CASE REPORT

Healthy Gums does it Matter? Amlodipine-Induced Gingival Overgrowth (AIGO): A Case Report.

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Abstract
In Malaysia, more than half a million adults, representing 2.5% of the population, are living with four major non-communicable diseases (NCDs): diabetes, hypertension, hypercholesterolemia, and obesity. As for hypertension, 29.2% or 1 in 3 adults in Malaysia has hypertension and 91% are on blood pressure medications. This includes dihydropyridine calcium channel blockers such as amlodipine, which is commonly used in primary care. We report a case from our primary care clinic involving a 70-year-old man with a known history of primary hypertension who developed painless gum swelling and discomfort while the patient was on T. amlodipine 10 mg. Oral examination showed diffuse gingival hypertrophy involving the upper and right lower gums. The condition resolved completely after discontinuation of the offending drug and substitution with an angiotensin-converting enzyme inhibitor. This case is notable because the gingival overgrowth developed only after 4 years of amlodipine 10 mg therapy. This paper aims to bring clinicians' attention to these adverse effects of amlodipine, so that timely and effective management can be given to the patient, avoiding complications and unnecessary treatment.

Keywords: D*ihydropyridine calcium channel blocker, gingival overgrowth, hypertension.*

Introduction

Gingival overgrowth (also referred to as enlargement or hyperplasia) is a benign, painless condition characterized by a marked increase in the size of the interdental papillae, with severity ranging from mild to very extensive. [1,2] Terms such as gum hypertrophy and gum hyperplasia are synonymous, describing the same histological finding of enlarged gingival tissue. The causes of gum overgrowth are multifactorial; however, genetic predisposition has been shown to play a key role in drug-induced cases. To date, more than 20 medications have been implicated in the development of gingival hypertrophy. [3] Calcium channel blockers are one of the recognizable drug-induced gingival hypertrophies, along with anticonvulsants and immunosuppressants. [4] Among calcium channel blockers, the dihydropyridine group (e.g., nifedipine, felodipine, amlodipine) is most often linked to gingival enlargement. [5] Amlodipine, a third-generation dihydropyridine, is widely prescribed for the management of hypertension and angina pectoris. [1] The reported prevalence of amlodipine-induced gingival overgrowth is around 3.3%, which is considerably lower than the prevalence associated with nifedipine, estimated between 14% and 83%. [6] Amlodipine is commonly administered in this class and is frequently used in the management of hypertension, especially in primary care settings.

Case report

A 70-year-old man presented with painless, progressively enlarging swelling of the upper and right lower gums over the past three months. The swelling was associated with gum discomfort, difficulty chewing, malalignment and, loosening of the affected teeth. His medical history included hypertension and dyslipidemia, for which he had been taking amlodipine 10 mg and simvastatin 10 mg daily for four years.

On physical examination, he appeared moderately built, well-nourished and showed no signs of anaemia. His vital signs were stable. Gingival overgrowth was noted throughout the maxilla, as shown in Figure 1(a), and over the right mandible as shown in Figure 1(b), predominantly in the right buccal region. The enlargement was firm, generalized, and outwardly expanded, without periodontal pockets, gingival inflammation, bleeding, or purulent discharge. Poor oral hygiene was evident, with local irritants observed around the teeth. Otherwise, laboratory results as shown in Table 1, including full blood count, C-reactive, protein and renal profile, were normal.

After correlating the clinical history and examination, other potential causes such as the use of alternative medications, nutritional deficiencies, and malignancies were excluded. Based on the clinical findings, a diagnosis of amlodipine-induced gingival overgrowth was made. Amlodipine was discontinued and replaced with an angiotensin-converting enzyme (ACE) inhibitor. Disease progression halted within a few days following the medication change. One month after switching to perindopril 4 mg daily, gingival swelling improved, however, the severe overgrowth and malposition required full dental extraction with denture replacement. The patient declined follow-up photos due to a reluctance to wear dentures.

Discussion

AIGO is considered a multifactorial condition, with its onset and severity influenced by factors such as the dose, duration, and plasma concentration of amlodipine, along with patient-specific elements including sex, genetic predisposition (fibroblasts with abnormal drug susceptibility and/or functional heterogeneity), oral hygiene status, preexisting gingival inflammation, and activation of growth factors. [7,8,9] The exact pathogenesis of AIGO remains unclear, but it is generally explained through a multifactorial model involving both noninflammatory and inflammatory pathways. [7,8] Proposed noninflammatory mechanisms include impaired collagenase activity due to reduced secretion of matrix metalloproteinases-1

and -3, decreased folic acid uptake, inhibition of aldosterone synthesis in the adrenal zona glomerulosa, and upregulation of keratinocyte growth factor. [1] Inflammatory processes may also play a role, triggered by the direct toxic effect of high drug concentrations in gingival crevicular fluid, which can reach levels up to 292 times higher than those measured in plasma. [9] This inflammation could lead to the upregulation of several cytokine factors such as fibroblast growth factor-2 (FGF-2), transforming growth factor-β1 (TGF-β1), interleukin-6 and interleukin-1β (IL-6, IL-1β), and platelet-derived growth factor-β (PDGF-β), predisposing the tissue to a localized toxic effect and the development of fibrotic gingival hyperplasia. [10] Released proinflammatory cytokines are also involved in mast cell migration, influencing fibroblast proliferation, extracellular matrix synthesis, and degradation. Furthermore, amlodipine may stimulate the production of IL-2 by T-cells, causing fibrosis. [9]

Amlodipine-induced gingival overgrowth (AIGO) typically occurs within the first three months of starting a dose of 10 mg/day and often begins as enlargement of the interdental papilla. [9] In our patient, however, gingival enlargement developed only after four years of continuous amlodipine therapy at 10 mg daily. The variable time course of gingival hypertrophy in this patient may be influenced by multifactorial causes, including genetic susceptibility and host response to drug-induced gingival fibroblasts, interleukins, and matrix metalloproteinases. In addition to these known risk factors, our patient did not practice daily tooth brushing, leading to poor oral hygiene. This was supported by a recent dental evaluation showing generalized periodontitis, which likely played an important role in the progression of gingival overgrowth. The strong relationship between inflammation and AIGO is highlighted by evidence that the condition can often be controlled, even with ongoing amlodipine use, through meticulous professional and individual oral hygiene. [6,11] Another possible contributing factor in our case is the patient's male gender, as AIGO occurs about three times more frequently in men than women. [12] This case highlights that AIGO can significantly impair quality of life if not addressed early, as seen in our patient who required extensive dental extractions and dentures despite resolution of gingival overgrowth after discontinuing amlodipine.

Medical doctors and dentists/periodontists should therefore be aware of the potential of amlodipine and other medications to cause or worsen gingival overgrowth, particularly as the condition may progress if left untreated. The gingival enlargement can create periodontal pockets inaccessible to normal brushing or flossing, impairing oral hygiene and predisposing patients to infections, caries, and periodontitis. [13] Hence, it is crucial to explain this adverse effect to patients, emphasizing the importance of maintaining good oral hygiene, especially since amlodipine remains one of the most commonly prescribed anti-hypertensive agents in long-term primary care.

Conclusion

AIGO is a rare but important side effect that can be easily missed, especially in primary care, It often develops within the first three months of starting a 10 mg/day dose, but in some cases, it may appear years later. This delayed onset is linked to several factors, including dosage, duration of use, individual genetics, and most importantly, poor oral hygiene — which can significantly worsen the condition. AIGO can be prevented and reversed with early recognition, proper dental care, and medication adjustments when necessary. It is vital for healthcare providers to stay alert, advise patients on good oral hygiene, and promote regular dental visits — especially for those using amlodipine long-term.

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Conflicts of interest
None to declare.

Ethical consideration
The patient provided verbal consent before the use of images and the case for publication.

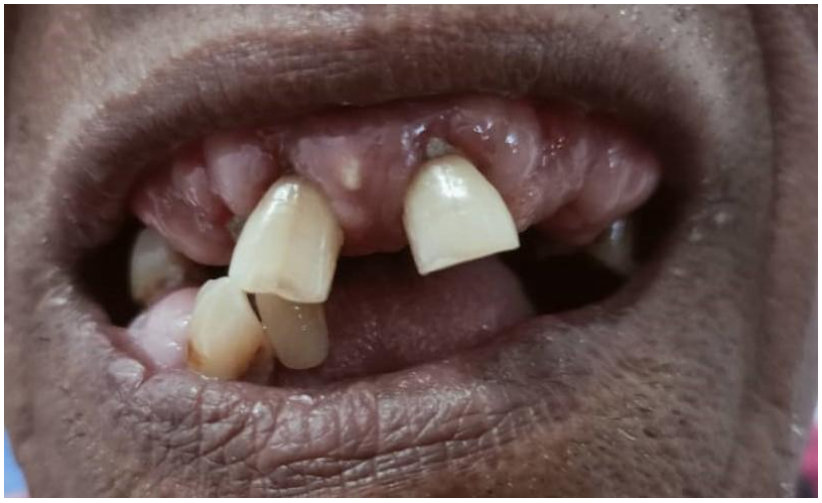

Figure 1(a) Gingival Overgrowth over maxilla area

Figure 1(b). Gingival Overgrowth over the right mandible near the buccal area

Table 1. Laboratory results

Parameter	Result	Reference Range
Urea	3.3	2.8 -7.2 mmol/L
Creatinine	69	59 -104 umol/L
Total white cells	6.4	4.08 – 11.37 10^9/L
Platelets	279	142 – 350 10^9/L
Hemoglobin	12.4	11.8 – 16.9 g/L
C-Reactive protein	0.1	< 0.5 mg/dL

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