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AMLODIPINE-INDUCED GINGIVAL HYPERPLASIA IN CHRONIC PERIODONTITIS: A CLINICAL CASE REPORT WITH ONE YEAR FOLLOW-UP

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ABSTRACT: Background: Drug-induced gingival overgrowth (DIGO) is a common side effect of certain medications used for non-dental purposes, notably anticonvulsants, calcium channel blockers (CCBs), and immunosuppressants. These drugs, despite differing pharmacologically, inhibit intracellular calcium ion influx, leading to a decrease in collagenolytic activity and an increase in fibroblasts and collagen synthesis, ultimately causing gingival overgrowth. **Case Presentation:** A 54-year-old male presented with significant gingival enlargement and periodontal disease. Clinical examination revealed generalized mild to moderate calculus, erythematous and indurated gingiva with severe periodontal attachment loss, and tooth mobility. Despite scaling and root planning, the gingival enlargement persisted, necessitating surgical intervention. Open flap debridement was performed, leading to a successful outcome with no recurrence of gingival enlargement after one year of follow-up. **Discussion:** The case highlights amlodipine-induced gingival overgrowth, a recognized side effect of CCBs. The exact mechanisms remain unclear, with both inflammatory and non-inflammatory pathways implicated. The inflammatory process involves cytokine upregulation, leading to fibroblast proliferation and fibrotic gingival hyperplasia. The case underscores the importance of early diagnosis, medication management, and surgical intervention in managing DIGO. **Conclusion:** DIGO is a significant side effect of systemic medications affecting periodontal tissues, with mechanisms that are not yet fully understood. Identifying risk factors and employing advanced molecular research is essential to developing effective prophylactic and therapeutic strategies.

INTRODUCTION: Drug-induced gingival overgrowth or enlargement is a side effect that arises after taking medications that are primarily used for non-dental therapies; hence, the overgrowth cannot be attributed to a change in the drug's intended pharmacological activity [1]. The three main medications that cause gingival hyperplasia are the anticonvulsants, calcium channel blockers, and immunosuppressants. Though they have different pharmacological profiles, they all work similarly at the cellular level by inhibiting intracellular calcium ion influx. The degenerative alterations are located in the connective tissue of the gingiva; there is an overabundance of collagen that resembles extracellular matrix accumulated with varied degrees of inflammatory infiltrates, primarily plasma cells [2].

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The mechanism of enlargement is brought on by a decrease in collagenolytic activity and an increase in fibroblasts and collagen synthesis. This is because the folate absorption is reduced by the fibroblast cells, and it prevents a collagenase enzyme called matrix metalloproteinase (MMP) from being activated.

As a result, the connective tissue matrix is less likely to degrade and remodel [3]. The drug concentration in bacterial plaque or crevicular gingival fluid directly damages the gingival tissue. Gingival overgrowth is brought on by irritation caused by dental plaque. Transforming growth factor beta 1 (TGF-β1) is upregulated in response to inflammation. Therefore, maintaining dental plaque management is essential for both treating and preventing DIGO throughout time [4].

Case Presentation: A 54-year-old male patient presented to the periodontics department with a chief complaint of progressively increasing gingival enlargement over the past six months. He also reported experiencing gingival bleeding while brushing. On examination, the patient exhibited generalized mild to moderate supra- and subgingival calculus, along with masticatory difficulties leading to tooth misalignment. Clinical evaluation revealed erythematous and indurated gingival tissue with widespread expansion extending to the interdental and marginal gingiva. The patient had periodontal pockets with an average attachment loss of 7–9 mm in also all the teeth, and significant tooth mobility grade III was observed in 41, 31 and grade II mobility in 32, 33, 42, 43 according to Miller's classification, 1950), with the remaining teeth showing slight grade I mobility. An interpretation of periodontal index (Russel A.L. 1956) showed established destructive periodontal disease. Radiographic examination revealed considerable horizontal bone loss extending to the middle third of the roots. Routine blood and urine tests were within normal limits.

The patient was diagnosed with stage III, grade C periodontitis with drug-induced gingival overgrowth, based on the attachment loss of more than 5 mm and an estimated bone loss/age percentage of 2.2. The primary objective of the periodontal treatment was to address both the drug-induced gingival enlargement and the underlying periodontal inflammation. After changing the patient's medication, phase I therapy, which included scaling and root planning, was initiated. Following three to four cycles of regular scaling and root planning, the inflammation was reduced; however, the gingival enlargement significantly persisted with probing pocket depths (PPD) of 7–9 mm in both the mandibular and maxillary arches. Consequently, open flap debridement was planned for all four quadrants.

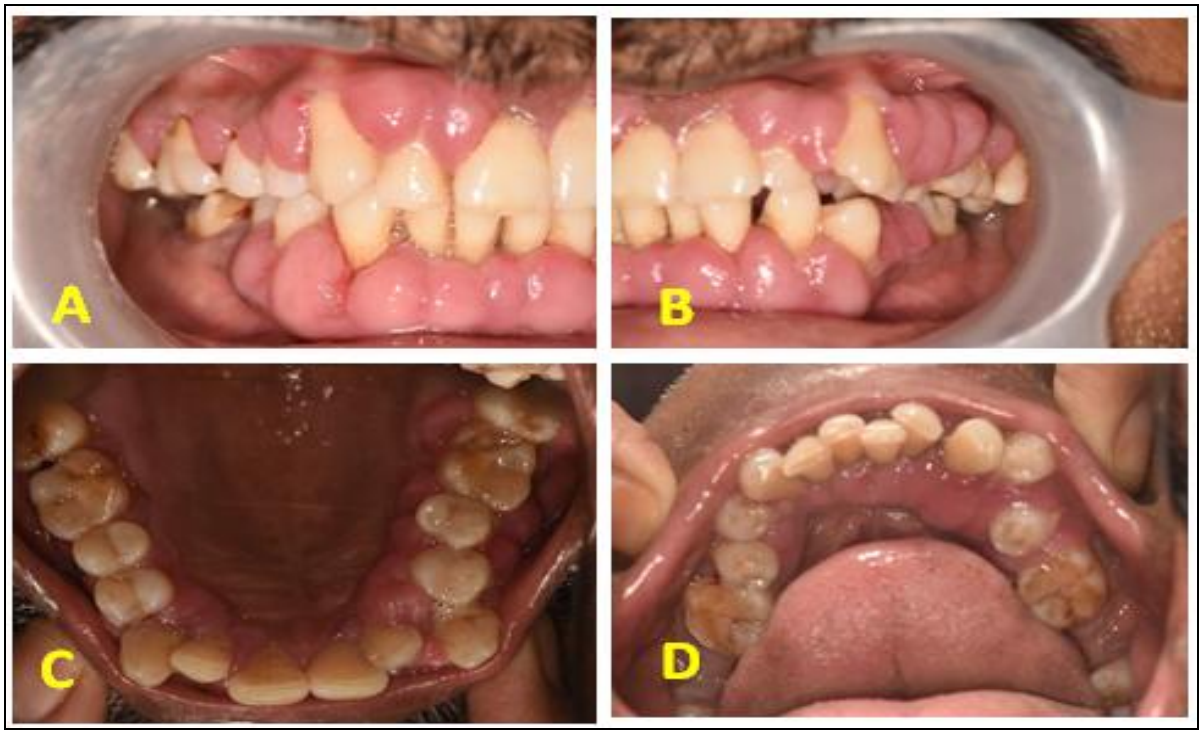

FIG. 1: THE CLINICAL PRESENTATION OF DRUG INDUCED GINGIVAL ENLARGEMENT IS ILLUSTRATED IN MULTIPLE FIGURES: FIGURES A AND B DISPLAY THE LEFT AND RIGHT SIDES, RESPECTIVELY, WHEREAS FIGURES C AND D SHOW THE MAXILLARY AND MANDIBULAR OCCLUSAL VIEWS, RESPECTIVELY

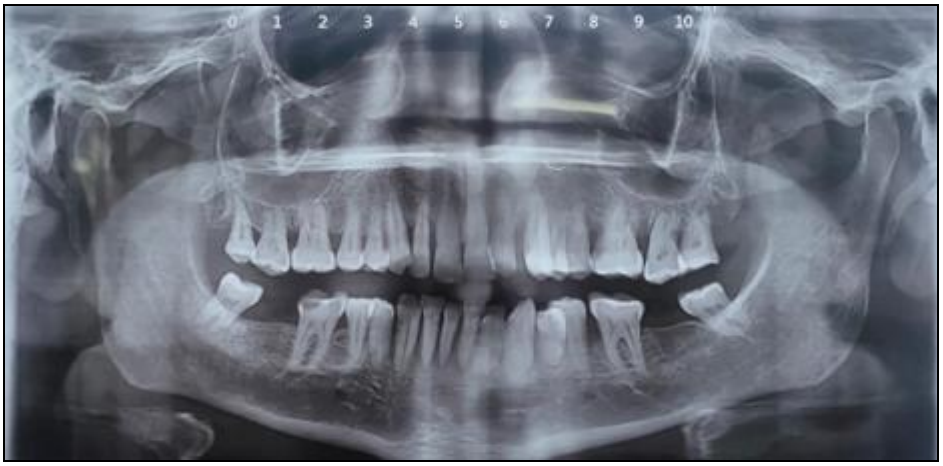

FIG. 2: GENERALIZED HORIZONTAL BONE LOSS EXTENDING TO THE MIDDLE THIRD OF THE ROOTS WAS OBSERVED IN THE ORTHOPANTOMOGRAPHY

Preoperative blood pressure was recorded on the day of surgery for the patient. A full-thickness mucoperiosteal flap was raised both buccally and palatally/lingually after internal bevel, crevicular, and interdental incisions were performed. Under 2% local anesthesia, extensive debridement was carried out using adrenalin (Lignocaine diluted 1:200000). The flaps were approximated and the inner surface of the tissues trimmed **Fig. 3**. The patient was discharged with instructions to take antibiotics and analgesics for five days, as well as to use a mouthwash containing 0.02% chlorhexidine, following a final examination for bleeding. A one-week interval was maintained between surgeries on each of the four quadrants with uneventful healing.

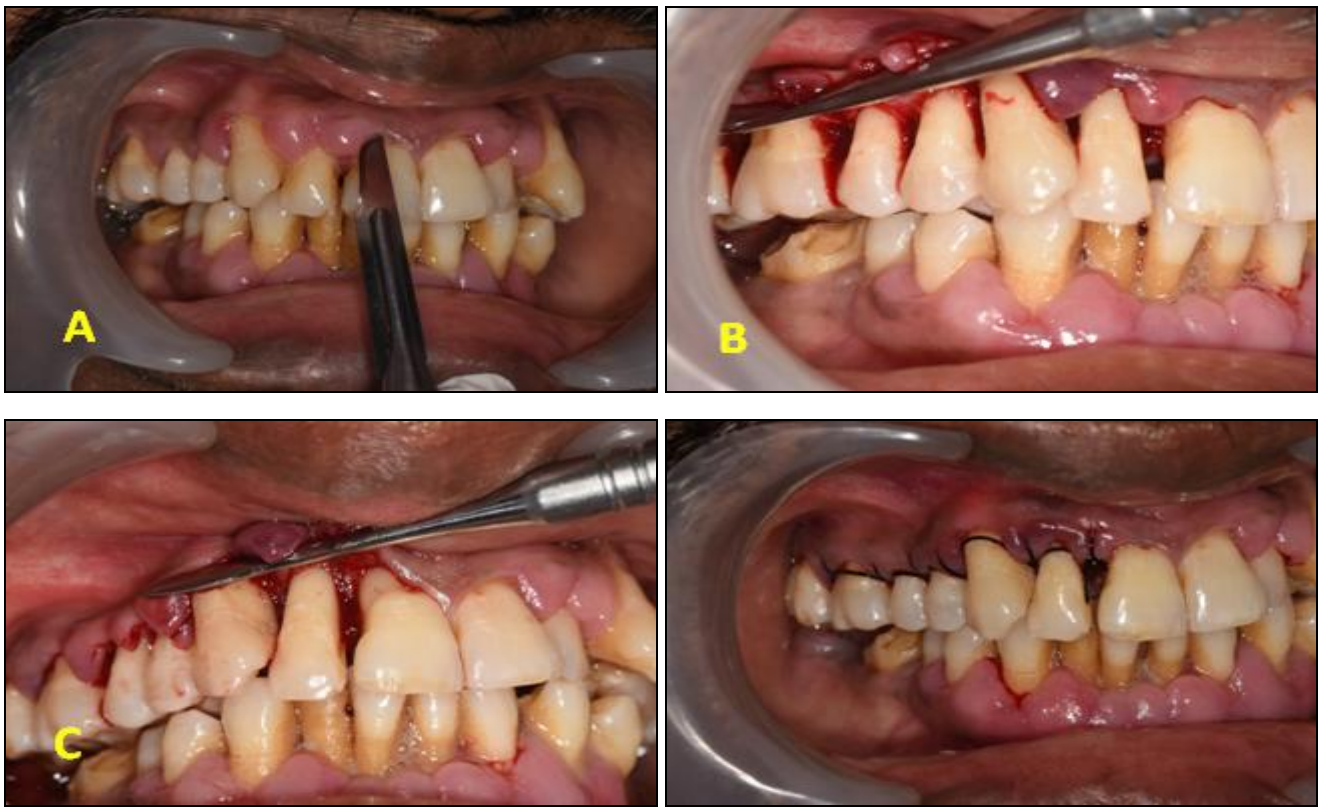

FIG. 3: ILLUSTRATES THE PROCEDURE OF OPEN FLAP DEBRIDEMENT, INCLUDING EXCESS TISSUE TRIMMING AND FLAP APPROXIMATION WITH CONTINUOUS SLING SUTURE, CARRIED OUT IN THE FIRST QUADRANT

With one-year follow-up after receiving supportive periodontal therapy, the patient showed no signs of gingival enlargement relapse as well as had appropriate periodontal health maintenance **Fig. 4.**

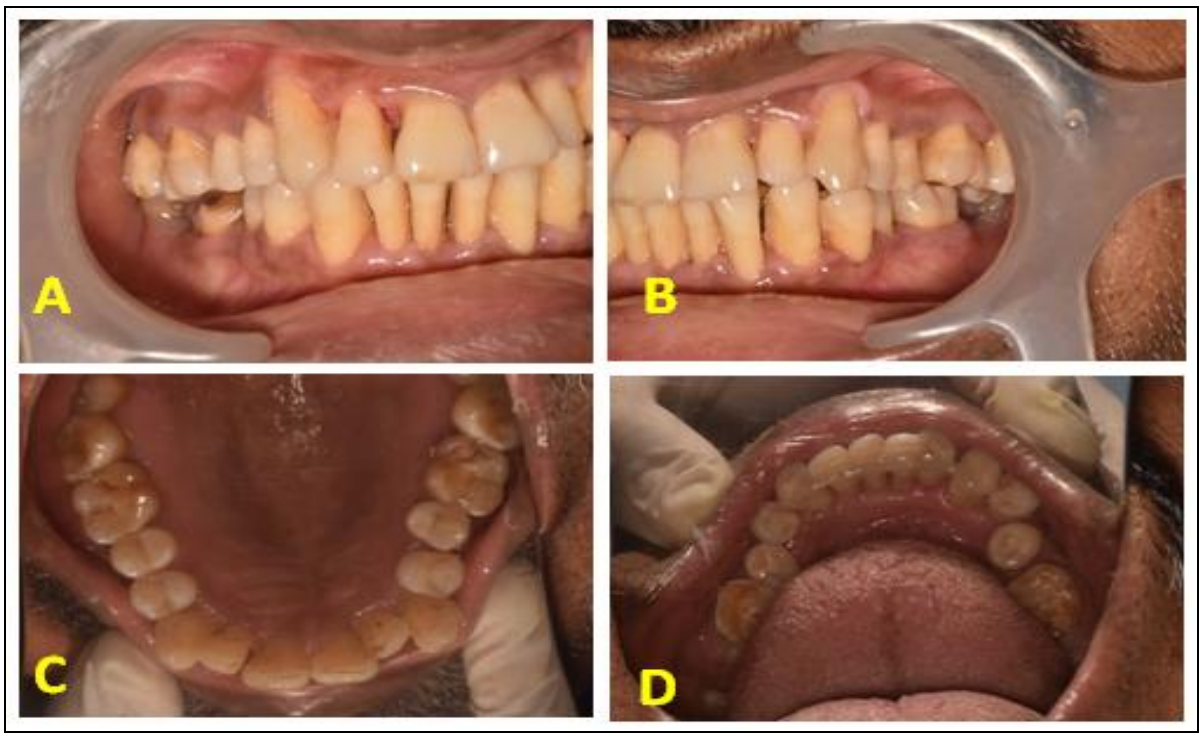

FIG. 4: ONE-YEAR FOLLOW-UP AFTER THE ACCESS FLAP SURGERY, THE PATIENT EXHIBITED NO SIGNS OF GINGIVAL ENLARGEMENT RECURRENCE

DISCUSSION: Seymour *et al.* originally reported gingival enlargement (GE) in 1994 as an adverse reaction of amlodipine, a dihydropyridine calcium channel blocker (CCB) used to treat hypertension and angina [3]. While it is widely known that CCBs can cause GE, the precise processes underlying this remain unclear. It has been proposed that both inflammatory and non-inflammatory mechanisms have a role in CCB-induced GE [5].

Studies show that 1.7% to 3.3% of patients experience amlodipine-induced gingival hyperplasia [6], with men 3.3 times more likely than women to experience this condition [7, 8]. An important risk factor for the emergence of medication-induced gingival growth is inadequate dental care[9]. Nevertheless, since the majority of research on the connection between bacterial plaque and GE is cross-sectional, there is not enough data to definitively determine whether gingival alterations are triggered by or as a result of bacterial plaque[10]. According to the non-inflammatory theory, this condition might be associated with decreased folic acid absorption, diminution of the adrenal cortex's ability to produce aldosterone, and an increase in keratinocyte growth factor and adrenocorticotropic hormone as an outcome [11]. It is thought that this drug causes aberrant sensitivity in fibroblasts, which leads to gingival hyperplasia in those who use it. These fibroblasts overproduce proteins, primarily collagen. It has been suggested that an individual's sensitivity or resistance to drug-induced gingival overgrowth may depend on the percentage of fibroblast subsets that respond fibrogenically to the medication [12].

Conversely, the inflammatory pathway plays a critical role in the way that medications and fibroblasts interact [5]. There may be direct negative consequences from the medication concentration in crevicular gingival fluid, which can be up to 292 times greater than in the blood. Fibroblast growth factor-2, transforming growth factor-β1, interleukin-6 (IL-6), IL-1β, and platelet-derived growth factor-β are among the cytokines that are upregulated during this drug-induced inflammation. This, in turn, stimulates fibroblast proliferation and results in fibrotic gingival hyperplasia [5, 13]. The standard course of treatment entails stopping the offending medication and successfully controlling local inflammatory variables like calculus and plaque. If these treatments are ineffective in reducing the overgrowth, surgery is regarded as a last option. These therapies work well, but they don't always stop recurrence. Before the functional

damage arises, surgical procedures should be carefully examined and usually done for cosmetic purposes [14]. Surgical intervention is necessary in the majority of instances with gingival overgrowth produced by amlodipine. Since the enlargement persisted despite many nonsurgical periodontal treatments, we decided to do open flap debridement on all four quadrants in order to get better functional and cosmetic results.

CONCLUSION: A typical side effect of systemic treatment on periodontal tissues is drug-induced gingival overgrowth. However, at best, we know very little about the pathogenesis of gingival overgrowth. Given the frequency and severity of drug-induced gingival overgrowth, it would be crucial to identify and look into relevant risk factors. Advanced molecular approaches are needed to clarify the biology of gingival overgrowth and provide fresh information for the future development of prophylactic and therapeutic strategies.

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