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Introduction
Chronic inflammatory demyelinating polyneuropathy (CIDP), characterized by slowly progressive or relapsing demyelinating polyneuropathy, is caused by an autoimmune mechanism. Although CIDP is heterogeneous, autoantibodies against neurofascin155 (NF155), a paranodal protein in peripheral nerves, are detected in 4%–18% of CIDP cases. Recent reports have shown that anti-NF155 antibody–positive CIDP is characterized by onset at a relatively young age, tremor, ataxia, and refractoriness to intravenous immunoglobulin (IVIg). However, only a few reports are available that provide specific details of the clinical treatment of these cases.

Methods
We report the cases of 4 patients with anti-NF155 antibody–positive CIDP who underwent sural nerve biopsies. Anti-NF155 antibody was detected by ELISA and cell-binding assay. All 4 patients had anti-NF155 antibody. The subclass was noted to be predominantly IgG4.

Case reports
Patient 1.
A 38-year-old woman developed impairment in hand dexterity, followed by limb weakness and gait. Eight months after onset, she could no longer stand independently. Neurological examination showed bilateral facial weakness and paresthesia, dysarthria, mild limb weakness, severe ataxia, and tremor. The administration of IVIg (0.4 g/kg for 5 days) and 2 courses of intravenous methylprednisolone (IVMP) (1 g/day for 3 days) was ineffective. However, her symptoms slowly improved after 4 sessions of plasma exchange (PE). She could then stand without an aid after 3 additional sessions of PE. Because she still could not walk, IVIg was administered again but was ineffective. She was eventually able to walk with a crutch after the administration of prednisolone (PSL) (30 mg/day) and cyclosporine A (CyA) (200 mg/day).

Patient 2.
A 40-year-old man had a history of CIDP treated with corticosteroids. He had been treated for 2 years, and CIDP had been in remission for 16 years prior to the recurrence. He developed paresthesia of distal limbs and gait disturbance. Treatment with PSL (30 mg/day) was started, but his symptoms showed no improvement. Neurological examination showed slight limb weakness, deep sensory disturbance, mild ataxia, and tremor. Although IVIg was administered, his symptoms did not improve. His paresthesia slightly reduced after 5 sessions of PE after 3 months. He continued to receive PSL (10 mg/day) for 18 months. However, paresthesia and mild ataxia slowly worsened. After 2 additional courses of IVMP and 4 sessions of PE were performed, but they were not effective.

Patient 3.
A 30-year-old woman had paresthesia of distal lower limbs. Lower limb weakness appeared 20 months after the onset of symptoms. Neurological examination showed moderate distal weakness in lower limbs and mild ataxia. Her paresthesia mildly improved following 3 courses of IVIg. Although 2 courses of IVIg and 7 sessions of immunoadsorption plasmapheresis (IAPP) using a tryptophan column (IMMUSORBA TR-300, ASAHI KAISEI MEDICAL, Japan) were not effective, her lower limb weakness and mild ataxia improved after 4 sessions of PE.

Patient 4.
A 42-year-old man had paresthesia of distal limbs and gait disturbance. Neurological examination showed mild distal limb weakness and ataxia. He was diagnosed with Guillain–Barré syndrome (GBS). He received IVIg, but it was not effective. Since his symptoms got worse, he was diagnosed with sural CIDP and again after 2 months from the onset. However, his symptoms did not improve. Four sessions of PE were then performed but were ineffective. Although rehabilitation was performed, he became bedbound. He had severe ataxia, tremor, moderate limb weakness, and muscle wasting of the distal limb after 11 months from the onset. Nine sessions of PE were performed in which his symptoms slowly started improving after 6 sessions. Because his neurological symptoms still remained, 1 course of IVMP was performed, followed by the administration of PSL (60 mg/day) and CyA (200 mg/day). During these treatments, he continued to recover. He could finally walk with an aid following 4 additional sessions of PE after 14 months from the onset.

Conclusion
1. Anti-NF155 IgG4 antibody–positive CIDP shows distinctive clinicopathological features.
2. The antibody may be directly associated with the pathogenic mechanisms of anti-NF155 IgG4 antibody–positive CIDP.

Table 1. Clinical information of 4 patients with anti-NF155 antibody–positive CIDP

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Onset form</th>
<th>Onset age</th>
<th>Assess</th>
<th>SEW</th>
<th>AntitNF155 IgG4</th>
<th>PSL (mg/day)</th>
<th>CyA (mg/day)</th>
<th>IVIg (g/day)</th>
<th>PE (sessions)</th>
<th>IVMP (g/day)</th>
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<tbody>
<tr>
<td>Patient 1</td>
<td>38</td>
<td>male</td>
<td>chronic</td>
<td>18</td>
<td>10 months</td>
<td>−</td>
<td>+</td>
<td>60</td>
<td>200</td>
<td>0.4</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Patient 2</td>
<td>28</td>
<td>male</td>
<td>chronic</td>
<td>12</td>
<td>18 months</td>
<td>−</td>
<td>+</td>
<td>60</td>
<td>200</td>
<td>0.4</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Patient 3</td>
<td>25</td>
<td>female</td>
<td>subacute</td>
<td>18</td>
<td>12 months</td>
<td>−</td>
<td>+</td>
<td>60</td>
<td>200</td>
<td>0.4</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Patient 4</td>
<td>42</td>
<td>male</td>
<td>chronic</td>
<td>20</td>
<td>20 months</td>
<td>−</td>
<td>+</td>
<td>60</td>
<td>200</td>
<td>0.4</td>
<td>8</td>
<td>1</td>
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Table 2. Electrophysiological examination of 4 patients with anti-NF155 antibody–positive CIDP

<table>
<thead>
<tr>
<th>Patient</th>
<th>Median nerve</th>
<th>Ulnar nerve</th>
<th>Tibial nerve</th>
<th>Sciatic nerve</th>
<th>Median motor latency (msec)</th>
<th>Peak SNAP amplitude (μV)</th>
<th>Distal SNAP amplitude (μV)</th>
<th>CMAP amplitude (mV)</th>
<th>Motor latency (msec)</th>
<th>CMAP amplitude (mV)</th>
<th>Sensory amplitude (μV)</th>
<th>CMAP amplitude (mV)</th>
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</thead>
<tbody>
<tr>
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<td>5.7</td>
<td>13.6</td>
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<td>9.4</td>
<td>5.4</td>
<td>12.3</td>
<td>4.01</td>
<td>6.2</td>
<td>3.1</td>
<td>13.0</td>
<td>4.01</td>
</tr>
<tr>
<td>Patient 2</td>
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<td>6.8</td>
<td>23.2</td>
<td>18.2</td>
<td>2.47</td>
<td>8.1</td>
<td>20.3</td>
<td>4.01</td>
<td>5.7</td>
<td>2.47</td>
<td>32.5</td>
<td>4.01</td>
</tr>
<tr>
<td>Patient 3</td>
<td>9.4</td>
<td>7.5</td>
<td>18.2</td>
<td>18.2</td>
<td>5.9</td>
<td>8.1</td>
<td>32.5</td>
<td>4.01</td>
<td>6.2</td>
<td>8.1</td>
<td>32.5</td>
<td>4.01</td>
</tr>
<tr>
<td>Patient 4</td>
<td>11.1</td>
<td>8.3</td>
<td>13.0</td>
<td>13.0</td>
<td>≤5</td>
<td>5.7</td>
<td>≤5</td>
<td>5.7</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
</tbody>
</table>

Figure. Pathological pictures of sural nerve biopsies from 4 patients with anti-NF155 antibody–positive CIDP.

There was no onion bulb formation, vasculitis, or inflammatory cell infiltration. A partial paranodal demyelination was observed in teased-nerve fibers from three patients (patient 1, 2, and 4). Abnormal paranodal lesions, such as loss of the transverse bands, were observed in all patients. These electron microscopic findings were not observed in control CIDP patients without anti-NF155 antibody.

References