

Limbic Encephalitis associated with the presence of voltage gated potassium channel antibody

A 43 year old man presented with episodes of limb weakness since childhood.

INTRODUCTION

Limbic encephalitis (LE) has typically been regarded as a paraneoplastic disorder and associated malignancies include lung (most commonly small cell lung carcinoma), testis, thymus, and breast¹⁻⁸. It is usually associated with antibodies to Hu (ANNA1 - antineuronal nuclear antibody), amphiphysin, anti-CV2 (CRMP5 - collapsin response-mediator protein-5), P/Q-type calcium channel, Purkinje cell cytoplasmic autoantibody type 2 (PCA-2) and Ma2⁹⁻²¹ but in recent years a different form of LE associated with voltage gated potassium channel antibodies (anti-VGKC-Abs) has been identified which may respond to immunotherapy and does not seem to be linked to a remote effect of a neoplastic process [see Buckley ACNR 2005]²²⁻²⁸. The clinical profile of this new syndrome includes seizures, memory impairment, hyponatraemia and behavioural changes.

CASE

A 56 year-old diamond merchant who trained as an industrial psychologist presented with a six month history of recurrent episodes of altered behaviour and episodes of vagueness which would involve lack of recall of his occupation and sudden outbursts of expletives. He had no relevant past medical history. He was extensively investigated with no diagnosis emerging and this included

EEG monitoring with no electrophysiological evidence of seizure activity during some of his aforementioned episodes. He was thought to be suffering from a non-epileptic attack disorder, although with time it became clear that these episodes were more obviously epileptic in nature (see video). Throughout this time he drank water excessively and continued to conduct his business from the hospital bed often writing lengthy but confused letters and indeed became increasingly confused and confabulated memories such as meeting Richard Branson in the hospital foyer. He also became uncharacteristically hostile with paranoid delusions concerning staff members.

General and neurological examinations were normal as was bedside cognitive testing. Routine haematological and biochemical investigations revealed hyponatraemia (Na = 122 mmol/l) which was shown to be the result of psychogenic polydipsia. Vasculitis serology was negative and CSF examination was normal (protein 0.45g/l, glucose 3.5g/dl (with no cells or evidence of microbiological organisms). Screening for malignancy including tumour markers, CT scan of chest, abdomen and pelvis and whole body PET was negative and he had a normal MRI (with contrast) scan of his brain and a brain FDG-PET revealed diffuse hypometabolism involving both hemispheres anteriorly and posteriorly (see Figure 1). Further EEGs did though demonstrate electrophysiological evidence of seizures.

Neuropsychological evaluation revealed mild impairment of frontal executive function and episodic memory.

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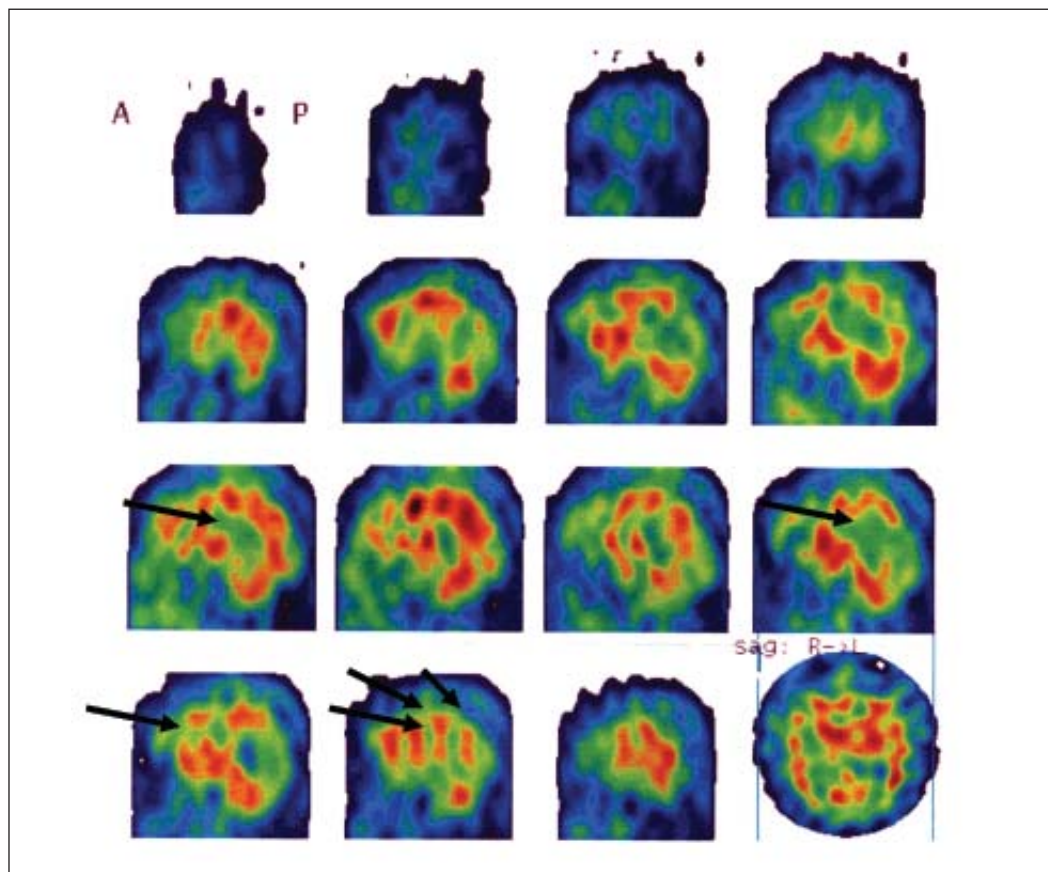


Figure 1. FDG-PET scan of the brain demonstrating the multiple areas of hypoperfusion. These are sagittal sections of the brain with A and P denoting anterior and posterior respectively starting with slices taken from the right on the top left moving sequentially across the page then moving down to the next row. Arrows indicate areas of hypoperfusion.

A diagnosis of limbic encephalitis was made and his serum VGKC-Abs were sent off and strongly positive - 2317pM (normal controls less than 100pM²⁹).

He was commenced on a course of intravenous immunoglobulin (0.4g per kilogram per day for 5 days) but his behaviour continued to be extremely erratic with episodes of aggression and confusion. Anti-epileptic medication was also started and this eventually controlled his seizures using a combination of phenytoin, gabapentin and levetiracetam. His serum sodium remained low despite attempts at strict fluid restriction although it became apparent that he was getting access to water by alternative means. As a result of his continuing problems, he was treated with plasma exchange and high dose oral prednisolone (60mg) and on this there was a gradual but definite improvement in his clinical state with resolution of his neuropsychiatric symptoms and cessation of his seizures. Furthermore his polydipsia resolved as mirrored by a return to normal serum sodium status in parallel to a drop in anti-VGKC antibody titre. After a total of 6

months of inpatient care he was discharged. At outpatient review 5 months after discharge he was well with no further seizures and had returned to his normal personality.

DISCUSSION

Initially described in 2001 by Buckley et al³⁰, VGKC-Ab limbic encephalitis presents acutely or subacutely with confusion, seizures and amnesia accompanied occasionally by hyponatraemia and usually by unilateral, or bilateral, medial temporal lobe signal change on MRI. Response to immunomodulatory therapy is usually, but not universally, good²²⁻²⁵.

The direct pathological role of the VGKC-Ab is unclear but evidence is growing to suggest this is the case²²⁻²⁵. The level of the antibody in the serum can be used as a helpful therapeutic marker allowing adjustments in immunomodulation to achieve the serological aim of lowering the antibody level.

ACKNOWLEDGEMENTS

The patient and his family are thanked for their full co-operation at all stages of the assessment and treatment. Thanks also to Prof J Hodges, Consultant in charge of the case.

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