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Non-Immune Causes of Longitudinally Extensive Transverse Myelitis: Lessons Learnt from A Tertiary Care Cohort

ABSTRACT

Background: Longitudinally extensive transverse myelitis (LETM) is often presumed to be immune-mediated. However, a substantial proportion of LETM arises from non-immune causes that closely mimic inflammatory myelitis, leading to diagnostic delays and inappropriate immunotherapy.

Objectives: The aim of the present study was to describe the clinical and radiological characteristics of LETM due to non-immune causes and highlight red flag features that differentiate these conditions from immune-mediated LETM.

Methods: We retrospectively reviewed LETM cases who presented to our tertiary care centre over a period of 6 years (2019–2025) and analysed cases due to non-immune causes.

Results: Out of a total 43 LETM cases, 27 cases with a non-immune cause were included in the present study. These included various etiological categories: infectious (n=11), vascular (n=5), nutritional (n=4), neoplastic/paraneoplastic (n=4) and compressive (n=3). The diagnostic delay in cases with vascular etiologies was more compared to other causes. 55% (5/27) of cases received immunotherapy before final diagnosis was established. Clinical and radiological diagnostic clues differentiating various etiologies were strikingly different compared to the immune mediated group.

Conclusion: Non-immune causes constitute a significant proportion of LETM in endemic regions. Recognizing red flag features is essential to avoid misclassification as immune-mediated LETM. Early identification of reversible etiologies such as vitamin B12 deficiency and spinal dural arterio-venous fistula significantly alters outcomes. Bottom of Form

Keywords: LETM; spinal infarct; subacute combined degeneration; spinal dural AV fistula; transverse myelitis

INTRODUCTION

Longitudinally extensive transverse myelitis (LETM), defined as "a T2-hyperintense spinal cord lesion spanning three or more vertebral segments", is often presumed to be associated with immune-mediated disorders such as Aquaporin-4 (AQP4) IgG positive neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD).[1-3] This prompts use of immediate immunotherapy when LETM is present, even before alternative etiologies are excluded.

It is important to note that LETM is not a diagnosis; it is a radiological pattern. It can be shared by a broad spectrum of diseases.[4-8] Vascular, infectious, compressive, nutritional, neoplastic, and paraneoplastic processes can all produce LETM, and frequently mimic inflammatory myelitis. The rate of misdiagnosis of LETM as immune-mediated, often receiving inappropriate immunotherapy, ranges from 17% to 74%.[9] Similar patterns are reported in Indian and Asian cohorts, where infectious and nutritional etiologies are more prevalent.[10-13]

It is well known that inappropriate immunotherapy like steroids worsens LETM secondary to vascular etiologies such as spinal dural arteriovenous fistulas (sDAVF).[14] Infectious myelitis may deteriorate with immunosuppression. Compressive and neoplastic lesions require urgent intervention, while nutritional myelopathies due to subacute combined degeneration of the cord (SACD) respond dramatically to replacement therapy.[15]

This prompted us to review our cases with LETM focusing exclusively on non-immune LETM, describing their clinical and radiological signatures and highlighting red flags that could prevent misdiagnosis.

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METHODS

We performed a retrospective observational study at a tertiary-care neurology centre in Mumbai over a period of 6 years (January 2019–October 2025). Permission was obtained from the Institutional Ethics committee prior to commencement of the study. Inclusion criteria were: (a) Clinical and radiological diagnosis consistent with transverse myelitis and (b) Magnetic resonance imaging (MRI) spine demonstrating longitudinal T2 hyperintensity extending across ≥3 vertebral segments. Patients with immune-mediated LETM (AQP4-positive NMOSD, seronegative NMOSD, MOGAD and other immune etiologies) were excluded. Data was collected from the outpatient records and hospital admission records. It included demographic details, clinical features, MRI characteristics, CSF profile, hemogram and biochemical parameters, infectious workup (tuberculosis, HIV, syphilis, viral serology as available), autoimmune profile (including NMO and MOG antibodies, ANA, ANA Blot, ACE, ANCA), and final etiological diagnosis were noted. The functional outcome was noted after treatment and at last follow up by the modified Rankin scale (mRS).

STATISTICAL ANALYSIS

Continuous variables such as age, symptom duration, and diagnostic delay were summarized as mean ± standard deviation (SD) to convey central tendency and dispersion. Categorical variables including sex, etiology category, level of cord involvement, and outcome categories, were presented as counts and percentages to illustrate distribution across groups.

RESULTS

Out of a total 43 cases with LETM, 27 cases with non-immune causes were included in the present study. The mean age at presentation was 43 years (range: 8 years to 73 years). Majority were males (18/27, 66.6%). The following were the predominant etiological categories noted: infectious or para-infectious (n=11), vascular (n=5), nutritional (n=4), neoplastic or paraneoplastic (n=4) and compressive (n=3) (Table 1). The various categories are described in detail. We also present few illustrative cases in each category to emphasize clinical and radiological red flags.

Table 1: Etiological categories in non-immune mediated LETM

Cause of non-immune mediated LETM	Total number, n (%)
Infectious or para-infectious	11 (40.7 %)
Vascular	5 (18.5 %)
Nutritional	4 (14.8 %)
Neoplastic or paraneoplastic	4 (14.8 %)
Compressive	3 (11.1 %)

A. Infectious causes

Infections were predominant cause for LETM in our cohort. These included tubercular myelitis (n=6), post viral myelitis (n=2), fulminant enteroviral myelitis (n=1), chikungunya myelitis (n=1) and HIV myelopathy (n=1). Two cases with TB myelopathy presented after initial treatment for disseminated tuberculosis with tuberculomas (Figure 2). Intramedullary conglomerate granulomas masqueraded as LETM in these cases. Besides, extradural soft tissue component was evident especially on contrast imaging. Viral etiologies—including chikungunya, post-viral myeloneuropathy, and post-COVID myelitis—presented acutely with paraparesis and bladder involvement. CSF was diagnostic in most cases along with serology for the viral markers. However, CSF pleocytosis was variable; normal cell counts did not rule out infectious myelitis in some cases. As a group, these cases had variable outcome despite appropriate therapy with anti-tubercular agents or anti-viral therapy. Especially, the fulminant enteroviral myelitis and post COVID myelitis cases received intravenous steroids and immunoglobulins and had a poor outcome (mRS=4) on follow up.

Table 2: Red Flags for Non Immune LETM

Etiology	Key Clinical Red Flags	MRI Red Flags
Vascular – sDAVF	Chronic, progressive course; worsening after steroids; fluctuating symptoms; imbalance out of proportion to sensory loss	Dorsal flow voids; serpiginous vessels; patchy enhancement; “missing-piece” sign; conus involvement
Vascular – Spinal Cord Infarction	Hyperacute onset; severe pain at onset; vascular risk factors; rapid progression to nadir	Anterior cord hyperintensity; “snake-eye” sign; restricted diffusion
Infectious – Tuberculosis	Prior TB history; subacute progression; may lack systemic symptoms	Nodular or granulomatous enhancement; patchy asymmetric LETM; associated vertebral or meningeal disease
Infectious – Viral / Post-COVID	Recent viral illness; fever, arthralgia, cytopenias; mono-phasic course	Central gray-matter–predominant T2 hyperintensity (“glass-eel” sign); minimal or no enhancement
Nutritional – Vitamin B12 Deficiency	Subacute gait ataxia; distal paresthesias; macrocytic anemia; peripheral neuropathy	Dorsal column–restricted LETM; inverted-V sign; no enhancement; no cord expansion
Neoplastic – Intramedullary Tumors	Relentless progression; band-like dysesthesia; no steroid response	Expansile cord lesion; heterogeneous enhancement; architectural distortion; irregular margins
Compressive Myelopathy	Severe axial back pain; mechanical worsening; bladder involvement; poor steroid response	Eccentric extradural compression; long-segment cord edema secondary to compression; Pan cake sign

Case 1: A 28-year-old male with a remote history of treated CNS tuberculosis presented with six weeks of progressively worsening lower limb weakness and gait imbalance, accompanied by new urinary urgency. Examination showed spastic paraparesis with a sensory level at T10. MRI spine revealed a long-segment T2 hyperintense lesion from D6–D11 consistent with LETM, characterized by patchy, asymmetric involvement, cord edema, and multiple small nodular enhancing foci (Figure 1 A-C). Autoimmune markers (AQP4-IgG, MOG-IgG) were negative. CSF demonstrated lymphocytic pleocytosis and elevated protein. In view of the patient's prior TB history and granulomatous-appearing enhancement, targeted testing was pursued; CSF gene xpert was positive for Mycobacterium tuberculosis, confirming tubercular LETM. Antitubercular therapy with adjunctive steroids led to gradual neurological improvement.

Red-flag pattern: Prior TB history, nodular/ granulomatous enhancement, lymphocytic CSF with high protein, positive GeneXpert, patchy non-central long-segment LETM.

Case 2: A 22-year-old previously healthy male presented with rapidly progressive paraparesis and acute urinary retention, occurring three days after a febrile illness marked by severe arthralgia and myalgia. On examination, he had spastic paraparesis with a sensory level at T10 and preserved cranial nerve function. Initial laboratory evaluation revealed anemia and thrombocytopenia, raising suspicion for a post-viral inflammatory process. MRI of the spine demonstrated a longitudinally extensive T2-hyperintense lesion involving the thoracic cord, with a striking central gray-matter–predominant pattern producing the characteristic "glass-eel appearance" (Figure 1D). There was no significant enhancement. CSF analysis showed lymphocytic pleocytosis with elevated protein but no oligoclonal bands. Autoimmune markers i.e AQP4-IgG and MOG-IgG were negative. On Serology Chikungunya IgM was positive, confirming the diagnosis of chikungunya-associated myelitis. He was managed with supportive care, steroids and physiotherapy, with gradual neurological improvement over few weeks, consistent with the typically monophasic and self-limited course of chikungunya-related spinal cord involvement.

Red-flag pattern: Viral prodrome, cytopenias, lymphocytic pleocytosis in CSF, central gray-matter "glass-eel" sign, negative autoimmune markers.

Case 3: A 32-year-old male, presented with an abrupt onset of lower limb weakness and urinary retention. His symptoms aggravated in the next 48 hours, without any prior trauma or systemic illness. On examination, he had spastic paraparesis with brisk reflexes and a sensory level at D8. His blood workup —including complete blood counts, inflammatory markers, and metabolic profile—was normal. CSF analysis showed normal cell counts and protein, and autoimmune markers (AQP4-IgG, MOG-IgG, ANA/ENA) were negative. MRI of the spine revealed a long-segment T2 hyperintense lesion extending from the mid-thoracic cord to the conus, without enhancement or significant cord expansion (Figure 1E). A detailed review of his recent history revealed a mild upper-respiratory illness one week prior, for which he had not sought medical attention. Nasopharyngeal RT-PCR performed during admission returned positive for SARS-CoV-2. The temporal association with recent infection, normal CSF findings, non-enhancing MRI, and negative autoimmune workup supported a diagnosis of post-COVID viral myelopathy, a para-infectious immune-triggered phenomenon increasingly recognized in the post-pandemic era. He was treated with high-dose steroids, IVIG, rituximab and supportive care, with gradual neurological improvement over the following weeks.

Red-flag pattern: Recent viral illness, normal CSF, non-enhancing long-segment lesion, negative autoimmune markers, monophasic course

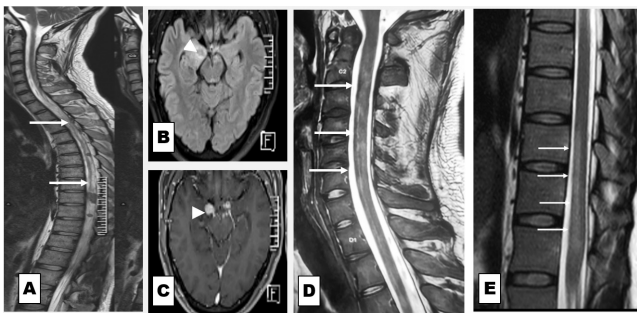

Figure 1(A to E): (A): MRI Spine sagittal T2W image showing longitudinally extensive T2 hyperintensity from C7 to D8 with cord edema (white arrows) and multiple small nodular lesions, suggestive of granulomatous etiology (seen in case 1); (B and C): MRI Brain axial FLAIR image and T1W post contrast image showing FLAIR-hypointense lesion with surrounding edema in the right medial temporal lobe with post-contrast nodular enhancement (arrow heads) suggestive of CNS tuberculosis with both spinal and intracranial involvement (seen in case 1); (D): MRI spine sagittal T2 weighted image showing the characteristic "glass-eel" appearance- slender, translucent, uninterrupted T2 signal involving the central cord in Chikungunya myelitis (white arrows) (seen in case 2); (E): MRI spine sagittal T2 weighted image showing long-segment T2 hyperintense lesion extending from the mid-thoracic cord to the conus, without enhancement or significant cord expansion in post-COVID myelitis (white arrows) (seen in case 3)

B. Vascular causes

Vascular causes noted were acute spinal cord infarction (SCI) (n=3) and sDAVF (n=2). These cases had a hyperacute to acute onset and severe deficits at presentation. In our cohort, all cases were initially misclassified as inflammatory LETM, and given immunotherapy (steroids, intravenous immunoglobulins and cyclophosphamide) with poor response or worsening after immunotherapy (both cases of sDAVF) before final diagnosis

was made. The mean delay in diagnosis was 2.6 months in the vascular group of which the mean delay in diagnosis in patients with sDAVF was 6 months. The presence of pain at onset, rapid progression, and vascular risk factors were key clinical clues. MRI features typical of SCI such as "snake eye sign" was seen in all 3 cases and restricted diffusion in 1/3 cases. The characteristic MRI features of sDAVF like flow voids and prominent venous engorgement were noted on retrospective review of prior imaging studies. The typical "missing puzzle piece sign" were also noted in sDAVF cases.

Case 4: A 61-year-old woman presented with a 3–4-month history of progressively worsening paraparesis and urinary retention. She had been treated elsewhere as seronegative NMOSD and experienced clinical deterioration following corticosteroid therapy. Examination revealed spastic paraparesis with a sensory level at T10. MRI review done at our centre demonstrated a long-segment thoracic T2 hyperintensity with prominent dorsal flow voids and patchy enhancement showing the characteristic "missing puzzle piece sign" (Figure 2A,2B and 2E). CSF analysis was normal. Spinal angiography confirmed a right L2 dural arteriovenous fistula, and endovascular embolization resulted in neurological improvement.

Red-flag pattern: Chronic progression, worsening after steroids, dorsal flow voids, conus involvement, missing puzzle piece sign, normal CSF study.

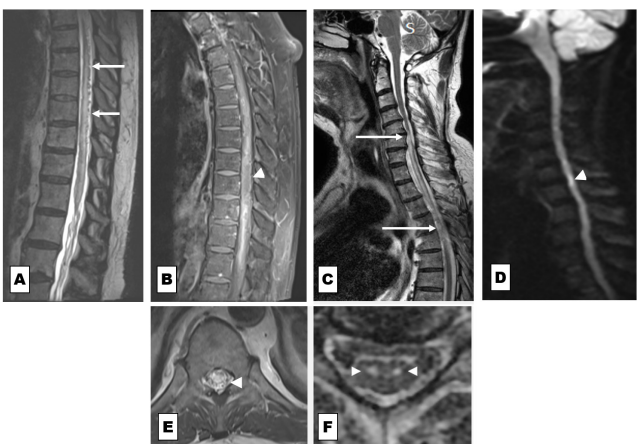

Figure 2 (A to F): (A): MRI Spine sagittal T2W image showing serpiginous dorsal flow voids with patchy areas of cord hyperintensity, suggestive of dilated venous channels (white arrows) in spinal dural arterio-venous fistula (sDAVF) (seen in case 4); (B): MRI spine sagittal T1W post contrast image showing the "missing puzzle sign" (arrow head)- absence of segmental post contrast enhancement - typical of venous hypertensive myelopathy seen in sDAVF (seen in case 4); (C and D): MRI spine sagittal T2 weighted image and diffusion weighted image - longitudinally extensive T2 hyperintensity extending from C6 to D5 (white arrows) (seen in case 5); (E): MRI spine axial T2W image showing the dorsal flow voids seen in sDAVF (arrow head) (seen in case 4) (F): MRI spine axial T2W image showing the classic snake-eye appearance, with bright, rounded foci in both anterior horns—highly suggestive of infarction in this vascular territory (seen in case 5)

Case 5: A 57-year-old male developed sudden, severe right upper limb pain while lifting luggage, followed within hours by quadriparesis and sphincter involvement. His medical history included deep-vein thrombosis and pulmonary embolism. MRI spine revealed anterior cervical cord T2 hyperintensity with the classic snake-eye appearance on axial images and restricted diffusion, consistent with acute ischemia (Figure 2C, 2D and 2F). CSF was normal. A diagnosis of anterior spinal artery infarction was established. He was treated with intravenous steroids and supportive management. His power improved gradually and was able to walk with a walker.

Red-flag pattern: Hyperacute onset, severe pain at onset, vascular risk factors, snake-eye sign, restricted diffusion on spinal imaging, normal CSF study.

C. Nutritional causes

Nutritional myelopathies secondary to vitamin B12 deficiency were noted in 4 cases. Anti-parietal cell antibody positivity and alcohol abuse were seen in one case each. Predominant vegetarian diet as an underlying risk factor was seen in all cases. These cases presented with acute to subacute onset predominantly sensory features and characteristic dorsal column involvement as seen in imaging studies. This signal is often reversible on treatment, as noted in one case. The response to therapy was dramatic and functional outcome was excellent in this group.

Case 6: A 62-year-old lady presented with a three-month history of progressive gait unsteadiness, distal paresthesias, and worsening fatigue. She denied bowel or bladder symptoms. She had a pure vegetarian diet and often fasted for religious purposes. Examination revealed impaired vibration and joint-position sense in both lower limbs, Romberg sign was positive with mild spasticity and preserved muscle strength. Her sensory level was ill-defined, but the pattern suggested dorsal column dysfunction rather than a classical transverse myelitis. MRI of the spine demonstrated a long-segment T2 hyperintensity confined to the dorsal columns, extending from C3 to T6, with the characteristic inverted-V sign on axial images. There was no enhancement or cord expansion (Figure 3A and 3B). Laboratory evaluation revealed macrocytic anemia and a markedly reduced serum vitamin B12 level. CSF analysis was normal. The constellation of dorsal column–predominant LETM, macrocytosis, and low B12 confirmed SACD. She was initiated on parenteral vitamin B12 replacement, with gradual improvement in gait and sensory function over subsequent weeks.

Red-flag pattern: Macrocytic anemia, peripheral neuropathy, dorsal column–restricted LETM, inverted-V sign, absence of enhancement, normal CSF

D. Neoplastic and Paraneoplastic causes

Neoplastic involvement of the spinal cord was seen in 3 cases (astrocytoma in 2 cases and primary spinal cord lymphoma in

one case), and paraneoplastic myelopathy in one case. Majority of these patients (3/4) received immunotherapy (steroids and IVIG) prior to referral to our centre. Although, expansile cord lesions were noted in all cases, absence of systemic disease and delay in diagnostic biopsy accounted for delay in final diagnosis. The functional outcome in these cases was poor (mRS=4). Paraneoplastic myelopathy was noted in one case who was a 35-yr-old lady, initially managed as CNS vasculitis and later diagnosed with B cell lymphoma (after a delay of 2 years), when metastatic deposits were noted in an abdominal wall abscess biopsy. She eventually succumbed due to severe urosepsis.

Case 7: A 62-year-old male presented with a two-month history of progressively worsening paraparesis and urinary retention. He reported no sensory level initially, but over time developed a vague band-like tightness around the mid-thoracic region. Examination revealed spastic paraparesis with impaired vibration sense and a sensory level at D8. There was no history of infection, autoimmune disease, or systemic malignancy. MRI of the spine demonstrated a long-segment T2 hyperintense lesion involving the mid-thoracic cord, but unlike inflammatory LETM, the lesion showed focal expansile morphology, heterogeneous enhancement, and distortion of normal cord architecture (Figure 3C and 3D). There was no clear central predilection, and the margins were irregular. CSF analysis was normal, and autoimmune markers (AQP4-IgG, MOG-IgG) were negative. Given the progressive course, cord expansion, and atypical enhancement pattern, a neoplastic etiology was suspected. He underwent D8–D10 laminectomy and biopsy, which confirmed a high-grade intramedullary astrocytoma. He was referred for oncological management.

Red-flag pattern: Expansile cord lesion, persistent heterogeneous enhancement, architectural distortion, normal CSF, lack of response to steroids, progressive course.

E. Compressive Myelopathy

Compressive myelopathy giving rise to LETM like features were seen in 3 cases. Two of these cases received intravenous steroids prior to referral to our centre as radiological features were confused with an immune mediated myelopathy. Pain was predominant symptom along with chronic progressive myelopathic features and absence of bowel and bladder involvement were noted. On review of imaging, characteristic "pan-cake sign" was noted in 2 cases.

Case 8: A 20-year-old female with history of birth asphyxia and developmental delay, presented with subacute quadriparesis and mild urinary urgency. This was preceded by a generalised tonic clonic seizure at home. She also complained of severe neck pain. She was noted to have quadriparesis with dystonic posturing of neck and hands, and bladder involvement in the form of urgency. MRI demonstrated a long-segment T2 hyperintensity from C2–T1, with disc bulges and "pan-cake" like enhancement pattern (Figure 3E-3G). She received intravenous methylprednisolone, with improvement in power, as relatives were reluctant for any neurosurgical intervention. The acute deterioration post seizure, normal CSF, and severe axial neck pain were discordant with an immune-mediated process. This case exemplifies that LETM may be seen in acute compressive myelopathy.

Red-flag pattern: Severe neck pain, eccentric compression, sharp transition zones, extradural pathology, inconsistent enhancement pattern.

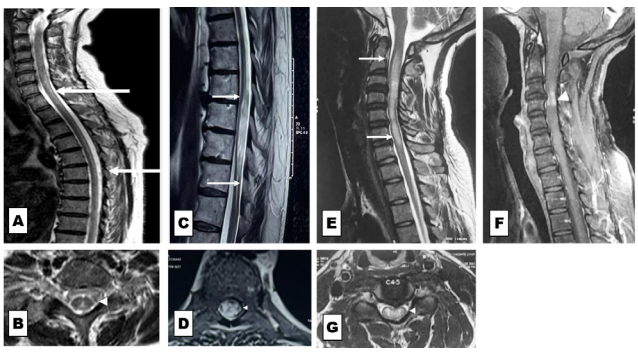

Figure 3(A to G): (A and B): MRI Spine sagittal T2W image and axial image showing longitudinally extensive hyperintensity extending from C7 to D8 (white arrows) with symmetric dorsal column involvement, forming the characteristic inverted "V" configuration (arrow head) in subacute combined degeneration of the cord respectively (seen in case 6); (C and D): MRI Spine sagittal T2W image and axial image showing longitudinally extensive mild expansile intramedullary lesion with heterogenous hyperintensity from D8 to D10 (white arrows), suggestive of an infiltrative neoplastic process with cord architecture distortion (arrow head) (seen in case 7); (E and F): MRI Spine sagittal T2W image and T1W post contrast image showing long-segment T2 hyperintensity from C2–T1, with disc bulges (white arrows) and "pan-cake" like enhancement pattern (arrow head) (seen in case 8); (G): MRI Spine axial T2W image showing disc bulge at C4- C5 level with cord signal (arrow head) in compressive myelopathy (seen in case 8)

DISCUSSION

The etiological breadth of LETM poses a major diagnostic challenge in real-world neurology. In our cohort of 43 patients, non-immune causes accounted for nearly two-thirds (27/43)—a proportion substantially higher than that reported in NMOSD-focused series.[16] Our study showed a striking male predominance, unlike the female preponderance noted in most immune-mediated series.[17]

Infectious myelitis was the most common non-immune cause seen in 40% of cases in our study. In a large retrospective Indian series comprising 64 LETM patients, non-immune causes (post-infectious myelitis, SACD, tuberculous myelitis, and sDAVF) accounted for around 25% of total cases.[10] In tuberculosis-endemic regions like India, spinal tuberculosis remains a critical differential for LETM.[14] Viral LETM—including varicella-zoster, HIV-associated myelitis, chikungunya, and post-COVID myelitis—

has been increasingly recognized, with several reports describing gray-matter-predominant lesions and monophasic para-infectious courses.[18-20]

An Argentine cohort also highlighted the heterogeneity of LETM, wherein idiopathic, neoplastic, and vascular etiologies (including dural fistulas) featured among non-NMOSD causes.[21] Vascular etiologies such as sDAVF are consistently reported as atypical causes of LETM and are frequently misdiagnosed as inflammatory myelitis.[22–24] These cases require a high index of suspicion and careful review of imaging to identify classical signs such as dorsal flow voids or the "missing puzzle-piece sign".[25] Early angiographic evaluation is recommended when suspected.[26]

Acute spinal cord infarction (SCI) is a rare cause, seen in about 5–8% of acute myelopathies.[27] It should be suspected in cases with catastrophic, hyperacute onset symptoms and negative autoimmune serology. In addition to classical signs like "pencil-like" lesions and the owl's-eye sign, vertebral body infarction can be a diagnostic clue.[28] Diffusion-weighted imaging abnormalities are highly specific and reported in up to 82% of cases.[29]

Nutritional myelopathy secondary to vitamin B12 deficiency can occur with risk factors such as vegetarian diet, alcohol abuse, autoimmune gastritis, malabsorption, and copper deficiency.[30-32] The dorsal column–restricted T2 hyperintensity with inverted-V sign and absence of enhancement are distinguishing imaging features. Unlike other etiologies, this subgroup demonstrates dramatic response to replacement therapy and excellent functional recovery.[33]

Neoplastic and paraneoplastic etiologies accounted for 14.8% of cases and were associated with the worst outcomes. The most common intramedullary spinal tumors are ependymomas followed by astrocytomas.[34] Expansile cord morphology, heterogeneous enhancement, architectural distortion, and lack of steroid response are important red flags. Paraneoplastic myelopathy is rare and often associated with amphiphysin-IgG or CRMP-5-IgG antibodies, though antibody-negative cases are reported.[35-36] Guidelines recommend surveillance for 6 months to 4 years for occult malignancy in suspected paraneoplastic syndromes.[37]

Compressive myelopathy was identified in 11.1% of patients and was occasionally confused with inflammatory etiologies, leading to inappropriate steroid use. Compressive myelopathy due to cervical spondylosis or stenosis may exhibit intramedullary T2 hyperintensity and T1 hypointensity. The transverse "pancake-like" post-gadolinium enhancement pattern is a useful clue.[38]

Collectively, our study emphasizes that LETM is a radiological pattern rather than a diagnosis. The pattern of gadolinium enhancement accompanying LETM on MRI can be an important clue to diagnosis, especially characteristic radiological features with each entity.[39] Red-flag indicators—hyperacute onset, severe pain, worsening after steroids, normal CSF, expansile lesions, dorsal flow voids, dorsal column restriction, granulomatous enhancement, and systemic risk factors—should prompt evaluation beyond immune-mediated causes.

Our study had certain limitations. This was a single-centre study with a modest sample size, limiting generalizability. Referral bias may have led to complex or atypical cases. Long-term functional outcomes were not uniformly available in all subgroups.

CONCLUSIONS

Non-immune causes constitute a significant proportion of LETM in endemic regions like ours. Misdiagnosis leads to unnecessary immunotherapy and delay in definitive management. A structured approach that integrates clinical red flags, MRI patterns, and targeted investigations is essential in order to avoid unnecessary immunotherapy and to ensure timely, etiology-specific treatment. Early identification of reversible etiologies such as B12 deficiency and sDAVF significantly alters outcomes.

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