

VADE MECUM ON HOLISTIC AND NONPAREIL MANAGEMENT OF THE PERPLEXING QUANDARY OF AMLODIPINE INDUCED GINGIVAL ENLARGEMENT

Dr. Nithiyanandam P.*, Dr. Bhuvaneshwari P., Dr. M. N. Akshaya and Dr. Francisk Donus S.

Department of Periodontology, Tamilnadu Government Dental College and Hospital,
Chennai, Tamil nadu, India.

Article Received on
23 July 2024,

Revised on 13 August 2024,
Accepted on 03 Sept. 2024

DOI: 10.20959/wjpr202418-33855



*Corresponding Author

Dr. Nithiyanandam P.

Department of
Periodontology, Tamilnadu
Government Dental College
and Hospital, Chennai,
Tamil nadu, India.

ABSTRACT

Introduction: Gingival enlargement is a known side effect of calcium channel blockers--especially the dihydropyridine group. It forms a major concern for the patient due to its unesthetic appearance.

Objective: To describe the diagnosis and management of amlodipine drug induced gingival enlargement. **Materials and Methods:** The case presented here is a 50-year-old female patient with drug induced gingival enlargement. Patient was a known hypertensive and was on medication- Amlodipine for past two years. Planned surgical intervention along with comprehensive management was the chosen treatment strategy. Meticulous oral hygiene maintenance, switchover to alternative drug by physician opinion, scaling and root planing and surgical excision of enlarged gingiva in lower anterior, periodontal flap surgery in upper anterior and vestibuloplasty in lower anterior region.

Results: The regression and prevention of recurrence of drug-induced gingival overgrowth were achieved through drug substitution, suitable non-surgical and surgical treatment, and excellent plaque control. Post surgical enlargement was found to be minimal, followed by prosthodontic rehabilitation. No recurrence was noted upto a follow up of one year. **Conclusion:** This case report provides a brief overview of amlodipine induced gingival enlargement and comprehensive management.

INTRODUCTION

The clinician faces a diagnostic conundrum when encountering gingival expansion, whether it be localized or generalized, as it exerts cosmetic ramifications and may create a niche for the growth of microbial flora. Numerous factors can contribute to it, such as genetics, inflammatory conditions, medications, or systemic diseases. Despite the lack of clarity surrounding the aetiopathogenesis, calcium channel blockers such as nifedipine and amlodipine are implicated. In 1994, Seymour *et al.* reported the first case of gingival overgrowth as a side effect of amlodipine, a more recent dihydropyridine drug used to treat angina and hypertension. Lafzi *et al.* has documented the quick development of gingival hyperplasia in patients who started using amlodipine at a dose of 10 mg per day within two months. Gingival hypertrophy often manifests clinically one to three months after starting the prescribed drug regimen.^[1-4]

PHARMACOLOGICAL PROFILE OF AMLODIPINE

Other members of the long-acting dihydropyridine group include felodipine, nifedipine, nicardipine, isradipine and nitrendipine.

Mechanism of action: Vasodilatation of peripheral and coronary arteries

DOSAGE: 2.5 or 5 grams, single dose (alone or in combination with atenolol)

ADVERSE EFFECTS: Headaches, facial flushing, dizziness, oedema, gingival hyperplasia.

ORAL EFFECTS: detectable in gingival crevicular fluid.

Significant sequestration of drug in patients exhibiting gingival overgrowth.

CASE REPORT

A 50-year-old female patient's main complaint, which she brought to the attention of the periodontology department at Tamilnadu Government dental college and hospital in Chennai, was swelling in her upper and lower gums for a period of three months. Based on the patient's medical history, it was determined that they were prescribed amlodipine (5 mg) for systemic hypertension two years prior. At three months, the patient noticed the gingival enlargement and intermittent bleeding of the gums. On general examination, the patient was moderately built and nourished. Intraoral examination revealed diffuse enlargement of the gingiva of both the upper and the lower jaws involving marginal gingiva, attached gingiva and the interdental papilla. The attached gingiva was erythematous, the surface was lobulated, and showed bleeding on probing. The probing depth was recorded to be in the range of 4 mm to 6mm.

Panoramic radiography showed the complete set of mandibular and maxillary teeth, as well as generalized spacing between the former, missing teeth in relation to the posterior and lower anterior teeth, generalized horizontal bone loss, and root stumps in relation to the upper right back tooth region. **FIG.(1)**



Fig. 1: Pre-Operative orthopantomography.

The patient was informed about the gingival hyperplasia and the side effects of the medication she had been taking for the past two years. Surgical periodontal treatment was part of the treatment plan because the enlargement had not responded well to professional debridement with scaling and root planning, so it was addressed for both functional issues and aesthetic reasons.

HISTOPATHOLOGY FINDINGS

H&E-stained microsections exhibiting fibrous hyperplasia-suggestive dense fibro-collagenous stroma with numerous tiny blood vessels and chronic inflammatory cell infiltration. **FIG.(2)**

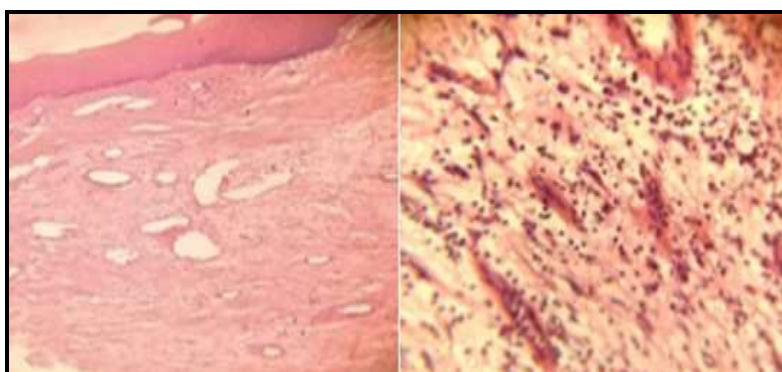


FIG. 2: Fibrous hyperplasia-suggestive dense fibro-collagenous stroma with numerous tiny blood vessels and chronic inflammatory cell infiltration.

TREATMENT

After the patient was referred to the doctor, the doctor consented to replace the medication (amlodipine) with an alternative hypertension medication, which included ACE inhibitors and β -blockers.

The patient was instructed to follow stringent oral hygiene practices and to rinse twice a day with 10 ml of 0.2% chlorhexidine mouthwash for one minute. After two weeks, she was requested to report back. In the meanwhile, the tissue had grown fibrous and the inflammation had decreased.

Root planing treatment is done, and patient asked to assess the subside of gingival growth after 4 weeks.

SURGICAL TREATMENT

FIRST VISIT

STEP 1: Patient consent obtained and local anaesthetic- 2% lignocaine hydrochloride was administered.

STEP 2: The sulcular incision is given around each tooth and through the lingual /palatal flap.

STEP 3: Each interdental papilla has a semilunar incision that dips apically from line angle of the tooth so that papillary incision line angle is less than 5 mm from the gingival margin allowing the interdental tissue to be dissected from the lingual /palatal aspect so that it can be moved intact with facial flap. The first modification of PPF was reported by Checchi et al. in 1988, where in the horizontal incision beneath the interproximal area, on opposite side of bone defect was deemed best as it allowed protection of the regenerated area from the oral environment.

STEP 4: Debridement is done with saline irrigation. **FIG. (6)**

STEP 5: Hemostasis achieved and 3-0 silk sutures placed. **FIG. (7)**

SECOND VISIT

Local anaesthetic-2% lignocaine hydrochloride is administered.

GINGIVECTOMY

External bevel incision is given in lower anteriors to remove excess hyperplastic gingival enlargement and 3-0 silk sutures placed.

VESTIBULOPLASTY BY KAZANJIAN TECHNIQUE

An incision is made in the mucosa of the lip and a large flap of labial & vestibular mucosa is reflected. Vestibule is deepened by supraperiosteal dissection. Flap of mucosa is turned downward from its attachment on the alveolar ridge. The flap is placed directly against the periosteum to which it is sutured. **FIG. (8)**

Coe-pak is placed into the deepened sulcus. The Coe-pak helps to hold the flap in its new position and to maintain the depth of vestibule during the initial stages of healing. Coe-pak is removed after 14 days. The labial donor site is left to granulate by secondary epithelisation. **FIG.(9)**

**FIG.(3)****FIG.(4)****FIG (5)****FIG.(6)****FIG.(7)****FIG.(8)****FIG.(9)****FIG.(10)**

FIGURES (3) (4) Preoperative picture showing calculus, stains with inflamed gingival enlargement. FIG. (5) after 14 days of Scaling and Root planning. FIG.(6) Papilla preservation flap done followed by debridement FIG.(7)3-0 silk sutures placed in palate FIG.(8) Gingivectomy, Vestibuloplasty by kazanjian technique followed by 3-0 silk sutures FIG. (9) after 14 days. FIG.(10) Temporary prosthetic replacement is done after 30 days.

DISCUSSION

Currently, over 20 medications, including oral contraceptives, have been linked to gingival overgrowth. However, there is ample evidence linking gingival hyperproliferation to three primary pharmacological classes: immunosuppressants, calcium channel blockers, and anticonvulsants.^[43]

Though each of these medications targets different primary target tissues with its pharmacological impact, they all appear to function similarly on gingival tissue, which is a secondary target tissue.

Here, we describe a 50-year-old hypertensive patient who was taking 10 mg of amlodipine twice a day when he developed gingival hypertrophy. Although amlodipine was previously thought to have a far lower incidence of gingival enlargement than nifedipine, a significant number of cases have lately come to light.

The incidence of amlodipine-induced gingival hyperplasia, a third generation calcium channel blocker, is very low, while nifedipine, a first generation calcium channel blocker, causes gingival overgrowth in roughly 20% of patients. It has been demonstrated that the frequency of amlodipine-induced gingival hypertrophy ranges from 1.7% to 3.3%.^[43-44]

Any cause for gingival overgrowth may be stressful since it raises the risk of periodontal disease and dental damage. In addition, it results in changes to appearance and clinical symptoms such as bleeding, inflammation, tenderness, speech difficulties, irregular tooth movement, and difficulties with dental occlusion.

Plaque-induced inflammation that results in edematous and hyperemic gingiva may at least worsen the abnormalities in gingival shape observed in DIGO. This keeps the cycle going by altering the gingiva's contour, which makes plaque removal more challenging. In this

instance, the advancement of periodontal disease may have been accelerated by these inflammatory gingival alterations, ultimately resulting in tooth loss.

According to the case study's findings, gingival overgrowth can still occur in edentulous ridges. This could be because of the overgrowth's persistence, which might not go away entirely after a tooth is extracted or because a particular subpopulation of gingival fibroblasts has incorporated itself into the mucosa of the alveolar ridge.

In 1941, Thompson and Gillespie recommended surgical intervention for DIGO. The amount of keratinized tissue present, the location of the base of pockets in relation to the mucogingival junction, the presence of bony defects, the extent and grade of gingival enlargement, and aesthetic considerations all influence the type of surgical technique used, whether it be a gingivectomy or a periodontal flap procedure. After receiving surgical periodontal therapy or nifedipine, individuals with severe gingival growth had a recurrence rate of around 40% within 18 months of beginning active treatment.^[14-15] If treatment is sustained, there may be a recurrence of gingival hyperplasia in addition to the persistence of other risk factors. Hence, the patient was referred to Department of Prosthodontics for fixed partial denture. **FIG. (10)**

CONCLUSION

One common side effect linked to the usage of three main pharmacological classes anticonvulsants, calcium channel blockers, and immunosuppressants is gingival overgrowth (GO). The whole extent of the processes involved in gingival overgrowth is still unknown. After analyzing all the data, it seems that three key variables—drug variables, plaque-induced inflammatory changes in gingival tissue, and genetic factors that control fibroblast heterogeneity are crucial for the expression of these gingival changes. Dental surgeons should be cognizant of medications while providing treatments linked to gingival overgrowth and should talk about these issues with their medical colleagues.

ACKNOWLEDGMENTS

The authors would like to acknowledge several colleagues who provided critical feedback on the paper including Dr. Thamarai selvi and Dr. Rachana Anagol. The principal author is also grateful for the mentorship of Dr. Bhuvaneshwari. P, who first identified this phenomenon for her. Most importantly, the authors are grateful for the generosity of the patient featured in this

vignette. Her willingness to share his private health issue in hopes of preventing this befalling other patients is fundamental to this report.

REFERENCES

1. A Rare Case Report of Amlodipine-Induced Gingival Enlargement and Review of Its Pathogenesis Sanjeev Joshi¹ and Sucheta Bansal.
2. Amlodipine-induced Gingival Hyperplasia – A Case Report and Review M Madi, SR Shetty, SG Babu, S Achalli.
3. Lauritano D, Martinelli M, Baj A, et al. Drug-induced gingival hyperplasia: an
4. In vitro study using amlodipine and human gingival fibroblasts. *Int J Immunopathol Pharmacol*, 2019; 33: 205873841982774. <https://doi.org/10.1177/2058738419827746>
5. Quenel L, Keribin P, Giran G, Tessier MH, Lesclous P. Amlodipine-induced gingival enlargement: a case report. *J Stomatol Oral Maxillofac Surg*, 2020; 121(3): 308-311. <https://doi.org/10.1016/j.jormas.2019.04.014>
6. Erken E. Amlodipine and gingival hyperplasia: case report with review of the literature. *Acta Med Mediterr*, 2016; 32: 1605. https://doi.org/10.19193/0393-6384_2016_5_138
7. Barclay S, Thomason JM, Idle JR, Seymour RA. The incidence and severity of nifedipine-induced gingival overgrowth. *J Clin Periodontol*, 1992; 19(5): 311-314. <https://doi.org/10.1111/j.1600-051X.1992.tb00650.x>
8. Aryal D, Shahi K, Shrestha SM. Amlodipine induced gingival overgrowth. *J Nep Soc Perio Oral Implantol*, 2018; 2(1): 30-32. <https://doi.org/10.3126/jnspoi.v2i1.23608>
9. El Ayachi H, Ennibi OK. Periodontal management of amlodipine-induced gingival hyperplasia in a hypertensive patient: a surgical approach. *Sci Dent J.*, 2021; 5(2): 91.
10. Devanoorkar A, Guttiganur N. Interdisciplinary approach in the management of medically compromised patient with drug-induced gingival enlargement. *JInterdiscip Dentistry*, 2019; 9(1): 44.
11. Deveci KC, Calisir M, Tanik A, Erdem MB. Antihypertensive drug-induced gingival hyperplasia: a case report. *Aydın Dent J.*, 2021; 7(1): 77-84.
12. El Ghoulbzouri H, Er-raji S, Ennibi O. Periodontal management of amlodipine-induced gingival over growth: a 2 years follow-up case report. *J Med Dent Sci Res.*, 2018; 5(1): 01-05.
13. Khairat RU, Jan SM, Bashir B, Behal R. Amlodipine induced gingival enlargement: a case report. *Int J Res Rev.*, 2019; 6(6): 203-207.

14. Kumar S, Chaubey KK, Srivastava A, Agarwal A. Management of amlodipine-induced gingival enlargement: a case report. *Chron Dent Res.*, 2020; 9: 48-51.
15. J, Bakutra G, Chandran S, Vishnoi S. Different treatment modalities for drug-induced gingival overgrowth: a case series. *Natl J Integr Res Med.*, 2018; 9(2): 106-109.
16. Mukherjee M, Ganguly R, Chatterjee D. Anti-hypertensive drug-induced gingival overgrowth. *Guident*, 2019; 12(8): 58.
17. Pauly G, Kashyap RR, Kini R, Rao PK, Bhandarkar GP, Shetty D. Appalling adverse effects of amlodipine in a chronic kidney disease patient: a case of drug-induced gingival overgrowth. *Pharmacol Toxicol Biomed Rep.*, 2018; 4(1): 6-7.
18. Raghu N, Deepak P, Suresh RM, Manjula MJ. Amlodipine-induced gingival hyperplasia. *Natl J Physiol Pharm Pharmacol*, 2021; 11(7): 803-805.
19. Rakesh BM, Sharma S, Chandana KH. A rare case of accelerated gingival overgrowth with high-dose amlodipine therapy. *J Pharmacovigil Drug Res.*, 2021; 2(1): 15-17.
20. Renzo G, Dario ND, Gianfranco G, Gabriele M, Luca T. The management of amlodipine-induced gingival overgrowth associated to generalized chronic periodontitis—a case report. *Int J Med Pharm.*, 2018; 11(1): 1-9.
21. Shome S, De A, Ghosh A, Saraf A. Amlodipine-induced generalized gingival overgrowth: a clinical case. *IP Arch Cytol Histopathol Res.*, 2021; 6(2): 1-3.
22. Sumra N, Kulshrestha R. Drug-induced gingival overgrowth: report of 2 cases. *J Dent Forecast*, 2018; 1: 1-3.
23. Sharma A, Joshi R, Laxmi Rana SR, Shrestha DB, Joshi PR, Khadka S. Amlodipine-induced gingival overgrowth in patients at a tertiary-level hospital of Nepal. *J Nep Soc Perio Oral Implantol*, 2018; 2(1): 2-5. <https://doi.org/10.3126/jnspoi.v2i1.23571>
24. Tejnani A, Mani A, Sodhi NK, et al. Incidence of amlodipine-induced gingival overgrowth in the rural population of Loni. *J Indian Soc Periodontol*, 2014; 18(2): 226-228. <https://doi.org/10.4103/0972-124x.131332>.
25. Gopal V, Quo BC, Chainani-Wu N. Amlodipine-induced gingival overgrowth with unusual presentation as a gingival mass and rapid regression after dose reduction. *Clin Adv Periodontics*, 2017; 7(1): 25-29. <https://doi.org/10.1902/cap.2016.160013>
26. Jayanthi R, Rajan PB. Amlodipine-induced gingival overgrowth. *J Assoc Physicians India*, 2016; 64(3): 87.
27. S. Pradhan and P. Mishra, “Gingival enlargement in antihypertensive medication,” *Journal of the Nepal Medical Association*, 2009; 48(174): 149–152.

28. T. D. Rees and R. A. Levine, "Systemic drugs as a risk factor periodontal disease initiation and progression," *Compendium of Continuing Education in Dentistry*, 1995; 16(1): 20–42.
29. "Drug associated gingival enlargement," *Journal of Periodontology*, 2004; 75(10): 1424–1431.
30. P. Garzino-Demo, M. Carbone, M. Carrozzo, R. Broccoletti, and S. Gandolfo, "An increase in gingival volume induced by drugs (phenytoin, cyclosporine and calcium antagonists). A review of the literature," *Minerva Stomatologica*, 1998; 47(9): 387–398.
31. J. S. Ellis, R. A. Seymour, J. G. Steele, P. Robertson, T. J. Butler, and J. M. Thomason, "Prevalence of gingival overgrowth induced by calcium channel blockers: a community-based study," *Journal of Periodontology*, 1999; 70(1): 63–67.
32. M. G. Jorgensen, "Prevalence of amlodipine-related gingival hyperplasia," *Journal of Periodontology*, 1997; 68(7): 676– 678.
33. M. G. Triveni, C. Rudrakshi, and D. S. Mehta, "Amlodipineinduced gingival overgrowth," *Journal of Indian Society of Periodontology*, 2009; 13(3): 160–163.
34. R. A. Seymour, J. M. Thomason, and J. S. Ellis, "The pathogenesis of drug induced gingival overgrowth," *Journal of Clinical Periodontology*, 1996; 23(3): 165–175.
35. A. Nyska, M. Shemesh, H. Tal, and D. Dayan, "Gingival hyperplasia induced by calcium channel blockers: mode of action," *Medical Hypotheses*, 1994; 43(2): 115–118.
36. R. I. Marshall and P. M. Bartold, "A clinical review of druginduced gingival overgrowths," *Australian Dental Journal*, 1999; 44(4): 219–232.
37. A. Lafzi, R. M. Z. Farahani, and M. M. Shoja, "Amlodipineinduced gingival hyperplasia," *Medicina Oral, Patologia Oral y Cirugia Bucal*, 2006; 11(6): E480–E482.
38. R. A. Seymour, "Calcium channel blockers and gingival overgrowth," *British Dental Journal*, 1991; 170(10): 376–379.
39. S. Sonmez, C. Cavdar, C. Gunduz et al., "Do MMP-1 levels of gingival fibroblasts have a role in the gingival overgrowth of cyclosporine-treated patients?" *Transplantation Proceedings*, 2008; 40(1): 181–183.
40. P. G. Raman, V. N. Mishra, and D. Singh, "Nifedipine induced gingival hyperplasia," *The Journal of the Association of Physicians of India*, 1988; 36(3): 231–233.
41. M. Mavrogiannis, J. S. Ellis, J. M. Thomason, and R. A. Seymour, "The management of drug-induced gingival overgrowth," *Journal of Clinical Periodontology*, 2006; 33(6): 434–439.

42. Amlodipine induced gingival enlargement Satya Ranjan Misra, 1 Sushmita Koduru Lakshmi, 1 Neeta Mohanty².
43. Hiperplasia Gingival inducida por Amlodipina – Reporte de una Caso y Revisión M Madi, SR Shetty, SG Babu, S Achalli.
44. Gingival enlargement improvement following medication change from amlodipine to benidipine and periodontal therapy Hidehiko Kamei¹ Maria Furui, 1 Tatsuaki Matsubara, ^{2,3} Koji Inagaki ⁴.