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Case Study

Unravelling The Mechanism of Phenytoin-Induced Gingival Hyperplasia: A Case Report

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ABSTRACT

Phenytoin is a widely used medicine for controlling seizures. However, it can cause unwanted side effects, one of which is gingival hyperplasia, a condition that many people overlook. This case involves a man who has had generalized tonic-clonic seizures for 11 years and was taking phenytoin. He started experiencing increasing gum swelling, which caused him discomfort and made it harder to keep his mouth clean. After a check-up, doctors diagnosed him with phenytoin-induced gum overgrowth. The treatment involved stopping the injectable version of phenytoin and switching to oral tablets. This helped the gum swelling slowly go away. The case shows that early detection and timely action can greatly improve patient results and prevent long-term mouth problems. It also shows the need to watch for mouth-related side effects in people taking phenytoin for a long time to ensure both seizure control and a better quality of life.

INTRODUCTION

Phenytoin, a hydantoin derivative is a drug of choice for many years to treat different types of seizure disorders. While it helps control seizures, it also has known side effects. One of the most common is gum swelling, which is not harmful but can be unsightly and affects people taking phenytoin for a long time. Three main groups of drugs—antiepileptics like phenytoin, immunosuppressants, and calcium channel blockers—can cause gum overgrowth. These drugs affect how the body uses calcium. They reduce the flow of calcium into cells, which changes how folic acid is used and limits the action of collagenase, an enzyme important for tissue

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repair. This side effect of phenytoin was first noticed by Kimball in 1939, within a year of phenytoin being introduced as an antiepileptic drug in 1938. Some theories explain how this happens, including the biochemical mechanistic unifying hypothesis by Brown and Arany. Less talked about, but still important, are phenytoin's effects on the immune system, which can make patients more likely to get infections from harmful microbes.

CASE PRESENTATION:

A 20-year-old male patient with history of Epileptic episodes for 11 years, admitted for the complaint of Breakthrough seizure. Patient was treated with initial dose - Injection Phenytoin 800 mg IV in 100 ml normal saline over 20 mins and maintenance dose - Injection 100 mg IV TDS on first day. Patient developed progressive Gingival hypertrophy after 2 days of Phenytoin therapy. Clinical examination revealed appearance of slightly yellowish, creamy white patches along with gum overgrowth, which later turned to be pigmented gum. Management involved withdrawal of Injection Phenytoin and included Tab. Phenytoin 100 mg (1-0-2). The patient showed significant improvement. Following the withdrawal of phenytoin injection, the gum swelling showed immediate and significant regression. However, as the swelling decreased, the affected areas, especially where the swelling was most noticeable, began to show dark pigmentation, making them darker than surrounding healthy gum tissue. This pigmentation continued even after the swelling completely resolved.

VITAL SIGN AND PHYSICAL EXAMINATION

Initial revealed stable hemodynamic with a temperature of 37.2°C, blood pressure of 110/70 mmHg, and a regular heart rate of 85 beats per minute. The respiratory rate remained stable at 24 breaths per minute, with oxygen saturation maintaining at 98 % on room air. Cardiovascular examination demonstrated regular heart sounds without any murmurs or additional heart sounds. Respiratory examination revealed clear breath sounds bilaterally without any adventitious. ECG stated right axis deviation.

PAST HISTORY:

Patient has history of epileptic seizures for the past 11 years and has been on medications including TAB. Phenytoin 100mg, TAB. Sodium valproate 200mg, TAB. Diazepam 5mg, TAB. Calcium. Despite regular intake of medication, the patient experienced a recent episode of epilepsy 3 months ago. Prior to the current presentation, the patient had ataxia. There was no documented history of drug allergies or adverse reactions to medications. A family history of seizures was notably absent.

LAB INVESTIGATION:

The total white blood cell count 8.4 x 103 cells/µL. Haemoglobin is 14.6 and platelet is 201 x 103/µL counts remained within normal parameters. Biochemical analysis of liver function tests, alanine aminotransferase (ALT) at 17 U/L and aspartate aminotransferase (AST) at 19 U/L were within normal range. Renal function parameters, including serum creatinine is 0.72 mg/dL and urea is 24mg/dL, were within normal limits. Serum electrolytes showed reduced levels of - calcium 7.8 mg/dl and magnesium 1.5 mg/dl.

DIAGNOSIS:

On 3rd day of phenytoin therapy, after examining, patient was diagnosed with gum hypertrophy.

COURSE IN THE HOSPITAL:

This adverse reaction was reported to Adverse drug monitoring centre, Government Medical College, Nagapattinam. The decision made was to stop the drug and casualty assessment was done using Naranjo scale and was found to be Probable. INJ. Phenytoin was discontinued after two days of therapy. The patient was subsequently shifted from injectable phenytoin to oral phenytoin (100 mg), while remaining medications in the regimen (TAB. Sodium valproate 200 mg, TAB. Diazepam and TAB. Folic acid) were unchanged. This modification resulted in marked clinical improvement and patient showed favourable outcomes. The patient was discharged on day 5 with complete follow-up.

DISCUSSION:

Phenytoin can lead to gum swelling, which is not only uncomfortable but also alters the shape of the gums. This condition is commonly seen in individuals taking phenytoin, but it can become more severe in those with poor oral hygiene or low levels of folate. This case illustrates several important points regarding the use of phenytoin. Gum swelling is a known side effect, but in this patient, it became quite significant. This might occur when the medication is not effective initially or when the patient has difficulty tolerating it, leading to acute inflammation. Additionally, phenytoin may slightly weaken the immune system, making patients more prone to infections.[3] Phenytoin-induced gum overgrowth is linked to complex changes in the body's chemistry and cell activity. It affects how the body absorbs folate, which in turn influences the production of certain proteins and enzymes. These enzymes are crucial for converting inactive collagenase into its active form within the gums. If there is insufficient active collagenase, it cannot break down excess connective tissue, resulting in increased tissue build-up. [2] Research suggests that gum overgrowth in phenytoin users is more related to increased connective tissue rather than actual growth. It is believed that reduced collagenase activity prevents the breakdown of material surrounding cells. This effect is further exacerbated by dental plaque, which causes inflammation and accelerates the accumulation of connective tissue. Therefore, both the drug's impact on the body and local inflammation contribute to this side effect.[4] These observations indicate that the process of gum overgrowth is influenced by bacteria in dental plaque, which leads to inflammation and stimulates the production of more connective tissue in the gums. Phenytoin, as one of the drugs associated with this issue, reduces folate levels in gum cells. This affects the production and function of certain enzymes required to convert inactive collagenase into an active form within the gums. Without active collagenase, the extra tissue formed due to inflammation does not break down, resulting in the side effect known as gum overgrowth.

CONCLUSION:

This case underscores the importance of thoroughly reviewing a patient's medication history before initiating phenytoin or any long-term treatment. It also highlights the limited awareness many patients have regarding the side effects of medications. Phenytoin-induced gum overgrowth results from a combination of poor folate metabolism, reduced active collagenase, and local inflammation caused by plaque.[2,4] Early identification, consistent dental check-ups, and informing patients about potential side effects are crucial in preventing severe gum changes. This case also emphasizes the need for collaboration among healthcare providers and the timely reporting of side effects to enhance patient safety and optimize treatment outcomes.

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