

Longitudinally extensive transverse myelitis patients



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Characteristics of Longitudinally Extensive Transverse Myelitis patients: a retrospective analysis of 40 consecutive cases at a tertiary care hospital from North-West India

Abstract

Longitudinally extensive transverse myelitis (LETM), characterised by spinal cord inflammation extending three or more vertebral segments may be caused by multiple disorders most common being neuromyelitis optica (NMO). Such is the frequent association between these two entities that there is a growing concern to regard them as being practically synonymous with each other. However, all potential etiologies should be considered in the assessment of LETM. We conducted retrospective analysis (2010-2014) of 40 patients of LETM for demographic features, clinical presentation, laboratory investigations and neuro-imaging. Result: Majority of the patients presented acutely with bladder dysfunction and paraparesis. Ten out of 40 (25%) were classified as NMO among which only 4 were serum NMO antibody positive. Among the rest, there were 6 patients of MS, 3 patients of tubercular, 2 patients each of ADEM, spinal AVM and postinfectious etiology, one patient each of SARD and SLE. A group of 13 patients remained in whom no causative factor could be identified from the available investigations. Conclusion: LETM even with optic neuritis does not universally represent a diagnosis of NMO and one needs to be cautious while making a diagnosis of NMO without consideration of other etiologies as the treatment and prognosis differs among different etiologies.

Abbreviations: MS (multiple sclerosis); AVM (arteriovenous malformation); SACD (subacute combined degeneration); ADEM (acute disseminated encephalomyelitis); TM (transverse myelitis).

Key words: Longitudinally extensive transverse myelitis; Neuromyelitis optica

Introduction

Longitudinally extensive transverse myelitis (LETM) is a relatively recent term designating a transverse myelitis(TM) that extends three or more vertebral segments vertically. These lesions, which may occasionally span the entire length of the spinal cord, are much rarer and in general associated with greater morbidity than the typical lesions of idiopathic TM or multiple sclerosis (MS) - associated TM(1).

The key discriminating feature of LETM lesions is their length. The most frequent cause of LETM is neuromyelitis optica (NMO). In recent times the association between these two conditions has been so heavily emphasized that when LETM is encountered, an erroneous diagnosis of NMO may be made prior to careful consideration of other potential etiologies of LETM(1).

Thus, early recognition and establishment of the aetiology of LETM from appropriate workup is essential for optimizing outcome and in some cases commencing appropriate treatment to prevent future attacks of central nervous system (CNS) inflammation.

Studies comparing clinical, laboratory and radiological profiles of the LETM patients are scarce, especially from the developing countries. Thus, this

study was conducted to review the characteristics of presentation and <https://assignbuster.com/longitudinally-extensive-transverse-myelitis-patients/>

etiological classification of LETM at SMS Medical College and Hospital, Jaipur, a tertiary care centre of North India.

Patients and Methods

The study is a retrospective analysis (2010-2014) of 40 patients classified as having LETM on the basis of clinical manifestations of myelitis and spinal MRI finding of lesions typically extending three or more vertebral segments in length, admitted in SMS Medical College and Hospital, Jaipur with the following objectives:-

To study the clinical, radiological and CSF profile of patients with LETM.

To determine the aetiology of the myelitis.

Patient demographics, presenting symptoms, clinical manifestations and investigations were recorded on data entry forms.

The investigations included routine blood profile along with markers of connective tissue disorders (ESR, CRP, ANA, Anti ds DNA), MRI (of involved spinal cord segments in T2-weighted images of spinal MRI and MRI Brain), CSF analysis (including oligoclonal bands) and serum NMO antibody (NMO Ab) which was done by indirect immunofluorescence method.

Results

40 patients were found to fulfil the LETM criteria. 22 among the 40 patients were less than 30 years age (55%). Overall Mean age was 28 years with male: female ratio of 1.8: 1, suggestive of male preponderance. Apart from

it no specific trend was observed among the study group in terms of their demographics.

The majority of patients presented with bladder dysfunction, paraparesis and quadriparesis. Most of the patients had an acute presentation. Collectively, thoracic spinal cord segment was most commonly involved. 12 patients had clinically significant vision impairment at the time of presentation of which 10 were classified as NMO according to Wingerchuck et al criteria, one case was classified as MS and another was a case of SACD (Table 1).

Table 1: Presenting Clinical features

Bladder-Bowel dysfunction	27 (67.5%) (65%)
Paraparesis	26 (65%)
Quadriparesis	14(35%)
Vision Impairment	12(30%)
Sensory level	
Dorsal	33(82.5%)
Cervical	7(17.5%)

Table 2: Radiological Findings

Number of Spinal cord segments in spinal MRI

3-6 22

> 6 18

B) MRI Brain

Normal 28

Abnormal 10

Not done 2

Cerebrospinal fluid (CSF) pleocytosis was seen in 55 % (22 out of 40 patients) ranging from 10 to 250 cells/cumm. Among 10 NMO patients, 5 showed CSF pleocytosis of which 2 had neutrophilic predominance. The maximum cell count among NMO patients was 35 cells with lymphocytic predominance. Apart from it, 3 patients of tubercular, 2 patients each of postinfectious etiology and ADEM , one patient of MS and 4 patients of undetermined etiology also showed CSF pleocytosis. The maximum CSF cell count was 250 cells in one of the tubercular patient with lymphocytic predominance. CSF proteins were elevated in 15 out of 40(37. 5%) patients of which 3 patients were each of MS and tubercular etiology, 2 patients each of NMO and postinfectious etiology and 5 patients were of undetermined category. Out of 40 patients, 18 had extensive lesions involving > 6 spinal cord segments . Among 38 patients in whom MRI brain was done, 10 showed <https://assignbuster.com/longitudinally-extensive-transverse-myelitis-patients/>

abnormalities, of which 5 patients were of MS, two were each of ADEM and tubercular etiology and another one was NMO (NMO Ab positive) (Table 2). Among the MS patients, abnormalities were seen involving deep white matter of bilateral cerebral hemispheres, corpus callosum, brainstem and basal ganglia.

Based upon the above-mentioned clinical presentation and investigations, patients were classified according to their etiologies (Table 3).

Table 3: Etiology of LETM patients

Neuromyelitis optica	10
MS associated	6
Tubercular	3
ADEM	2
Postinfectious	2
Spinal AVM	2
Nutritional(SACD)	1
SLE	1
Undetermined	13

10 patients were of NMO fulfilling revised diagnostic criteria for neuromyelitis optica by Wingerchuk et al (7). In 8 out of 10 patients NMO antibody was sent, 2 patients refused for it. 4 out of them were NMO Ab positive and remaining 4 were negative. Among 10 NMO patients only one patient had lesions in MRI brain typical of NMO (Figure 1&2)).

Four of ten patients in whom serum NMO Ab was done showed positivity and one of the NMO Ab positive patient had brain MRI abnormality involving brainstem, posterior part of corpus callosum, left parietal periventricular white matter. Six patients were of MS fulfilling the revised McDonald criteria for diagnosis of MS. Three patients were of tubercular myelitis , two patients each were of ADEM , postinfectious etiology, and spinal AVM. One was having nutritional cause in form of vitamin B12 deficiency and one patient had SLE (ANA & dsDNA positive). Rest of the patients could not be categorised to a definite etiology from the available investigations.

Discussion

In our series, common presenting symptoms were bladder dysfunction, paraparesis, quadriparesis, and visual impairment. Majority of the patients studied suffered from bladder dysfunction and paraparesis.

It is a difficult task to determine the underlying etiology of LETM and it is worth exploring each case for subtle clues that may point toward the correct underlying diagnosis as the prognosis and long-term treatment decision differs in each category. Till now there are no studies describing association

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of clinical features and demographic features with the etiology of the myelitis (2).

In our series the maximum CSF cell count (250) was in tubercular patient. Maximum CSF cell count in NMO and MS patients was 35 and 30 respectively.

It is now well established that LETM does not universally represent a diagnosis of NMO, even in the setting of optic neuritis. However, in our series demyelinating disorders were found to be the most common cause of LETM and NMO was the most common etiology among demyelinating disorders.

All NMO patients fulfilled the criteria laid down by Wingerchuk et al (3). Among ten NMO patients, four were NMO antibody positive. Three main laboratory techniques are utilized in identifying the antibodies. In our patients it was done by the indirect immunofluorescence method which has the reported sensitivity and specificity of 86% and 91% respectively (4). At present, it is unclear whether there is truly a subset of patients with clinical NMO that are NMO antibody negative, or if this is a result of inadequate sensitivity of existing immunoassays to detect the antibody, or inadequately sensitive and specific diagnostic criteria, or a combination of all of these factors.

Although a regular follow up was not available in all NMO patients, a telephonic survey revealed that four NMO patients, of which two were seronegative and in two NMO antibody was not done, had no relapse and are doing well. Apart from this, one patient died from subsequent relapse and one could not be assessed in follow up. Among the four NMO antibody
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positive patients, who were under regular follow up, two (50%) presented with relapsing- remitting form of illness. One was 25 years old male who initially had 4 episodes of paraparesis with near complete recovery each time and developed vision impairment in the fifth episode and another was a 12 year old girl who had four relapses with simultaneous occurrence of vision impairment and paraparesis in the first episode. Thus, 4 patients had a monophasic disease course in 1 year follow up. However, a diagnosis of monophasic NMO should be considered with caution, because more than 90% of patients with NMO ultimately develop a relapsing course. One prospective Class I study found that the presence of aquaporin-4-specific autoantibodies (AQP4) predicts recurrence of TM or conversion to NMO(5). So was our observation in the form that out of the 3 patients who had relapse, 2 were NMO antibody positive. Therefore, we speculate that AQP4 antibody status, particularly seropositivity, has some predictive value.

Median age of onset of NMO is in the fourth decade. In our series all NMO patients were below 40 years of age except one who was a 52 years old female (figure 3). Interestingly this patient apart from late onset, also presented with slowly progressive paraparesis of one year duration which has not been described earlier in the literature.

In spinal NMO lesions, the central part of the cord is commonly affected, including both grey and white matter with peripheral sparing (figure 3). These imaging features may therefore help to differentiate MS from NMO in patients who present with LETM(6).

Among the NMO antibody positive patients, one had typical brain lesions of NMO (Figure 1). In patients with clinical and radiological features otherwise typical for NMO, 60–85% of cases have been shown to have abnormal brain lesions. Lesions involving the diencephalon and brainstem distinctly atypical for MS have been commonly reported in NMO patients. These distinctive lesions predominately involve the hypothalamus and can extend to brain tissue surrounding the third and fourth ventricle and aqueduct of Sylvius and seem to be characteristic brain lesions of NMO(7).

There were 13 patients in whom a definite etiological diagnosis could not be made from the feasible investigations. This group is usually described in the literature as 'idiopathic'. However, the idiopathic nature is a diagnosis of exclusion. In our series whether these patients were belonging to the category of postinfectious or some other form of demyelinating etiology was not clear from the investigations that were done in these patients as these patients were also later lost to follow up.

Among 3 patients who were classified as tubercular on the basis of reactive CSF and positive TB PCR, one had intramedullary spinal tuberculomas (Figure 4). Intramedullary tuberculomas (IMT) are seen in only 2 out of 100, 000 cases of tuberculosis and 2 out of 1, 000 cases of central nervous system tuberculosis, are even rare as a cause of LETM(8). Out of these three, one had complete recovery with ATT and remaining 2 had poor outcome with bedridden status.

Among 40 LETM patients, we were able to categorise only two patients as ADEM on clinical and radiological grounds (Figure 5). Both patients were of

paediatric age (14 and 16 years) group, had complete and rapid recovery with no recurrence on 6 month follow up, which made the diagnosis even more certain, and correlated with the fact that monophasic course is the hallmark of ADEM. MRI features of ADEM that are unusual in MS are symmetric bilateral disease, relative sparing of the periventricular white matter and deep grey matter involvement (9). However, 22% of ADEM patients had a periventricular lesion pattern indistinguishable from that seen in MS (10). Similar radiological features were observed by us in both patients (Figure 5 and 6). The radiological features of spinal cord involvement in ADEM in adults have not been well studied. In a small Dutch series, one-third of patients had lesions extending more than two vertebral segments on spinal MRI at presentation (11). Approximately 75% patients with ADEM have a preceding infection, and by definition there will be evidence of demyelination within the brain, as well as in the spinal cord, as seen in our patients (Figure 6). These features may help to differentiate ADEM from NMO spectrum disorders.

Among the metabolic causes, subacute combined degeneration (SACD) of the cord due to vitamin B12 deficiency can produce longitudinally extensive hyperintense signal on MRI imaging as seen in one of our patient (Figure 7). Generally T2 weighted scans demonstrate focal high signal abnormalities in the white matter of the dorsal and posterior columns in SACD (12).

In conclusion, the differential diagnosis of LETM is broad. Although characteristically associated with NMO, this diagnosis accounts for less than half of cases of isolated LETM in adults, and may be even less common in

children. Patients presenting with LETM require a thorough work-up to exclude other treatable causes particularly infectious and inflammatory.

The management of LETM is dependent on distinguishing inflammatory from non-inflammatory aetiologies and in identifying patients who are at high risk of further attacks.

Figure Legends

Figure 1: MRI brain showing hyperintensities (arrowheads) involving brainstem, left parietal periventricular white matter, posterior part of corpus callosum in seropositive patient of NMO (12 year old girl)

Figure 2: MRI cervical spine T2 weighted sagittal and axial images of same patient showing predominant involvement of central grey matter (arrowheads).

Figure 3: MRI cervical spine T2 weighted sagittal and axial images of 52 years old NMO antibody positive female showing predominant involvement of central grey matter.

Figure 4: T2 weighted sagittal and axial images showing hyperintensity (arrowheads) in cervical cord with contrast enhancement suggestive of tuberculoma.

Figure 5: MRI cervicodorsal spine, T2 weighted sagittal and axial images of a 16 year old girl with ADEM. MRI brain of the same patient showed lesions (arrowheads) in basal ganglia, brainstem and cortex typical of ADEM.

Figure 6: MRI brain and spine of a 14 years old male with ADEM showing hyperintensities in brain involving bilateral periventricular white matter and long segment hyperintensity in the cord extending upto conus.

Figure 7: Hyperintense signal in posterior aspect (arrow) of cervicodorsal cord in T2 weighted axial and sagittal images of SACD patient.

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