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PHENYTOIN-INDUCED GINGIVAL ENLARGEMENT: MULTIDISCIPLINARY CLINICAL MANAGEMENT: A CASE REPORT

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ABSTRACT

Introduction: Gingival overgrowth, recognized since long as a deleterious side-effect of chronic phenytoin therapy, whenever occurs, lasts throughout the period of drug therapy and is difficult to manage owing to its insidiously progressive nature, leading to frequent recurrences.

Methods: This case report documents a case of severe gingival enlargement associated with periodontitis in a patient under antiepileptic therapy, along with brief review of literature concerning etiopathogenesis, and provides a rational model for its clinical management.

Conclusions: It is important that clinicians become aware of the potential etiologic agents of drug induced gingival enlargement and its characteristic features in order to be able to prevent, diagnose and successfully manage it.

Key words: *periodontitis; phenytoin; gingival enlargement; periodontal therapy*

INTRODUCTION

Phenytoin is an anti-epileptic drug commonly used as a therapeutic agent in patients with epilepsy, either alone or in combination with other anticonvulsant drugs. Advantages of phenytoin include its effectiveness, low cost, availability, and frequency of administration. Among the side effects of phenytoin therapy, gingival enlargement is a well-recognized adverse effect, occurring on average among approximately 50% of patients receiving this drug. [1] A summary of estimated prevalence rates for drug (anticonvulsants) -associated gingival enlargement is shown in Table 1. [2]

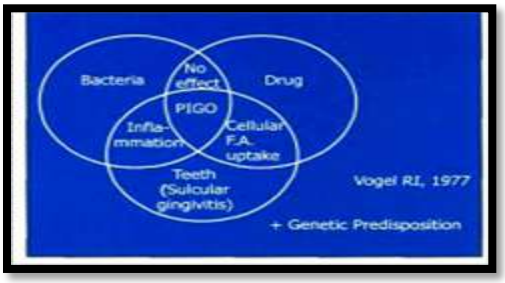

Figure 1- Phenytoin induced gingival enlargement-multifactorial model by Vogel.

Although several studies have been conducted regarding phenytoin-induced enlargement, the pathogenesis of this gingival lesion still is not understood. The literature has suggested an association between phenytoin-induced gingival enlargement and a variety of conditions, including multiple anti-epileptic therapies, plaque accumulation, host genetic predisposition, and reduced serum folate levels. [3] [Figure: 1]

Management of gingival hyperplasia requires understanding etiopathogenesis of the condition. Drug-induced gingival hyperplasia may improve with substitution of other drugs that minimally affect the gingiva, along with reinforcement of good home care oral hygiene regimens and periodic professional surgical excision of hyperplastic gingivae. [4]

This case report clearly describes the challenges that oral and medical health practitioners face when developing appropriate prevention and treatment programs for epileptic patients, particularly those with periodontal disease, emphasizing multidisciplinary planning for the prevention and treatment of gingival lesions in these medically compromised patients.

Figure 2- Preoperative intraoral view of the mandibular arch showing severe gingival enlargement

CASE HISTORY

Diagnosis:

A 20-year-old female reported to the outpatient department of our institute complaining of progressive swelling in the gums since one year. The patient had been taking phenytoin over a period of four years, for seizure control. Intraoral examination revealed moderate-to-severe overgrowth of a firm, dense and fibrotic consistency that involved both the maxillary and mandibular arches.[Figures: 2-3]Full-mouth periodontal charting, including assessment of probing depth and clinical attachment level, revealed

deep pockets throughout the mouth, and abundant plaque and calculus deposits. The radiographic findings, which corroborated those of the clinical examination, revealed generalized alveolar bone loss. [Figure: 4]

Figure 3- Preoperative intraoral view of the maxillary arch. showing generalized gingival enlargement

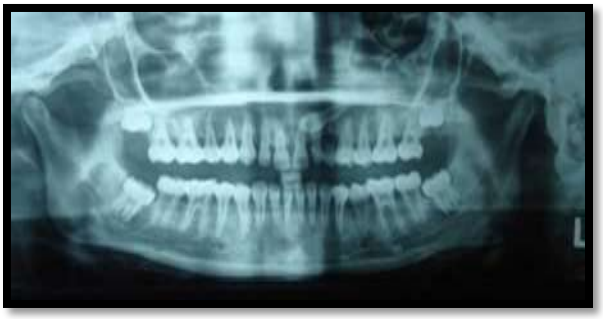

Figure 4- Preoperative panoramic radiograph of the maxillary and mandibular arches showing generalized alveolar bone loss

Medical and dental management:

The patient initially underwent phase 1 periodontal therapy that comprised scaling, root planning and oral hygiene instructions. The neurophysician gradually tapered phenytoin over a period of one month replacing it with phenobarbitone. The patient was well compensated showing no episode of recurrent seizure activity. One month later Phase 2 therapy was performed, involving periodontal surgery in all four quadrants utilizing an internal bevel gingivectomy [Figure:5]combined with open-flap debridement.[Figure-6]The patient was followed up regularly; no recurrence of gingival overgrowth was observed six months after the surgery. [Figures: 7-8]

Figure 5- Internal bevel gingivectomy procedure on the right maxillary quadrant

Figure 6- Open-flap debridement

Histopathologic Findings:

The microscopic evaluation of these sections revealed parakeratinized stratified squamous acanthotic epithelia with thin long rete ridges extending into the connective tissue. The underlying connective tissue showed dense wavy bundles of collagen fibres containing numerous fibrocytes and fibroblasts. Some sections in the connective tissue

exhibited infiltration of chronic inflammatory cells, a few scattered multinucleated giant cells and areas of neovascularization. [Figure: 9]

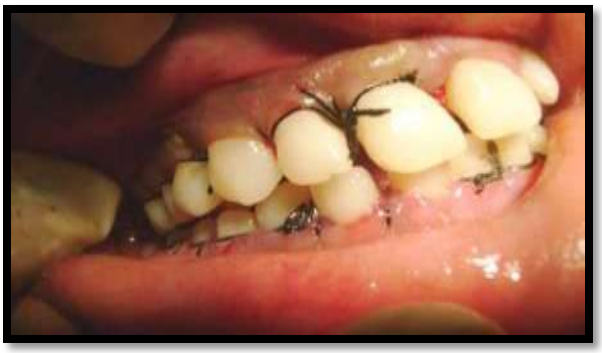

Figure 7- Frontal view of the maxillary and mandibular arches 2 weeks after surgery

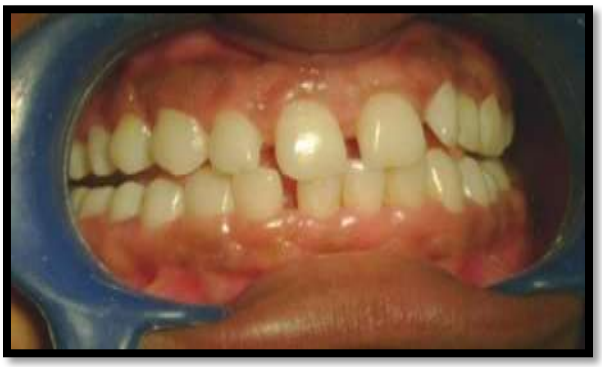

Figure 8- Frontal view of the maxillary and mandibular arches 6 months after surgery

DISCUSSION

Gingival enlargement in individuals using phenytoin first was described in 1939.[5] The precise mechanism by which drug-induced gingival enlargement occurs is still not completely understood, although a number of hypothesis have been suggested.[6]

Three significant factors, which are important in the expression of these gingival changes, and can be considered, are: drug variables, plaque-induced inflammatory changes in the gingival tissues and genetic factors – the latter determining the heterogeneity of the gingival fibroblasts. [7] Based upon this knowledge, a combined treatment approach, including periodontal therapy and medication adjustments is required for prevention and management of phenytoin-induced gingival enlargement.

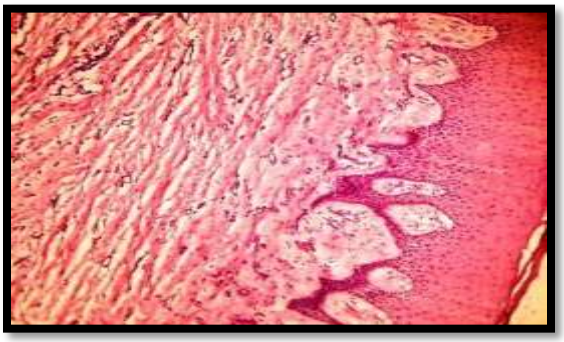

Figure 9 - Photomicrograph of histopathological specimen illustrating the presence of a thickened acanthotic epithelium with elongated rete ridges and densely fibrous connective tissue

Clinical manifestation of gingival enlargement frequently appears within one to three months after initiation of treatment with phenytoin .Gingival overgrowth normally begins at the interdental papillae and is more frequently found in the anterior segment of the labial surfaces. Gradually, gingival lobulations are formed increasing the plaque retentive areas which in turn, predispose to the development and/or enhancement of the overgrowth. Disfiguring gingival overgrowth triggered by these medications is not only esthetically displeasing but often impairs nutrition and access for oral hygiene, resulting in an increased susceptibility to oral infection, caries, and periodontal diseases.[8]

Several studies have demonstrated the benefits of a preventive periodontal program, including a dental prophylaxis and reinforcement of oral hygiene at frequent intervals, for patients taking phenytoin.[9]A

preventive dental program should be initiated for patients as soon as they begin taking phenytoin, especially when periodontal attachment loss is present, because although gingival enlargement that occurs can be treated, the alveolar bone loss is irreversible, compromising tooth supporting apparatus permanently. Recently, the feasibility of phenytoin substitution has increased with the addition of a new generation of anticonvulsants such as lomatrigine, gabapentin, sulthiame, and topiramate. Reducing the dose of the drug or suppressing it and substituting another are the logical options for controlling gingival enlargement induced by anti-epileptic drugs.

Pharmacologic Agent	**Trade Name**	**Prevalence**
Phenytoin	Dilantin	50%
Sodium valproate (valproic acid)	Depakene, Depacon, Epilim, Valpro	Rare
Phenobarbitone	Phenobarbital, Donnatal	<5%
Vigabatrin	Sabril	Rare
Carbamazepine	Tegretol	None reported

Table 1.Estimated Prevalence of Drug (Anticonvulsants)-Associated Gingival Enlargement according to the most frequently reported Prevalence Rates[2]

In the present case, the patient's neurologist prescribed phenobarbitone as a substitute for phenytoin. Phenobarbital remains a commonly prescribed alternative anti-epileptic medication that has some association with gingival overgrowth; however, compared to phenytoin, this side effect occurs infrequently.

Phenytoin withdrawal and scaling and root planing reduced gingival hyperplasia and inflammation effectively in this patient; however, surgical treatment was required to eliminate residual gingival overgrowth. The remaining excess tissue and calculus were removed using a conventional flap after the physician determined the patient's risk status in relation to proposed surgical procedures. After surgery, healing was uneventful and significant regression of the initial condition (gingival suppuration, bleeding on probing, gingival hyperplasia, and periodontal pockets) was observed.

The patient was placed on a maintenance and follow-up program to prevent recurrence of periodontitis and hyperplasia. A three month interval for periodontal maintenance therapy has been recommended for patients taking drugs associated with gingival enlargement.[10]

The maintenance program consisted of a medical history update, re-evaluation of clinical periodontal parameters, prophylaxis, and additional instruction concerning oral hygiene.

CONCLUSION

Current studies on the pathogenetic mechanism of phenytoin-induced gingival enlargement are focusing on the direct and indirect effects of these drugs on gingival fibroblast metabolism.

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.

The present case reflects the complexity of managing cases of phenytoin-induced gingival enlargement associated with periodontitis and reinforces the need for multidisciplinary treatment care and more rational anti-epileptic therapies.

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