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Research Article

Typical and Atypical NMOSD - Its Implications

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Abstract

Background: Neuromyelitis optica (NMO) has evolved from Devic's classical description to a broader disease spectrum of NMO Spectrum Disorder (NMOSD), from monophasic illness to a polyphasic illness with multiple recurrences, disease confined to optic nerve and spinal cord to now brain stem, cerebrum and even with endocrinopathy due to hypothalamic involvement [1], coexisting infections [2] and a variety of autoimmune diseases, including non-organ specific autoimmune diseases and co-existent autoantibodies without diseases [3].

Objectives: To report, the epidemiological characteristics, clinical presentations, recurrence rate, treatment and response to therapy in 23 patients with NMO spectrum disorder among the Indian population.

Materials and Methods: An observational, retrospective analysis of our prospectively maintained data base of patients during the period of May 2018 - June 2018 who satisfied International Panel for NMO Diagnosis (IPND) revised criteria [4] of NMOSD was done.

Results:

1. 23 case records of NMOSD were retrieved. 14 cases were aquaporin4 positive and 9 were aquaporin4 negative.
2. Mean age is 39.6 years. Median age is 42 years (Range 17 - 64). Female to male ratio is 1:2.8.
3. Clinical presentations included longitudinally extensive transverse myelitis being the most common followed by optic neuritis, area postrema syndrome, seizures and brainstem encephalitis.
4. Two had associated herpes simples virus encephalitis, one CSF VDRL positivity. Two had associated retro viral disease.
5. Two had ANA, Anti ds DNA antibody positive vasculitis.
6. One had CSF oligoclonal bands in CSF and an open ring enhancement on MRI suggestive of tumefactive demyelination.

Discussion and Conclusion:

Contrary to current literature there is unusual male preponderance in our study population.

- Atypical lesions(Red flags) or course should suggest additional work up for associated diseases and prompt treatment ofwhich can lead to a significant recovery.
- Aquaporin 4 antibody positivity, severity at presentation, associated diseases and relapse rate determine the prognosis.

Keywords: Typical NMOSD; Atypical NMOSD; NMOSD Associated Diseases

Abbreviations

AQP4: Aquaporin-4; CSF: Cerebrospinal Fluid; CBA: Cell Based Assay; DTI: Diffusion Tensor Imaging; hlas: Human Leukocyte Antigens; IPND: International Panel for NMO Diagnosis; IV IgG: Intravenous Immunoglobulin; LETM: Longitudinally Extensive Transverse Myelitis; MRI: Magnetic Resonance Imaging; MTR: Magnetisation Transfer; MOG-iggs: Myelin Oligodendrocyte Glycoprotein; NMO: Neuromyelitis Optica; NMOSD: NMO Spectrum Disorder; ON: Optic Neuritis; PRES: Posterior Reversible Encephalopathy Syndrome; SLE: Systemic Lupus Erythematosus

Introduction and Review of Literature

The first account of a patient with visual loss and spinal cord disease was made by Antoine Portal in the 19th century. Pescetto, Durrant, Lockhard and Clarke also contributed to similar descriptions early on [7]. The association of visual loss with spinal cord disease was described by Allbutt in 1870. A decade later, Erb gave the first detailed description of NMO [5]. Eugene Devic, French neurologist mentioned the term "neuromyelitis optica" for the first time in 1894. He, along with his student Fernand Gault, described a clinical syndrome characterized by optic neuritis and acute transverse myelitis [5,8,9]. Also, there were reports of patients with relapsing course of the disease by Beck in 1927 and McAlpine in 1938) [5].

In 2004 Lennon and Wingerchuk isolated neuromyelitis optica immunoglobulin G (NMO-IgG) antibody, a specific marker to differentiate NMO and MS [7]. A year later Lennon and colleagues discovered selective binding of NMO-IgG antibody to the aquaporin-4 (AQP4) water channel [10]. In 2006 Wingerchuk and colleagues revised the diagnostic criteria for NMO which have been commonly used over the years. As per the revised criteria optic neuritis (ON), acute myelitis and at least two of three supportive criteria that included continuous spinal cord magnetic resonance imaging (MRI) lesion encompassing over three vertebral segments, brain MRI not fulfilling diagnostic criteria for MS and aquaporin-4 immunoglobulin G (AQP4-IgG) seropositivity should be present. The above diagnostic criteria had a sensitivity of 99% and specificity of 90% for NMO [11]. Eventually, new discoveries in the area of immunopathophysiology and radiology of NMO lead to the conclusion that a broader spectrum of clinical disease exists. "Neuromyelitis optica spectrum disorders" (NMOsd) not only includes AQP4-IgG seropositive patients with NMO, but also other limited forms of the disease [8,12].

The "International consensus diagnostic criteria" for neuromyelitis spectrum disorders was published by International Panel for NMO Diagnosis (IPND) in 2015 according to which the general term of NMOsd should be used for all those patients who satisfy the clinical criteria and is further subclassified into NMOsd with or without AQP4-IgG positivity based on the basis of serologic testing, as shown in figure 1. The diagnosis of NMOsd with AQP4-IgG is made when at least one of the six typical core syndromes is present (optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOsd-typical diencephalic MRI lesions, symptomatic cerebral syndrome with NMOsd-typical brain lesions); along with seropositivity for AQP4-IgG detected by the best available method and when alternative diagnoses are excluded. Such a diagnosis can be made in a patient seronegative for AQP4-IgG when at least two core clinical features occur as a consequence of one or more clinical attacks, and all of the following conditions are met: (a) at least one core clinical feature must be NMO-typical (optic neuritis, acute myelitis with longitudinally extensive transverse myelitis (LETM) or area postrema syndrome); (b) clinically proven dissemination in space (two or more different core clinical syndromes) with additional MRI requirements specific for each clinical syndrome (See figure 1) [4].

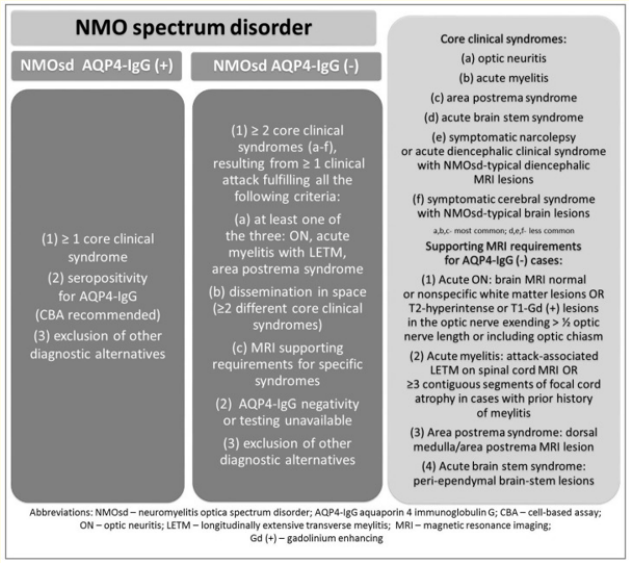

Figure 1: Diagnostic criteria for neuromyelitis spectrum according to International panel for neuromyelitis optica (NMO) diagnosis (2015).

As per the IPND recommendation, NMOsd diagnosis can be made only when the patient has experienced at least one clinical attack. Seropositivity for AQP4-IgG or MRI lesions characteristic for NMOsd are inadequate for the diagnosis in the absence of symptoms. In addition, isolated clinical attack of the disease is not adequate foe diagnosis in AQP4-IgG seronegative patients. Also, there are no clinical features that completely exclude NMOsd, but a few of them might point to an alternative diagnosis. Red flags those point an alternative diagnosis in NMOsd include the following: progressive clinical course with no association between deterioration and disease relapse, atypical duration of attack (< 4 hours or > 4 weeks), incomplete/partial transverse myelitis, oligoclonal bands in the cerebrospinal fluid (CSF), sarcoidosis, malignancy, chronic infections (e.g. HIV, syphilis) and some MRI features (e.g. Dawson fingers, cortical lesions, peripheral spinal cord lesions or lesions of less than three vertebral segments). Neuromyelitis optica occurs more common in women [8,12]. As per literature across the world, female to male ratios range from 2:1 to 10:1. Relapsing illness is more common in women (90%) [12]. Median age of onset is 39 years. The disease may also occur at extremes of age [8] and the prevalence is about one to three per 100,000 populations [12]. It is less common (1% - 2%) in Caucasians, people from North America or Australia and most common occurrence (20% - 48%) is found in the West Indian and Asian population [8,13]. It is predominantly a sporadic disease, but reports of familial cases have also been documented (in about 3% of patients) [4,12,14]. The hypothesis that NMO is a complex genetic disease was made because of infrequent familial aggregation of cases, the absence of multigenerational pedigrees and lack of distinctive features in familial cases [14]. Human leukocyte antigens (HLAs) associations of neuromyelitis optica, such as DRB1*0301 in white population, and DPB1*0501 in Asian population pose a greater risk to acquire illness [8].

Neuromyelitis optica can be a monophasic or relapsing illness. As per the literature across the world, 80% - 90% of patients have a relapsing course of illness. The most typical clinical features of NMO include ocular pain with diminution of vision (optic neuritis), acute transverse myelitis with papraparesis/paraplegia, sensory loss and bladder dysfunction [8,12]. Other features include Lhermitte's sign, paroxysmal tonic spasms or radicular pain can accompany acute myelitis [5,8,12]. Involvement of cervical spinal cord extending into brainstem may result in nausea, hiccups and even respiratory failure [8,12]. Less common clinical syndromes include endocrine abnormalities, encephalopathy, coma, cerebral syndromes and the posterior reversible encephalopathy syndrome (PRES) [12]. After the first attack of the disease, 60% of patients experience another relapse within one year and 90% within three years [8,12]. Interestingly, AQP4-IgG seropositive patients with recurrent optic neuritis (ON) or the first episode of LETM are particularly at high risk of relapse [12]. Optic neuritis and LETM may occur simultaneously but usually they occur sequentially as different episodes [8,12]. Relapses are characterized by symptoms progressing over several days, and then slowly improving over weeks or months and are more frequent and more severe when compared to those of MS. Recovery is incomplete leading to accumulated disease burden and disability early in course [8,12]. Although patients with monophasic illness experience more impairment from attacks than patients with relapsing illness, their long-term outcome is usually better. As the duration of illness passes five years, over a half of patients with relapsing course might have developed unilateral or bilateral blindness, or they need help for ambulation [8]. The percentage of patients with permanent monoplegia or paraplegia is also higher in the relapsing illness than the monophasic group (52% and 31% respectively) [5]. Also, respiratory failure is more common in the relapsing group (33% Vs 9%) [5]. The prognosis of relapsing NMO is poor in comparison with MS [5].

Initially, brain MRI is usually normal, except for enhancement of optic nerve or brainstem lesions in some. On follow-up imaging nonspecific brain lesions may be found which are typically, clinically silent and do not meet criteria to fulfill MS [5,8,12]. 10% of patients fulfilling the NMO diagnostic criteria might develop brain lesions over time in follow-up imaging that meet MS criteria [8,12]. Abnormalities in normal-appearing grey matter and normal or mild changes in normal-appearing white matter in magnetisation transfer (MTR) and diffusion tensor imaging (DTI) has also been reported in NMO patients [8]. This may be a strong evidence of retrograde neuronal degeneration and selective or more severe destruction of grey matter marked by over expression aquaporin-4 [8].

Spinal cord MRI has great value in the diagnosis of NMO. The changes include longitudinal, contiguous lesions extending over three or more vertebral segments [5,8,12]. The sensitivity and specificity is 98% and 83% respectively in diagnosis of NMO [11]. Additional typical findings are cord swelling and gadolinium enhancement [5]. Few patients eventually develop focal spinal cord

atrophy. Of note, T2-weighted longitudinally extensive lesions may not develop early in course of disease. Also, they might contract or resolve over time [11].

Cerebrospinal fluid (CSF) examination may be useful in differentiating NMO from MS. CSF pleocytosis (> 50 cells/mm^3) with a neutrophilic predominance and elevated protein (100 to 500 mg/dL) is a common finding in NMO and not in MS [5,8,12]. Oligoclonal IgG bands are helpful in differentiating NMO from MS. They are present in 85% - 90% of patients with MS, but are seldom found in patients with NMO (15% - 30%) [5,8,12].

Aquaporin-4 (AQP4-IgGs, also called NMO-IgGs) antibodies are a specific biomarker and are important in the diagnosis of NMO [7,8,10,13]. These have a sensitivity of 73% and specificity of 91% in the diagnosis of a clinically defined NMO [7,8]. The sensitivity and specificity however depend on analytical methods used for the identification of AQP-4-IgG and is the best for cell-based assays (CBA). Other autoimmune disorders related to NMO such as Asian optic-spinal MS, recurrent ON, recurrent myelitis with LETM, ON or myelitis associated with certain organ-specific and non-organ specific autoimmune disorders may also be associated with antibody positivity [8]. Of note, 10% - 25% of NMO patients can be seronegative for AQP4-IgG [8]. In those who are AQP4-IgG seronegative two other autoantibodies were detected: autoantibodies against aquaporin-1 (AQP1-Abs) [14] and antibodies against myelin oligodendrocyte glycoprotein (MOG-IgGs) [15]. However, some NMO patients may be seropositive for both AQP4-IgG and AQP1-Ab. MOG-antibody disease, which essentially is a NMO spectrum disease can present at any age, presents most commonly with optic neuritis, shows slight female preponderance and uniformly prevalent across all ethnic groups. It is often a relapsing illness with risk of relapse determined by the duration of immunosuppression. The prognosis is typically favourable, but patients can be left with significant sphincter and erectile dysfunction, cognitive impairment and poor visual acuity. The maximum disability is due to onset attack [16].

Strong association between LETM or optic neuritis (ON) and other autoimmune diseases, especially systemic lupus erythematosus (SLE) and Sjögren's syndrome (SS) [5,8,12,17] is put forward by many studies. The spectrum also includes autoimmune hypothyroidism, pernicious anemia, immune thrombocytopenic purpura, primary sclerosing cholangitis and ulcerative colitis [5,8]. The association of NMO with autoimmune diseases is about 30% [5,8]. Systemic autoimmune diseases, as well as the presence of non-organ specific autoantibodies are found at similar frequencies in NMO and MS. Strangely, NMO patients frequently have a family history of autoimmune diseases [8] and thereby it has been concluded that NMO could be a manifestation of a genetic tendency toward humoral autoimmunity. An alternative explanation is that NMO could arise as a complication of a specific or nonspecific systemic autoimmune disease [18] and in which case the illness should precede NMO. However, reports of patients who develop SLE or SS before NMO onset and those who manifest NMO before the diagnosis of SLE or SS gives evidence of strong association [18]. The association with thyroid disease (the most common co-existing autoimmune disease), myasthenia gravis or celiac disease is well reported [18]. It might also be triggered by a nonspecific infection that can perturb the immune system (e.g. self-reactive lymphocyte, AQP4-IgG production, inflammatory cytokines, BBB disruption) and thus modulates NMOSD [2].

The mainstay of treatment for NMO is immunosuppressive therapy but due to less prevalence, large controlled clinical trials are lacking and treatments are often based on small case series. Steroids, azathioprine, intravenous immunoglobulin (IV IgG), plasmapheresis as well as an anti-CD20 monoclonal antibody have been well studied [19].

The factors indicating a worse prognosis are the following: frequent relapses during the first two years of the disease, the high severity of the first attack and, interestingly, coexistence of systemic lupus erythematosus (SLE) or other non-organ-specific autoimmune disorders or the presence of auto antibodies [8]. The five-year survival is 90% in monophasic patients and 68% in relapsing patients. In the second group deaths are typically due to respiratory failure [5].

Materials and Methods

The study population consisted of patients with NMOSD from our prospectively maintained database at Department of Neurology, Government General Hospital, Guntur during the period of May 2016 - June 2018 who satisfied International Panel for NMO Diagnosis (IPND) revised criteria [4]. The patient who had relapses and remission with variable degree of recovery between episodes were labeled as polyphasic illness as compared to patients with simultaneous or closely related ON and LETM (< 30 days) or progressive without recurrence, that is, monophasic illness. We performed observationally, retrospective analysis of this cohort, to study the

epidemiological characteristics, clinical presentations, associated diseases, recurrence rate, treatment and response to therapy.

Results

- 23 case records of NMOSD were retrieved and analysed.
- 15 are males (65.25%) and 8 are females (34.7%) (Table 1).
- 14 cases (60.8%) were aquaporin4 positive and 9(39.1%) were aquaporin4 negative (Table 2).
- Mean age is 39.6 years. Median age is 42 years (Range 17 - 62).
- Aquaporin4 antibody positivity in males is 6 (40%) (Table 3) and females are 8 (100%) (Table 4).
- Female to male ratio is 1:2.8.
- Clinical presentations included longitudinally extensive transverse myelitis with optic neuritis being the most common in 13 patients (56.5%) followed by isolated longitudinally extensive transverse myelitis in 5 patients (21.7%) and isolated optic neuritis in 2 patients (8.6%), Area postrema syndrome in 2 patients (8.6%), brainstem encephalitis in 1 patient (4.3%) (Table 5).
- Total number of patients with associated diseases is 7 and of them 5 (71.4%) are males and 2 (28.5%) are females (Table 6).
- Two had associated herpes simples virus encephalitis, one CSF VDRL positivity.
- Two had associated retro viral disease.
- Two had ANA, Anti ds DNA antibody positive vasculitis.
- One had CSF oligoclonal bands in CSF and a ring enhancing pattern (open) on MRI suggestive of a tumefactive demyelination.
- Average relapse rate was one per patient per annum. A total of 18 relapses occurred. Longitudinally extensive transverse myelitis with optic neuritis was the most frequent manifestation during relapse in 6 patients (33.3%), followed by Isolated Optic Neuritis in 4 patients (22.2%), Isolated myelitis in 3 patients (16.6%), Area postrema syndrome in 2 patients (11.1%), Brainstem syndrome in 2 patients (11.1%), Cortical involvement in 1 (5,5%) (Table 1).
- All patients received Inj. Methyl Prednisolone. In addition, 16 patients (69.5%) required additional immunosuppression with IVIG in 3 (13.1%), Azathioprine in 9 (39.1%), Rituximab in 3 (13.1%), Methotrexate in 1 (4.3%).
- Two patients expired both with brainstem involvement, one during the first episode and the other during relapse.

Sex Ratio							
Female	8 (34.7%)						
Male	15 (65.2%)						
Age Groups							
Group	5 - 10 years	10 - 20 years	20 - 30 years	30 - 40 years	40 - 50 years	50 - 60 years	60 - 70 years
N%	-	2	5	4	6	6	1
Course							
Monophasic	7 (30.4%)						
Polyphasic	16 (69.5%)						
Site of recurrence	Myelitis (LETM) + Optic Neuritis	Myelitis (LETM)	Optic Neuritis	Area Posterma	Brain stem	Cortical Involvement	
N = 18 (%)	6 (33.3%)	3 (16.6%)	4 (22.2%)	2 (11.1%)	2 (11.1)	1 (5.5%)	
Type of treatment	IVMP alone	IVIG	PLEX	Azathioprine	Rituximab	Methotrexate	
N = 23(%)	7 (30.4%)	3 (13.1%)	-	9 (39.1%)	3 (13.1%)	1 (4.3%)	

Table 1: Demographic data.

Total number of patients	Serum Aquaporin4 antibody positive	Serum Aquaporin4 antibody negative
23	14	9
100%	60.8%	39.1%

Table 2: Aquaporin 4 antibody positivity.

Total number of male patients	Serum Aquaporin4 antibody positive (male)	Serum Aquaporin4 antibody negative (male)
15	6	9
100%	40%	60%

Table 3: Males with aquaporin4 antibody positivity.

Total number of female patients	Serum Aquaporin4 antibody positive (female)	Serum Aquaporin4 antibody negative (female)
8	8	0
100%	100%	0%

Table 4: Females with aquaporin 4 antibody positivity.

Total number of patients	Males with associated diseases	Females with associated diseases
7	5	2
100%	71.4%	28.5%

Table 6: Proportion of patients with associated diseases.

Total number of NMOSD patients	Longitudinally extensive transverse myelitis and optic neuritis	Isolated Optic neuritis	Isolated Longitudinally extensive transverse myelitis	Area postrema syndrome	Brainstem encephalitis
23	13	2	5	2	1
100%	56.5%	8.6%	21.7%	8.6%	4.3%

Table 5: Clinical presentation.

Discussion

Neuromyelitis optica makes up a substantial proportion of inflammatory demyelinating disorders of the CNS in noncaucasian populations such as Afro-Brazilians (15%), East Asians (up to 48%) and Indians (9%) [20-22].

According to worldwide reports, it is a female preponderant illness with ratios that range from 2:1 to 10:1. Moreover, up to 90% of relapsing NMO patients are women [12]. On contrary to it in the current study Female to male ratio is 1:2.8. Male preponderance was reported earlier by a study from India [23]. The median age of onset is 39 years, however, the disease may also occur in children and in the elderly [8]. The age of onset in NMO ranges from childhood to late adulthood with the decrease in the incidence after the fifth decade; the median age of onset is in late 30's. Mean age of onset 27 years, comparable to western cohorts. In our study the median age is 42 and the mean age is 39.6 years. Also, there is an equal distribution of patients across second to fifth decade.

An antecedent viral illness was reported in 30% of patients with monophasic and 23% of patients with recurrent NMO [5]. In the current study, 5 out of 23 (21.7%) patients had coexisting infectious disease with positive serology. Two patients had coexisting Herpes Simplex Virus Encephalitis. One had a positive CSF VDRL. Two had coexisting Retro Viral Disease.

Neurosyphilis-optic neuritis is relatively uncommon. It can present in any four stages of syphilis and its mode of onset can be variable, as acute, subacute, or chronic progressive. Screening for neurosyphilis is important in bilateral optic neuritis cases with poor response to steroid, positive serum treponemal test, history of untreated syphilis, HIV infection and/or constricted pattern of visual field defect. Neurosyphilis can also rarely manifest as a form of LETM that should be treated by intravenous penicillin [24]. In the current study one patient presented with chronic progressive myelopathy with CSF VDRL and serum aquaporin4 antibody positivity. He neither responded to penicillin no to immunosuppression. He now has residual paraplegia.

25 - 30% of NMOSD patients suffered from a prodromal flu-like illness. Introduction of LPS, an important bacterial component, failed to produce a typical MS or NMOSD lesion. Sellner., *et al*. analyzed parainfectious NMOSD reports published between 1975 and 2009 and found on average a high prevalence of monophasic courses (88%) and a generally poor prognosis (with only a complete recovery in 25% of cases) in NMOSD patients. Taken together, these findings strongly suggest that infectious agents may trigger or exacerbate the development of NMOSD in genetically susceptible patients. *Mycobacterium* and *Mycoplasma* sp. share homologous epitopes to human AQP4, pulmonary or renal tuberculosis may, for example, induce lymphocytes that are sensitized against a bacterial epitope with selfproteins such as AQP4. Then, the entry of self-reactive lymphocytes, or their productions, into the CNS could potentially break down our CNS immunological tolerance and damage astrocytes. *H. pylori* neutrophil-activating proteins (HPNAP) - recruitment of neutrophils and monocytes. *H. pylori* might evoke or trigger the development of NMOSD by either skewing T-cell differentiation towards Th1 and Th17 phenotypes or by increasing the level of cytokines and leukocytes. Vacuolating A (VacA) cytotoxin

derived from *H. pylori* could exert chemotactic on bone marrow derived mast cells TNF-a. Tight-junctions between the BBB and the cerebrovascular basal lamina could be disrupted presumably letting more T cells and AQP4- specific antibodies into the CNS. Infections such as herpes virus (Herpes simplex, Epstein-Barr virus and cytomegalovirus), human T lymphotropic virus 1 (HTLV-1), dengue virus, *Borrelia burgdorferi* (Lyme), tuberculosis, *Mycoplasma pneumoniae*, and *Streptococcus pneumoniae* can manifest as LETM and/or optic neuritis [2].

Interestingly, though most of the infectious myelitis cases reported absence of AQP4-Ab, several cases have shown that NMOSD with AQP4 can develop several days after zoster infection. These findings might imply at least some pathogenic overlap between these two distinctive diseases of NMOSD and herpes zoster [2].

Given the rarity of NMO and the lack of information on its prevalence in less developed countries where HIV/AIDS is known to be prevalent, it is too early to comment on whether NMO is seen with greater than expected frequency in HIV positive patients. However, there are accumulating reports suggesting an excess of MS or MS-like illnesses in HIV/AIDS patients and this observation could be extended to include NMO, since both diseases are characterized by inflammatory demyelination, with significant overlap in neuropathogenesis. Macrophages are the primary CNS cell types capable of supporting HIV reproduction. Detection of early viral life cycle markers in astrocytes implies that astrocytes, too, are infected by HIV, which could conceivably predispose HIV/AIDS patients to NMO, a disease typified by damage to the astrocytes. However, while it is tempting to speculate on the possibility of an excess of NMO in patients living with HIV, further epidemiological and clinical studies are needed to elucidate the association between these two diseases. Limited information exists about treatment of NMO in HIV-infected patients. With the advent of HAART, immunosuppressants once strictly contra-indicated in HIV positive individuals are now attempted, especially in those less immunocompromised. For example, mycophenolate and rituximab have been safely used in such patients for organ transplantation and lymphoproliferative disorders respectively [25,26]. In the current study two HIV positive patients presented with Optic neuritis and longitudinally extensive transverse myelitis. One of them responded to Steroid and the other did not. In fact, the other has a cortical lesion suggestive of tumefactive demyelination. Her serum Aquaporin4 antibodies were positive and CEF is negative for oligoclonal bands and infectious serology. Her CD4 improved with Anti-Retroviral therapy. She required Azathioprine for immune suppression along with ART.

Two of the patients in the current study have associated ANA and Anti ds DNA vasculitis. One of them had a relapsing course and the other had a chronic progressive course. According to several studies, the occurrence of optic neuritis and/or transverse myelitis in AQP4-IgG seropositive patients with systemic autoimmune disease (e.g. SS or SLE) should not be regarded as a vasculitic complication of a systemic disorder, but as the coexistence of these two diseases [8,18].

Conclusion

- NMOsd is an autoimmune, demyelinating which most often presents with longitudinally extensive transverse myelitis and/or optic neuritis.
- Other clinical presentations include area postrema syndrome, brainstem syndrome.
- The current study has contradicting results when compared to literature from India and across the world.
- It can be a common disease among males. The current study has a male predominance (65.4%) and Male to Female ratio of 2.8:1.
- It can occur in elderly age group. The age of onset is more with mean age of 39.6 years and a median age of 42 years. Most of the patients were spread between second to fifth decades.
- Aquaporin4 positivity was 60%. It is positive 40% males and surprisingly 100% female patients.
- In the current study 7 of 23 (30.4%) had coexisting disease (infectious or auto immune diseases).
- Has a restricted clinical profile in spite of a wide variety of disease associations.
- Early extensive evaluation, diagnosis and prompt treatment especially in presence of atypical presentations, Red flags can lead to a significant recovery.
- Aquaporin 4 antibody positivity, severity at presentation, importantly associated diseases and relapse rate determine response rate and thus prognosis introduction should reflect the background, purpose and significant of the study that is carried out.

Conflict of Interest

Nil.

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