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(CASE REPORT)

Non-surgical management of amlodipine-induced gingival enlargement

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Abstract

Introduction: Gingival enlargement is a pathologic condition involving enlargement of the keratinized gingiva. Several factors can contribute to gingival enlargement, including calcium channel blockers. In this paper, we report a case of a middle-aged woman with hypertension who was treated for periodontal disease with gingival enlargement after switching her medication from amlodipine.

Case presentation: A 45-year-old female patient visited the periodontology department of RSGMP Universitas Airlangga complaining of swollen gums. The patient reported that she did not notice when it began, but she was now concerned as they were increasing in size, and it felt painful sometimes since a month ago. Medically, the patient has had hypertension for the past five years (after giving birth to her last child) and has been taking amlodipine 10mg irregularly for the past three years. The patient was diagnosed with moderate generalized chronic periodontitis stage II grade B with drug-induced gingival enlargement.

Case management: A non-surgical approach was given to the patient, including effective plaque control and reducing, discontinuing, or substituting the suspected medication and local application of antibiotics.

Conclusion: The optimal treatment approach involves modifying the medication and using conservative periodontal therapy. Surgical intervention should be contemplated solely when the condition fails to respond to alternative therapy. Determining the most effective treatment for each patient and implementing an interdisciplinary approach with collaboration among medical and dental professionals is essential.

Keywords: Drug induced gingival enlargement; Amlodipine; Calcium channel blocker; Periodontal non-surgical treatment

1. Introduction

Gingival enlargement is a pathologic condition involving enlargement of the keratinized gingiva and usually presents with diverse clinical manifestations [1]. There are four degrees of gingival enlargement, including the absence of gingival enlargement (Grade 0), enlargement concerned with the interdental papilla (Grade I), enlargement involving the papilla and marginal gingiva (Grade II), and enlargement covering three-fourths or more of the tooth crown (Grade III) [2].

Several variables may contribute to gingival enlargement, including plaque control, periodontal factors, gender, genetic aspects, and drugs and their relative potency. Medications linked to drug-induced gingival enlargement are generally classified based on their therapeutic effects: immunosuppressants, anticonvulsants, and calcium channel blockers [2]. Calcium channel blockers (CCB) are commonly prescribed to treat conditions including hypertension. These medications can be characterized chemically as phenylethylamine derivatives (verapamil), benzothiazepine

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derivatives (diltiazem), and dihydropyridines (nifedipine and amlodipine) [3]. Other factors that may contribute to calcium channel blocker-induced gingival overgrowth are the duration of treatment, concurrent drugs, plaque, oral hygiene, and hormonal factors [2].

In this article, we report a case of a woman in her middle age with hypertension who was managed for her periodontal disease with gingival enlargement by altering her medication from amlodipine to another hypertension medicine.

2. Case presentation

A 45-year-old female patient visited the periodontology department of Rumah Sakit Gigi dan Mulut Pendidikan Universitas Airlangga complaining of swollen gums. The patient reported that she did not notice when it began, but she was now cautious because it gradually increased in size and had been occasionally unpleasant for a month.

The patient previously went to the community health center and was given mefenamic acid, amoxicillin, and metronidazole. However, after taking the medication, the patient experienced nausea, vomiting, and swollen eyes, so she did not continue taking it. The pain subsided, but there was still no sign of improvement in the gums. The patient has not had scaling and root planing since three years ago. She admitted to brushing her teeth only once in the morning and experiencing bleeding gums when brushing her teeth.

Medically, the patient has had hypertension for the past five years (after giving birth to her last child). On her first visit to the periodontology department, her blood pressure was 164/103 mmHg. The patient has been taking amlodipine 10mg irregularly for the past three years. Initially, the medicine was consumed after consulting with a general practitioner, but she continued at her own will. The patient claimed to have no drug or food allergies.

No cervical lymphadenopathy or swelling was revealed during the extra-oral examination; however, there was marked halitosis. Intraorally, there was severe gingival enlargement affecting the maxillary gingiva palatal and buccal, extending from the posterior of both sides to the anterior, and also gingival enlargement affecting the mandible extending from the posterior of both sides to the anterior (Fig 1). The mucosa covering the area was not intact, fragile, mobile, and oedematous. A periodontal examination was performed, which included bleeding on probing (BOP) and probing pocket depth (PPD) to examine oral hygiene.

Figure 1 Intraoral photograph at first examination

At baseline before scaling and root planing, the periodontal examination showed an average PPD of 5.1 mm, the deepest PPD was 9 mm, and BOP was noted in 100% sites. Panoramic radiograph examination revealed moderate generalized bone loss especially on the mandible (Fig 2).

Figure 2 Radiographic at the first visit

Due to the conditions, the patient was diagnosed with moderate generalized chronic periodontitis stage II grade B with drug-induced gingival enlargement as a result of poor oral hygiene and the medication of calcium channel blocker.

3. Case management

The most effective treatment of DIGO is withdrawal or substitution of medications, therefore before the initial treatment started, we referred the patient to an internist to get the hypertension properly treated and reported the probability of drug use that causes gingival enlargement. After the consultation, the internist suggested taking amlodipine 10 mg every morning and checking whether the patient had taken the medicine regularly before considering the drug substitution.

After two months, on the second visit, the blood pressure was not well controlled yet but better than the first at 138/93 mmHg. Intraorally, no improvement was seen in the gingival condition. Severe gingival enlargement affected the maxillary gingiva palatal and buccal, extending from the posterior of both sides to the anterior. Gingival enlargement also affected the mandible, extending from the posterior of both sides to the anterior (Fig 3). Initial periodontal therapy was done to the patient, including meticulous oral hygiene instruction using a toothbrush twice daily, supragingival calculus scaling, and chlorhexidine gluconate mouthwash prescription. In order to determine the following therapy, we consulted again with the internist, and the patient was given amlodipine 10 mg and lisinopril.

Figure 3 Intraoral photograph after regular consumption of antihypertensive for two months

On the third visit the following month, the patient reported no longer feeling pain. Although we asked for consideration in changing the prescription for hypertension, in the intraoral examination, there was a slight improvement in the gingival condition (Fig 4A). The enlarged gingiva was tender and marked red in color but it did not bleed easily on probing compared to the previous visit. Examination of hard tissue revealed increased mobility in relation to 42 41 31 32. As the enlargement reduced, scaling of calculus that was previously hidden was done. The gingival bleeding upon scaling was present but it was slightly less than the previous visit. The patient was then instructed to pay a visit again after two weeks. Before visiting the periodontology department, the patient visited the internist and was given nifedipine 30 mg.

After two weeks, there was minimal change especially on the lower anterior gingiva but some worse enlargement was seen on other regions (Fig 4B). Scaling and root planing was repeated, and chlorhexidine gluconate mouthwash was prescibed again. We raised suspicion that it required to change the antihypertensive to a medication other than the calcium channel blocker group so we consulted the patient condition to the internist again. The patient was asked to visit the periodontology department in a month. Unfortunately, due to personal reasons the patient visited the periodontology department after two months.

There was no significant improvement on the fifth visit (Fig 4C). Patient revealed that a month before the current visit, nifedipine was replaced with angiotensin 2 receptor inhibitor, candesartan 8 mg, instead of calcium channel blocker antihypertension. Scaling and root planing was done as the routines and as the adjunctive to the mechanical periodontal treatment, it was decided to use local antibiotic, metronidazole 25% gel. The gel was applied to the gingival pockets directly using syringe.

Two months later, on the sixth visit, the patient remarked that it was easier to do oral hygiene routines. Intraorally, the gingival showed better condition than the previous visits, it seemed to be firmer and the enlargement was obviously seen (Fig 4D). There was also significant reduce in gingival bleeding during the routine scaling and root planing. Metronidazole 25% gel was applied again as it gave positive results on the therapy. And two weeks after, the gingival condition seems to improved a lot. The enlargement can only be seen on the interdental papillary (Fig 4E). As the alternative from the previous visit, minocycline 2% gel was applied to the pocket to get better results after the routine scaling and root planing. We did not prescribed mouthwash to avoid the side effects from the continous usage of the chlorhexidine mouthwash.

Figure 4 Intraoral photograph a month after initial treatment (A), a month and a half after initial treatment (B), three months after initial treatment (C), a month after drug replacement (D), three months after drug replacement (E)

During the latest visit, there was a notable improvement in gingival condition (Fig 5A). The results of periodontal reevaluation showed an average PPD of 4.5 mm with the deepest PPD was 7 mm and BOP was observed in 29% sites.

Figure 5 Application of minocycline gel and intraoral photograph four months after drug replacement (A), eight months after initial treatment (B)

During the latest visit, eight months after initial treatment and there was a notable improvement in gingival condition (Fig 5B). Despite the better condition of gingival enlargement as it became firmer, we decided to postpone the pocket reduction surgery due to the patient's unstable blood pressure and prefer periodical control as maintenance until the patient's systemic condition improved. After all these treatments, the intraoral conditions of patient showed a great improvement after changing the drugs into a non CCB drugs and the adjunctive therapy from local antibiotic, minocycline.

4. Discussion

Gingival enlargement (GE) may arise from various causes, and it is essential to identify the specific cause prior to periodontal treatment. Numerous pharmaceuticals have been documented as contributors to gingival enlargement,

including calcium channel blockers (CCBs), cyclosporin, and phenytoin [2]. Nifedipine is the CCB most frequrntly linked to gingival enlargement. The prevalence of gingival enlargement associated with nifedipine is significantly higher, ranging from 14% to 83%, in contrast to other CCBs, such as verapamil and amlodipine, which have a prevalence of 4.2% and 3.3% respectively [4]. However, multiple studies have indicated that amlodipine appears to be associated with more severe gingival enlargement [5].

Calcium channel blockers are commonly prescribed medications for patients with hypertension and gingival enlargements (GEs) typically manifest within 2 to 15 months of therapy with CCB [6, 9]. GEs predomimnantly affect the buccal and anterior regions more frequently than the rest of the dental arch, sparing the edentulous crests. They can also be localized or generalized. The prolonged use of amlodipine for three years resulted in severe generalized gingival enlargement (GE). In the patient of this case, the condition affected the palatal and buccal sides of the mouth and the anterior and posterior regions of the maxillary and mandible. Poor dental hygiene of the patient exacerbated the GE, leading to tooth mobility.

Several mechanisms have been suggested for drug-induced GE. However, the particular explanation, including the pathophysiology of gingival enlargement generated by CCBs, remains uncertain. Various mechanisms have been proposed, such as the increasing of keratinocyte growth and inhibition of apoptosis, the decrease in matrix metalloproteinases which prevents collagen breakdown, and the influence of factors like plaque buildup and hormonal imbalance that can enhance the hyperplastic transformation of gingival tissues [7].

A study by Drozdzik hypothesized that profibrotic medicines promote keratinocyte proliferation while reducing apoptosis. Tumor growth factor (TGF)-β1 reduces the expression of epithelial E-cadherin while increasing fibroblast-specific protein-1 (FSP-1) and αvβ6 integrin. Consequently, epithelial cells of gingiva detach from adjacent cells, undergoing biochemical alterations that lead to the acquisition of mesenchymal cell characteristics, remarkably resembling fibrogenic (fibroblast-like cells). The changes include increased resistance to apoptosis, a notable rise in extracellular matrix sythesis, and enhanced migratory capacity [8,9]. Additionally, certain studies reported decreased apoptosis and enhanced cell proliferation, contributing to the hyperplastic characteristics of gingival enlargement [3].

Oral hygiene is likely to have a major influence on DIGO. Bacterial plaques facilitate the drug accumulation at targeted sites and trigger an inflammatory response, resulting in fibroblast proliferation, which aids in drug-induced GE [2]. Gingival enlargement severity is directly related to the degree of plaque formation and inflammation induced by plaque [3]. A study proposed that inflammation is essential for the onset of drug-induced GE, as fibroblasts in non-inflamed gingiva exhibited reduced activity or inactivity, even when exposed to drugs [5].

The initial treatment for gingival enlargement induced by calcium channel blockers (CCBs) involves a non-surgical approach, including effective plaque control and reducing, discontinuing, or substituting the suspected medication. Discontinuing CCBs or switching to an alternative medication frequently leads to improvement in gingival enlargement. When CCBs are utilized appropriately, the consideration of an alternative class of antihypertensive medication is warranted. The reintroduction of this drug is inadvisable due to a high recurrence rate [10]. The treatment that is believed to be the most effective for drug-induced gingival enlargement is the withdrawal or substitution of the causative medications, resulting in the resolution of gingival lesions within 1 to 8 weeks post-discontinuation [9]. The patient's clinical presentations demonstrated improvement after one month, consistent with prior research indicating that switching from nifedipine to an alternative antihypertensive medication resulted in the regression of gingival enlargement.

In addition to non-surgical treatment, the patient also received local antibiotic application. It offers benefits and enhanced safety compared to systemic antibiotics [11]. Minocycline and doxycycline possess antibacterial properties and demonstrate additional functions, including anti-inflammatory and resistance to alveolar bone resorption. A latest systematic review discovered that sustained release of minocycline is more effecient than mechanical debridement alone in reducing periodontal pocket depth [12]. The findings are suitable to the case of this patient: local antibiotic applications improved the gingival conditions more than mechanical debridement alone.

It is advisable to undertake appropriate dental and periodontal care to eliminate dental plaque and mitigate inflammation. Periodontal pocket reduction surgeries, including gingivectomy, aim to eliminate pockets and enhance oral hygiene. However, in cases of significant alveolar bone loss, as observed in this patient, the loss of multiple teeth necessitates prosthetic rehabilitation (4). This patient demonstrates moderate to severe alveolar bone loss accompanied by unstable blood pressure. Given these conditions, we propose the implementation of conservative management, which includes regular in-office oral hygiene procedures and enhanced collaboration among medical and dental specialists

5. Conclusion

Healthcare practitioners need to understand that calcium channel blocker therapy may induce gingival enlargement as an adverse consequence. The optimal treatment approach involves modifying the medication and using conservative periodontal therapy. Surgical intervention should be contemplated solely when the condition fails to respond to alternative therapy. Due to its complicated nature and susceptibility to recur with sustained pharmaceutical use, it is essential to determine the most effective treatment for each patient and implement an interdisciplinary approach with collaboration among medical and dental professionals.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors state that there is no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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