Case Series

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Longitudinally extensive transverse myelitis, a disabling disorder with a good prognosis: a case series from Nepal

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Introduction: Longitudinally extensive transverse myelitis (LETM) is a rare spinal cord disorder with variable etiologies and presentations. It can present solely or as an association with other neurological disorders.
Methodology: It was a series of cases of LETM in a tertiary care hospital.
Clinical presentation and outcomes: The initial three cases presented with bilateral lower extremity weakness and were diagnosed as transverse myelitis while, the fourth case, already diagnosed as LETM presented with seizure followed by loss of consciousness. All four cases had a good prognosis to date with continued physiotherapy.
Conclusion: The early diagnosis of the disease helps to guide the optimal management and decide the potential need for physiotherapy.

Keywords: longitudinally extensive transverse myelitis, neuromyelitis optica spectrum disorder, weakness

Introduction

Longitudinally extensive transverse myelitis (LETM) is a rare entity of spinal cord inflammation, defined as a hyperintense lesion extending over three or more vertebral segments on spinal MRI[1]. Neuromyelitis Optica Spectrum Disorder (NMOSD) is the most important etiology of LETM. Acute myelitis with LETM is included as one of the core clinical characteristics in the diagnosis of NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status[2]. Other etiologies associated with LETM include multiple sclerosis (MS), postinfectious myelitis, spinal cord infarction, systemic lupus erythematosus, acute disseminated encephalomyelitis (ADEM), Sjogren syndrome, and occasionally idiopathic[3,4]. Therefore, excluding other differentials of LETM is crucial before diagnosing LETM. Early diagnosis of LETM and prompt initiation of immunotherapy is pivotal for optimal recovery, and preventing disability and mortality[5]. Despite of increasing prevalence of LETM in East Asian countries compared to Western countries, there have been very limited studies from Nepal[3]. Therefore, we have presented the first case series of LETM comprising four hospital-admitted cases.

HIGHLIGHTS

- Longitudinally extensive transverse myelitis is a rare disabling spinal cord disorder.
- It has wide variation in etiologies, presentations, and prognosis.
- We present a case series of four cases with good prognosis till date.
- The early recognition and diagnosis of the disease is important for good prognosis of the disease.

Methodology

This study was a series of prospective cases of LETM in a tertiary care hospital. All the cases were diagnosed as LETM. The detailed demographic, clinical, and management information was collected accordingly. The cases were kept on follow-up wherever possible. The emphasis was given more on physiotherapy after the discharge from the hospital. It was conducted in accordance with the Preferred Reporting Of CasE Series in Surgery (PROCESS) guidelines[6].

Cases presentation

Case 1

A 20-year-old male presented in the outpatient department (OPD) with sudden onset bilateral lower extremity weakness,

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which had progressed to involve bilateral upper extremities over the course of 3 days. He also complained of numbness and tingling sensation in the limbs and difficulty with micturition. However, there was no history of fever, systemic viral disease, diarrhea, vomiting, falls, or trauma. There was no history of similar illnesses in the past. On examination, the patient was vitally stable, conscious, and well-oriented. There were no signs of meningeal irritation, and his higher mental and cerebellar functions were intact. On motor examination, the power was normal (5/5 on the Medical Research Council (MRC) scale) in the lower limbs but slightly decreased (4/5) in the upper limbs. The deep tendon reflexes (DTRs) were brisk in all four limbs, and the Babinski sign was bilaterally positive. On sensory examination, there was a decreased sense of vibration in the left upper and right lower limbs.

Laboratory investigations revealed a raised total leukocyte count (TLC) (13 290 cells/mm^3), raised C-reactive protein (CRP) (9 mg/l), and normal erythrocyte sedimentation rate (ESR). CSF protein electrophoresis was negative for oligoclonal bands. RFTs, LFTs, and serum electrolytes were within normal limits. An MRI of the cervical spine was done, which showed a T2 hyperintense signal at C3-C4 to D1 with patchy enhancement and mild cord expansion. The central part of the cord and more than two-thirds of the cord circumference were involved. Mild cerebellar tonsillar ectopia and mild degenerative changes at L4-L5 were noted on MRI screening of the whole spine. The patient was diagnosed with LETM based on the clinical and neuroimaging findings. He was managed with pulsed injection methylprednisolone for 5 days, along with oral gabapentin and proton pump inhibitors for supportive care. At the time of discharge, the patient was hemodynamically stable, but the weakness in the upper limbs persisted. He was discharged on oral prednisolone, gabapentin, and mycophenolate mofetil. The caretakers were advised to arrange regular physiotherapy for the patient.

Case 2

A 36-year-old female presented to the neurology OPD with a complaint of weakness in the lower limbs for 3 months. It had progressed to involve the upper limbs too. It was associated with a tingling sensation, numbness in all four limbs, and blurred vision in the left eye. There was no history of fever, viral illness, diarrhea, vomiting, falls, or trauma. She had a similar episode 2 years ago, during which she developed bilateral lower extremity weakness rendering her unable to walk. The episode lasted for a few weeks and resolved spontaneously. On examination, the patient was vitally stable, conscious, and well-oriented. There were no signs of meningeal irritation, and his higher mental and cerebellar functions were intact. Motor examination showed slightly decreased power (4/5) in all four limbs. The DTRs were brisk, and the Babinski sign was bilaterally positive. The vibration sense was decreased in the left upper and right lower limbs.

Visual Evoked Potential (VEP) revealed prolonged P100 latency from the left side, indicative of optic neuritis. Contrast-enhanced magnetic resonance imaging (CEMRI) showed multifocal areas of short and long segment eccentric lesions involving the cervical cord (C3-C5) and dorsal cord (D8-D9) with peripheral enhancement in the cervical cord. These findings were suggestive of a demyelinating lesion. Additional findings included mild central canal dilation at the C6-C7 level and diffuse disk bulging at the L4 to L5 level. Based on the findings, the patient was admitted and managed as a case of NMOSD. She was managed with pulsed intravenous methylprednisolone therapy and oral gabapentin. She showed improvement within a few days and was ambulatory.

Case 3

A 16-year-old female patient presented with a complaint of high-grade fever documented at 102°F along with progressive bilateral lower limb weakness for 10 days. She also had sensory complaints of numbness and tingling in the lower limbs. The weakness had gradually progressed to involve the upper limbs. On examination, her GCS was 15/15 (E4V5M6). The power was 0/5 in both lower limbs and 2/5 in both upper limbs on the MRC scale. Reflexes were brisk, and planters were bilaterally upgoing. CSF analysis revealed TLC of 68 cells/mm^3 (89% neutrophils), decreased glucose (28 mg/dl), and raised CSF protein levels (103 mg/dl). CSF protein electrophoresis was negative for IgG oligoclonal bands. CEMRI of the head and spine showed long segment T2/FLAIR hyperintensity with mild thickening of the spinal cord and relative sparing of conus medullaris. There was subtle enhancement of the cord in the central and peripheral portions, predominantly at the T9-T12 level. Subcortical T2/FLAIR hyperintense foci with no diffusion restriction/contrast enhancement were reported in the bilateral precentral gyrus, the central part of the pons, and the upper medulla. She was seronegative for Anti-NMO IgG (AQP4-IgG) and Anti-MOG antibodies. She was admitted to the ward and managed as a case of LETM-NMOSD with intravenous pulsed methylprednisolone, oral steroids, mycophenolate mofetil, and supportive therapy. On discharge, the power in the upper limbs had improved (4/5) while it was still 0/5 in the lower limbs. She was discharged on oral prednisolone, gabapentin, and mycophenolate mofetil and was advised to continue physiotherapy.

Case 4

A 56-year-old diabetic and hypertensive female presented in the OPD with a chief complaint of fever for 2 days, accompanied by an episode of transient loss of consciousness that occurred 1 day prior. The episode was associated with abnormal body movements, frothing from the mouth, and bowel incontinence. Our patient was a known case of LETM diagnosed 1 year ago and currently receiving cyclophosphamide pulsed therapy and oral steroids. On examination, she was conscious, well-oriented, and afebrile at the time. Her blood pressure and pulse were 70/50 mmHg and 79 b/m, respectively. On motor examination, power on the right side was normal (5/5), decreased (2/5) in the left upper and 1/5 in the left lower limb. After relevant investigations, she was diagnosed as a case of septic shock secondary to hospital-acquired pneumonia (HAP) on top of community-acquired pneumonia (CAP) and complicated urinary tract infection (UTI). She was treated with vasopressors, antibiotics, and steroids. At the time of discharge, she was clinically and hemodynamically stable. The basic clinical information of all cases is given in Table 1.

Discussion

The incidence of transverse myelitis is one to eight cases per million people per year and LETM is a rare but disabling

Table 1

Summary table with basic clinical information of four cases

Cases	Clinical features	On examination	Investigations	Management	Diagnosis
1	20 Y/M presented with weakness of B/L lower limb for 3 days progressive now involving upper limb associated with tingling, numbness, and retention of urine	Vitals-stable CNS- GCS 15/15 Tone- Normal Power- 4/5 on the upper limb and normal on the lower limb. Reflex- brisk Plantar- B/L upgoing, sensory- decreased to vibration on the left upper and right lower limb	MRI of C-spine with a screening of the whole spine: Long segment T2 high signal intensifying the spinal cord at C3-C4 to D1 suggestive of likely acute demyelination. Predominant involvement of the central part of the cord is noted	Prednisone 60 mg OD Mycophenolate 250 mg for 1 week then 500 mg	Longitudinal extensive transverse myelitis (C3/4-D1)
2	36 Y/F presented with lower limb weakness followed by upper limb for 3 months with tingling, numbness, and blurred vision. With two episodes in the past which has subsided on its own	Vitals- stable CNS- GCS 15/15 Tone- Normal Power 4/5 on all limbs, reflex- brisk Plantar- B/L upgoing, sensory- decreased to vibration on LUL and RLL	Visual Evoked Potential (VEP)- features of delayed P100 latency likely sec. to optic neuritis. Contrast-enhanced MRI (CEMRI)- multifocal areas of eccentric lesion involving C3-C5 and D8-D9. Oligoclonal band- not documented on CSF	Methylprednisolone	Longitudinal extensive transverse myelitis- NMOSD
3	16 Y/F presented with fever and weakness of B/L lower limbs, which was progressive by involving upper limbs with difficulty swallowing	Vitals- stable CNS- GCS 15/15 (E4V5M6) Power Lower limb 0/5 upper limb ⅖ Reflex-brisk, plantar B/L upgoing	CSF- TLC 68/mm3 (N-89%, L11%) Glu- 28 mg/dl, protein 103 mg/dl Blood c/s Klebsiella present MRI of head and spine-features suggestive of demyelinating etiology	-Methylprednisolone Steroids -Mycophenolate -Gabapentin	Longitudinal extensive transverse myelitis - NMOSD
4	56 Y/F k/c/o HTN, DM, and longitudinally extensive transverse myelitis under medication presented with: Fever for 2 days with transient loss of consciousness Associated with abnormal body movement of upper extremities, frothing, and bowel inconsistency for one day	BP- 70/50 mmHg RR- 24/min, PR- 79 bpm Spo2- 98% via NC S/e- CNS: GCS 15/15 Tone- Normal, power- decrease on Lt. Side Plantar B/L down going	TLC-5880 RBS-237 mg/dL Urine RME- RBC /WBC/ bacteria in significant amounts. Blood c/s- MSCONS seen HRCT chest- Opacity present suggesting CAP	IV fluids Vasopressor IV antibiotics	Longitudinal extensive transverse myelitis. Septic shock secondary to HAP on top of CAP and complicated UTI

condition subtype[7–9]. It has varied presentation depending upon its different etiologies with a likely poor outcome[3]. Even etiologies can vary in different regions[10]. It shows the importance of clinical studies from all over the world. There are few studies from Nepal on LETM. Here, we have presented the first case series, including four hospital-admitted cases.

In our study, three cases (75%) were the first episode of LETM while the remaining one case (25%) was a chronic case with residual neurological deficit. Age group 21–40 years was seen as most commonly affected, that is two cases (50%), and female preponderance, that is three cases (75%). The most common clinical presentation was quadriparesis, that is three cases (75%), followed by sensory alteration, paraparesis, and bladder involvement. MRI showed the most frequent spinal cord lesion in the cervicothoracic region in three cases (75%) with no brain involvement but brainstem involvement in 1 case (25%). When it is compared with the recent retrospective study of 19 patients from Nepal, in contrast, they have reported male preponderance (68.42%), bladder involvement as the most common finding (78.94%) followed by quadriparesis (42.10%), and MRI imaging finding of thoracic cord lesion being the most commonly affected area (52.63%) with the cervicothoracic region the least (15.78%)[11].

Etiologically, our two cases (50%) had Neuromyelitis Optica Spectrum Disorders (NMOSD) consisting of one case being seronegative NMOSD (both AQP4-IgG and MOG-IgG negative) and one case with unknown antibody status. The remaining two cases (50%) had unknown etiology. The previous study from Nepal reported 36.84% of patients with AQP4-IgG positive NMOSD, 21.05% of patients had unknown etiology and 42.10% of patients had etiologies that include postinfectious transverse myelitis, leukemic transverse myelitis, and cervical spondylotic myelopathy[11]. The study from Thailand also reported similar findings with NMOSD being the most common etiology (37.5%) followed by infections (12.5%), systemic lupus erythematosus (SLE) (12.9%), idiopathic (10%), clinically isolated syndrome (CIS) (10%), multiple sclerosis (MS) (2.5%), spinal dural arteriovenous fistula (AVF) 5%, acute disseminated encephalomyelitis (ADEM) (5%), 2.5% to each of spinal cord infarction, schwannoma, and vitamin B12 deficiency[10]. The etiological heterogeneity of LETM is found for different regions and populations. Studies from Spain, France, and Western Australia have reported higher rates of MS and lower rates of NMO as causes of LETM[12–14].

Patients with LETM require proper evaluation to identify the NMOSD group of patients because of its high risk of relapse and require early and aggressive immunosuppression[1,15]. Patients with suspected LETM need a thorough workup that should include an MRI of the brain and spinal cord, analysis of cerebrospinal fluid (CSF), and blood investigation to detect cause-specific markers[9]. LETM is one of the six core clinical characteristics of NMOSD and is incorporated into the diagnostic criteria of its subtypes (NMOSD with AQP4-IgG and NMOSD without AQP4-IgG or unknown AQP4-IgG status). In patients with clinical features suggestive of NMOSD but without AQP4-IgG, testing of MOG-IgG should be done. If the result is MOG-IgG negative too, it is then known as seronegative NMOSD and if it is positive, it is a MOG antibody-associated disease which has different pathology as compared to NMOSD. We can differentiate LETM due to NMOSD from MS by LETM with central cord lesions, the presence of AQP4-IgG in seropositive cases, and usually an absence of oligoclonal bands in CSF[2]. However, both in MS and NMOSD, the location of spinal cord lesions was more common in the cervical than the thoracic cord[16]. Other investigations may be necessary to rule out alternative diagnoses.

Specific treatment of LETM depends upon the underlying cause. It mainly differs by whether it is inflammatory or noninflammatory etiology, where inflammatory etiologies are responsible for the majority of cases. Noninflammatory causes have specific treatments like antimicrobial therapy for syphilis, neuroborreliosis, parasitic infections, surgery for dural fistula, and treatment of vitamin and mineral deficiency whereas, for inflammatory etiologies, management can be divided into acute and prophylactic treatment where acute treatment mainly involves immunosuppressive agents or plasma exchange therapy depending upon the severity of disease and risk of relapse[15]. In NMOSD, at least 5 years of maintenance therapy is required[17]. In our cases all three acute cases were treated with intravenous methyl prednisone and all four cases were given maintenance therapy with mycophenolate mofetil.

The prognosis of LETM depends on its etiology. NMOSD is the most common etiology in Asia, when associated with AQP4-IgG positivity, it is associated with brainstem lesions as well as a high chance of relapse and therefore it needs early immunosuppressant treatment[18,19]. The majority of patients with NMOSD have only partial or no recovery from myelitis with only 17% achieving complete recovery regardless of AQP4-IgG status[20]. A study has reported that recurrence was associated with the number of the spinal cord involved; however, recurrence is not associated with worse outcomes[21].

Our study has several limitations. Important limitations are the limited number of cases and no proper follow-up findings. Similarly, we could not find the exact cause for some of the cases due to the unavailability of required investigations.

Conclusion

LETM is a rare and disabling condition with varied presentations and etiologies. The high degree of clinical suspicion, thorough evaluation with MRI of the brain and spinal cord, CSF, and blood analysis can reveal the etiologies that can guide the management. Acute treatment as well as maintenance therapy with an immunosuppressant is necessary for NMOSD, the most common etiology of LETM.

Ethical approval

As is a case report, therefore, it did not require ethical approval from ethics committee.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

B.D.: conceptualization and writing – original draft; K.B., S.B., Q.U.A.M., and R.P.: writing – original draft; B.D.P. and B.U.R.: writing – review and editing; S.A. and P.P.: resources and data validation; R.C.S. and R.P.: conceptualization, supervision, and writing – review and editing. All the authors read and approved the final manuscript.

Conflicts of interest disclosures

The authors report no conflict of interest.

Research registration unique identifying number (UIN)

Registration is not required for the case series.

Guarantor

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