

CASE REPORT**VALPROATE INDUCED HYPERAMMONEMIC ENCEPHALOPATHY**

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Valproate is a commonly prescribed anticonvulsant drug. It has a potential to cause hyperammonemia even in the presence of normal liver function tests. This hyperammonemic state can lead to encephalopathy referred as Valproate induced hyperammonemic encephalopathy (VHE). Here we present a case of valproate induced hyperammonemic encephalopathy in a young male caused by initiation of valproate therapy.

Keywords: Neurology; Valproate; Encephalopathy

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INTRODUCTION

Sodium valproate is a widely used drug used for epilepsy, bipolar disorder and migraines. Hyperammonemic encephalopathy (VHE) is one of the rare adverse effects of valproate. In literature, it is usually described in context of underlying liver disease or urea cycle disorders. However, it can present in the absence of any underlying pathology even with normal serum valproate levels. It typically presents with symptoms of encephalopathy characterized by altered sensorium, lethargy, vomiting, increase frequency of seizures and variable neurological deficit. Up to 50% cases can be asymptomatic.¹

Treatment for valproate induced encephalopathy is mainly supportive along with withholding valproate. The aim is to reduce ammonia production by stopping catabolism. Protein diet restriction and L-carnitine use can be useful. Ammonia level greater than 4 times the upper limit of normal is an indication for hemodialysis.^{2,3} Here we present a case of hyperammonemia encephalopathy in a young male.

CASE REPORT

Seventeen years old male patient who was a known epileptic for the last two years, presented with decreased level of consciousness.

He had his first episode of generalized tonic clonic seizure at the age of 15, since that, he was taking levetiracetam. He remained fit free on this treatment for two years. One month prior to presentation, his medication was switched to sodium valproate by General practitioner. After the start of sodium valproate, he remained well for one week but later his condition started to deteriorate. He developed multiple episodes of vomiting, changes in sleep pattern, fluctuating level consciousness and

low-grade fever, along with an increase in frequency of seizure and was brought to the emergency department. On arrival he was vitally stable except temperature of 100 F. He was confused and drowsy but arousable to verbal command and planters' response were bilaterally upgoing.

His family history was positive for epilepsy with two of his siblings being diagnosed with the same condition. One of his brothers had died due to status epilepticus.

On initial lab work up all base line investigations including Complete Blood Picture, C-Reactive Protein, Liver Function Tests Renal Profile were in normal limits. Serum valproate level was within therapeutic range. MRI brain with contrast revealed no abnormality. CSF analysis was also normal. EEG showed recurrent generalized interictal epileptiform discharges in the form of spike and sharp waves with intermixed theta range slowing. Keeping in view the normal biochemical profile in the setting of clinical encephalopathy along with positive EEG findings, valproate induce encephalopathy was considered for which serum ammonia levels were sent. They were raised more than two times upper limit of normal. Sodium Valproate was stopped and he was given phenytoin and leveracetam for seizure control. Along with supportive treatment, dietary protein restriction, Intravenous dextrose, the patient was also started on L-carnitine. He started showing gradual clinical improvement, his ammonia levels also started declining. After 3 weeks his ammonia levels normalized and he regained his prior functional status.

DISCUSSION

Literature review suggests that VHE may not be as rare as we see in our clinical settings. Suhal Shah *et al.*, described VHE in a middle aged female who was

started on valproate therapy for bipolar disorder.⁴ A study on 347 patients who were taking valproate for mood stabilization, described hyperammonemia in 36% of patients. 43.2% patients were symptomatic and valproate discontinuation normalized ammonia levels in most patients.⁵ In another study, dose-dependent association between valproate and blood ammonia level was described in 55% cases taking valproate for some reason.⁶

Although its pathogenesis is not completely understood yet hyperammonemia is the main cause of encephalopathy. Multiple risk factors have been proposed that includes simultaneous topiramate therapy, dietary factors like excessive protein intake, urea cycle defect. It may be acute or subacute. In our case, it was subacute picture we couldn't elaborate the underlying genetic disorder (if any) due to limited lab facilities in our setup. Furthermore, among urea cycle defect, ornithine transcarbamylase (OTC) deficiency is the most common cause of hyperammonemia. It is X linked recessive disorder so unlikely to be present in adult males with negative family history.^{2,5}

Treatment aims towards reducing ammonia production along with withholding valproate. Dietary protein restriction and fulfilling caloric requirement by intravenous glucose and lipids is done. Hemodialysis is recommended in case where Ammonia is more than 4 times upper normal limit.⁵

In our patient, we conservatively managed the patient with IV dextrose, L carnitine, protein restriction initially then its reintroduction as per

dietician guide. In our case serum ammonia was not that high to warrant hemodialysis. Although his recovery was slow yet complete.

CONCLUSION

VHE is a rare however can have fatal outcome if not recognized and managed in time. Physician should be vigilant while initiating Valproate therapy to patient. Any sudden change in mental status after it, should raise the suspicion of VIH in order to provide a timely diagnosis and management.

Authors Contribution:

All authors contributed equally to the case report.

Conflict of interest:

Nil

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