Amlodipine-induced reversible gum hypertrophy

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ABSTRACT
Gingival hypertrophy is a common manifestation of any pathology affecting gingival and periodontal regions. It commonly follows inflammatory disorders, Vitamin C deficiency, leukemia and due to drugs such as anticonvulsants, immunosuppressants, and calcium channel blockers. Amlodipine is a third generation dihydropyridine derived calcium channel blocker commonly used to treat hypertension. Here, we describe the case of a 45-year-old hypertensive woman who was on amlodipine for 1 year and subsequently developed one of its rarest adverse effects, i.e., gingival hypertrophy.

INTRODUCTION
Calcium channel blockers are commonly used drugs for treating hypertension owing to their superior efficacy, tolerability, and safety profile. Gingival hypertrophy is a rare side effect of this class of drugs, most of the cases having been reported with the use of nifedipine. The third generation dihydropyridine derived calcium channel blocker amlodipine has replaced nifedipine as a first choice drug largely, owing to its slow hepatic degradation resulting in longer duration of action and lesser adverse effects. The incidence of gingival hypertrophy associated with amlodipine is very rare and very few cases have been reported in medical literature. We hereby describe a rare case of amlodipine-induced gingival hypertrophy in a 45-year-old woman who was being treated by this antihypertensive drug for 1 year.

CASE REPORT
A 45-year-old woman presented to the Medicine Outpatient Department with complaints of gum swelling since 1 month [Figure 1]. It was gradually progressive, involving both upper and lower gums, associated with redness, pain and malalignment of her teeth. There were no signs of ulceration or bleeding. She had significant difficulty in eating food.

Her general examination was unremarkable, except for the red and swollen gums. She was a known hypertensive and was controlled on amlodipine 10 mg O.D. for the past 1 year. Routine investigations including hemogram, electrocardiogram, renal and liver functions were within normal limits. Other possible causes of gingival hypertrophy were carefully excluded, including usage of any other drug.

We substituted amlodipine with telmisartan 40 mg O.D. and advised her to maintain proper oral hygiene. On follow-up after 3 months, her gum swelling had significantly subsided [Figure 2], while she remained normotensive on the newly prescribed drug.
DISCUSSION

Gingival hypertrophy is a common clinical manifestation of gingival and periodontal disease. It involves proliferative overgrowth of the gingiva, resulting in coverage of teeth, pain, difficulty in eating, infection, abscess, ulceration, and bleeding.\[^{3}\] It can also delay the eruption of teeth by causing mechanical obstruction.\[^{4}\] The common causes of gingival hypertrophy include inflammatory diseases, leukemia, Vitamin C deficiency and drugs.

Currently, the etiology of drug-induced gingival overgrowth is not entirely understood but is clearly multifactorial. There is ongoing debate whether drug-induced gingival overgrowth is due to hyperplasia of the gingival epithelium or of submucosal connective tissue, and/or both. Furthermore, the effect of age, sex, and duration and dosage of the drug in the pathogenesis of gingival overgrowth is not clearly understood. One of the main reasons is that clinical and epidemiologic studies are primarily retrospective, and they are unable to fully clarify this association.\[^{3,4}\]

Some of the risk factors known to contribute to gingival overgrowth include the presence of gingival inflammation (i.e., gingivitis) resulting from poor oral hygiene. Furthermore, the presence of dental plaque may provide a reservoir for the accumulation of phenytoin or cyclosporine. In orthodontic patients, gingival overgrowth has been suggested to be due to nickel accumulation and epithelial cell proliferation.\[^{3,4}\]

The most common drugs implicated in drug-induced gingival hyperplasia include anticonvulsants (phenytoin, valproate, lamotrigine, and ethosuximide), immunosuppressants (cyclosporine), and calcium channel blockers (nifedipine, amlodipine, verapamil). The prevalence of gingival hypertrophy with calcium channel blockers is as high as 38%.\[^{3}\] Nifedipine is the one most commonly associated with gingival hypertrophy, with an incidence of 20%.\[^{1}\] Amlodipine usage is a rare cause of gingival hypertrophy, with a prevalence rate of 3.3%.\[^{2}\]

The pathogenesis of drug-induced gingival hypertrophy is still unclear.\[^{6}\] It may be a direct effect of the drug or any of its metabolites on gingival fibroblasts. Gingival fibroblasts are stimulated by several mediators, including mast cells,\[^{7}\] resulting in recruitment of a large number of inflammatory cells. Not all patients taking the implicated drug are affected, thus there is heterogeneity in the response of gingival fibroblasts. Other factors such as genetics, pharmacokinetics, and inflammation may also be important.

The primary aim of nonsurgical approaches is to reduce the inflammatory component in the gingival tissues and thereby avoiding the need for surgery.

Meticulous removal of plaque on a frequent basis helps in the maintenance of attachment levels. Patients at risk from, or who have developed drug-induced gingival overgrowth will benefit from effective oral hygiene measures, professional tooth cleaning, scaling, and root surface instrumentation. For some patients, these measures alone can reduce the gingival overgrowth to acceptable levels, for others, it can make surgical correction easier.

The initial step of treatment is reducing the dose of prescribed drug or discontinuation. Maintenance of adequate oral hygiene and plaque control is essential to prevent any complications. In severe and refractory cases, gingivectomy is the preferred surgical treatment.\[^{8}\] Alternatively, an argon laser can be used to treat drug-induced gingival hypertrophy.\[^{9}\]

CONCLUSION

With the increasing number of hypertensive patients and usage of amlodipine to render them normotensive, the clinician must be sensitized to the development
of gingival hypertrophy as a rare but possible side effect of this very popular drug, and must revise his prescription accordingly.

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REFERENCES
