EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 9
605-609
Year: 2016

PERIODONTAL MANAGEMENT OF PHENYTOIN INDUCED GINGIVAL ENLARGEMENT: A CASE REPORT

[1]Dr. Sowmya N. K., *[2]Dr. Khyati Chandra, [3]Dr. Gayathri G. V. and [4]Dr. D. S. Mehta

[1]Reader, Department of Periodontology, Bapuji Dental College and Hospital, Davangere.
[2]Post Graduate Student, Bapuji Dental College and Hospital, Davangere.
[3]Professor, Department of Periodontology, Bapuji Dental College and Hospital, Davangere.
[4]Head of the Department, Department of Periodontology, Bapuji Dental College and Hospital, Davangere.

Corresponding Author: Dr. Khyati Chandra
Post Graduate Student, Bapuji Dental College and Hospital, Davangere.

Article Received on 20/07/2016 **Article Revised on 11/08/2016** **Article Accepted on 01/09/2016**

ABSTRACT
Gingival enlargement is a common clinical feature of gingival and periodontal diseases. It is not an uncommon side effect of certain systemic drugs. Drug-induced gingival enlargement is the term now used to describe medication-related gingival hypertrophy or hyperplasia, Gingival overgrowth (GO) is a side effect associated with some distinct classes of drugs, such as anticonvulsants, immunosuppressant, and calcium channel blockers. Drug-induced gingival enlargement is the term now used to describe medication-related gingival hypertrophy or hyperplasia, a condition commonly induced by three main classes of drugs: anticonvulsants, antihypertensive calcium channel blockers and the immunosuppressant cyclosporine. The pathogenesis of drug-induced gingival enlargement is uncertain and there appears to be no unifying hypothesis that links together the three commonly implicated drugs. Epilepsy is the most common chronic neurological disorder in human. Antiepileptic drug phenytoin is one of the main drug responsible for drug induced gingival overgrowth (DIGO) that alters the extracellular matrix metabolism affecting the gingival tissue. The prevention and m management of drug induced gingival enlargement remains unsatisfactory. The problem is compounded by the high recurrence rate arising from chronic usage of the listed medications and persistence of risk factors. The present case report describes the treatment of a patient with a phenytoin-induced gingival enlargement and its management which includes both non-surgical and surgical management followed by supportive therapy leading to a predictable and an excellent outcome.

KEYWORDS: Phenytoin, Gingival overgrowth, prevention, Drug Induced Gingival Overgrowth, Antiepileptic drug management.

Gingival hypertrophy or hyperplasia induced by medication is termed as drug induced gingival enlargement. Anticonvulsants/anti-epileptics, immunosuppressants anti-hypertensives are the three main classes of drugs responsible for the drug induced gingival enlargement. Various risk factors like age, drug dose, genetic factors, plaque induced inflammation are contributing to the establishment of the enlargement, though the hypothesis and the pathogenesis is uncertain. Antiepileptic drug phenytoin is one of the main drug responsible for drug induced gingival overgrowth that alters the extracellular matrix metabolism affecting the gingival tissue. However, the pathogenesis of such drug induced gingival overgrowth remains fulfilled by some inconsistent findings.

This case report highlights the phenytoin induced gingival overgrowth (PIGO) in a 24-year-old female patient and its management which includes both non-surgical and surgical management followed by supportive therapy leading to a predictable and an excellent outcome.

CASE REPORT
A 24-year-old female patient reported to the department of periodontics with a chief complaint of generalized swollen gums which had bleeding on slightest incitement. Patient also complained of forwardly placed teeth and few missing teeth in the upper front tooth region of jaw. On eliciting the medical history, the patient was epileptic since the age of 10 and was on medication and the reported drug regimen was 300mg/day phenytoin and 100 mg/day phenobarbital. Multidisciplinary approach was considered for the treatment of the patient. Patient gave a history of an epileptic attack around 2 years back when she lost her right maxillary central incisor due to trauma. Periodontal examination revealed pale pink, enlarged, firm and

fibrotic gingiva with pronounced stippling. There was generalized bleeding on probing with high gingival bleeding index (80%), probing pocket depths was 2-3mm beyond the mucogingival junction in more than 30% of the teeth with presence of subgingival calculus. Bone loss was also confirmed by radiographic assessment. Routine blood investigations revealed a normal blood picture. A diagnosis of Phenytoin induced gingival overgrowth and chronic generalized periodontitis was made and no other risk factors were recognized. The patient's physician was consulted in earlier appointments and no consent was given regarding the change or substitution of the medication but the patient was given consent for periodontal surgical procedure with necessary precautionary measures. In view of this, the treatment plan consisted, initially, of conservative therapy with dental education, motivation and scrupulous oral hygiene instruction, in combination with scaling and root planing. Patient was explained about the maintenance of the oral hygiene and was advised to use 0.2% chlorhexidine mouthwash (10 ml for 7 days) twice daily. The proposed therapy was found to be effective for improving the clinical parameters evaluated (gingival bleeding index reduced to 34.7%), reduction but not complete resolution of the pocket depth post phase I therapy. Since there was persistence of periodontal pockets associated with bone loss periodontal surgical procedure was considered and the patient was explained the same with its future course if left untreated. Written informed consent was obtained for periodontal surgery from the patient. After anaesthetizing the area under strictly aseptic conditions, sounding of the alveolar bone was performed to assess and identify the areas of osseous defects. Using Bard Parker knife with #15 blade, the initial scalloped internal bevel incision was made atleast 3 mm coronal to the mucogingival junction (MGJ) including the creation of interdental papillae. The same blade was used to thin the gingival tissues in a buccolingual direction to the MGJ. At this point, the blade established contact with the bone and full and partial thickness flap was elevated. Using orban's knife the base of each papillae connecting facial and lingual incisions was incised. The excised tissues were removed with curettes. Following scaling and root planing, flaps were repositioned on top of the alveolar crest, and sutures were placed using an interrupted technique with black braided 3-0 silk sutures. The surgical site was covered with periodontal dressing. The post-operative instructions were given including only liquid, semisolid or finely minced foods for the first 24 hours, application of ice intermittently on the face over the operated area. Chewing on the un-operated side of the mouth. Post-operative medication included an antibiotic (amoxicillin 500mg TID for 3 days) and anti-inflammatory analgesic drug (paracetamol TID after meals for 3 days). Patient was recalled after one week for the suture removal and the healing was satisfactory and uneventful. The patient was recalled after 1 month for observing the healing process which was much satisfactory (fig:2). The same treatment protocol was followed for the remaining quadrants.

DISCUSSION

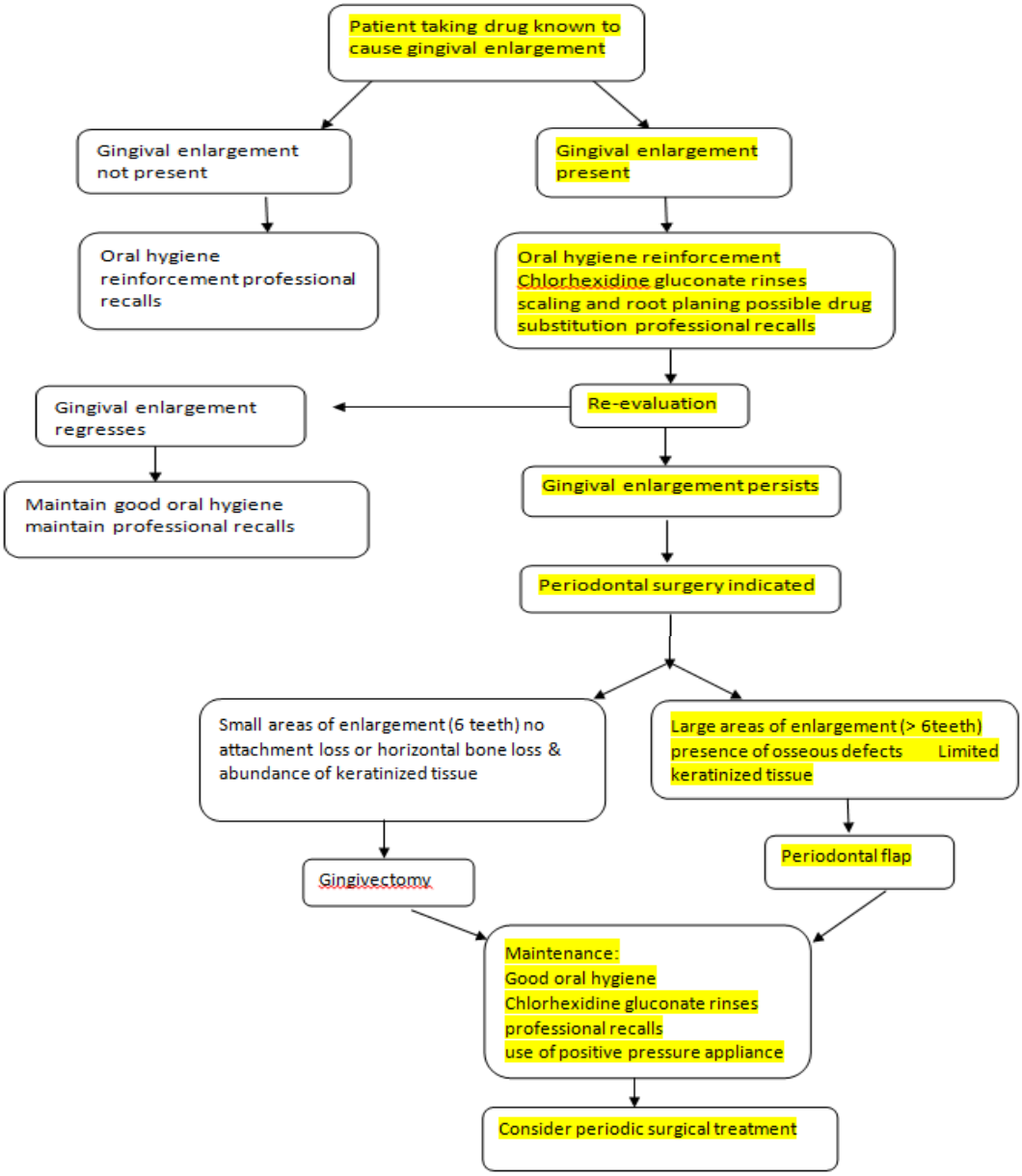
Phenytoin remains the drug of choice for treatment for grand mal, temporal lobe, and psychomotor epilepsy since it was first introduced in the 1930s. Drug-induced gingival overgrowth, also known as gingival hyperplasia secondary to drugs, was first reported in the dental literature in the early 1960s in institutionalized epileptic children who were receiving therapy with phenytoin (Dilantin) for the treatment of seizures.[1,2,3] phenytoin induced gingival overgrowth is a multifactorial pathology. Kato et al have suggested that it is probably due to an imbalance in collagen degradation rather than increase in its synthesis. These authors also showed reduction in the expression of genes encoding collagen types I and III concomitantly with a higher density of these fibers in gingival overgrowth. Thus it was suggested that phenytoin induced gingival overgrowth is probably due to an imbalance in collagen degradation rather than increase in collagen synthesis.[4]

This Impairment in collagen metabolism is seen as a consequence of enzymatic degradation of matrix metalloproteinases(MMPs) and Integrin mediated endocytosis leading to collagen accumulation during gingival overgrowth.[5] Apart from this, reduction of MMPs is also responsible for the phenytoin induced gingival overgrowth as in a study by Kato et al gene expression of Matrix Metalloproteinases (MMP)-1, 2, and 3 was reduced by phenytoin administration, while the tissue inhibitor (TIMP) TIMP-1 mRNA was markedly augmented.[6] There is a possible association between Gingival overgrowth and epithelial mesenchymal transition (EMT).[7] Gingival enlargements does not occur in all patients receiving phenytoin; when it does occur, there are 3 types:[8]

- **Type I:** Non-inflammatory hyperplasia. Substitution of phenytoin with another anti-epileptic drug is the only method of eliminating this hyperplasia. Subsequent to substitution,
the enlargement disappears after a few months.
- **Type II:** Chronic inflammatory enlargement not related to phenytoin use. This enlargement is caused entirely by local irritants, and resembles inflammatory enlargement in patients not receiving phenytoin.
- **Type III:** Combined enlargement. This is a combination of hyperplasia caused by phenytoin and inflammation by local irritation.

In our case, it was the type III gingival enlargement caused by use of phenytoin as it was a combination of drug induced hyperplasia of the gingiva concomitant with its inflammation contributed by the presence of local irritants. Treatment of drug induced gingival overgrowth (DIGO) should be based on the medication being used and the characteristic feature of a particular case. First consideration should be given to possibility of

substitution or changing the medication in accordance with the physician's consent. If the drug substitution had been done, it would have been essential to allow for a 6-12-month period to elapse between discontinuation of the offending drug and the possible resolution of the gingival enlargement.[8] In our case, it was phenytoin induced gingival overgrowth, carbamazepine[3] and valproic acid were the drug substitution both which are known to induce lesser enlargement. But the physician did not consent for either the change or substitution of the medication. So we commenced our treatment protocol which firstly included a strict emphasizing and motivation on plaque control measures as it is known that good oral hygiene decreases the degree of gingival enlargement, improves overall gingival health with regular motivation and professional care after therapy which are important to maintain long term results.[9] Gingivectomy and periodontal flap surgery are the two treatment options in cases which do not regress even after strict plaque control measures or drug substitution whenever feasible. The clinician's decision to choose any of the surgical technique is modifiable and made on the case to case basis. The factors to be considered are presence or absence of osseous defects, position of the periodontal pocket in relation to the mucogingival junction and the amount of keratinized gingiva. Our case required osseous recontouring due to persistence of pocket depth beyond mucogingival junction and absence of minimum 3mm of keratinized gingiva which made periodontal flap surgery as the treatment of choice that could have been treated with gingivectomy otherwise. The advantage of gingivectomy over periodontal flap surgery is the ease and the swiftness of the technique. The management of the drug induced enlargement can be done by.[10]



The highlighted text explains the treatment protocol followed in this particular case

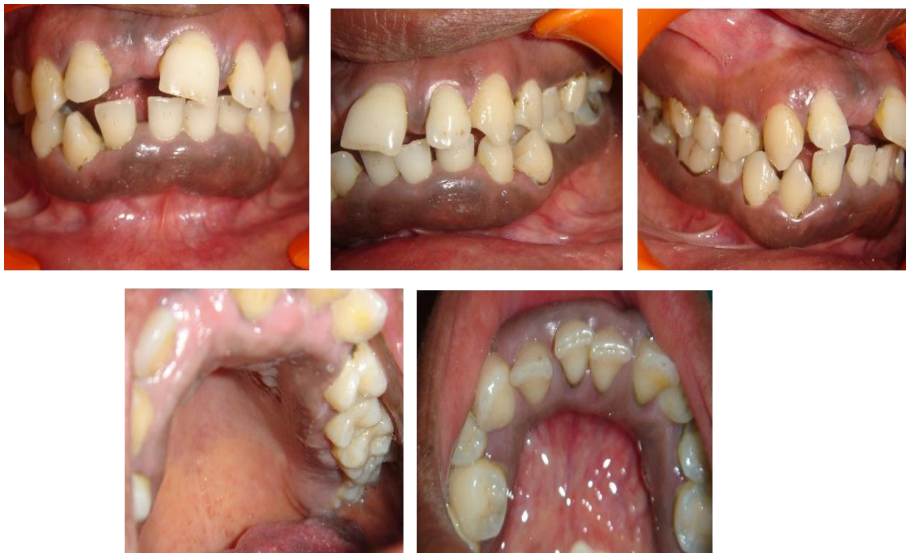


Fig1: Preoperative view

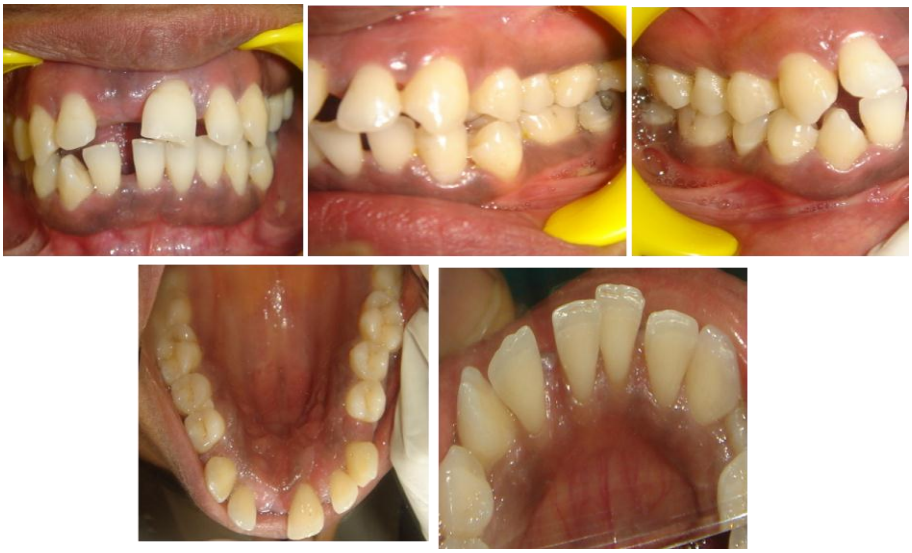


Fig 2: Post-operative view

CONCLUSION

Every case of drug induced gingival enlargement should be treated in a systematic manner encompassing consultation with patient's physician, substitution of the drug if possible, non-surgical and surgical periodontal therapy (gingivectomy/periodontal flap surgery), followed by supportive periodontal therapy. Phenytoin induced gingival overgrowth being the most common adverse drug reaction in individuals on antiepileptic therapy and poor oral hygiene as one of the important risk factor in the further progression of gingival enlargement, the importance of meticulous oral hygiene maintenance should not be undervalued. Considering the alternative to the medication should be considered if viable that can arrest or lessen the severity of the pathology. Surgical correction as in the mentioned case becomes the last recourse for those who do not respond well to other modalities.

REFERNCES

1. Thomason JD, Fallaw TL, Carmichael KP, Radlinsky MA, Calvert CA. Gingival hyperplasia associated with the administration of amlodipine to dogs with degenerative valvular disease (2004-2008). *J Vet Intern Med*., 2009; 23: 39-42. [Medline].
2. Vorkas CK, Gopinathan MK, Singh A, Devinsky O, Lin LM, Rosenberg PA. Epilepsy and dental procedures. A review. *N Y State Dent J*., 2008; 74: 39-43. [Medline].
3. Mohan RP, Rastogi K, Bhushan R, Verma S. Phenytoin-induced gingival enlargement: a dental awakening for patients with epilepsy. *BMJ Case Rep*., 2013; 23: 2013.
4. Gurgel BC, de Morais CR, da Rocha-Neto PC, Dantas EM, Pinto LP, Costa Ade L.Phenytoin-induced gingival overgrowth management with periodontal treatment. Braz Dent J., 2015; 26: 39-43.
5. Kato T, Okahashi N Ohno T, Inaba H, Kawai S, Amano A. Effect of phenytoin on collagen

accumulation by human gingival fibroblasts exposed to TNF-alpha in vitro. Oral Dis., 2006; 12: 156-62.
6. Kato T, Okahashi N, Kawai S, Kato T, Inaba H, Morisaki I, Amano A. Impaired degradation of matrix collagen in human gingival fibroblasts by the antiepileptic drug phenytoin. J Periodontol. 2005; 76: 941-50.
7. Sume SS, Kantarci A, Lee A, Hasturk H, Trackman PC. Epithelial to mesenchymal transition in gingival overgrowth. Am J Pathol, 2010; 177: 208-18.
8. Carranza FA Jr. Treatment of gingival enlargement. In: Carranza FA Jr., Newman MG, eds. Clinical Periodontology. 8th ed. Philadelphia: WB Saunders Company; 1996; 672-76.
9. Kara C, Demir T, Tezel A. Effectiveness of periodontal therapies on the treatment of different aetiological factors induced gingival overgrowth in puberty. Int J Dent Hyg, 2007; 5: 211-17.
10. Carranza FA Jr. Treatment of gingival enlargement. In: Carranza FA Jr., Newman MG, eds. Clinical Periodontology. 8th ed. Philadelphia: WB Saunders Company, 2006; 920-21.