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# Amlodipine - A Novel Offender of Gingival Overgrowth—A Case Report

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## ABSTRACT

**Aim:** There are only few cases presented with Amlodipine induced gingival enlargement so far. The main purpose of this case report is to discuss about Amlodipine-influenced gingival enlargement in a 56 years old female hypertensive patient and its peri-odontal management and maintenance.

**Case Report:** In this case report, patient with a history of hypertension for past 2 years and presenting with Amlodipine induced gingival enlargement and various approaches to manage it were discussed.

**Discussion:** One of the common clinical features of gingival disease is the gingival enlargement, otherwise termed as Gingival Overgrowth. Gingival enlargement occurs as a side effect following administration of certain drugs. The most common drugs causing gingival enlargement are Anticonvulsants for eg Phenytoin, immuno-suppressants like Cyclosporine and calcium channel blockers (Nifedipine). Amlodipine - a third generation calcium channel blocker is found to be associated with Gingival overgrowth even when prescribed in a very low dose of about 5mg.

**Conclusion:** The results of this case report suggested that the combined non-surgical and surgical therapy resulted in complete healing of the gingival overgrowth with less post operative complication.

**Key Words:** Drug-Induced Gingival Overgrowth (DIGO), Calcium Channel Blockers (CCBs), Gingivectomy and Amlodipine

## INTRODUCTION

One of the common clinical features of gingival and peri-odontal disease is the increase in the size of the gingiva. Current terminologies used to describe this condition are Gingival enlargement and gingival overgrowth (GO). *An overgrowth or increase in size of the gingiva is called as Gingival enlargement.*<sup>1</sup> Various etiologic factors have been associated with this condition, of which the two most common causes are inflammation and medications used. Certain systemic drugs prescribed for non-dental treatment have an unwanted side effect on the gingiva. *Kimball* in 1939, was the first to describe about Drug-induced gingival enlargement with chronic usage of phenytoin- an anti-epileptic drug. More than 20 prescribed medications are associated with this condition.<sup>2</sup> *Drug influenced gingival enlargement is defined as an enlargement resulting in whole or in part from systemic drug use.*<sup>1</sup>

The other drugs associated with gingival overgrowth are broadly classified into 3 categories according to their therapeutic actions, i) anticonvulsants ii) immuno-suppressants and iii) calcium channel blockers (CCBs)<sup>3</sup>. Among these drugs CCBs especially Nifedipine causes gingival overgrowth in about 10% of patients<sup>2</sup>. Amlodipine - a dihydropyridine derivative, induced enlargement of the gingiva is usually less common. *Jorgensen* in 1997 reported that the prevalence of gingival overgrowth in patients taking Amlodipine is about 3.3%<sup>4</sup>. It is indicated in the management of both hypertension and angina.

The mechanism behind the GO is not well documented. Both inflammatory and non-inflammatory mechanisms have been suggested. Non-inflammatory mechanism suggests a defective collagenase activity due to an increased uptake of folic acid, a blockage in the synthesis of aldosterone in adrenal cortex with a consequent feedback increase

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in adrenocorticotrophic hormone (ACTH) levels and an up-regulation of keratinocyte growth factor. The inflammatory theory suggests that inflammation develops as a result of a direct toxic effect of drug concentration in gingival crevicular fluid and with bacterial plaque. This inflammation leads to an up-regulation of several cytokine factors particularly the transforming growth factor beta 1 (TGF- $\beta$ 1)<sup>5</sup>. In addition, Inflammatory Enlargements generally are complications secondary to any other type of enlargement, creating a combined gingival enlargement<sup>6</sup>. The management of this combined enlargement always require combined treatment.

## CASE REPORT

A patient named Mrs. Vasanthi 56 years old female came to our hospital with a chief complaint of bleeding and swollen gums and mild gnawing pain occurs occasionally. On intraoral examination enlarged gingiva with generalized bleeding on probing with presence of local factors like plaque and calculus were observed (Fig 1). Patient's medical history reveals that she is hypertensive and under medication (T. Amlong 5mg once daily) for past 4 years. Enlargement involves marginal gingiva as well as interdental papilla of mandibular anteriors, premolars and certain maxillary teeth regions. On the basis of history given by the patient and clinical features it was diagnosed as Amlodipine -induced gingival overgrowth compounded with plaque induced chronic periodontitis.

## CASE MANAGEMENT

A complete blood investigation was taken to rule out other systemic diseases. Patient's physician was consulted regarding the dental treatment procedure under Local anaesthesia and opinion was obtained, substituting the drug was not advised for this particular case. Patient was subjected to initial Phase I therapy (Fig 2) which included complete scaling and root planing (SRP) with adjunct prescription of antibiotics (Cap. Moxikind 500mg tds for 5 days, T. Flagyl 400mg bd for 5 days). Patient recalled a couple of week after SRP and was instructed to maintain good oral hygiene with the use of mouth rinses (Chlorhexidine). A drastic response was noticed after two week in the revisit. It resulted in Regression of the size of enlargement with some amount of fibrotic component left unresolved (Fig 3). A surgical therapy was planned to completely eliminate the remaining amount of gingival enlargement. Under local anaesthesia, bleeding points were marked; the remaining enlargement was excised by giving an external bevel incision along the marked points with NO.15 scalpel (Fig 4, 5). After the surgical gingivectomy procedure, saline + Betadine irrigation was done. Periodontal dressing was placed after achieving hemostasis. Post operative in-

structions and analgesics were given. Healing was uneventful without any post-operative complications. The patient was asked to report after few weeks and observed to remain asymptomatic. Oral hygiene instructions were given and patient is under maintenance phase with no signs of recurrence (Fig 6). The histopathological study report shows the presence of dense infiltration of chronic inflammatory cells and perivascular inflammatory infiltrate and connective tissue shows dense bundles of collagen fibres with fibroblasts. And the epithelium shows hyperplasia, acanthosis and intracellular edema (Fig 7).

## DISCUSSION

The mechanism by which calcium antagonists induce gingival overgrowth is yet to be explained. Nifedipine induced gingival overgrowth was first reported in the year 1980s by Lederman *et al.*, and Ramon *et al.*, soon after Diltiazem, Verapamil and in cases with Amlodipine and Felodipine were also described. The severity of gingival overgrowth in patients taking these medications correlates well with poor plaque control and is always correspond with the degree of Plaque-induced inflammation<sup>7</sup>. Seymour *et al.*, stated that the pathogenesis of drug-induced gingival enlargement is a multifactorial model which involves an interaction of several factors, which expands on the interaction between drug and metabolite with the gingival fibroblasts. The predisposing factors are age, genetic predisposition, pharmacokinetic variables, drug-influenced alterations in gingival connective tissue homeostasis, histopathology, ultrastructural factors, inflammatory changes and drug-induced actions on growth factors<sup>8</sup>. Gingival overgrowth influenced by Amlodipine usually begins at the interdental papilla, which occurs within 6 months of taking medications at a dose of 10mg/day. Few cases have reported at a dose of 5 mg of Amlodipine when used more than 6 months<sup>8</sup>. The treatment option for such case should always start with Non-surgical therapy; the main aim of this approach is to reduce the inflammation thereby allowing it to resolve since few patients respond well along with substitution of the drug. In this present case scenario, the patient's physician was not willing to substitute the drug. When gingival enlargement persisted even after eliminating the inflammatory components, then there is a need of periodontal surgery. It is the clinician's decision to choose the technique whether scalpel gingivectomy, periodontal flap surgery, electrocautery or laser excision. Fardel and Lygre in 2015 stated that surgical treatment was more effective than non-surgical treatment in reducing the size of overgrowth.<sup>5</sup> It was reported that more than 75% of patients using CCBs needed treatment for Gingival overgrowth and replacing the drug with non-CCB antihypertensive significantly reduces the Gingival Overgrowth<sup>5</sup>.

## CONCLUSION

In this present case the combined non-surgical and surgical therapy resulted in complete healing of the gingival overgrowth with less post operative complication. Yet there is a need of post therapy maintenance and long term follow up in order to evaluate the long term recurrence of gingival overgrowth in patients who had not replaced Amlodipine with alternative drug. Within the limitation of the present study it has been concluded that combined treatment would be more effective in managing combined enlargement cases.

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Figure 1: Pre-operative.



Figure 3: Two week after SRP.



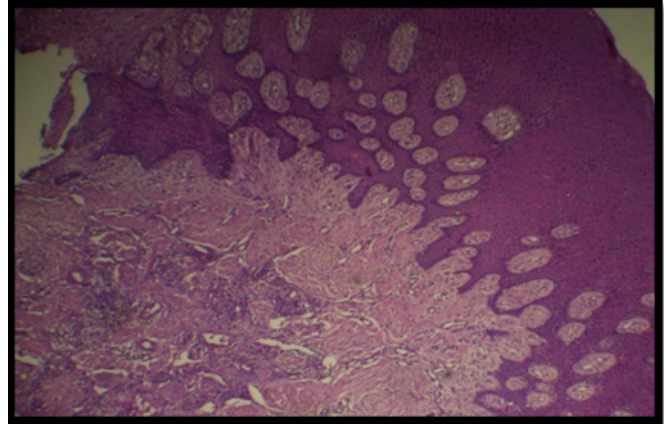
Figure 2: Immediately after SRP.



Figure 4: Before Surgical gingivectomy.



**Figure 5:** Immediate post operative (After gingivectomy).



**Figure 7:** Histopathological photomicrograph.



**Figure 6:** One month post surgical.