

Idiopathic Transverse Myelitis: An Experience in A Tertiary Care Setup

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ABSTRACT

Objective: To observe the clinical, laboratory and radiological features of idiopathic transverse myelitis in patients presenting to the Department of Neurology Civil Hospital Karachi, and to assess the outcome in terms of clinical recovery at four weeks.

Methodology: A prospective observational study in which patients were identified according to a Performa developed on the basis of diagnostic criteria provided by Transverse Myelitis Consortium Working Group.¹ Patients presenting with acute myelopathy other than Idiopathic transverse myelitis were excluded clinically and radiologically on the basis of same diagnostic criteria. MRI Spinal Cord, MRI brain, visual evoked potentials and CSF analysis of all patients were done. Data was analyzed on Microsoft excel 2007.

Results: Seventy two patients, 58.3% males and 41.6% females with a mean age of 28 years were identified as idiopathic transverse myelitis over a period of seven years, from July 2003- June 2010. Weakness of limbs was the commonest first symptom at onset, occurring in 27(37.5%) patients and duration of onset from the beginning of symptoms to completed weakness ranged from 10 hours (< 1day) to 28 days, with a mean of 5.04 days. Paraplegia was commoner than quadriplegia occurring in 69.4% of patients. Four (5.5%) patients had no imaging abnormalities. Normal MRI brain and normal visual evoked potentials were mandatory for the selection of patients for the study to rule out other causes of spinal cord demyelination. Eleven (15.3%) patients had normal CSF examination.. Elevated protein ranging from 50mg% to 128mg% was present in all subjects with abnormal CSF. Mild lymphocytic Pleocytosis was present in 33 (54.09%) patients. Oligoclonal bands were absent in all patients.

Response to methyl-prednisolone was judged in terms of recovery in motor power, improvement in sphincter control and resolution of sensory signs and symptoms. Twenty seven patients (37.5%) made complete recovery or were left with minimal residual deficit at the end of four weeks (MRC grades 5-4), 31(43%) made partial recovery with moderate disability (MRC grade 3) and 14 (19.4%) patients were left with severe disability or did not improve at all (MRC grades 0-2). Factors associated with poor recovery included delayed presentation after achieving maximum deficit, syrinx formation and extensive MRI lesions.

Conclusion: Idiopathic transverse myelitis is not an uncommon disease in our population. It did not behave very differently from what is reported in the international literature, with myelitis most commonly involving the dorsal spine, spanning over more than two spinal segments and showing complete or partial recovery in majority of cases with timely presentation for treatment.

INTRODUCTION

Acute transverse myelitis (ATM) is a focal inflammatory disorder of the spinal cord resulting in motor, sensory and autonomic dysfunction.¹ It has an incidence of 1-8 new cases per million people per year.² ATM can affect individuals of all ages with bimodal peaks between the ages of 10-19 and 30-39 years of age.³⁻⁴ No specific gender predominance, familial predisposition or geographical distribution is seen. Transverse myelitis has a wide spectrum of etiologies,

like auto-immune reaction to systemic infection or vaccination, as a part of systemic autoimmune disorders or acquired demyelinating diseases, or as result of direct infection of spinal cord.⁵ Idiopathic ATM is a diagnosis of exclusion when no etiologic phenomena can be identified. De Seze et al classified acute non-compressive myelopathies etiologically, : i) those related to multiple sclerosis, ii) systemic disease (e.g. systemic lupus erythematosus (SLE), anti-phospholipid syndrome, Sjogren's disease), iii) parainfectious, iv) delayed radiation myelopathy, v) spinal cord infarct and iv) idiopathic myelopathy.⁶

Most of the studies have broadened their inclusion criteria to include all acute myelopathies which has a wider spectrum with diverse etiologies and as a result idiopathic transverse myelitis is rarely reported. Local data comparing clinical, laboratory and

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radiological features of the idiopathic ATM with international literature are few. Thus we aimed to identify the clinical and radiological profile of acute idiopathic transverse myelitis among our patients and to observe their clinical outcome after conventional therapy.

MATERIALS AND METHODS

We evaluated prospectively all patients presenting to Neurology OPD who on clinical examination were diagnosed as cases of myelopathy, during a period of seven years, from July 2003- June 2010. A Performa was developed, based on diagnostic criteria provided by Transverse Myelitis Consortium Working Group,¹ to maintain uniformity of assessment. Informed consent was taken from the patients prior to their enrolment into the study.

Patients presenting with acute myelopathy other than idiopathic transverse myelitis were excluded on clinical and radiological grounds. Patients with history of symptom progression for more than 4 weeks and less than 4 hours were excluded, as per diagnostic criteria.¹ Post traumatic, para-infectious, post-vaccinal, postradiation myelopathy or any congenital or acquired obvious vertebral column deformity were excluded clinically. Patients with previous history of any transient, recovered or residual weakness, imbalance, vision loss, double vision, or sphincter loss were also excluded to rule out the multiple sclerosis clinically. Fever at presentation, recurrent genital infection, major systemic illness leading to immunosuppression was also included in our exclusion criteria.

All these patients underwent MRI examination to ascertain the nature of myelopathy, and to rule out spinal cord compression. MRI facility was not available in our setting and it was difficult to maintain the uniformity in terms of MRI strength over seven years of observation period. However, centers offering 1.5 tesla MRI were preferred in all doubtful cases in addition to ordering contrast enhanced studies. Patients having, on MRI, prolapsed intervertebral disc causing significant compression at the clinically predicted level, spinal cord tumors, and syrinx not associated with demyelination, vertebral osteomyelitis, arteriovenous malformation and significant thinning of spinal cord with normal signals were excluded.

All these patients also underwent MRI examination of the brain to rule out silent plaques of demyelination or vasculitis to rule out multiple sclerosis, acute disseminated encephalomyelitis and syndromes of systemic vasculitides. Visual evoked potentials were performed for all patients to rule out multiple sclerosis and neuromyelitis optica at presentation. Normal MRI

brain and normal visual evoked potentials were therefore considered mandatory for the selection of patients for the study.

CSF examination was done in all patients including the oligoclonal bands. In addition to routine investigations which included blood complete picture, blood sugar, blood urea nitrogen, creatinine, electrolytes, urine detailed report and chest-ray; these patients also had specific investigations to rule out associated conditions and secondary myelopathy. These included liver function tests, hepatitis B & C serology, ANA profile and vitamin B12 levels. Patients having positive tests were not included. We also planned to carry out ACE levels, APLA profile, Complement levels, and SS-A and SS-B antibodies when suggested by clinical features. However none of patients had to undergo these investigations because of lack of clinical features suggestive of the associated disorders. NMO Ig-G antibodies test was not done as it is not available in Pakistan. Spinal angiograms were not considered necessary where onset of symptoms was more than 4 hours as per diagnostic criteria¹ or where spinal MRI with contrast was not suggestive of spinal arteriovenous malformation.

All patients were administered Methyl-prednisolone 1gm IV for 5 days followed by tapering doses of oral prednisolone over 15 days.

We studied the clinical, radiological and laboratory profile of the patients at first presentation. We didn't aim to follow up the patients over longer periods than 4weeks. It was not practically possible because most of our patients came from the remote areas they usually do not turn up to the follow up after complete clinical recovery or stability. So it is difficult to comment on recurrence of myelitis either as recurrent idiopathic transverse myelitis or its conversion to the multiple sclerosis or eventually development of Neuromyelitis optica.

Data was analyzed on Microsoft Excell 2007. In addition to demographic features, for nature of first symptom, duration of symptom onset to maximum weakness, clinical pattern of motor weakness, presence of sensory (loss of pain sensation to pin-prick) deficit, presence of spinal shock, associated sphincter control loss, MRI appearance of lesions, CSF pleocytosis, CSF proteins and response to high dose steroids at end of 20 days therapy.

RESULTS

Seventy-two patients fulfilled our criteria for idiopathic transverse myelitis. There were 42 (58.3%) males and 30 (41.6%) females. Ages ranged from 9 years to 45

years with a mean age of 28 years. Maximum number of patients, 49 (68.05%) belonged age range of 21-40 years. Weakness of limbs was the commonest first symptom at onset, occurring in 27 (37.7%) of patients. See figure 1.

Duration of onset from the beginning of symptoms to completed weakness ranged from 10 hours (< 1day) to 28 days, with a mean of 5.04 days. Maximum number of patients 26 (36%) had symptom progression over less than 24 hours; only 4 patients had symptom progression extending over 4th week. Weakness of limbs, paraparesis or quadriplegia, was present in all patients at the completion of progression of symptoms, majority of the patients had paraplegia 50 (69.4%) as compare to the quadriplegia 22(30.5%). Weakness on MRC grade ranged from 0-3 at the most in involved limbs in all cases. At the completion of progression of symptoms, Sphincter involvement occurred in 61 (84.7%) patients, well defined sensory level was present in 65 (90.02%) patients, while spinal shock was observed in only 17 (23.6%).

High intensity signal on T2W sequences occupying more than two-third of the cord diameter was seen in 64 (88.8%) of patients. Cord swelling, suggested by absence or thinning of surrounding CSF rim was seen in 31(43.05%) of patients. Associated syrinx was seen in 7(9.7%) patients mimicking spinal cord tumor. Patients presents with cord swelling, syrinx or normal MRI (total 42 patients 58.3%) also underwent contrast enhanced MRI. Out of them 20 (47.6%) had focal peripheral cord enhancement with maintenance of the cord contour. The enhancing area was much smaller as compared with the extent of hyperintensity on T2-weighted images. In 68 (94.4%) patients lesions occupied more than two spinal segments. In 12 (17.68%) cases lesions were within cervical region and mostly 50 (69.9%) located in dorsal spine. In five patient (7.35%) lesions extended from cervical to dorsal spine; the largest extending from C6-D8. One patient (1.47%) had MRI abnormality in conus medullaris. MRI brain was normal in all patients.

Motor level corresponded well with level of MR abnormality in all patients while sensory level varied from the usual 3-4 segments below to more than 10 segments below the MRI lesion in some cases. CSF was normal in 11 (15.2%) patients. Findings were abnormal in remaining 61 (84.7%) patients. Elevated protein ranging from 50mg% to 128mg% was present in all those subjects. Pleocytosis in the range of 6-40 cells, predominantly lymphocytes, was present in 33 (54.09%) patients. Oligoclonal bands were absent in all patients.

All the patients received only pulse steroids. Response to methyl-prednisolone was judged at 4 weeks in terms of recovery in motor power, improvement in spasticity, improvement in sphincter control and resolution of sensory signs and symptoms. Twenty seven patients (37.5%) made complete recovery or were left with minimal residual evidence at the end of four weeks (MRC grades 5-4). Patients with moderate disability 31(43%) who made partial recovery were either left with spasticity (Modified Ashworth Scale 1-2) or weakness (MRC grade 3). Patients, who were left with severe disability or did not improve at all, 14 (19.4%), had severe residual weakness (MRC grades 0-2) and/or residual spasticity (Modified Ashworth Scale 3-4). None of our patient expired during hospital stay and none required ventilatory support.

Patients with poor responsiveness included who presented later than two weeks after reaching maximum neurological deficit (6 patients), patients who developed syrinx (7 patients) and one patient whose lesion extended up to fourteen segments in cervico-dorsal regions.

Figure 1: Presenting Symptoms (%) At Onset

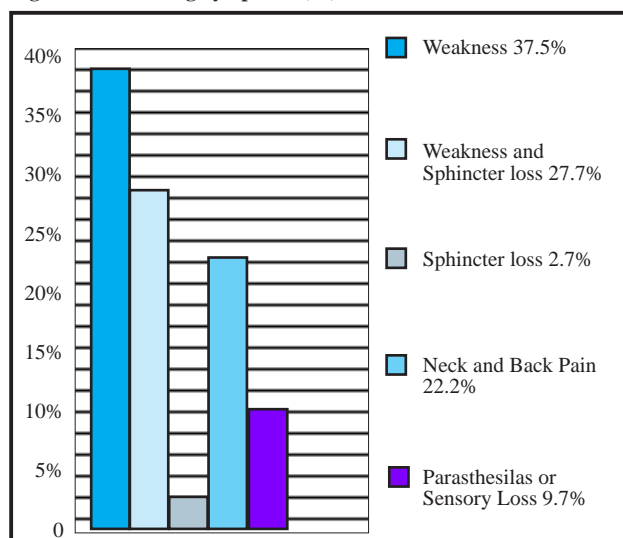


Table 1: Findings of Spinal Cord MRI of the Patients

Total no of spinal cord MRI done	72
Normal MRI	4 (5.5%)
High intensity signal on T2W	68(94.4%)
Site of high intensity signal on T2W images	Cervical (17.68%) Dorsal (73.5%) Cervico-dorsal (7.35%) Conus medullaris (1.47%)
Cord swelling	31 (3.05%)
Associated syrinx	7 (9.7%)
Contrast MRI done	42 (58.3%)
Contrast enhancement seen	20(47.6%)

DISCUSSION

Our patients showed M:F ratio of 1.4:1. Literature however, depicts no gender predisposition.² Similarly our patients were mainly younger, mean age 28 years, than the two peaks of incidence described for idiopathic ATM, that is, 10-19 years and 30-39 years.²⁻³ However, Saleh et al quote a mean age of 31 years in their study which is closer to our data.⁷

Most of our patients had acute presentation of symptoms although we identified 4 cases whose symptom progression continued for 23-28 days from the onset of first symptom. A mean duration of 5.04 days from onset to nadir may have its effects on prognosis and outcome, because patients from remote areas may not reach on time or those who are not diagnosed earlier, time window for effective treatment is reduced. Christenson et al reported duration of 1-20 days from symptom onset to maximum deficit.⁸

Weakness was the first symptom in most of our patients as shown in figure 1, while three other studies report pain⁹ or sensory symptoms^{8,10} as the first manifestation of myelitis. Paraparesis was more common in our patients and when present as a part of quadriparesis was more severe than upper limb weakness.

MRI is mandatory in the diagnosis of transverse myelitis to rule out the presence of structural lesions, especially those amenable to urgent neurosurgical intervention. Lesions associated with idiopathic transverse myelitis usually span at least two vertebral segments¹ as we also found in our study, such lesions usually enhance with intravenous gadolinium administration. Table 1 shows the MRI characteristics of our patients. Majority of our patients had dorsal myelopathy which is generally supported by the literature. However, Misra et al and Murthy et al found high frequency of cervical spinal cord involvement, 7 out of 10 and 9 out of 13 respectively.¹¹⁻¹² Cervical myelopathy was however not as uncommon as is reported in western literature. We did contrast MRI in 42 patients, 20 (47.6%) showed focal peripheral cord enhancement as a sign of inflammation. Although there was no post contrast enhancement in remaining 22 patients, but CSF analysis showed mild lymphocytic pleocytosis with elevated proteins meeting the diagnostic criteria of idiopathic transverse myelitis.¹

Normal MRI results should prompt a reconsideration of the diagnosis of myelopathy in favor of other disorders of the central or peripheral nervous system. We had to resort to the literature when patients with all clinical signs of myelopathy as well as responsiveness to steroids were encountered. We had

four such patients in series. Clinically Isolated Myelopathy with Normal MRI is not only well reported.¹³ but had been observed in one fifth cases of referred to United Kingdom neuroscience center.¹⁴

There may be a large disparity between the clinical sensory level and the level of the lesion in spinal cord disease. This has been explained on the basis of pain and temperature fibers crossing obliquely to reach the contralateral spinothalamic tracts two or three segments higher. Although this is true, it accounts only for sensory levels a few segments below the lesion, and does not explain the large discrepancies of up to 9-11 segments described in various studies and up to 10 segments in our study.^{11,15}

In our study CSF was normal in 11 (15.2%) patients. If the CSF is normal, then the diagnosis of idiopathic acute transverse myelitis would not be possible under the proposed criteria.¹ Further, the clinical findings present in those individual were not consistent with a vascular myelopathy either. So we label those patients as possible acute idiopathic transverse myelitis.¹

CSF was abnormal in the remaining 61 patients (84.7%). Elevated protein ranging from 50mg% to 128mg% was present in all those patients. Pleocytosis was seen in the range of 6-40 cells, predominantly lymphocytes, in 33 (54.9%) patients. Oligoclonal bands were absent in all patients. This result matches the CSF findings described in international literature for the diagnosis of idiopathic transverse myelitis.¹

Only those patients with normal visual evoked potentials were included in our study, to rule out neuromyelitis optica at presentation. However normal visual evoked potentials do not absolutely preclude an eventual diagnosis of NMO. The diagnosis of idiopathic transverse myelitis may be changed to NMO over time because a clinically apparent optic neuritis may follow weeks or months after the acute spinal cord syndrome.¹

Although no randomized controlled trials recommending the treatment of idiopathic transverse myelitis are present, high dose steroids are still considered the first line therapy. This is either inferred from various case reports or extrapolated from successful trial of patients with multiple sclerosis. Approximately 50-70% of patients are reported to have partial or complete recovery and can ambulate with or without aid, according to various researchers.¹⁶⁻¹⁷ We also witnessed good steroid responsiveness as none of the patient progressed to ventilatory failure or death during hospital stay, although 14 patients were left with severe disability or no improvement at all.

Younger age at onset, severity of weakness, presence of spinal shock, back pain, rapid onset transverse myelitis, extensive hyperintensity on spinal cord neuroimaging and electrophysiological evidence of anterior horn cell involvement have all been quoted as bad prognostic factors for acute transverse myelopathies.^{8,18-20} Fourteen (19.4%) patients in our study showed poor recovery at 4 weeks (MRC Grade 0-2). We found delayed presentation (more than two weeks after reaching the maximum deficit, 6 patients), extensive lesions (1 patient) and presence of syrinx (7 patients) associated with poor recovery.

Because of the lack of follow up there are few limitations of our study. We need further studies to categorize acute idiopathic transverse myelitis as recurrent acute idiopathic transverse myelitis, development of neuromyelitis optica or multiple sclerosis in future.

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