CASE REPORTS

Is valproate encephalopathy under-recognised in older people? A case series

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Abstract

Background: valproate (VPA) is an antiepileptic drug with a broad spectrum of efficacy. Although usually well-tolerated, it may have side-effects of which encephalopathy is one of the most serious.

Objective: to describe the clinical characteristics of valproate encephalopathy (VE) in five older patients with remote symptomatic seizures treated with rapid VPA loading.

Design: case series.

Setting: teaching hospital

Patients: five patients (71–89 years old) with underlying cerebrovascular disease or dementia and symptomatic seizures.

Results: VE was characterised by decline in conscious level and (in some cases) increase in seizure frequency. Three of the five patients had elevated ammonia levels. EEG showed generalised slow activity, in some cases accompanied by additional epileptic discharges. The condition was reversible in four patients after VPA discontinuation. One patient died.

Conclusions: older people may be at particular risk of VE because of co-morbid pathology, age-related metabolic changes and co-medication.

Keywords: valproic acid, valproate, epilepsy, encephalopathy, older people, elderly

Introduction

In older patients with epilepsy, sodium valproate (VPA) is sometimes regarded as the antiepileptic drug of first choice because of its good tolerability and cardiovascular safety [2, 5, 6, 7]. Although there are currently no evidenced based guidelines for the use of VPA in the treatment of status epilepticus (SE) rapid oral titration or intravenous infusion of VPA are also increasingly used to treat seizure emergencies [1–4]. One of the most serious adverse events of VPA therapy is valproate encephalopathy (VE) [8]. Although VE is, in general, reversible if VPA is discontinued, more severe and even fatal cases have been reported [8]. In adult epileptology, VPA-induced encephalopathy is regarded as a rare complication, although a considerable number of cases have been reported [8, 9–18, 19, 20]. Here, we describe five older patients with epilepsy who developed signs and symptoms suggestive of VE during initial VPA treatment.

Methods

Consecutive case series of five older patients with VE presenting to the Centre Hospitalier de Luxembourg, between September 2002 and April 2006

Illustrative case report (case 1)

An 83-year-old woman was admitted because a first generalised tonic-clonic seizure was followed by simple-partial SE with myoclonic movements of the left arm and leg. She had a history of dementia but had never received antiepileptic drugs. There was no indication of liver disease. Brain magnetic resonance imaging showed vascular leuкоencephalopathy and cortical atrophy. A lumbar puncture revealed no abnormalities. The patient received intravenous VPA (2000 mg over 24 h). Intravenous phenytoin (PHT) was added because of an incomplete response to VPA. In the first 24 h, a VPA serum level of 102 µg/ml (reference range; 50–100 µg/ml) and a
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Figure 1. (A) EEG of patient 1 showing generalised slow activity with some epileptic discharges suggestive of acute encephalopathy. (B) EEG of the same patient after discontinuing VPA, showing slow alpha activity with some intermittent theta activity, i.e. normalisation of the EEG pattern.

PHT serum level of 15.0 µg/ml (reference range, 5–20 µg/ml) were achieved. Despite this treatment the patient remained somnolent and showed an increase in seizure activity. Ammonia levels were elevated to 474 µg/dl (normal range, 28–80 µg/dl). The EEG showed changes suggesting a toxic encephalopathy (continuous polymorphic theta and delta waves over both hemispheres) and epileptic discharges. VPA was stopped because of the decline in conscious level and elevated ammonia. Ammonia levels returned to normal within a few days. Seizures were controlled by PHT monotherapy and the patient recovered completely 48 h later.

For further information on cases 1–5 see Appendix 1 in the supplementary data on the journal website (http://www.ageing.oxfordjournals.org/).

Discussion

The characteristic signs of VE are an impairment of consciousness (sometimes progressing to stupor and coma), focal or bilateral neurological symptoms and signs, and often an increase in seizure frequency [8]. The differentiation from prolonged postictal states or non-convulsive SE can be challenging, especially without access to EEG. In all our patients, we observed a significant clinical deterioration after the first administration of VPA. Case 2 demonstrates that VE can also occur with rapid oral VPA titration. Switching from VPA to a different antiepileptic drug resulted in prompt improvement (although case 3 deteriorated due to septicemia). As described previously, the EEG in our patients was characterised by (reversible) generalised slow activity and increased epileptiform discharges (Figure 1) [8]. The difficult differential diagnosis suggests that VE is probably under-recognised, especially in patients with pre-existing brain disorders. Patients with age-related metabolic changes (age range: 71–89 years in our patients), cognitive decline and other disturbances of brain function (e.g. vascular leukoencephalopathy) may be at particular risk of VE.

For further discussion of pathophysiological aspects of VE see Appendix 2 in the supplementary data on the journal website (http://www.ageing.oxfordjournals.org/)

Key points

- Older people are at risk of CNS toxic effects of valproate (VPA).
- Critically ill older patients with symptomatic epilepsy treated with rapid loading of VPA may be more prone to developing valproate encephalopathy (VE).
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- VE may be more common in older patients than previously thought.

Conflict of interest
None

References
The list of 30 references supporting this article has meant that only the most important are listed here and are represented by bold type throughout the text. The full list of references is available on the journal website (http://www.ageing.oxfordjournals.org/) as Appendix 3.


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Ablation of supraventricular tachycardia in a 96 year old

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Abstract
Atrioventricular nodal re-entrant tachycardia (AVNRT) is a common arrhythmia that is frequently encountered in clinical practice. Though more common in the younger population, it affects individuals of all ages. The elderly in particular are usually more symptomatic and more frequently require emergency treatment including urgent hospital admissions. We report on a 96-year-old lady who presented with troublesome supraventricular tachycardia that was difficult to control with drug treatment. Electrophysiologic testing revealed AVNRT that was ablated successfully using the standard technique with no complications. She continued to do well at follow-up 1 month after the ablation. This case highlights the need to routinely offer this highly effective technique as the first-line treatment to the elderly along the same indications as those commonly observed among younger patients.

Keywords: AVNRT, ablation, elderly