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Etiologic Profile of Non-Compressive Myelopathy in a Large Tertiary Care Centre of North West Part of India

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Abstract: ***The term myelopathy describes pathologic condition that cause damage or dysfunction of spinal cord, meningeal or perimeningeal space. Here we tried to determine the etiological profile of non-compressive myelopathies in a tertiary care centre of north west India. Objectives-1. To study the clinical and radiological features of non- compressive myelopathies. 2. To determine the causes of non-compressive myelopathies. Material and Method: An observational study was carried out in the neurology department of a large tertiary care centre of north west India from May 2018 to June 2020.Total number of patients were 70. MRI brain and spine along with visually evoked potential test and cerebrospinal fluid analysis were done in all 70 cases.Results- Out of 70 patients, 50 (71.4 %) were males and 20 (28.57 %) females. Mean age of presentation was 31.95 years. Patients were subdivided on the basis of age into groups - <18 years (15 patients-21.4 %), 18-45 years (42 patients-60 %) and >45 years (13 patients-18.5 %).Onset of illness was acute to sub-acute in nature in all the cases. Bladder and bowel involvement was seen in maximum cases (55 cases-78.6 %).Patients found to have long segment myelitis (50 patients-71.4 %), short segment myelitis (13 patients-18.5 %) and spinal cord without changes (7 patients-10 %). Demyelinating illness was most common in occurrence- 20 cases out of 70 (28.6 %) comprising 10 NMO positive (14.3 %), 8 MOG positive (11.4 %) and 2 multiple sclerosis cases (2.8 %). Six cases (8.6 %) each of tubercular myelitis and post infectious (non-tubercular) ATM including 1 case (1.4 %) of post herpetic myelitis were found along with five cases (7.1 %) of sub acute combined degeneration and 2 cases (2.9 %) of spinal AVM (Arterio-venous malformation) 31 (44.3 %) cases remained undiagnosed due to non-affordability to further blood tests. Conclusion: Most common cause was found to be demyelinating illness followed by tubercular, post infectious and vitamin B12 deficiency cases.***

Keywords: long segment myelitis, tubercular myelitis, MOG

1. Introduction

The term myelopathy describes pathologic condition that cause damage or dysfunction of spinal cord, meningeal or perimeningeal space. Demyelinating disease, traumatic injuries, vascular diseases, infections, inflammatory or autoimmune processes may affect the spinal cord due to its confinement in a very small space. Although there are plenty of published data on each of the non-compressive myelopathies, there has been no Indian study on the overall etiological spectrum in the light of newer diagnostic criteria and latest serological tests. Many studies from India were carried out during the period when even serological test for neuromyelitisoptica (NMO) was not available. Ours is the first study mentioning about myelin oligodendrocyte glycoprotein antibody (MOG) disorder. Here we tried to determine the etiological profile of non-compressive myelopathies in a tertiary care centre of northwest India.

Aim and Objectives

- To study the clinical and radiological features of non-compressive myelopathies
- To determine the causes of non-compressive myelopathies.

2. Material and Methods

Study Design- An observational study was carried out in the neurology department of a large tertiary care centre of north-west India from May 2018 to June 2020 and data was collected as per the proforma designed for the purpose. Total number of patients were 70.

Inclusion Criteria-Patients with acute, sub-acute and chronic neurologic dysfunction consistent with myelopathy (with or without co-existing encephalopathy, neuropathy or radiculopathy) were included.

Exclusion Criteria-(1) Patients of myelopathy who did not undergo MRI spine (2)Spinal cord compression on MRI explaining patient's neurologic dysfunction (3) Motor neuron disease (4) Degenerative ataxias (5) Trauma

Acute-to-subacute myelopathy (ASM) was defined as spinal cord dysfunction lasting at least 48 hours and reaching nadir within 21 days of symptom onset, as per Transverse Myelitis Consortium Working Group[1].

Patients were questioned about onset of illness, progression, symptoms such as skin rash, photosensitivity, joint pain, bone pain, edema, jaundice, anaemia, gastrointestinal bleeding, cough, chest pain, exposure to radiation and other toxic substances, travel details and high risk sexual behavior.

We looked for evidence of systemic disease or malignancy. Detailed neurological examination was performed in each case including evaluation of higher functions, cranial nerves along with fundus, motor and sensory system, cerebellar functions, reflexes, examination of skull, spine, peripheral vessels and nerves. MRI brain and spine along with visually evoked potential (VEP) test and cerebrospinal fluid (CSF) analysis were done in all 70 cases.

3. Results

Out of 70 patients with non-compressive myelopathy, 50(71.4%) were males and 20 (28.57%) females. Mean age of presentation was 31.95 years similar to previous study by Prabhakar et al[2] and Das. [3]

Patients were subdivided on the basis of age into 3 groups - <18 years(15 patients-21.4%), 18-45 years(42 patients-60%) and >45 years(13 patients-18.5%) (Table1).Onset of illness was acute to sub-acute in nature in all the cases. Clinical features of non-compressive myelopathy are listed in Table-1.Bladder and bowel involvement was seen in maximum cases (55 cases-78.6%), followed by paraparesis (50 cases-71.4%). Quadriparesis was seen in 20 cases (28.6%) and visual impairment in 18 cases (25.7%).Fever preceded the onset of illness in 20 cases (28.5%) of non-compressive myelopathy – 6 (8.6%) cases of post infectious acute transverse myelitis (ATM), 5 (7.1%) cases in NMO, 2 (2.8%) cases in MOG, 7(10%) cases in which cause could not be established either due to financial constraints or due to negative routine workup.

MRI brain and spine were done in all 70 cases and were found to be normal in 7 cases (10%). Radiologically, patients were found to have long segment myelitis (50 patients-71.4%), short segment myelitis (13 patients-18.5%) and spinal cord without changes (7 patients-10%) (Table-2). Sixty three cases (90%) had spinal cord changes of which 48 (68.5%) cases had dorsal cord involvement, 19 (27.1%) cases had cervical cord involvement, conus involvement was seen in 9 (12.8%) cases and 6 (8.6%) cases had brainstem involvement. Cord involvement was central T2 hyperintensity spanning 3 or more than 3 segments called as longitudinally extensive transverse myelitis (LETM) which was found in 50 cases out of 70 (71.4%) of which 16 (32%) were of demyelinating disorder comprising NMO(8 cases-16%) and MOG(8 cases-16%), remaining others included tubercular myelitis (6 cases-12%), post infectious etiology (2cases-4%), spinal AVM(2 cases-4%) and SACD(1case-2%).Cause in 23 cases of LETM out of 50 could not be established (46%).Out of 13 cases (18.5% of 70 cases) of short segment myelitis,4 cases(30.7%) were post infectious myelitis,2 cases each of (15.4%) of NMO disorder and MS,1 (7.7%)case of syrinx and 4 (30.7%) cases remained undiagnosed.MRI spine was normal in 7 out of total 70 cases of which 3 cases each were of SACD and post infectious myelitis and1 case(1.4%) remained undiagnosed.MRI brain abnormality along with cord changes was found in 10 out of total 70 cases (14.3%) of which 6 had brainstem involvement (8.6%),2 cases(2.9%) had periventricular hyperintensities and 1 case(1.4%) each of fronto parietal sulcalhyperintensity and CNS tuberculoma were found.

Overall, demyelinating illness was most commonin occurrence- 20 cases out of 70 (28.6%) comprising10 NMO positive(14.3% of overall cases) , 8 MOG positive(11.4%)and 2 multiple sclerosis cases (2.8%) (Table-3). Sixc ases (8.6%) each of tubercular myelitis and post infectious (non-tubercular)ATM including 1 case (1.4%) of post herpetic myelitiswere found. There were five cases (7.1%)of sub acute combined degeneration and 2 cases (2.9%) of spinal AVM(Arterio-venous malformation).Out of 70 cases, cause of illness could not be established in31 (44.3%) cases due to non-affordability to further blood tests. However, in these cases CSF viral panel and CB –NAAT were negative along with routine blood tests including serum vitamin B12 level which were found to be normal. Eight cases of these 31 (25.8%) were NMO-MOG negative and did not fulfill the criteria of aquaporin negative NMO-SD[4], so were included in this group of unknown causes.

Out of 15 patients in first age group of less than 18 years, demyelinating disease was the most prevalent cause –NMO and MOG cases were 6 out of 15 (40%),3 cases(20%) were post infectious(non-tubercular), 1(6.6%) tubercular myelitis and 5(33.3%) unknown. Out of 42 patients in age group of 18-45 years, cause could not be found in19 cases (45.2%). Demyelinating illness again was found to be the commonest cause in 13 cases out of 42 (30.9%), followed by 4 cases(9.5%) each of SACD and tubercular myelitis ,1 case(2.4%)each of spinal AVM and post infectious(non-tubercular).In age group of >45 years, out of 13 cases mixed etiology was found –2 cases(15.4%) were of post infectious ATM,1(7.7%) each of NMO, tubercularmyelitis, AVM and SACD and cause could not be found in 7cases (53.8%).

VEP was performed in all 70 cases and p100 latencies were found to be bilaterally prolonged in all 18 cases of demyelinating illness (25.7%).CSF analysis was done in all cases of non-compressive myelopathy as routine study along with viral panel for HIV, HSV-1, 2, CMV, EBV and CB-NAAT. Gross CSF abnormality was found in 11 (15.7%) cases where all had lymphocytic pleocytosis with raised proteins in cases of tubercular myelitis and demyelinating illness except one case where it was neutrophilic in nature. Oligoclonal bands were found in 2 cases (2.9%).

4. Discussion

In our study of 70 patients with non-compressive myelopathy, 50 (71.4%) were males and 20 (28.57%) females (Table-1).Patients were categorized on the basis of age into 3 groups - <18 years, 18-45 years and >45 years. Bladder and bowel involvement was seen in maximum cases followed by paraparesis, quadriparesis and visual impairment. Fever preceded the onset of illness in 20 cases (28.5 %) of non-compressive myelopathy – 6 (8.6%) cases of post infectious acute transverse myelitis (ATM), 5 (7.1%) cases in NMO, 2 (2.8%) cases in MOG,7 (10%) cases in which cause could not be established either due to financial constraints or due to negative routine workup.

MRI brain and spine were done in all cases to rule out compression. They were found to be normal in 7 out of 70 cases (10%) while 63(90%) cases had spinal cord changes (Table-2).Previous studies conducted showed normal MRI in 7 to 50% cases. In our study, LETM was found in NMO (16%) and MOG (16%) positive cases mainly, others included tubercular myelitis (12%), AVM(4%), post infectious etiology (4%) and SACD(2%).Twenty three cases (74.2%) in unknown etiology group had LETM. Out of 13 cases (18.5% of 70 cases) of short segment myelitis,4 cases(30.7%) were post infectious myelitis, 2 cases each of (15.4%) of NMO disorder and MS,1 case (7.7%) of syrinx and 4 (30.7%) cases remained undiagnosed. Out of 5 cases (7.1%) of SACD, 1 case each of LETM (1.4%) and short segment myelitis (1.4%)was found while rest 3 cases (4.3%) had no spinal changes. MRI spine was normal in 7 out of total 70 cases of which 3 cases each were of SACD and post infectious myelitis and1 case(1.4%) remained undiagnosed.MRI brain abnormality along with cord

changes was found in 10 out of total 70 cases (14.3%) of which 6 had brainstem involvement (8.6%) which were demyelinating (NMO-MOG)in nature, 2 cases (2.9%) of MS had periventricular hyperintensities and 1 case(1.4%) each of fronto parietal sulcalhyperintensity and CNS tuberculoma were found.

Many studies conducted in India showed prevalence of non-compressive myelopathy as 14 to 62%.In our study, out of 70 cases of non-compressive myelopathy, major bulk was formed by longitudinally extensive transverse myelitis (50cases-71.4%) (Table-3,4) which was mainly demyelinating in nature. All cases had acute to sub acute onset of illness.In India post infectious myelitis was considered to be the commonest cause but of late with the advent of better immunological testing, demyelinating disease is on the rise.In31 cases(44.3%), cause of illness could not be established due to financial constraints to further blood tests. Eight of these 31 cases (25.8%) were NMO-MOG negative but did not fulfill the criteria of aquaporin negative NMO-SD,so were included in this group of unknown causes.

Demyelinating illness was most common in occurrence in people below 45 years age whereas etiology of non-compressive myelopathy was varied in elderly age group. There were 20 demyelinating cases(28.6%) out of total 70 comprising 10(14.3%)NMO positive, 8 (11.4%) MOG positive and2 MS cases (2.9%).There were 6(8.6%) cases each of tubercular myelitis and post infectious(non-tubercular) ATM,5 (7.1%) cases of sub acute combined degeneration and 2(2.8%) cases of spinal AVM. In a study conducted by Prabhakar et al [1]from 1997 to 1999, acute transverse myelitis (ATM) was the commonestetiology followed by vitamin B12 deficiency myelopathy. In a study by Kayal A.K. et al[5], median age was 35 years, male: female ratio was 1.4:1 and most common causes were found to be neuromyelitisoptica spectrum disorder and multiple sclerosis (MS).

Myelin oligodendrocyte glycoprotein (MOG) –IgG disease is a novel entity, not documented in any of the earlier studies. Eight MOG positive cases (11.4%) documented in our study were young adults, ranged from 10-35 years age with male preponderance but sex predisposition (ratio of 3:1) is contrary to what is found in literature. All cases presented with myelitis as first episode. All 10 NMO cases showed female preponderance with 4:1 ratio, with age group less than 45 years. Only 1(1.4%) case was reported in elderly female of 61 year. Two cases of multiple sclerosis were found.

Acute complete transverse myelitis (ACTM) was defined as relatively symmetric moderate or severe loss of motor and sensory modalities caudal to the level of the lesion. Acute partial transverse myelitis (APTM) was labeled when there was incomplete or patchy involvement of at least one spinal segment with mild to moderate weakness and asymmetric or dissociated sensory symptoms and occasionally, bladder dysfunction. As perFord B et al [6] ATM is a monophasic illness usually focal, so difficult to differentiate between post-infectious form versus demyelinating illness as in both lesion can be asymmetrical and longitudinally extensive. Patchy focal cord hyperintensityis seen mainly in multiple sclerosis, CSF –OCB is important marker for the same, which could be performed in only 3 cases in our study, two of which turned out to be positive for MS. So exact number of ATM could not be assessed. As per Prabhakar et al [2]in ATM group, mean age was 30.35 years, antecedent event was observed in 41.9% case,25 cases out of 31 cases(80.6%)had symmetrical involvement and most of the cases had severe deficit at onset.

Visually evoked potential study was done in all cases which was found to be abnormal in 18 (25.7%) cases, all of them were in demyelinating category.

CSF analysis for infective etiology was done in all cases as routine CSF study along with viral panel for HIV, HSV-1,2,CMV,EBV and CB-NAAT. Gross CSF abnormality was found in 11 (15.7%)cases where all had lymphocytic pleocytosis with raised proteins in cases of tubercular myelitis and demyelinating illness except one case where it was neutrophilic in nature. Mild protein elevation was seen in 9(12.8%) cases of demyelinating illness and post infectious myelitis. Oligoclonal bands were found in 2 cases (2.8%).In a study by Prabhakar et al [2],CSF analysis in 23 patients of ATM revealed rise in proteins (mean 147.95mg%, range 20-1200 mg/dL) and pleocytosis (mean 20.78/cumm, range 0-200 mm3) with oligoclonal band (OCB) positive in 28% cases of ATM.

5. Conclusion

Non-compressive myelopathy is a broad spectrum disorder. Overall most common cause was found to be demyelinating illness followed by almost equal number of tubercular, post infectious and vitamin B12 deficiency cases. In none of the previous studies MOG Ab disorder was diagnosed being a novel entity. A major limitation of the study was the financial constraints due to which some patients could not be evaluated further. Finding out the exact cause of non compressive myelopathy is crucial not only for the treatment of patient but it also helps in understanding the overall prognosis.

References

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Table 1

A.	**Age of patients**	**Number of cases(n=70)**
1.	<18 years	15(21.4%)
2.	18-45 years	42(60%)
3.	>45 years	13(18.6%)
B.	**Sex of patients**	**Number of cases(n=70)**
1.	Male	50(71.4%)
2.	Female	20(28.6%)
C.	**Clinical presentation**	**Number of cases(n=70)**
1.	Bladder and bowel involvement	55 (78.6%)
2.	Paraparesis	50 (71.4%)
3.	Quadriparesis	20 (28.6%)
4.	Visual impairment	18 (25.7%)

Table 2

S.NO (A)	*Type of spinal lesion*	*Number of cases*
1.	Longitudinally extensive transverse myelitis	50 (71.4%)
(a)	NMO disorder	8 (16%)
(b)	MOG disorder	8 (16%)
(c)	Tuberular myelitis	6 (12%)
(d)	Post infectious myelitis	2(4%)
(e)	Spinal AVM	2 (4%)
(f)	SACD	1 (2%)
(g)	Undiagnosed	23(46%)
2.	Short segment myelitis	13 (18.6%)
(a)	Post infectious myelitis	4(30.7%)
(b)	MS	2(15.4%)
(c)	NMO	2(15.4%)
(d)	Syrinx	1(7.7)
(e)	Undiagnosed	4(30.7%)
3.	No change	7 (10%)
S.NO (B)	Type of brain lesion	Number of cases
1.	Brain stem hyperintensity	6(60%)
(a)	NMO disorder	4(40%)
(b)	MOG disorder	2(20%)
2.	Periventricular hyperintensity (MS cases)	2(20%)
3.	CNS Tuberculoma	1(10%)
4.	Fronto-parietal sulcalhyperintensity	1(10%)

Table 3

S.NO.	Etiology of non compressive myelopathy	Number of cases (n=70)
1.	Demyelinating disorder	20 (28.6%)
(a)	NMO	10 (14.3%)
(b)	MOG	8 (11.4%)
(c)	MS	2 (2.9%)
2.	Post infectious	6 (8.6%)
3.	Tubercular myelitis	6 (8.6%)
4.	SACD	5 (7.1%)
5.	Spinal AVM	2 (2.9%)
6.	Undiagnosed	31 (44.3%)

Table 4

S.NO.	Etiology of non compressive myelopathy in <18 years age	No. of cases (n=15)
1.	Demyelinating disorder	6 (40%)
(a)	MOG	3(20%)
(b)	NMO	3(20%)
(c)	MS	0
2.	Post infectious	3(20%)
3.	Tubercular myelitis	1(6.7%)
4.	Undiagnosed	5(33.3%)
S.NO.	**Etiology in 18-45 years age**	**No. of cases (n=42)**
1.	Demyelinating disorder	13(30.9%)
(a)	NMO	6(14.2%)
(b)	MOG	5(11.9%)
(c)	MS	2(4.8%)
2.	SACD	4(9.5%)
3.	Tubercular myelitis	4(9.5%)
4.	Spinal AVM	1(2.4%)
5.	Post infectious myelitis	1(2.4%)
6.	Undiagnosed	19(45.2%)
S.NO.	**Etiology in >45 years age**	**No. of cases (n=13)**
1.	Post infectious	2(15.4%)
2.	Demyelinating disorder	1(7.7%)
(a)	NMO	1(7.7%)
(b)	MOG	0
(c)	MS	0
3.	Spinal AVM	1(7.7%)
4.	SACD	1(7.7%)
5.	Tubercular myelitis	1(7.7%)
6.	Undiagnosed	7(53.8%)

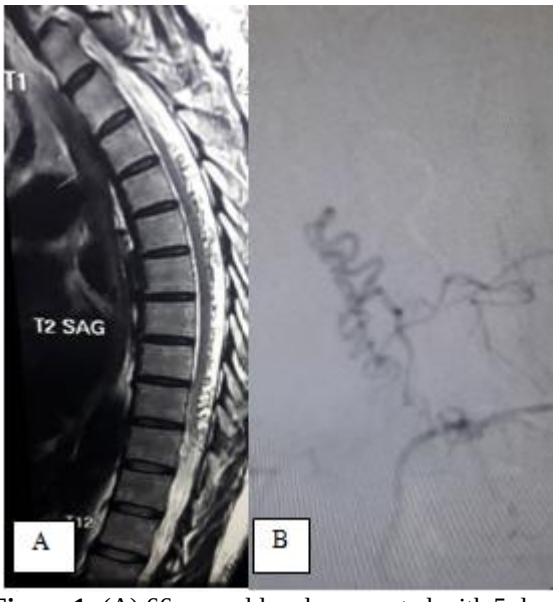

Figure 1: (A) 66 year old male presented with 5 days history of sudden onset low back ache with paraparesis , MRI T2 weighted image showed spinal AVM(dural AV fistula) extending from dorsal region D3-D10. (B) Spinal DSA showing dural AVF supplied by left radiculomeningeal artery at D10 spinal level .

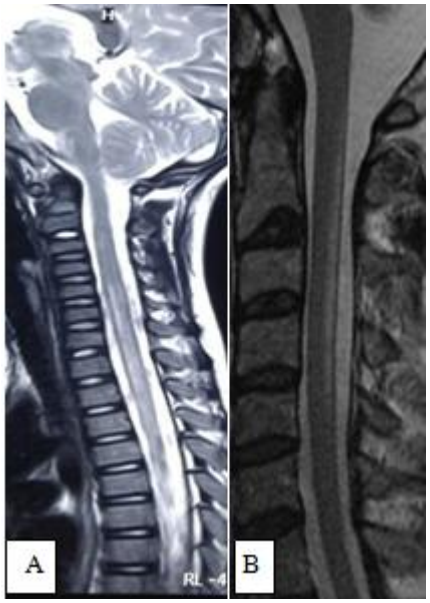

Figure 2: (A) 13 yr old male with acute onset quadriparesis with MRI spine T2 weighted image showing lesion in cervico–dorsal region(C5 to D4 level) with mid brain hyper intensity , was found to have MOG antibody disorder. (B) 45 year old male patient with SACD with MRI spine T2 weighted image showing hyperintensity in cervical cord posteriorly.

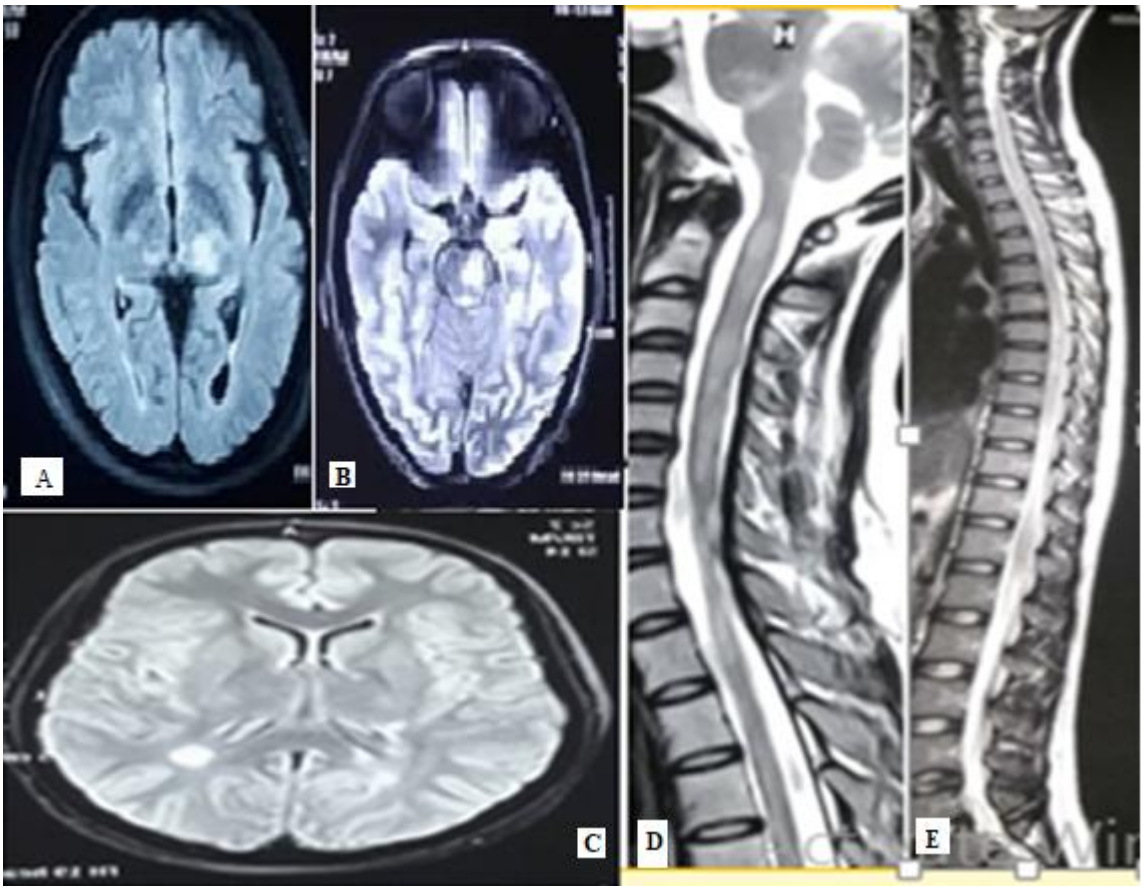

Figure 3: (A) 42 year old female with MRI brain T2 flair image showing bilateral asymmetric (left>right) thalamic hyperintensity in a case of NMO positive disorder. (B) 10 year old male child with MRI brain T2 flair image showing hyperintensity predominantly in left mid brain in a case of MOG disorder. (C) 35 year old female with MRI brain T2 FLAIR image showing periventricular lesion in a case of MS. (D) 38 year old female with MRI spine T2 weighted image showing patchy cervical and dorsal hyperintensity in a case of MS. (E)32 year old male with MRI spine T2weighted image showing LETM extending through cervical and dorsal cord.