

## Neuromyelitis Optica Spectrum Disorder: A Case Report

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### Abstract

A 66 year old woman suffering from recurrent attacks of neuropathic burning pain over the past 6 years, affecting first the sacral region and then progressively different locations on the face, was referred to our facility. She had severe paraparesis and signs of brainstem dysfunction leading to respiratory failures. After an extensive investigation including brain and spinal cord MRI and laboratory findings, such as positive test for aquaporin-4 immunoglobulin G antibodies (AQP4-IgG), the patient was found to suffer from neuromyelitis optica spectrum disorder (NMOSD) without optic neuritis. She was initially treated with corticosteroids followed by plasmapheresis. She partially recovered regarding her respiratory function but remained paraplegic. She was placed on azathioprine and died a few months afterwards.

**Keywords:** Neuromyelitis optica; Central nervous system; Multiple sclerosis; Cerebrospinal fluid; Systemic lupus erythematosus; Antinuclear antibodies

### Introduction

Neuromyelitis optica (NMO), also known as Devic's disease, is a serious, idiopathic and inflammatory demyelinating syndrome of the central nervous system (CNS). This devastating disease is classically characterized by selective and severe attacks of the optic nerve and spinal cord with or without recovery, and is potentially fatal [1]. It causes sudden loss of vision in one or both eyes, varying degrees of weakness or paralysis in the legs or arms, loss of sensation and/or bladder and bowel dysfunction. Although originally considered as a variation of multiple sclerosis (MS), clinical, radiological, pathological and especially immunological data have led to a novel definition of this clinical entity [2]. Early differentiation between NMO and MS is particularly important because the course of NMO is more severe and the treatment strategies for attack prevention are different. Immunotherapy approved for MS treatment is ineffective and appears to aggravate NMO [3]. Immunosuppressive therapy is the treatment of choice for reducing NMO relapses. The association of NMO with the specific biomarker AQP4-IgG is considered as an additional criterion supporting the diagnosis (sensitivity and specificity for NMO respectively 91% and 100%) [4].

### Case Report

We present here an atypical case of NMO. The medical history of our patient includes hypertension, diabetes, hyperlipidemia, anemia, chronic constipation and depression. Neurological diseases were not reported in the family. She was hospitalized several times in our department. In 2009 she suffered from neuropathic pain affecting the sacral region bilaterally radiating to the hips. Her lumbar spine and plexus MRI was normal. Pain was resolved progressively with treatment with oxycodone and carbamazepin. Then in 2010 she developed atypical pain affecting the face unilaterally. She was treated with pregabalin. Treatment was pursued for one year and significant improvement was noticed. Her neuropathic pain symptoms completely resolved. Paraneoplastic markers including ANTI HU and ANTI RI were negative. The following immunological markers ANTI SSA, ANTI SS, ANTI RNP, JO1 AB-B, ANTI SCL170AB-B and ANTI CENTROMER-B were negative. Skin biopsy revealed small fiber neuropathy with mild reduction in the small nerve fiber innervation to sweat glands. Her brain MRI scan was normal. In 2013 she developed unspecified neuropathic pain affecting progressively different locations of the face and later on severe burning chest pain going from side to side. During her hospitalization she suffered as well from an episode of vertical oscillopsia leading to lack of balance. She was treated with

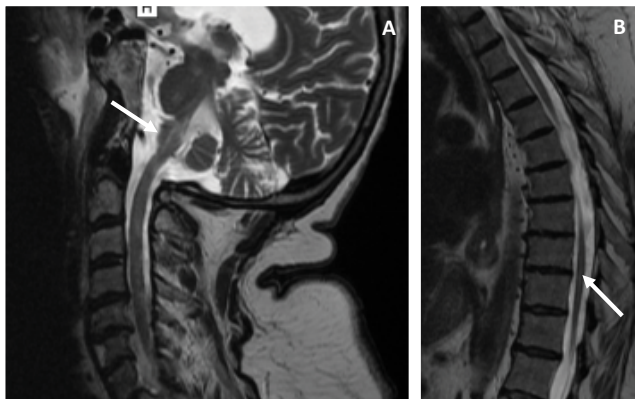
gabapentin and pregabalin, and improvement was observed. No specific disease was found. In March 2015, new neurological signs were observed. The patient complained from progressive weakness of the legs, recurrent falls and urine incontinence. Two months afterwards, neurological examination revealed cerebellar signs in the hands, severe paraparesis of both lower limbs with positive Babinski sign, spinal cord sensory level at T4 and signs of brainstem dysfunction leading to respiratory failures. Investigations revealed hemoglobin of 9.1 g/dl, MCV of 80 fL, leucocytosis and high proportion of neutrophils (87%). Cerebrospinal fluid (CSF) analysis demonstrated mild pleocytosis (10 leucocytes/mm<sup>3</sup>) with predominance of monocytes (60%). An elevated concentration of protein and glucose (81 and 107 mg/dl respectively) was observed as well. Testing for antibodies to HIV, HBC, HVC and Lyme disease in serum was negative. Gram staining revealed no organism. Antinuclear antibodies (ANA), anti-beta-2-glycoprotein, anticardiolipin and lupus anticoagulant antibodies were undetectable. Neurosyphilis tested by VDRL and fluorescent treponemal antibody absorption (FTA-ABS) in serum and CSF was negative. No oligoclonal bands were found in serum and CSF of our patient. Fabry and Gaucher's diseases were tested negative. Sarcoidosis was suspected but angiotensin converting enzyme negative tested in serum and CSF revealed no pathological values. Tumor markers were tested negative. Systemic Lupus Erythematosus (SLE) revealed to be negative. Due to the suspicion of Wernicke syndrome, that revealed negative later on, she was treated with thiamine. The neuromyelitis optica spectrum disorder was presumed and the patient was treated with methylprednisolone 1 gram for 5 days. A partial improvement in her clinical status was noted. Thoracic spine T2-weighted MRI revealed lesions in the medulla oblongata and spinal cord at the levels of T8-T9 and T11 (Figures 1 and 2). FLAIR MRI demonstrated periependymal lesions in brainstem (Figure 3). Brain MRI revealed lesion in periventricular white matter (Figure 4). CT and CT angio scans were not indicative of any other pathology. Seropositivity for aquaporin-4-immunoglobulin G antibodies confirmed the hypothesis, the patient was found to suffer from NMOSD without optic nerve involvement. The patient was treated

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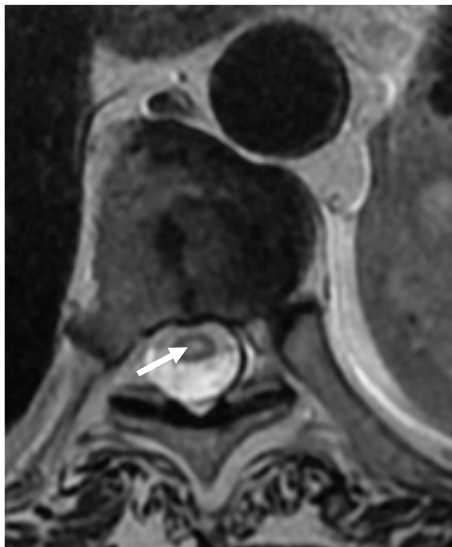
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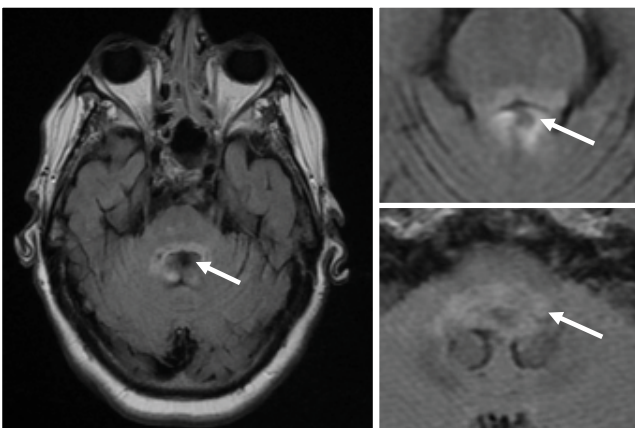
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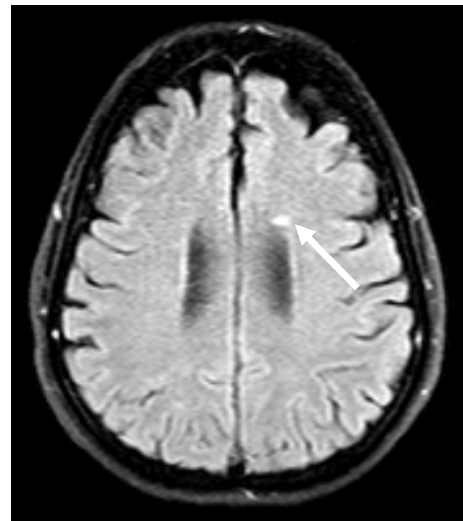
**Figure 1:** Sagittal T2-weighted MRI showing hyperintense lesions involving the medulla oblongata (A) and involvement of mid-thoracic spinal cord (T8-T9) and lower thoracic spinal cord at T11 level along with cord atrophy (B).



**Figure 2:** Axial T2-weighted MRI showing high-intensity lesion in central spinal cord.



**Figure 3:** Axial T2-weighted fluid-attenuated inversion recovery (FLAIR) MRI showing peri-aqueductal high intensity areas and focal high-intensity lesion in central pons.



**Figure 4:** Axial T2-weighted fluid-attenuated inversion recovery (FLAIR) MRI showing high intense lesion in periventricular white matter.

with plasmapheresis 5 times. Although her respiratory function partially improved, she did not fully recover and remained paraplegic. To reduce relapses, she was placed on azathioprine 150 mg daily, a chronic immunosuppressive therapy. After a few months she died, probably due to cardiorespiratory failure.

## Discussion

Through this case study we illustrate the complexity of neuromyelitis optica diagnosis and treatment challenges due to the broad spectrum of symptoms. Close attention to the severe development of the disease is strongly recommended. The patient presents atypical characteristics of the disease with initial symptoms of recurrent neuropathic pain without optic neuritis. The presence of CNS symptoms outside the optic nerves and spinal cord has until recently excluded the diagnosis [5]. In a minority of patients this disorder may also target other parts of the brain, especially the brainstem and hypothalamus. AQP-4-IgG exclusively detected in NMO patients have allowed the identification of cases beyond the traditional phenotype [6]. These limited forms of the disease not meeting full clinical criteria are classified as NMOSD [4]. We highlight here the importance to relate the clinical findings as well as brain and spinal cord lesions observed on MRI with the new revised diagnostic criteria. These new criteria remove the absolute restriction on CNS involvement beyond the optic nerves and spinal cord. In our case, pain probably caused by inflammatory lesions in the spinal cord may be a key factor leading to diagnosis. Pain is indeed highly prevalent in NMO patients. Severe neuropathic pain can occur in the early stages of the disease and can even be the first clinical symptom [7]. NMO was often misdiagnosed as MS or perceived as a type of MS due to the similarity of the symptoms, but it is a distinct condition. It has a unique pathology and immunopathogenesis, and a different clinical evolution [8]. NMO is usually not associated with brain lesions at disease onset. They occur over time in later phases of the disease in the majority of patients. It carries a poorer prognosis especially for patients with relapsing disease [5]. Most attacks are moderate or severe and remissions are often incomplete. Neurologic disability accumulates in a stepwise fashion and patients usually die because of respiratory failure associated with attacks of myelitis [2]. Supernumerary oligoclonal bands of IgG are frequently detected in the CSF of MS patients but are threefold less frequent in NMO. They were not detected in our patient.

The cause of NMO is usually unknown, although it may appear after an infection or may be associated with another autoimmune condition. Findings suggest that in some of the patients, infections could be associated with the development and relapse of the disease [9]. In our case, viral and bacterial infections were not detected. The combination of neurological impairments which occur in NMO patients can also be seen in other autoimmune diseases such as Systemic Lupus Erythematosus (SLE) that was negative in our patient. In conclusion, early differential diagnosis from other related diseases sharing the same clinical features is particularly crucial. Accurate and prompt treatment with intravenous corticosteroid therapy has to be initiated in the acute phase. An aggressive immunosuppressive treatment focused on preventing future relapses and initiated as soon as the diagnosis is set, is of vital importance due to the poor prognosis of this disease.

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