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Case Report
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Cranial Nerve Injury and Neuropathy Around the Nodes of Ranvier with Positive Anti-NF186 Antibody: A Case Report

*Dong S[1], Sun M[1], Chen C[1], Wang J[2], Jin Q[3] and Cheng H[1]**

[1]Department of Neurology, The First Affiliated Hospital of Nanjing Medical University, China

[2]Department of Nephrology, The First Affiliated Hospital of Nanjing Medical University, China

[3]Department of Neurology, The Affiliated Sir Run Run Hospital of Nanjing Medical University, China

Abstract

Autoimmune nodopathy with Neurofascin-186 (NF-186) antibody positive is rare to report. This case report describes a patient with NF-186 antibody positive. This patient suffered from recurrent unclear speech accompanied by dysphagia. Hormone therapy was effective initially. But one month later, he experienced worsening speech and difficulties in swallowing, chewing, and moving his head. Further examination showed that both serum and cerebrospinal fluid anti-NF186 IgG antibody tests were positive. The patient again received hormone treatment, but this time it was ineffective. Subsequently, he received plasma exchange therapy, all neurological impairments improved significantly.

Keywords: Autoimmune nodopathy; NF-186 antibody; Cranial nerve injury

Introduction

Autoimmune Nodopathy is a new concept proposed in recent years. Such cases were initially thought to be Guillain-Barre Syndrome (GBS) or Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), which are associated with antibodies around the nodes of Ranvier [1,2]. However, there is increasing evidence that autoimmune nodopathies are very different from GBS and CIDP pathogenesis. Autoimmune nodopathies have distinct clinical manifestations and warrant different treatments. Here, we describe a patient who manifested with cranial nerve impairment and positive anti-Neurofascin-186 (NF-186) antibody.

Case Presentation

A 70-year-old male patient suffered from recurrent unclear speech accompanied by dysphagia starting from June 29th, 2021. Initially, the symptoms lasted for several minutes. On June 30th, the symptoms did not go away and worsened at night. The patient went to a local hospital. No obvious abnormalities were found after head CT examination, he received antiplatelet drugs and statins immediately. Furthermore, Magnetic Resonance Imaging (MRI) did not reveal any infarct and the patient showed no remission after microcirculation treatments. The patient was subsequently treated with hormone therapy (dexamethasone 10 mg/day intravenous drip, reduced gradually). One week later, his symptoms were significantly relieved. One month later, he experienced worsening speech and difficulties in swallowing, chewing, and moving his head. This time, he was admitted to our hospital. After taking a detailed history, we learned that the patient was diagnosed with bilateral blepharoptosis in 2018 and had a history of hypertension. Physical examination showed that the vital signs were stable. In addition, cardiopulmonary and abdominal examinations were normal. Neurological examination results were as follows: Conscious, oriented, bilateral eyelid ptosis (covering the upper edge of the pupil to the level of 4 to 8 o'clock), bilateral peripheral facial paralysis, severe dysphonia (the patient just only pronounces monosyllabic words), and no bilateral pharyngeal reflex. The neck and shoulder muscle force were grade III. The muscle strength and tension of the limbs were normal. Ataxia and sensory examination were normal. Bilateral pathological signs and the meningeal irritation sign were negative. Blood tests including biochemical profile, thyroid function, tumor markers, infectious disease (HIV/HBV/HCV/syphilis), and other standard measures were normal. Neuroimaging and neuromuscular electrophysiological tests (involving only the limbs) showed no abnormalities. The protein and cell amount in Cerebrospinal Fluid (CSF) was normal. The serum anti-NF186 IgG antibody test was positive (1:10) (Figure 1A) and the cerebrospinal fluid anti-NF186 IgG antibody was positive (1:1) (Figure 1B).

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Correspondence:
Hong Cheng, Department of Neurology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, 210029, China, Tel: +86-025-68306050; E-mail: chenghong@njmu.edu.cn

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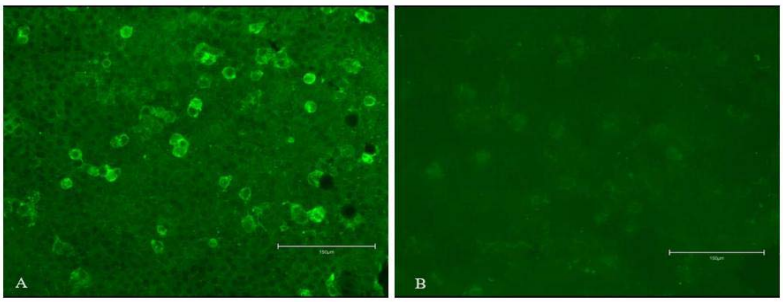

Figure 1: (A) Serum anti-NF186 IgG antibody test was positive (1:10). **(B)** Cerebrospinal fluid anti-NF186 IgG antibody was positive (1:1).

The patient again received hormone treatment, but this time it was ineffective. Subsequently, after he received plasma exchange therapy, all neurological impairments (including blepharoptosis) improved significantly.

Discussion

The EFNS/PNS guidelines (2021) suggest that autoimmune nodopathies are not CIDP variants as they have distinct clinical features and show no overt inflammation or macrophage-mediated demyelination [3]. The nodes of Ranvier are an important structure of myelinated nerve fibers that can be divided into the nodal region, para-nodal region, and para-nodal region. The internal molecular structure is extremely complex and can be divided into signal transduction proteins, cytoskeletal/structural proteins, ion channels and related proteins, adhesion molecules, and so on [4]. Neurofascin-155 (NF155), NF186, anti-contact protein, and anti-contact protein-related proteins are common nodal and para-nodal antigens that have been frequently reported in peripheral neuropathy cases such as GBS, CIDP and multiple sclerosis. NF186 is a cell adhesion protein located in the Langair node region that is co-anchored with voltage-gated Na+ channels at the beginning of the Langair node or axial projection. As a transmembrane protein, NF186 has six immunoglobulin-like domains, four fibronectin type III domains, and one mucin domain [5]. As an important adhesion protein in the nodes of Ranvier, NF186 has attracted much attention, although there are few reports. Meta-analysis of CDIP and GBS showed that anti-NF186 antibody positive patients account for only 0% to 2.03% of total CIDP and GBS cases [6]. Autoimmune nodopathies that are NF186 antibody positive have a later age of onset. They always occur in subacute or chronic condition and may be accompanied by focal segmental glomerulosclerosis, Sjogren's syndrome, or other autoimmune diseases [7]. Unlike other autoimmune nodopathies, anti-NF186 antibody positive patients rarely present with tremor and pathological pain. Some patients have prodromal infections and seem more susceptible to respiratory failure and other cranial nerve impairments. In the existing literature, all cases showed symptoms of peripheral nerve damage and show may have additional Cranial Nerve (CN) impairments (CN III, IV, V, VI, VII, IX). However, in the present case, multiple cranial nerves (CN III, V, VII, IX, X, XI, and XII) were involved. Electrophysiological examination is an important tool for diagnosis of autoimmune nodopathies. In previous case reports, demyelination and/or axonal damages were found in most cases with positive anti-NF186 antibody. However, in the present case, no abnormal changes were found on electrophysiological examination. This may be because the patient only presented with cranial nerve impairments and so electrophysiological examination was limited to peripheral nerves of the extremities. A study of 16 serum anti-NF186 antibody positive patients found that 7 had central nerve injuries, 9 had peripheral nerve injuries, and 12 had elevated CSF proteins [8]. Protein-cell separation in CSF is characteristic of CIDP, which is caused by protein exudation into the CSF due to an inflammatory reaction at the nerve root. However, in this case, protein-cell separation in the CSF did not occur, which may be related to the course of relapsing-remitting. Similar to this case, Sonali et al. [9] and Anudeep et al. [10] reported two patients with GBS in which no protein-cell separation was found in their relapsing-remitting course. Immunotherapy is important for autoimmune nodopathies, including Intravenous Immunoglobulin (IVIg), hormones, and plasmapheresis therapies. Notably, patients may have different responses [7]. Autoimmune nodopathies with anti-NF155 antibody positive patients always have poor response to IVIg and hormone treatments. Because the anti-NF155 IgG4 antibody rarely binds Fc receptor, plasmapheresis can achieve satisfactory results to remove the antigen-antibody complex. NF-186 is an isomer of NF-155. Patients with positive anti-NF186 antibodies may have similar characteristics. In the present case, the patient initially improved significantly after hormone therapy, but hormone therapy effects were not obvious after the second attack. Eventually, the patient recovered rapidly after plasma exchange. Some studies have reported that rituximab works at treating autoimmune nodopathies [11]. Rituximab can improve the immune response by reducing the number of CD20+ B cells. Although rituximab is convenient to use, comprehensive evaluation of immune status is required before using it and the long-term efficacy is still under review.

Conclusion

In summary, autoimmune nodopathies with positive NF-186 antibody are a kind of peripheral neuropathy with a late onset and low incidence. Such patients tend to present with cranial nerve injuries and a serious condition. Early recognition and immunotherapy are important for this disease.

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