Indian J Pharmacol. 2013 Nov-Dec; 45(6): 636–637. PMCID: PMC3847262
doi: 10.4103/0253-7613.121388

Phenytoin-induced cerebellar atrophy in an epileptic boy

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Received 2013 Apr 16; Revised 2013 Jun 7; Accepted 2013 Aug 6.

Abstract

Epilepsy is an important health problem due to its high prevalence and potential for causing long-term morbidity. It is commonly treated in children with phenytoin sodium. It has wide pharmacokinetic variability and a narrow therapeutic range that leads to toxicity. Here, we report a case of phenytoin-induced cerebellar atrophy in a 16-year-old epileptic boy who presented to the hospital with a viral infection.

KEY WORDS: Adverse drug reaction, antiepileptic drugs, antiseizure drugs, cerebellar atrophy, phenytoin

Introduction

Children constitute approximately 40% of India's population but information on adverse drug reactions occurring in them is limited.[1] Phenytoin sodium (PHT) is one of the commonest antiepileptic drug (AED) used in children in India.[2] The drug has wide pharmacokinetic variability and has a narrow therapeutic range that leads to toxicity. There is some evidence of the association of long-term use of PHT and toxicity like cerebellar atrophy. Such cerebellar changes have been reported even with the long-term use of nontoxic levels of phenytoin.[3] However, such reporting is very scarce in pediatric population. Here, we report a case of reversible cerebellar atrophy induced by PHT in a 10-year-old boy.

Case Report

A 16-year-old boy was admitted to the hospital with fever and weakness. His systemic examination was normal. His past history included history of seizure for the last 10 years. He was on oral PHT, 5 mg/kg daily once daily. After initiating therapy with PHT 10 years back, he was seizure free for 2 years. Then he started getting seizures that required adjustment in his medication. Patient was also occasionally prescribed clobazam, 5 mg, oral, as and when required. The episodes used to last for a brief period of over 6-7 days.

He would then be seizure free for the next 3-4 months. Seizures used to occur at every 3-4 months interval. The boy had history of birth asphyxia and delay in developmental milestones. His previous MRI scans of brain revealed no abnormality. There was no family history of seizure. The boy was managed conservatively for viral fever. After the patient recovered, he was evaluated again due to complaint of difficulty in walking. CNS examination revealed normal mentation with cerebellar signs including gaze-evoked nystagamus, truncal, and appendicular ataxia. MRI scan of the brain was advised and it showed cerebellar atrophy as shown in Figure 1. The patient had no other neurological and other systemic problems other than epilepsy. Serum phenytoin level was high (30 mcg/ml) and PHT was withdrawn immediately. Patient was started on valproic acid and followed up. The causality assessment was done using the Naranjo scale.[4] The causal analysis showed a probable association of the ADR with phenytoin.

Discussion

Epilepsy is a common neurological disorder that is managed with antiepileptic drugs. PHT is one of the commonest and the first line antiepileptic drug. PHT is used in both generalized and partial epilepsies and avoided in myoclonic epilepsy. This drug is generally safe and is commonly used throughout the world. However, a sizeable proportion of patients may develop drug induced adverse effects that include sedation, gum hypertrophy, lymphadenopathy, chorea, ataxia, etc.[5,6] There are a few reports on cerebellar atrophy after long-term use of PTH. These adverse effects are usually reported if the drug serum levels are above the therapeutic range. They have also been reported if the drug level is within the normal range.[7,8] These effects are, however, reversible on reducing the dose of PHT.[2] Our patient presented with severe cerebellar disorder and he was on the drug for 10 years. But he started recovering steadily after withdrawing the drug. Hence, a regular monitoring for adverse drug reaction should be considered in patients who are on drugs on long term basis. These reactions could be idiosyncratic or dose-dependent which again may be acute or chronic in nature. Since most of these effects are reversible, it is important to identify the clinical manifestations related to drug toxicity and to manage them appropriately. Also, it warns the need for regular monitoring of plasma concentration, accurate dosing, and identification of adherence issues in patients on phenytoin.

Footnotes

Source of Support: Nil

Conflict of Interest: None declared

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Axial T1 image of brain showing bilateral cerebellar atrophy in an epileptic boy on phenytoin