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CASE REPORT

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Longitudinally extensive transverse myelitis as an initial manifestation of sarcoidosis: A rare case and its management

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Key Clinical Message

Sarcoidosis-induced LETM represents a rare but life-threatening neurological manifestation of sarcoidosis, characterized by spinal cord inflammation, and associated neurological deficits. Sarcoidosis should be included in the differential diagnosis of LETM, particularly in patients with no lung involvement. Prompt recognition and management are obligatory to optimize outcomes and prevent long-term disability.

Abstract

Sarcoidosis is a multisystem inflammatory granulomatous disorder characterized by the formation of noncaseating granulomas. Although sarcoidosis commonly affects the skin, lymph nodes, and lungs, neurological involvement of sarcoidosis has also been reported. Longitudinally extensive transverse myelitis (LETM) is a rare but well-documented serious manifestation of neuroscoidosis. We report a case of LETM caused by sarcoidosis in a 53-year-old male who presented with progressive bilateral lower extremity weakness, urinary retention, and paresthesia. Laboratory evaluations revealed elevated inflammatory markers. Magnetic resonance imaging of the spine showed hyperintense signals consistent with transverse myelitis. Cerebrospinal fluid analysis revealed lymphocytic pleocytosis and elevated protein levels. Chest computed tomography showed hilar lymphadenopathy. A biopsy of the intrathoracic lymph node showed noncaseating granulomas consistent with sarcoidosis. A diagnosis of sarcoidosis-induced LETM was made after ruling out all other possible etiologies. His condition improved gradually after starting high-dose prednisone, mycophenolate, and rehabilitation strategies. Our case underscores the importance of prompt diagnosis and management of sarcoidosis-induced LETM and highlights that sarcoidosis must be included among differential diagnoses of LETM, especially in cases with no lung involvement.

KEYWORDS
longitudinally extensive transverse myelitis, myelopathy, neurosarcoidosis, sarcoidosis, transverse myelitis

1 | INTRODUCTION

Sarcoidosis is a multisystem inflammatory granulomatous disease of unknown etiology, characterized by the formation of pathologically multiple noncaseating granulomas.[1] Sarcoidosis has the potential to involve every organ system of the body and mainly affects the respiratory system, lymph nodes, and skin.[2] However, its wide range of clinical manifestations may present diagnostic challenges, especially in cases with atypical manifestations. Neurosarcoidosis is a rare but serious manifestation of sarcoidosis with a reported incidence of 5% in all cases of sarcoidosis; however, it was observed to vary from 5% to 10% in some series.[3] Neurological involvement of sarcoidosis can involve the central or peripheral nervous system or both. Neurological manifestations of sarcoidosis are shown in Figure 1.[4,5] Longitudinally extensive transverse myelitis (LETM) is a rare, life-threatening manifestation of sarcoidosis, which is not widely reported in the literature.[6] We report a case of LETM as a first presentation of sarcoidosis.

2 | CASE HISTORY AND EXAMINATION

A 53-year-old male with a history of type 2 diabetes mellitus was brought to the emergency department with complaints of progressive bilateral lower limb weakness, numbness, and tingling sensations for the last 3 weeks. He reported that these symptoms developed gradually and worsened without any relieving or aggravating factors. He also complained of intermittent urinary retention for the previous 5 days. He complied with his medication, including atorvastatin and insulin. He had no history of trauma, falls, travel history, or recent infection. He quit smoking 20 years ago and did not report illicit drug use or alcohol abuse.

On initial evaluation, he looked anxious, hemodynamically stable, and was well oriented to time, place, and person. Neurological examination revealed bilateral lower limb weakness (3/5 on the Medical Research Council Scale), hyperreflexia in lower limbs, and reduced sensation to pinprick and light touch below the level of the T4 dermatome. Cranial nerves were intact, and skin, cardiovascular, and respiratory system examinations were nonsignificant.

3 | METHODS AND DIAGNOSIS

He underwent laboratory evaluations, which were within normal range except for elevated erythrocyte sedimentation rate of 34 (reference value: <15 mm/h) and c-reactive protein of 8.1 (reference value: 0.8–1 mg/dL). Brain magnetic resonance imaging (MRI) was unremarkable, and spine MRI revealed T-2 hyperintense signals involving the thoracic spine, suggesting transverse myelitis (Figure 2A,B). His cerebrospinal fluid analysis showed

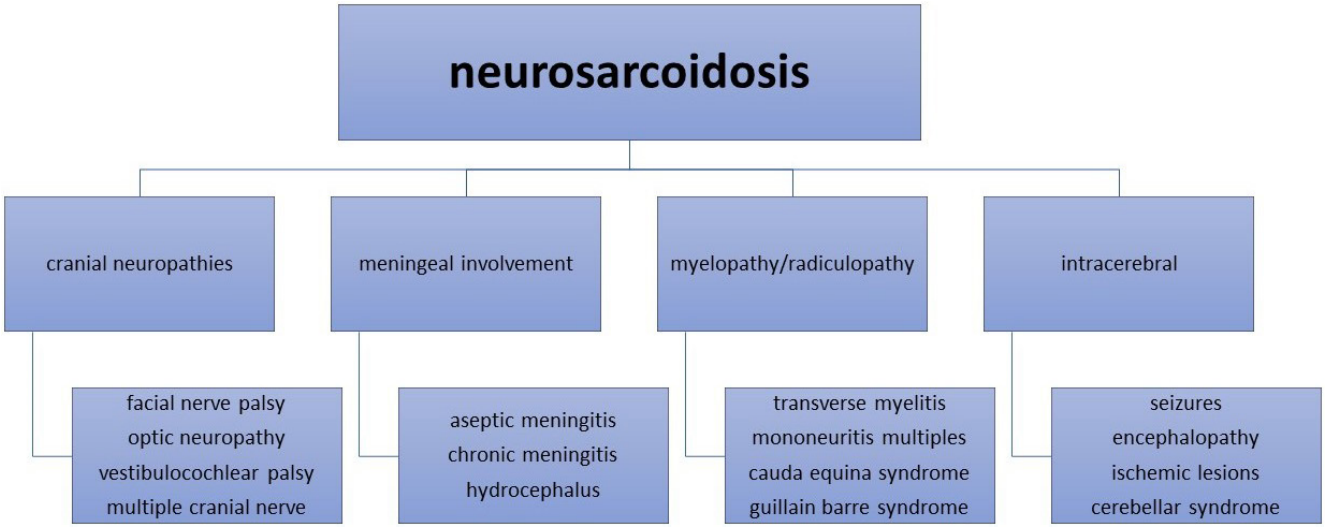

FIGURE 1 Neurological manifestations of sarcoidosis.

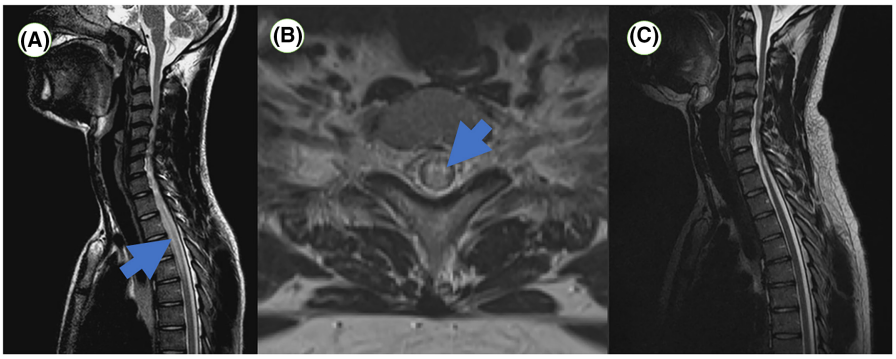

FIGURE 2 T2-weighted spinal MRI showing hyperintense signals (blue arrows) from C8-T4 (A) sagittal view, (B) axial view. Disappearance of hyperintense signals after 8 weeks of therapy (C). C, cervical; MRI, magnetic resonance imaging; T, thoracic.

lymphocytic pleocytosis with an elevated protein level. Computed tomography of the chest was performed, which revealed hilar and mediastinal lymphadenopathy (Figure 3). His blood culture was negative, and infectious workups including tuberculosis, human immunodeficiency virus, and hepatitis screening and autoimmune workups, including antinuclear antibody, aquaporin-4 antibodies (AQP4-Ab), and myelin oligodendrocyte glycoprotein (MOGP), were negative. Nerve conduction study and electromyography of the lower limb were consistent with myelopathy. Based on his clinical picture and imaging results, he underwent intrathoracic lymph node biopsy, which was consistent with the diagnosis of sarcoidosis, revealing noncaseating granulomas.

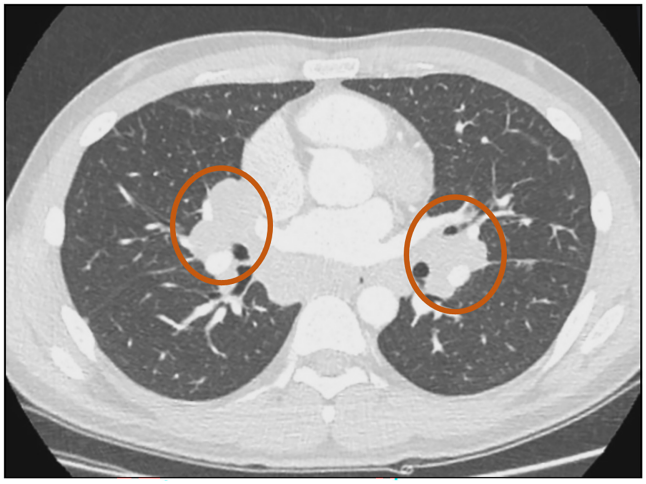

FIGURE 3 CT chest demonstrating hilar lymphadenopathy (circle). CT, computed tomography.

4 | TREATMENT AND FOLLOW-UP

A probable diagnosis of acute transverse myelitis induced by sarcoidosis was made. He was commenced on methylprednisolone of 1 g/daily for 5 days, followed by a tapering dose of oral steroid of 40 mg/daily. His condition started improving gradually with the resolution of sensory disturbance and mild improvement in motor function. Detailed systemic evaluation, including eye examination and pulmonary function tests, did not reveal involvement of other organ systems. A repeat spine MRI 8 weeks later demonstrated a significant reduction in contrast enhancement (Figure 2C). Mycophenolate mofetil was added to his regimen 2 months later with ongoing rehabilitation and close monitoring.

5 | DISCUSSION

Longitudinally extensive transverse myelitis is a rare neurological disorder characterized by spinal cord inflammation, resulting in sensory, motor, and autonomic dysfunction.[7] ATM can occur idiopathically or have a diverse etiology, such as infections, autoimmune, or inflammatory conditions (Figure 4).[8,9]

Sarcoidosis-induced LETM represents an uncommon but important sarcoidosis manifestation and is diagnosis per exclusionism. Only a limited number of cases have been reported on sarcoidosis-induced LETM, but the literature is steadily expanding. LETM, as a first presentation of sarcoidosis, has also been reported in a few cases, underscoring the importance of considering sarcoidosis among differentials of myelopathy. Wang et al. underlined a case series of sarcoidosis-induced TM in nine patients. Analysis revealed that the median age of disease onset was 49.1 years old, and eight patients presented with LETM as the first manifestation of sarcoidosis. The diagnosis was confirmed using MRI and CSF analysis, followed by chest imaging. All patients reported improved outcomes after using steroids and immunosuppressive agents.[10] Scott et al. reported two cases of LETM as the first presentation of sarcoidosis in previously healthy patients, as in our case. Imaging findings were consistent with

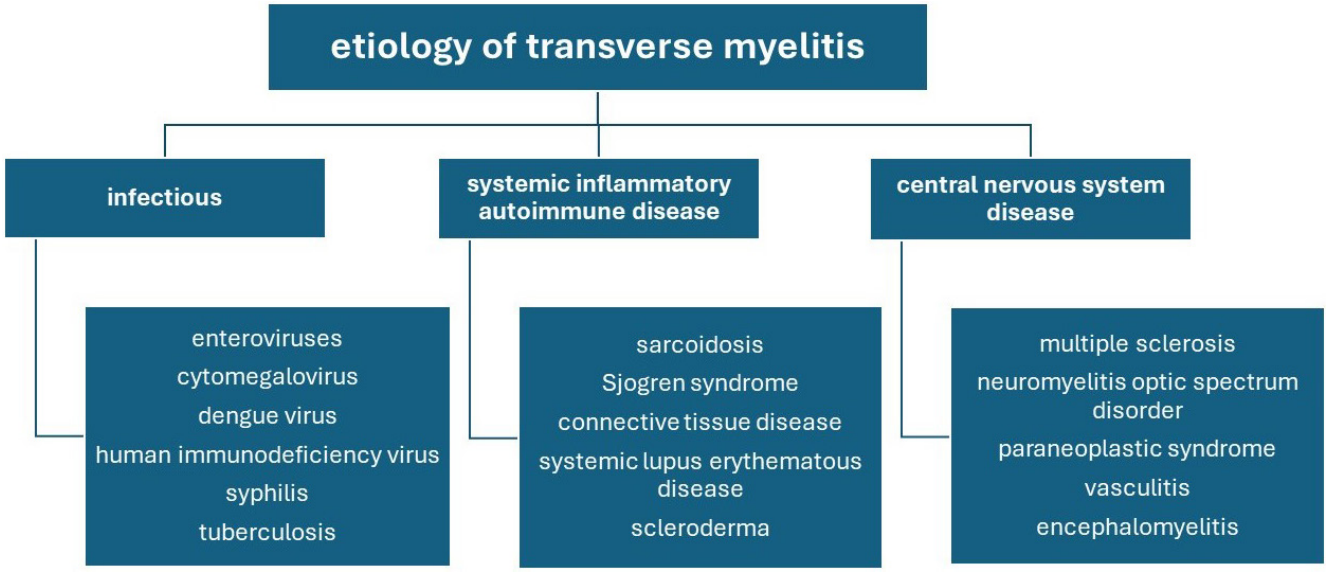

FIGURE 4 Etiology of transverse myelitis.

transverse myelitis, and a biopsy of lymph nodes revealed noncaseating granulomas. Both patients showed clinical improvement after commencing high dose of steroids.[6] Patel et al. also highlighted a case of transverse myelitis as the first presentation of sarcoidosis in a 62-year-old female. Her imaging findings and biopsy results were consistent with sarcoidosis-induced transverse myelitis, and her condition improved gradually after commencing high-dose steroids.[11] We have tabulated the reported cases of sarcoidosis-induced LETM in the last 10 years (Table 1).[6,11–15]

The exact pathophysiological mechanisms of sarcoidosis-induced TM remain poorly understood. Noncaseating granuloma in sarcoidosis induces an inflammatory response and subsequent tissue injury in the spinal cord and surrounding structures.[16] Granulomatous infiltration of the spine can cause inflammation, disrupt neuronal pathways, and impair blood flow, leading to typical clinical features of myelopathy.[16] In addition to granulomatous infiltration, immune-mediated mechanisms, aberrant T-cell activation, and cytokine (interleukin-2) production may perpetuate inflammation with subsequent tissue injury.[4] The diversity of clinical manifestations implies the involvement of various pathogenic mechanisms, highlighting the need for additional research into the immunological and genetic factors contributing to transverse myelitis in sarcoidosis.

A comprehensive evaluation, including clinical, radiological, laboratory, and biopsy findings, is required to diagnose sarcoidosis-induced LETM. Neuroimaging, particularly MRI spine and positron emission tomography (PET) CT, plays a central role in visualizing spinal cord abnormalities, including hyperintensity, cord edema, or focal lesions indicative of inflammation.[10,13] CSF analysis may reveal lymphocytic pleocytosis, elevated protein levels, and occasionally oligoclonal bands suggestive of cord inflammation. Serum biomarkers such as erythrocyte sedimentation rate, c-reactive protein, interleukin-2, and angiotensin-converting enzyme levels may also be elevated in sarcoidosis but lack specificity for both sarcoidosis and neurosarcoidosis.[17] Additionally, systemic investigations, including chest imaging and eye examination, are essential to rule out systemic involvement, which is characteristic of sarcoidosis. The challenges still lie in differentiating sarcoidosis-induced transverse myelitis from other etiologies of inflammatory myopathies despite the availability of these diagnostic modalities, necessitating the importance of careful omission of alternative etiologies.[13,17] In our case, the patient's MRI was consistent with myelopathy, and biopsy findings were suggestive of sarcoidosis. He was diagnosed with sarcoidosis-induced LETM after ruling out all other possible etiologies.

Neurosarcoidosis treatment is based on expert opinion and small retrospective disease, as limited data are available on the optimal treatment options for neurosarcoidosis (Figure 5).[18] Corticosteroids such as prednisone are usually prescribed as initial treatment and are typically initiated at high doses. Failure of corticosteroid monotherapy is common due to disease severity or high-dose prednisone toxicity.[19] Therefore, steroid-sparing or second-line agents such as methotrexate, mycophenolate, azathioprine, or cyclophosphamide are often recommended in combination with steroids except for neurosarcoidosis of the fascial nerve, which often responds to a few weeks of steroid monotherapy.[18] Methotrexate has been the most widely

TABLE 1 Reported cases of sarcoidosis-induced LETM.

Author et al.	Age/ Sex	Clinical presentation	Prior sarcoidosis	Biopsy source	Location of abnormal radiological findings	Treatment	Follow-up and outcome
Scott et al.[6]	47/M	Limb weakness, urinary retention, numbness, backache	No	Lung	LETM: entire spine	Steroids, plasma exchange therapy, infliximab	6 months: improved, MRI: normalized
Scott et al.[6]	56/M	Right-sided hemiparesis, neck pain	No		LETM: C2-C7	Steroids, infliximab	9 months: minimal improvement
Patel et al.[11]	62/F	Lower extremity weakness, sensory disturbance, urinary retention	No	Lung	LETM: C2-T4	High-dose steroids, methotrexate	Several months: improved, MRI: normalized
Mana et al.[12]	37/F	Paraplegia, urinary incontinence, saddle anesthesia	No	Lung	LETM: entire spine	Steroids, infliximab	3 months: improved
Cicia et al.[13]	60/M	Neuropathic pain, paresthesia	No	Lung	LETM: C5-D2	Methylprednisolone, prednisone, mycophenolate mofetil	9 months: improved, CT chest: normalized
Gupta et al.[14]	53/M	Acute urinary retention, weight loss, lower extremity weakness	No	Lymph node	LETM: T3-T12	Methylprednisolone, plasma exchange therapy	No response to treatment
Rodrigues et al.[15]	53/M	Limb weakness, urinary retention, ataxia	No	Lung	LETM: D4-D6, D10-D12	High-dose steroid, plasma exchange therapy, IVIG	1 year: improved

Abbreviations: C, cervical; CT, computed tomography; F, female; IVIG, intravenous immunoglobulin; LETM, longitudinally extensive transverse myelitis; M, male; MRI, magnetic resonance imaging; T, thoracic.

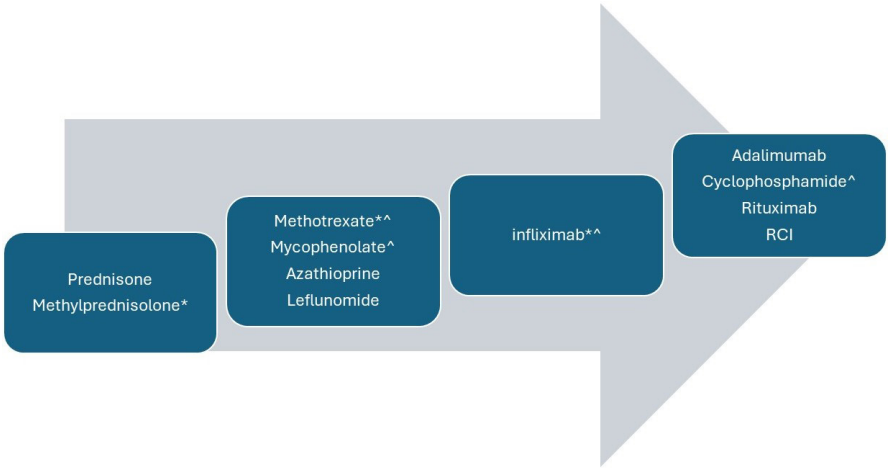

FIGURE 5 Approach to management of neurosarcoidosis. *indicates therapies which may be used for severe or progressive disease, ^indicates drugs that have been reported specifically for neurosarcoidosis, RCI, repository corticotropin injection.

used steroid-sparing agent for neurosarcoidosis, and the response rate has been reported to be 63% in one study.[20] To treat neurosarcoidosis more effectively, mycophenolate may also be used; however, mycophenolate has severe toxicity. Biologic agents such as infliximab have also shown efficacy in selected cases.[21,22] Physical and occupational therapy are also crucial in improving functional outcomes, especially in patients with residual neurologic deficits. The treatment regimen depends on many factors, including the severity of nervous system involvement, treatment response, tolerability, and associated potential risks. Our patient responded to mycophenolate, which has a better tolerability profile than other immunosuppressive agents, as compared to other immunosuppressive agents in one article.[15]

6 | CONCLUSION

Sarcoidosis-induced LETM represents a rare but life-threatening neurological manifestation of sarcoidosis, characterized by spinal cord inflammation and associated neurological deficits, necessitating comprehensive diagnostic evaluation. Sarcoidosis should be included in the differential diagnosis of LETM, particularly in patients with no lung involvement. Prompt recognition, diagnosis, and management are obligatory to optimize outcomes and prevent long-term disability. Diagnosis requires comprehensive clinical, laboratory, and radiological evaluations with histological findings. Management often involves a combination of corticosteroids and immunosuppressive agents with rehabilitation strategies to prevent disease relapse or progression. Further research is warranted to elucidate the underlying mechanisms of neurosarcoidosis and discover targeted therapies to improve patient outcomes.

AUTHOR CONTRIBUTIONS

Binayak Singh: Conceptualization; investigation; methodology; supervision; writing – original draft. **Zahoor Ahmed:** Investigation; methodology; writing – review and editing. **Anjali Mandal:** Supervision; writing – original draft; writing – review and editing. **Muhammad Zia Ali:** Methodology; writing – original draft; writing – review and editing. **Fnu Sanjna:** Investigation; methodology; writing – review and editing. **Rakhi Bai:** Investigation; methodology; supervision; writing – original draft; writing – review and editing. **Aman Kumar:** Investigation; methodology; supervision; writing – original draft; writing – review and editing. **Fnu Girish:** Investigation; methodology; supervision; writing – review and editing. **Fnu Karishma:** Investigation; methodology; writing – original draft. **Fnu Sonam:** Data curation; investigation; methodology; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data and supporting files of this article are available from the first and corresponding author upon reasonable request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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