Amlodipine-Associated Gingival Hyperplasia: A Case Report and Review of Literature

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Gingival overgrowth can be adverse reaction of calcium channel blockers. Although nifedipine is commonly associated with this process, some case reports have also implicated amlodipine as a possible etiology. Here we present a case of a 59-year-old Pakistani female who developed gingival hyperplasia secondary to amlodipine use. We believe that the knowledge about amlodipine-associated gingival hyperplasia is necessary for dentists, so they can accurately diagnose this condition and provide appropriate management.

KEYWORDS: Drug-induced gingival overgrowth (DIGO), gingival hyperplasia, amlodipine

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INTRODUCTION

Gingival overgrowth is hereditary or acquired enlargement of attached gingiva.[1] It results from increased proliferative activity of fibroblasts that cause accumulation of extracellular matrix and collagen in gingival connective tissue. While hereditary gingival hyperplasia may be seen in association with multiple syndromes and conditions, acquired is attributed to chronic trauma, granulomatous diseases, nutritional deficiencies, endocrine problems, neoplastic diseases and medications.[2] There are several medications that have been implicated as a direct cause of gingival overgrowth. The common ones include anticonvulsants, cyclosporin, antibiotics, oral contraceptives and calcium channel blockers.[1]

Calcium channel blockers are a class of antihypertensives. Although little is known about the exact mechanism by which they cause gingival overgrowth, there are a couple of explanations available in the literature. The first explanation claims that calcium channel blockers decrease folic acid uptake by cells, thus retarding aldosterone synthesis and increasing adrenocorticotropic hormone activity. This interferes with collagenase synthesis leading to build up of collagen in gingival tissues. The second theory claims that build of drug concentration in the gingival crevicular fluid causes inflammation in the gingival tissues. The release of inflammatory cytokines in the gingiva leads to excessive collagen deposition.[3]

The most calcium channel block linked to gingival hyperplasia is nifedipine.[4,5] Since amlodipine has an identical mechanism of action to nifedipine, it is commonly used as a replacement drug to nifedipine when adverse effects like tachycardia, facial flushing and gingival overgrowth arise. However, the literature now documents a correlation between gingival overgrowth and amlodipine.[6-8]

Here we present a case of a 59-year-old Pakistani female who developed medication-related gingival overgrowth. Our patient was taking amlodipine among other antihypertensives. Since amlodipine is commonly prescribed antihypertensive medication, our case is a good reminder for dentists to consider amlodipine as a potential cause for gingival hyperplasia.

CASE REPORT

A 59-year-old female was seen in the Oral Medicine clinics at Riphah International University with a complaint of bleeding gums, halitosis and gingival enlargement for over one month. Her medical history was positive for unstable hypertension and a prior episode of myocardial infarction. She was currently taking telmisartan 80mg, metoprolol 100mg, aspirin 75mg, amlodipine 5mg, valsartan 50 mg, atorvastatin 10mg and alprazolam 0.5mg. She has been on this medication for almost 3 years.

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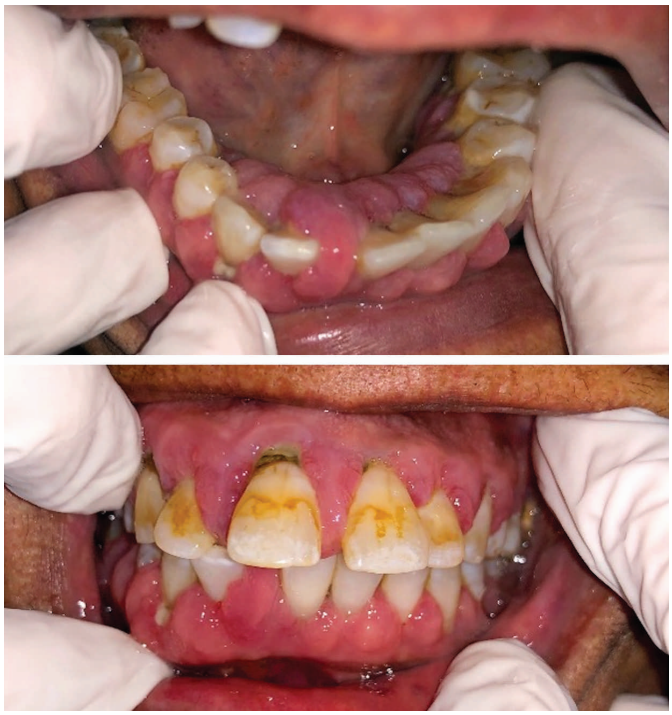
On clinical examination gingival hyperplasia was identified. While the attached gingiva of both jaws was involved, it was more pronounced in the anterior region (Figure 1). The most affected area was mandibular lingual region. The hyperplasia was accompanied by heavy calculus deposits, periodontal pocketing and bleeding on probing. There was intrinsic staining noted on the anterior maxillary teeth.

Figure 1: Patient on first appointment

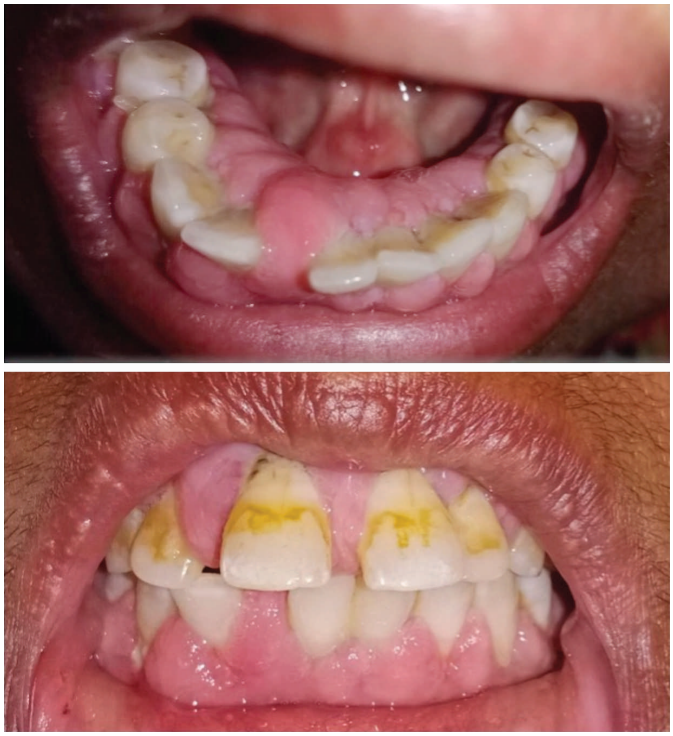


We discussed the condition with the patient and explained potential causes of gingival hyperplasia. Following exclusion of other causes of gingival enlargement, a diagnosis of medication-associated gingival overgrowth was made. The patient was referred to the Periodontology department for oral hygiene prophylaxis (scaling and polishing of teeth). We also wrote a letter to patient's physician recommending discontinuation of amlodipine.

Following the plaque and calculus removal, the patient was prescribed chlorhexidine rinse and antibiotics for 1 week. She then saw her physician who updated her medications but persisted with use of both amlodipine and metoprolol. The cardiologist did modify the treatment plan after numerous attempts from us to get in touch with him.

On follow up the patient no longer had complaints of halitosis and gingival bleeding. However, some degree of gingival hyperplasia still persisted (Figure 2). Our patient was offered gingivectomy to get rid of the extra tissue, but she refused. She remains on follow up and gets her calculus and plaque deposits removed through instrumentation regularly.

Figure 2: Patient seen on 3-month follow up.



DISCUSSION

An increasing number of drugs are involved in causing gingival hyperplasia. The common drugs involved in causing this are calcium channel blockers, anticonvulsants, immunosuppressants and β-blockers. Since our patient was using a medicine implicated in gingival overgrowth; amlodipine, drug-associated gingival overgrowth remained the only option in our differential diagnosis. Drug-induced gingival overgrowth shows a female predilection, women between the ages of 45 to 60-years are mostly affected.[7,9] Our patient was also female between the favored age group.

Amlodipine is classified as a dihydropyridine in the category of calcium channel blockers. FDA has approved amlodipine for managing hypertension and coronary artery diseases. It reduces hypertension by blocking the voltage gated L-Type channels. This prevents activation and phosphorylation of myosin, contraction of vascular smooth muscle, and increase in blood pressure. The same mechanism of action also prevents the precipitation of angina.[10]

Like all medications, amlodipine is associated with some adverse effects. These include pulmonary and peripheral edema, heart failure, dizziness, headaches, nausea and abdominal pain. In the head and neck region, amlodipine is associated with gingival overgrowth, taste alterations (dysgeusia), total loss of taste sensations (ageusia) and smell disturbances (dysosmia).[11]

The mechanism of gingival overgrowth is a consequence of changes in size of cell, division of cells, increased matrix production, angiogenesis in gingiva and altered phenotype of fibroblasts. This coupled with reduced metalloproteinase production causes enlargement of gingival tissues.[12] The enlargement of the gingiva can sometimes become more likely if other medications like metoprolol, a common β-blocker, is being used. A study has shown that over 25% of patients using both amlodipine and metoprolol were more likely to develop gingival overgrowth.[13] Our patient was using both medications at the time of presentation.

Amlodipine-associated gingival hyperplasia presents as generalized painless swelling of the gingiva. Prominent involvement of interdental papillae initiating soon after drug consumption is usually seen.[14] The hyperplasia can range from localized bead-like enlargements of interdental papillae to pronounced gingival overgrowth. Both arches are commonly involved. The anterior gingiva is more prominently involved.[15] The overgrowth is firm to hard on palpation. Loss of scalloped margins, gingival bleeding and erythema due to inflammation may also occur. Bleeding on probing may be a rare finding. Mobility and eventual loss of teeth is noted in chronic cases. Since only dentate areas demonstrate gingival hyperplasia, loss of teeth often results in resolution of overgrowth. Patients see dentists due to esthetic or functional concerns.[15,16] While most of these features were noted in our patient, there was also a complaint of halitosis.

Diagnosis of drug induced gingival enlargement made based on thorough dental and medical histories, clinical presentation and histology, where appropriate. Evaluation and complete record of location, nature and extent of involvement, probing depth, presence of plaque or calculus needs to be made. Other causes of gingival overgrowth like chronic trauma, granulomatous diseases, nutritional deficiencies, endocrine problems, and neoplastic diseases need to be ruled out.[2] Common serology investigations including complete blood picture, glucose tolerance test and renal function tests can rule out leukemia, infection, diabetes and renal failure. Pregnancy tests may be needed for women in child-bearing age. Histopathology of the enlarged tissues shows proliferation of fibroblasts and collagen. The collagen is often thick and ropy in appearance and streaming vertically. The surface oral epithelium may exhibit hyperkeratosis, acanthosis and elongated rete-ridges. Sprinkling of chronic inflammatory cells may be seen.[17] Absence of multinucleated giant cells or neoplastic cells also helps in establishing definitive diagnosis.[2]

Management of drug-associated gingival overgrowth requires discontinuation of the offending agent and surgical excision of excess tissue. Recurrence is a frequent problem, especially in cases when the medication cannot be stopped.[18] Non-surgical intervention includes scaling and root planning along with irrigation of all subgingival pockets with 1% chlorhexidine. This gets rid of harmful organisms and prevent secondary inflammation. Oral hygiene instructions are strongly recommended.[19] It was difficult for us to proceed with management due to reluctance of the cardiologist in switching medications. It took us several phone calls and 2 letters before the medications were discontinued. Our patient refused any invasive procedures, she chose to undergo scaling and polishing was given a chlorhexidine mouthwash. We believe that this is the reason why her hyperplastic tissue persisted on the 3 months follow up.

In conclusion, we discuss a case of gingival overgrowth associated with a common antihypertensive medication; amlodipine. We believe that this knowledge is necessary for dentists so they can correctly identify medication-associated gingival hyperplasia and appropriately manage this condition by coordinating with the patient's physician.

CONFLICT OF INTEREST

None declared

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