



Is My Medication the Culprit of My Confusion – Valproic acid Induced Hyperammonemic Encephalopathy

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INTRODUCTION

- ❖ Valproic acid (VPA) is used as an anticonvulsant, and as a mood stabilizer in bipolar and psychotic disorder. Therapeutic plasma levels are between 45 and 125 ug/ml.
- ❖ VPA-induced hyperammonemic encephalopathy (VHE) is a rare but possibly fatal adverse event, characterized by impaired cognition, lethargy, impaired consciousness, and apathy.
- ❖ It can occur shortly after initiation of VPA or even in those who have been on long-term VPA.

CASE PRESENTATION

- ❖ A 64-year-old man with history of seizure disorder on chronic sodium valproate therapy, 1250mg twice daily, was admitted to our hospital for altered mental status.
- ❖ He was hemodynamically stable and physical examination including neurological examination was unremarkable, except for Glasgow Coma Scale score of six.
- ❖ CT head did not reveal any intracranial abnormalities. CBC, CMP, lactic acid were within normal limits.
- ❖ UA was positive for a UTI, and patient was started on IV antibiotics.

HOSPITAL COURSE & MANAGEMENT

- ❖ Despite completion of appropriate treatment for UTI, patient remained encephalopathic.
- ❖ This prompted further work up including urine toxicologic screening, lumbar puncture, and ammonia level. The results were within normal limits, except for an elevated plasma ammonia level at 93 umol/L.
- ❖ EEG was negative for subclinical seizure activity.
- ❖ There was no history of liver disease, malignancy, or alcohol use disorder in this patient.
- ❖ Lactulose was administered, however patient did not have adequate bowel movements and his ammonia level continued to remain elevated.

DIAGNOSIS

- ❖ After ruling out other potential contributing factors of acute encephalopathy and hyperammonemia, VHE was suspected although VPA level was within therapeutic range.
- ❖ Given the diagnosis, VPA was promptly discontinued and substituted with levetiracetam. Patient also received 3 doses of 0.4 mg intravenous naloxone over the course of 4 days.
- ❖ His ammonia levels declined rapidly to 42 umol/L and his mental status showed improvement.

DISCUSSION

- ❖ In the light of this case, we illustrate the possibility of developing VHE in a patient who has been on chronic VPA and the consideration of naloxone in treating VHE.
- ❖ The mechanism of action of naloxone in treating VHE is unclear, but postulated to be related to gamma-aminobutyric acid (GABA) antagonistic effects and reversal of central nervous system depression.

CONCLUSION

- ❖ Ammonia levels should be checked in patients on VPA therapy who develop new onset of neurologic symptoms.
- ❖ Physicians must be aware of this rare idiosyncratic reaction as it can occur when the VPA level is within the reference range and with normal liver enzyme levels.
- ❖ Adjustment of dose or withdrawal of VPA may be necessary.
- ❖ Naloxone could be an effective therapy and should be considered for the management of VHE.