Acute visual dysfunction following Phenytoin induced Toxicity

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Abstract

Aim: Acute Visual Dysfunction may be caused by Acute Phenytoin Toxicity

Method: An 18 year old female with prior generalized tonic-clonic seizures developed blurred vision, diffuse corneal opacity (OD), and ankyloblepharon after Phenytoin administration for seizures. Colour vision was found to be normal with Ishihara pseudo-isochromatic charts and visual fields (Humphrey's automated perimeter) show gross concentric constriction in both eyes. Fundus examination revealed increased CD ratio in both eyes. Patient also developed multiple cutaneous maculo-papular lesions and Steven-Johnson syndrome like exfoliation of skin around lips and perioral area. Serum free-phenytoin concentration measured reveals toxic levels of Phenytoin with no other prior co-morbid retinopathy or optic nerve defect.

Results: Phenytoin was withheld, and Leviteracetam administered for seizures and the patient experienced a partial recovery in skin lesions with administration of Prednisolone and in conjunction with reducing serum levels of Phenytoin. Two weeks later the skin lesions have partially subsided, perioral area healed but Bilateral Ankyloblepharon persists and surgical release may be advised.

Conclusion: Phenytoin toxicity may cause acute visual dysfunction as previously unknown phenomenon.

Keywords: Acute phenytoin toxicity, Ocular manifestation, Symblepharon, SJS-Steven Johnson Syndrome.

I. Introduction

Since its discovery in 1908, phenytoin has become one of the well-studied anticonvulsants. With an average monthly cost of $30, it has also become one of the most widely used anticonvulsants, listed on the World Health Organization's List of Essential Medicines. However, with its narrow therapeutic index and its pervasive daily use, considering potential phenytoin overdose or toxicity from chronic use is key to early management and prevention of further toxicity.[1][2][3].

Phenytoin is a commonly prescribed antiepileptic drug. Due to its saturation (zero-order) pharmacokinetics, phenytoin carries a special risk of dose-related toxicity that is an important issue in emergency medicine. Excessive self-medication, misunderstanding of the prescription order, and probable drug interaction were the three leading causes of acute phenytoin intoxication. Unsteady gait, dizziness/vertigo, nausea/vomiting, general weakness, and drowsiness were the most common presenting symptoms. Although acute phenytoin intoxication causes no mortality and has a good outcome, the unsteady gait increases the risk of injuries caused by falls. The management of acute phenytoin intoxication includes temporary withdrawal of phenytoin and supportive care.[4]

We are reporting a case of a patient who received phenytoin therapy for generalized tonic clonic seizures and developed ocular manifestations borne of acute toxicity.

II. Case Study

An 18 year old female presented to the Medicine OPD with prior 3 year history of generalized tonic-clonic seizures under herbal medication for the condition and was prescribed Phenytoin (300mg HS/PO) for the condition, with instructions for regular

follow-up. 15 days later the patient presented in the emergency department with (Figure 1) severe maculo-

Figure 1 : Maculo-popular Rashes over lipe & face

papular rash with crust over face and extremities and perioral lesions with haemorrhagic eruptions over lips and oral ulcers and redness of both eyes and blurring of vision. She was immediately institutionalised for further treatment. She denied any history of prior episode of any such reaction in the past, with any other drug intake with no over the counter prescription and had no vision abnormalities in the recent past. She also denied of any substance abuse in the recent past. Neither she nor her family has any history of diabetes, hypertension and negative history of ocular trauma in the recent past.

On investigation, biochemical parameters show mild eosinophillia (5%) with moderate Anaemia (10.6 g/dL) which improved over 5 days (11.5 g/dL) and slightly raised RDWA (60.6 fL). Liver function tests show raised bilirubin levels(0.3 mg/dl) raised SGPT (74.6 IU/L) and ALP (289 IU/L). Serum Phenytoin levels were 17.0 mcg/ml. Rest of the reports were within normal limits. Based on the patient's medical history, clinical presentations, and lab reports, a diagnosis of Phenytoin toxicity was considered.

Ophthalmic examination revealed uncorrected visual acuity of OD 20/125 (log mar 0.7) and OS 20/60 (log mar 0.5). Slit lamp examination revealed bilateral bulbar conjunctival congestion with diffuse corneal oedema with superficial stromal infiltration, with epithelial defect staining positive with fluoroscein, with bilateral inflammation near lateral Canthi with palpebral conjunctiva adherent to bulbar conjunctiva (Figure 2), and mild anterior Blepharitis in both eyes.

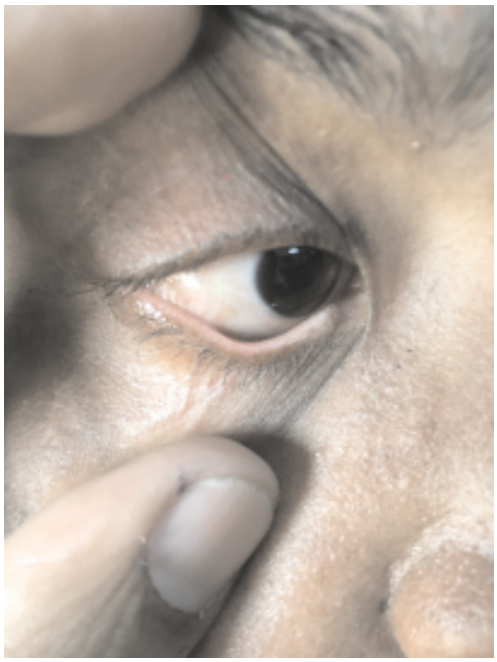

Figure 2 : Palpebral Conjunctiva Adherent at Canthi

Colour vision was found to be normal with Ishihara pseudo-isochromatic charts and visual fields (Humphrey's automated perimeter) show gross concentric constriction in both eyes. Fundus examination revealed increased CD (0.4-0.5) ratio in both eyes with normo-tensive IOP in both eyes (OD-14.6, OS-12.2).

Phenytoin was immediately discontinued and patient was maintained on oral Leviteracetam for seizures, along with supportive care for skin and perioral lesions with I / V Methyl Prednisolone for initial 3 days followed by oral Prednisolone for maintenance. For ocular condition patient was commenced on topical Moxifloxacin 0.5% QID along with CMC gel 1% BD for alleviate FB sensation, and oral Antioxidants, with advice for follow-up after 2 weeks.

After a fort night facial and perioral lesions have subsided, along with disappearance of corneal opacity, along with improvement in ocular symptoms and visual acuity. But the ankyloblepharon has not improved and may need surgical correction once the ocular inflammation has subsided.

III. Discussion

Phenytoin has a narrow therapeutic range of 10-20 mcg/mL.[5,6] At plasma concentrations below 10 mcg/mL, elimination follows first order. However, at higher concentrations, including those in the therapeutic range (10-20 mcg/mL.), the metabolic pathway becomes saturated and elimination shifts to zero order [5]. Half life of phenytoin varies between six and twenty four hours at plasma concentration less than 10 mcg/ml, but increases with higher concentrations[5,7]. As a result, plasma concentration rises disproportionally even with small increase in dose [8][6]. Toxicity generally correlates with the increasing plasma levels. The increased half life due to zero order pharmacokinetics can also result in prolonged duration of toxic symptoms[9].

The toxic effects seen with chronic treatment are primarily dose related cerebellar-vestibular effects.3 It may also cause other central nervous system effects, behavioural changes, increased seizure activity, gastrointestinal symptoms, hirsutism, gingival hyperplasia, osteomalacia and megaloblastic anaemia[7,8,6]. Chronic phenytoin ingestion leads to its accumulation in the cerebral cortex, resulting in atrophy of cerebellum, causing ataxia and nystagmus[10]. Signs of phenytoin toxicity usually manifest at phenytoin levels above 15 mcg/mL[11]. Our patient had serum phenytoin levels of 17.0 mcg/ml. Previous studies point out that phenytoin toxicity may develop over months to year after starting the drug[12]. These effects can be reversed by withdrawing or reducing the dose of Phenytoin[7,13].

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