Total external ophthalmoplegia induced by phenytoin: A case report and review of literature

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A 28-year-old male developed total external ophthalmoplegia following oral administration of phenytoin. The case is reported and its significance is discussed.

Key Words: External ophthalmoplegia, Phenytoin induced ophthalmoplegia, phenytoin toxicity.

Introduction

There have been imnumerable reports concerning phenytoin toxicity, but few have mentioned its effects on eye movements other than nystagmus.1 Ophthalmoplegia has been reported with administration of large doses of Phenytoin,2,3 Phenobar-

References


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bitone, Primodone, Carbamazepine and Amitriptyline. Spector et al[7] reported that phenytoin could induce total external ophthalmpoplegia irrespective of oral or intravenous administration. Incomplete[4] as well as complete ophthalmpoplegia[5] has been reported with phenytoin even within therapeutic range. We present a patient with phenytoin intoxication who developed disturbances in the ocular movements.

**Case Report**

A 28-year-old mentally retarded male, with IQ-55, had generalized tonic-clonic epilepsy for two years. He was placed on carbamazepine (Tegretol) 800mg per day. However, due to financial reasons, he was irregular with his treatment. Subsequently, he was placed on Diphenyl hydantoin (300mg per day). After about two weeks of the change in the drug treatment he reported inability to move his eyes. He denied excessive ingestion of the drug. The pupils were 5mm in diameter, round, equal and reacting well to light. The gaze was fixed directly forward. The patient did not move his eyes on command and could not follow the light. The eyes could not be moved by head turning or neck bending or by irrigation of the ears with ice water. Fundi were normal. The rest of the neurological examination was normal. The cerebrospinal fluid examination was normal. The CT of the head was normal. The phenytoin drug level was 22 microgm per ml. The phenytoin was withdrawn and he was given loading dose of phenobarbitone, followed by its maintenance dose. On the fifth day, he could move his eyes about 10° in horizontal (lateral and medially) but was unable to move them in the vertical direction. On the seventh day, the horizontal movements had improved and he could move the eyes slightly downward but not upward. Irrigation of the left ear with ice cold water produced no movements of the eyes but irrigation of right ear produced occasional nystagmus with fast component to the left. On the eleventh day his eye movements were normal. He was seizure-free on 120 mgm of phenobarbitone per day.

**Discussion**

Phenytoin is a vestibular depressant.[8] Spector et al[7] observed that the return of vestibulocular response in their patients with phenytoin intoxication lagged behind the return of consciousness and other reflex activities and attributed it to its depressant effect on the vestibuloocular system which may be out of proportion to its actions on other levels of the neuraxis. The oculomotor unresponsiveness to cold caloric irrigation may occur even when the blood phenytoin level is within the accepted therapeutic range.

GABA mediates the inhibition of oculomotor neurons produced by the vestibular system. Phenytoin increases the postsynaptic potentials produced by GABA in the cerebral cortex and the spinal cord. Spector et al[7] attributed the unresponsive cold caloric irrigation with phenytoin to an increased effectiveness of GABA-induced inhibition at the synapses of the vestibulo-ocular motor system. The lag in the recovery of the oculovestibular response in the present case could be explained with the above said hypothesis.

The cerebellum has an inhibitory role over the vestibulocular reflex through Purkinje cells. Phenytoin increases the rate of Purkinje cell discharge.[9] Whether this phenytoin-augmented Purkinje cell firing would act in a manner analogous to electric stimulation of the cerebellar cortex and result in the depression of transmission through the vestibular nucleus and affect the normal function of the vestibuloocular apparatus is unclear. The majority of the reported cases of phenytoin-induced ophthalmpoplegia recovered completely over a variable period with normalization of the phenytoin level.

The present case is unique; in spite of the drug toxicity the patient was alert and had bilateral external ophthalmpoplegia with loss of oculocephalic and oculovestibular reflexes. The recognition of this entity is important to avoid unnecessary investigations in a patient on phenytoin.

**References**


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**Calvarial malignant fibrous histiocytoma**


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