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VALPROATE INDUCED CEREBELLAR SYNDROME

Psychiatry

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ABSTRACT

Valproate-induced hyperammonemic encephalopathy is a rare event clinically characterized by altered sensorium, vomiting, headache, irritability and focal neurological deficits. The pathogenesis of this dreadful complication is not well understood, although hyperammonemia has been implicated in causation of encephalopathy. In this case report, we bring to light a case of valproate-induced encephalopathy who presented mainly with difficulty in walking and speech, body tremelousness. High index of suspicion of valproate-induced hyperammonemic encephalopathy is required if diffuse ataxia is present as it is a potentially reversible clinical disorder.

KEYWORDS

Encephalopathy, hyperammonemia, cerebellar syndrome

INTRODUCTION

Sodium valproate is a commonly used drug for the treatment of seizure disorders, migraine, bipolar disease and chronic pain. It is known to cause a serious complication, hyperammonemic encephalopathy which is characterized by acute onset of impaired consciousness, confusion, headache, vomiting, seizures, ataxia.[1] In this submission, we present a case of valproate-induced hyperammonemic encephalopathy where the clinical presentation was restricted to cerebellar clinical features.

CASE REPORT

A 25-year-old male presented with acute onset tremulousness, confusion difficulty in walking and speech. He was a known case of Bipolar Disorder treated initially with Lithium (900 mg/day) and recently switched over to sodium valproate (1000 mg/day) before the onset of this acute complication. The general examination revealed normal vitals with presence of asterixis. The patient showed bilateral cerebellar signs in the form of defective coordination in both upper and lower limbs with difficulty in walking and slurring of speech. The motor and sensory examination, and deep tendon reflexes were normal.

Investigations including hemogram, liver function tests, renal function parameters, serum electrolytes and blood sugar showed normal results. Thyroid function tests (T3, T4, Thyroid stimulating hormone) and nutritional parameters including vitamin B12 levels were also found in normal range. However, serum ammonia level was raised to 111 μmol/L (normal range 12-47 μmol/L). The levels of serum valproate and carbamazepine were found to be in the normal range (serum valproate: 60 ug/mL [range: 50 to 100 μgm/mL] and serum lithium levels after discontinuation of lithium<0.5 μgm/mL [range: 0.5 to 1.5 μgm/mL]). Electroencephalography revealed generalized slowing in delta range suggestive of encephalopathy [Figure 1]. Patient underwent magnetic resonance imaging of cranium, which turned out to be normal. With this background of clinical observations and laboratory assessment, a diagnosis of valproate-induced hyperammonemic encephalopathy was considered. The valproate was replaced by Oxcarbamazepine (300mg) two times a day along with carnitine supplementation. The patient showed rapid recovery and was able to walk independently after a week. His serum ammonia level normalized on repeat serum ammonia estimation (20 μmol/L).

DISCUSSION

The symptoms of hyperammonemia are difficult to be recognized in psychiatric patients owing to their comorbid condition. It is suggested that patients taking valproic acid should be closely monitored for mental status changes,confusion, focal neurologic deficits,delirium and this monitoring can help in early detection of encephalopathic changes.[2]

Ammonia levels and drug levels should be checked immediately if a patient develops lethargy or any neurological symptoms. Ammonia levels are best monitored in the blood, while Valproic acid levels can be best monitored in saliva, so both levels are closely checked timely.[3] Although valproate-induced hepatic dysfunction is a well known clinical entity, less commonly the drug can also produce an encephalopathy of non-hepatic origin by producing hyperammonemia, and is called as valproate-induced non-hepatic hyperammonemic encephalopathy.[4]

Other causes of non-hepatic hyperammonemia include recent drugs intake including 5-FU, asparaginase and enflurane, hematologic diseases like multiple myeloma and acute myeloblastic leukemia,disorders of pancreas including hyperinsulinemia, hyperglycemia, distal renal tubular acidosis and total parenteral nutrition.[5]

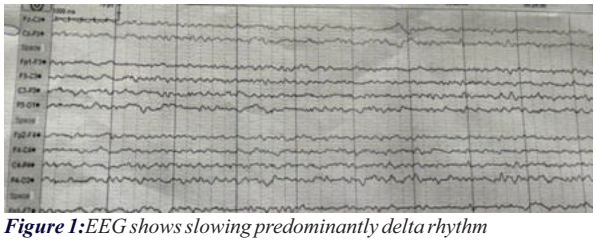

Figure 1:*EEG shows slowing predominantly delta rhythm*

CONCLUSION

Hyperammonemia with encephalopathy is a rare side effect of valproic acid toxication that carries a risk of high mortality. Rising ammonia levels can be asymptomatic most of the time but may give rise to symptoms ranging from mild confusion to coma and death. We conclude that valproic acid should be stopped immediately with the increase in ammonia levels in patients taking valproic acid, and also physicians and psychiatrist should be vigilant of the past history and ongoing current medications of the patient. Patient medication lists should be reviewed for drug interactions causing high ammonia. Doctors prescribing valproic acid should closely monitor the mental status in patients taking valproic acid to reduce mortality.

REFERENCES

1. Stahl SM. Prescriber's Guide: Stahl's Essential Psychopharmacology [Internet]. 7th ed. Cambridge University Press; 2020
2. Dreifuss FE, Langer DH. Side effects of valproate. The American journal of medicine. 1988; 84 (1) : 34-41 .
3. M, Fagiolino P, Maldonado C, et al. Hyperammonemia associated with valproic acid concentrations. Biomed Res Int. 2014; 2014 : 217269 .
4. Segura-Bruna N, Rodriguez-Campello A, Puente V, Roquer J. Valproate-induced hyperammonemic encephalopathy. *Acta Neurol Scand.* 2006;114:1–7.
5. Alqahtani S, Federico P, Myers RP. A case of valproate-induced hyperammonemic encephalopathy: Look beyond the liver. *CMAJ.* 2007;177:568–9.