

Inappropriate vasopressin secretion due to limbic encephalitis secondary to LGI1 antibodies

Sonakshi Sharma, Ian Holdaway

Voltage-gated potassium channels (VGKC) are membrane-signaling proteins that respond to changes in voltage or ligand concentration across the cell membrane.¹ Antibodies against proteins associated with the VGKC complex (such as leucine-rich, glioma-inactivated protein 1 (LGI1)) are a rare, but treatable cause of non-paraneoplastic autoimmune limbic encephalitis.^{2,3} Hyponatremia has been noted in up to 90% of these patients,^{2,4} with at least half being secondary to the syndrome of inappropriate antidiuretic hormone secretion (SIADH).^{3,5,6} The exact mechanism of SIADH in this condition is unclear.

We describe a case of LGI1 limbic encephalitis presenting with generalised tonic-clonic seizures, confusion, memory loss, and SIADH, with minimal sodium response to fluid restriction, but rapid normalisation after immunotherapy, suggesting a pathogenic role of the LGI1 antibodies in the induction of SIADH.

Case report

A 59-year-old man (on no regular medications) was admitted in June 2015 with two generalised tonic-clonic seizures. He had a past history of a seizure (2007), with a normal EEG, and an MRI brain showing non-specific white matter change. Examination during the admission was unremarkable. Investigations revealed serum sodium of 125mmol/L (135–145) secondary to SIADH (urine sodium 33mmol/L, urine osmolality 415mosm/L, plasma osmolality 269mosm/L, 0930h serum cortisol 524nmol/L (normal 200–700) and normal thyroid function with serum free thyroxine 13.3pmol/L (normal 9–19), and TSH 1.8mIU/L

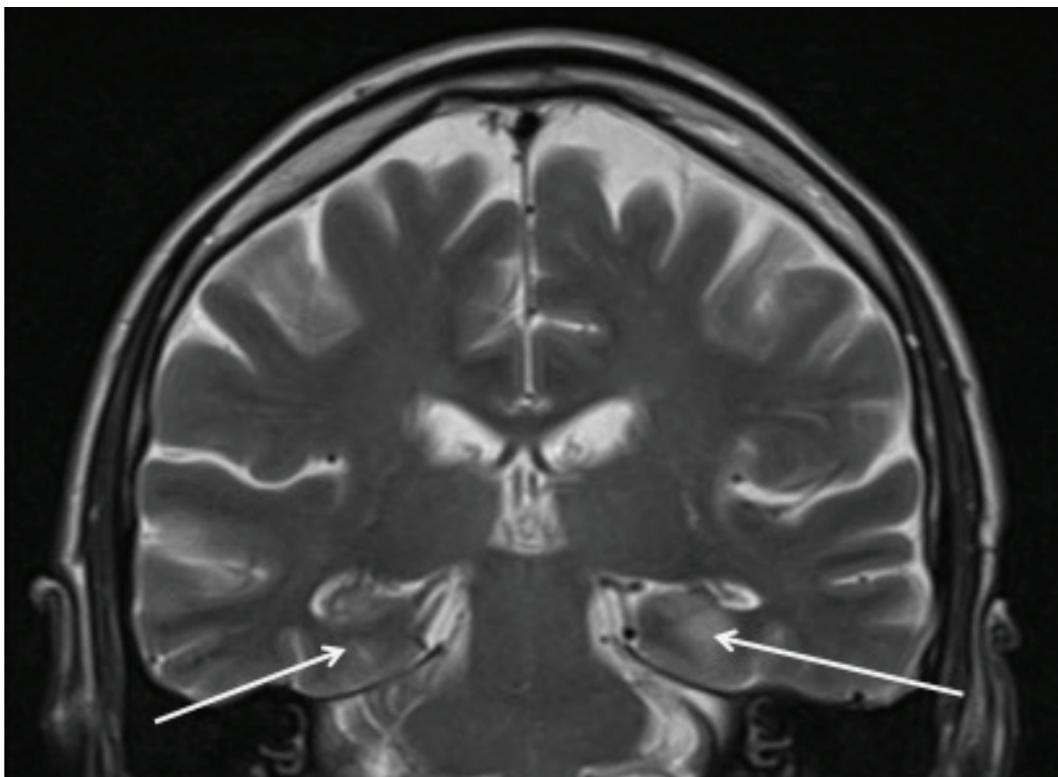
(normal 0.4–4)). Clinical assessment indicated he was euvolaemic. The cause of the SIADH and seizures was unclear. Levetiracetam was started and he was discharged with fluid restriction of 1.2L. His wife noted confusion and episodic memory loss at home, with difficulty remembering passwords and basic computer skills.

He was admitted with another seizure in July 2015, and serum sodium was 122mmol/L at the time. An MRI brain showed signs of limbic encephalitis that had developed since 2007 (Figure 1). CT scan of the chest, abdomen, and pelvis was entirely normal. His volume status was again felt to be normal and a repeat serum cortisol was 534nmol/L at 0730hrs. The Endocrinology service was consulted for the SIADH (minimally responsive to 800ml fluid restriction despite clinical euvolemia) and suggested that this was most likely secondary to the limbic encephalitis, which may be an autoimmune (rather than paraneoplastic) phenomenon. The CSF was positive for antibodies to the LGI1 protein. Treatment was commenced with intravenous Methylprednisone (followed by oral Prednisone), intravenous immunoglobulin (IVIG) and Azathioprine, and the serum sodium normalised promptly. The patient was reviewed in clinic in October 2015 and was noted to have significant improvement along with normal sodium levels off fluid restriction.

Discussion

LGI1 is a secreted neuronal protein that forms part of the VGKC complex and plays an important role in maturation and normal functioning of synapses. It

Figure 1: Coronal T2 MRI scan showing hyperintensity in the medial aspect of the temporal lobes, including the hippocampus, consistent with limbic encephalitis.



is expressed in the hippocampus, hypothalamus, midbrain, pons, medulla and cerebellum, as well as the renal tubules (where the exact location is uncharacterised as yet), prostate, sebaceous glands and reproductive organs.^{3,7,8} There are several potential mechanisms by which LGI1 antibodies may cause SIADH, including direct action on the hypothalamic nuclei to increase ADH production, or via action on renal tubules to increase sensitivity to ADH. The hippocampus has efferent fibers to the hypothalamus, and another possibility is that disruption of normal synaptic function of LGI1 in the hippocampus may affect ADH release from the hypothalamus.^{5-7,9}

SIADH also occurs in limbic enceph-

alitis caused by herpes simplex virus, with case reports confirming successful normalisation of serum sodium with fluid restriction and salt tablets.¹⁰ The particular correlation of SIADH with autoimmune limbic encephalitis is important, because these patients may be resistant (or only partially responsive) to fluid restriction alone.⁶ The presence of difficult-to-treat SIADH in a patient presenting with seizures and memory impairment, with an unremarkable CSF exam, may serve as a clue to the diagnosis of LGI1 limbic encephalitis. These patients require immunosuppressive therapy (rather than anti-epileptic drugs) for treatment of seizures, LGI1 antibodies and normalisation of serum sodium.

Competing interests:

Nil.

Consent

Verbal informed consent was obtained from the patient for publication of this case report and any accompanying images.

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