A Case of Unusual Cause of Ataxia in a Child with Seizure Disorder

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Introduction

Ataxia is defined as an inability to coordinate voluntary muscular movements, a neurological symptom that can be seen in a myriad of diseases and condition such as postinfectious sequelae in chickenpox.\textsuperscript{2} Drugs such as phenytoin, valproate, thallium, metabolic causes abetalipoproteinemia, Hartnup disease and degenerative causes like ataxia telangiectasia, spinocerebellar ataxia and Friedreich ataxia.\textsuperscript{3} In this report, we highlight a case of sudden onset of diffuse ataxia in 13yr old female child who presented with breakthrough seizure while EEG being normal.

Case Report

A 13yr old female child who is a known case seizure disorder with was brought to the hospital with complaint of breakthrough seizures while on valproate medication. The dose of the valproate was increased and subsequently tablet clobazam was added and admitted in intensive care unit for observation. Next day, on general examination, the child presented with normal vitals but showed bilateral cerebellar signs in the form of defective coordination of upper and lower limbs in the form diffuse ataxia and with scanning speech. Initial investigations were normal and subsequently MRI was advised which showed focal nodular lesion on left periventricular region in left frontal lobe suggestive of heterotopia and Electroencephalography was normal. The child continued to have ataxia and recurrence of seizure on day 3 of admission for which serum ammonia was sent in suspicion of drug induced ataxia and was found to be high 135 microgram/dl (normal:10-80 microgram/dl). With this background of clinical and laboratory assessment a diagnosis of valproate induced hyperammonemia was considered. With continued seizure activity and acute complication of ataxia, valproate was replaced by oral lacosamide 50 mg/day along with tablet clobazam and carnitine supplementation. The patient showed gradual improvement in gait and speech over 2 to 3 days.

Discussion

Ataxia is defined as impaired coordination of voluntary muscle movement, it is a physical finding not a disease and has varied causes such as postinfectious sequelae of infections like varicella zoster virus, Toxoplasmosis, Ebstein barr virus. Metabolic causes are abetalipoproteinemia, Hartnup disease, refsum disease.\textsuperscript{4} Degenerative causes are ataxia telangiectasia, Friedreich ataxia and...
spino-cerebellar ataxia. Drugs like valproate, phenytoin and thallium are other cause. Valproic acid has a broad spectrum use in treating epilepsy, bipolar disorders, prophylaxis and treatment of migraine and neuropathic pain. Although valproate induced hepatic dysfunction leading to encephalopathy is well known entity, less commonly the drug can cause hyperammonemia through nonhepatic origin called as valproate induced non hepatic hyperammonemic encephalopathy.

Valproic acid causes hyperammonemia by following mechanisms 1) valproic acid undergoes omega oxidation and forms 4en valproic acid which inhibits carbamoyl phosphate synthetase I, a key enzyme in urea cycle 2) decreased production of mitochondrial acetyl coA which decreases N-acetylglutamate, an activator of carbamoyl phosphate synthetase I. The increased retention of ammonia leads to acute complication of drowsiness, scanned speech with reversible ataxia. Hyperammonemia induces activation of astrocytes thereby causing cerebral edema and neuroinflammation which leads to increased expression of GABA transporter GAT-3 mainly in astrocytes which in turn increases GABAergic tone and causes cognitive impairment. The clinical spectrum of hyperammonemia constitutes irritability, drowsiness, coma and occasionally paradoxical seizures with cerebellar signs. Discontinuing the drug reverses the ataxia gradually over a period of 2 to 3 days and supplementation with carnitine shifts the metabolism of valproate towards beta oxidation, resulting in less production of toxic metabolites via omega oxidation.

**Conclusion**

In light of this case report, we hereby conclude that blood ammonia levels must be monitored in patients who develop new onset neurological symptoms lethargy, impaired consciousness, cerebellar signs like gait ataxia with gastrointestinal symptom vomiting and abdominal pain while on valproate as it can lead to hyperammonemia encephalopathy and cerebellar signs even when liver function test are normal. High index of suspicion of valproate induced hyperammonemic encephalopathy is required if ataxia is present as it is a potentially reversible clinical disorder. Hence length of valproate along with its dosage and serum levels of valproate and ammonia do not correlate with onset and severity of valproate induced encephalopathy. Although L-carnitine, lactulose and neomycin have been used adjunctively in some patients, discontinuation of valproate remains the mainstay of treatment.

**End Note**

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**References**