

doi: <http://dx.doi.org/10.18203/2319-2003.ijbcp20150396>**Case Report****Amlodipine induced gingival hyperplasia: a case report****Parul Elsa Thomas<sup>1</sup>, R. Tolstoy<sup>2</sup>, L. Britto Duraisingh<sup>3\*</sup>**

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**Received:** 09 May 2015**Revised:** 13 July 2015**Accepted:** 05 July 2015**\*Correspondence to:**

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**ABSTRACT**

A 55-year-old South Indian male with hypertension, benign prostate hypertrophy and old myocardial infarction was admitted with painless inflammation of gingiva. He received amlodipine 5 mg once a day, atorvastatin 10 mg once a day, aspirin 75 mg once a day and rabeprazole 20 mg once a day for past 5 months. The patient in the case presented had gingival hyperplasia as a result of managing his hypertension with amlodipine. Calcium channel blockers are one of the most widely used anti-hypertensive and are known for causing gingival hyperplasia as an adverse effect. It may develop as a result of two inflammatory and non-inflammatory pathways. The problem completely resolved when the offending drug was withdrawn and he was switched over to an angiotensin receptor blocker. The present case is interesting as it occurred with a low dose of amlodipine (5 mg) and appeared on administration for 5 months. This paper aims at drawing the attention of clinicians toward adverse effects of amlodipine along with a brief review on the management of hyperplasia without surgical interventions.

**Keywords:** Amlodipine, Gingival hyperplasia, Hypertension

**INTRODUCTION**

Amlodipine is a new dihydropyridine calcium channel blocker that is used in management of both hypertension and angina.<sup>1</sup> It is structurally similar to nifedipine and pharmacodynamically comparable to it.<sup>2</sup> In hypertension, the therapeutic dose of amlodipine is 5 mg once or twice daily or 10 mg once daily. The frequent adverse drug reactions (ADR) are a headache, facial flushing, dizziness, edema, gingival hyperplasia.<sup>3</sup>

The incidence of gingival hyperplasia has been reported as 10-20% in patients treated with calcium antagonists in

the general population. The proposed non-inflammatory mechanism of gingival hyperplasia by amlodipine include defective collagenase activity due to decreased uptake of folic acid, blockage of aldosterone synthesis in adrenal cortex and consequent feedback increase in adrenocorticotropin hormone (ACTH) level and upregulation of keratinocyte growth factor (GF). The inflammatory mechanism includes upregulation of several cytokine factors such as transforming GF-beta (TGF-beta). The prevalence of gingival overgrowth induced by amlodipine is 1.7-3.3%. Although there have been several studies examining these results are conflicting, with previous estimates ranging from 20% to 83%.

## CASE REPORT

A 55-year-old male patient was admitted for gingival swelling. Past medical history showed hypertension, benign prostatic hypertrophy, and myocardial infarction for which the patient received amlodipine 5 mg once daily, atorvastatin 10 mg once daily, aspirin 75 mg once daily, and rabeprazole 20 mg once daily for the past 5 months. The patient had a painless and gradual enlargement of gingiva within 4 weeks of the duration of drug use. Gingival overgrowth was found throughout the maxilla and mandible. This was found to be firm and generalized. The gingiva showed an outward enlargement with the lack of periodontal pockets. There was no gingival inflammation. Bleeding and purulent discharges were also absent. Oral cavity examination revealed diffuse gingival hypertrophy of both upper and lower gums. Gingival biopsy specimens were subjected to microscopic examination and this demonstrated hyperplasia of the connective tissue, thickening of overlying epithelium, and rete ridge elongation along with few inflammatory cells. History and clinical examination were correlated and other potential causes including use of other drugs, nutritional deficiencies, and malignancies were excluded. Based on clinical and histological evidences amlodipine induced gingival hyperplasia was confirmed for this patient. We substituted an angiotensin receptor blocker (ARB) (olmesartan) for amlodipine, within 3 months the gingival hypertrophy regressed completely.

## DISCUSSION

Gingival enlargement or gingival overgrowth is the preferred term for all medication related gingival lesions previously termed as gingival hyperplasia or gingival hypertrophy.<sup>3</sup> It has multifactorial etiologies such as hereditary (familial), malignancies, and drugs that has been frequently associated with inflammatory changes in gingiva.<sup>4</sup> The patients medicated with certain drugs may be implicated in this unwanted side effect of drug-induced gingival overgrowth (DIGO).

An increasing number of medications are associated with gingival overgrowth. Currently more than 20 prescription medications are associated with gingival enlargement.

Drugs associated with gingival overgrowth can be broadly divided into three categories – anti-convulsants, calcium channel blockers, and immunosuppressants.<sup>5</sup> Although the pharmacological effect of each of these drugs are different and directed toward various primary target tissues, all of them seem to act similarly on a secondary target tissue, that is the gingival connective tissue causing common clinical and histopathological findings.

Clinical manifestations of gingival enlargement frequently appear within 1-3 months after initiation of treatment

with associated medications. It normally begins at the interdental papillae and more frequently found in the anterior segment of the labial surfaces. Gradually gingival lobulations are formed that may appear inflamed or fibrotic in nature depending on the degree of local factor induced inflammation. However, the fibrotic enlargement is normally confined to the attached gingiva, but may extend coronally and interfere with esthetics, mastication or speech. Disfiguring gingival overgrowth triggered by these medications is not only esthetically displeasing, but often impairs nutrition and assess for oral hygiene resulting in an increased susceptibility for oral infection, caries, and periodontal diseases. DIGO usually occurs within the first 3 months of starting amlodipine at a dose of 10 mg/day and begins as an enlargement of the interdental papilla.<sup>6</sup>

It may develop as a result of direct toxic effects of concentrated drug in the cervicular gingiva. The underlying mechanism remains to be fully understood. However, two main inflammatory and non-inflammatory pathways have already been suggested. The proposed non-inflammatory mechanism include defective collagenase activity due to decreased uptake of folic acid, blockage of aldosterone synthesis in the adrenal cortex and consequent feedback increase in ACTH level and upregulation of keratinocyte GF. Alternatively inflammation may be due to gingival fluid and/or bacterial plaques. This inflammation could lead to upregulation of several cytokine factors such as TGF-beta.

Many studies have been conducted which showed that amlodipine cannot induce gingival hyperplasia at 5 mg OD dose even if taken for more than 6 months. It can be caused only at a dose of 10 mg/day. The present case is unique in that even 5 mg/day dose of amlodipine caused gingival hyperplasia after 5 months of use.

Untreated gingival hypertrophy might lead to bleeding, infection abscess, ulceration, cosmetic deficiency, and functional difficulty (e.g., chewing, talking). Treatment of drug-induced gingival hypertrophy includes cessation of the drug and replacing the affecting drug with another agent is also recommended when possible.

Gingivectomy with carbon dioxide or yttrium-aluminum-garnet laser is recommended for patients who have moderate to severe gingival enlargement that does not resolve when the dose is reduced, proper oral hygiene is maintained or after a short course of antibiotics. In the majority of patients for whom drug discontinuation or substitution is not possible and for whom prophylactic measures have failed, surgical excision of gingival tissue remains the only treatment option. ADR assessment was done using Naranjo's scale. The score was found to be 5 which indicated probable ADR.

## CONCLUSION

Our patient's amlodipine induced massive gingival hyperplasia completely resolved when amlodipine was replaced by an ARB (olmesartan). Amlodipine is a commonly prescribed anti-hypertensive drug, so every physician should be aware of this potentially harmful side effect, particularly if adverse oral symptoms arise during the period of drug use. Painful surgical interventions should be avoided whenever possible.

## ACKNOWLEDGMENTS

We take this opportunity to thank PSG Hospitals for providing necessary facilities and continuous support in all our activities.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

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**Cite this article as:** Thomas PE, Tolstoy R, Duraisingh LB. Amlodipine induced gingival hyperplasia: a case report. Int J Basic Clin Pharmacol 2015;4:805-7.