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Case Report

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Conservative Management Of Nifedipine Influenced Gingival Enlargement - A Case Report

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Abstract
Gingival enlargement is a well documented unwanted effect associated mainly with phenytoin, cyclosporine, and the calcium channel blockers3, 10. Amongst the calcium channel blockers, nifedipine is the most widely used10. It may cause aesthetic disfigurement, speech disturbances, difficulty in mastication. It may also impede effective tooth cleaning, cause abnormal tooth movement, or force the teeth out of alignment. The management of drug influenced gingival enlargement is a challenge for the periodontist, mainly due to less understanding of its pathogenesis, difficulties in selection of proper line of management and recurrence of the enlargement. Gingival enlargement can be managed locally and systemically with a combination of medical and dental treatment. Co-operative teamwork and good communication between the patient, their doctor and their dentist are essential.
This report discusses the importance of conservative approach (scaling and root planing along with drug replacement) in the management of a case of nifedipine influenced gingival enlargement. The need for extensive surgery was almost completely alleviated after this approach.

Key Words
mastication, collagen, drug. nifidipine

Introduction

"Gingival enlargement or overgrowth" is now the preferred term for all medication-related gingival lesions previously termed "gingival hyperplasia or hypertrophy". These earlier terms did not reflect the histologic composition of the pharmacologically modified gingiva. Drug-induced gingival overgrowth was first reported by Kimball in 1939 associated with chronic use of the anti-epileptic drug phenytoin[11].

Nifedipine is the calcium channel blocker that is most frequently implicated in drug induced overgrowth. Estimates of the prevalence of nifedipine-induced gingival overgrowth ranges from 20% to 83%6. Nifedipine was first associated with overgrowth in 1984 (Lederman et al. 1984, Ramon et al. 1984). It has been reported as causing clinical overgrowth of the gingiva in 5 of 34 patients treated with the drug for a period of 1 year or more (Barak et al. 1987)[5]. Drug-induced gingival overgrowth appears to be more prevalent in children and adolescents and has a predilection for the anterior gingival tissues. Gingival changes can occur within 3 months of dosage (Hassell 1981, Seymour 1991, Seymour & Jacobs 1992)[10].

The treatment of drug influenced gingival enlargement is a challenge for the periodontist due to difficulty in the selection of proper line of management and its high recurrence rate. Comprehensive treatment of these cases is multidisciplinary in nature. Dentists and physicians should first consider the nonsurgical approach, including the removal of local factors and replacement of the offending drug. If the nonsurgical approach is not effective, periodontal surgery can remove the enlarged gingival tissues.

This paper aims at drawing the attention of dentists towards the conservative management of nifedipine induced gingival overgrowth along with providing a brief review of the pharmacologic profile of this drug and its effects on the gingiva.

Pharmacological Profile (Nifedipine)

- FORMULA: $C_{17}H_{18}N_2O_2$
- It is a dihydropyridine calcium channel blocker (other members:- amlodipine, nicardipine, isoradipine, nitrendipine & felodipine).
- CHEMICAL DESIGNATION: 1,4-Dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5- pyridine dicarboxylic acid, dimethyl ester**[Figure 1]**.

Mode Of Action

- Nifedipine is a calcium-ion-influx inhibitor in cardiac and smooth muscle which does not change serum calcium concentrations. Other drugs of this class include Verapamil, perhexiline maleate and prenylamine lactate. The precise mechanism by which this relieves angina is believed to include relaxation and prevention of coronary artery spasm as well as reduction of oxygen utilization by the myocardium. The mechanism at the cellular level is the prevention of calcium-dependent ATPase from breaking down the formed ATP, thereby decreasing high-energy phosphate consumption, mechanical tension and oxygen requirements of the myocardium. The myocardium therefore functions at a lower energy level. Nifedipine and phenytoin have similar pharmaco-physiologic effects at the cellular level despite differences in target tissue[8].

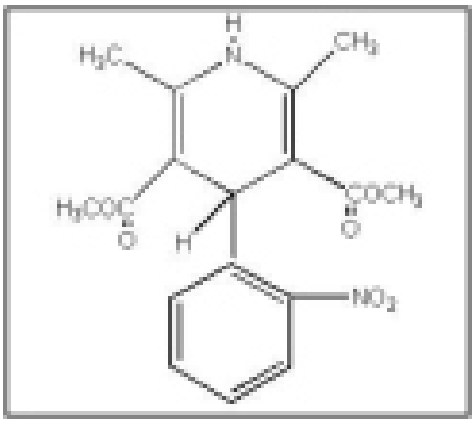

Figure 1

Dosage: 2.5 or 5 grams, single dose (alone or in combination with Atenolol)

Adverse Effects

Side effects of nifedipine are rare. However, headaches, dizziness, nausea, and tiredness have been reported usually occurring at the beginning of the treatment and decreasing as the treatment progresses[11]. Facial flushing, oedema, gingival hyperplasia have also been reported.

Nifedipine is in the FDA pregnancy category C. This means that it is not known whether this medication will be harmful to an unborn baby. It should not be taken without consulting a doctor during pregnancy. Nifedipine passes into breast milk. A person over 65 years of age may be more likely to experience side effects from nifedipine. A lower dose of this medication may then be prescribed by the doctor.

Significant sequestration of drug occurs in patients exhibiting gingival overgrowth.

Clinical And Histologic Features

It starts as a painless, beadlike enlargement of the interdental papilla and extends to facial and lingual gingival margins. It may partially or completely cover the tooth surfaces. If there is underlying periodontal disease then the tissues may appear inflamed[2]. It tends to be more severe in areas where plaque accumulates. Otherwise the gingival enlargement is distributed symmetrically and anterior teeth are more severely affected than the posterior teeth[12]. Gradually, gingival lobulations are formed that may appear inflamed or more fibrotic in nature, depending on the degree of local factor- induced inflammation. The fibrotic enlargement normally is confined to the attached gingiva but may extend coronally and interfere with esthetics, mastication, or speech. Disfiguring gingival overgrowth triggered by this medication is not only aesthetically displeasing but often impairs nutrition and access for oral hygiene, resulting in an increased susceptibility to oral infection, caries, and periodontal diseases[13].

Biopsies of the patients treated with nifedipine show a slight to moderate hyperkeratosis, thickening of the spinous layer, fibrosis of the underlying connective tissue with fibroblastic proliferation, and some increase of the number of capillaries with slight chronic perivascular inflammation[11].

Pathogenesis

a) Role of Fibroblasts: Because only a subset of patients treated with this medication will develop gingival overgrowth, it has been hypothesized that these individuals have fibroblasts with an abnormal susceptibility to the drug. It has been showed that fibroblast from overgrown gingiva in these patients are characterized by elevated levels of protein synthesis, most of which is collagen. It also has been proposed that susceptibility or resistance to pharmacologically induced gingival enlargement may be governed by the existence of differential proportions of fibroblast subsets in each individual which exhibit a fibrogenic response to this medication.

b) Role of Inflammatory Cytokines: A synergistic enhancement of collagenous protein synthesis by human gingival fibroblasts was found when these cells were simultaneously exposed to nifedipine and interleukin-1b(IL-1b), a proinflammatory cytokine that is elevated in inflamed gingival tissues. In addition to IL-1b, IL-6 may play a role in the fibrogenic responses of the gingiva to these medications.

c) Role of Matrix Metalloproteinase (MMP) Synthesis and Function: Because most types of pharmacological agents implicated in gingival enlargement have negative effects on calcium ion influx across cell membranes, it was postulated that such agents may interfere with the synthesis and function of collagenases.

Case Report

A 25 year old male reported to the O.P.D. of Periodontology Department of Government Dental College & Hospital, Amritsar. The patient complained of massive swelling of gums with respect to upper and lower front teeth since 3 months accompanied with bleeding from gums while eating and brushing, and foul odour. He also complained of continuous mild pain and a feeling of heaviness in upper and lower jaw**[Figure 2]**.

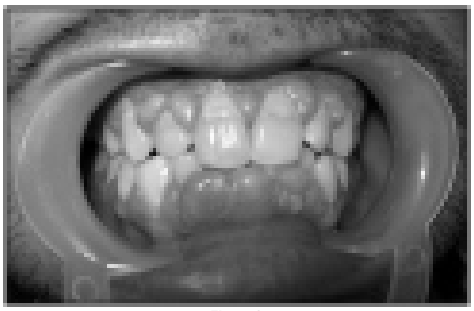

Figure 2

History Of Present Illness

- HOPI dated back to 3 months when the patient first noticed swelling of gums in relation to front teeth which massively increased in size within 20 days.
- Bleeding from gums while eating and brushing and foul odour was experienced.
- He also complained of continuous mild pain and a feeling of heaviness in both upper and lower jaws.

Past Medical History

- The past medical history dated back to 5 years when the patient reported to a private medical physician with a complaint of pain while urination and itching sensation. Blood and urine examination were performed and biopsy done and it was diagnosed that the right kidney was shrunken in size.
- 2 years later he became hypertensive.
- The patient was put on some medication(records unknown) to regulate his blood pressure.

5 months back the medication was changed to NIFEDIPINE 30MG (TAB. NICARDIA CD RETARD) once daily.

Investigations And Examination

After the patient reported to our department : *blood investigations* were performed and reported to be within normal limits.

Intraoral examination revealed that :

All teeth were present.

Left maxillary and right mandibular 2nd molars were grossly decayed.

Enlargement of the marginal and interdental gingiva on the facial aspect with respect to maxillary and mandibular anterior teeth was present.

In region of 31, 32, 41, 42 massive gingival enlargement was seen which was pale pink in colour and fibrotic in consistency covering more than half of the crowns.

At isolated places, particularly in lower anterior region, inflammatory changes were seen.

Range of probing depth of gingival sulcus was recorded in between 3mm to 8mm.

Mild fluorosis was present and occlusion was found to be normal.

Radiographic examination: revealed no bone loss.

Histopathology : microscopic examination of the biopsy specimens demonstrated a connective tissue hyperplasia, proliferation of overlying epithelium, and elongated reteridges penetrating the connective tissue together with few inflammatory cells**[Figure 3]**.

Differential Diagnosis

- Gingivitis associated with local factors
- Gingivitis associated with hormonal imbalance(e.g. pregnancy, puberty)
- Gingival fibromatosis
- Leukemic enlargement

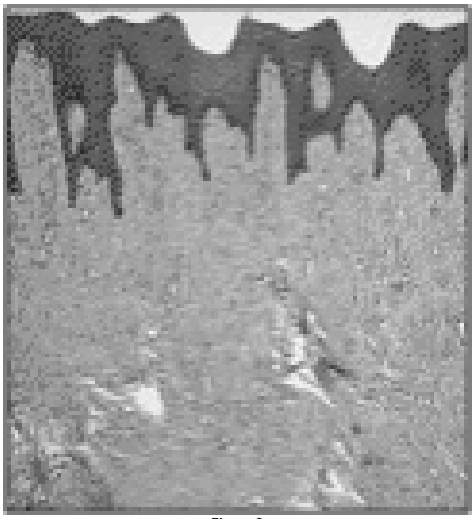

Figure 3

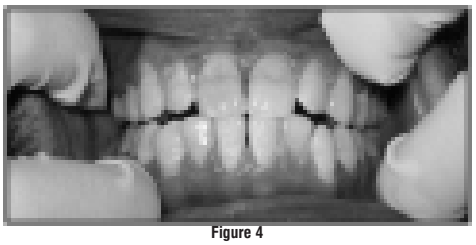

Figure 4

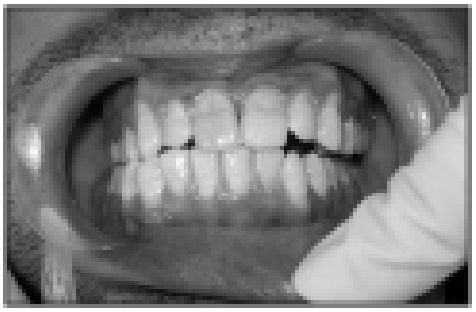

Figure 5

Provisional Diagnosis

- BASED ON CLINICAL PRESENTATION AND PAST HISTORY – Nifedipine Influenced Gingival Enlargement.

Final Diagnosis

- Nifedipine influenced gingival enlargement based on the clinical and histopathologic evidences.

Case Management

- Referral to the physician: patient was referred to his medical physician who replaced NIFEDIPINE 30 mg/day with ATENOLOL 50 mg/day.
- Phase I therapy: Rigorous oral hygiene instructions included: scaling and gingival massage, antiseptic washings (0.2% chlorhexidine use) to control plaque were administered as an essential part of the management to prevent recurrence.
- Maintenance Phase: After 3 months, there was a marked reduction in the enlargement**[Figure 4]**. Maintenance phase was continued for five months during which the patient was advised to maintain meticulous oral hygiene and follow recall visits once every month. There was near complete resolution of the enlargement after 5 months and the patient is extremely satisfied with the results achieved**[Figure 5]**.

Discussion

- Gingival enlargement, with its potential cosmetic implications and also providing new niches for the growth of microorganisms is a serious concern for both the patients and clinician.
- Amongst the several pathogenesis of drug influenced gingival enlargement the plaque induced inflammatory changes is pivotal. The nature of the relationship between plaque and the expression of gingival enlargement is unclear[7,9,4,1]. Oral hygiene plays a decisive role in the development of gingival enlargement.
- In the present report, a marked reduction of the enlargement occurred following scaling and root planing. This goes in accordance with the findings of Hancock R[5].

Conclusion

- The use of medications with the potential to contribute to the development of gingival enlargement is likely to increase in the years to come.
- Whenever possible, treatment should generally target on drug substitution and effective control of local inflammatory factors such as plaque and calculus.
- This is the most practical and effective way to control the recurrence of enlargement.
- When these measures fail to cause resolution of the enlargement, surgical intervention (GINGIVECTOMY) is recommended.
- 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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