Limbic Encephalitis: Under-Recognition of Voltage-Gated Potassium Channel Antibodies

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Dear Sir,

Fukushima et al. [1] reported a case of steroid-responsive limbic encephalitis (LE) without clear aetiology. Their patient presented with generalised and complex partial seizures, amnesia, hyponatraemia and bilateral medial temporal lobe high signal on fluid-attenuated inversion recovery magnetic resonance images (MRI). This symptom myriad is best described within the rubric of LE. LE is traditionally considered a paraneoplastic phenomenon; hence the appropriately intensive search for occult malignancy by Fukushima et al. [1]. However, recently voltage-gated potassium channel antibodies (VGKC-Ab) have been shown to be a more reversible, infrequently malignant cause of LE [2].

The patient described by Fukushima et al. [1] also demonstrated prominent hormonal abnormalities, including the syndrome of inappropriate ADH (SIADH) and impaired thyrotropin-releasing hormone secretion. In keeping with this, previous descriptions of VGKC-Ab-associated LE have reported SIADH (in 80% of cases), significant appetite and weight gain (in 30%) and occasional abnormal thyroid function. However, SIADH is not a specific feature for VGKC-Ab-associated LE, since ADH is secreted from some small cell lung cancers, and 1% of all small cell

lung cancer is associated with anti-Hu paraneoplastic LE.

Since the report of Fukushima et al. [1], we have shown the serum of their patient to be strongly positive for VGKC-Ab (2,354 pM). The antibody titre decreased during treatment to 901 pM. This test is a radioimmunoassay utilising the binding of ¹²⁵I-radiolabelled α -dendrotoxin to specific potassium channels. The results are expressed as picomoles of ¹²⁵I-dendrotoxin-VGKC-binding sites per litre of serum [3]. Results below 100 pM are considered negative, although we have found 5% of elderly subjects to have a titre between 100 and 400 pM [2].

Previously, we have demonstrated the presence of VGKC-Ab in two patients initially considered to have Hashimoto's encephalopathy [3]. Hashimoto's encephalopathy, in contrast to VGKC-Ab LE, often presents with prominent stroke-like episodes and frequent tremor. However, there is also some overlap: Hashimoto's encephalopathy patients often have neuropsychiatric presentations, sleep disturbances, can show medial temporal lobe MRI abnormalities [4], demonstrate thyroid hormone abnormalities and often show an excellent steroid response.

These cases illustrate the need to consider VGKC-Ab-associated LE in the dif-

ferential diagnosis of confusion with seizures. It is evident that the VGKC-Ab-positive subgroup of LE is under-recognised. While the clinical distinction between subtypes of such 'limbic encephalitis' is complex, neuroendocrine abnormalities may provide a clue as to the likely, often non-paraneoplastic, aetiology.

References

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