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LETTER TO THE EDITOR

Anti-neurofascin 186 antibody in amyotrophic lateral sclerosis: a case report

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Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease, which causes muscle weakness, atrophy, fasciculation and spasticity. An autoimmune mechanism has been proposed to be involved. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired neurological disorder with heterogeneous presentation, which is characterized clinically by weakness and impaired sensory function evolving over 2 months or more. Motor CIDP accounts for only 1–10% of patients with CIDP, which presents as weakness but with normal sensation clinically and electrodiagnostically [1]. Anti-nodal/paranodal antibodies have been discovered in a small subset of patients fulfilling 2010 European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) criteria for CIDP. The 2021 EFNS/PNS guidelines proposed to name the conditions as "autoimmune nodopathy" and not to regard them as CIDP variants [1]. The clinical features of patients with motor neuron disease lacking upper motor neuron signs may resemble those of motor CIDP. Recently, a 75-year-old woman reported a 5-year history of progressive muscle weakness and amyotrophy. Despite seropositivity for anti-neurofascin (NF) 186 antibody, physical examination and electromyography were indicative of ALS.

Case report

A 75-year-old woman had 4-year history of weakness and amyotrophy originating in the right upper limb and extending to the left upper limb. She had hypertension for 30 years and controlled it well. None of her family members had neurological disorders. At the time of our initial evaluation examination revealed asymmetric distal predominant weakness and atrophy in the bilateral thenar muscles and interosseus. Proximal muscles of the upper limbs were only minimally affected. Fasciculations were observed in bilateral thenar muscle and first dorsal interosseous muscle. It also showed a slightly decreased muscle tone in upper limb. The bilateral biceps and triceps reflex were 1+ and the bilateral knee jerk were 2+. Pathologic reflexes were absent. There were no sensory deficits in limbs. Romberg sign was absent. There was no tongue wasting or fasciculation. Blood count and routine biochemical tests were within normal ranges. Tumor markers and thyroid function were normal. The protein level of CSF was slightly high (0.55 g/L, normal range = 0.25–0.45 g/L). Other CSF analyses (cell counts, glucose, chlorine and immunoglobulin G) were normal. Serum anti-ganglioside antibodies, paraneoplastic antibodies, anti-NF155 antibody, anti-contactin-1 antibody and anti-contactin-associated protein 1 antibody were negative. Anti-NF186 antibody was positive at a titer of 1:100 by a cell-based assay (CBA) using NF186-transfected cells (antibody against NF186 and the serum of an anti-NF186 antibody-positive autoimmune nodopathy patient served as positive control, while the serum of a healthy control served as a negative control). Nerve conduction study revealed a marked reduction in compound muscle action potential (CMAP) amplitude of bilateral median and ulnar nerves, while a slight decline in CMAP of right tibial nerve. However, there was no evidence of conduction block and delayed

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conduction velocity. The sensory studies were normal. Needle EMG showed large, long-duration motor unit potentials (MUPs) with reduced recruitment and fibrillation potentials in bilateral C5-T1 and right L2–S1-innervated muscles. She was diagnosed with lower motor neuron syndrome based on EMG findings and the absence of upper motor neuron signs on the examination. Because of the apparent increase in the anti-NF186 antibody, she received treatment with intravenous immunoglobulins (2 g/kg), which manifested no significant improvement. Within one year after admission, muscle weakness and amyotrophy had spread to the lower limbs. She needed support to walk because of muscle weakness in both lower limbs. Examination showed that the bilateral knee jerk was 3+. The Babinski and Hoffman signs were present. Needle EMG showed large, long-duration MUPs with reduced recruitment and fibrillation potentials in bilateral C5–T1, bilateral L2–S1-innervated muscles and the right T7 and left T10 paraspinal. Anti-NF186 antibody was still positive at a titer of 1:100 (CBA). She was diagnosed with probable ALS based on EMG findings and the presence of upper motor neuron signs on the examination according to the revised El Escoria criteria. The total disease course of the patient was more than 5 years.

Discussion

Anti-NF186 antibody was initially reported to be associated with autoimmune nodopathy patients showing subacute-onset, sensory ataxia, conduction block and cranial nerve involvement [1]. Anti-NF186 antibody was also reported in patients with multiple sclerosis, Guillain-Barré syndrome and multifocal motor neuropathy [2, 3]. Previous studies suggested a potential association between ALS and autoantibodies, including anti-LRP4 antibody, anti-cytosolic 5′-nucleotidase 1A antibody and so on [4, 5]. To our knowledge, we reported the first case of ALS with sera anti-NF186 antibody positivity. The anti-NF186 antibody titer of the present case was 1:100, which was within the reported range.

In the absence of typical clinical pattern or consistent electrophysiologic features, anti-NF186 antibody positivity should not prompt physicians to diagnose autoimmune nodopathy. The present case highlighted the importance of the match between clinical and electrophysiological features to confirm or refute a suspected diagnosis. Furthermore, we also stress the significance of follow-up and the risk of misdiagnosis by overreliance on positive antibody. The mechanism by which anti-NF186 antibody is produced and the role of anti-NF186 antibody in ALS remains elusive. Further larger studies to evaluate the percentage and the diagnostic value of anti-NF186 antibody in ALS are worthwhile.

Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

Competing interests No funding was received to assist with the preparation of this manuscript.

Ethical approval The article does not contain any studies with human participants.

Informed consent Informed consent was obtained from the patient.

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