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Neuromyelitis Optica Spectrum Disorder: An Overview

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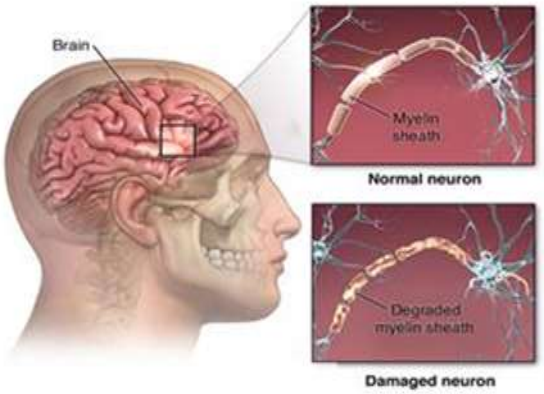
ABSTRACT :-

Neuromyelitis optica spectrum disorder (NMOSD) is a rare, autoimmune demyelinating disease of the central nervous system, primarily targeting the optic nerves and spinal cord. It is often associated with antibodies against aquaporin-4 (AQP4), leading to severe inflammation, demyelination, and axonal damage. Clinically, NMOSD manifests with recurrent episodes of optic neuritis, longitudinally extensive transverse myelitis, and, in some cases, brainstem or cerebral involvement. Early and accurate diagnosis is crucial, as NMOSD requires distinct therapeutic strategies from multiple sclerosis. Advances in immunopathology have led to the development of targeted treatments, including monoclonal antibodies that reduce relapse rates and disability progression. This review discusses the pathophysiology, clinical features, diagnostic criteria, and emerging treatment strategies for NMOSD, highlighting the need for personalized management approaches to improve patient outcomes.

Keywords :- Neuromyelitis optica , multiple sclerosis, vision loss, autoimmune disorder , AQP4 .



Introduction :-

Neuromyelitis optica spectrum disorders (NMOSD) are a spectrum of autoimmune diseases characterized by acute inflammation of the optic nerve (optic neuritis, ON) and the spinal cord (myelitis).[1][2][3] Episodes of ON and myelitis can occur simultaneous. A relapsing of this disease is common if it is left untreated

Neuromyelitis optica (NMO) is a particular disease within the NMOSD spectrum. It is characterized by optic neuritis and extensive myelitis. In more than 80% of NMO cases, the cause is immunoglobulin G autoantibodies to aquaporin 4 (anti-AQP4).

There are 2 types of NMO:

Relapsing form : It get recovered and periodically flares-up. It is more common type. Women are more likely to have this form than men.

Monophasic form : It involves a single attack which lasts a month or two, then may be free from attacks for several years. Both men and women are equally have this form.

Causes:-

NMOSD is an autoimmune disorder caused by attacks on the nervous system. In over 80% of cases, anti-AQP4 IgG autoantibodies are responsible, while 10–40% of the remaining cases involve anti-MOG antibodies. (19)The cause of other cases remains unknown and likely varies.(23)

The exact trigger for autoimmunity is unclear, but genetic and environmental factors contribute. Being female, particularly in AQP4-IgG-positive NMOSD, (19)is the strongest risk factor. Certain HLA alleles are also linked to NMOSD.(19)

Previously, NMO was associated with systemic diseases, and some cases may be paraneoplastic. (24)Lupus can generate NMO-IgG autoantibodies, leading to lupus-related NMO. (25)The discovery of anti-AQP4 has spurred further research into NMOSD's causes.

Symptoms: -

1. Spinal Cord Effects –

The most common initial symptom of NMOSD is spinal cord inflammation (myelitis)(4), leading to dysfunction such as muscle weakness, paralysis, sensory loss, spasms, bladder/bowel issues, or erectile dysfunction. (1)(4)(2)(7)(8)(9)Myelitis is often transverse, affecting both sides of the body.

2. Optic Effects –

The second most common symptom is optic nerve/chiasm inflammation (optic neuritis, ON), causing varying degrees of vision loss, including reduced acuity, visual field defects, or color blindness. NMOSD-related ON is more severe than in MS, often affecting both eyes and causing permanent damage.

3. Brain Effects –

Less commonly, NMOSD affects the brainstem,(4) causing respiratory issues, vomiting, hiccups, pain, or spasms. (1)(4)Brain lesions are common but often asymptomatic, though cognitive deficits and depression may occur. Diencephalic lesions are more frequent in AQP4-IgG NMOSD.(1)(4)

4. Disease Course –

The disease typically follows a relapsing-remitting course but can be progressive. Deficits may be temporary or permanent, especially without treatment.

5. Fatigue –

Fatigue affects up to 77% of NMOSD patients and significantly impacts quality of life.(10)(11)(12)

6. Comparison with MS : -

NMO and MS can appear similar but are distinct diseases. NMO was once mistaken as a variant of MS, but they differ in pathogenesis, symptoms, imaging, cerebrospinal fluid findings, disease progression, and prognosis. MS may rarely mimic NMO, but they are generally unrelated conditions.(1)

PATTHOPHYSIOLOGY :-

- Role of AQP4 in NMOSD

AQP4 is the most widely expressed water channel in the brain, spinal cord, and optic nerves, localized to astrocyte foot processes at the blood-brain barrier. (13)(14)It is also found in the kidneys, stomach, airways, glands, and muscles, (15)but these organs are protected from antibody-mediated damage by local complement inhibitors, which are absent in the brain.(16)

- AQP4 Antibodies and Pathogenesis

AQP4-IgG antibodies (predominantly IgG1) trigger interleukin-6 (IL-6) production in AQP4-expressing astrocytes, weakening the blood-brain barrier. Binding to AQP4 leads to complement- and cell-mediated astrocyte damage and internalization of the glutamate transporter EAAT-2(17). This astrocyte dysfunction disrupts support for surrounding neurons and oligodendrocytes, resulting in granulocyte infiltration, oligodendrocyte damage, and demyelination. (18)Unlike MS, NMOSD demyelination is secondary to astrocyte injury.

Epidemiology:

Neuromyelitis optica (NMO) prevalence varies by region, ranging from 0.5 to 10 cases per 100,000 people.(19) Unlike multiple sclerosis (MS), its prevalence is not linked to latitude. (19) NMO is more common in women, who make up over two-thirds of patients and more than 80% of those with the relapsing form.(20)

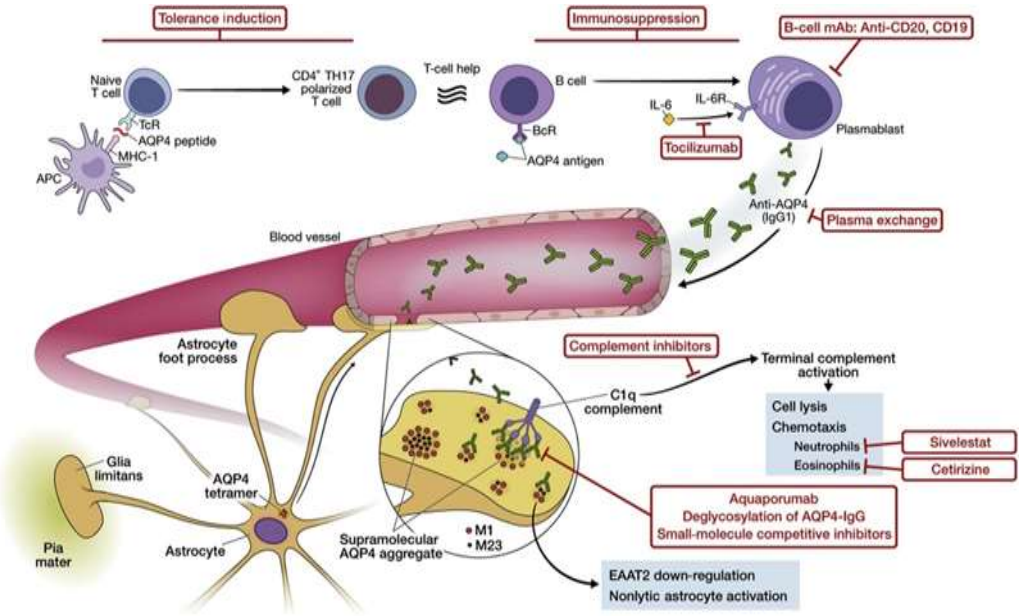
A retrospective study found that 1.5% of neurological patients had Neuromyelitis optica spectrum disorders (NMOSD), with an MS:NMOSD ratio of 42:7. Among NMOSD patients, 77% had long spinal cord lesions, 38% experienced severe optic neuritis, and 23% had brain or brainstem lesions. Only 56% met criteria for clinically definite NMO at follow-up.(21)

NMO is more common in Asians than Caucasians. In Japan, optic-spinal multiple sclerosis (OSMS), which accounts for 30% of MS cases, may be identical to NMO. In tropical and subtropical regions, MS is rare, but when present, often takes the form of OSMS.(22)

Most NMO patients have no affected relatives, and the condition is generally considered nonfamilial. Rarely, NMO may occur alongside other autoimmune diseases, paraneoplastic syndromes, or infections, though some cases remain idiopathic.

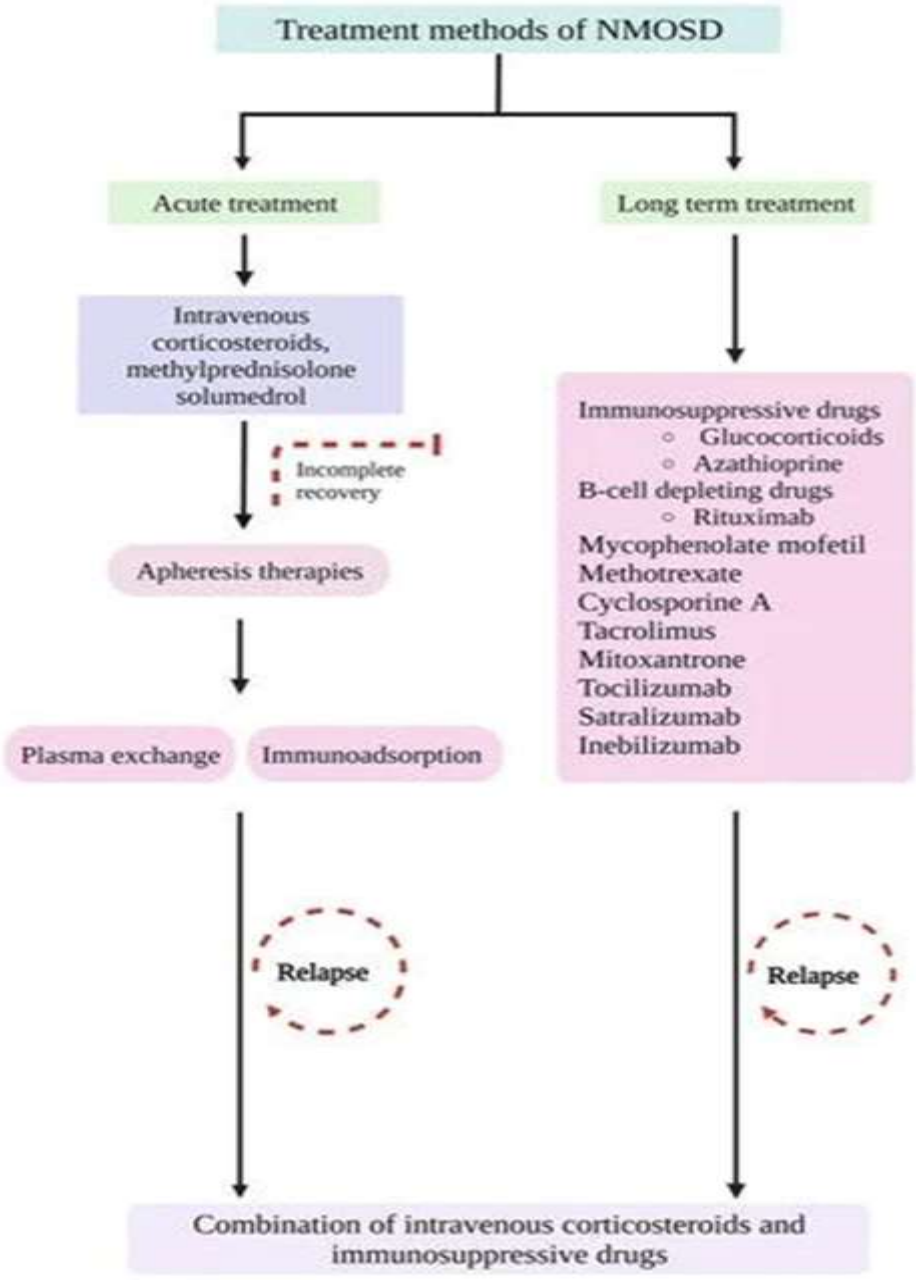
History :-

Neuromyelitis optica (NMO) was first associated with optic nerve and spinal cord disorders in the late 18th and early 19th centuries. (26)However, sustained medical interest began in 1870 with Sir Thomas Clifford Allbutt's report. In 1894, Eugène Devic and Fernand Gault described 16 cases linking optic neuritis and myelitis, establishing NMO as a distinct entity.



In 2002, researchers at the Mayo Clinic identified a humoral mechanism behind NMO, a (27) and by 2005, aquaporin-4 (AQP4) was confirmed as the disease's primary target. This led to diagnostic advancements, including the detection of AQP4-IgG antibodies. However, some AQP4-negative cases were later linked to anti-MOG IgG(28), while others remain idiopathic.

Treatment for MNOSD



Conclusion :-

Our understanding of NMO has evolved significantly in the past decade, and future research is expected to bring even more breakthroughs. The next challenge is to apply these discoveries to clinical trials and develop more effective treatments. More importantly, the insights gained from NMO could help unravel the mechanisms behind other demyelinating diseases, particularly multiple sclerosis (MS)

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