Management of Phenytoin-Induced Gingival Enlargement: A Case Report

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ABSTRACT

Phenytoin-induced gingival enlargement is an illustrious and often reported gingival lesion. Patients undergoing treatment for epilepsy with phenytoin are frequently affected. Occurrence of such lesions among younger age groups is more than adults. Oral hygiene maintenance can modify Phenytoin-induced gingival enlargement, hence it plays a crucial role in control of this lesion. The clinical and microscopic appearance of drug-induced gingival enlargement caused due to any drug is similar, while the mechanisms of action may be dissimilar. This case report features phenytoin induced gingival enlargement in a young cooperative patient who was treated successfully.

KEYWORDS: Anticonvulsants, Drug-Induced, Epilepsy, Gingival Enlargement, Phenytoin.

INTRODUCTION

The term 'Drug-induced gingival enlargement' (DIGE) refers to gingival hypertrophy or hyperplasia caused due to long term use of a drug such as phenytoin (PHT). This condition is also induced by two other classes of drugs: antihypertensive calcium channel blockers such as nifedipine, verapamil, diltiazem and immune suppressants cyclosporine (cyclosporin A).[1]

Epilepsy, the most common chronic neurological disorder in humans, has a prevalence of approximately 1% in developed countries, rising to 2% in less developed nations.[2]

PHT (5,5 diphenylhydantoin) was first introduced as an antiepileptic drug by Merritt & Putnam in 1938.[3] Within a year of its initial clinical use, reports linking PHT to gingival enlargement appeared in the literature.[4]

The year 2014, marked the 75th anniversary of the discovery, by Dr. O. P. Kimball, that administration of diphenylhydantoin (Phenytoin; PHT) on a long term regimen for control of grand mal seizures is often accompanied by enlargement of the soft tissues surrounding the teeth.[5] This condition is frequently referred to as phenytoin-induced gingival enlargement (PIGE).

Yet, 3/4th of a century later, PHT remains as the drug of choice in seizure therapy worldwide although it may also be used in cases of neuralgias and cardiac arrhythmias.[6] It is estimated that about 30 to 50% of patients taking PHT develop significant gingival alterations.[2]

Other anticonvulsants such as sodium valproate, phenobarbitone, vigabatrin and primidone have also been associated with gingival enlargement but the cases of gingival changes after long term use of these drugs in adult patients have been rarely reported.[7]

After the commencement of treatment with the

How to cite this article:
Nasha A, Zade RM, Ramesh A, Shetty S, Zade V, Boddun M. Management of Phenytoin-Induced Gingival Enlargement: A Case Report. Int J Dent Med Res 2014;1(4):64-68.

associated medications, the clinical manifestations of gingival enlargement often appear within 1 to 3 months. But the pathogenesis of PIGE is yet unsure.[8]

CASE REPORT

A 17 year old male was referred to Department of Periodontology, Chhattisgarh Dental College and Research Institute, Rajnandgaon with the chief complaint of generalized swollen gums since 8 months. The patient hesitate meeting people because of unesthetic appearance and presence of severe oral malodor [Figure 1].

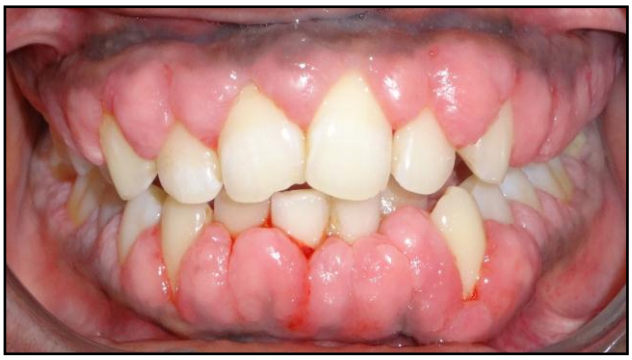

Figure 1: Preoperative facial view of the patient

Medical history showed that the patient had epilepsy since the age of 9 and had tried various types of treatments but did not get much benefit. For the last 8 months, the patient had been put on PHT (Eptoin 100 mg tds). The patient did not receive any prior dental therapy.

Since then, the drug was not changed and was associated with gradual gingival enlargement. On clinical examination, the gingival tissues were bead shaped, pale pink in color, enlarged, firm, and fibrotic [Figures 2 and 3]. Generalized bleeding on probing was present. Oral hygiene was poor.

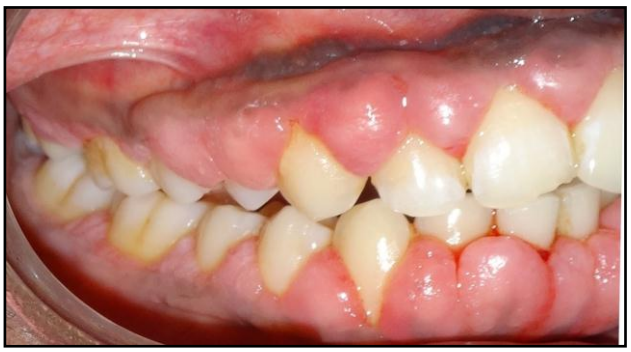

Figure 2: Right side preoperative view

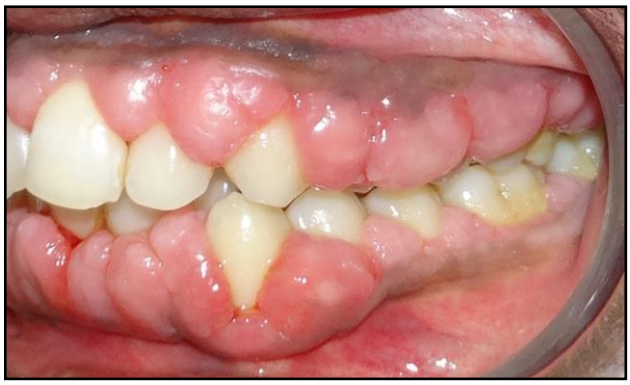

Figure 3: Left side preoperative view

Complete hemogram values were under normal limits. A diagnosis of generalized DIGE was made. With the consent of the patient and his physician, complete oral prophylaxis was performed and 0.2% chlorhexidine mouthwash (10 ml BID for 7 days) was prescribed to the patient.

After 1 week, the gingival condition improved and the patient was asked to maintain oral hygiene with a soft toothbrush and warm saline gargles and to discontinue the chlorhexidine mouthrinse.

The neurological condition of the patient did not permit the substitution of PHT immediately; so the patient was informed about the chances of recurrence and was recalled for supportive periodontal therapy after 1 month, 3 months, and 6 months.

Substantial enlargement of gingival tissues was present at the 6-month recall visit, hence surgical excision was planned. The patient was informed about the surgical procedure, and a written consent was obtained for periodontal surgery.

Following the administration of local anesthesia (2% lignocaine with 1:80,000 adrenaline), the pockets on each surface were explored with a periodontal probe and marked with a pocket marker. Each pocket was marked in several areas to outline its course on each surface.

The initial scalloped internal bevel incision was then made starting apical to the points marking the course of the pockets with a No. 15 blade including the creation of new interdental papillae. [Figures 4].

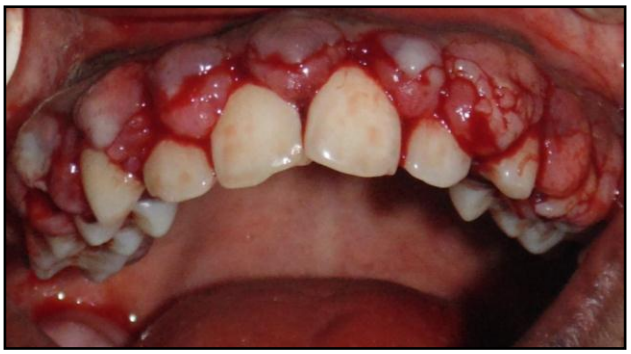

Figure 4: Internal bevel incision.

The incision was carried out to a point apical to the alveolar crest. Thinning of the flap was done along with the initial incision in the buccolingual direction up to the mucogingival junction. Care was taken to retain enough amount of attached gingiva after removal of the pocket wall.

A crevicular incision was made from bottom of pocket to the bone followed by interdental incision to detach the connective tissue from the bone. The triangular wedge of tissue thus created was removed with the help of curettes.

Following scaling and root planing, the flaps were positioned on the root-bone junction [Figures 5 and 6] and continuous sling sutures were placed using black braided 3-0 silk sutures [Figures 7 and 8]. Postoperative medications and instructions were given to the patient.

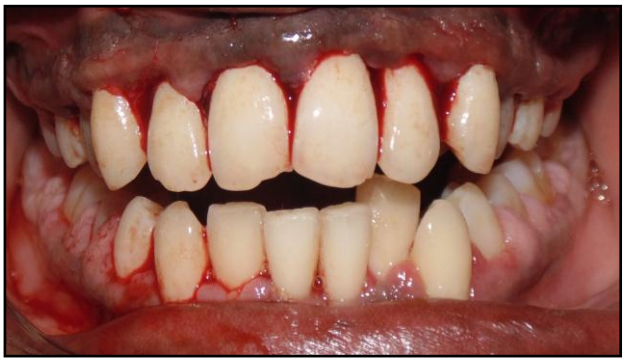

Figure 5: Adaptation after excision of enlarged tissue in upper arch

Sutures were removed after 7 days. The healing was uneventful. The same procedure was carried out for both upper and lower arch with a gap of 7 days between the two periodontal surgeries. The 2 week post-operative results were satisfactory due to adequate plaque control [Figures 9].

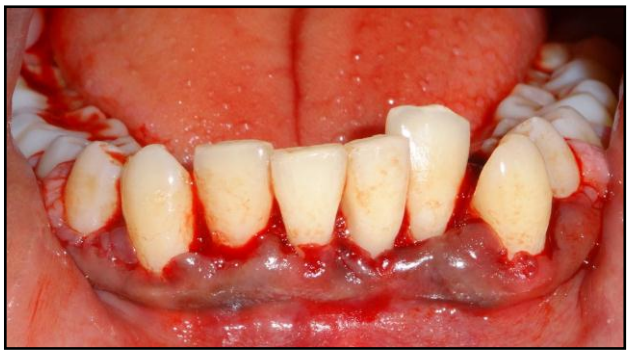

Figure 6: Adaptation after excision of enlarged tissue in lower arch

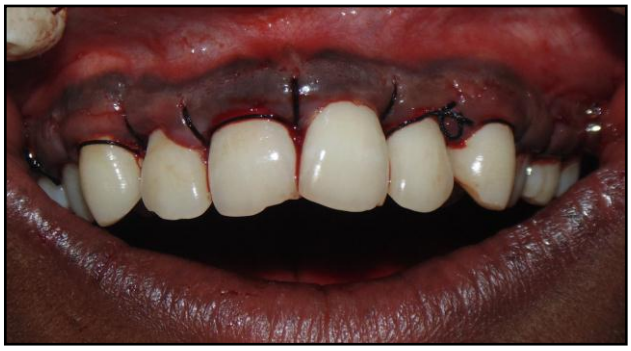

Figure 7: Post-operative suturing in upper arch

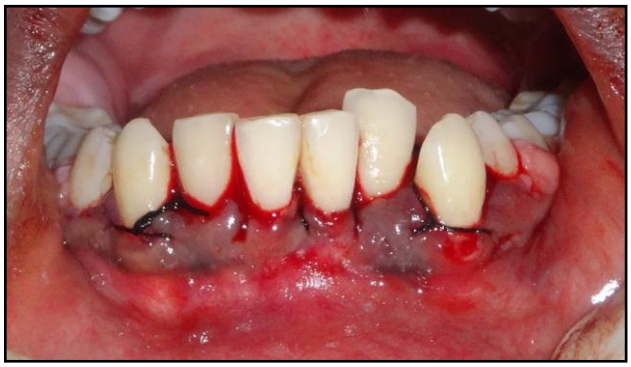

Figure 8: Post-operative suturing in lower arch

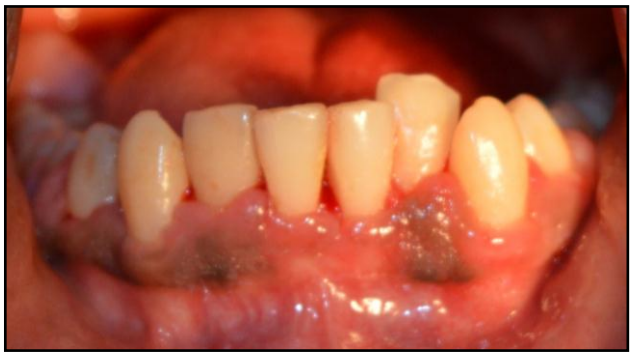

Figure 9: 2 week Post-operative view of lower arch

The excised tissues were sent for histopathological examination. Microscopic examination of soft tissue

specimen revealed gingival hyperplasia showing hyperplastic epithelium with thin elongated rete pegs penetrating deep into the connective tissue. Connective tissue showed dense collagen fibers bundles along with blood vessels and chronic inflammatory cells.

Patient's oral hygiene maintenance and esthetics has improved sufficiently which has resulted in absence of malodor and significant increase in patient's quality of life.

DISCUSSION

A patient with gingival enlargement presents with some of the common clinical symptoms like unpleasant appearance, hindrance during speech and mastication, malalignment of teeth, occlusion difficulty, increased frequency of caries and development of periodontal diseases. The association between PHT and gingival enlargement exists since decades.[9]

Microscopic analyses of PIGE biopsies show a surplus tissue of apparently regular composition or with an increased amount of collagen and number of fibroblasts. Often, the overlying surface epithelium presents rete pegs elongating into the underlying lamina propria. The results from one study suggested that sodium valproate may be considered a safe alternative to PHT for the treatment of adult-onset epilepsy.[10]

Most of the studies to evaluate pathogenesis of DIGE involving anticonvulsants have been done with PHT.[9] While the mechanisms of action may be dissimilar, the clinical and microscopic appearance of DIGE caused due to any drug is alike.[11] It begins as a firm, nodular enlargement of the interdental papilla, within 3 months of taking drugs like PHT, which is limited to keratinized portions of the gingiva. Since all lesions show an increase in the connective tissue component, so the target cell is the gingival fibroblast.[12] This case also presented similar clinical features.

Seymour et al., in their review on the pathogenesis of drug induced gingival overgrowth, the risk factors considered include age, sex, drug variables, concomitant medication, periodontal variables and genetic factors.[10] Gingival inflammation is often associated and is a requirement for development of the enlargement. The presence of plaque acts as a cofactor in the etiology of DIGE. In this case, severe gingival inflammation was also present.

The pharmacokinetics of inducing drugs and the gingival binding affinity of these drugs are determinants in the pathogenesis of DIGE.[9] A recent study concluded that the CYP2C9 gene polymorphism is responsible for modification of the inflammatory response to PHT.[13]

The hypothesis that DIGE is a side effect with a multifactorial etiology is supported by the review of various investigations into its pathogenesis. The inflammatory changes that occur within gingival tissue appears to coordinate the communication between drugs and fibroblasts.[2]

CONCLUSION

PIGE is not a rare phenomenon and it is one of the most widespread unwanted effects of systemic medication on the periodontal tissues. The three important factors which are significant in the expression of these gingival changes are drug variables, plaque-induced inflammatory changes in the gingival tissues, and genetic factors which determine the heterogeneity of the fibroblast. Yet, our understanding of the pathogenesis of gingival overgrowth is partial. Hence, it is important to identify and explore possible risk factors concerning to both prevalence and severity of PIGE to provide ample information for the design of future preventive and therapeutic approach.

ACKNOWLEDGEMENT

The authors acknowledge the staff and students of the Department of Periodontics, Chhattisgarh Dental College and Research Institute, Rajnandgaon, Chhattisgarh for supporting in their work.

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Source of Support: Nil
Conflict of Interest: Nil