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Surgical management of phenytoin-induced gingival enlargement – A rare case report

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Abstract

Phenytoin-induced gingival enlargement presented as an abnormal growth of the gingiva due to the adverse effect of phenytoin therapy. Phenytoin-induced gingival enlargement is more commonly evident to occur in children and young adults. The enlargement affects aesthetics, speech, masticatory function, normal oral hygiene practice and even in severe cases causes malocclusion. Management of Phenytoin-induced gingival enlargement includes decreasing the use of phenytoin, meticulous oral hygiene practice to reduce inflammation and surgical excision of fibrotic gingival overgrowth by gingivectomy followed by gingivoplasty. This case report presents phenytoin-induced severe gingival enlargement in a 35-year-old female since the age of 10 years.

Keywords: Gingival enlargement, Phenytoin, External Bevel Gingivectomy, Epilepsy, Seizures, Drug-induced overgrowth.

Introduction

Gingival enlargement is presented as an increase in the size of the gingiva. It can occur due to various etiological factors including commonly prescribed drugs. Right now, it is evident that more than 20 prescription medications are related to gingival enlargement. Among

these drugs, the antiepileptic agent phenytoin has been widely associated with induce Gingival enlargement.

Phenytoin (PHT; 5, 5- diphenylhydantoin) was first introduced as an anti-epileptic drug in 1938. Since then, it has been used for the management of various seizures and also use in the condition of neuralgias and cardiac arrhythmias.[1] It is calculated that approximately 30% to 50% of patients under phenytoin prescription can develop significant gingival changes.[2] The first evidence of gingival enlargement associated with the chronic use of phenytoin was made in 1939.[3] Other anticonvulsants like valproic acid, carbamazepine, phenobarbital and vigabatrin have also been associated with gingival overgrowth. Other drugs like the immunosuppressant Cyclosporine A and some calcium channel blockers (Dihydropyridines, Diltiazem and Verapamil) also induce gingival enlargement.

This drug-induced overgrowth starts in the papillary region and later involves the margins and the gingival attachment. It characterizes as a lobulated and thickened appearance either partially or completely covering the tooth surfaces. It appears pink to a deep bluish-red depending on the amount of inflammatory infiltrate and secondary inflammation may induce edema, ulcerations and bleeding. The anterior teeth are more commonly, mainly the buccal surface. Patients may complain about aesthetics, discomfort, difficulty in mastication and speech, impediment of oral hygiene activities resulting in halitosis and to severe extents even malocclusion may occur.[4]

Case Presentation

This is a case report of 35 years old female patient presented to the Department of Periodontology, Punjab Government Dental College & Hospital Amritsar, with a Chief complaint of gingival bleeding with swollen gums and Halitosis. She gave a history of epilepsy since the age of 10 years and taking the anti-epileptic drug phenytoin 100 milligrams 3 times a day and is continuing at the time she visited the department. Her mother noticed painless and beadlike overgrowth in papillary gingiva between mandibular incisors teeth which slowly involved marginal gingiva after 3 months of medication and progressively increased covering the two-thirds crown of teeth within 6 months. It was causing difficulty in maintaining oral hygiene, mastication, speech and unsightly aesthetics.

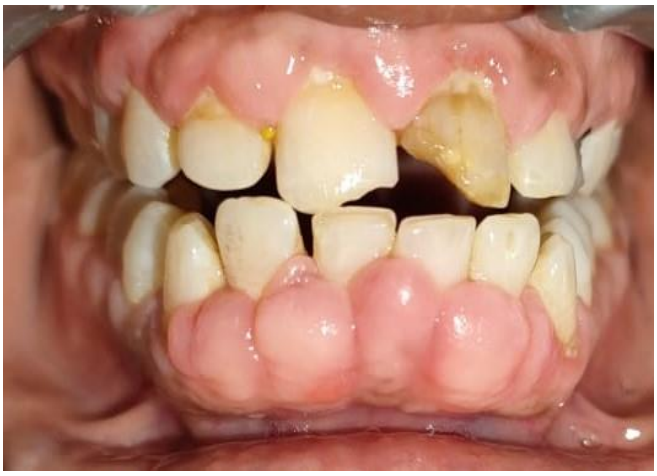

Figure 1: Preoperative view of Gingival enlargement

On Extra-oral Examination patient had incompetent lips with a convex profile. The bilateral symmetry of the face was present. Intra-oral Examination revealed pale pink colored gingiva with diffuse, nodular gingival enlargement involving both maxillary and mandibular arch. Generalized Loss of stippling and bleeding on probing was seen. Gingiva was with firm margins, rolled out contour with dense fibrotic consistency. Diffuse gingival enlargement covering almost 2/3rd of clinical crown height was seen (figure 1). Oral hygiene was poor with local deposits without any signs of exudation. There was a lack of true periodontal pockets and the presence of a coronal increase in gingival size making Pseudo-pockets of 5mm - 7 mm (figure 2). The clinical diagnosis and medical history given by the patient & her

mother were suggestive of phenytoin-induced gingival enlargement.

Figure 2: Pseudo pocket in maxillary anterior teeth

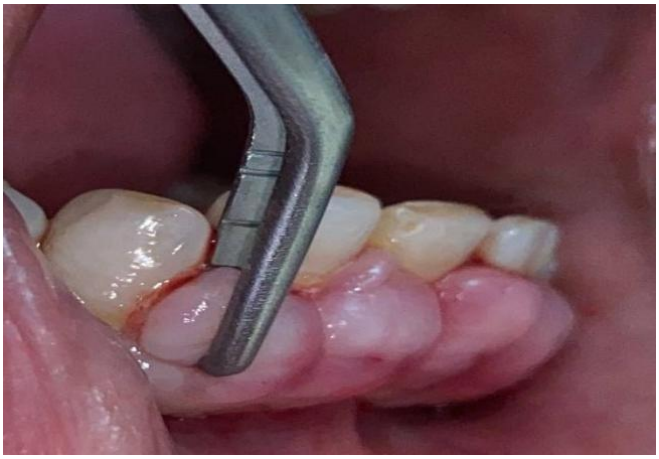

Figure 3: Bleeding points produced using Crane-Kaplan pocket marker

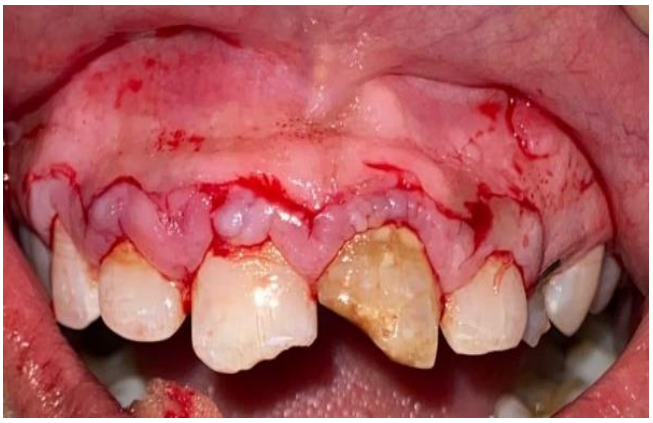

Figure 4: External Beveled incision apical to base of pocket

To determine whether an alternative drug or the dosage of the same medication could be modified, the patient was advised to go to her doctor to inform him concerning the gingival enlargement put on by phenytoin use but according to him medication could not be deferred or changed.

Treatment started with a thorough oral prophylaxis (Scaling and Root Planing) and guidance on oral hygiene. Surgical excision by External Bevel Gingivectomy as suggested by *Zentler* using a scalloped incision was planned. Blood chemistry was insignificant. Patient consent was obtained. For acute care settings, the insertion of a peripheral intravenous (IV) line was kept for therapeutic purposes. Crane-Kaplan Pocket Marker was used to draw bleeding sites at various locations around each tooth in the area following appropriate local anesthesia using Lignocaine with 1:80,000 adrenaline (figure 3). The series of bleeding points that were created served as a guide for the incision and described the depth of the pocket in the area that was needed to get therapy. B. P. blade no 15c was used for external bevel incision and to produce thin and properly festooned margins of the remaining gingiva. The beveled incision was made at a level apical to the base of the pocket to create a "physiologic" gingival margin contour (figure 4). The incision was made in a buccal direction. Following the first incision, a secondary interdental incision was made, and the incised tissues were gently removed with a Gracey curette. Also, Curettes was used to remove any remaining tissue tabs and granulation tissues (figure 5).

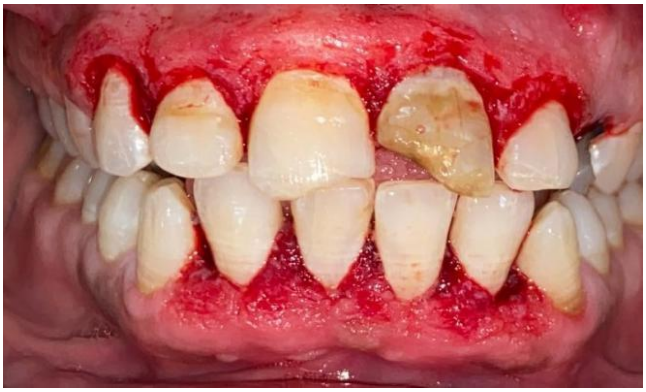

Figure 5: Post Gingivectomy view

The exposed tooth surfaces were meticulously scaled to eliminate calculus deposits and the surgical area was flushed with normal saline + 5% povidine solution. The wound site was covered with a Periodontal dressing (Coe Pack) to shield the incised area during healing and the excised tissue was sent for histopathological studies (figure 6,7).

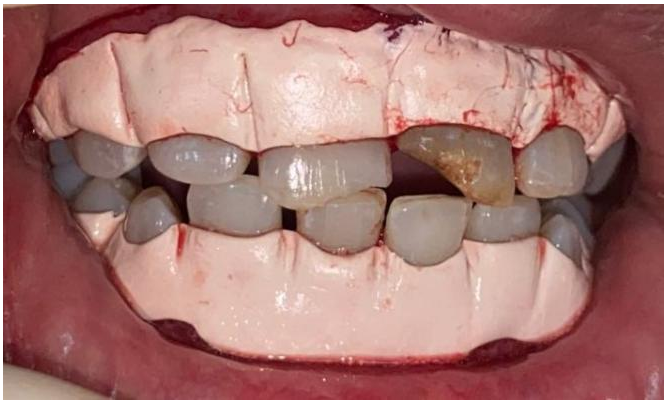

Figure 6: Periodontal dressing (Coe-Pack)

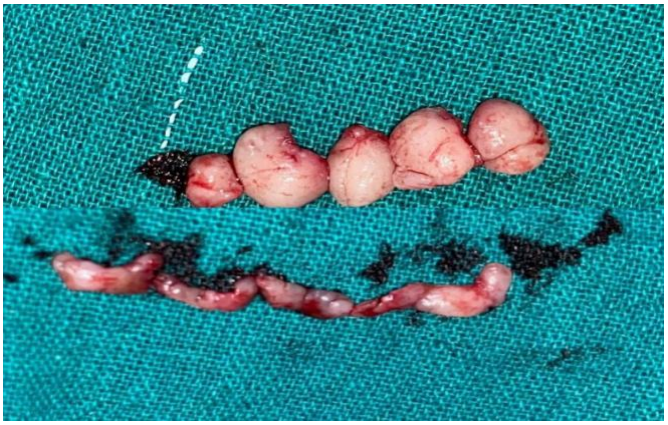

Figure 7: Excised Gingival Tissue

Analgesic/antibiotic drugs and oral care were administered as part of the post-operative care. In addition, the patient was provided 0.2% Chlohex HEAL mouth rinse twice a day for 15 days. She was recalled after 7 days for periodontal dressing removal and she was scheduled for follow-up visits after 15 days, 1 month, 3 months, 6 months, and 1 year to check the gingival condition and oral hygiene maintenance.

The histopathological examination of gingival biopsy specimens revealed connective tissue hyperplasia, acanthosis of the overlying epithelium, hyper-keratinized and slightly proliferating stratified squamous epithelium and elongated rete ridges, as well as a few scattered inflammatory cells (figure 8). Deeper connective tissue revealed extensive connective tissue infiltrates, as well as nerve bundles and blood arteries. The stroma of connective tissue was dominated by fibroblasts (figure 9). Fibroepithelial hyperplasia was diagnosed as the lesion. It was suggestive of Phenytoin-induced gingival hyperplasia based on clinical and pathological data.

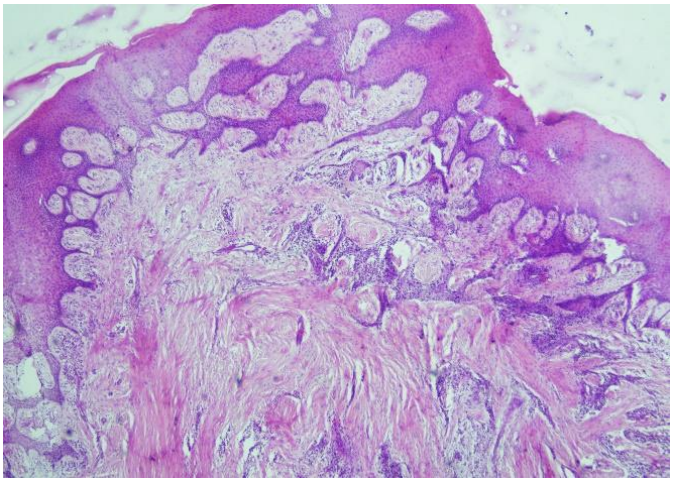

Figure 8: Histopathological picture of excised tissue showing keratinized squamous epithelium and elongated rete ridges (H & E, 10X)

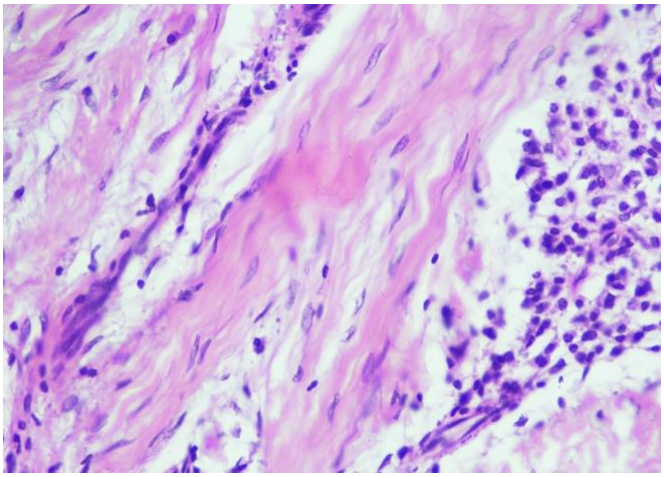

Figure 9: Histopathological picture of excised tissue showing dense fibro-collagenous connective tissue with predominance of fibroblasts (H & E, 40X)

The patient was conscientious about keeping proper dental hygiene.

After a 3-month follow-up period and the patient's findings remained steady, with no recurrence of enlargement (figure10).

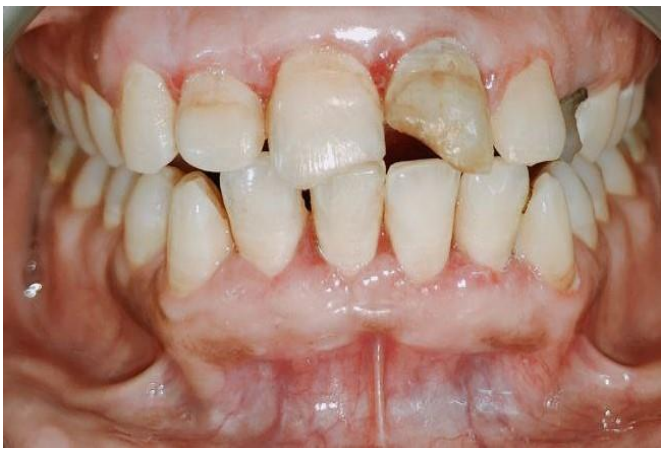

Figure 10: 3 months follow up view

Discussion

Phenytoin-Induced Gingival Overgrowth (PIGO) occurs in older children and young adults, rarely seen in edentulous patients. Dummett[5] suggested that after taking PHT, GO becomes apparent in the first 3 months while Aas[6] suggested that the overgrowth is more rapid in the first year. This patient was on phenytoin since the age of 10 years and start noticing gingival enlargement just after 6 months of medicine.

The etiologies of PIGO are multiple and complex associated with cellular and molecular level changes including fibroblasts, cytokines, growth factors, and genetic susceptibility. It has been found that in gingival fibroblast monolayer cultures, there was an increase in collagen production and a decrease in its degradation in response to Phenytoin.[7] The inactivation of collagenase by fibroblasts in response to phenytoin has also been reported.

In fibroblasts, interleukins (IL) 1a, 1b, and tumor necrosis factor (TNF)-a induced a significantly higher generation of prostaglandin E2 and upregulates the release of arachidonic acid after 9 months of phenytoin therapy.[8] The decrease in epidermal growth factor receptor (EGF-R) metabolism after phenytoin therapy. The single-nucleotide polymorphisms in the coding region of cytochrome CYP 2C alter the phenytoin metabolism.

The treatment for PIGO usually starts with tapering or stopping the dose. It is better to substitute the drug to remove the main etiological factor for gingival enlargement. In cases of low-grade gingival enlargement, the condition can be reversed after a duration of 4 months of stopping phenytoin.[9] In severe cases of PIGO requires gingivectomy to establish normal contour of gums, but recurrence can occur on continued exposure to Phenytoin.

When starting PHT therapy, the intra-sulcular method of brushing, inter-dental cleansing and mouth rinse with Chlorhexidine can avoid aggravating the condition. Folate supplementation as a preventive[10] and therapeutic measure for PIGO is effective.

We suggest that a patient on phenytoin therapy should be informed well about the adverse effects of a

medicine. Patients should maintain oral hygiene properly and can take folate supplements as a preventive therapy. The clinician must take proper medical and dental history for better diagnosis and treatment planning. This patient underwent a surgical procedure, gingivectomy and gingivoplasty due to severe condition of PIGO. The consulting doctor should prescribe an alternative drug for Phenytoin as it deteriorates the quality of life of the patient causing adverse conditions like gingival enlargement that not only concern aesthetically but also cause difficulty in speech and eating.

Conclusion

Medical practitioners should prescribe phenytoin drug and its dose carefully. Patient should be informed about the adverse effects of the drug and motivated to consult the dentist regularly for a check-up to early diagnosis of any susceptibility to the drug. So, it can be treated early. In cases of present history of seizures, clinicians should be well-equipped to handle any emergency during surgery.

References

1. G. N. Guncu, F. Cxaglayan, A. Dincxel, A. Bozkurt, S. Sayg, and E. Karabulut, “Plasma and gingival crevicular fluid phenytoin concentrations as risk factors for gingival overgrowth,” Journal of Periodontology, vol. 77, pp. 2005–2010, 2006.
2. T. Modeer, H. Domeij, I. Andur ´ en, M. Mustafa, and G. ´ Brunius, “Effect of phenytoin on the production of interleukin-6 and interleukin-8 in human gingival fibroblasts Journal of Oral Pathology and Medicine, vol. 29, no. 10, pp. 491–499, 2000.
3. O. P. Kimball, “The treatment of epilepsy with sodium diphenyl hydantoinate,” The Journal of the American Medical Association, vol. 112, pp. 1244–1245, 1939.
4. Bharti V, Bansal C. Drug-induced gingival overgrowth: the nemesis of gingiva unravelled. J Indian Soc Periodontol 2013;17:182–7
5. Dummett CO. Oral tissue reactions from dilantin medication in the control of epileptic seizures. J Periodontol 1954;25:112–22.
6. Aas E. Hyperplasia gingivae diphenylhydantoinea. A clinical, histological, and biochemical study. Acta Odontol Scand 1963;21:1–142.
7. Vernillo AT, Schwartz NB. The effects of phenytoin (5,5- diphenylhydantoin) on human gingival fibroblasts in culture. J Periodontal Res 1987;22:307–12.
8. Modeer T, Brunius G, Iinuma M, Lerner UH. Phenytoin potentiates interleukin-1-induced prostaglandin biosynthesis in human gingival fibroblasts. Br J Pharmacol 1992;106:574–8.
9. Little TM, Girgis SS, Masotti RE. Diphenylhydantoininduced gingival hyperplasia: its response to changes in drug dosage. Dev Med Child Neurol 1975;17:421–4.
10. Arya R, Gulati S, Kabra M, Sahu JK, Kalra V. Folic acid supplementation prevents phenytoin induced gingival overgrowth in children. Neurology 2011;76:1338–43.