Phenytoin Misadventure in Epilepsy: A Case Report

Sunita Sah[1]

[1]Department of Dental Medicine, Purbanchal University Teaching Hospital, Gothgaun, Morang, Nepal

Correspondence :
Sunita Sah. Email: suneitasoni@gmail.com

ABSTRACT

Gingival overgrowth is a pathologic event frequently associated with systemic use of certain medications and is often referred to as Drug-induced gingival overgrowth (DIGO). The degree of pathogenicity depends on the type of drug, its dose and duration; oral hygiene; individual susceptibility; genetic factors; and environmental influences. DIGO can be localized which may remain confined to papilla or can be generalized involving marginal gingiva that may completely cover the crowns of the teeth thereby causing aesthetic and functional problems. The first-line treatment of DIGO is substitution of related medications in combination with dental biofilm control and regular periodontal maintenance.

Keywords: Drug-induced gingival overgrowth; drug substitution; systemic medication

INTRODUCTION

The most common cause of gingival overgrowth (GO) is the systemic use of certain medications, often called drug-induced gingival overgrowth (DIGO).[1] The first sign of DIGO can be observed as early as three months. It can be localized, which may remain confined to interdental papilla or can be generalized involving marginal and attached gingiva that may completely cover the crowns of the teeth. DIGO frequently results in biofilm accumulation that may lead to periodontal disease.[2] The first-line treatment of DIGO is substitution of related medications in combination with non-surgical periodontal therapy (NSPT) which includes elimination of local factors, dental biofilm control and regular periodontal maintenance.[1] This paper reports a case of 22-year-old male patient with generalized gingival overgrowth covering three-fourth of the crown that dramatically reduced itself within few months of drug substitution and biofilm control, without any surgical intervention.

CASE REPORT

A 22-year-old male patient was referred from the Department of Conservative Dentistry and Endodontics to the Department of Periodontology and Oral Implantology for the management of enlarged gingiva. He had reported to the Department of Internal Medicine 12 years back with the chief complaint of frequent altered behaviour and loss of consciousness. He was prescribed inj. Midazolam (for acute management) followed by diazepam 5 mg BD on a regular basis for the same. Despite regular medication, the patient reported the first episode of seizures six years later, during which he got his upper front teeth fractured. He was then diagnosed

Citation
Sah S. Phenytoin Misadventure in Epilepsy: A Case Report. J Nepal Dent Assoc. 2024 Jul-Dec;24(39):33-7.

with epilepsy, for which diazepam was substituted with Phenytoin (100 mg TDS). On dental history, endodontic treatment of upper front teeth was done about five and a half years back.

The patient noticed his gums getting enlarged after a few months of Phenytoin use. It was gradually progressive and was associated with difficulty in oral hygiene maintenance and eventually halitosis, which impaired his esthetic and psychosocial behavior.

On intra-oral examination, there was generalized GO covering three-fourth of the crown on labial aspect of both upper and lower arches (Bokenkamp's Grade-III GO)[3] with minimal deposits, and fracture of 21 involving the pulp chamber (Ellis Class III # as shown in figure 1A and 1B).[4] On radiographic examination (IOPAR), 11 and 21 showed linear radio-opacity in the radicular portion suggestive of endodontic treatment as shown in figure 1C. There was no radiographic bone loss evident. A provisional diagnosis of Phenytoin-induced gingival overgrowth (PIGO) was made.

After obtaining the written informed consent, NSPT was performed and the patient was referred to the Department of Internal medicine for possible drug substitution. Phenytoin was substituted with Levetiracetam (Verocet™) 1500 mg in two divided doses for 10 days followed by 2 gm in two divided doses for 6 months. The GO resolved significantly to Bokenkamp's Grade-I[3] within eight months after the drug substitution (figure 2A, 2B and 2C). Thereafter, functional crown lengthening through internal bevel gingivectomy of 21 was done. The post-operative picture at two weeks has been shown in figure 3.

Figure 1: Pre-operative [1A-labial view, 1B-right lateral view, 1C-Intraoral periapical radiograph (IOPAR)]

Figure 2: After 8-months of drug substitution (2A-labial view, 2B-right lateral view, 2C-left lateral view)

Figure 3: Labial view after 2-weeks of functional crown-lengthening procedure

DISCUSSION

DIGO has primarily been associated with the systemic administration of anticonvulsants, calcium channel blockers, and the immune-suppressants. The prevalence of DIGO associated with Phenytoin, Cyclosporine and Calcium channel blockers are 50%, 30% and 10-20%, respectively.[5] However, the prevalence varies significantly and it depends upon the population being investigated. Limited evidences are available regarding other drugs causing DIGO.[1]

The first scientific report on DIGO was published in 1939, which was associated with diphenylhydantoinate (Phenytoin).[6] Phenytoin, introduced in 1938, is a first-line antiepileptic drug commonly used for the treatment of grand mal, temporal lobe, and psychomotor seizures.[5] Phenytoin-induced gingival overgrowth (PIGO) has been known for more than 70 years. Clinical onset of PIGO can occur as early as one month, and severity can be seen in 12-18 months.[7] In the present case, the patient noticed his enlarged gums after a few months of phenytoin use.

PIGO is of major concern to the patient because it frequently occurs on the anterior aspect of jaws, and the entire dentition can be covered in severe cases. PIGO is characterized by enlargement of interdental papillae and increased thickening of the marginal tissues, thereby, causing aesthetic and functional problems, such as malposition of teeth, and difficulty in speech.[8] In the present case, the patient complained about compromised aesthetic, psychosocial behavior and difficulty in mastication but no problem in speech.

DIGO is associated with pseudo-pocket formation, biofilm accumulation and impaired oral hygiene maintenance that may lead to periodontal disease. Therefore, substitution of related medication in combination with NSPT is often required to improve the overall gingival health.[1] In the present case, firstly, NSPT was instituted, and then the patient was referred to the Department of Internal Medicine for the possible substitution of Phenytoin. Phenytoin was replaced by Levetiracetam (Verocet). GO is a common side effect of 1st generation antiepileptic medications like Phenytoin, but very rare with the newer ones. Levetiracetam (2nd generation antiepileptic drug),[9] though this drug is generally safe, but in rare instances, GO has been documented.

If any drug substitution is attempted, it is important to allow a 6 to 12 months period to elapse between discontinuation of the offending drug and substitution with an alternative drug.[1] This lapse of time is considered so that the effect from the residual serum levels of drug on the gingival fibroblasts that cause increase in the extracellular matrix content is completely eliminated.[5] In the present case, the GO resolved significantly within few months of the drug substitution. By the end of eight months, GO subsided thereby resembling to its normal architecture. This is in accordance with the study by Lee HC et al.,[10] Chang et al.,[11] Aljehani et al.[12] who have also successfully treated DIGO with drug substitution in combination with NSPT.

In many patients, GO persists even after possible drug substitution and NSPT. In such cases, surgical removal of the DIGO either by gingivectomy or gingivoplasty should be considered.[1] In the present case, surgical intervention was not required as the GO dramatically reduced itself within few months of drug substitution and NSPT. Functional crown lengthening of 21 was done and then patient was referred back to Department of Conservative Dentistry for prosthetic rehabilitation. Patient is on frequent recall visit for periodontal care and maintenance for adequate biofilm control.

REFERENCES

1. Newman MG, Takei HH, Klokkevold PR, Carranza FA. Newman and Carranza's Clinical Periodontology, 13th edition. Elsevier; 2018.
2. Mavrogiannis M, Ellis JS, Thomason JM, Seymour RA. The management of drug-induced gingival overgrowth. J Clin Periodontol. 2006 June;33(6):434–9. [Pubmed] [DOI]
3. Bökenkamp A, Bohnhorst B, Beier C, Albers N et al. Nifedipine aggravates cyclosporine A-induced gingival hyperplasia. Pediatr Nephrol. 1994 Apr;8(2):181-185.[Pubmed] [DOI]
4. B S, Gopikrishna V. Grossman's Endodontic Practice - 13th edition. 2014.
5. Farook FF, M. Nizam MN, Alshammari A. An Update on the Mechanisms of Phenytoin Induced Gingival Overgrowth. TODENTJ. 2019 Dec 31;13(1):430–5. [DOI]
6. Kimball OP: The treatment of epilepsy with sodium diphenyl hydantoinate, JAMA 112:1244–1245, 1939. [DOI]
7. Marshall, R. I., & Bartold, P. M. (1999). A clinical review of drug-induced gingival overgrowths. Aust Dent J, 44(4), 219–232. [Pubmed] [DOI]
8. Pihlstrom BL. Prevention and treatment of Dilantin-associated gingival enlargement. Compend Suppl. 1990 Mar 6;(14):S506-510. [Pubmed] [DOI]
9. Lyseng-Williamson KA. Spotlight on levetiracetam in epilepsy. CNS Drugs. 2011 Oct 1;25(10):901–5. [Pubmed] [DOI]
10. Lee HC, Wu CN, Yuan K. Self-correction of pathologic tooth migration after nonsurgical periodontal treatment in a metabolic syndrome patient with severe periodontitis and drug-influenced gingival enlargement. J Indian Soc Periodontol. 2021;25(4):350–4. [Pubmed] [DOI]
11. Chang CC, Lin TM, Chan CP et al. Nonsurgical periodontal treatment and prosthetic rehabilitation of a renal transplant patient with gingival enlargement: a case report with 2-year follow-up. BMC Oral Health. 2018 Aug 20;18(1):140. [Pubmed [DOI]
12. AlJehani YA. Nonsurgical Management of Phenytoin-induced Gingival Hyperplasia. J Contemp Dent Pract. 2015 Apr 1;16(4):319–21. [Pubmed] [DOI]