Clinical Case Reports

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CASE REPORT

Fulminant neuromyelitis optica in a Finnish woman – a case report

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Funding Information
No sources of funding were declared for this study.

Received: 28 February 2016; Revised: 8 May 2016; Accepted: 28 May 2016

Clinical Case Reports **2016; 4(8): 782–785**

doi: 10.1002/ccr3.624

Key Clinical Message

Neuromyelitis optica is a rare inflammatory, demyelinating disease of the central nervous system that predominantly targets the optic nerves and spinal cord. Our case represents an unusual and severe course of neuromyelitis optica. Despite several forms of treatment, our patient died after a severe and short-term attack.

Keywords

Case report, demyelination, neuromyelitis optica, treatment.

Background

Neuromyelitis optica (NMO) or Devic's disease is a rare inflammatory, demyelinating disease of the central nervous system (CNS) that predominantly targets the optic nerves and spinal cord [1]. The disease was first described in 1870 by Albutt and 24 years later, Devic described the clinical characteristics of NMO – optic neuritis and acute transverse myelitis. The syndrome was eponymously named Devic's disease [2].

The discovery of a specific NMO immunoglobulin (NMO-IgG) opened a new era in the classification and understanding of the pathogenesis of NMO [3]. NMO-IgG binds to aquaporin-4, which is the main channel that regulates water homeostasis in the CNS.

Diagnostic criteria for NMO with aquaporin-4 antibodies (AQP4-Ab) requires at least one core clinical characteristic, a positive test for AQP4-Ab using best available detection method (cell-based assay recommended) and exclusion of alternative diagnoses [1]. The core clinical characteristics are, for example, optic neuritis, acute myelitis, acute brainstem syndrome, symptomatic narcolepsy, or symptomatic cerebral syndrome with typical NMO brain lesions [1].

Neuromyelitis optica must be distinguished from other demyelinating diseases, for example, multiple sclerosis. The presence of AQP4-Ab differentiates NMO from multiple sclerosis (MS) with high specificity [4]. In contrast to typical MS, the clinical events in NMO are usually more severe [5, 6]. Cerebrospinal fluid (CSF) findings in NMO are also known to differ significantly from those in classical MS. CSF-restricted oligoclonal IgG bands are absent in most NMO patients. Cerebrospinal fluid pleocytosis is a common finding (50%) in NMO. However, pleocytosis is usually mild, and frequently includes neutrophils, eosinophils, activated lymphocytes, and/or plasma cells [6, 7]. AQP4-Ab are also detectable in the CSF of most AQP4-Ab-seropositive patients with NMO [8].

The incidence and prevalence of NMO are not well known. Studies carried out in Europe, South East and Southern Asia, the Caribbean and Cuba suggest that the incidence and prevalence of NMO ranges from 0.05–0.4 to 0.52–4.4 per 100,000, respectively [9]. The disease is

mainly sporadic, although a few familial cases have been reported [10].

We describe a case of an unusual and severe course of NMO affecting almost the entire spinal cord and brain.

Clinical Details

A 45-year-old woman was referred to hospital with acute-onset chest pain. Examination on the day of admission revealed normal results as regards ECG, troponin I, and computed tomography (CT) of the chest and abdomen. The next day, the patient reported headache and neurological examination showed right-sided hemiparesis and afferent pupillary defect of the left eye suggesting an afferent optic nerve defect. Within a few hours, the patient showed a rapid neurological deterioration with progressive tetraplegia and global decline. Brain CT, precerebral, and intracranial vessel CT angiography showed no abnormalities. Magnetic resonance imaging (MRI) of the brain was also normal. MRI of the spinal cord showed myelitis in the spinal cord segments C2 to Th5 (Fig. 1A). CSF examination revealed polymorphonuclear pleocytosis (leukocytes 1210×10^6/L, neutrophils 95%) and an increased total protein concentration (2273 mg/L). Oligoclonal banding was negative. Due to spinal cord MRI and CSF findings, infectious transverse myelitis could not be excluded and the patient was treated with dexamethasone, acyclovir, ceftriaxone, ampicillin, and levofloxacin. Dexamethasone was given for 5 days according to the treatment protocol of bacterial meningitis. Possible infectious etiology was treated with wide-range antibiotic therapy.

The next day, the patient's condition worsened; she became comatose and had a respiratory failure that required assisted ventilation; this might be caused by bilateral phrenic nerve involvement as its roots originate from C3 to C5 where the lesion was also seen (Fig. 1A). Brain MRI showed high signal changes in thalami, internal capsule, and corpus callosum (Fig. 1B) and also similar changes in pons, medulla oblongata, cerebellum, and middle cerebellar peduncle (Fig. 1C). These changes were also seen in the periventricular area and hippocampus. Spinal cord MRI showed progression at levels C2 to Th11. The MRI findings were mostly consistent with acute demyelination. Treatment with methylprednisolone and immunoglobulin was attempted and as serum AQP4-Ab was confirmed as positive (indirect immunofluorescence assay was used, the titer was 19.85, normal <10) and the patient did not respond to the treatment, the patient was also treated by means of plasmapheresis. These treatments failed to achieve any improvement and the patient died after 7 weeks.

Histological examination of the CNS revealed extensive, sharply limited demyelination and axon defect (Fig. 2A and B). The spinal cord was almost entirely affected. Only the lumbar area was partly spared. Extensive demyelination was also seen in the thalamus, pons, and medulla oblongata. The chiasma and tractus opticus were entirely demyelinated. Smaller demyelination foci were found in the periventricular area of the hippocampus and in the corpus callosum. Demyelination was verified by showing both CD68-positive macrophage infiltration and beta-APP positivity as signs of axonal damage.

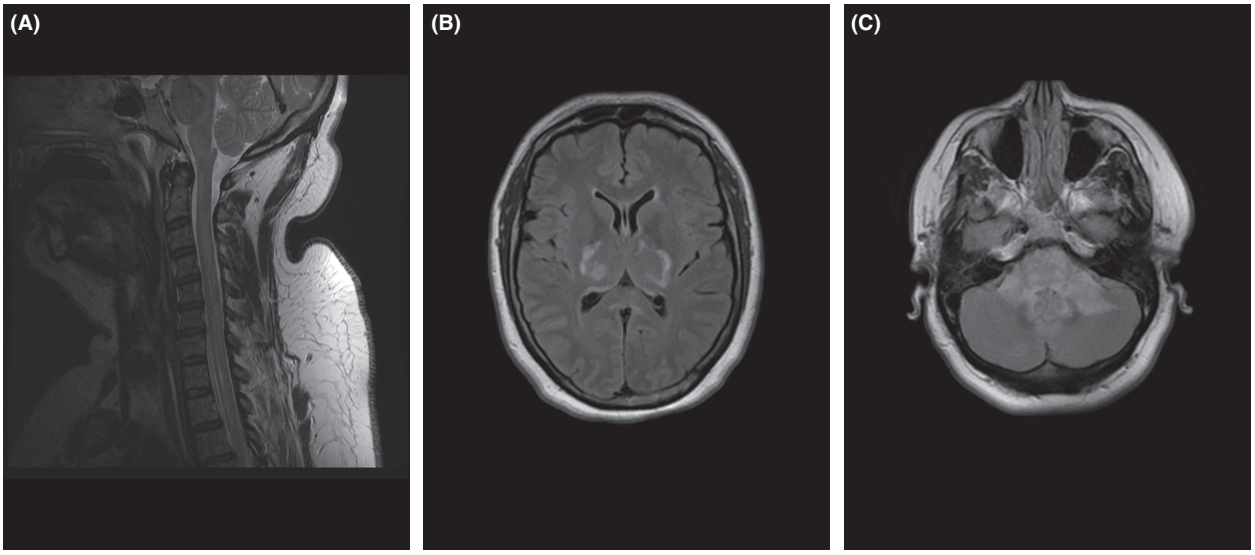

Figure 1. (A) Sagittal T2-FSE MRI of the spinal cord showing high signal changes. (B) Axial T2-FLAIR brain MRI showing high signal changes in thalami, internal capsule, and corpus callosum. (C) Axial T2-FLAIR brain MRI showing high signal changes in pons, medulla oblongata, cerebellum, and middle cerebellar peduncle.

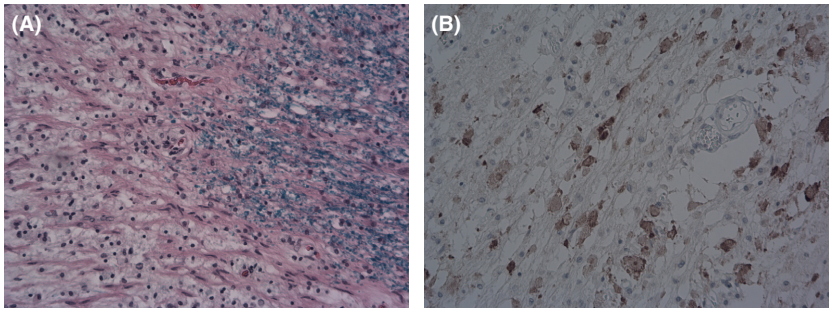

Figure 2. Histologic slides of chiasma opticum. (A) The Kluver-stained sections show demyelination, lack of blue. (B) The axon defect is shown by immunostaining (brown staining) of beta-amyloid precursor protein (APP).

Discussion

This is the first case report of NMO described from Finland from the AQP4-Ab era. There is only one older publication of a Finnish NMO patient from the pre-AQP4-antibody era [11]. Our case showed an unusual and severe course of the disease.

The patient was referred to hospital with an acute-onset chest pain, which is an unusual first symptom of NMO. Examination on the day of admission revealed no explanation for the chest pain. We reason the symptom was caused by myelitis.

In our case, demyelination affected almost the entire spinal cord, sparing only partly the lumbar cord, which is unusual at first myelitis. Lesions involving the lumbar or sacral spinal cord in addition to the cervical and thoracic portions have been reported only in 11% of patients at first myelitis. Previous reports have revealed that 92% of the patients have at least one spinal cord lesion extending over three or more vertebral segments at their first myelitis. Median extension was six segments [6].

It has been reported that seropositive women have more severe clinical attacks than males, as evidenced by high lesion load in the spinal cord and other types of coexisting autoimmunity [6].

The brain was also widely affected. Brain MRI abnormalities are relatively common and may be relatively unique by virtue of localization and configuration [12], as seen also in our patient.

The histopathological findings in the CNS, CSF, and AQP4-Ab seropositivity are consistent with neuromyelitis optica-type demyelination, although the disease course of our case was not typical of NMO due to its rapid and severe course. According to hospital-based observational studies, mortality of NMO ranges from 2.9% to 25% and is disease-related in the majority of the cases [9]. Jarius et al. reported that disease duration at the time of death ranged from 6 months to 23.6 years [6]. Our patient died after a severe and short-term first attack. The disease duration is considerably shorter than previously reported [6, 9]. In addition, our patient's histological examination revealed extensive, sharply limited demyelination of the spinal cord and brain in the acute phase of the disease. To the best of our knowledge, histopathological reports in the acute phase of the disease are rare.

The treatment in this particular case was targeted to multiple causes of the symptoms due to the unknown etiology in the beginning of the disease. Later on, the patient was treated according to the current guidelines of NMO. Acute attacks and relapses of NMO are generally treated with intravenous glucocorticoids followed by plasmapheresis for refractory or progressive symptoms [13, 14]. However, there are no controlled trials evaluating the treatment of NMO, and recommendations are primarily supported by data from observational studies and by the clinical experience of experts.

Despite several forms of treatment, the patient did not survive. A major challenge remains as regards treatment of this devastating condition.

Acknowledgments

Neuropathological examination was performed by Hannu Tuominen, MD, PhD, neuropathologist, Oulu University Hospital.

Conflict of Interest

None declared.

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