Case report

Presence of both anti-contactin 1 and anti-neurofascin 140 antibodies in a case of chronic inflammatory demyelinating polyneuropathy

Hsin-Pin Lin, Kwo Wei David Ho, Miguel Chuquilin*

Department of Neurology, University of Florida, Gainesville, FL 32610, United States

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ABSTRACT

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired disorder of peripheral nerves and nerve roots. Its cause is unknown, but recently antibodies to nodal and paranodal proteins have been discovered in a small subset of CIDP patients. These contactin and neurofascin-related immune-mediated neuropathies are thought to be variants of CIDP and often respond better to B-cell depletion treatment with rituximab as the antibodies are often in the IgG4 subclass. Here, we report a patient with both anti-contactin 1 and anti-neurofascin 140 antibodies whose presentation resembled phenotypes of both CIDP variants.

1. Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) typically presents with symmetric motor and sensory symptoms that progress or relapse beyond eight weeks. Patients with CIDP are usually treated with immune modulating therapy using intravenous immune globulin (IVIg), plasma exchange, or glucocorticoids. Recently, antibodies to nodal and paranodal proteins have been discovered in a small subset of CIDP patients [1–3]. These contactin and neurofascin-related immune-mediated neuropathies are thought to be variants of CIDP and often respond better to B-cell depletion treatment with rituximab as the antibodies are often in the IgG4 subclass. Here, we describe a CIDP patient with both anti-contactin 1 and anti-neurofascin 140 antibodies. Her clinical presentation resembled phenotypes of both CIDP variants.

2. Case

A 20-year-old African American female presented with 2-month history of bilateral numbness and tingling in the hands and legs, bilateral leg weakness and gait imbalance that had worsened abruptly to the extent that she could not ambulate without assistance. Four months ago, she had left-sided facial numbness and tingling, drooling, and dysarthria that occurred after flu-like symptoms and spontaneously resolved after 6 weeks. Physical exam showed bilateral lower extremity edema, areflexia, weakness in both proximal and distal muscles, decreased vibration and pinprick sensation distal to the knees and impaired proprioception. CSF showed albuminocytologic dissociation. 24-h urinary protein was 2.8 g. ESR 62 mm/h, CRP 5.7 mg/L. Vitamin and copper levels were normal. Only scl-70 was positive on ANA panel. HIV, RPR, Lyme IgG and IgM were negative. Brain, cervical and thoracic spine MRI were normal. Nerve conduction study (NCS) showed prolonged F wave latencies, greater in lower than upper extremities.

The patient was diagnosed with CIDP and received three treatment courses of IVIg 2 g/kg. She had moderate improvement after the first treatment, but did not respond to the last two. Her symptoms worsened and she became wheelchair-bound again. Contrast lumbar spine MRI showed diffuse enlargement and enhancement of the cauda equina to the sacral plexus (Fig. 1). Repeat NCS showed severe axonal and demyelinating neuropathy, with motor more than sensory and lower more than upper extremity involvement.

Because of patient’s young age, significant proteinuria and the severity of her disease, further work up was performed. Serum vascular endothelial growth factor level and skeletal bone survey were ordered to evaluate for POEMS syndrome. Tests for serum antibodies to CNTN1, neurofascins (NF155, NF186, and NF140) and β-Tubulin [1] were ordered to look for known CIDP variants. Sural nerve biopsy was normal, indicative of predominantly proximal demyelinating process. There was no evidence of vasculitis, proteinaceous deposit, or amyloid deposition. Whole body CT scan showed no evidence of malignancy or lymphadenopathy. Serum was positive for IgG to Contactin 1 (CNTN1) and...
Neurofascin 140 (NF140). The patient was started on methylprednisolone 1 g/day for five days, followed by 1 g/day once a week and her symptoms improved significantly. Her proteinuria also improved. Kidney biopsy was consistent with primary membranous glomerulonephritis (she used nonsteroidal anti-inflammatory drugs for migraines). She had significant weight gain and rituximab was offered as an alternative. The patient declined due to fear of side effects.

3. Discussion

Our patient had both anti-CNTN1 and anti-NF140 antibodies and her clinical presentation resembled phenotypes of both CIDP variants with early axonal involvement, severe leg weakness and likely concomitant autoimmune disorder.

Anti-CNTN1 antibodies have been found in a small subset of patients with CIDP and GBS (1% to 7%) [2,3]. CNTN1 is an axonal adhesion protein. It interacts with contactin associated protein 1 (CNTNAP1/CASPR1) on the axon side and NF155 on the glial side to form the paranodal axo-glial junctions. Patients with anti-CNTN1 seropositive CIDP often have severe clinical phenotype. They are associated with predominantly motor with early axonal involvement, sensory ataxia, and paresthesia. Patients tend to respond well to corticosteroids and rituximab, but not to IVIg therapy [3].

The anti-NF140/186 IgG seropositive CIDP was recently described by Delmont et al. [2]. NF140, similar to NF186, is a neuronal isoform of neurofascin, located at the nodes of Ranvier to form nodal complexes and to cluster sodium channels at the nodes. Anti-NF140/186 antibodies were detected in 2% of their CIDP group. These patients showed subacute onset, severe leg weakness at disease nadir, sensory ataxia, conduction block and cranial nerve involvement. They had good response to treatment with steroids and IVIg when the antibodies were of IgG4 subtype. Interestingly, similar to our case, four out of five patients described also presented with a concomitant autoimmune disorder: one had retroperitoneal fibrosis; one had anti-Ro/SS-A antibodies; and two had focal segmental glomerulosclerosis [2].

CIDP is a heterogeneous disorder. If a patient with CIDP shows distinct clinical presentations or lacks response to IVIG, testing for CNTN1 and neurofascin antibodies may help guide therapy.

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Conflict of interest

The authors declare no conflict of interest.

Author contributions

Hsin-Pin Lin and Kwo Wei David Ho conceptualized the manuscript. Hsin-Pin Lin created the first draft of the manuscript. Kwo Wei David Ho and Miguel Chuquilin critically reviewed the article and provided revisions for intellectual content.

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