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Case Report

A rare case of phenytoin-induced cerebellar atrophy

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ABSTRACT

Epilepsy is a common health problem and affects humans of any age. Phenytoin is indicated in all types of seizure except in absence epilepsy. It has a wide range of pharmacokinetic properties with a narrow therapeutic range thus often leading to toxicity. Long-term neurological side effects of phenytoin include cerebellar atrophy. Therefore, monitoring of plasma levels should be done in patients on long-term phenytoin. Here, we describe a case of cerebellar degeneration in a post-operated brain abscess patient on chronic phenytoin therapy.

Keywords: Epilepsy, Phenytoin, Toxicity cerebellar atrophy

INTRODUCTION

Epilepsy is a common neurological disease with a high prevalence of more than 10 million India.[1] Phenytoin is a widely prescribed anticonvulsant used in patients of all age groups for treatment and prevention of various types of epilepsy and status epilepticus, except for absence seizures. Acute intoxication of phenytoin causes encephalopathy and ataxia, whereas chronic intake of phenytoin is a known cause of cerebellar atrophy.[2]

CASE REPORT

A 30-year-old male patient with a history of brain abscess at left parietal lobe, operated 15 years back with residual right hemiparesis, now presents with 3 years of progressive imbalance and slurring of speech.

On examination, the patient was conscious, oriented, and unable to stand without support. There was gaze evoked nystagmus, scanning cerebral speech. No other cranial nerves were involved. On motor examination, there was mild hypotonia, reduced power of both upper limb and lower limb of right side 4–/5. The right-sided reflexes were brisk and the right plantar response was extensor. Cerebellar signs were positive in the upper limb and lower limb. Thus, the possibility of pancerebellar involvement was considered.

The patient was on phenytoin sodium 100 mg TID for the past 15 years. His seizures were well controlled. Hence, the possibility of phenytoin-induced ataxia was considered. All routine tests were normal. The patient was evaluated with magnetic resonance imaging brain which showed diffuse cerebellar atrophy [Figures 1 and 2]. Serum phenytoin levels were >60 mg/mL. Hence, the possibility of phenytoin-induced cerebellar degeneration was considered.

Phenytoin dose was then tapered gradually. Levetiracetam was introduced for prevention of seizures. Serum phenytoin level became normal. The patient was followed up after 3 months. Ataxia was mildly reduced which shows permanent degeneration of cerebellum due to chronic phenytoin toxicity.

DISCUSSION

Phenytoin, formerly known as diphenylhydantoin, is a potent anticonvulsant used to treat and prevent generalized tonic-clonic seizures, complex partial seizures, and status epilepticus. Phenytoin was formerly the most commonly used anticonvulsant agent, but it is getting replaced by better tolerated newer agents.[3] Phenytoin which was synthesized in 1908 as a barbiturate analog does not cause central nervous system depression; rather, it may produce excitement and muscular rigidity in toxic levels. Antiepileptic effect is due to the slowing of recovery rate of inactivated voltage sensitive neuronal Na+ channels thus limiting repetitive action potential firing.[4] Plasma levels of phenytoin vary when changing from rapid release tablets to extended release form or from parenteral to oral form; thus, frequent blood level monitoring is needed.[4]

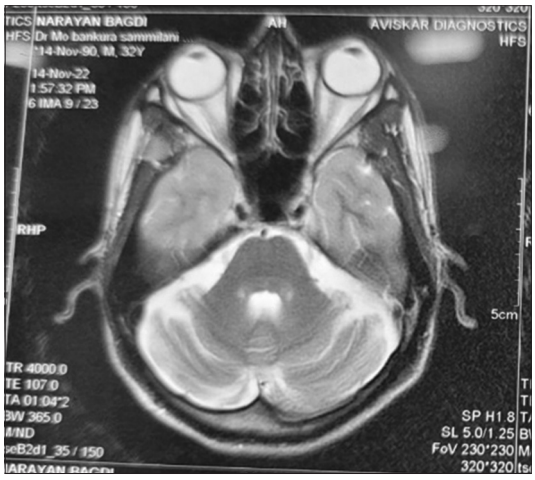

Figure 1: T2 Weighted Axial view showing prominent cerebellar atrophy.

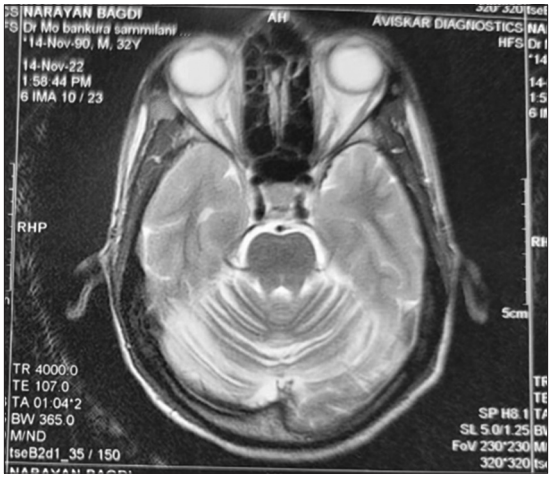

Figure 2: Magnetic resonance imaging T2-weighted image showing gross cerebellar atrophy.

Studies and case reports showing cerebellar atrophy after long-term use of phenytoin are published before.[5,6] Long-term dose-dependent neurological side effects of phenytoin therapy are cerebellar atrophy, cerebral atrophy, and brain stem atrophy. Skull hyperostosis, gum hypertrophy, and megaloblastic anemia are other known effects of chronic phenytoin therapy.[2] Phenytoin itself may cause diffuse atrophy of Purkinje cells of the cerebellum[7] which is also seen in long-term non-toxic plasma levels of phenytoin.[8] Cerebellar atrophy in epileptic patients is also attributed to seizure-mediated cell loss secondary to hypoxic-ischemic injury.[9] Hence, the cumulative effect of hypoxia due to repeated seizures is an important cause of cerebellar degeneration.[5] Other differential diagnoses of cerebellar atrophy include alcoholic atrophy, multisystem atrophy, and Ataxia telangiectasia.[2] Magnetic resonance imaging (MRI) brain is the best investigation to look for cerebellar damage as evident from size of sulci and foliae.[10]

MRI of our case shows reduction in cerebellar volume and diffuse cerebellar atrophy.

CONCLUSION

Due to the narrow therapeutic range and several adverse effects of chronic phenytoin therapy, frequent monitoring of plasma drug levels should be done. Accurate dosing and early identification of toxicity is recommended.

Ethical approval

The research/study complied with the Helsinki Declaration of 1964.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the

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