Non-Hyperammonaemic Valproate Encephalopathy

Ged Hawthorn (Senior Clinical Pharmacist)
Orange Health Service

Objective:
To report a rare and atypical presentation of valproate induced non-hyperammonaemic encephalopathy.

Clinical Features:
A 72yr old female presented to ED with increasingly erratic behaviour, decreased level of consciousness, hypothermia and seizures. Past medical history included bipolar disorder, hyperthyroidism, and a resting tremor.

Current Medications:
The Patients husband had been administering additional valproate 500mg doses on top of her 1g bd usual regimen to “calm her down”.

Case Progress:
The Patient was intubated and transferred to ICU. She was worked up for infective and neurological causes. The pharmacist suggested the possibility of valproate hyperammonaemic encephalopathy. Valproate was ceased and an ammonia level was taken which returned within limits. She was slow to wake, had persistent motor weakness, was not following commands and remained intubated on nil sedation days 1-5.

Cultures/Pathology
LP, Blood- Nil growth
Valproate Level= 107 mg/L (high)
Ammonia Level= 29 micromoles/L (within Range)
LFTs- Within range
Carnitine Levels- Low with non-specific abnormalities not consistent with inborn error.

Interventions:
The pharmacist conducted a literature search and proposed that a carnitine deficiency could be causing a shift in metabolism of valproate from mitochondrial beta oxidation to cytoplasmic reticulum omega oxidation, resulting in accumulation of neurotoxic 4-en-VPA. Carnitine IV supplementation was commenced on Day 5.

EEG- Generalised slow wave activity consistent with encephalopathy. No epileptiform activity.

Outcomes:
The patient was extubated on day 6, 1 day after commencement of carnitine. GCS was 15 and she was transferred to the ward. Carnitine levels returned later confirming a carnitine deficiency.

Conclusion:
This case demonstrates the value of the pharmacist in highlighting atypical medication related causes of admission. Appropriate withdrawal of the implicating agent and adequate treatment resulted in a quick resolution of the symptoms.

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