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MANAGEMENT OF AMLODIPINE INDUCED GINGIVAL OVERGROWTH – REPORT OF TWO CASES

Dr. Puja Sarkar*, Dr. Suchisuvra Bagchi and Dr. Prasanta Bandyopadhyay

P-34, Motijheel Avenue, Kolkata – 700074.

***Corresponding Author: Dr. Puja Sarkar**
P-34, Motijheel Avenue, Kolkata – 700074.

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ABSTRACT
Several drugs have been claimed to be associated with gingival overgrowth as an adverse effect of their usage. Such drugs include calcium channel blockers (CCB), phenytoin and cyclosporine etc. Among the CCBs, Amlodipine has been used with increasing frequency over the past few years and has been reported to cause gingival overgrowth. The exact reason for such enlargement has not yet been conclusively determined, but several risk factors have been proposed of such enlargement. Here we present a series of cases of Amlodipine induced gingival enlargements with their treatment including surgical management.

KEYWORDS: Drug induced gingival overgrowth, Calcium channel blockers (CCB), Amlodipine, Gingivectomy.

INTRODUCTION

Gingival overgrowth is a known side effect associated with the use of several drugs. Almost 20 such drugs have been indentified to produce drug induced gingival overgrowth. They have been broadly categorized into threemajor groups according to their therapeutic actions, namely- anticonvulsants, immunosuppressants and calcium channel blockers (CCBs).[1] Torpet et al in the year 2004 reported that the prevalence with the use of CCBs might be as high as 38%.[2] Of this large group of drugs, the dihydropyridines (i.e., nifedipine, nitrendipine, felodipine) are the agents most frequently related to drug induced gingival overgrowth.[3]

Amlodipine is a new dihydropyridinecalcium channel blocker used in management of both hypertension and angina.[4] It is structurally similar to nifedipine and pharmacodynamically comparable to it.[5] Ellis *et al*. first reported drug induced gingival overgrowth with amlodipine.[6] Lafzi et al. (2006) had reported, rapidly developed gingival hyperplasia in patient receiving 10 mg per day of amlodipine within two months of onset.[7] The prevalence of gingival overgrowth in patients taking amlodipine was reported to be 3.3% that is much lower than that of nifedipine which was 47.8%.

The clinical manifestation of amlodipine induced gingival overgrowthvaries a lot ranging from mild to moderate swelling with smooth, shiny surface involving interdental, marginal & /or attached gingiva to multiple bead like enlargements involving the aforementioned sites of the gingiva. The color of the lesionis generally pale pink. However in presence of inflammation there may be reddish discolouration of the marginal gingiva.

The disfiguring gingival overgrowth triggered by these medications is not only esthetically displeasing, but often impairs nutrition and access for oral hygiene resulting in an increased susceptibility for oral infection, caries and periodontal diseases.

In the present report, the management of a series of amlodipine induced gingival overgrowth has been presented.

CASE REPORT

CASE- 1

A 40 years old female was referred to the Department of Periodontia at Dr. R. Ahmed Dental College and Hospital, Kolkata with complaints of enlargement of gums involving both upper & lower arches for last 6 months.

Medical history of the patient revealed that she had been suffering from essential hypertension & was under anti-hypertensive therapy taking amlodipine 5mg as a monotherapy for last 1 year. Contradictory to the literature survey this patient started to notice gingival enlargement after 6 months of using 5 mg of amlodipine whereas other reports 10 mg of amlodipine per day was required to develop amlodipine induced gingival overgrowth.[6]

Intraoral examination revealed the presence of peculiar bead like enlargement (Fig.1) including interdental, marginalaswellas attached gingiva & covering almost

middle 1/3 rd of maxillary & mandibular teeth with formation of pseudo pocket. The gingival surface of the enlargement appeared smooth, shiny surface with a firm consistency. The most conspicuous observation was the absence of commonly present gingival inflammation inspite of havingbead like gingival enlargement which favors plaque accumulation leading to inflammatory changes.

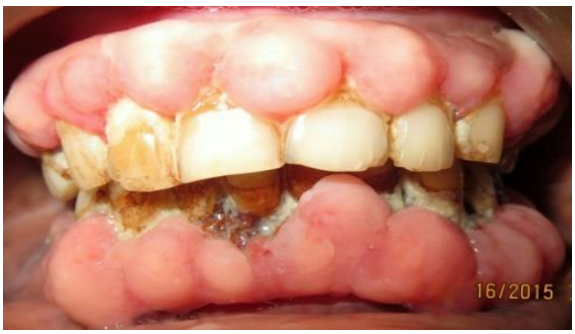
Investigation: Patient was advised for complete hemogram & the results of all the parameters were found within normal limit. OPG showed generalized horizontal bone loss.

On the basis of patients history & clinical features, a clinical diagnosis of amlodipine induced GO was made.

Treatment: Treatment started with non-surgical periodontal therapy including scaling and root planning. Patient was educated and motivated for maintenance of proper oral hygiene.

Patient was then referred to the concerning physician for substitution of the drug amlodipine, if possible. The patient was then switched over to atenolol 100 mg daily as a monotherapy by the physician.

After 3 months of completion of non-surgical periodontal therapy & drug substitution a dramatic response was observed. Regression in the size of gingival enlargement with some remaining fibrous component in the gingiva of the lower jaw was noted. Residual deformity of the gingiva was planned to be corrected surgically to remove the tissue & proper contouring of the gingival margin was achieved.



Case 1: Fig (1)- shows I/O

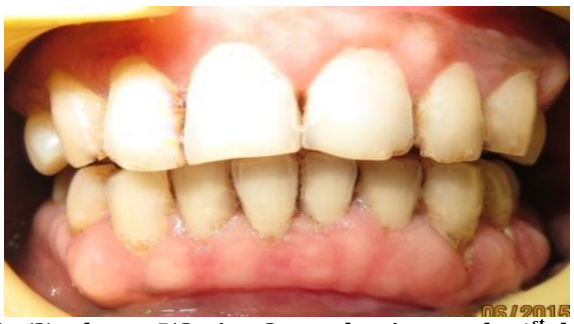


Fig (2)- shows I/O view 3 months view on the 1st day of visitafter non-surgical periodontal therapy

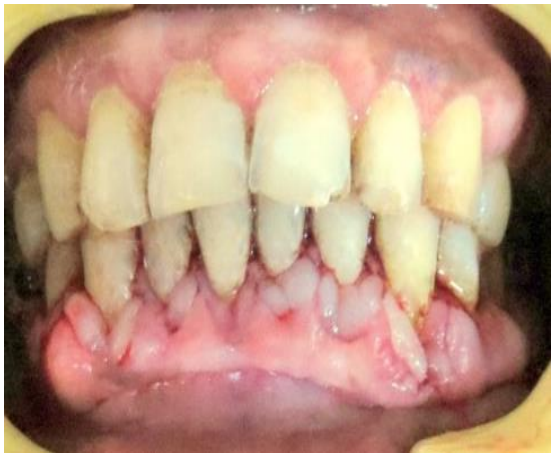


Fig.(3)- shows I/O view with internal bevelincision

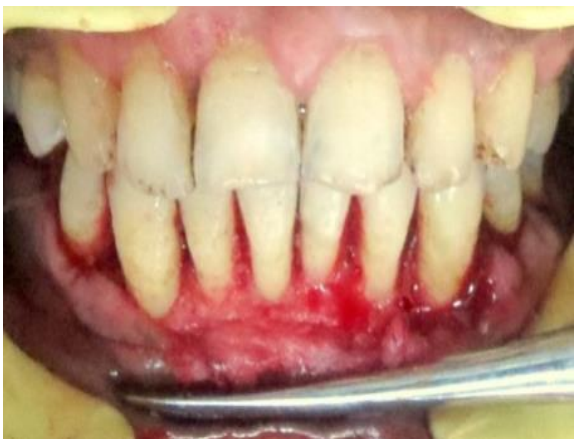


Fig.(4)- shows I/O view after tissue excision & flap reflection

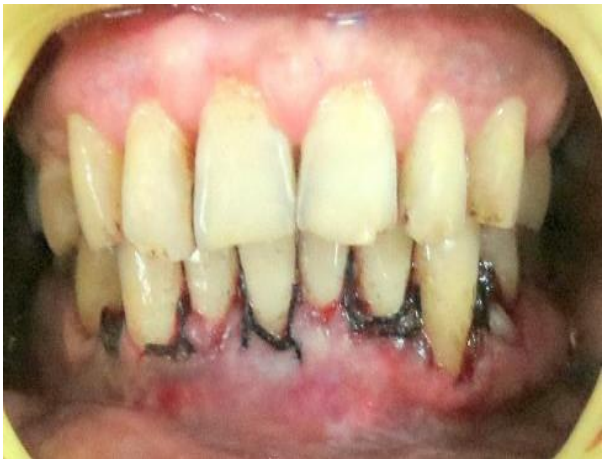


Fig.(5)- shows I/O view after stabilization of flap by suturing

Followupvisit: On seventh day of follow-up visit periodontal pack was removed. Healing procedure was found to be uneventful.

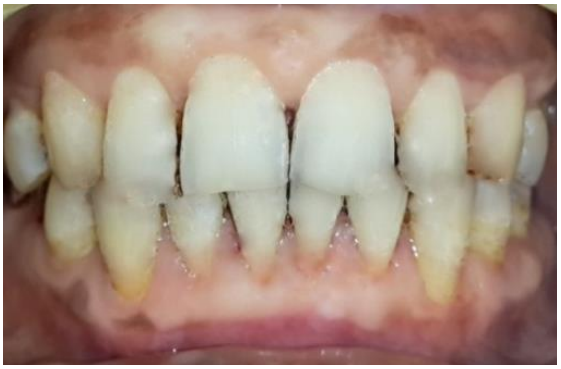


Fig.(6)- shows I/O view on 6 months follow-up visit

H/P: Histopathological (H/P) examination revealed the presence of a mixture of dense & loose fibrous component with mild chronic inflammatory cells infiltrate in the connective tissue.

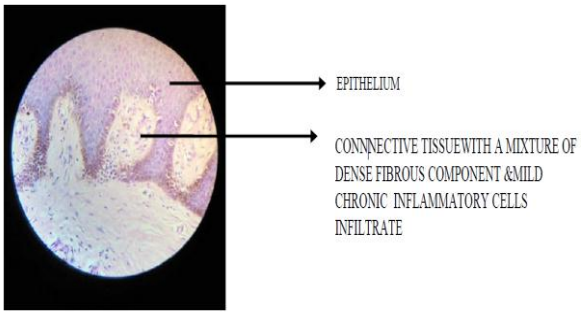


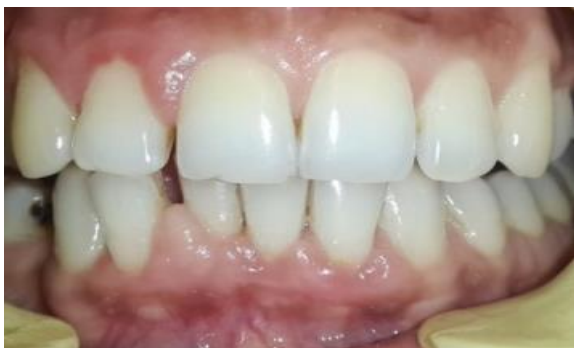
Fig (7)-shows H/P report of the excised tissuewith a mixture of dense fibrous component & mild chronic inflammatory cells infiltrate in the connective tissue.

CASE – 2

A female patient of 45 years reported with complaints of swelling of lower front gum for last 2 months. Patient was under treatment of essential hypertension and was taking amlodipine 5 mg once daily for last 6 months.

Intraoral examination revealed presence ofmild gingival enlargement with smooth shiny surface only in lower anterior tooth region involving themarginal & papillary gingiva.

Investigation: OPG revealed generalized horizontal bone loss. Report ofhemogram and other blood test were within normal limit.



Case 2: Fig.(1)-shows pre-operativeI/O view

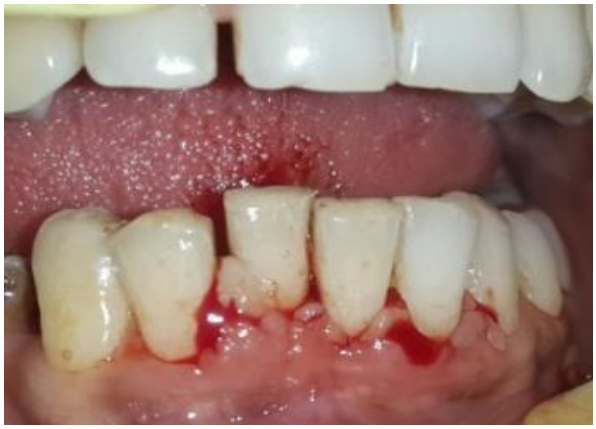


Fig (3)- shows I/O view after surgical incision after suture placement

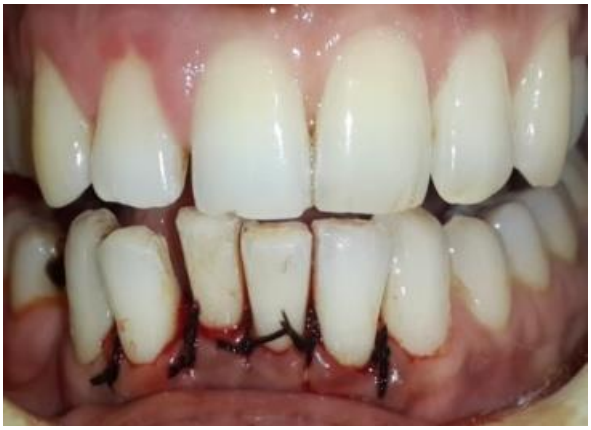


Fig (2)- showsI/O view after surgical incision after suture placement

Treatment: After Phase-I therapy patient was referred to her physician for drug substitution, if possible. Amlodipine was substituted to losartan 50 mg once a day. Remaining excess gingiva was corrected bygingivectomy. Healing was uneventful.

Followup visit: Patient was recalled after every 3 months. The 9-month follow-up visit is shown [Fig.(4)].

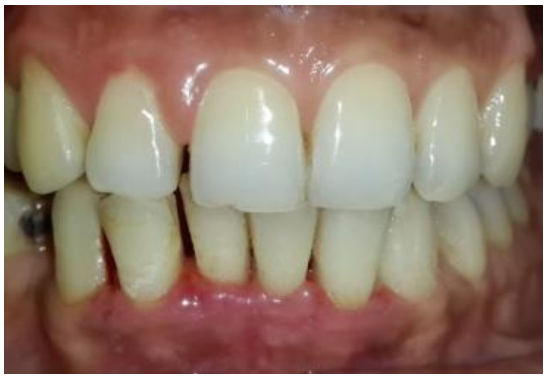


Fig.(4)- Clinical outcome on 9 monthsfollow-up visit

DISCUSSION

Gingival overgrowth is now a recognised undesirable effect associated with many of the calcium channel blockers such as amlodipine. The underlying mechanism

of gingival enlargement still remains to be fully understood. Several possible mechanisms and pathways have been proposed over the years.

However, there is lack of general consensus on this issue. Below are some of the most cited causes and risk factors of gingival overgrowth:

1. ***Role of matrix metalloproteinases***

The hallmark of the enlargement is the increase in the amount of connective tissue matrix dominated by collagen fibers. Collagen synthesis is controlled by matrix metalloproteinases and the tissue inhibitor of metalloproteinases. Collagen fibers are degraded via an extracellular pathway by secretion of collagenases and via an intracellular pathway via phagocytosis by fibroblasts. CCBs affect calcium metabolism by reducing the calcium influx into the cells, leading to a reduction in the uptake of folic acid, thus limiting the production of active collagenase.[8] As a result of the reduction in collagen degradation, increased collagen accumulation occurs.

Other possible pathways for the gingival enlargement is overproduction of extracellular ground substance characterized by increased presence of sulfated mucopolysaccharides (glycosaminoglycans).[9]

2. ***Role of inflammatory cytokines***

Proinflammatory cytokines, such as interleukin-1β and interleukin- 6 seem to have a synergistic effect in the enhancement of collagen synthesis by human gingival fibroblasts.[10]

3. ***Role of fibroblasts***

The finding that the majority of patients treated with CCBs do not develop gingival enlargement lead to the discovery of a subset of fibroblasts that are susceptible to CCBs. A genetic predisposition of different fibroblasts phenotypes to CCB may be related to the human lymphocyte antigen.[12] Other genetic predisposition could influence the metabolism of CCBs, as these drugs are metabolized by the hepatic cytochrome P450 enzymes. Cytochrome P450 genes exhibit considerable polymorphism, which results in inter-individual variation in enzyme activity.

RISK FACTORS

- **Dental plaque and oral hygiene level**

The oral bacterial biofilm is a common risk factor for all forms of inflammatory periodontal diseases and its presence exacerbates CCB-induced gingival enlargement. The severity of gingival enlargement is well correlated with poor oral hygiene.

- **Dosage**

There is lack of a clear correlation between dosage of nifedipine and gingival overgrowth.[8] Some reports on amlodipine suggest that a daily dose of 5mg or higher could be a risk factor for gingival overgrowth in some patients.

CONCLUSION

Stringent maintenance of oral hygiene, switchover to alternative drugs and surgical therapy if required, remains the main stay of available treatment modalities. Better results were obtained where drug substitution along with oral prophylaxis were followed.

REFERENCES

1. Ishida H, Kondoh T, Kataoka M, Nishikawa S, Nakagawa T, Morisaki I et al. Factors influencing nifedipineinduced gingival overgrowth in rats. J Periodontol, 1995; 66: 345–350.
2. Torpet LA, Kragelund C, Reibel J, Nauntofte B. Oral adverse drug reactions to cardiovascular drugs. Crit Rev Oral Biol Med, 2004; 15: 28–46.
3. Seymour. R. A. Calcium channel blockers and gingival overgrowth. British Dental Journal, 1991; 170: 376-379.
4. Joshi S, Bansal S. A rare case report of amlodipine-induced gingival enlargement and review of its pathogenesis. Case Rep Dent. 2013; 20: 138-248.
5. Jorgensen MG. Prevalence of amlodipine-related gingival hyperplasia. J Periodontol. 1997; 68(7): 676-8.
6. Ellis JS, Seymour RA, Steele JG, Robertson P, Butler TJ, Thomason JM. Prevalence of gingival overgrowth induced by calcium channelblockers: a community-based study. J Periodontol, 1999; 70: 63-7.
7. Lafzi A, Farahani RM, Shoja MA. Amlodipine induced gingival hyperplasia. Med Oral Patol Oral Cir Bucal. 2006; 11: E480–2.
8. Barclay S, Thomason JM, Idle JR, Seymour RA. The incidence and severity of nifedipine- induced gingival overgrowth. J Clin Periodontol, 1992; 19: 311–314.
9. Lucas RM, Howell LP, Wall BA. Nifedipine-induced gingival hyperplasia. A histochemical and ultrastructural study. J Periodontol, 1985; 56(4): 211–215.
10. Johnson RB, Zebrowski EJ, Dai X. Synergistic enhancement of collagenous protein synthesis by human gingival fibroblasts exposed to nifedipine and interleukin- 1- beta in vitro. J Oral Pathol Med, 2000; 29: 8–12.
11. Pernu HE, Knuuttila MLE, Huttenen KRH, Tiilikainen ASK. Drug-induced gingival overgrowth and class I1 major histocompatibility antigens. Transplantation, 1994; 57: 1811– 1813.