CASE REPORT

Gingival Hyperplasia due to Nifedipine – In A Young Patient

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ABSTRACT

Introduction: Gingival hyperplasia is well known side effect associated with number of drugs calcium channel blockers like amlodipine, immunosuppressant drugs like cyclosporine, anticonvulsants like phenytoin, sodium valproate etc.

Case Report: A case of Nifedipine induced gingival enlargement in a 26 years old female is discussed after just 3 months of drug intake.

Conclusion: Patients receiving Calcium channel blockers may develop gingival hypertrophy which is usually reversible with discontinuation of the drug.

Keywords: Gingival Hyperplasia, Calcium Channel Blockers (CCB's), Nifedipine

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INTRODUCTION

The use of CCBs in managing patients with heart diseases was pioneered by Fatt and Katz[1] and subsequent work by Fleckenstein.[2] This class of drug exerts its action by binding to L-type calcium channels located on vascular smooth muscles, cardiac myocytes, Sinoatrial and Atrioventricular node. The first generation of these drugs was developed in 1970s and included derivatives of dihydropyridines, phenylalkylamines and benzothiazepines. The first generation of CCBs had multiple side effects which included tachycardia, facial flushing and gingival overgrowth.[3] Subsequently the drug induced gingival overgrowth was also observed in later generations of dihydropyridines which included nitrendipine,[4] oxydipine[5] and amlodipine.[6] Gingival hyperplasia is a well-documented complication of other drug classes like immunosuppressant's and anti-convulsants other than antihypertensives, which leads to unpleasant appearance and predisposes to periodontal disease due to harboring of gingival sulcus with pathogenic bacteria.

CASE REPORT

A 27 yrs. Old female patient with Stage II hypertension diagnosed for the first time in 2001 at the age of 15 yrs. but she stopped taking medications for her medical condition. In April 2013 she presented to our hospital for headache and left sided weakness. Her blood pressure in upper limbs revealed stage II (180/100mmHg) hypertension. Subsequent CT scan (Head) showed infarct in right Internal capsule and putamen. Clinical examination showed upper motor neuron type of left sided hemiparesis and abdominal bruit. On general examination her lower limb pulses were weak with low blood pressure (130/80mmHg) as compared to upper limbs. USG Abdomen was normal. Blood investigations were within normal limits. ECG showed Left axis deviation with left ventricular hypertrophy. Echocardiography revealed left ventricular hypertrophy with grade I diastolic dysfunction. Renal Doppler Study reported bilateral renal artery stenosis. Patient underwent renal angiography which revealed non visualization of Left renal artery with dual arteries supplying the right kidney which were diffusely stenosed. Abdominal aorta had diffuse stenosis before origin of right renal artery extending up to the aortic bifurcation. Multiple dilated collateral blood vessels were visible. Patient was put on Tab. Nifedipine 20mg TDS, Tab. Metoprolol 25mg BD, Tab Prazosin 10mg BD for control of hypertension. Her condition stabilized with treatment and was discharged with recovering hemiparesis. The patients' blood pressure was well controlled with medications. After about 3 months of regular treatment she noticed abnormal shape and size of gums (Figure-1).

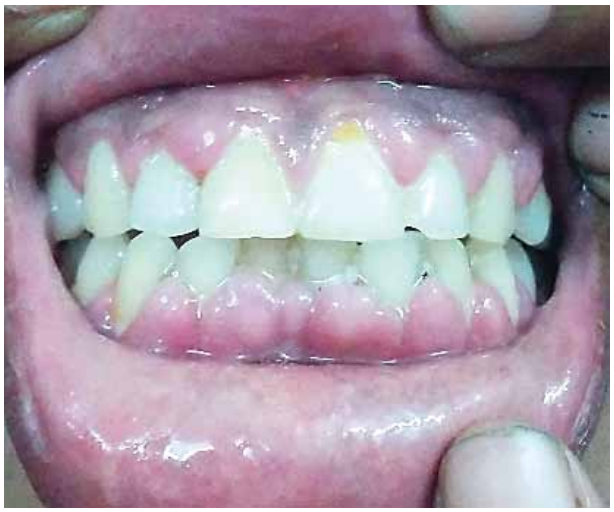

Figure-1: Showing Gingival Hyperplasia

She noticed that the gingival hyperplasia was gradually progressive and was associated with pain and gum bleeding. On examination there was generalized and firm overgrowth of gingiva throughout maxillary and mandibular alveolar ridges.

Histo-pathological examination of lobulated gums revealed hyperplastic gingival epithelium with underlying fibro- cellular connective tissue and features of dense chronic inflammation (Figure-2).

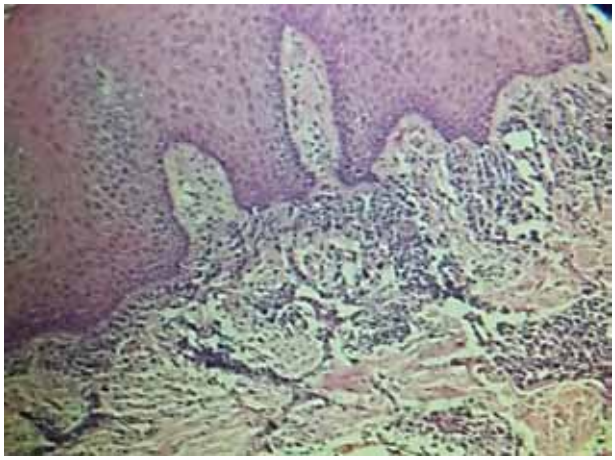

Figure-2: Showing Hyperplastic gingival epithelium with fibrocellular connective tissue and features of dense chronic inflammation

A diagnosis of drug induced gingival hyperplasia secondary to antihypertensive medication due to nifedipine was considered. Accordingly her antihypertensive medications were changed to Metoprolol 25mg BD, Prazosin 10mg BD and Methyldopa 250 mg TDS.

DISCUSSION

Several possible pathways and mechanisms have been proposed as a cause of gingival enlargement but the pathogenesis is still not well understood. Some causes are considered in the etiopathology of this condition which includes matrix metalloproteinases, inflammatory cytokines and fibroblasts. Risk factors which contribute to this condition include dental plaques, poor oral hygiene, age, gender and dose of the medication. Some studies have also shown that patients having these gingival lesions have a genetic predisposition and a high frequency of HLA antigens and genetic markers like HLA-DR2 and cytochrome P-450.[7] On the other hand presence of genetic markers like HLA-B37 and HLA-DR1 provide some protection against gingival overgrowth.

The gingival enlargement can be localized or generalized and ranges from mild increase of interproximal gingival papillae to a severe enlargement of marginal and papillary tissues. In severe cases the papillae and surrounding tissues are enlarged with a lobulated appearance. The changes are more obvious in anterior teeth and facial/buccal surfaces. Histologically the changes are due to an exaggerated connective tissue response rather than epithelial cell proliferation. There is an accumulation of extracellular matrix proteins like collagen, amorphous ground substance and glycosaminoglycans. Plasma cells and to a lesser degree lymphocytes dominate the accompanying inflammatory infiltrates.The extracellular matrix is degraded by secretion of collagenases and phagocytosis by fibroblasts. CCB's affect the calcium metabolism by reducing influx of calcium in the cell and thereby affecting folic acid uptake. This limits the production of active collagenase and leads to accumulation of excessive collagen.[8]

The inflammatory cytokines like IL-6 have been shown to enhance proliferation of fibroblasts and also increase glycosaminoglycan synthesis.A subset of fibroblasts related to specific human lymphocyte antigen may be more susceptible to CCBs induced gingival enlargement.[4] Poor oral hygiene affects the gingival overgrowth by affecting the oral bacterial biofilm.Age is not considered as a risk factor as mostly the drug is used in middle aged individuals.

Gender may play a role in drug induced gingival overgrowth as males are found to be more susceptible.[10] Nifedipine affects androgen metabolism and increases conversion of testosterone to 5a-dihydrotestosterone. This active metabolite increases collagen synthesis and also decreases its degradation.[10]

Several case reports have implicated Nifedipine in gingival enlargement as it is more lipophilic and penetrates the cell membrane more quickly thereby playing a ma-

jor role in the pathogenesis of drug induced gingival enlargement. The variation in half life and volume of distribution of nifedipine in comparison to amlodipine also contributes to the etiopathogenesis.[9] This pharmacokinetic property enables nifedipine to achieve higher peak plasma levels as compared to amlodipine affecting drug induced gingival enlargement.

Our patient presented with gingival hypertrophy after 3 months of continuous use of 60mg nifedipine per day. The gingival enlargement can be detected clinically as early as 1-3 months following the initial dose of CCB. Several case reports have pointed out the incidence of drug induced gingival enlargement due to CCBs in middle and old aged patients as they are often prescribed in this age group.Our patient presented as a young hypertensive due to bilateral renal artery stenosis. This differs from the usual age group of patients presenting with gingival hypertrophy. In our case report the patient belongs to female gender, this differs from other studies which suggests male predilection of gingival hypertrophy.[10] After stoppage of nifedipine there was much resolution of the gingival hypertrophy after about 2-3 months. (Figure-3)

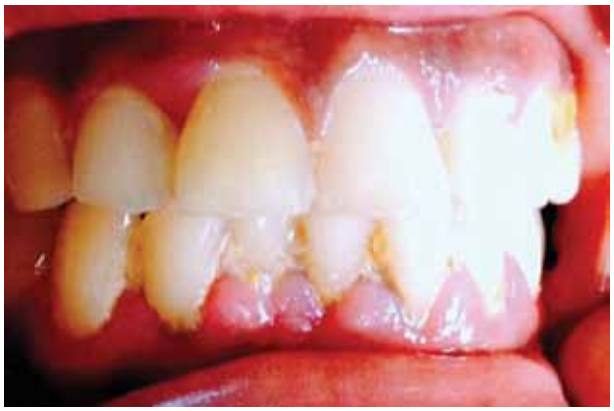

Figure-3: Resolution of gingival hypertrophy

CONCLUSION

CCB's are an essential part of management of hypertension and heart diseases but a troublesome and often overlooked side effect in the form of gingival hypertrophy can occur. Stoppage of the culprit drug is essential as failure to do so can lead to progression and or recurrence of disease. Surgical and non-surgical techniques can only provide temporary relief.

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