

Management of initial and surgical management of amlodipine-induced gingival enlargement with multifactorial etiology: a case report with 6 months follow-up

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ABSTRACT

Drug-induced gingival enlargement can be seen as a side effect of systemically used drugs such as calcium channel blockers, anticonvulsants, and immunosuppressants. One of these drugs is amlodipine, a dihydropyridine derivative calcium channel blocker used in the treatment of high blood pressure and coronary artery disease. Amlodipine-induced gingival overgrowth is rarely seen compared to other calcium channel blockers. The aim of this case is to present the diagnosis of gingival overgrowth due to amlodipine use and the identification of other etiologic factors such as labial frenulum, phase 1 initial, and phase 2 surgical treatment approaches. A 56-year-old female patient presented to our clinic with severe gingival overgrowth, intense bleeding, difficulty feeding, and pain. The anamnesis revealed that she had hypertension and had been taking amlodipine derivative Norvasc 10 mg once a day for 8 years. A look inside the mouth showed that there was a lot of gum tissue growing over the crowns from the labial and palatal sides, mainly in the front of the maxilla. Phase 1 treatment was initiated. As a result of the consultation with the patient's cardiologist, the hypertension medication Norvasc 10 mg was replaced with Candexil 16 mg by the medical physician. The preoperative tension and blanch test was positive, and the labial frenulum was seen to mobilize the free gingival margin of the central teeth. After the same session of gingivoplasty, the labial frenulum was removed by a frenectomy operation. After the operation, antibiotics, analgesics, and mouthwash were prescribed. The patient stated that he did not have any problems after the operation. 6-month follow-up showed uneventful healing. No recurrence of gingival growth was found in the 1st, 3rd, and 6th month follow-ups. In conclusion, this case report shows that non-surgical periodontal treatment alone isn't always enough to treat drug-induced gingival overgrowths. The gingival shape should be changed so that the patient can properly clean their teeth, and drug-induced gingival overgrowths, like the one in this case, may have more than one cause and may need additional surgery like a labial frenectomy.

Keywords: Amlodipine, gingival overgrowth, calcium channel blocker, labial frenectomy, surgical periodontal therapy

INTRODUCTION

An increase in the size of the gingival connective tissue matrix is what amlodipine-induced gingival overgrowth (AIGO) is. The connective tissue matrix is composed of many components, including collagen, fibrin, and fibronectin. Misregulation of collagen synthesis and degradation is thought to trigger drug-induced growth. Gingival fibroblasts produce more collagen when exposed to amlodipine.¹

Amlodipine is a dihydropyridine derivative calcium channel blocker (CCB) used in the treatment of hypertension. It has structural similarities to nifedipine, which frequently causes gingival hypertrophy. Amlodipine has a long half-life of 30 to 50 hours. It has been reported that AIGO usually develops within three months after initiation of the drug at a dose of 10 mg/day.²

The general prevalence of gingival overgrowth due to CCB is 38%. The prevalence of AIGO is between 1.7% and 3.3%. The male-female ratio was found to be 3.3.³ There are few cases of amlodipine-related gingival hyperplasia in the current literature.⁴

When the gums enlarge, deep pockets can form that cannot be reached with toothbrushes and dental floss, making it difficult for the patient to maintain oral hygiene. This makes the host more susceptible to oral infections, caries, and periodontitis. When AIGO is diagnosed, the first step is to change the medication in consultation with a doctor. CCB should not be discontinued to avoid complications such as stroke and angina. In addition to professional plaque cleaning, the patient should be motivated to practice oral hygiene.²



In this case report, our aim was to diagnose AIGO, determine the multifactorial etiologies, and present the treatment management. Non-surgical periodontal treatment may not always be sufficient in AIGO. A reliable method of treating AIGO is a combination of surgical and nonsurgical periodontal treatment with drug replacement.

CASE

A 56-year-old woman presented to the Periodontology Clinic of Dicle University Faculty of Dentistry with complaints of severe gingival enlargement, intense bleeding, and pain (Figure 1). In the anamnesis, it was learned that she had hypertension and had been taking Norvasc, a 10 mg amlodipine derivative, once a day for eight years. Intraoral examination revealed a growth covering all upper teeth and increasing anteriorly. The gingival index was recorded at 3, and intense spontaneous bleeding was observed (Figure 1).



Figure 1. Phase 1 pre-treatment

It was determined that the gingival growths reached the incisal edges of the teeth. The patient was consulted by a cardiologist. The amlodipine derivative Norvasc was replaced with Candexil 16 mg, an angiotensin II receptor antagonist. Phase I treatment was initiated. During 4 sessions, scaling, root surface smoothing, and gingival curettage procedures were continued, and oral hygiene habits were reviewed (Figure 2).



Figure 2. 2 months after drug replacement and phase 1

After 3 months, the patient was re-evaluated (Figure 3). Despite significant improvement in the gingival margin with nonsurgical periodontal treatment, phase 2 surgical treatment was planned to give the gingiva a knife-edge shape and prevent food retention. In the tension test, it was determined that the labial frenulum mobilized the free gingival margin of the central teeth, and a frenectomy operation was planned simultaneously with the gingivectomy operation to prevent food retention, protect the keratinized gingiva, and prevent gingival recession.



Figure 3. 3 months after drug replacement

Kirkland and Orban blades were used to give the gingiva a knife-edge shape (Figure 4). Then, the labial frenulum was clamped with a needle holder, and an incision was made from the posterior side with the scalpel leaning against the needle holder. On the anterior side of the needle holder, a half-thick incision was started from the most anterior part of the frenulum, two incision lines were joined at the end of the needle holder, and a lozenge-shaped piece of tissue was removed. The incision line was slightly extended to the right and left sides, the fibers that move the free gingival margin were dissected, and the periosteum was scraped with a periosteal elevator to prevent the cut fibers from re-adhering. The wound lips were dissected with tissue scissors and closed with simple sutures with 3.0 silk sutures. Since the incision line expanded in a triangular shape, a small coronal part of the wound was left for secondary healing (Figure 4).

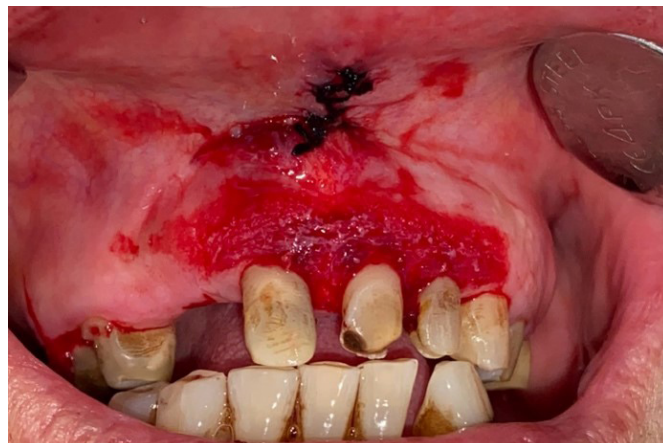


Figure 4. After operation



RESULTS

Recovery was uneventful at the 1-week postoperative follow-up. The patient reported simple postoperative symptoms such as mild pain and tightness in the frenulum area. Sutures were removed on postoperative day 14 (**Figure 5**). Mild scarring was seen in the frenulum area (**Figure 6**). One-month follow-up showed that the gingival thickness and shape were in appropriate form (**Figure 7**). Gingival overgrowth was not observed again at the six-month postoperative follow-up (**Figure 8**). The patient with AIGO was successfully followed up for a total of nine months, including three months preoperatively and six months postoperatively.



Figure 5. 2 weeks after operation



Figure 6. After sutures are removed



Figure 7. 1 month after operation



Figure 8. 6 months after operation

DISCUSSION

Gingival overgrowths cause speech and chewing difficulties, poor oral hygiene, and an unaesthetic appearance. Gingival overgrowth is also a serious concern for clinicians, as it provides a favorable environment for the growth of microorganisms.⁵

A study of 150 cardiac patients found that amlodipine at a dose of 5 mg/day did not cause AIGO, even when used for more than 6 months. On the contrary, Seymour et al. reported three patients with poor oral hygiene who developed gingival enlargement due to amlodipine use for at least three months.⁴ AIGO is now considered to be not uncommon.²

Age is not a valid risk factor for gingival overgrowth associated with the use of CCBs, as CCB medications are generally suitable for middle-aged and older adults.⁶ This is supported by a study of more than 800 patients treated with calcium channel blockers, in which age was not identified as a significant risk factor.⁷

Gingival overgrowth only happens in some people who take the same medication at the same dose or frequency. Because of this, some doctors think that drug-induced gingival overgrowth (DIGO) may be linked to a genetic tendency, but the exact genetic link has not been found.⁸ The only genetic marker investigated in relation to DIGO is human lymphocyte antigen expression (HLA). Since HLA phenotypes are determined before transplantation, investigation of this marker has been limited to organ transplant patients. Several studies have reported the relationship between HLA expression and the incidence of drug-induced gingival overgrowth, but the results were not found to be significant.⁶

Many etiopathogenetic mechanisms have been proposed for DIGO; however, the exact cause is not known. Since many drugs with variable pharmacodynamics may cause DIGO, it may have a multifactorial pathogenesis.⁸ One hypothesis states that anticonvulsants, immunosuppressants, and CCBs all cause cation flux inhibition.⁹ Folic acid is actively transported to gingival fibroblasts, but there is less cation flow. This means that fewer cells take in folate, which in turn lowers the production and activation of matrix metalloproteinases. These are enzymes that break down collagen. This decreases collagenase activity, leading to decreased collagen degradation and thus connective tissue accumulation, which eventually manifests as DIGO.¹⁰



Folic acid has been added to food sources for more than 20 years to help prevent neural tube birth defects and other congenital anomalies. As the amount of folate in food sources has increased over the past 20 years, the prevalence of DIGO has decreased. However, there is currently insufficient evidence to prove a cause-and-effect relationship between increased folate intake for public health and a progressive decline in the incidence of DIGO over the years.¹⁰

The etiology of DIGO is multifactorial. Bacterial plaque is an important factor, and the severity of gingival overgrowth is directly proportional to the degree of plaque accumulation and plaque-induced inflammation.¹¹

Surgical treatment of DIGO involves reorganization of the gingiva with a scalpel, blades, or laser. Successful therapeutic management of DIGO includes plaque control, topical folic acid, and topical azithromycin.¹⁰

CONCLUSION

In this report, we present the treatment of a patient with AIGO treated with surgical and non-surgical methods following drug exchange and a six-month follow-up after surgery. Different periodontal surgeries may also be needed to prevent the recurrence of DIGO. Although our 6-month results are stable, long-term follow-up studies are needed.

ETHICAL DECLARATIONS

Referee Evaluation Process: Externally peer-reviewed.

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