# CASE REPORT

## *Management of Amlodipine-induced gingival enlargement – a case report*

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**Abstract**

*Gingival overgrowth is a multifactorial condition which clinically manifests as an increase in size of gingiva, often associated with inflammatory changes. Among various factors certain drugs, such as anticonvulsants, immuno-suppressive drugs, calcium channel blockers have been shown to produce similar gingival overgrowths in certain susceptible patients. Amlodipine, a calcium channel blocker used for management of hypertension, angina pectoris, coronary artery spasm and cardiac arrhythmias, has shown to cause gingival overgrowth that may be localized or generalized, mild to severe, affecting esthetic and function of the patient. In the present case a 53-year old female patient reported with amlodipine-induced gingival enlargement as she was on medication for hypertension since last 3 years. The present case was managed starting with Phase-1 therapy, drug substitution followed by surgical management and further maintenance.*

**Keywords:** *Amlodipine, calcium channel blockers, gingival overgrowth*

### INTRODUCTION

Gingival overgrowth is one of the most important clinical feature of gingival pathology. It has multifactorial etiologies and found to be frequently associated with inflammatory changes in the gingiva. Other conditions are hereditary (familial), malignancies and those resulting from adverse effects associated with systemic administration of certain drugs.[1]

Drugs associated with gingival overgrowth can be broadly categorized into three major groups according to their therapeutic actions, namely anticonvulsants, immunosuppressive drugs and calcium channel blockers.[2] Currently, more than 20 prescribed medications are found to be associated with gingival enlargement.[3] Although the pharmacologic effect of each of these drugs is different and directed toward various primary target tissues, all ofthem seem to act similarly on a secondary target tissue, that is, the gingival connective tissue causing common clinical and histopathological finding.

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Amlodipine is a new dihydropyridine calcium channel blocker that is used in the management of both hypertension and angina. It acts by inhibiting the calcium ion influx in cardiac and smooth muscle cells resulting in coronary and peripheral arterial vasodilation, reduced heart rate, decreased myocardial contractibility and oxygen utilization by the myocardium and slow atrioventricular conduction.[4] Ellis et al.[5] first reported amlodipine-induced gingival overgrowth.

Drug induced gingival overgrowth (DIGO) can be localized or generalized, mild to severe enlargement interfering with esthetics, mastication, speech, and access for oral hygiene, resulting in an increased vulnerability to bacterial infections including periodontal diseases and dental caries.[6,7]

In the present case patient reported with amlodipine-induced enlargement (5 mg once daily) using since last 3 years.

There are very less data supporting enlargement at 5 mg once/daily dose of amlodipine even after taking for more than 6 months.[8]

### CASE REPORT

A 53-year old female patient reported in the Department of Periodontics, Kothiwal dental college and research centre, Moradabad with a chief complaint of enlarged and bleeding gums in upper front teeth region for 6 months (Fig. 1).

She had recently discontinued brushing due to enlarged and bleeding gums.

Intra oral examination revealed diffuse enlargement involving interdental papilla, marginal gingiva and

attached gingiva in relation to teeth #14 - #24 and also in lower anteriors.

**Figure 1: Pre-operative view**

Gingiva was pinkish-red in colour with rolled out margins and interdental papillae causing loss of normal gingival scalloping (Fig. 2).On palpation gingiva appeared fibrotic with some areas of edematous component. Poor oral hygiene status of the patient was assessed from the presence of localirritating factors and bleeding on probing was observed.

**Figure 2: Post application of plaque disclosing agent**

The pocket probing depth was recorded and found to be localized in the affected area within range of 4-6 mm.

Patient was subjected to complete hematological investigation and all the parameters were found to be within normal range. Orthopantomogram revealed generalized horizontal bone loss (Fig. 3).

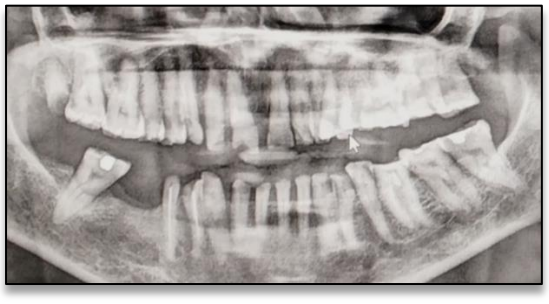

**Figure 3: Orthopantomogram**

Treatment plan was made and explained to the patient which was well accepted by her. It include Phase-1 therapy (scaling, root planing and oral hygiene instructions) using plaque disclosing agent to educate the patient about local causative factors plaque and calculus, drug substitution by consultant physician which was changed to Atenolol 100 mg once/daily and surgical intervention (Internal bevel gingivectomy).

Patient was instructed to maintain good oral hygiene with the use of chlorhexidine 0.2% twice/daily. After patient satisfying the criteria surgical intervention was carried out.

**SURGICAL PROCEDURE**

After achieving adequate anaesthesia internal bevel gingivectomy incision was taken using Bard Parker blade no. 11 extending from distal to tooth #14 to distal to tooth #24 (Fig. 4). Thereafter full thickness flap was elevated using periosteal elevator followed by crevicular and interdental incision to detach the interdental tissue and gingival collar from the bone.

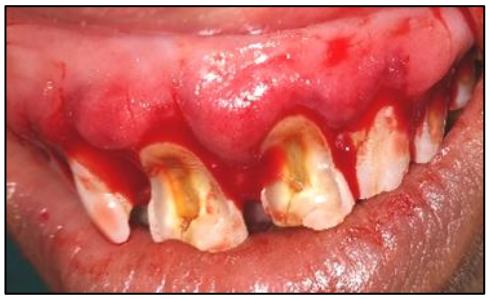

**Figure 4: Par-operative (internal bevel incision)**

Now by using curettes gingival collar and granulation tissue was removed and proper scaling and root planing performed. Wherever required flap was thinned from inner side for better adaptation, then flap was placed back against the teeth and secured with non-resorbable suture in interrupted manner. Excised tissue was sent for histological investigation.

0.2% Chlorhexidine mouthwash twice/daily was continued, analgesic with proper oral hygiene measures were advised. At a follow-up visit after 7 days, the sutures were removed and after 1 month follow up the wound was found to heal normally without any recurrence (Fig. 5). Histopathological report revealed presence of fibrous component and

inflammatory cell infiltrate chiefly lypmphocytes and plasma cells in connective tissue stroma.

**Figure 5: 1 month Post-operative view**

## DISCUSSION

Despite the popularity and wide acceptance of calcium channel blockers by the medical community, its oral impact of causing gingival overgrowth should be recognized and discussed. The prevalence rate reported for nifedipine-induced gingival overgrowth is highly variable, ranging from 6% to 83%,[9,10] while for amlodipine-induced gingival overgrowth was 3.3%.[11]The first sign of overgrowth can be observed as early as 3 months after drug institution usually starting from anterior labial surface in interdental papillae which may gradually convert into massive diffuse enlargement involving marginal and attached gingiva. It was reported that plaque-induced inflammation can exacerbate the effect of medications, leading to a combined effect on the gingival tissues. However some investigators believe that inflammation is a prerequisite for gingival overgrowth that could be prevented by proper plaque control.[12,13]

The pathogenesis of Drug induced gingival overgrowth (DIGO) is complex. The main mechanism is mediated through defective function of gingival fibroblasts. On interaction with Amlodipine and gingivalfibroblasts, overproduction of collagen and extracellular ground substance occurs and leads to increase in the gingival size. The drug interferes with the calcium metabolism of fibroblast cells and hence reduces the production of the degrading enzyme collagenase.[13]

There are two proposed pathways:- inflammatory and non-inflammatory pathways. The proposed non-inflammatory mechanism includes 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 up regulation of keratinocyte growth factor.[14] Alternatively, inflammation may develop as a result of direct toxic effects of concentrated drug in gingival crevicular fluid and/or bacterial plaque. This inflammation could lead to the up regulation of several cytokine factors such as interleukin-6 (IL-6), IL-1β, platelet-derived growth factor subunit B (PDGF BB),fibroblast growth factor 2 (FGF 2), transforming growth factor-$\beta$1 and connective tissue growth factor (CTGF).[15,16]

Not all the individuals taking medication develop gingival overgrowth because it was suggested that oral hygiene practice, existence of differential proportions of fibroblast subset in each individual and functional heterogenicity exists in gingival fibroblasts in response to various stimuli are responsible.[17]

Treatment is generally targeted on drug substitution and effective control of local inflammatory factors. However, when these measures fail to cause resolution of the enlargement, surgical intervention is recommended.[18] Most reports of amlodipine gingival overgrowth have required surgical intervention.[19] In the present case patient responded well with the drug substitution and oral hygiene maintenance led to reduction in severity of the growth. However growth was not completely resolved, so surgical intervention was carried out. For surgical management gingivectomy/gingivoplasty or periodontal flap surgery can be performed. In the present case internal bevel gingivectomy was performed for elimination of gingival enlargement, healing with primary intention and less discomfort to the patient. One month post-operative showed uneventful healing without any re-occurrence.

## CONCLUSION

Observing that the gingival hyperplasia can occur with amlodipine even at a small dose (5mg), physicians and dentists should be aware of the medications that can induce gingival hyperplasia and be able to identify changes in the oral cavity in such patients and to prevent, diagnose, and successfully manage them. It can be treated non-surgically and surgically with combined effort of medical and dental physician. So, co-operative teamwork between the patient, his physician, and the dental health care professional is mandatory to minimize and successfully treat such unwanted side effects of drugs.

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