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Case Report

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Phenytoin Induced Gingival Enlargement - Consultative Planning Between Oral Care Practitioners And Physicians: A Case Report

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Abstract
Diphenylhydantoin has been one of the most effective drugs available for the control of epileptic seizures. However, its usefulness is limited by a side effect that often leads to a severe, disfiguring overgrowth of the soft tissue. Incidence rates have ranged from 3 to 93%, but about 50% of patients on long-term phenytoin therapy develop gingival enlargement. Long-term phenytoin can also lead to a coarsening of the face, enlargement of the lips, and thickening of the scalp and face. Both genders and all races are susceptible to phenytoin-induced gingival enlargement. Those affected are largely adolescents and young adults, and less frequently, the elderly. Gingival enlargement becomes clinically noticeable within 2 to 3 months after initial administration of phenytoin and reaches its maximal severity after 12 to 18 months. This presentation describes the diagnosis and management of drug induced gingival enlargement associated with anti-epileptic therapy (phenytoin and phenobarbitone). This report demonstrates the significance of consultative planning between oral care practitioners and physicians for the prevention and treatment of such gingival lesions.

Key Words
phenytoin, gingival enlargment, electrocautery

Introduction:

Gingival overgrowth is well recognized unwanted effect associated with three major drugs/drug groups – phenytoin, ciclosporin and the calcium channel blockers. The prevalence of this unwanted effect varies between drugs, and a variety of risk factors have been identified in relation to the expression of drug-induced gingival overgrowth (DIGO).[1] Phenytoin is the most studied, its association with gingival enlargement dating back to 1939.[2]

Though numerous studies on this gingival lesion have been conducted, the pathophysiology of phenytoin-induced gingival enlargement (PIGE) is still not well understood. However, associations between factors relating to dental hygiene[3], phenytoin utilization[4], host genetic predisposition, multiple anti-epileptic therapy[5], reduced serum folate levels[6] and PIGE have been suggested.

The prevalence of PIGE varies from 13% in a community based study[7], to 50% in institutionalized patients[3]. Generally, a higher prevalence has been found in adolescents and children than in adults. In a paediatric study of 79 children taking phenytoin alone or in combination with other antiepileptic agents, 67% had gingival overgrowth[8].

Many different types of therapy have been tried to reduce or eliminate deep pockets by gingival surgery. Treatment of drug-induced gingival enlargement is based on the clinical features. DIGO is a common clinical problem that often requires intervention.

Today most periodontists use a surgical blade to incise or excise soft tissue. Classic gingival surgery primarily deals with the treatment of pockets – i.e., gingival sulci that are deepened due to a proliferation or an increase in bulk of gingival tissue in a coronal direction, with or without apical migration of the epithelial attachment. The surgical treatment is the definitive therapy of the DIGO, although the recurrence is frequent even with well conducted periodontal maintenance. The common surgical technique is the simple excision of the excessive gingival tissue with secondary healing – external bevel gingivectomy (EBG). The internal (reverse) bevel gingivectomy (IBG) often is used instead of an EBG if the tissue to be excised is thick and a long external bevel incision would be required to create knife-edged margins. It is accepted that gingival surgery (both EBG and IBG) is essentially limited to the treatment of pseudopockets. Other surgical technique which can be used are electrocautery and laser.

Case Report:

A 22 year female patient reported to the Dept. of Periodontontics, Subharti Dental College and Hospital, with swollen and bleeding gums and inability to eat on right side over 6 months. Past medical history indicated that she had epilepsy and was treated with Phenytion (400 mg/day, single dose orally) for the last 5 years. Since 1 year, patient noticed a gradual and painless enlargement of gingiva. The initial intra oral examination revealed a generalized and firm overgrowth of the gingiva on maxillary and mandibular arch **(Figure 1)**. The overgrowth was more prominent on the anterior region of the mandibular and maxillary arch. According to Bokenkamp[9] grading of gingival

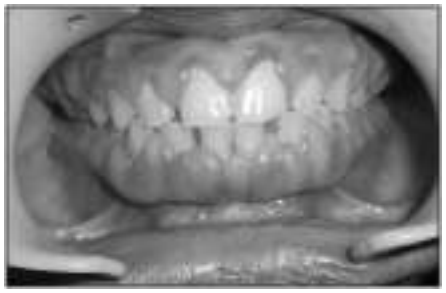


Figure 1

enlargement, Grade II gingival enlargement was present in relation to posterior teeth while Grade III enlargement in relation to 13 to 23 and 33 to 43. Marginal gingiva was reddish pink in color and rest of the gingiva was pink. Gingiva was leathery in consistency with purulent discharge, and bleeding on probing was present **(Figure 2, 3)**. On Microscopic examination, the gingival biopsy specimens showed connective tissue hyperplasia, acanthosis of the overlying epithelium with elongated retepegs and a few sparse inflammatory cells. The lesion was diagnosed as Phenytion -induced gingival overgrowth based on clinical, histological and medical evidences **(Figure 4)**.

Treatment:

Ideally, the treatment of choice for medically induced gingival overgrowth would be discontinuation of the associated medication. Nevertheless, this approach is often not possible. Effective treatment of a condition such as this generally focuses on correction of the aesthetic and/or functional problems that result, and can be divided into either nonsurgical or surgical alternatives[10]. Non-surgical techniques can limit the occurrence of this unwanted affect, reduce the extent of plaque-induced gingival inflammation and reduce the rate of recurrence. Phenytion sodium was substituted with Carbamazepine 200mg twice daily. Along with this, a strict oral hygiene regimen was followed consisting of oral hygiene instructions with frequent and correct brushing of teeth, professional scaling and prescription of chlorhexidine gluconate mouth wash [0.2%] two times a day. Surgical reduction of the overgrown tissues is frequently necessary to accomplish an aesthetic and functional outcome (Hallmon and Rossman,). Definitive treatment involves surgical elimination of the excess gingival tissue through implementation of gingivectomy procedure and electrocautery. The clinician's decision to choose between these two surgical techniques should be made on an individual basis, encompassing careful consideration of the following aspects: the extent of area requiring surgery; the presence of periodontitis and osseous defects; the amount of keratinized gingival, and the position of the base of the pockets in relation to the existing mucogingival junction. As the width of attached gingiva was sufficient and there was no underlying osseous defects external bevel gingivectomy (EBG) was done under local anesthesia **(Figure 5)** and electrocautery **(Figure 6)** was used to give proper contour and shape to gingiva. Periodontal dressing was placed and post operative instructions were given. Amoxicillin 500mg (tid for 5 days) and Ibuprofen 400mg were prescribed. After completion of the treatment, patient was put on maintenance phase **(Figure 7)**.

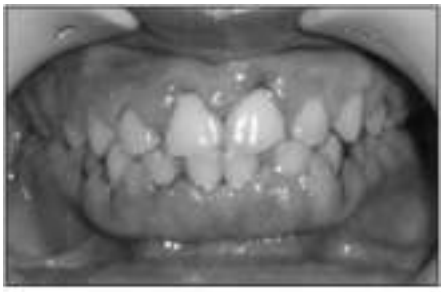
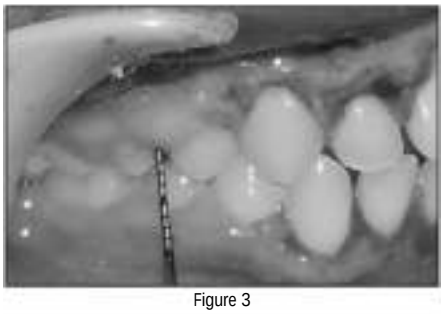


Figure 2



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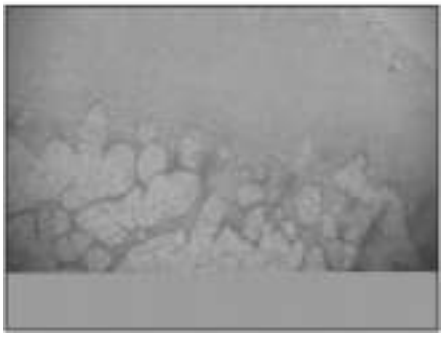


Figure 4

Discussion

Firm evidence of the involvement of phenytoin as the principal iatrogenic factor in the development of gingival enlargement has been presented in the literature[11]. Duration of treatment and phenytoin plasma levels have also shown a significant correlation to gingival enlargement in some studies[12]. Others, could not establish any statistically valid relationship between total plasma phenytoin levels, duration of treatment and gingival enlargement[13]. These relationships are likely to be complicated by a number of factors such as variable phenytoin plasma protein binding, nonlinear phenytoin elimination as well as nonlinear effect relationships[14]. Phenytoin is a drug with high plasma protein binding and the free phenytoin concentrations are better correlated with both efficacy and toxicity. A reduced plasma protein binding favours tissue distribution, particularly to those tissues with high phenytoin binding affinity such as the gingival fibroblasts[3]. The high plaque levels would suggest that despite the majority of patients claiming to brush their teeth daily (77%) they were not achieving effective plaque removal.

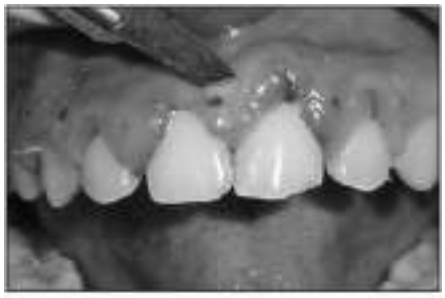
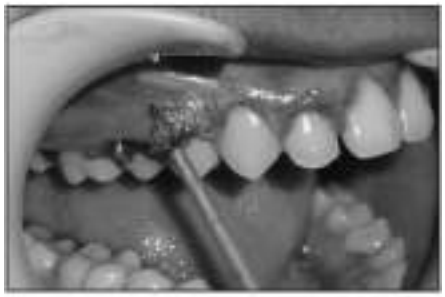


Figure 5



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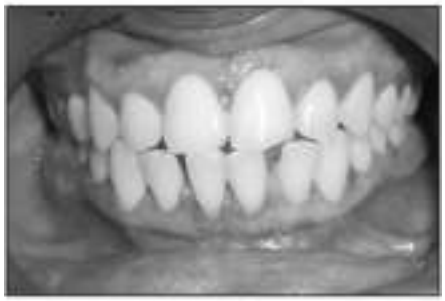

Figure 7 Post Op 3 Months

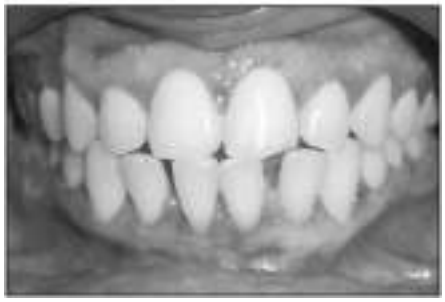

Figure 7 Post Op 5 Yrs

Some authors[15] argued against the link between gingival enlargement and plaque. They believed that gingival enlargement is a phenotypic presentation of the host's genetic response / susceptibility to the mitotic effect of phenytoin. Their argument was substantiated by the observation that some patients with high plaque levels had normal gingival tissue while others with no detectable plaque, exhibited clinically obvious gingival enlargement. This characteristic decline in folate level has been suggested to be one of the important promoters of PIGE[6]. Although a variety of non-surgical measures have been shown to be of some value in the management of DIGO, surgical correction of gingival overgrowth is still the most frequent treatment. Such treatment is only advocated when overgrowth is severe. However, in the day-to-day management of individual patients it is perhaps more important to consider the impact that gingival changes may have on the patients quality of life or their ability to maintain a healthy periodontium. From the patient's prospective, surgical correction of DIGO should result in little or no post-operative pain or sequelae, good aesthetics and a reduced risk of recurrence. Currently, the surgical management of DIGO includes the scalpel gingivectomy, overgrowth flap surgery, electrosurgery and laser excision.

Scalpel Gingivectomy

The surgical treatment of choice is the gingivectomy, which was first advocated for drug-induced gingival overgrowth in 1941[16]. The soft tissue wall of the pocket is excised[17]. As there is, in nearly all circumstances, adequate attached gingiva, there is little fear of creating mucogingival problems with this technique. Conventionally the excess tissue is released by means of a long bevel incision which should ideally allow the complete removal of pocket tissue as part of the excised tissue mass, particularly in the inter-dental region. If the tissue is greatly thickened in the horizontal plane, a shallower initial incision may be required to gain access to the inter-dental area, followed by a separate re-contouring of the remaining tissue to reduce its bucco-lingual width, if necessary. With this approach the increased bulk of the tissue can be removed, the soft tissue pockets are eliminated and the crowns of the teeth exposed. This procedure improves access to any faulty restorations or calculus deposits, facilitating their elimination. The procedure is used extensively and the technique is straight-forward, accurate and causes minimal damage to the surrounding tissues. As it may be regarded as the ''standard treatment'', it is often compared with other techniques, however, there are few studies on recurrence rates, patient satisfaction with aesthetics and incidence of post-operative complications after such surgery. Peri-operative haemorrhage is the main disadvantage of scalpel excision, and this can be significant in highly vascularized and inflamed overgrown gingival tissues[18]. Aesthetic outcomes have also been poorly evaluated after scalpel gingivectomy and again the only evidence comes from a comparative study[19] Patients with overgrowth were treated by either flap surgery or gingivectomy. Those treated by the latter method appeared to have a ''smoother'' gingival surface than when treated by a flap procedure. Numbers in this study were small and long-term benefits need to be considered. Further work in this area is required.

Electrosurgery

Electrosurgery techniques have been used in dentistry for the past 70 years.

Although such techniques produce adequate haemostasis, they have the disadvantage

of causing a surrounding zone of thermal necrosis, which may impede wound healing. Reports in the literature have confirmed delayed healing of electrosurgery wounds when compared with scalpel wound healing[18]. This is probably due to the production and accumulation of excessive latent heat, which can be significant if electrosurgery is performed inappropriately. The amount of latent heat produced is dependant upon instrumentation variables, such as type of waveform, size of cutting electrode, time required for incision and the energy produced at operating site[20]. Nevertheless, surgical intervention using conventional means (scalpel) may sometimes be technically difficult and/or impractical for example in children or mentally handicapped, or in patients suffering from impaired haemostasis. In these situations the use of electrosurgery may be advantageous[21]

Conclusion:

The use of medications with the potential to contribute to the development of gingival overgrowth will likely increase in the years to come. Among the old and relatively newer pharmacologic agents involved in gingival enlargement, overall, phenytoin still has the highest prevalence rate (approximately 50%), with calcium channel blockers and CsA-associated enlargements about half as prevalent. If possible, treatment is generally targeted on drug substitution and effective control of local inflammatory factors such as plaque and calculus. When these measures fail to cause resolution of the enlargement, surgical intervention is recommended. These treatment modalities, although effective, do not necessarily prevent recurrence of the lesions. Newer molecular approaches are needed to clearly establish the pathogenesis of gingival overgrowth and to provide novel information for the design of future preventative and therapeutic modalities.

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