

A Case report on Phenytoin induced Gingival Hyperplasia

¹V. Lalruatsanga, ²Mohammed Jaseel, ³M Sandhya, ⁴Aloof, ⁵Shaikh Shabaz

^{1,2,3,4,5}Pharm.D Intern

Department of Pharmacy Practice,
TVM College of Pharmacy, Bellary, Karnataka, India

Abstract- Phenytoin is a commonly used antiepileptic drug prescribed for the management and prevention of epilepsy. Chronic uses of phenytoin can lead to gingival hyperplasia and other adverse effects. An 80 years old male patient was presented with gingival hyperplasia, difficulty in walking and giddiness, the patient had a history of seizure disorder 3 years back and was regularly on Tab. Phenytoin 100mg. Naranjo scale and WHO causality scale was used to assess the relationship between the drugs and the unwanted clinical events. This case emphasizes the importance of periodic therapeutic drug monitoring of phenytoin and the importance of maintenance of oral hygiene for the prevention of gingival hyperplasia and also alerts the physician about the toxic manifestation of phenytoin in patients on long term therapy.

Keywords: Phenytoin, Gingival Hyperplasia, Therapeutic drug monitoring.

Introduction

Epilepsy is a neurological disorder characterized by sudden, recurrent unprovoked seizure which disturbed the mental functioning and movement of the body by abnormal electrical signaling in the brain ^[1]. Phenytoin is the most common antiepileptic drug prescribed for the management and prevention of epilepsy ^[2].

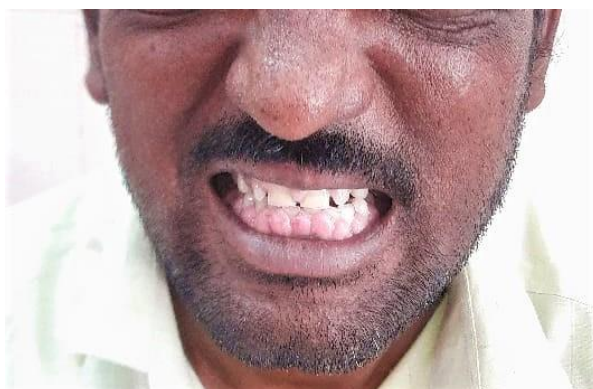
To ensure safety and prevent toxicity, diligent monitoring is essential for phenytoin due to its narrow therapeutic range of 10-20 mg/dl ^[3]. Prolonged use of phenytoin may result in gingival hyperplasia and various other adverse effects, such as ataxia, nystagmus, slurred speech, and tremors ^[4]. Phenytoin stands out as the most prevalent drug associated with gingival hyperplasia among various medications, occurring in approximately 50% of patients using phenytoin. ^[5] The degree of hyperplasia is influenced by the dosage, emphasizing the need for monitoring serum phenytoin concentrations in instances of phenytoin-induced toxicity. ^[1].

Here we report a case of phenytoin induced gingival hyperplasia in a patient with history of seizure disorder with chronic use of phenytoin.

Case report

An 80-year-old male patient admitted to the Department of General Medicine, VIMS, Bellary, Karnataka, reported difficulties in walking, swaying on both sides, and increased dizziness over the past month, with a worsening condition in the last week. The patient had a history of a seizure three years ago and had been consistently taking Tab. Phenytoin 100mg 2-0-3. There were no previous complaints of limb weakness, fever, vomiting, involuntary micturition, chest pain, or breathlessness, and the patient had no other comorbidities.

Fig 1: Overgrowth of the gingiva



Upon examination, the patient exhibited ataxia, swaying on both sides, impaired tandem walking, and gingival hypertrophy as shown in fig 1. Muscle power in both lower limbs was graded as 5/5 according to the Medical Research Council scale. No nystagmus, dysdiadochokinesia, or nodular skin lesions were observed. Liver function tests, including AST (13 U/L), ALT (24 U/L), ALP (148 U/L), and total bilirubin (0.3 mg/dL), were within normal range. However, the serum phenytoin level exceeded toxic threshold at 37.9 mcg/ml.

Based on both subjective and objective findings, the patient received a diagnosis of phenytoin toxicity. The phenytoin dosage was initially reduced from 2-0-3 to 1-0-2 on the first day and further adjusted to 1-0-1 on the second day. Additionally, Tab. Clobazam 10mg was initiated on the fourth day as part of the treatment plan.

Discussion

Phenytoin is frequently prescribed as an antiepileptic medication for the treatment of various seizure disorders and status epilepticus. The signs and symptoms of phenytoin toxicity usually align with the serum phenytoin level, and it is noteworthy that phenytoin has a narrow therapeutic range of 10–20 mcg/ml. Additionally, the pharmacokinetics of phenytoin exhibit non-linear behavior even when within the established therapeutic range^[5].

As the dose of phenytoin increases, the enzyme system responsible for its metabolism gradually becomes saturated, leading to a decrease in the elimination rate of phenytoin^[3,6]. The adverse effects associated with phenytoin encompass ataxia, cerebral atrophy, confusion, hypotension, gingival hyperplasia, bullous dermatitis, tissue necrosis, nystagmus, and osteomalacia. In our patient, the observed toxic effects include ataxia and gingival hyperplasia. Gingival hyperplasia, also known as gingival hypertrophy, is a common side effect of chronic phenytoin use. This condition involves fibrotic enlargement of the gingiva and is often attributed to various etiological factors, with phenytoin being the most prevalent. The mechanism underlying gingival overgrowth is proposed to involve alterations in collagen degradation, impacting calcium metabolism levels of MMPs and TIMPs, as well as integrin expansion. This fibrosis is characterized by the presence of numerous fibroblasts exhibiting an activated synthetic and proliferative phenotype, influenced by deregulated cytokines^[7].

Chronic phenytoin ingestion leads to its accumulation in the cerebral cortex resulting in atrophy of cerebellum causing ataxia^[3]. Movement abnormalities can often be attributed to antipsychotic and centrally acting dopaminergic agents; however, anticonvulsants can also occasionally contribute to such effects. Studies have associated the use of phenytoin with facial abnormalities, myoclonus, and dystonia. Research findings indicate that phenytoin can be toxic to the cerebellum in both clinical and laboratory settings. Moreover, in humans, degeneration of Purkinje cells has been observed following a single phenytoin overdose.

Most patients who undergo these involuntary movements typically exhibit elevated plasma phenytoin levels, as observed in our case (37.9 mcg/ml), where the plasma level was deemed toxic during the diagnostic assessment.

Considering the pharmacokinetics, limited therapeutic index, and individual variability in phenytoin metabolism and excretion, the symptoms exhibited by the patient in our investigation were apparent^[8].

Assessment of ADR

The causality assessment was done by using both WHO causality assessment algorithm and Naranjo's scale. Based on time temporal relationship the reaction was attributed to medication. So, it was probable according to WHO scale and it was probable according to Naranjo's scale with a score of 6.

Conclusion

This case emphasizes the critical role of regular therapeutic drug monitoring for phenytoin and underscores the importance of maintaining oral hygiene to prevent gingival hyperplasia. It alerts physicians to be vigilant about the potential toxic manifestations of phenytoin in patients on prolonged therapy. Furthermore, it highlights the significance of educating both patients and their caregivers about the clinical manifestations of phenytoin toxicity for early recognition and appropriate intervention. By sharing our findings, we seek to increase awareness, enhance diagnostic accuracy, and encourage the implementation of evidence-based approaches for effectively managing this adverse effect.

Consent of the patient

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Author agreement statement

This is an original work done and we solemnly declared that the manuscript has not been published before in any other journals. We also confirmed that all the mentioned orders are aware of all declarations and agree to them.

REFERENCES:

1. Singh P, Tomar N, Kaushik M, Ahmad S. Phenytoin Induced Gingival Enlargement and Its Management-A Case Report. 1. The Association of Monocyte Lymphocyte Ratio and IFN- γ /IL-4 Ratio on Status of Sputum Conversion in Tuberculosis Patients with Post Intensive Phase 1 Anak Agung Gede Ocha Rama Kharisma Putra, I Ketut Suryana, Ida Bagus Ngurah Rai, Ni Wayan Candrawati, Ida Ayu Jasminarti Dwi Kusumawardani, I Gede Ketut Sajinadiyasa, Ni. 2022 Apr;22(2):112.
2. AlJehani YA. Nonsurgical management of phenytoin-induced gingival hyperplasia. J Contemp Dent Pract. 2015 Sep 1;16(4):319-21.
3. Menon VB, Kurian J, Undela K, Ramesh M, Gowdappa HB. Phenytoin toxicity: A case report. Journal of Young Pharmacists. 2015;7(3):272.
4. Pathakamuri N, Sah SK, Shariff A, Dhurappanavar SN, Pradhan J, Pradhan A, Matad SS, Shivukumar S, Khonglein D, Gosi M, Patil VS. Chronic use of Phenytoin Induced Ataxia: A Case Series of Six Patients. Journal of Young Pharmacists. 2022 Apr;14(2):249.
5. Urolagin SS, Swaroop D, Agrawal C, Dholakia P, Karalwad MB. Management of phenytoin-induced gingival enlargement in a patient with antiphospholipid antibody syndrome: a rare case report. Journal of Indian Society of Periodontology. 2016 Sep;20(5):561.
6. Miller C, Joyce DM. Phenytoin toxicity. WebMD. Medscape. New York. 2012.
7. Gurgel BC, Morais CR, Rocha-Neto PC, Dantas EM, Pinto LP, Costa AD. Phenytoin-induced gingival overgrowth management with periodontal treatment. Brazilian dental journal. 2015 Jan;26:39-43.
8. Shah K. A Case Report-Phenytoin Induced Ataxia.