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Case Report

Prise en charge combinée non chirurgicale et chirurgicale d'une hyperplasie gingivale induite par la nifédipine chez un adulte atteint d'insuffisance rénale chronique : à propos d'un cas clinique.

Combined Non-Surgical and Surgical Management of Nifedipine-Induced Gingival Enlargement in an Adult with Chronic Kidney Disease: A Case Report

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RESUME

L'hyperplasie gingivale est un effet secondaire connu de certains inhibiteurs calciques, en particulier la nifédipine. Ce cas clinique décrit la prise en charge parodontale d'un homme de 41 ans atteint d'une hyperplasie gingivale généralisée induite par la nifédipine, survenant dans un contexte de maladie rénale chronique et d'hypertension artérielle. Le traitement a consisté en un remplacement de la nifédipine par l'irbésartan, un traitement antibiotique, un détartrage et un surfaçage radiculaire, entraînant une amélioration notable de l'arcade mandibulaire. Une gingivectomie chirurgicale a été nécessaire pour l'arcade maxillaire en raison d'une hyperplasie persistante. Le suivi à quatre mois a montré une absence de récurrence, soulignant l'efficacité d'une approche personnalisée associant substitution médicamenteuse, traitement parodontal complet et chirurgie ciblée pour la gestion à long terme de ce type de cas.

MOTS CLES : Nifédipine, hyperplasie gingivale, chirurgie parodontale, insuffisance rénale chronique, parodontite.

ABSTRACT

Gingival enlargement is a well-known side effect of certain calcium channel blockers, particularly nifedipine. This clinical case describes the periodontal management of a 41-year-old man with generalized gingival hyperplasia induced by nifedipine, occurring in the context of a chronic kidney disease and arterial hypertension. Treatment included replacing nifedipine with irbesartan, administering antibiotic therapy, scaling, and root planing, which led to significant improvement in the mandibular arch. Due to persistent hyperplasia in the maxillary arch, surgical gingivectomy was performed. A four-month follow-up showed no recurrence, highlighting the effectiveness of a personalized approach combining drug substitution, comprehensive periodontal therapy, and site-specific surgery for the long-term management of such cases.

KEYWORDS: Nifedipine, gingival enlargement, periodontal surgery, chronic kidney disease, periodontitis.

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1. Introduction

Drug-induced gingival enlargement (DIGE) is a well-recognized adverse drug reaction characterized by abnormal gingival tissue overgrowth, first described in patients receiving phenytoin in the 1930s^[1]. Since then, DIGE has been associated mainly with three classes of medications: anticonvulsants (Phenytoin), immunosuppressants (Cyclosporine), and calcium channel blockers (CCBs) which are used in the management of cardiovascular diseases^[2].

Given that CCBs are frequently prescribed in patients with systemic cardiovascular conditions, it is useful to acknowledge the range of comorbidities often accompanying hypertension. Beyond chronic kidney disease (CKD), these include cardiovascular disorders such as left ventricular hypertrophy, metabolic conditions including diabetes mellitus, and vascular or neurologic complications such as cerebrovascular events and retinal damage^[3]. Awareness of these comorbidities is essential for the comprehensive management of patients receiving antihypertensive therapy.

Among CCBs associated with gingival enlargement, nifedipine has been most frequently implicated, followed by amlodipine and verapamil. The prevalence of nifedipine-induced gingival enlargement has been reported to range from 20% to over 80%, depending on dosage, treatment duration, plaque accumulation, and individual susceptibility^[2]. Other antihypertensive agents, such as angiotensin II receptor blockers, are not commonly associated with gingival overgrowth and are therefore considered suitable alternatives^[4].

The pathogenesis of DIGE is multifactorial and involves complex interactions between drug-induced fibroblast stimulation, altered collagen metabolism, inflammatory mediators, and genetic predisposition. Poor oral hygiene and pre-existing periodontal disease

significantly increase the severity of gingival enlargement^[5].

This case report describes the combined non-surgical and surgical management of nifedipine-induced gingival enlargement in an adult patient with

chronic kidney disease, highlighting diagnostic challenges and therapeutic considerations.

2. Observation

A 41-year-old male presented with a chief complaint of swollen gums. The patient reported progressive gingival swelling over the preceding two months.

The patient had been diagnosed, one year prior, with stage 3b chronic kidney disease (eGFR of 31 mL/min/1.73m² with a serum creatinine level of 2.5 mg/dL) and essential hypertension^[6]. Blood pressure values were medically controlled under antihypertensive therapy. He was on nifedipine (Loxen LP® 50 mg, three times daily) and moxonidine (0.4 mg, once daily). In addition to pharmacological management, a nephroprotective diet and lifestyle modifications were prescribed as part of the comprehensive management of the patient's CKD and hypertension.

Intraoral examination revealed generalized fibrotic gingival enlargement, especially in the maxillary and mandibular anterior regions. The gingiva was firm, lobulated, and with a pink color. Clinical inflammatory markers were significant, with a Gingival Index (GI) of 3 and a Sulcus Bleeding Index (SBI) of 5^[7,8]. Suppuration was observed in the maxillary sextants and mandibular anterior region. Probing depths ranged from 3 mm to 10 mm.

Panoramic radiography showed generalized, predominantly horizontal alveolar bone loss of mild to moderate severity.



Figure 01: Panoramic radiography demonstrating a generalized, mainly horizontal pattern of alveolar bone loss with mild to moderate severity, consistent with generalized periodontitis.

According to the 2017 classification framework, the primary diagnosis was Generalized Periodontitis, Stage IV, Grade B^[9].

A secondary diagnosis of nifedipine-induced gingival enlargement was established based on medication history, clinical presentation, and improvement following substitution^[9].

Differential diagnoses such as hereditary gingival fibromatosis, leukemic enlargement, and chronic inflammatory gingival hyperplasia were excluded based on medical and hematologic findings.

The treatment consisted of:

1. Drug Substitution: The patient's nephrologist replaced nifedipine with irbesartan (Aprovel®), a selective angiotensin II receptor antagonist. The patient responded well to the drug substitution, with blood pressure values maintained within physiological limits.

2. Initial Periodontal Therapy: A systemic antibiotic was prescribed (Rovamycine® 03MUI twice daily for 7 days) followed by full-mouth scaling and root planing. Due to their poor prognosis, extraction of the root of tooth 23, the roots of tooth 16, and tooth 17 was indicated and performed.

3. Surgical Phase: Persistent fibrotic enlargement in the maxillary region necessitated gingivectomy using a scalpel. No surgical intervention was performed in the mandibular arch.

4. Maintenance: Periodontal maintenance was performed monthly. At 4 months, gingival health was stable and no recurrence was noted.

At follow-up, the gingival tissues exhibited healthy contours with firm consistency. The suppuration previously noted in the maxillary and mandibular regions completely resolved. Probing depths were reduced and ranged between 2 and 4 mm, with absence of sites ≥ 5 mm and no bleeding on probing. The patient reported improved comfort and better compliance with oral hygiene practices. Additionally, clinical attachment gains were noted in areas that had previously shown signs of inflammation.

Following periodontal stabilization, the patient was referred to the Department of Prosthodontics for replacement of the missing teeth.

Importantly, after the substitution of nifedipine with irbesartan, the patient's hypertension remained well-controlled, with blood pressure values maintained within physiological limits throughout follow-up, highlighting the effectiveness and safety

of the therapeutic adjustment in the context of both systemic and periodontal management.

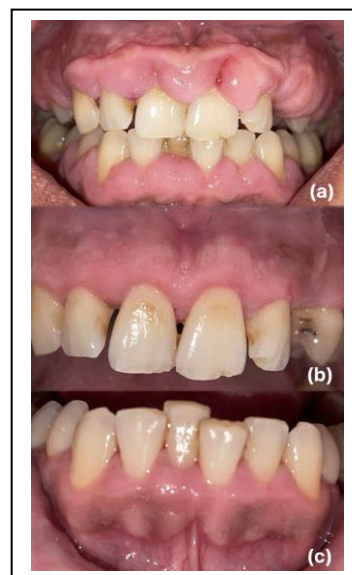


Figure 02: Clinical photographs showing the gingival condition of the patient before and after treatment: (a) Pre-treatment of the maxillary and mandibular anterior regions showing generalized gingival enlargement.; (b) Maxillary anterior region 4 months after gingivectomy, showing resolution and restored gingival contours; (c) Mandibular anterior region 4 months after successful nonsurgical therapy alone.

3. Discussion

The development of nifedipine-induced gingival enlargement is the result of complex molecular and cellular mechanisms involving increased gingival fibroblast proliferation, reduced collagen degradation, and accumulation of extracellular matrix (ECM)^[5].

Calcium channel blockers such as nifedipine disrupt intracellular calcium homeostasis in gingival fibroblasts, which impairs folate uptake and leads to altered collagenase activity and reduced degradation of ECM components such as collagen and glycosaminoglycans, resulting in their accumulation in the gingival connective tissue. Disturbed calcium signaling also affects fibroblast and keratinocyte behavior and modifies cell-adhesion molecules and matrix-remodeling enzymes, thereby contributing to connective tissue overgrowth^[10-12].

Profibrotic signaling pathways, notably transforming growth factor- β (TGF- β), are upregulated in the context of nifedipine intake; TGF- β is a key regulator of ECM synthesis and stimulates fibroblast proliferation and connective

tissue growth factor (CTGF), further enhancing fibrogenesis^[10,12].

In addition to direct cellular effects, inflammatory mechanisms play a crucial role. Elevated levels of proinflammatory cytokines and growth factors such as vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and matrix metalloproteinase (MMP) have been documented in saliva and gingival crevicular fluid of patients with calcium channel blocker-associated gingival enlargement, suggesting that chronic inflammation amplifies fibroblast activity and dysregulated ECM turnover. Plaque accumulation and poor oral hygiene are well-established local modifiers that exacerbate inflammatory mediator expression and gingival enlargement severity, highlighting the interplay between pharmacologic action and environmental triggers^[11].

Drug substitution represents a cornerstone in the management of DIGE. Several authors have reported significant regression of gingival enlargement following replacement of nifedipine with alternative antihypertensive agents, particularly angiotensin II receptor blockers. In the present case, substitution with irbesartan, combined with meticulous plaque control, resulted in marked improvement in the mandibular arch, confirming literature data suggesting that early-phase enlargement may be reversible^[13].

However, persistent fibrotic gingival enlargement in the maxillary arch failed to resolve without surgery and necessitated gingivectomy. This finding aligns with studies by Mavrogiannis *et al.*, who emphasized that long-standing fibrotic lesions often fail to resolve completely despite drug substitution and scaling and root planing, thus requiring surgical intervention to restore gingival architecture and facilitate oral hygiene^[14].

The differential response observed between the mandibular and maxillary arches can be explained by the stage and chronicity of the lesions, as well as local tissue characteristics. Early-phase DIGE is characterized primarily by increased fibroblast proliferation and extracellular matrix accumulation, which remain reversible once the offending drug is withdrawn and inflammation is controlled^[13]. This likely accounts for the marked regression observed in the mandibular arch following substitution of nifedipine with irbesartan and meticulous plaque control. In contrast, the resistance of the maxillary arch to non-surgical therapy suggests a higher degree

of fibrosis, with dense collagen bundles, reduced vascularity, and diminished fibroblast turnover. Such mature fibrosis is less responsive to drug substitution alone and requires surgical intervention, as reported in previous studies^[14].

Local anatomical factors may further contribute to site-specific differences. The maxillary gingiva is often thicker and more fibrotic, and may retain plaque more readily, amplifying local inflammatory mediator expression and sustaining ECM accumulation^[15].

Systemic evidence supports the concept that CKD can significantly influence gingival inflammation, immune regulation, collagen metabolism, and wound healing, thereby plausibly delaying the regression of DIGE in susceptible individuals. CKD is characterized by immune dysregulation and persistent low-grade systemic inflammation, including altered lymphocyte and monocyte/macrophage function and elevated levels of pro-inflammatory mediators such as tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and matrix metalloproteinase-1 (MMP-1) in gingival crevicular fluid. The accumulation of uremic toxins further impairs host immune responses to periodontal pathogens, facilitating bacterial persistence, sustained inflammation, and infection-associated alveolar bone loss. Moreover, CKD-related metabolic disturbances—including vitamin deficiencies, metabolic acidosis and oxidative stress—compromise connective tissue homeostasis by reducing collagen synthesis, impairing angiogenesis, and delaying wound repair^[16]. Collectively, these systemic alterations provide a biologically feasible explanation for prolonging inflammatory-fibrotic responses and slowing regression of drug-induced overgrowth in certain sites.

Following drug withdrawal, partial normalization of calcium-dependent and profibrotic signaling pathways may occur. It is biologically plausible that such recovery is more pronounced in regions with less established fibrosis, where ECM turnover remains relatively dynamic, whereas densely fibrotic tissues with stabilized collagen architecture exhibit limited spontaneous remodeling and therefore maintain persistent enlargement.

These findings underscore the site- and lesion-specific nature of DIGE regression and emphasize the need for a tailored, multidisciplinary management strategy combining drug substitution, nonsurgical therapy, surgical intervention when necessary, and

structured maintenance for optimal long-term outcomes.

4. Conclusion

This case underscores the importance of early recognition and multidisciplinary management of drug-induced gingival enlargement in medically compromised patients. In individuals with chronic kidney disease and hypertension, careful coordination with the treating physician is essential to ensure both periodontal stability and systemic control. The substitution of nifedipine, combined with comprehensive nonsurgical therapy and site-specific surgical intervention, resulted in complete remission without recurrence at four months. This report highlights that individualized treatment planning and strict maintenance are critical for long-term periodontal health in patients receiving calcium channel blockers.

5. Patient Consent

Written informed consent was obtained from the patient for publication of this case report and all associated images.

6. Conflict of Interest Statement

The authors declare no conflicts of interest related to this publication.

7. Références.

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