

## Neuromyelitis optica (NMO)

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CC-BY 4.0Keywords Neuromyelitis Optica (NMO);  
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## Abstract

Neuromyelitis Optica (NMO or Devic's syndrome) is a rare demyelinating disease of the CNS that predominantly affects the spinal cord and optic nerves and shares many clinical and radiological features with multiple sclerosis. We report a case regarding a 53 year old woman who was admitted initially with hiccups and paraesthesias but was not evaluated during first 2 episodes and presented with severe progression of NMO. NMO was diagnosed with Seropositivity for NMO-IgG and longitudinally extensive spinal cord lesions (3 or more spinal segments).

## Introduction

Neuromyelitis Optica (NMO or Devic's syndrome) is a demyelinating disease of the central nervous system that predominantly affects the spinal cord and optic nerves and shares many clinical and radiological features with Multiple Sclerosis (MS) [1-3]. NMO is now considered a disease entity rather than a subtype of MS after discovery of a novel, pathogenic autoantibody (termed NMO-IgG or AQP4-Ab) in 2004 [4, 5].

NMO is a rare syndrome constituting less than 1% of demyelinating disease [6, 7]. Clinical, MRI, and spinal fluid features from several case series are illustrated in Table 1 [8]. The current prevalence estimates of prevalence of NMO in Japan is approximately 14 per 1,000,000, and of northwest England is approximately 4 per 1,000,000 [9, 10] with a female-to-male ratio of 3:1. The mean age of onset is approximately 40 years old, but cases also have been reported in childhood. Devic's disease is more common in asians than caucasians. The Mayo clinic proposed a revised set of criteria for diagnosis of Devic's disease in 2006 (Table 2).

## Case report

A 53 year-old woman was admitted in a local hospital on November 2013 with complaints of hiccups and vomiting from 7 days, paraesthesias of left upper limb and lower limb from 5 days. Patient completely recovered and relieved of symptoms in a period of 30 days. Her routine investigations (Complete blood count, differential count, renal function tests, liver function tests, B12 levels, folic acid levels, hemoglobin, FBS, and PPBS) were normal during that episode. However, thyroid profile was abnormal which was suggestive of hyperthyroidism for which she took no medication. Relatives denied any illicit drug usage or alcohol consumption. No history of fever with chills, cough with expectoration and shortness of breath. No history of diabetes mellitus, hypertension or ischemic heart disease. Patient was completely asymptomatic till 2015.

In March 2015 patient was brought to emergency room with complaints of bilateral lower limb paralysis, bilateral upper limb weakness (distal >proximal) and band like sensation over the chest and hiccups. Clinical examination revealed normal higher mental functions, Mini Mental Status Examination (MMSE) of 28/30. Vision is diminished to counting fingers in right eye. Other cranial nerves were normal. Hypertonia was noted in all limbs. CNS examination revealed power of 3/5 in bilateral upper limb muscles around shoulder and elbow joints and 2/5 around wrist joint.

Lower limb power was 0/5 on admission but improved to 1/5 over a period of 15 days. Upper limb reflexes were 2+ and knee and ankle reflexes were 3+. Babinski's reflex was present bilaterally. Sensory system examination revealed loss of joint position and vibration sense till bilateral anterior superior iliac spine (ASIS). Pain and temperature sensations were intact. Superficial reflexes were present except abdominal reflex. Other systemic examination was normal.

Antibodies to HSV1, HSV2, CMV, EBV, HBV, VZV, HCV and HIV in serum and cerebrospinal fluid, as well as sarcoidosis and tumor markers in serum revealed no abnormality. Polymerase chain reaction in CSF for HSV1 and HSV2 was negative. Cerebrospinal fluid analysis demonstrated no oligoclonal bands. Immunological tests for ANA titer were 1: 320, tests for anti-ENA, anti-dsDNA, anti-cardiolipin, anti-β2GPI, lupus cells, and cryoglobulins were negative.

MRI Brain and whole spine revealed 1) Hyperintensity in cervical cord at the level of lower half of C6 and upper half of C7 vertebral body (Figures 1-3). 2) Hyperintensity in thoracic cord at level of T7, T8 and T9 (Figures 4-6). 3) Hyperintensity in right optic nerve head (Figure 7, 8). The clinical features and investigations fit in to criteria of neuromyelitis optica.

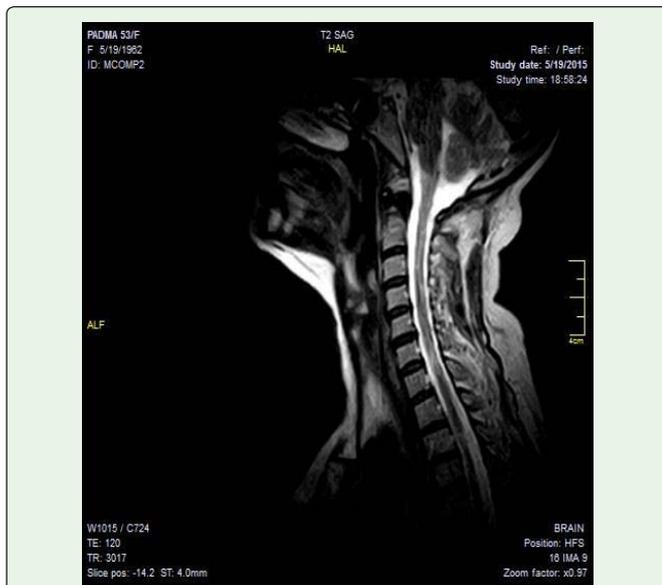
Patient was started on Prednisolone 1gm/day (30mg/kg per day or maximum 1gm/day) for 5 days and Azathioprine (2.5-3 mg/kg/daily). Patient showed marginal improvement in motor symptoms. Patient after a period of 3 months of treatment requires 2 person supports for performing daily activities. Hiccups completely resolved, sensory symptoms improved by 80%. Patient was started on Thyroxine 25mcg and increased to 75mcg.

**Table 1:** Clinical, MRI, and spinal fluid features from several case series.

Feature	Number (Proportion)
Women/men	87/36 (2.3:1)
Average age at onset	37
Monophasic/polyphasic	72/40 (1.8:1)
Optic neuritis presentation	50 (45%)
Transverse myelitis presentation	43 (38%)
Combined ON/TM presentation	19 (17%)
Autoimmune disease/antibodies	28/104 (27%)
Antecedent infection	22/91 (24%)
Normal brain (MRI)	48/63 (76%)
Abnormal spinal cord (MRI)	55/58 (95%)
CSF pleocytosis	63/85 (74%)
>50 cells/mm <sup>3</sup>	27/84 (32%)
CSF polymorphonucleocytes	34/67 (51%)
CSF oligoclonal bands	23/77 (30%)

**Table 2:** Mayo clinic criteria for NMO.

Absolute criteria:
1. Optic neuritis
2. Acute myelitis
Supportive criteria:
1. Brain MRI not meeting criteria for MS at disease onset
2. Spinal cord MRI with contiguous T2-weighted signal abnormality extending over three or more vertebral segments, indicating a relatively large lesion in the spinal cord
3. NMO-IgG seropositive status (The NMO-IgG test checks the existence of antibodies against the aquaporin 4 antigen.)



**Figure 1:** MRI cervical spine showing Hyperintensity at the level of C6-C7.



**Figure 2:** MRI cervical spine showing Hyperintensity at the level of C6-C7.



**Figure 3:** MRI cervical spine showing Hyperintensity at the level of C6-C7.

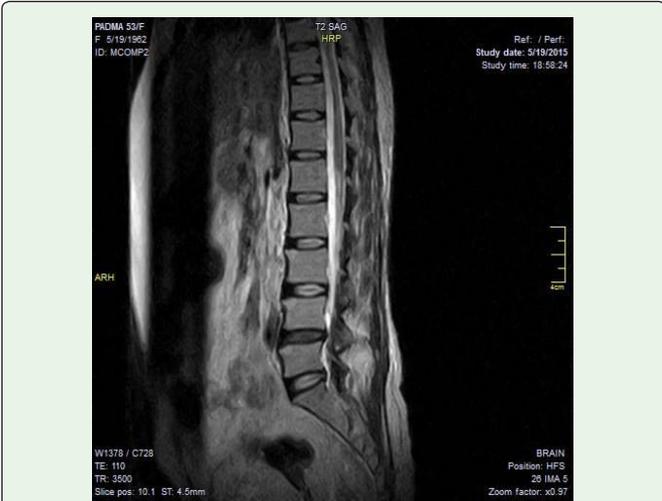


Figure 4: MRI Spine showing Hyperintensity at level of T7, T8 and T9.

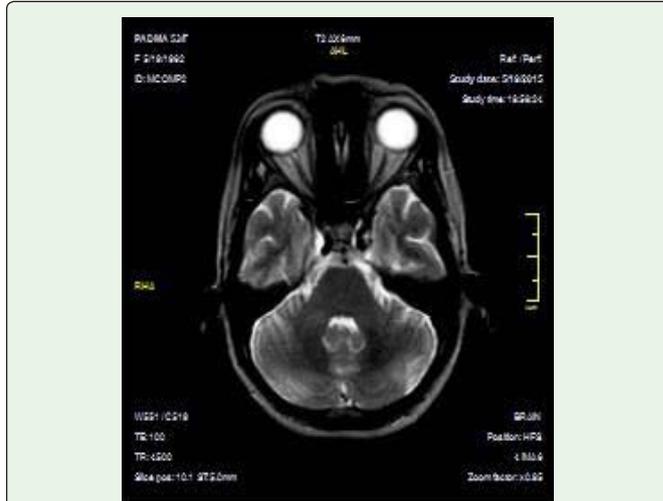


Figure 7: MRI Brain showing Hyperintensity in right optic nerve head.



Figure 5: MRI Spine showing Hyperintensity at level of T7, T8 and T9.

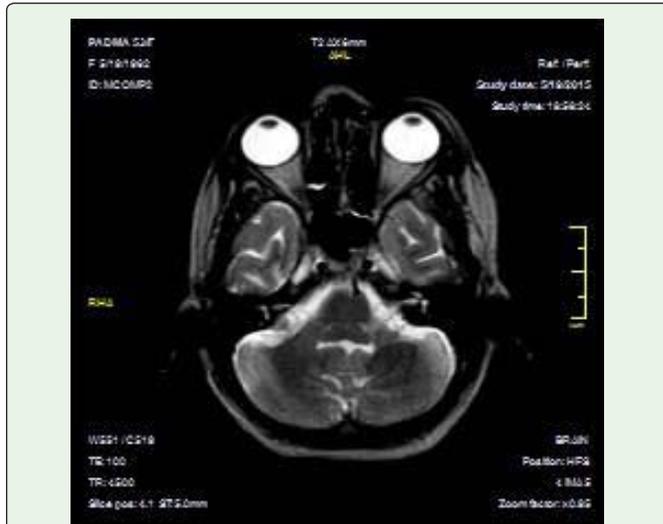


Figure 8: MRI Brain showing Hyperintensity in right optic nerve head.

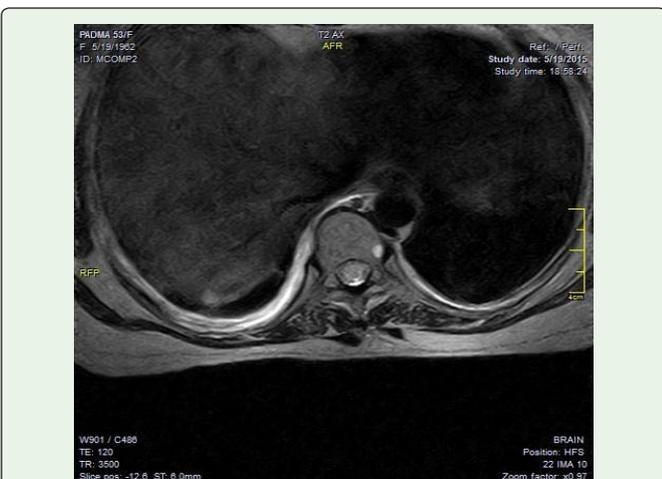


Figure 6: MRI Spine showing Hyperintensity at level of T7, T8 and T9.

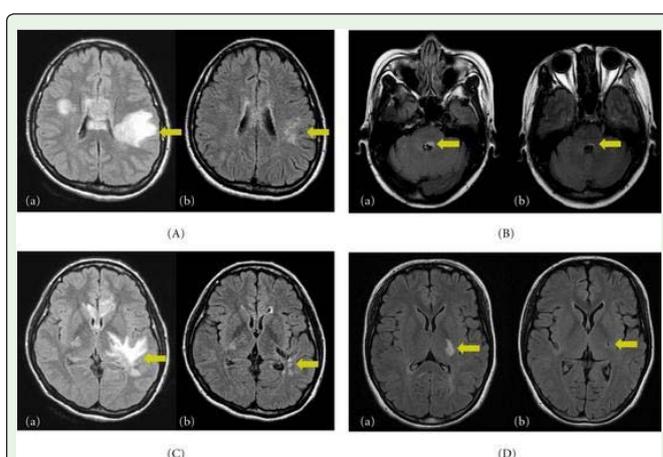


Figure 9: MRI findings at acute manifestation and after symptoms resolved.

**Table 3:** Diagnostic criteria of NMO<sup>a</sup>

Major criteria (all criteria are required but may be separated by an unspecified interval)
(i) Optic neuritis in one or more eyes
(ii) Transverse myelitis, clinically complete or incomplete, but associated with radiological evidence of spinal cord lesion extending over three or more spinal segments on T2-weighted MRI images and hypointensity on T1-weighted images when obtained during acute episode of myelitis
(iii) No evidence for sarcoidosis, vasculitis, clinically manifest systemic lupus erythematosus or Sjögren's syndrome, or other explanation for the syndrome
Minor criteria (at least one must be fulfilled)
(1) Most recent brain MRI scan of the head must be normal or may show abnormalities not fulfilling Barkhof criteria used for McDonald diagnostic criteria, including <sup>b</sup> :
(i) non-specific brain T2 signal abnormalities not satisfying Barkhof criteria as outlined in McDonald criteria
(ii) lesions in the dorsal medulla, either in contiguity or not in contiguity with a spinal cord lesion
(iii) hypothalamic and/or brainstem lesions
(iv) "Linear" periventricular/corpus callosum signal abnormality, but not ovoid, and not extending into the parenchyma of the cerebral hemispheres in Dawson finger configuration
(2) Positive test in serum or CSF for NMO-IgG/aquaporin-4 antibodies
<sup>a</sup> These criteria exclude limited or inaugural syndromes that may be NMO, such as recurrent transverse myelitis with longitudinally extensive spinal cord lesions or recurrent ON; further study is warranted to clarify their relationship with NMO, especially in the setting of seropositivity for NMO-IgG/AQP4 antibodies.
<sup>b</sup> Periodic surveillance with brain MRI scanning is necessary to monitor for the emergence of new lesions that may lead to a revised diagnosis.

## Discussion

Devic's disease is a severe idiopathic immune-mediated inflammatory demyelinating disease that predominantly involves the spinal cord and optic nerves. The cardinal clinical features of the disorder are longitudinally extensive transverse myelitis and optic neuritis. More than 90% of patients with NMO have repeated relapses rather than monophasic disease. Clinical events can occur simultaneously or can be separated by long duration of months to years. Optic neuritis can be unilateral or bilateral. Several differences exist in the characteristics and outcomes of patients with the monophasic and relapsing forms.

Systemic autoimmune diseases are associated commonly with NMO compared to MS oligoclonal bands are seen in 85-90% of MS cases but only 20-30% of NMO cases. Diagnosis of NMO was made based on the clinical findings of optic neuritis and repeated transverse myelitis on MRI and seropositivity for NMO-IgG. The isolated testing for NMO-IgG autoantibody is highly specific (91%; 85-99%) and sensitive (73%; 58-76%), and has less common occurrence in MS. Its target antigen is the AQP4 water-pump channel, an integral protein of astrocytic plasma membranes and is highly concentrated in the astrocyte foot processes.

The distribution of AQP4-rich areas in the central nervous system, especially in the central spinal cord, hypothalamus, periventricular area and periaqueductal areas is highly indicative of NMO lesions. Spinal cord histopathology in NMO found loss of AQP4 in acute inflammatory lesions surrounding immunoglobulin and complement-deposited hyalinized small vessels which suggests humorally-mediated microangiopathy leading to spinal cord lesions in NMO.

Detection of acute brain abnormalities in NMO spectrum disorder is based on T2-weighted or fluid-attenuated inversion recovery (FLAIR) hyperintense signals. The brain lesions in T2 or FLAIR MRI shrink or disappear on follow-up scans, and acute lesions sometimes lead to chronic T1 hypointense lesions, suggesting cell death and cavitation (Figure 9), [11].

Brain MRI abnormalities in AQP4 autoimmunity are localized in the periependymal regions, where AQP4 is expressed maximally. Periependymal lesions surrounding the 3rd ventricles were reported previously as "diencephalic lesions," [12] which includes the thalamus and hypothalamus. The anterior border of the midbrain which is adjacent to the third ventricle can also be involved. Hypothalamic lesions were found in 5.0% of NMO cases in the USA [13], 5.3% in Japan [14], and 0% in Cuba [15]. Hypothalamic lesions are found in 13.3% of multiple sclerosis patients. The lesions in MS were small and triangular or lobulated in shape, whereas in NMO, they are usually more extensive [16-18]. Some reports have described hypothalamic lesions accompanied by symptoms in NMO-IgG/AQP4-Ab-positive patients, which include syndromes of inappropriate anti-diuretic hormone secretion (SIADH), narcolepsy, hyperprolactinemia, secondary amenorrhea, hypothermia, hypotension, hypersomnia, obesity, hypothyroidism and galactorrhea.

Other lesions described were brainstem lesions Adjacent to the fourth ventricle, periependymal lesions surrounding the lateral ventricles, lesions involving the corticospinal tracts, extensive hemispheric lesions and cortical involvement and leptomeningeal enhancement. The criteria for the NMO spectrum included ON or myelitis associated with brain lesions typical of NMO; these were hypothalamic, corpus callosal, periventricular, or brainstem lesions (Table 3), [19].

Before the era of NMO-IgG/AQP4-Ab, brain MRI abnormalities were described in 13-46% of patients with NMO. The incidence of brain abnormalities reported increased to 50-85% of patients fulfilling the 1999 NMO criteria [2] with the exception of the brain MRI criterion or revised 2006 NMO criteria and to 51-79% of AQP4-Ab-seropositive patients [20, 21].

In conclusion this case report illustrates the importance of Magnetic resonance imaging in diagnosis of Neuromyelitis optica, which is a rare disorder. Differentiation of NMO from Multiple sclerosis is very important as the management differs.

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