated protein, low glucose, elevated IgG index, presence of oligoclonal bands, and elevated CSF ACE concentration.[13] In our patient, CSF findings were normal.

Differential diagnosis includes infections, granulomatous diseases, benign tumors and malignancies, vasculitis, lupus, and neuromyelitis opica spectrum disorder. Rarely, multiple sclerosis can also have similar presentation. Sarcoidosis as a cause of LETM is very uncommon.

Clinical criteria for diagnosis of Neurosarcoidosis, Consensus 2018 have classified cases as definite, probable, and possible based on histopathology. A definite diagnosis is confirmed by biopsy from nervous tissue with MRI, CSF, and/or electromyography/nerve conduction study findings typical of granulomatous inflammation of the nervous system, while probable neurosarcoidosis is when biopsy from any other systemic site shows the presence of non-caseating granuloma in the presence of positive imaging or CSF findings with or without EMG/NCS findings typical of granulomatous inflammation of the nervous system. Without biopsy, it is possible.

The first-line treatment therapy is steroids. Second-line steroid sparing therapy is used in patients who fail to improve on steroids. It includes methotrexate, mycophenolate, and azathioprine. Third-line therapy consists of anti TNF alpha agents. However, relapses are still common in patients on anti TNF agents and there is an increased risk of infections.[14] Rituximab and JAK inhibitors have also shown improvement in symptoms of NS, but the role is still unclear. Moreover, investigation should be done for varicella zoster virus infection and fungal infections if there is apparent worsening of NS even in a known patient of NS.[15]

## Conclusion

Diagnosis is difficult to be made in a case of NS without any systemic manifestations. It is important for the clinician to have a high index of suspicion of NS in a case of LETM before labeling it idiopathic because it is a treatable cause.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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