Case Report
A 30-year interval between myelitis and optic neuritis in a patient with neuromyelitis optica: a case report and literature review

Zhuo Wang1*, Lichao Sun2*, Xinyue Zhang1, Zan Wang1, Weihong Lin1

Departments of 1Neurology and Neuroscience Center, 2Emergency, The First Hospital of Jilin University, Changchun 130021, Jilin, China. *Equal contributors.

Received December 31, 2017; Accepted September 5, 2018; Epub October 15, 2019; Published October 30, 2019

Abstract: Purpose: To report a patient with neuromyelitis optica (NMO) in whom myelitis developed 30 years after the detection of optic neuritis. Case presentation: A 48-year-old man presented to our hospital with chief complaints of unexplained numbness and swelling in both lower extremities since 9 months. Since the last two months, he developed progressive numbness of the limbs, clumsiness and headache. Thirty years ago, he was diagnosed with optic neuritis in the right eye and underwent ophthalmological examinations. His best corrected visual acuity was light perception in the right eye. 30-2 Humphrey visual field analyzer demonstrated central, temporal and inferior scotomas in the left eye. Cervical magnetic resonance imaging (MRI) showed abnormal intramedullary signals at C3-6 level, which appeared hyperintense on sagittal T2-weighted and fluid-attenuated inversion recovery (FLAIR) imaging. Anti-aquaporin-4 (AQP4) antibodies in cerebrospinal fluid (CSF) were strongly positive (+++). The clinical, radiological and laboratory features met the criteria for the diagnosis of NMO. Conclusion: Patients with optic neuritis should be evaluated to exclude or evaluate the possibility of development of NMO because of the long interval between optic neuropathy and spinal cord injury. The AQP4 antibody, cerebral and spinal MRI and other related tests are needed to better assess the risk of development of NMO.

Keywords: Neuromyelitis optica, optic neuritis, myelitis, magnetic resonance imaging

Introduction
Neuromyelitis optica (NMO), also known as Devic’s disease or Devic syndrome, is a putative autoimmune inflammatory demyelinating disorder of the central nervous system (CNS), which predominantly involves the optic nerves and the spinal cord [1]. Autoantibodies against the water channel aquaporin-4 (AQP4) are implicated in the pathogenesis of a spectrum of inflammatory CNS disorders of varying severity; these disorders share a common serum biomarker NMO-IgG [2]. In a French case-series of 125 patients with NMO, the average interval between development of optic neuritis and myelitis was 15 months [3]. Ogasawara et al reported an NMO patient in whom myelitis occurred 25 years after the detection of optic neuritis [4]. Herein we report a patient with NMO who had a 30-year interval between optic neuritis and myelitis.

Case report
A 48-year-old man presented to our hospital with a history of unexplained numbness and swelling in both lower extremities since 9 months. Since the last two months, he developed progressive numbness of the limbs, which was associated with clumsiness and headache. Thirty years ago, the patient developed sudden loss of vision in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital. He had residual visual deficiency in the right eye, and was diagnosed with optic neuritis at a local hospital.

30-2 Humphrey visual field analyzer revealed central, temporal and inferior scotomas in the left eye.
A case of neuromyelitis optica

Fundus photography showed optic atrophy in the right eye while the left optic disc was normal. All other cranial nerves were normal. The limb muscle strength was level 4. The muscle tension was high in upper limbs, but normal in lower extremities. Deep tendon reflexes in limbs were normal. The pain diminished from below T2 levels. There was no deep sensory deficit or ataxia. Chaddock sign and Babinski sign were positive on the left side. Chaddock sign was positive and Babinski sign was negative on the right side. Cervical magnetic resonance imaging (MRI) showed abnormal intramedullary signals at C3-6 level, which appeared hyperintense on sagittal T2-weighted and fluid-attenuated inversion recovery (FLAIR) imaging (Figure 1).

Brain MRI was unremarkable. Pulmonary computed tomography (CT) showed bilateral secondary pulmonary tuberculosis. Cerebrospinal fluid (CSF) pressure was normal; CSF protein was 0.56 g/L; Pandy reaction was positive (+); CSF leukocyte count was 17×10^6/L; IgG level was 75.60 mg/L; serum and CSF anti-AQP4 antibodies were strongly positive (+++); serum and CSF oligoclonal bands (OCB) were negative; the permeability of the blood-brain barrier (BBB) was 6.9 (normal reference level <5.0); serum myelin basic protein (MBP) level was 11.538 µg/L (normal reference level <2.5); CSF myelin basic protein (MBP) was 4.910 µg/L (normal reference level <3.5). Flash visual evoked potential (FVEP) demonstrated decreased amplitude of P2 wave and an ambiguous waveform in the right eye; however, left eye was normal in this respect. Pattern visual evoked potential (PVEP) demonstrated no effective waveform in the right eye, while PVEP in the left eye was normal. Antinuclear antibody (ANA) series showed that Sjogren’s syndrome antibody (SSA) was strongly positive (+++), and granule-type was positive (1:1000). Serological tests for tuberculosis showed positive LAM-IgG and 38KD-IgG. Erythrocyte sedimentation rate (ESR) was 35 mm in the first hour. Bilateral salivary gland ultrasound revealed uneven echo. The clinical, radiological and laboratory findings were consistent with the diagnosis of NMO.

The patient was treated with high-dose pulsed steroid and anti-tuberculosis therapy, which was followed by oral steroid therapy for six months. One month after the start of treatment, there was improvement in numbness of the extremities, especially the lower extremities. No aggravation of tuberculosis was observed. At one year follow-up, right eye vision was maintained at the pre-treatment level; however, there was no numbness in his extremities. The study was approved by the Ethics Committee at the First Hospital affiliated to the Jilin University. Written informed consent was obtained from the patient for publication of this case report.

Discussion

In 2006, Wingerchuk et al proposed the revised criteria for diagnosis of NMO: (1) optic neuritis; (2) acute myelitis; (3) at least two of the following three supportive criteria, a) contiguous spinal cord MRI lesion extending over ≥ 3 vertebral segments; b) brain MRI findings not consistent with multiple sclerosis (MS); c) NMO-IgG seropositivity [5]. These diagnostic criteria are associated with 94% sensitivity and 96% specificity.

A previous study showed a direct association between the severity of disease at onset and prognosis. There is more probability of relapse when the onset of symptoms is mild. Conversely, occurrence of severe symptoms at onset increases the probability of an unremitting disease course [6]. Another study showed a high rate of incomplete or no recovery from myelitis from the beginning, and those chances of complete recovery decrease with increase in the
A case of neuromyelitis optica

number of subsequent relapses [7]. Mild symptoms or a benign long-term course does not rule out the diagnosis of NMO [7]. In a study by Pirko et al, 26.9% and 42.3% of patients with optic neuritis developed MS or NMO in 5 years and 10 years, respectively [8]. Patients who develop binocular acute visual loss and pain, either simultaneously or successively, are more prone to NMO [9]. It is worthwhile to note that brain MRI has an important role in predicting the risk of development of NMO or MS.

Recently, occurrence of NMO in combination with various other autoimmune diseases such as systemic lupus erythematosus (SLE), Sjogren’s syndrome (SS), and thyroiditis has been reported, with the first two accounting for the majority [10]. Elevated serum levels of autoantibodies such as ANA, anti-cardiolipin antibodies (ACLA), anti-neutrophil cytoplasmic antibodies (ANCA), and anti-thyroid antibodies (AThA) have been reported [11]. Occurrence of NMO in combination with SS is associated with some distinct clinical manifestations such as a propensity for involvement of cervical spinal cord, wider lesions in the longitudinal range, and a tendency for relapse [12]. Steroid therapy in combination with cyclophosphamide was shown to be effective in inducing remission [13]. Other treatment modalities include plasma exchange, intravenous immunoglobulin, or rituximab [7].

In our study, we analyzed the clinical features of myelitis and optic neuritis of a patient who presented with NMO. The patient was diagnosed with optic neuritis at the age of 18 years and had residual visual deficiency ever since. However, the disease remained in quiescence. The involvement of limbs and spinal cord started gradually 30 years later. Bilateral salivary gland ultrasound revealed uneven echo but there was no dryness of mouth and eyes. He declined labial gland biopsy. We suspected SS in this patient although it could not be confirmed. The patient denied any history of tuberculosis; however, secondary pulmonary tuberculosis was diagnosed on the basis of lung CT and positive antitubercular antibodies. He was administered anti-tuberculosis treatment to prevent aggravation of the tuberculous pathology owing to high-dose pulse steroid therapy. CSF examination showed no evidence of tuberculosis infection in the CNS. It was suggestive of an association between active tuberculosis and NMO [14]. Anti-tuberculosis treatment may improve loss of nerve function, and reduce its recurrence in NMO patients [15]. The reason of the extraordinarily long time interval in this patient is not fully understood; life pressure or stress factors may have potentially stimulated autoimmunity to provoke myelonic injury [16].

In summary, we present comprehensive clinical, radiological (MRI), and laboratory features of a patient with NMO. In patients diagnosed with optic neuritis, the possibility of development of NMO after a prolonged interval should be considered. Since it is crucial to diagnose and treat NMO at an early stage, detailed history of the patient with respect to the onset of optic neuritis, disease course, ocular involvement (monocular or binocular), symptoms of myelitis such as past or present sensory, motor or autonomic nervous system dysfunction are important. Moreover, investigation of AQP4 antibody, cerebral and spinal MRI and other related tests may help assess the risk of development of NMO, identify potential predictors of worse clinical outcomes, and facilitate appropriate immunotherapy as soon as possible. At the same time, screening for other autoimmune diseases may help guide the best therapeutic strategy and minimize the chances of recurrence.

Disclosure of conflict of interest

None.

Address correspondence to: Weihong Lin, Department of Neurology and Neuroscience Center, The First Hospital of Jilin University, Changchun 130021, Jilin, China. Tel: +86-13944116869; E-mail: linweihong321@126.com

References

A case of neuromyelitis optica


