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Autoimmune limbic encephalitis

Editor – We read with interest the recent article by Derry *et al* (*Clin Med* October 2011 pp 479–82) concerning limbic encephalitis (LE). There are important additional issues leading on from this succinct article that may be useful to the general physician when considering a LE diagnosis.

As reflected in the article, the diagnosis of autoimmune encephalitis (AE) and, more specifically, LE is a difficult one with no causative agent identified in up to two-thirds of encephalitic patients referred to specialist centres.[1]

As mentioned in the article, recent work has indicated potassium channels are not the antigenic target in LE and it is in fact Anti-LGI1 (Leucine-rich glioma inactivate 1).[2,3] In addition, other studies suggest that another auto-antigen 'CASPR2 - contactin-associated protein-like 2' (expressed in hippocampal neurons) is associated with illnesses previously attributed to anti-VGKC antibodies such as drug-refractory epilepsy, encephalitis, peripheral nerve dysfunction, or a combination of both: Morvan syndrome or neuromyotonia.[4–7] Therefore, the term 'anti-VGKC' encephalitis is no longer in routine use.

The authors rightly illustrate the cardinal symptoms of LE as being severe short-term memory impairment with psychiatric symptoms such as personality change, depression, anxiety, hallucinations, confusion, and complex partial (often temporal) and generalised seizures.[8,9] It must be recalled that auto-antibodies may take some weeks to process and often LE treatment will have to be initiated prior to definitive diagnosis. With this in mind, there are other clinical features that may assist in pointing the clinician towards the diagnosis of LE. Features classically associated with anti-LGI1 encephalitis include faciobrachial tonic seizures[7] and, in 40% of patients, myoclonus.[2] With regards to initial blood tests, hyponatraemia is a common finding in patients with anti-LGI1 encephalitis being found in patients both with and without underlying malignancy, indicating that it is not purely a paraneoplastic phenomenon.[10] Autonomic instability is also described.

Once LE has been identified, it is essential to exclude paraneoplastic aetiology such as anti-Hu or anti-Ma2 associated LE as tumour treatment and, if possible, removal is associated with better outcomes than immunomodulatory therapy alone.[3] It is important to note that the encephalitic presentation will precede the identification of the neoplasm in up to three quarters of patients.[9,11,12]

Thankfully, as the article points out, non-paraneoplastic LE is associated with good outcomes if recognised early and treated aggressively. However, the clinician must be alert to the fact that residual neurological deficits may be subtle, difficult to elicit and, in some cases, sufficient to preclude the patient's return to work.

It is clear that the earlier AE or LE is diagnosed and therapy started, the better the outcome. We recently published an AE review containing a clinical algorithm for work-up, diagnosis, and treatment of autoimmune encephalitis[13] that – in conjunction with important articles such as Derry *et al*'s – we hope will assist the neurologist and generalist alike in early AE diagnosis and treatment.

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The changing landscape of anticoagulation and atrial fibrillation

Editor – We read with great interest the article by Breen and Hunt which presented an overview of the new oral anticoagulants (*Clin Med* October 2011 pp 497–9). We wish to highlight three new studies published since their review was

prepared, with important relevance to the topic of stroke prevention in atrial fibrillation (AF).

AVERROES was a double-blinded study comparing the use of the novel factor Xa inhibitor apixaban (5 mg twice daily) versus aspirin, in nearly 6,000 patients with AF, who were, either intolerant or unwilling to take oral vitamin K antagonist therapy.[1] There was a considerable reduction in the rate of the primary endpoint of stroke and systemic embolus (SSE) in the apixaban group (1.6% per annum *v* 3.7% per annum; $p<0.001$), despite similar rates of intracranial haemorrhage, major bleeding and death.[2]

The double-blinded ROCKET AF study compared once daily (20 mg) oral Xa inhibitor rivaroxaban with dose-adjusted warfarin among 14,264 AF patients at higher risk for stroke. The rate of the primary endpoint of SSE was similar between rivaroxaban (1.7% per annum) and warfarin (2.2% per annum). While there were similar rates of major and non-major bleeding, rivaroxaban did lead to significantly fewer reports of intracranial and fatal bleeding.

Finally, in the largest ever randomised stroke prevention in AF study, the double-blinded ARISTOTLE study randomised 18,201 patients to either oral apixaban (again 5 mg twice daily) or dose-adjusted warfarin.[3] Not only was apixaban non-inferior but actually superior to warfarin for the SSE primary endpoint (1.27% *v* 1.60% respectively). Furthermore, the rates of major bleeding (2.13% *v* 3.09%), all cause mortality (3.52 *v* 3.94%) and haemorrhagic stroke (0.24% *v* 0.45%) were all significantly reduced with apixaban.

These data, along with previously published data from the single-blinded RELY study using the oral direct thrombin inhibitor dabigatran, provide consistent evidence to suggest that AF anticoagulation practice is set to dramatically change in the very near future.

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