Expanding the Concept of Paraneoplastic Neuromyelitis Optica: A Cohort Description with Histological Staining

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Background

- Neuromyelitis optica (NMO) is an autoimmune Central Nervous System (CNS) syndrome distinct from MS.
- NMO is frequently associated with aquaporin-4 (AQP4) antibodies, found in 60 to 70% of patients.
- Paraneoplastic neurological syndromes are remote effects of cancer caused by an autoimmune response initiated by self-antigens expressed on cancer cells.
- Based on the potential relationship between cancer and a neurologic syndrome, definition exists for definitive or possible PNS.
- Paraneoplastic NMO has been previously described.
- The link between NMO and cancer needs further investigation.

Objectives

- To describe a large case series of paraneoplastic NMO.
- To confirm AQP4 expression by cancer cells can trigger NMO.

Methods

- 10 patients were identified from a database of 155 NMO patients followed at the UBC NMO Clinic.
- A retrospective chart review was done looking at demographics, NMO history, AQP4 serostatus and cancer history.
- Serum AQP4 status was done by a cell-based assay (CBA).
- Pathological samples of cancer, when available, were stained with AQP4 (Courtesy Dr. Raffaele Iorio).

Table 1: Paraneoplastic NMO cohort description

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age at NMO onset</th>
<th>AQP4 status at cancer diagnosis</th>
<th>Type</th>
<th>Time of NMO to cancer diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>54</td>
<td>Positive</td>
<td>LETM</td>
<td>14 months</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>61</td>
<td>Positive</td>
<td>LETM</td>
<td>6 months</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>41</td>
<td>Positive</td>
<td>LETM</td>
<td>8 months</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>49</td>
<td>Positive</td>
<td>Neurologic syndrome</td>
<td>8 years</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>54</td>
<td>Negative</td>
<td>LETM</td>
<td>2 years</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>62</td>
<td>Positive</td>
<td>LETM</td>
<td>14 years</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>59</td>
<td>Positive</td>
<td>LETM</td>
<td>10 years</td>
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<tr>
<td>8</td>
<td>F</td>
<td>65</td>
<td>Positive</td>
<td>LETM</td>
<td>9 years</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>52</td>
<td>Negative</td>
<td>LETM</td>
<td>15 years</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>65</td>
<td>Positive</td>
<td>LETM</td>
<td>9 months</td>
</tr>
</tbody>
</table>

Discussion

- The prevalence of paraneoplastic NMO in our cohort is consistent with a prevalence of 5-12% found in other series.
- Ovarian serous carcinoma and adrenocortical carcinoma are cancer subtypes not previously described in association with NMO.
- Expression of AQP4 on cancer cells provides a possible pathological link between cancer and NMO.
- As found in most of our patients, a subsequent occurrence of cancer is common in paraneoplastic syndromes.
- Higher age may be a possible confounder, but is described in previous paraneoplastic NMO cohort.
- Clinicians should have a higher level of suspicion for cancer screening in elderly patients presenting with NMO.

Conclusion

- We described 10 new cases of paraneoplastic NMO and 2 new cancer histological subtypes.
- We showed in a case of ovarian cancer that cancer cells express AQP4, suggesting AQP4 antibodies could be produced as part of an antineoplastic immune response leading clinically to NMO.

References