Voltage-gated potassium channel
antibody-associated limbic encephalitis

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Abstract

We are emphasising the importance of considering a rare diagnosis, voltage-gated Potassium channel antibody-associated limbic encephalitis, in an 80-year-old gentleman who presented with memory impairment, seizure and hyponatraemia. He was found to have high titre of voltage-gated potassium channel antibodies in his serum. He was given high-dose steroids and he responded biochemically and clinically with marked improvement in symptomatology.

Keywords: encephalitis, limbic encephalitis, VGKC antibody-associated encephalitis, older people

Case report

An 80-year-old gentleman, with a history of dual chamber pacemaker inserted in 2011 for sinus arrest, presented with falls. He was commenced recently on carbamazepine for generalised tonic clonic seizures.

His general physical and systemic examinations were unremarkable; his abbreviated mental score was 10/10. His blood tests showed sodium of 121. Other baseline blood tests were normal. 24-h electrocardiogram showed functioning pacemaker. CT head showed moderate global atrophy. After extensive investigations, low sodium was thought to be due to antiepileptic.

The neurology team diagnosed him as immune-mediated encephalitis based on increasing falls, short-term memory loss (reported by his wife and evening ward staff), seizures and low
sodium. Serum voltage-gated potassium channel (VGKC) antibodies were requested and were strongly positive. His cerebrospinal fluid (CSF) results were within normal limits. Herpes simplex, varicella zoster, enterovirus polymerase chain reaction (PCR) and treponema pallidum were all negative. He was started on prednisolone 60 mg with tapering off in 4 months. He showed a remarkable improvement in his memory noted by family with no further seizure, improved sodium level and decrease in VGKC antibody titre on 1-, 2- and 6-month follow-up.

**Discussion**

VGKC antibody-associated limbic encephalitis (immune mediated) is a rare disease (43 reported cases in literature review in 2009 [1]) but should be considered, along with herpes simplex encephalitis and Korsakoff’s syndrome, in the differential diagnosis of patients presenting with subacute amnesia [2].

First defined in 1968 [3] it is a clinical syndrome of subacute onset and presents with cognitive impairment, seizures and MRI changes. Patients are usually middle aged, unlike our elderly patient [4]. Although presentation here was very mild, mainly with falls but usually they present with subacute memory impairment and a range of psychiatric features such as confusion, disorientation and behavioural changes [4]. The cognitive impairment is due to limbic system involvement and MRI brain may reflect these changes. The seizures are often difficult to control and arise from the temporal lobe [4].

This encephalitis was initially associated with carcinoma. However, the raised levels of VGKC antibodies seen in Morvan’s syndrome [5], a syndrome with similar cognitive impairment, prompted a team in Oxford to measure VGKC antibodies in this condition. They also noted that antibody levels declined with improvement in symptoms [6].

Recently, specific targets of VGKC antibodies have been identified. These include the cell-surface antigens leucine-rich glioma inactivated 1 (LG1) which are predominantly associated with limbic encephalitis and faciobrachial dystonic seizures [7]. LG1 antibodies are epileptogenic [8]. Mutations in these channels resulted in intractable seizures in patients [9] and experimental animals [10].

Hyponatraemia is common and due to syndrome of inappropriate ADH secretion (SIADH), which may be resistant to treatment [4]. Electroencephalogram (EEG) findings may include diffuse slowing as seen in encephalopathy or focal, usually temporal, sharp waves [4]. CSF findings may show mild lymphocytosis and raised protein [4].

A decline in the VGKC antibodies level is seen in most patients with parallel improvement in neuropsychology, sodium level and seizure control with varying combinations of plasma exchange, intravenous immunoglobulin (IVIg) and high-dose oral steroids [2,4]. Steroids are slowly tapered off over months, titrated against clinical state and VGKC antibody levels [4]. MRI changes can show resolution, but if medial temporal atrophy remains then this could explain persisting cognitive impairment [4].

(Table 1).

**Conclusion**

VGKC antibody-associated limbic encephalitis is not as rare as was previously thought. Early treatment may prevent mortality associated with intractable seizures and electrolyte disturbances [4] and the morbidity associated with cerebral atrophy [2].

Therefore, it is suggested that the antibodies should be checked early in patients presenting with subacute onset of disorientation, confusion and memory loss particularly when associated with medial temporal lobe signal change in the relative absence of cerebellar and brainstem involvement on MRI or clinically, in the presence of SIADH.

**Key points**

• Cognitive impairment with encephalitis.
• LG1 antibodies associated encephalitis.
• Encephalitis involving the medial temporal lobe.
• Cognitive impairment, seizures, low sodium levels.

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Table 1. An overview of investigation findings in some causes of limbic encephalitis

<table>
<thead>
<tr>
<th>Cause of Encephalitis</th>
<th>Herpes simplex encephalitis</th>
<th>Paraneoplastic limbic encephalitis</th>
<th>VGKC-limbic encephalitis</th>
<th>Neuropil limbic encephalitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI temporal lobe signal change</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>EEG abnormalities</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>CSF abnormalities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raised white cells</td>
<td>++ (10–20/μl)</td>
<td>+ (10–100/μl)</td>
<td>+/- (&lt;1/mm³)</td>
<td>++ (7–81/μl)</td>
</tr>
<tr>
<td>Raised protein</td>
<td>++ (0.6–6 g/l)</td>
<td>++ (0.5–1.7 g/l)</td>
<td>+/- (&lt;0.8 g/l)</td>
<td>++ (0.5–1.5 g/l)</td>
</tr>
<tr>
<td>Hyponatraemia</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Serum antibody</td>
<td>-</td>
<td>Anti-Hu, Anti-Ma, CRMP5/CV2, ANNA-3</td>
<td>VGKC Ab</td>
<td>Anti-neuropil Abs</td>
</tr>
<tr>
<td>Underlying tumour</td>
<td>No</td>
<td>Yes (lung, testis, lymphoma)</td>
<td>Rarely (thymoma)</td>
<td>Yes (teratoma, thymoma)</td>
</tr>
<tr>
<td>Treatment</td>
<td>Aciclovir</td>
<td>Treat tumour ± immunosuppression</td>
<td>IVIg/plasma exchange and high dose steroids</td>
<td>Treat tumour ± immunosuppression</td>
</tr>
</tbody>
</table>

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Conflicts of interest

None declared.

References


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