ORIGINAL ARTICLE

Etiological Spectrum of Non-compressive Myelopathies in Tertiary Care Centre

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Abstract

Aims: To study the clinical, radiological, cerebrospinal fluid profile of non-compressive myelopathy and to study various etiologies of non-compressive myelopathies in causation of quadriplegia and paraplegia.

Study Design: Observational study.

Place and Duration of Study: Department of Neurology, Govt. Medical College, Kota in year 2015 and 2016.

Methodology: All the patients presented with myelopathy and MRI spine not showing any significant compression included in study. To know the etiology of non-compressive myelopathy patients were investigated including routine blood tests, cerebrospinal fluid analysis and visual evoked potentials, MRI of the brain, and immunological, infectious, and metabolic profile based on the pattern of involvement.

Results: The study had 80 patients with a median age of 38 years and male: female ratio 1.5:1. Patients were divided into acute myelopathy and chronic myelopathy. Forty four patients presented with acute myelopathy whereas 36 patients had chronic myelopathy. The causes of Acute myelopathy were post infectious myelitis (13), neuromyelitis optica spectrum disorder (NMOSD) (6), multiple sclerosis (MS) (2), connective tissue disorders (1), acute disseminated encephalomyelitis (4) and Idiopathic (18). The causes of Chronic myelopathy were Vitamin B12 deficiency (8), MS (2), mixed connective tissue disease (1), Copper deficiency (1), hepatic myelopathy (1), radiation (1), hereditary spastic paraparesis (1) and idiopathic (21).

Conclusion: Underlying etiology like demyelinating, infectious/post infectious, autoimmune or nutritional was found in 52% patients of non-compressive myelopathy.

INTRODUCTION

Non-compressive myelopathy have varied etiology ranging from infectious, nutritional, demyelinating, toxic, heredo-familial to degenerative conditions. The causative etiology is somewhat different in India as compared to the western countries. In India infectious, para-infectious and nutritional causes predominate over demyelinating and hereditary causes. There are multiple studies on the etiological spectrum of non -compressive myelopathies in past, however there has been only few Indian study post era of newer diagnostic criteria and post discovery of neuromyelitis optica (NMO) spectrum disorders. The previous studies from India were carried when serological test for NMO was not available[1,2]. This study was carried out in an attempt to determine the etiological spectrum of non-compressive myelopathies in a tertiary care hospital.

Material and Method

It was an observational study carried out in the Department of Neurology, Government Medical College, Kota, from January 2015 to December 2016, and the data were collected prospectively. The study was aimed to determine the causes of non-compressive myelopathies, and to study the clinical and radiological features of non-compressive myelopathies.

Patients presenting with acute or chronic paraparesis or quadriparesis consistent with myelopathy (with or without coexisting neuropathy, radiculopathy or encephalopathy,) were included in the study. Patients were excluded from the study if (a) Magnetic resonance imaging (MRI) of spine showing spinal cord compression explaining patient's neurologic dysfunction, (b) Patients of myelopathy who did not undergo MRI of the spinal Cord or did not give consent (c) diagnosis consistent with motor neuron disease (MND) and (e) degenerative Cerebellar ataxias associated myelopathy. All the Patients were evaluated clinically including onset, duration, and progression of neurological symptoms and history related to any clue to etiology of myelopathy like history suggestive of connective tissue disorders, toxin, high risk behavior or malignancy or treatment of malignancy. Patients were also looked for evidence of systemic disease or malignancy in the general and systemic examinations.

All patients underwent relevant routine biochemical analysis including complete hemogram , liver function tests, renal function tests serum electrolytes, thyroid profile, urinalysis and appropriate neuroimaging studies were carried out in all the patients. All cases with no obvious clinically significant compression visible on MRI which can explain the symptoms underwent further investigations which included serum HIV, VDRL, ESR, X-ray chest, collagen disease profile (ANA, RA factor, anti-dsDNA, and ant phospholipid antibody),

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Table 1: Clinical and demographic profile (n=80)

Characteristics	n (%)
Sex	
Male	48 (60%)
Female	32 (40%)
Motor manifestations	
Quadriparesis	54 (67.5%)
Paraparesis	24 (30%)
Bibrachial weakness	1 (1.25%)
Monoparesis	1 (1.25%)
Spasticity	28 (35%)
Flexor spasms	4 (5%)
Sensory manifestations	
Posterior column sensory loss	41 (51.25%)
Spinothalamic sensory loss	36 (45%)
Paresthesia	46 (57.5%)
Others	
Sphincter involvement	52 (65%)
Peripheral neuropathy	9 (11.25%)
Optic neuritis/atrophy	3 (3.75%)
Type of myelopathy	
Acute- Subacute	44 (55%)
Chronic	36 (45%)
Relapsing myelopathy	3 (3.75%)
Symmetrical	63 (78.755)
Asymmetrical	17(21.25%)

Table 2: Etiology of acute to subacute myelopathy(n=44)

Etiology	n (%)
NMOSD	6(13.6%)
Multiple sclerosis	2(4.54%)
Connective tissue disorders	1(2.27%)
Infectious/post infectious myelitis	13(29.54%)
Acute disseminated encephalomyelitis	4(9.09%)
Idiopathic	18(40.9%)

Table 4: Etiology of chronic myelopathy (n=36)

Etiology	n (%)
Multiple sclerosis	2(5.5%)
Vitamin B12 deficiency	8(22.2%)
Copper deficiency	1(2.7%)
Mixed connective tissue disease	1(2.7%)
Hepatic myelopathy	1(2.7%)
Radiation	1(2.7%)
Hereditary spastic paraparesis	1(2.7%)
Idiopathic	21(58.3%)

serum vitamin B12 level, copper level, angiotensin converting enzyme (ACE) levels, antibody against aquaporin-4 (AQP4-IgG) and visual evoked potentials (VEPs). MRI was done using 1.5 Tesla MRI. Cerebrospinal fluid (CSF) analysis included routine investigations like total count, differential counts, protein, and sugar. Further CSF investigations like ADA , immunoglobulin G (IgG) index and oligoclonal bands (OCBs); , viral polymerase chain reaction (PCR) and venereal disease research laboratory (VDRL) test were done depending upon clinical scenario. Ultrasound abdomen and computerized tomography scans of thorax and abdomen were done in patients suspected to have systemic disease or malignancy.

Table 3: Imaging and cerebrospinal fluid profile of acute-to-subacute myelopathy

Characteristic	Idiopathic (n=18)	NMOSD (n=6)	MS (n=2)	ADEM (n=4)	Infectious/postinfectious (n=13)
MRI					
Short segment myelitis	6(33.3%)	0	0	2(50%)	10(76.9%)
LETM	2(11.1%)	6(100%)	2(100%0	2(50%)	2(15.38%)
No signal change	10(55.5%)	0	0	0	1(7.6%)
CSF					
Pleocytosis	19(5.55%)	4(66.66%)	1(50%)	½(50%)	4(13.76%)
Protein >45 mg/dL	5(27.7%)	5(83.3%)	2(100%)	½(50%)	6((46.15%)
OCBs	0	0	1(50%)	0/0	0/0

Case Definitions

Acute myelopathy was defined as spinal cord dysfunction lasting at least 48 h and reaching nadir within 21 days of symptom onset. Subacute myelopathy was defined as progression of symptoms for 3-6 weeks from onset. Chronic myelopathy (CM) was defined as spinal cord dysfunction of insidious onset and progressing gradually over months to years. The diagnosis of multiple sclerosis (MS) was based on 2010 Revised McDonald Criteria. NMO spectrum disorder (NMOSD) was diagnosed based on 2015 International Panel for NMO Diagnosis criteria.[3]

Results

Eighty patients with diagnosis of non-compressive myelopathy were included in study, out of which 48 were male and 32 were females with male: female ratio 1.5:1. Mean age of study population was 38 years. Demographic and clinical profile of 80 patients summarized in Table 1.

Acute-subacute myelopathy was diagnosed in 44 (55%) patients. The median age was 33 years (range, 6– 65 years). The common causes were NMOSD, multiple sclerosis (MS), connective tissue disorders, post infectious myelitis, acute disseminated encephalomyelitis (Table 2). No etiology was found in 17/44 (36.36%) patients. Out of 13 cases of infectious/ post infectious myelitis, most common antecedent infection was Dengue virus seen in 8 patients; others had upper respiratory and gastrointestinal tract infection preceding the myelitis. MRI was suggestive of hyper intense signal on T2-weighed images in 32/44 patients and was normal in 12 patients. Out of 33 patients with abnormal MRI, 14 had hyper intense signals extending 3 or more than 3 segments (LETM), whereas rest 18 had short segment myelitis (Table 3).

Chronic myelopathy was diagnosed in 36(45%) patients. The median age was 43 years (range, 24–70 years). The causes of CM were progressive MS, mixed connective tissue disease, Vitamin B12 deficiency, Copper deficiency, hepatic myelopathy, radiation, and hereditary spastic paraparesis (Table 4). No etiology was found in 21/36 (58.3%) patients.

Discussion

Myelopathy can cause considerable morbidity due to either paraparesis or quadriparesis. Many studies are done in the past in India about etiological spectrum of non-compressive myelopathy however only few studies are done after the discovery of aquaporin-4 antibodies and after newer proposed diagnostic criteria's like for NMOSD diagnostic criteria and Revised McDonald Criteria.

A non-compressive myelopathy usually affects patients in the prime of their life. In our study median age of the study population was 38 years, with slight male predominance with male: female ratio 1.5:1. Similar results were seen in previous studies done in India like Prabhakar et.al.[2] which had mean age of 34 years.

In previous studied done in India, the most common cause of non compressive myelopathy was Acute transverse myelitis (ATM). In study from eastern India by Das et. al. had 82 patients enrolled between July 1994 and June 1996,[1] the most common cause of non-compressive myelopathy was ATM 24 (29.3%), and etiology was not found in 23 (28.0%) patients. In another study from North India by Prabhakar et.al., the most common cause of non-compressive myelopathy

were ATM (54.4%) and B12 deficiency. However these studies were done before serological test for AQP4-IgG was available. Some of these cases could have been MS or NMOSD. According to Transverse myelitis consortium working group[4] (TMCWG), ATM is classified according to Idiopathic and secondary to diseases like MS, NMOSD and connective tissue disorders. So in our study rather than making broad diagnosis of ATM, patients were classified according to etiology of ATM, because treatment and prognosis differ according to etiology of ATM.

In our study patient was diagnosed as post-infectious ATM if had a clear history of febrile illness within 30 days preceding onset of myelitis. Serological test for infection were done according to history of febrile illness. All serological tests could not be done for all infections due to financial limitation. Most common infection preceding ATM in our study was Dengue infection, which was seen in 8/13 post infectious ATM. This may be related to high prevalence of dengue in this region. One patient had preceding Chikungunya infection. In others exact etiological infection could not be found out in 4/13(30.76%) patients. In study done by Marchioni et.al. specific serological evidence of infection was found only in 5.7% patients in post infectious neurologic syndromes.[5]

NMOSD was seen in 6/44 patients with acute to subacute myelopathy. It was most common cause of LETM (6/14, 42.8%). The median age of presentation of NMOSD was 36 years with strong female preponderance (5/6). Most common location of myelitis was cervico-dorsal cord (100%). In retrospective Indian study of 44 patients with NMOSD, the most common location of myelitis was cervico-dorsal cord (77.5%) like seen in our study, however the median age of presentation was 26.5 years.[6] Post discovery of aquaporin-4 antibodies, a multicenter study done in 288 patients showed the common causes of acute non compressive myelopathy were NMO (17.0%), MS (10.8%), and para infectious (17.3%). Etiology was not found in 45 (15.6%).[7] So post discovery of aquaporin 4 antibodies, more and more patients who were previously diagnosed as idiopathic or remained undiagnosed are now being diagnosed as NMOSD and MS.

In our study, the most common cause of chronic non compressive myelopathy was Vitamin B12 deficiency. The common causes of Vitamin B12 deficiency in our patients were secondary to strict vegetarian diet, alcohol consumption and malnutrition and. Antiparietal antibody could not be done due to financial reasons. The most common type of presentation of Vitamin B12 deficiency was Myeloneuropathy. T2 hyperintense signal of cord were seen in 3/8 patients and were most commonly located to posterior and lateral column in both cervical and thoracic region. Most common cause of Vitamin deficiency was pernicious anemia in study of 143 patients of neurologic disorder due to vitamin B12 deficiency by Healton EB et al,[8] however in our country most common cause of Vitamin B12 deficiency may be dietary insufficiency. Other causes of chronic myelopathy were primary progressive MS, hepatic myelopathy, copper deficiency, radiation and Hereditary spastic paraparesis, however majority of chronic myelopathies were idiopathic.

Conclusion

This study showed that non-compressive myelopathy primarily affects patients in third to fourth decade of life. Patients are in there prime of life and are predominately earning members of family. Various causes of non-compressive myelopathy were found in 52% of patients; however etiology remained undiagnosed in 48% of patients. The common cause of acute to sub-acute myelopathy includes post infectious myelitis, NMOSD and MS whereas most common cause of chronic myelopathy was Vitamin B12 deficiency. Etiology could not be found out in 48% patients, however paraneoplastic panel, antibodies against myelinoligodendrocyte glycoprotein (anti-MOG) and complete infectious panel were not done in patients and there was no long term follow up, as some etiologies could have been found out on follow up. The study help us to understand better the etiological spectrum of non-compressive myelopathy.

References

1. Das K, Saha SP, Das SK, Ganguly PK, Roy TN, Maity B. Profile of non-compressive myelopathy in Eastern India: A 2-year study. *Acta Neurol Scand* 1999; 99:100-5.
2. Prabhakar S, Syal P, Singh P, Lal V, Khandelwal N, Das CP. Non-compressive myelopathy: Clinical and radiological study. *Neurol India* 1999; 47:29-9.
3. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology* 2015; 85:177-189. doi:10.1212/WNL.0000000000001729.
4. Transverse Myelitis Consortium Working Group. Proposed diagnostic criteria and nosology of acute transverse myelitis. *Neurology* 2002; 59:499-505.
5. Marchioni E, Ravaglia S, Montomoli C, Tavazzi E, Minoli L, Baldanti F, *et al.* Postinfectious neurologic syndromes: A prospective cohort study. *Neurology* 2013; 80:882-9.
6. Barhate KS, Ganeshan M, Singhal BS. A clinical and radiological profile of neuromyelitis optica and spectrum disorders in an Indian cohort. *Ann Indian Acad Neurol* 2014; 17:77-81.
7. de Seze J, Lanctin C, Lebrun C, Malikova I, Papeix C, Wiertlewski S,*et al.* Idiopathic acute transverse myelitis: Application of the recent diagnostic criteria. *Neurology* 2005; 65:1950-3.
8. Healton EB, *et al*. Neurologic aspects of cobalamin deficiency. *Medicine* 1991; 70:229-44.