Case Report

Amlodipine-induced gingival overgrowth: a case report

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Abstract

Gingival overgrowth is frequently observed as side effect in patients taking certain drugs such as calcium channel blockers, anticonvulsants and immunosuppressant. This can have a significant effect on the quality of life as well as increasing the oral bacterial load by generating plaque retention sites. Amlodipine, a third generation calcium channel blockers has been shown to promote gingival overgrowthalthough in very limited cases reported. We report a case of amlodipine-induced gingival enlargement in a 54-year-old hypertensive patient taking amlodipine at a dose of 5 mg.

Introduction

Gingival enlargement or Gingival overgrowth (GO) is one of the most important clinical features of gingival pathology. Its etiology is multifactorial and is associated with inflammatory changes in thegingiva. Other factors related to this condition are hereditary, malignancies and those resulting from adverse effects associated with systemic administration of certain drugs. Medications mainly implicated are the anticonvulsant such as phenytoin,calcium channel blockers (CCB) such as nifedipine and amlodipine, immunosuppressant such as cyclosporine.[1]

Amlodipine, a dihydropyridine derivative is a third generation calcium channel blocker, which has shown to have longer action and weaker side effect compared to the first generation such as nifedipine.[2] Ellis et al. first reported gingival sequestration of amlodipine and amlodipine-induced gingival overgrowth.[2]The prevalence of GO in patients taking amlodipine was reported to be 3.3%, (Jorgensen, 1997) which is lower than the rate in patients taking nifedipine 47.8% (Neryet al., 1995).[3,]

[4] Very few cases of amlodipine-induced gingival hyperplasia have been reported in the dental literature although there are numerous reports of nifedipine-(another member of calcium channel blockers) induced gingival overgrowth till date. Lazy et al[5]had reported rapidly developed gingival hyperplasia in patient received 10 mg per day of amlodipine within two months of onset. There are less data on reports of hyperplasia with amlodipine at a dose of 5 mg, even after taking it for more than 6 months .[3]

Thereby presenting a case of amlodipine induced gingival enlargement occurred at a dose of 5mg within 6months of use.

Case Report

A 54-year-old female patient came to the Department of Periodontics, Govt. Dental College and Hospital, Ahmedabad with the chief complaint of extensive gingival enlargement along with foul odour, bleeding and fetid discharge from gums for six months. Patient

was not aware of such growth until six months when she noticed a small bead-like nodular enlargement of the gums that gradually progressed to the present size covering almost the entire teeth interfering with further cleaning of teeth.Her past medical history revealed that the patient was hypertensive for last 1 year and was under medication (Amlodipine 5 mg, once daily) from last 6 months.The patient was moderately built and nourished. Her vital signs were within the normal range. Intraoral examination revealed generalized enlargement of attached gingival extending up to marginal and interdental gingiva.[FIGURE-1].Poor oral hygiene status of patient was assessed by the presence of local irritating factors which surrounded the teeth.A generalized nodular enlargement of the marginal and interdental gingiva on facial aspect was noticed. In upper and lower left regionlocalized gingival enlargement was seen which was bright red in colour and fibrotic in consistency.Range of probing depth of gingival sulcus was recorded in between 5 to 9 mm.

After correlating history and clinical-examination, diagnosis of chronic generalised periodontitis superimposed by combined type of gingival enlargement was made,basically a drug induced one, complicated by inflammatory changes due to plaque accumulation. Histopathological report revealed few areas of hyperplastic orthokeratinized and parakeratinised stratified squamous epithelium and connective tissue exhibiting mixture of dense and loose fibrous component. Inflammatory cell infiltrate with PMLs and dilated blood capillaries with few areas of calcifications were also evident. Radiographically generalized bone loss was present.

Case management

A non-surgical treatment was planned for the patient. Scaling and root planing was performed. Patient was referred to the physician for drug substitution. The physician substituted the drug with tab. Normadate 100 mg (Labetolol). Patient was instructed to maintain good oral hygiene with the use of 0.2% chlorhexidine oral rinses. Patient reported after 1 month with regression in the size of gingival enlargement.[FIGURE 2] Following oral prophylaxis and substitution of amlodipine, significant improvement in the gingival tissues was observed. However,radiographic investigation of this patient revealed the presence of generalized underlying bone loss. The gingival contours were un-esthetic, difficult to maintain and favoured plaque accumulation leading to further destruction of the attachment apparatus. Hence, phase II periodontal therapy was planned for the patient.Under local anaesthesia, the enlargement was resected segment wise by a modifiedwidman flap procedure. There were no postoperative complications and the healing was uneventful.[FIGURE 3] Follow up was done one to three monthly [FIGURE 4] Regular oral hygiene reinforcement and scaling was done for her. Patient is still on regular follow up and has to undergo a prosthetic rehabilitalion programme.

Discussion

The use of medications with the potential to contribute to the development of gingival overgrowth is likely to increase in the coming years . The prevalence rate of this disorder has been reported to vary: 10% to 50% for phenytoin , 8% to 70% for cyclosporine A and 0.5% to 83% for nifedipine[4,6,7]. Calcium channel blockers are considered potential etiologic agents of drug-induced gingival hyperplasia. In patients with hypertensive heart disease the prevalence of gingival overgrowth associated with

amlodipine is lower than that associated with other calcium channel blocking agents including nifedipine (Jorgensen et al.1997).[3] Although few cases of amlodipine induced hyperplasia have been reported, the present case was interesting as it occurred with a low dose of amlodipine (5mg) and appeared on administration for 6 months.

The pathogenesis of gingival overgrowth is uncertain and treatment is still largely limited to the maintenance of an improved level of oral hygiene and surgical removal of the overgrowth tissues. It has been hypothesized that these individuals have fibroblasts with an abnormal susceptibility to the drug. It has also been proposed that susceptibility or resistance to pharmacologically induced gingival enlargement may be governed by the existence of differential proportions of fibroblast subsets in each individual which exhibit a fibrogenicresponse to this medication.[8] A synergestic enhancement of collagenous protein synthesis by human gingival fibroblasts is found when these cells are exposed simultaneously to calcium channel blockers and elevated levels of interleukin-1β (a proinflammatory cytokine) in inflamed gingival tissues.[9] Interleukin-6 which also plays a role in fibrogenic responses,targets fibroblasts which trigger the proliferation of fibroblasts and exert the positive regulation on collagen and glycosaminoglycans synthesis. So this cytokine has been proposed to play a pathogenic role in fibrotic gingival enlargement [10]. Pharmacological agents implicated in gingival enlargement have negative effects on calcium ion influx across cell membranes, it was postulated that such agents may interfere with the synthesis and function of collagenases.[11]

Gingival hyperplasia 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. Most studies show an association between the oral hygiene status and the severity of drug induced GO. This suggests that plaque-induced gingival inflammation may be important risk factor in the development and expression of the gingival changes (Barclay et al.,1992).[12] In our case the environmental factors such as poor plaque control hadcontributed to worsen the existing gingival enlargement and therefore complicate the oral hygiene procedures (Ikawa et al., 2002)[13] It has been shown that there was significant reduction of nifedipine-induced GO by thorough scaling and root planing and scrupulous plaque control (Hallmon and Rossmann, 1999)[6]Treatment consists of stopping the offending drug, effective oral hygiene measures, professional tooth cleaning, scaling, and root planning. If gingival enlargement persists after careful consideration of the previously mentioned approaches, these cases need to be treated by surgery, either by gingivectomy or flap surgery. Surgical reduction of the overgrown tissues is frequently necessary to accomplish an aesthetic and functional outcome.[6]

In present case patient was subjected to planned sessions of scaling and root planing with substitute drug followed by flap surgery. On evaluating the patient after the period of 3 months drastic change in the clinical picture of gingiva with complete loss of inflammatory component was seen.Postoperative results found to be extremely satisfactory both esthetically and functionally .

Conclusion

The use of medications with the potential to contribute to the development of gingival overgrowth is likely increase in the years to come. Its also seen that the gingival hyperplasia could occur with

amlodipine even at a small dose (5mg).So newer molecular approaches are needed to clearly establish the pathogenesis of gingival overgrowth and to provide novel information for the design of future preventative and therapeutic modalities. Also cooperative 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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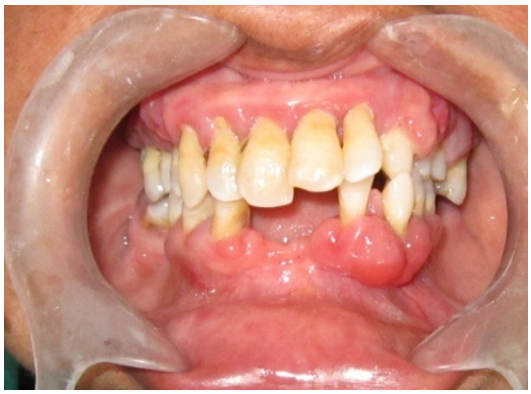


FIGURE 1: FACIAL VIEW OF PATIENT

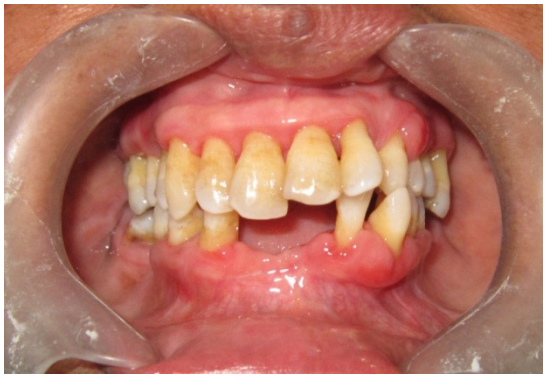
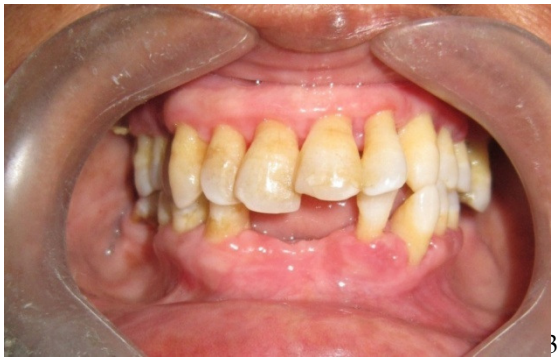


FIGURE 2: FACIAL VIEW AFTER PHASE I THERAPY ANDDRUG SUBSTITUTION



3:
AFTER SURGICAL THERAPY

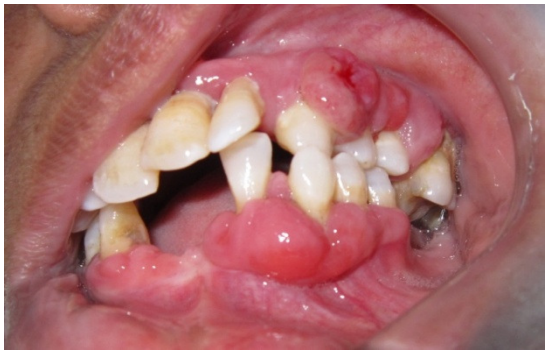
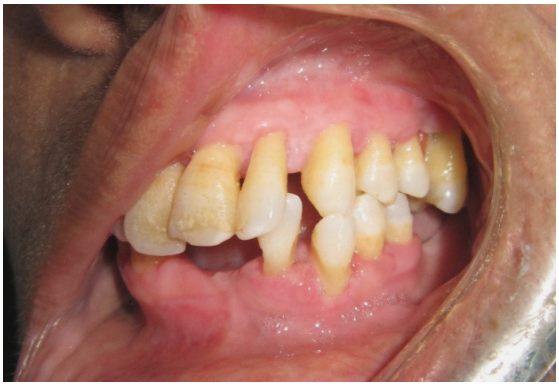


FIGURE 4:COMPARISON OF PRE AND POSTOPERATIVE



AFTER 3 MONTHS