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Amlodipine - Induced Gingival Enlargement: Report of Two Cases

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Abstract

Gingival enlargement is one of the adverse effects associated with the administration of several drugs including amlodipine, which is a calcium channel blocker used in the treatment of hypertension and angina. Amlodipine-induced gingival enlargement results in problems with esthetics, mastication, speech and oral hygiene maintenance and if not treated, may lead to more serious oral complications. Hence, it remains a challenge for the periodontists to diagnose and manage such cases effectively. Two cases of amlodipine-induced gingival enlargement were treated by drug substitution, scaling and root planing with periodontal maintenance and full mouth periodontal flap surgery in one of the cases.

Keywords

Calcium channel blocker, amlodipine, drug-induced gingival enlargement, drug substitution

Introduction

Gingival enlargement represents an over-exuberant response to a variety of local and systemic conditions. Drug-induced gingival enlargement is a well-documented adverse effect of certain systemic medications. Three families of drugs that are primarily associated with drug-induced gingival enlargement are anticonvulsants, calcium channel blockers and

immunosuppressants. It is estimated that 30% to 80% of the patients consuming these drugs are at risk of developing gingival enlargement.[1, 2] However, genetic factors, environmental influences, drug dosage, and poor plaque control can affect the development and severity of drug-induced gingival enlargement.[1,3]

Calcium channel blockers are routinely prescribed for hypertension, angina, cardiac arrhythmia and kidney transplantation with cyclosporine. Amlodipine is a third generation dihydropyridine calcium channel blocker commonly used as a long-acting antihypertensive drug, prescribed in a therapeutic range of 2.5 to 10 mg daily.[2, 4] Amlodipine-induced gingival enlargement is comparatively less prevalent (1.7% to 3.3%) as compared to gingivalenlargements induced by other calcium channel blockers such as nifedipine (6%to 83%), diltiazem (74%) and verapamil (21%).[4-6]

Clinical onset of gingival enlargement may appear within 1 to 3 months of using amlodipine with frequent predilection for the labial aspect of the anterior gingiva. It begins as bead like enlargements of the interdental papillae which may gradually extend to the marginal and attached gingiva resulting in massive folds of tissue that may extend coronally and partially or completely obscure the teeth, thus presenting aesthetic and functional difficultiesfor affected patients. The resultant impaired oral hygiene maintenance, biofilm accumulation, malpositioning of teeth, increased susceptibility to oral infection, caries and periodontal diseases may pose a risk for the general health of the patient.[1, 2, 5, 7, 8]

Case Presentation

Case 1

A 56-year old female presented with the chief complaint of bleeding gums since three months. Past medical history elicited that the patient was hypertensive for which she received amlodipine (10 mg/day) for the last 2 years. 2 months prior she had undergone extraction of 31 and 41 due to severe mobility. 1 month prior she started noticing gradual increase in the size of the gingiva with spontaneous bleeding and purulent discharge in relation to her mandibular right and left posterior teeth. The enlargement of the gingiva was associated with difficulty in chewing andhalitosis.

Intraoral examination revealed poor oral hygiene, generalized grade II combined gingival enlargement (fibrotic + inflammatory). The enlarged gingiva was reddish pink with melanin pigmentation, lobulated surface, firm in consistency, painless with bleeding on probing. There was generalized 8-9 mm probing depth. Anterior tongue thrust with pathological migration of maxillary and mandibular anterior teeth were present. Grade III mobility of 32, 42 were observed (Figure 1). Hemogram values were within normal range. Orthopantomogram (OPG) revealed generalized horizontal bone loss. Based on the patient's history and clinical features, clinical diagnosis of drug-induced gingival enlargement wasestablished.

The patient was referred to her physician for drug substitution. Amlodipine was omitted as per the advice of physician, switching over to monotherapy of losartan 50 mgoncedaily. Supragingival and subgingival scaling and root planing (SRP) were performed. Patient was educated and motivated for maintenance of proper oral hygiene. Two weeks after SRP, significant reduction in the enlargement was observed. After 2 months of phase-I therapy,

remaining excess gingival tissue and periodontal pockets were corrected by full mouth periodontal flap surgery (Figure 2). Healing following the procedure was uneventful (Figures 3 and 4). Meticulous oral hygiene maintenance protocol wasreinforced.

Case 2

A 48-year old female presented with the chief complaint of swollen gums since 3 months. Patient was apparently asymptomatic prior to 3 months when she started noticing bead like enlargement of gingiva in relation to her maxillary and mandibular anterior teeth which gradually increased to the present size. As the enlargement was painless, the patient neglected the same until 15 days prior when she started noticing further increase in the size of the gingiva with spontaneous bleeding and purulent discharge from gingiva in relation to maxillary anterior teeth. Past history elicited that the patient was diabetic since 3 years and under metformin 500 mg and hypertensive since 5 months for which she was taking amlodipine (5mg/day). Past dental history revealed congenitally missing 12 and 22, extraction of 24, 25, 26, 41, 46, 47 five years back due to un-restorabledecay.

Intraoral examination revealed poor oral hygiene with generalized grade II combined (fibrotic plus inflammatory) gingival enlargement. The gingiva was erythematous with a lobulated surface. On palpation, the gingiva was soft to firm in consistency with bleeding on probing. Probing depth evaluation revealed presence of pseudopockets (generalized 4-5 mm) (Figures 5 and 6). OPG showed no bone loss. Hemogram, blood glucose levels and HbA1 c value were within normal range.

Drug substitution to monotherapy of labetalol 100 mg (normadate) once daily was advised by the physician. Thorough SRP was performed along with patient education and motivation for oral hygiene maintenance. Three months later, significant regression in the size of the gingiva with minimal amount of fibrotic component was observed (Figure 7).

Discussion

Amlodipine-induced gingival enlargement has the potential to compromise the quality of life due to the concomitant unesthetic appearance, impaired nutrition, interference with speech and mastication and further deterioration with formation of new niches for the periodontopathogenic bacteria. Therefore, it may be considered a serious adverse drug reaction.[5, 8, 9]Early diagnosis and appropriate management can prevent the risk of latent complications.[8, 10]

The treatment is based on the clinical presentation of the case. Drug cessation or substitution to other class of antihypertensive medications, in consultation with patient's physician is the most effective treatment option.[2, 11]When this treatment approach is taken, it is suggested that it may take from 1 to 8 weeks for regression of the enlargement.[2, 9, 12] In the present cases, amlodipine was substituted by losartan 50 mg in the first case and labetalol 100 mg in the second case, resulting in clinically significant regression of the gingival enlargement in both thecases.

The severity of gingival enlargement in patients taking amlodipine correlates well with poor plaque control and is commensurate with the degree of plaque-induced inflammation.[2] Seymour et al[5] reported that the patients with poor periodontal conditions developed gingival hyperplasia upon chronic usage (at least three months) of amlodipine.

Tejnaniet al[6] observed that despite of long-term amlodipine consumption, patients with good oral hygiene did not show any signs of gingival enlargement.

The changes instituted with the drug should always be in combination with scaling and root planing (SRP) and oral hygiene instructions. Scaling and root planing eliminates the inflammatory component, which accounts for 40% of tissue enlargement. Hence elimination of local factors and regular maintenance of good oral hygiene help to decrease the degree and severity of the gingival enlargement and improve the overall gingival health.[9, 11]

The pathogenesis of drug-induced gingival enlargement is complex. The main mechanism is mediated through defective function of gingival fibroblasts as they are responsible for the matrix deposition of gingival tissues. The non-inflammatory pathway include defective collagenase activity due to decreased uptake of folic acid, blockage of aldosterone synthesis in adrenal cortex, and consequent feedback increase in adrenocorticotropic hormone level and upregulationofkeratinocytegrowthfactor.Inflammatory mechanismmayinvolveupregulation of several cytokines such as interleukin-6 (IL-6), interleukin-1β (IL-1β), and growth factors such as platelet-derived growth factor subunit B (PDGFB), fibroblast growth factor 2 (FGF2), and transforming growth factor-β (TGF- β).[1,8, 13]

Surgical elimination of enlargement involves gingivectomy and flap surgery. Gingivectomy is preferred when the gingival enlargement involves small areas (up to six teeth) with no evidence of attachment loss and presence of at least 3 mm of keratinized tissue. It may be performed using conventional scalpel technique, lasers or electrosurgical techniques. Periodontal flap surgery is preferred when the gingival enlargement involves larger areas (more than six teeth) with evidence of attachment loss and osseous defects. Although the periodontal flap approach may be technically more difficult, it results in better post-surgical healing, less post-operative discomfort, less post-operative bleeding, primary closure of the surgical site and early institution of post-surgical home care as compared to gingivectomy approach.[2, 9,11]

Recurrence has been observed as early as 3 to 6 months post-treatment especially when optimal plaque control is not maintained.[11, 14] However, with regular and meticulous periodontal maintenance protocol, no recurrence was observed in both the cases.

Conclusion

Amlodipine-induced gingival enlargement may result in serious emotional and social problems due to poor esthetic and functional implications. Indeed, all dental professionals should carefully review the patient's medical history for prescribed calcium channel blockers and closely examine and monitor gingival tissue changes as an integral part of comprehensive oral examination. Awareness, timely diagnosis and management along with meticulous plaque control will help to control this entity in routine dentalpractice.

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Figures

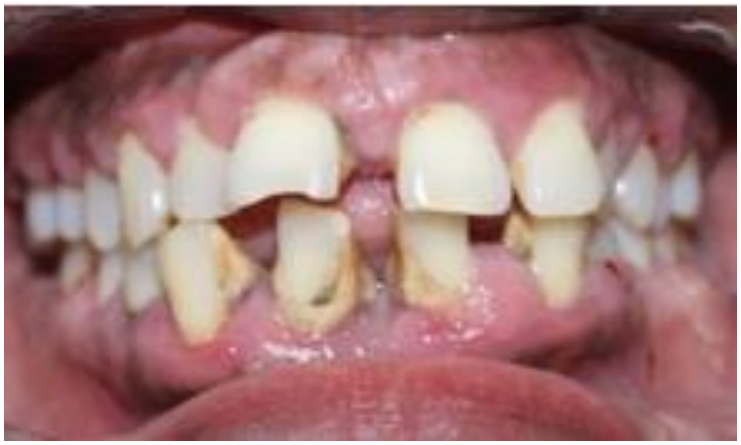

Fig.1: Pre-operative facial view (Case 1)

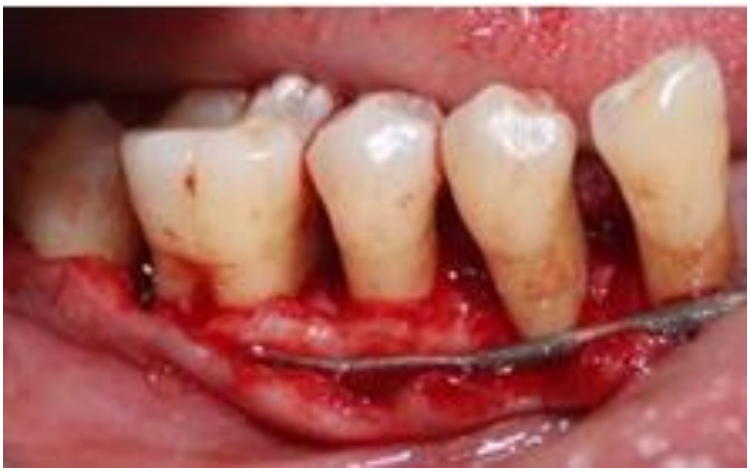

Fig.2: Periodontal flapsurgery (Case 1)

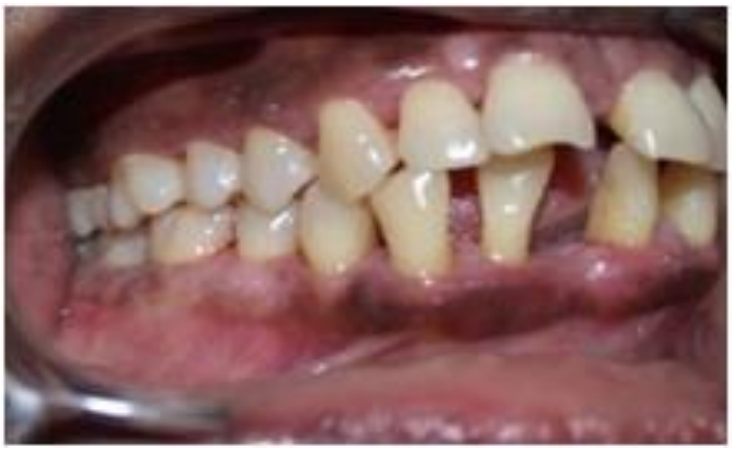

Fig.3: Post-operative right lateral view (Case 1)

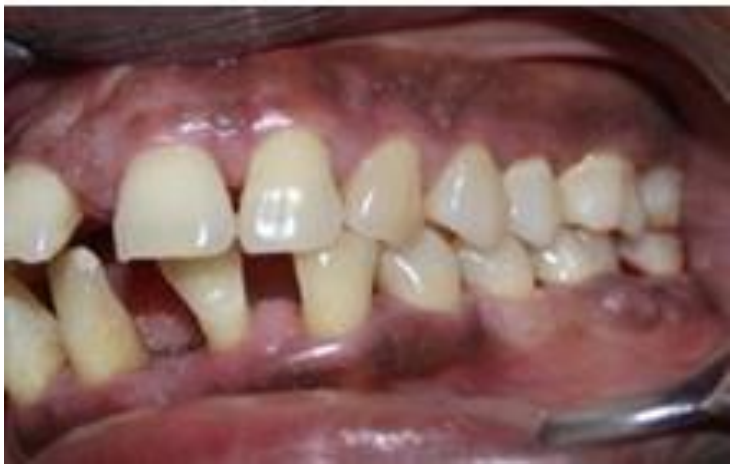

Fig.4: Post-operative left lateral view (Case 1)

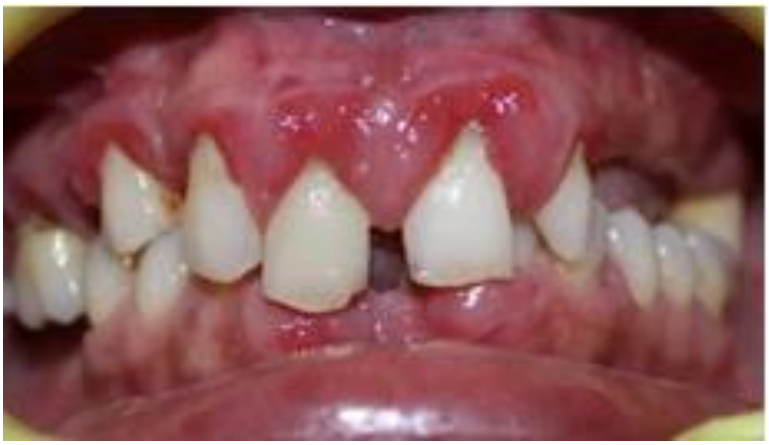

Fig. 5: Pre-operative facial view (Case 2)

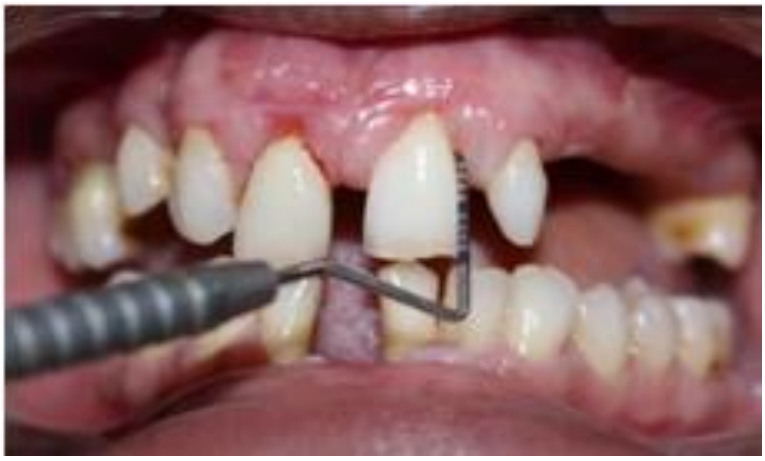

Fig.6: Probing depthevaluation (Case 2)

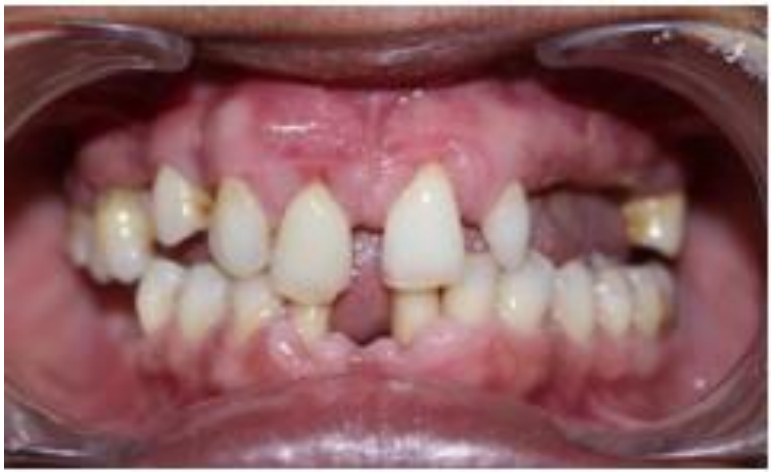

Fig. 7: Post-operative facial view (Case 2)