“Reversible Leigh’s-like Brain Abnormalities with Vigabatrin”- A Case Series

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Introduction

Vigabatrin, used for epileptic spasms and refractory epilepsy, is an irreversible inhibitor of γ-aminobutyric acid (GABA) trans- aminase, are thought to emerge from increased levels of GABA.

Significant adverse effects are visual field defects, movement abnormalities and rare cases can have Vigabatrin-associated brain abnormalities on magnetic resonance imaging (VABAM)

Objective

To describe the occurrence of Vigabatrin associated brain abnormalities on MRI in two children receiving combination therapy with oral steroids and Vigabatri

Methods

A case series of two cases of VABAM who presented to pediatric neurology OPD of a tertiary care centre

Results

Case 1: A 5 months-old girl, with epileptic spasms, was treated with synthetic adrenocorticotropic hormone, Clonazepam and Levetiracetam. Due to poor response, she received oral Prednisolone (2mg/kg/day body weight), and Vigabatrin (100 mg/kg/day). Three weeks later, she developed excessive sleepiness and dull activity.

Case 2: A 6.5 months-old female presented with global developmental delay, epileptic spasms, cerebral vision impairment. The spasms were controlled within a week with the combination therapy of oral prednisolone (3mg/kg/day) and Vigabatrin (130mg/kg/day), but within 3 weeks child showed neuroregression with encephalopathy, poor feeding, choreiform movements and oromandibular and appendicular dystonia.

Etiological Workup

The etiology of epileptic spasms was cryptogenic for case 1 as whole exome sequencing was unremarkable.

Case 2 revealed pathogenic heterozygous (X-linked) missense variation in ALG13 (X-linked developmental and epileptic encephalopathy)

MRI Changes

In both the cases, neuroimaging (MRI) in acute stage showed changes in globi pallidi, thalami, hypothalamus, and brain stem.

Vigabatrin was stopped immediately after suspecting VABAM.

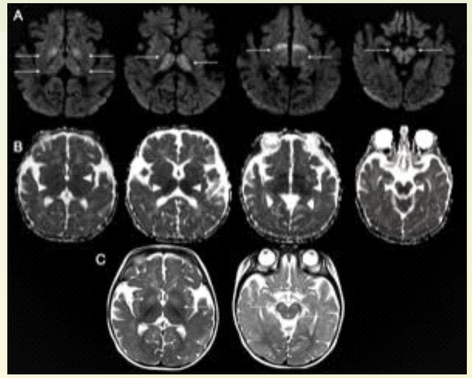

Figure 1. Age of six months on vigabatrin for three weeks (100 mg/kg/d): DWI sequence (A) shows increased signal and ADC sequence (B) shows restricted diffusion in globi pallidi, thalami, hypothalamus, and midbrain. T2 axial with signal changes in the globi pallidi and midbrain (arrows) and faint but apparent high signal changes in the thalami.

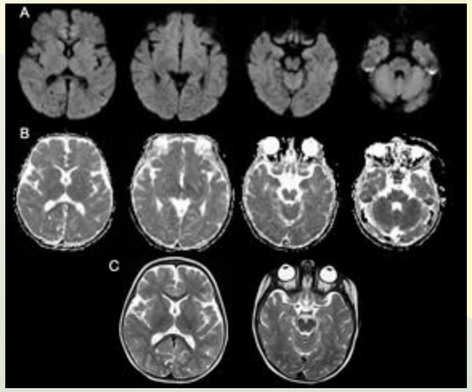

Figure 2 : Age of sixteen months, off vigabatrin for ten months: DWI (A) and ADC (B) shows a complete reversal of the cytotoxic edema and restricted diffusion changes in the globi pallidi, thalami, hypothalamus, and midbrain.

© T2 axial images shows an age-appropriate normal appearance with complete resolution of the high signal changes previously seen in the globi pallidi, thalami, hypothalamus, and midbrain

Follow up

The encephalopathy and movement abnormalities resolved over 3-4 weeks in both children. Complete resolution on follow-up imaging, is highly suggestive of Vigabatrin-associated brain abnormalities on MRI (VABAM)

Discussion

- Incidence : 21-34%
- The pathophysiology of VABAM is unknown.
- Sustained, high-dose VGB induces reversible intramyelinic edema and microvacuolation in brain white matter, thalamus, deep cerebellar nuclei, and brainstem in rodents and dogs.
- In human infants, reported with higher peak and average doses, can occur with usual therapeutic doses also.
- Risk factors include age younger than 12 months, presence of cryptogenic epileptic spasms, concomitant hormonal therapy
- VABAM, clinically can be symptomatic or asymptomatic.
- Symptomatic VABAM presents with movement disorders (including choreoathetosis, myoclonus, titubation, abnormal eye movements, dystonia, opisthotonos, and tremor), dysautonomia (including bradycardia and respiratory arrest), and acute encephalopathy.
- The MRI changes seen in basal ganglia (globi pallidi), brainstem (dorsal midbrain, medial longitudinal fasciculi, pons), thalami and dentate nuclei, as well as hypothalamus and the corpus callosum.
- Diffusion weighted imaging more sensitive than T2W for VABAM
- Mostly (88%) partially or completely reversed on cessation or dose reduction of VGB.
- VGB-HT (vigabatrin with hormonal therapy) leads to fulminant symptomatic VABAM. The temporal association of clinical deterioration with onset of combination therapy suggests possible potentiation of VGB toxicity when used in combination with hormonal therapy.

Conclusion

Toxicity of Vigabatrin (VABAM) mimics Leigh’s disease radiologically and clinically (neuro regression), and is reversible

References

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