Amlodipine Induced Gingival Overgrowth: A Case Report

Shoyab Khan *, Antush Mittal*, Kanteshwari I. K..**

ABSTRACT:

Healthy gums are pale pink or pigmented, which tightly wrap around the necks of the teeth. Gingival enlargement is an unwanted adverse effect of some drugs such as cyclosporin, phenytoin and calcium channel antagonists.
This can be a cosmetic problem, interfere with eating and speech, impede effective tooth cleaning or force the teeth out of alignment.
It is a serious concern for both the patient and the clinician due to unesthetic appearance and formation of new niches for periodonto-pathogenic bacteria. Among the calcium channel blockers gingival hyperplasia has most frequently been described as a side effect following administration of nifedipine. The incidence with amlodipine is much lower, however there have been few reports showing the association of this drug with gingival enlargement. This case report presents gingival hyperplasia as an adverse effect of amlodipine in patient on this drug for the last 2 years.

Key Words: Amlodipine, Gingival Enlargement, Calcium channel blockers.

INTRODUCTION

An overgrowth or increase in size of the gingiva is termed as Gingival Enlargement[1], which was earlier named as Gingival hyperplasia, Gingival Overgrowth or Gingival hypertrophy etc. Gingival enlargement is a well known consequence of administration of some anticonvulsants, immunosuppressants and calcium channel blockers and may create speech, mastication, tooth eruption and esthetic problems.[2] Currently, more than 20 prescription medications are associated with gingival enlargement.[3]

Calcium channel blockers are used in the management of various cardiovascular disorders like angina and hypertension. These drugs have been reported to be associated with gingival hyperplasia since 1984.[4] Of this large group of drugs, the dihydropyridines are most frequently implicated in gingival enlargement especially nifedipine. The overall prevalence of nifedipine induced gingival overgrowth appears to be approximately 38%.[4]

Gingival hyperplasia due to the concomitant unesthetic appearance and the formation of new niches for the periopathogenic bacteria is considered a serious adverse drug reaction.[5]

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Amlodipine induced gingival overgrowth was first reported by Seymour *et al*[6] and there have been only few reported associations of gingival overgrowth with this drug. Amlodipine such as nifedipine can be detected in gingival crevicular fluid. Gingival sequestration of amlodipine associated with gingival hyperplasia has also been reported.[6]

This article discusses a case of amlodipine-induced gingival hyperplasia and also reviews the relevant literature.

CASE REPORT

A 41 year-old female patient was reported at the Department of Periodontics at Dr. D. Y. Patil Dental College & Research Centre, Nerul, Navi Mumbai complaining of "swollen gums in oral cavity" which was progressively increasing. Past medical history revealed that the patient suffered from Hypertension since 6 years, but started receiving amlodipine (5mg/day) since last 2 years only. The painless and gradual overgrowths of gingival were noticed from one and half year before reporting to the clinic. The patient was otherwise free from any kind of distress or anxiety.

Upon clinical examination, generalized firm gingival overgrowth with rolled out margins & lobulated papillae were found wrt maxillary and mandibular arch, particularly at the buccal side (Fig. 1). On lingual aspect, the gingival overgrowth was minimal.

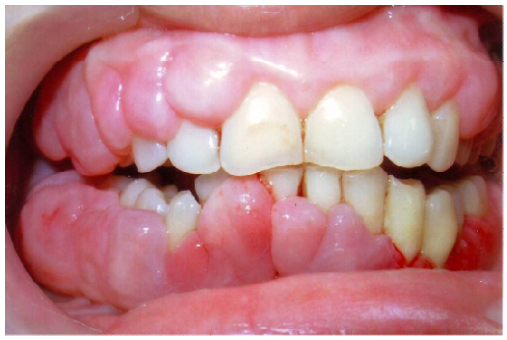
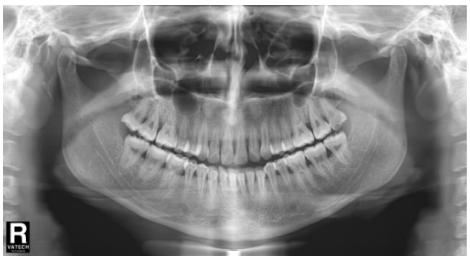
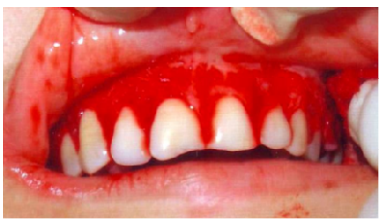


Fig. 1 Pre Operative Photograph

Generalized pseudo pockets measuring 3 – 10 mm and generalized bleeding on probing were present. The lack of true periodontal pockets was a prominent feature of gingival overgrowth indicating rather an outward enlargement of gingiva. On application of digital pressure there was a generalized discharge of purulent exudate. Oral hygiene was poor with excessive local deposits as the patient was unable to maintain good oral hygiene.

Treatment plan for the patient consisted of Initial phase therapy with thorough oral prophylaxis (Scaling and Root Planing) and oral hygiene instructions. Subsequently, the gingival overgrowths were surgically excised by External Bevel Gingivectomy (Fig. 2, 3 & 4). Post operative care included analgesic/antibiotic medications and strict oral care. The excised tissues were submitted for the histopathological examination.





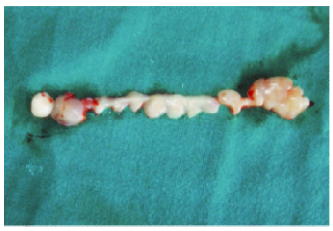
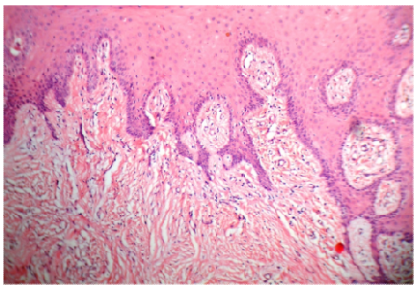


Fig.2 Pre Operative OPG of the patient Fig 3: Intra Operative Photograph Fig.4: Surgically sectioned tissue



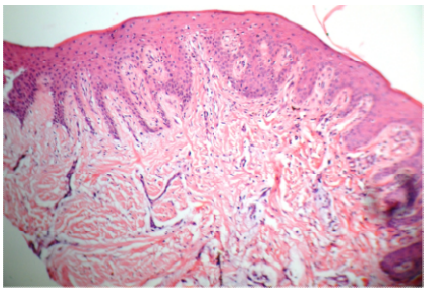
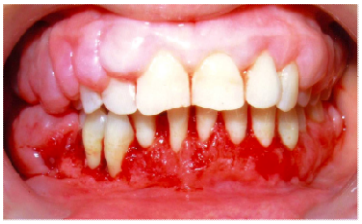
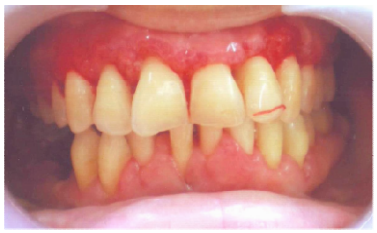


Fig.5 a) Histopathological picture at 10 x b) Histopathological picture at 40 x





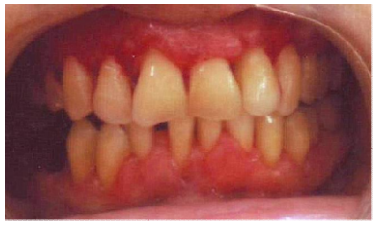


Fig.6. Immediate Post Op Fig.7. 15 days follow up Fig8. 6 months follow up

Microscopic inspection of the gingival biopsy specimens demonstrated a connective tissue hyperplasia, acanthosis of overlying epithelium, hyperkeratinised and proliferated stratified squamous epithelim and elongated rete ridges together with few sparse inflammatory cells (Figure 5 a & b). Deeper connective tissue showed severe connective tissue infiltrates with some nerve bundles and blood vessels. The lesion was diagnosed as fibroepithelial hyperplasia and was suggestive of amlodipine-induced gingival hyperplasia based on clinical and histological evidences. With a follow up period of 6 months (Fig. 6, 7 & 8), results were stable and patient was not showing recurrence of enlargement suggesting External Bevel Gingivectomy as an optimal treatment modality for such lesions.

DISCUSSION

Gingival overgrowth 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. Calcium channel blockers are considered potential etiologic agents of drug-induced gingival overgrowth.[7] Although the incidence of nifedipine-induced gingival hyperplasia is about 10%.[6], very few reports of amlodipine-related gingival hyperplasia does exist in the extant literature[6, 8, 9]. The present case is interesting as it occurred with a low dose of amlodipine (5 mg) and appeared only on long term administration (6 - 7 months). Several factors may influence the relationship between the drugs and gingival overgrowth. Those factors includes age, genetic predisposition, pharmacokinetic variables, poor oral hygiene, periodontal disease, periodontal pocket depth, gingival inflammation, degree of dental plaque, duration and dose of a drug, histopathology, ultra structural factors, inflammatory changes and drug action on growth factors.

The pathogenesis of gingival overgrowth is uncertain and not all patients taking calcium channel blockers develop overgrowth, suggesting a genetic predisposition. A marked heterogeneity of response of gingival fibroblasts to calcium channel blockers has been reported. Also, the dihydropyridines are metabolized by enzyme CYP3A4, a member of P450 enzyme family.

Cytochrome P450 genes exhibit genetic polymorphism which results in inter-individual variations in levels of enzyme activity.[10] It is also believed that nifedipine and other chemically related drugs share the capacity to alter calcium metabolism at cellular level.[11]

The underlying mechanism behind drug induced gingival hyperplasia may also involve inflammatory and non inflammatory pathways. The proposed non inflammatory mechanisms include defective collagenase activity due to decreased uptake of folic acid, blockage of aldosterone synthesis in adrenal cortex and consequent feedback increase in ACTH level and upregulation of keratinocyte growth factor. Alternatively, inflammation may develop as a result of direct toxic effects of concentrated drug in crevicular gingival fliud and/ or bacterial plaques. This inflammation could lead to the upregulation of several cytokine factors such as TGF-β1 (Transforming growth factor).[12, 13.]

Seymour[14] stated that interaction between the drug and gingival tissues appear to be enhanced by gingival inflammation caused by inadequate oral hygiene.

In a series of 150 cardiac patients, it was found that amlodipine at a dose of 5 mg/day cannot induce gingival hyperplasia even if taken for more than 6 months[9]. Contrarily, Seymour et al[6] reported three patients with poor periodontal conditions who developed gingival hyperplasia upon a chronic usage (at least three months) of amlodipine.

Barclay *et al*[15] suggested that plaque induced gingival inflammation may be important risk factor in the development and expression of the gingival changes.

Abirami *et al*[16] presented a case report on gingival hyperplasia induced by amlodipine in hypertensive patient on increasing doses of amlodipine from 10 mg to 25 mg daily for six weeks and showed regression of gingival hyperplasia after the withdrawal of amlodipine.

Drug withdrawal resulted in improvement which is the first step for management of drug induced overgrowth. We conclude that the overgrowth could occur with amlodipine even at a small dose (5mg) and it could occur even after 6-7 months of drug administration. Hence the possibility of amlodipine induced overgrowth should be considered for a low dose as well as a late presentation.

Finally, we emphasize that gingival overgrowth could be a side effect of amlodipine even with a very short term and low dose administration.

CONCLUSION:

Gingival enlargement is a recognized and common adverse effect of cyclosporin, phenytoin and calcium channel antagonists. The prevalence of gingival overgrowth induced by chronic medication with amlodipine is uncertain and rare in occurrence. This case report presents a clinical picture of a patient with poor periodontal condition and gingival overgrowth due to chronic use of amlodipine for two years.

Patient was advised change of medication in consultation with her physician, Scaling and Root Planing had been performed and she had been recalled for gingivectomy in

maxillary and mandibular arch which gives complete resolution of enlarged gingivae with stable results maintained for 6 months follow – up period.

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