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Amlodipine Induced Gingival Enlargement: A Case Report

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Abstract
Exuberant proliferation of gingival soft tissues in response to local and systemic conditions leads to gingival overgrowth which may create speech problems, difficulty in mastication, altered tooth eruption, and esthetic problems. Gingival enlargement can also occur as a side effect of certain drugs like calcium channel blockers, anti-convulsants and immunosuppressants given for systemic diseases. Hypertension is the major risk factor for cardiovascular diseases. Amlodipine has been widely used from past 2 decades in the management of hypertension and stable angina because of its good efficacy and safety compared with other antihypertensive medications. Here we report a rare case of Amlodipine induced severe gingival enlargement in a 61year old hypertensive male patient taking a dose of 10 mg per day in two divided doses.

Keywords: Amlodipine, gingival enlargement, Calcium channel blockers

Introduction

Gingival enlargement is one of the important clinical sign of pathological changes of gingiva [3]. During gingival enlargement fibrotic, hyperplastic and hypertrophic changes are observed which cannot be differentiated. Various etiological factors causing gingival enlargement includes acute or chronic inflammation, heredity, drugs, systemic diseases and conditions and neoplastic changes [3]. More than 20 medications are associated with gingival enlargement. Drugs causing gingival enlargement includes calcium channel blockers, anticonvulsants and immunosuppressants [6]. Amlodipine is new calcium channel blocker belonging to third generation dihydropyridine which is used in treatment of hypertension and stable angina [5,10]. Amlodipine-induced gingival enlargement is rare and only few cases has been reported in dental literature [6]. Excessive proliferation of gingival tissues interferes with speech, esthetics, tooth eruption and mastication [2]. There is increased susceptibility to oral infection, caries and periodontal disease due to impaired intake of nutrients and poor oral hygiene [3]. Early prevention and prompt treatment reduces gingival overgrowth, inflammation caused by bacteria, dental caries, tooth movement and its exfoliation.

Case Description

A 61 years old male patient visited the Department of Oral Medicine and Radiology with a chief complaint

of swelling in lower gum since 1 month. Patient noticed the swelling 1 month back which was initially small in size and gradually progressed to the present size. His past medical history revealed that he was hypertensive since 7 years and was under medication Amlodipine besilate 5 mg [Amlip -5] twice daily (was prescribed twice but was sometimes consuming thrice) since 2years. He also gave a history of paralytic attack 6 years back and was on medication aspirin gastroresistant and atorvastatin [Atorva ASP 75].

He was poorly built and nourished and his gait was unsteady as he had weakness on the left leg and arms due to paralysis and general physical examination revealed bilateral pedal edema on the legs.

On Intraoral examination generalized gingival enlargement with lobulations in the marginal, attached and interdental gingiva was evident, the surface was pink in color with loss of scalloping and stippling in the lower jaw i.r.t 43,46,47 and 37 [figure 1]. On palpation, the swelling was firm in consistency. Teeth present were 37,43,46 and 47 with 46 and 47 showing grade III mobility and grade II mobility was evident in 43 and 37. Based on the drug history and clinical examination a provisional diagnosis of drug-induced gingival enlargement due to amlodipine was given. OPG was taken which revealed generalized severe bone loss was present with a floating tooth appearance associated with root resorption till the middle third of the root in relation to 46 and 47. [figure 2]

Patient was advised to undergo total extraction, biopsy with gingivectomy and change of the Anti-hypertensive drug(Amlodipine)under physician's advice. He is kept under follow-up.

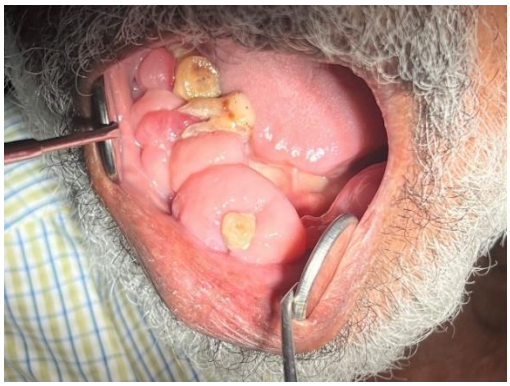


Figure 1 Showing Amlodipine-induced gingival overgrowth

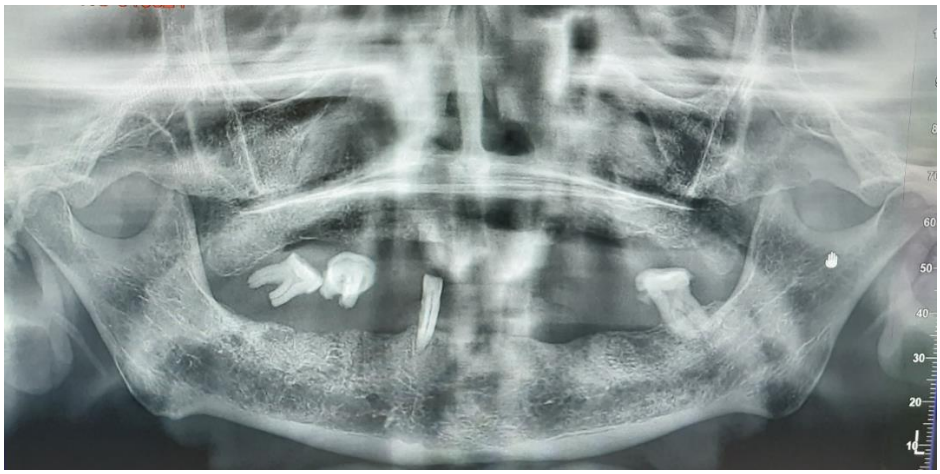


Figure 2 : Orthopantomogram [OPG] showing generalized severe bone loss with a floating tooth appearance associated with root resorption till the middle third of the root in relation to 46 and 47.

Discussion

Three main drug categories associated with drug-induced gingival enlargement include Immunosuppressants, Anticonvulsants, and Calcium Channel Blockers. The incidence of gingival overgrowth is highest for phenytoin.[9] Other drugs causing gingival enlargement include Phenobarbitone, Vigabatrin, Cyclosporin, Nifedipine, Verapamil, Diltiazem, etc. [Graph 1].

Calcium channel blockers are a group of drugs used for the treatment of hypertension, coronary artery spasms, cardiac arrhythmias, and angina pectoris [3]. They are considered as first choice medications in elderly patients with hypertension and angina [3]. Calcium ions are required to maintain tone in the vasculature. Calcium channel blockers inhibit the influx of calcium ion across cell membrane of heart and smooth muscles thereby reducing intracellular calcium. This leads to coronary and peripheral vessel dilation, decreased peripheral resistance and improved oxygen supply to myocardium [1].

Drug induced gingival enlargement can occur in patients with good oral hygiene with little or no plaque deposits or it may be absent in patients with poor oral hygiene [3]. Clinically growth of gingival soft tissues begins as a painless bead like enlargement of interdental papilla. Further progression of its growth extends to facial and lingual gingival margin [8]. The enlargement appears to be separated by linear groove which appears to be projected from beneath gingival margin [8]. Gingiva may appear pink in color with erythematous areas and lobulated surfaces and margins of gingiva appears to be rolled out [8].

Various risk factors which predispose to drug induced gingival enlargement includes genetic predisposition, poor oral hygiene, male sex and middle-aged adult [5]. [flow chart 1]

Gingival inflammation due to plaque triggers the release of various cytokines which acts on fibroblasts causing increased cell proliferation and collagen synthesis. Higher levels of interleukin 1α is evident in patients taking amlodipine [4]. Amlodipine acts on gingival fibroblasts causing increased connective tissue matrix volume by inhibiting the collagenase enzyme. Connective tissue matrix consists of collagen, fibrin, fibronectin and several other components. This enzyme plays a role in the turnover of collagen in the connective tissue [4]. Inhibition of collagenase enzyme causes impaired regulation of collagen synthesis and degradation.[13] Activation of collagenase occurs in presence of calcium. Amlodipine inhibits the influx of calcium ion leading to disruption in collagen breakdown [1].

Calcium channel blockers has on effect on androgen metabolism by converting testosterone into active metabolite which targets certain population of fibroblasts leading to increased collagen synthesis or inhibition of degradation of collagen by acting on collagenase. Hence males are more susceptible for drug induced gingival enlargement due to high levels of androgen hormone compared to females [4].

Polymorphism of genes leads to increased expression of cytosolic protein that blocks the apoptosis of cells. Apoptosis enables lysis of cell which are defective thereby limiting the inflammation. Cell cycles can be longer and size of the cell can be larger if there is impaired regulation of cell cycle [4].

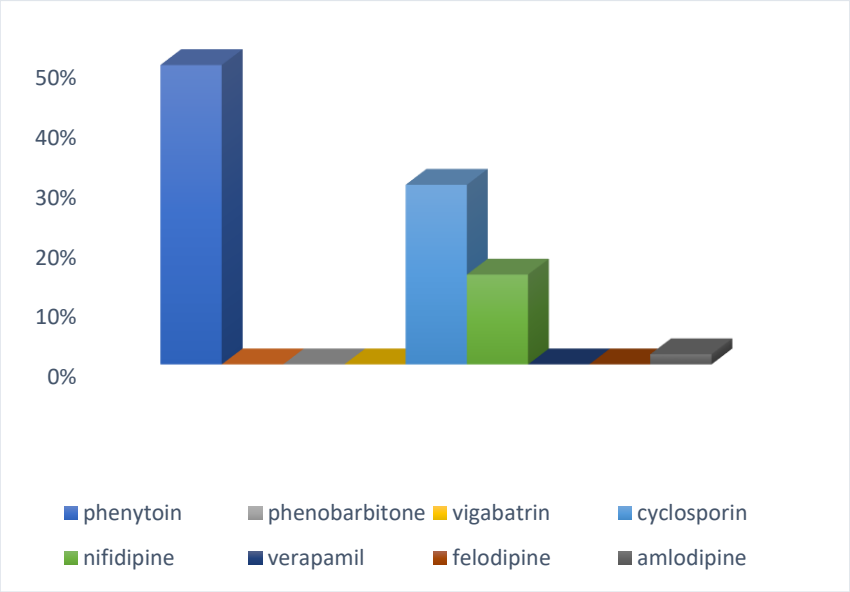
Amlodipine-induced gingival overgrowth is 3.3 times more common in males compared to females.[14] The initial signs of Amlodipine-induced gingival overgrowth begin as an enlargement of the interdental

papilla of keratinized gingiva followed by an increase in connective tissue components and gingival inflammation.[11,12] This implies that the interplay among drug metabolites, gingival fibroblasts, and cellular and biochemical mediators of inflammation results in Amlodipine-induced gingival overgrowth.[11]

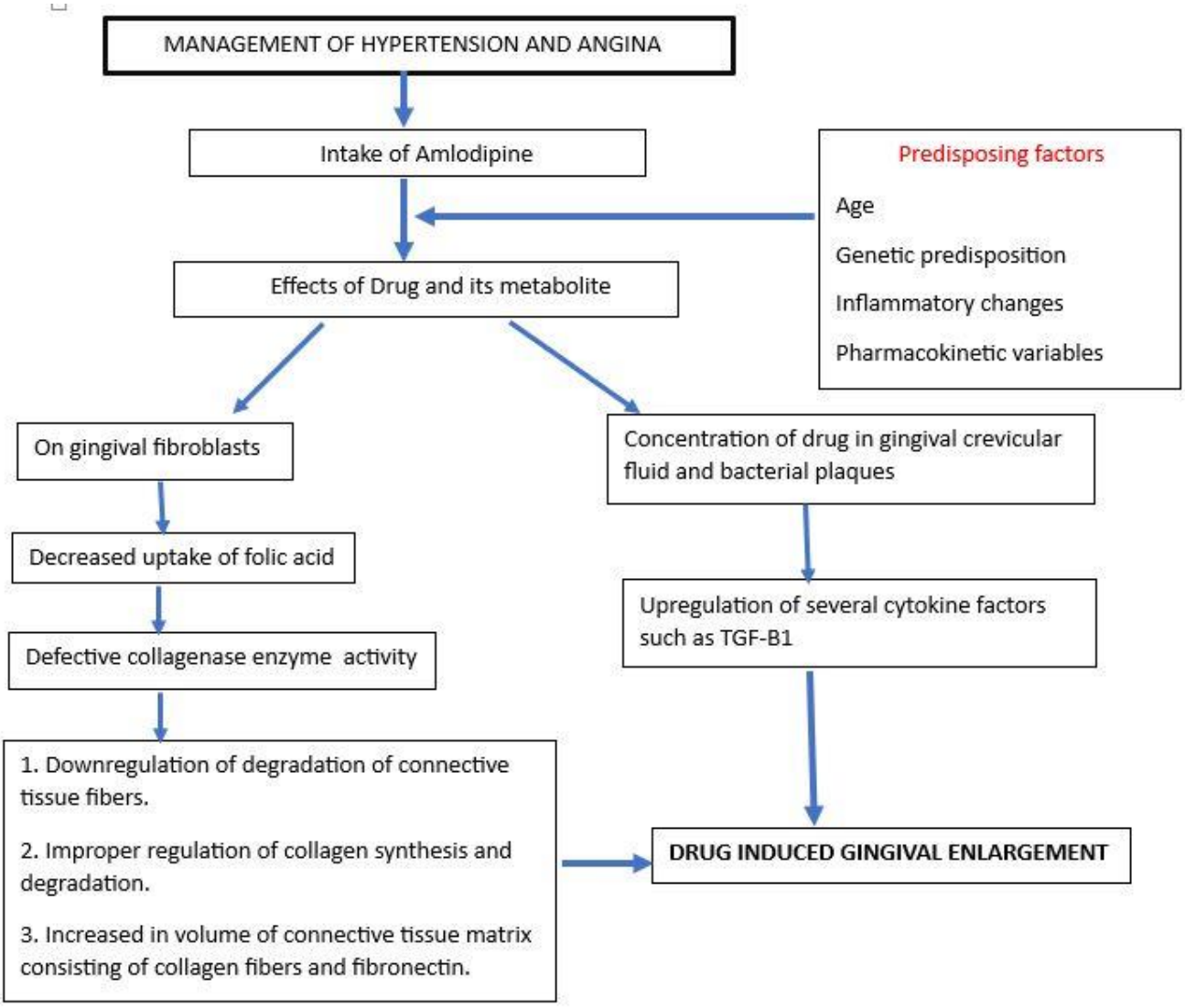
Use of statin medication [HMG CO -A reductase inhibitors] for treating cardiovascular disease has an impact on periodontium. Statins reduces the levels of proinflammatory cytokines IL-1B IL-6, IL- 8, and increases the levels of anti-inflammatory mediators IL-10 and other chemokines thus promoting wound healing and regeneration [7]. Anti-inflammatory properties for these drugs vary according to the dose and type of the drug used. Several studies on statins proves that there is significant reduction in bone resorption and increased bone regeneration by use of atorvastatin [7]. In our case we noted severe gingival enlargement and bone loss with root resorption. Studies showed that chances of drug induced gingival enlargement is rare in patients taking amlodipine [6] and bone resorption is less in patient under atorvastatin medication.

On Histopathological examination all the drug categories shows similar findings. variable thickness of parakeratinized epithelium covers the connective tissue stroma. Excessive accumulation of collagen, fibrin and amorphous ground substance in the connective tissue stroma along with varying degrees of inflammatory cell infiltrate is evident. Plasma cells are abundant [6] .

Drug induced gingival enlargement is treated in various phases depending on the severity of individual case. Various therapeutic options include scaling and root planning, drug substitution, surgical therapy and periodic maintenance and follow up [3]. [flow chart 2]



Graph 1 Showing Prevalence Rates of Various Drug Induced Gingival Enlargement [6]



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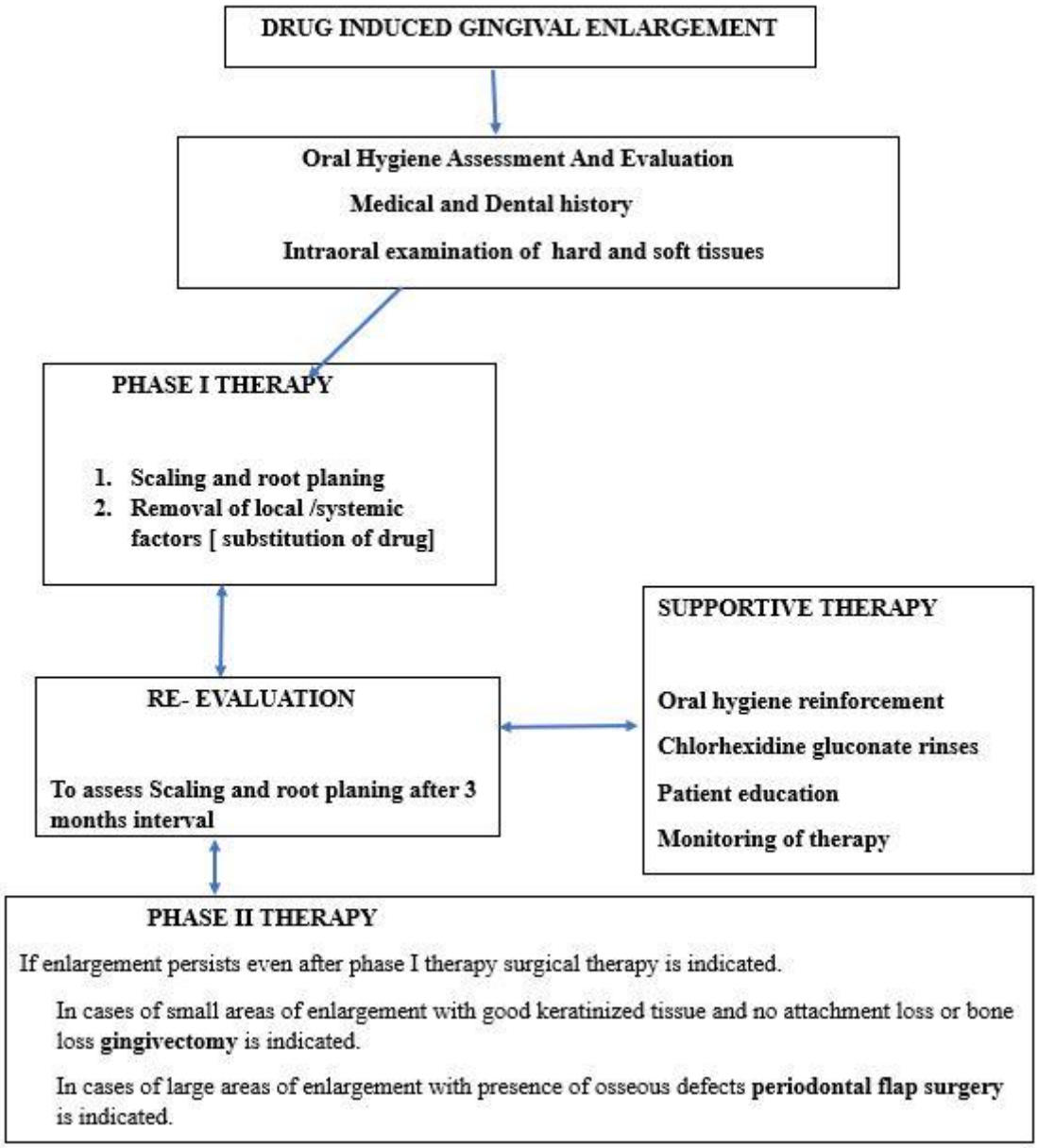

Flow Chart 2: Treatment Algorithm for Drug-Induced Gingival Enlargement[3,6]

Conclusion

Treatment plan varies for every individual depending on the severity of the case. Physicians should inform the patient about the possible consequences of using this drug and also maintain proper oral hygiene. For effective management of Drug-induced gingival enlargement, proper identification of etiological factors, and associated risk factors, maintenance of oral hygiene, elimination of local factors, and surgical excision of lesion in severe cases is essential for improving esthetics and function.

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