International Journal of Innovative Research and Advanced Studies (IJIRAS)
Volume 4 Issue 7, July 2017

ISSN: 2394-4404

# Neuromyelitis Optica - Case Report And Literature Review On Current Concepts

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***Abstract:*** ***Neuromyelitis optica is an inflammatory disorder of the CNS, in which immune system attacks myelin of the neurons located at the optic nerve and spinal cord producing simultaneous or sequential optic neuritis and myelitis. Once thought as a variant of MS, its discrimination from it is of paramount importance, since they have different clinical course and treatment modalities. Previous NMO diagnostic criteria was revised and modified by The International Panel for NMO Diagnosis (IPND) as NMO spectrum disorders (NMOSD), which includes serologic testing, clinical features or MRI findings related to optic nerve, spinal cord, brainstem, or cerebral lesions.***

***Herewith we report a case of 58y/f diagnosed as NMO as per clinical presentation and imaging studies and also we highlight upon the current concepts by reviewing the literature.***

***Keywords: Neuromyelitis optica spectrum disorders, Devic's disease, Multiple sclerosis, Aquaporin-4***

## I. INTRODUCTION

NMO, which is clinically represented by vision loss with acute myelitis, was first described by Clifford Albutt in 1870 and later described by Devic & his student fernand Gault in 1894. The term Devic's disease was coined by Acchoite in 1907 and is now considered as an autoimmune channelopathy, featured by production of disease specific auto antibody against aquaporin 4 in the year 2004. Clinical attacks may vary, be relapsing in 85% or monophasic in 15% with relation to positive or negative antibody status.

## II. INCIDENCE

Though case reports and series have been documented, only few epidemiological studies are available in the literature documenting a prevalence of $2.5/10^5$ & incidence of $0.1/10^5$ in a caribean study. A recent Danish study estimated a higher prevalence of $4.4/10^5$. The onset is usually around the fourth decade of life, but may occur at any age from early childhood to elderly patients with a female predominance (4). Although sporadic, familial NMO has been reported in 3% in some cohorts.

## III. CASE REPORT

58Y/F, a farmer, presented with sudden, painless and simultaneous loss of vision in both eyes of 2 days duration followed by inability to use both upper & lower limbs of one day duration. Clinical examination showed dilated and non reacting pupils with visual acuity limited to no perception of light in both eyes. opthalmological evaluation showed bilateral optic neuritis. Spinomotor examination showed UMN QUADRIPARESIS, associated with sensory deficits for all

ISSN: 2394-4404

modalities and autonomic dysfunction. No previous similar episodes.

Basic investigations and CT Brain done were normal. CSF analysis showed neutrophil pleocytosis. MRI whole Spine with brain screening reported as normal brain with T2 hyperintense lesion in the spinal cord from C2 to D3 level suggestive of LETM. Aquaporin antibody test not available and ANA were negative.

NMO was diagnosed as per criteria and patient was started on bolus doses of injection Methylprednisolone 1000mg in 100ml of NS for 5 days followed by advice on oral prednisolone of 1mg/kg daily for 2weeks with gradual tapering. During the course of I.V steroids, patient had improvement in her vision in both eyes from 6$^{th}$ day with visual acuity of finger counting with incomplete recovery of motor disability & was referred to higher neurological centre for further evaluation.

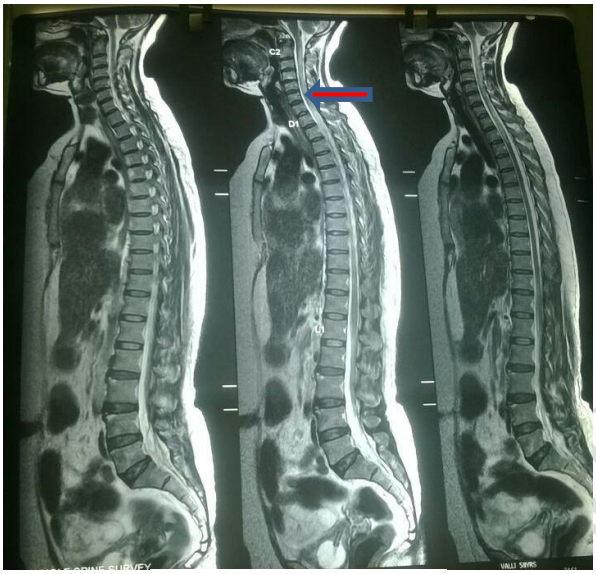

*Figure 1: MRI Whole Spine*

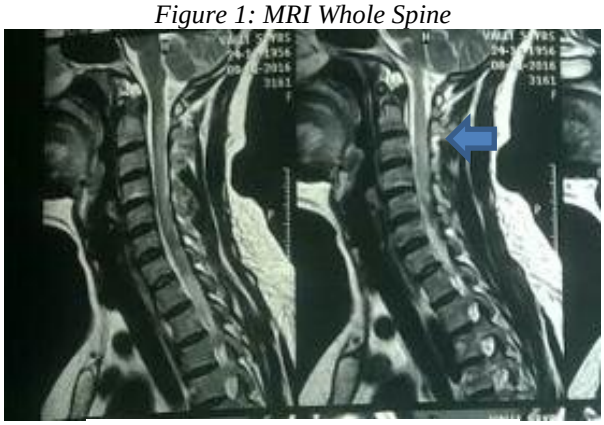

*Figure 2: showing LETM from C2 to D3*

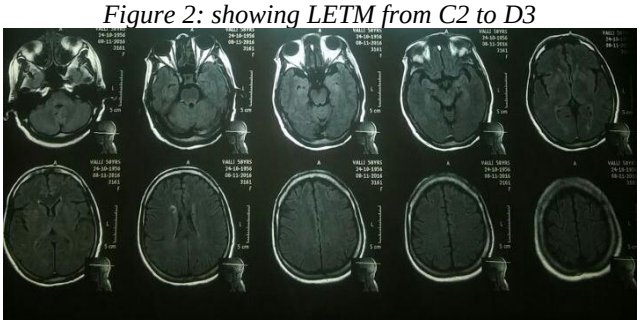

*Figure 3: MRI Brain*

## IV. DISCUSSION

### PATHOGENESIS

NMO is a disabling inflammatory condition targeting astrocytes in optic N & spinal cord. Aquaporin 4, a predominant water channel located in astrocyte foot processes around BBB, is critical in maintaining water homeostasis in the settings of physiological stress. Differential expression of these explains the pathological preference. MS is a CD4 mediated, while NMO is a humorally mediated autoimmune disease, featured by destruction of astrocytes by inflammatory mediators and complement fixation associated with weakening of BBB. Myelin bearing oligodendrocytes are the primary target in MS, while astrocytes are first lost in NMO & demyelination occurs as a secondary event.

### EVOLUTION OF NMO CRITERIA

Early studies identified patients with NMO as those with disease exclusive to the optic nerves and spinal cord. Subsequent studies revealed that 60% of patients develop brain MRI abnormalities involving AQP4-rich periventricular regions, which led to revised diagnostic criteria for NMO, including brain involvement and NMO-IgG seropositivity as additional features.

*Table 4. Wingerchuk et al.'s 1999 diagnostic criteria for neuromyelitis optica[8].*

| Diagnosis requires all absolute criteria and one major supportive criterion or two minor supportive criteria |
|---|
| Absolute criteria |
| 1. Optic neuritis |
| 2. Acute myelitis |
| 3. No evidence of clinical disease outside of the optic nerve or spinal cord |
| Supportive criteria |
| Major |
| 1. Negative brain MRI at onset (does not meet criteria for MS) |
| 2. Spinal cord MRI with signal abnormality extending over ≥3 vertebral segments |
| 3. CSF pleocytosis of >50WBC mm$^3$ OR >5 neutrophils/mm$^3$ |
| Minor |
| 1. Bilateral optic neuritis |
| 2. Severe optic neuritis with fixed visual acuity worse than 20/200 in at least one eye |
| 3. Severe, fixed, attack-related weakness (MRC grade ≤ 2) in one or more limbs |

Revised diagnostic criteria by Wingerchuk et al. (2006)
Two absolute criteria: (i) optic neuritis, (ii) myelitis.
At least two of three supportive criteria:

- ✓ presence of a contiguous spinal cord MRI lesion extending over three or more vertebral segments,
- ✓ MRI Brain features not satisfying the revised McDonald diagnostic criteria for MS, and
- ✓ NMO-IgG positivity in serum

Further experiments changed the concept as NMO spectrum disorders which includes brainstem & cerebral lesions in 2015.

**2015 IPND Neuromyelitis Optica Spectrum Disorder (NMOSD) Diagnostic Criteria**

**NMOSD With AQP4-IgG**
1. At least 1 core clinical characteristic (at right)
2. Positive test for AQP4-IgG*
3. Exclusion of alternative diagnoses**

**NMOSD Without AQP4-IgG or Unknown AQP4-IgG Status**
1. At least 2 core clinical characteristics (at right) resulting from 1 or more clinical attacks and satisfying all of the following requirements:
   a) At least 1 of: ON, acute myelitis with LETM, or APS
   b) Dissemination in space (≥2 different core characteristics)
   c) MRI requirements, if applicable (at right)
2. Negative test(s) for AQP4-IgG* or testing unavailable
3. Exclusion of alternative diagnoses**

* Using best available detection method (cell-based assay strongly recommended).
** Evaluation for alternative diagnoses guided by "red flags."

SOURCE: International Panel for Neuromyelitis Optica Diagnosis in affiliation with The Guthy-Jackson Charitable Foundation International Clinical Consortium. www.guthyjacksonfoundation.org/special-projects-and-programs/ipnd-diagnostic-criteria/. Accessed Aug. 24, 2015.

**Core Clinical Characteristics of NMOSD**
***Most common:***
1. Optic neuritis (ON)
2. Acute myelitis
3. Area postrema syndrome (APS): episode of otherwise unexplained hiccups or nausea and vomiting

***Less common:***
4. Acute brain stem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

**Supporting MRI Requirements for NMOSD Without AQP4-IgG**
1. **Acute optic neuritis:** brain MRI normal or demonstrating only nonspecific white matter lesions; OR optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm
2. **Acute myelitis:** spinal cord MRI showing attack-associated lesion extending ≥3 contiguous segments (LETM); OR ≥3 contiguous segments of focal cord atrophy in patients with prior history of acute myelitis
3. **Area postrema syndrome:** dorsal medulla/area postrema MRI lesion
4. **Acute brain stem syndrome:** peri-ependymal brain stem lesions

ATYPICAL FEATURES OF NMO:

Apart from typical optic neuritis & myelitis, patient may be presented with intractable hiccups, nausea, vomiting, painful tonic spasms, hypersomnia representing cranial involvement. There may be associated autoimmune disorders like Hypothyroidism, pernicious anaemia, ulcerative colitis, primary sclerosing cholangitis and idiopathic thrombocytopenic purpura in 40% of individuals.

MANAGEMENT

*TREATMENT OF ACUTE EXACERBATION:* Initial or recurrent acute episodes are usually treated with high-dose intravenous methylprednisolone or plasmapheresis(1–1.5 l plasma volume per exchange) in patients with severe symptoms that fail to improve or progress despite treatment with corticosteroids. Intravenous Immunoglobulins (IVIG), can be given for corticosteroid-refractory attacks, in view of humoral immunopathogenesis.

*RELAPSES:* Immunomodulatory drugs are not recommended as they worsen the clinical course. Commonly Immunosuppressives, like Azathioprine with prednisolone or Rituximab are primarily indicated for alleviating relapses as first-line therapy. If it is ineffective or the patient develops steroid-dependence for clinical remission, alternative immunosuppressive therapies need to be considered like Cyclophosphamide, Mitoxantrone, Mycophenolate mofetil or Intermittent plasma exchange.

*SUPPORTIVE AND SYMPTOMATIC TREATMENT:* For improving the quality of life which includes symptoms like spasticity, tonic spasms, NMO-related pain syndromes, bladder & bowel symptoms, sexual dysfunction and cognitive impairment. Some patients with high cervical cord lesions will require long-term mechanical ventilation. The European panel suggests that NMO cases with clinical evidence of SLE or SS should be treated according to ACR and European League against Rheumatism (EULAR) treatment protocols for neurological manifestations of systemic autoimmune disorders.

*NOVEL THERAPIES:* Following drugs are introduced, some under clinical trials for patients refractory to first-line therapies, which may also provide additional options for patients with severe clinical presentations like

- ✓ Tocilizumab, a human monoclonal antibody directed against the IL-6 receptor
- ✓ Eculizumab, a human monoclonal antibody directed against C5 protein which prevents its cleavage to C5a and C5b, the latter of which initiates the cytolytic terminal membrane attack complex (MAC) of the complement cascade.
- ✓ Aquaporumab, a recombinant human monoclonal antibody against AQP4 antibody.
- ✓ Complement inhibitor CD59, a glycophosphoinositol (GPI)-anchored membrane protein on astrocytes that inhibits that terminal C5b-C9 membrane attack complex (under trial)
- ✓ Granulocyte-targeted therapies: Silvestat is a neutrophil elastase inhibitor that is involved in neutrophil migration and phagocytosis that is currently being used in Japan to treat acute respiratory distress syndrome.

## V. CONCLUSIONS

There are changing concepts right from NMO diagnosis, pathogenesis and management, which needs to be distinguished from MS due to divergent course, treatment strategies and outcome. Autoimmune disorders must also be taken into account while diagnosing NMOSD.

The current management of NMOSD recommendation is acute treatment with IV steroids as well as PLEX in patients without a significant response to steroids. Long-term management is important to prevent relapses with rituximab, MM, and AZT being the most common immunosuppressant agents widely in use and should be initiated as soon as the diagnosis is made because prevention of attacks is the key issue for reducing permanent disability. The emerging novel therapies, currently under investigations are the promise of critical care management in NMOSD. Development of a drug with selective effect and reduced toxicity should be the target of future investigation.

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