CASE REPORT

Sodium valproate-related hyperammonaemic encephalopathy

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SUMMARY

A 59-year-old man with a background of poststroke epilepsy, lung cancer, chronic obstructive pulmonary disease and hypertension, presented to the medical assessment unit with acute confusion and altered consciousness. Medications included sodium valproate, aspirin and antihypertensives. On examination he was confused, with his Glasgow Coma Scale fluctuating between 10 and 14. Routine blood tests, thyroid function tests, serum sodium valproate level, urine dip, CT of the brain and cerebrospinal fluid analysis were all normal. EEG revealed changes consistent with an encephalopathic process. Serum ammonia was elevated (75 µg/dL), consistent with a diagnosis of valproate-related hyperammonaemic encephalopathy. Sodium valproate was changed to a different antiepileptic drug and his confusion gradually resolved. Valproate-related hyperammonaemic encephalopathy is a treatable condition which should be considered as a diagnosis in anyone taking sodium valproate with new onset confusion, even in the presence of therapeutic sodium valproate levels and normal liver function tests.

BACKGROUND

Sodium valproate is a commonly prescribed medication used to treat epilepsy, mood disorders and migraine. This case is an important reminder of the mechanism of sodium valproate-associated encephalopathy and highlights that normal valproate levels do not exclude this diagnosis. A failure to appreciate this leads to a delay in the recognition and treatment of this potentially life-threatening condition.

CASE PRESENTATION

A 59-year-old man was admitted to the medical assessment unit with acute confusion and drowsiness. On the day prior to admission, he was reported to be his usual self and there was no history of cognitive impairment. He denied any systemic symptoms on systems review. In particular, there was no history of recent seizures, urinary incontinence, tongue biting or falls.

He had a medical history of poststroke epilepsy, lung cancer (resected), chronic obstructive pulmonary disease and hypertension. His medications included sodium valproate, aspirin, antihypertensives and inhalers.

He drank 40 units of alcohol per week and was an ex-smoker. Following his stroke, he had carers twice daily.

On examination his Glasgow Coma Scale fluctuated between 10 and 14, and he scored 3/10 on the Abbreviated Mini Mental State Examination. He was

afebrile and observations were within normal limits. There were no new neurological signs and the rest of the routine examination was unremarkable.

INVESTIGATIONS

Full blood count, U+Es, liver function tests and C reactive protein were normal. Sodium valproate level was in the therapeutic range at 85 mg/L (normal 50–100 mg/L). A urine dip and chest X-ray were normal. A CT of the brain showed an old ischaemic infarct, but no acute changes.

After ruling out infective and structural cerebral causes of confusion (eg, metastasis or a subdural haemorrhage), the working diagnosis was a possible postictal state.

After 72 h, however, there had been no improvement in the confusion. A lumbar puncture and EEG were then carried out to look for evidence of encephalitis and non-convulsive status epilepticus, respectively.

Cerebrospinal fluid constituents, including cytology were normal. The EEG was reported to be a diffusely slow recording in keeping with an encephalopathic process, with no evidence of epileptiform activity.

The patient was then discussed with a neurologist, who advised to check the ammonia level to look for evidence of valproate-induced hyperammonaemia. This was raised at 75 µg/dL (normal 15–45).

TREATMENT

Sodium valproate was stopped and replaced with levetiracetam.

OUTCOME AND FOLLOW-UP

After a few days of stopping sodium valproate, the confusion resolved and the patient was discharged back home.

DISCUSSION

Sodium valproate is a commonly prescribed drug used to treat epilepsy, mood disorders and migraine. Hyperammonaemia has been reported to occur in 27% of patients taking sodium valproate, many of whom are asymptomatic.¹

When encephalopathy develops, coma and death may ensue if the cause is not recognised and valproate stopped.

The condition may potentially be exacerbated if the confusion is misdiagnosed as a postictal state and the sodium valproate dose subsequently increased.

The exact mechanism by which valproate may cause high serum ammonia has not been fully

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elucidated but it has been reported that there is a positive correlation between the dose of valproate and the development of hyperammonaemia and also between plasma levels of sodium valproate and ammonia.²

Importantly, however, there are also reports of hyperammonaemia occurring in the presence of normal valproate levels,³ as was the case with our patient.

It is also important to highlight that hyperammonaemia related to sodium valproate may occur with normal liver

function tests thus the mechanism does not appear to be related to hepatotoxicity.⁴

In summary, valproate-associated hyperammonaemic encephalopathy is a serious, yet easily treatable condition. It is therefore important to check the serum ammonia level in anyone taking sodium valproate who presents with an alteration in behaviour or consciousness.

Contributors EJP wrote the article, which was reviewed by FZ.

Competing interests None.

Patient consent Obtained.

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Learning points

- ▶ A normal sodium valproate level does not exclude sodium valproate-associated encephalopathy.
- ▶ Ammonia levels should be checked in anyone taking sodium valproate with an altered mental state.
- ▶ Hyperammonaemia can occur despite normal liver function tests.

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