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The Management of Amlodipine-induced Gingival Overgrowth Associated to Generalized Chronic Periodontitis- A Case Report

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Authors' contributions

This work was carried out in collaboration between both authors. Authors GR and TL designed the study, wrote the protocol and first draft of the manuscript. Authors DND, GG and MG managed the literature searches, and managed the analyses of the study. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

This case report describes the management of an 60 years-old female who presented with generalized chronic periodontitis associated with amlodipine-induced gingival overgrowth. The clinical examination showed generalized edematous gingival tissues, with gingival overgrowth, and presence of bacterial plaque and calculus on the surfaces of the teeth. Patient was a known hypertensive, and she was on medication with amlodipine from past three years. Diagnosis was determined based on history, clinical findings and radiographic examination. With the consent of physician for substitution of amlodipine, treatment consisted of meticulous oral hygiene instruction, scaling, root surface instrumentation, prophylaxis, and daily chlorhexidine mouth rinses. After this stage, periodontal surgery for pockets and excess gingival tissues elimination was performed. The patient has been enrolled in a supportive periodontal maintenance program, and after 3-years, there has been no recurrence.

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Keywords: Case report; gingival overgrowth; gingival enlargement; amlodipine; generalized chronic periodontics.

1. INTRODUCTION

"Gingival overgrowth" (GO) or "gingival enlargement" (GE) comprises any clinical condition in which is present an increase in the size of the gingiva. Since no increase in number of cells and/or in cells volume are present, GO and GE are preferred terms to describe that conditions previously labelled as "gingival hyperplasia" and "gingival hypertrophy" [1]. GO has been associated with multiple factors including congenital diseases, hormonal disturbances, long-term poor oral hygiene, inflammation, neoplastic conditions, and adverse drug reactions [1]. Among the drugs that induce GO, calcium channel blockers (CCB)s have been widely related to this condition [2]. CCBs, also called calcium antagonists, represent a group of drugs specifically developed to assist in the management of cardiovascular conditions, including hypertension, angina pectoris, coronary artery spasm and cardiac arrhythmia. CCBs may be classified on the basis of their chemical composition as benzothiazepine derivatives (diltiazem), phenylalkylamine derivatives (verapamil) or substituted dihydropyridines (amlopidine, felodipine, isradipine, nicardipine, nifedipine, nitrendipine, oxodipine, nimodipine and nisoldipine). CCBs, acting on calcium ion influx across the cell membrane of cardiac and smooth muscle cells, interfering or block the mobilization of calcium intracellularly. Ellis et al. [3], in 1993 first reported three cases of gingival sequestration of amlodipine and amlodipine-induced GO since then, several cases have been reported [4-8].

Chronic periodontitis is a disease that develops mainly in adults, as having its onset after the age of 35 years; and affects 18% of the population [9]. Features of chronic periodontitis have been listed in the 1999 International Workshop [9] as follows:

- most prevalent in adults, but can occur in children and adolescents;
- amount of destruction is consistent with the presence of local factors;
- subgingival calculus is a frequent finding;
- associated with a variable microbial pattern;
- slow to moderate rate of progression, but may have periods of rapid progression; can be associated with local predisposing factors (e.g., tooth-related or iatrogenic factors);
- may be modified by and ⁄ or associated with systemic diseases (e.g., diabetes mellitus, HIV infection);
- can be modified by factors other than systemic disease such as cigarette smoking and emotional stress.

Chronic periodontitis has been further classified as localized or generalized depending on whether < 30% or > 30% of sites are involved. Severity is based on the amount of clinical attachment loss (CAL) and is designated as slight (1-2 mm CAL), moderate (3-4 mm CAL) or severe (> 5 mm CAL) [10].

The aim of this paper is to report a case of amlodipine-induced GO, associated with a generalized chronic periodontitis. (AAP), presenting the management of the patient, and emphasizing on an objective treatment plan.

2. CASE PRESENTATION

The patient is a 60-year-old female, who had noticed an enlargement of her gingiva two years previously, in association with teeth migration and bleeding. Medical history revealed that the patient was hypertensive from last three years and she was taking amlodipine 10mg. She never was a smoker. On extra-oral examination, no cervical lymphadenopathy and no swelling were observed; while a halitosis was present. Intraoral examination revealed overgrowth of the vestibular and lingual gingiva, extending from tooth 33 to 43 and from tooth 13 to 23, and covering almost all of the crown of interested teeth (Figs. 1,2,3). The periodontal examination revealed deep pockets throughout the mouth with CAL > mm 5 with bleeding on probing in all the sites, and distolabial migration of the mandibular central and lateral incisors, which presented a Grade II mobility.

Special investigations included an full mouth Rx examination (Fig. 4) showing an generalized interproximal bone reabsorption more accentuated in the frontal-mandibular area The supposed diagnosis was GO associated with severe chronic generalized periodontitis, due to a combination of poor oral hygiene and the use of BBCs medication. Patient's physician was consulted regarding substitution of amlodipine,

and with the physician consent, a substitute was prescribed. The patient initially underwent cause/related periodontal therapy that included oral hygiene instruction, reinforcement and evaluation of the patient's plaque control; supra and subgingival scaling and root planing to remove microbial plaque and calculus. Fig. 5 was taken following the root surface debridement. Under local anaesthetic with infiltrations using 2% lidocaine with 1:80,000 epinephrine, internal bevel periodontal flap was used to remove the overgrowth gingival tissue and to remove the periodontal pockets (Fig. 6). Postoperatively, a Coe-pac dressing was used to cover the surgical site. Histopathological examination of tissue removed revealed hyperkeratotic epithelium characterized by long, thin interlacing rete pegs. The underlying connective tissue shows the presence of fibroblastic proliferation with abundant collagen fibers and numerous inflammatory cells. The diagnosis was gingival overgrowth with chronic inflammation'. (Fig. 7) After 10 days, at the suture removal, a lingual resin adhesive blocking was used to stabilize the teeth from 33 to 43 (Figs. 7,8). The patient has been enrolled in a supportive periodontal maintenance program, and after 3-years, there has been no recurrence (Fig. 9).

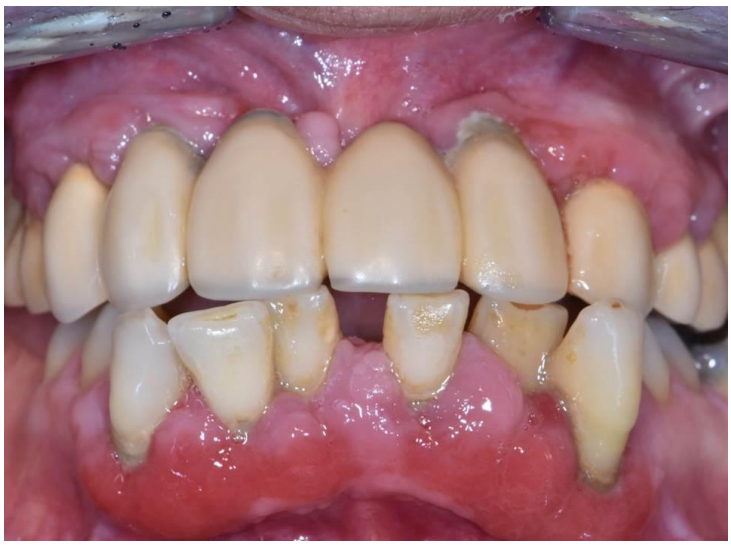


Fig. 1. Clinical situation at the first visit

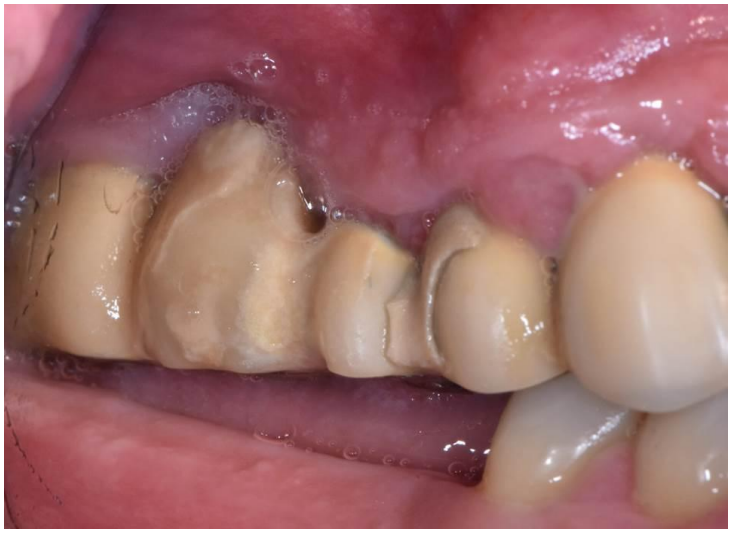
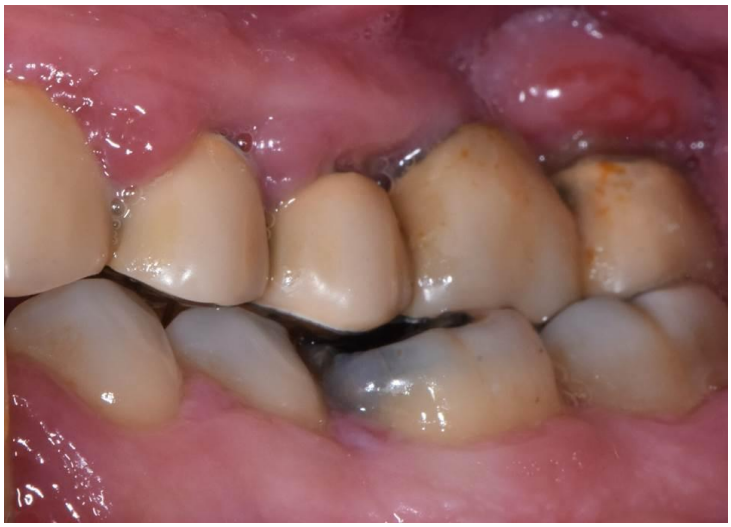


Fig. 2. Clinical situation at the first visit



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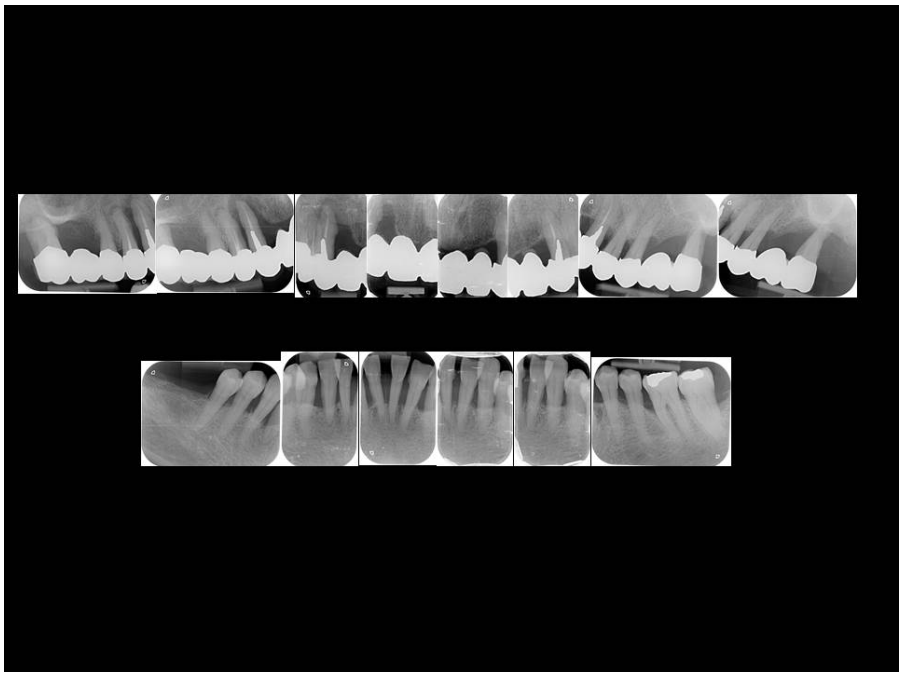

Fig. 4. Radiographic examination

3. DISCUSSION

In the patient of the present case report, the poor plaque control, and the amlodipine medication were identified as possible synergistic causative agents.

The pathogenesis of GO induced by amlodipine is still uncertain, however, several factors, affecting the relationship between amlodipine and GO have been called into question, (for a review see [10,11]). Because only a subset of subjects treated with this amlodipine will develop GO, it has been hypothesized that fibroblasts of these patients have an abnormal susceptibility to the drug. It has been reported that fibroblast from overgrown gingiva in these patients are characterized by elevated levels of protein synthesis, most of which is collagen [12]. It also has been proposed that susceptibility or

resistance to pharmacologically induced GO may be governed by the existence of differential proportions of fibroblast subsets in each individual which exhibit a fibrogenic response to this medication [12]. The possible hypothesis to explain the overgrowth is that the fibroblast contains strongly sulfated mucopolysaccharides those are ground substance precursors. After an interaction between amlodipine and gingival fibroblasts, overproduction of collagen and extracellular ground substance occur and lead to increase in the size of gingiva. The drug interferes with calcium metabolism of fibroblast cells and hence reduces the production of degrading enzyme collagenase [13]. Although the role of plaque has not clearly defined in most amlodipine-induced GO, there is no doubt that the resulting gingival inflammation can contribute an additional level of enlargement. In patients treated with amlodipine, the presence of chronic periodontitis could represent a predisposing condition of GO since a synergic effect has been

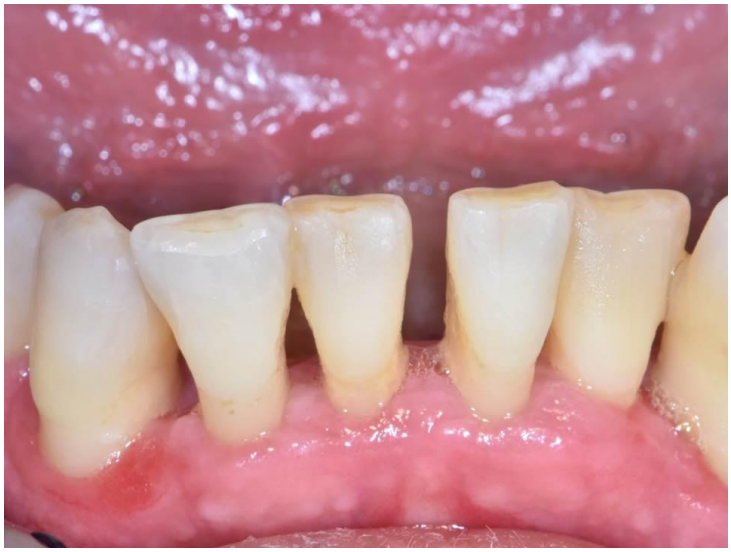

Fig. 5. Clinical situation after the gingival calculus removal, and the root surface debridement

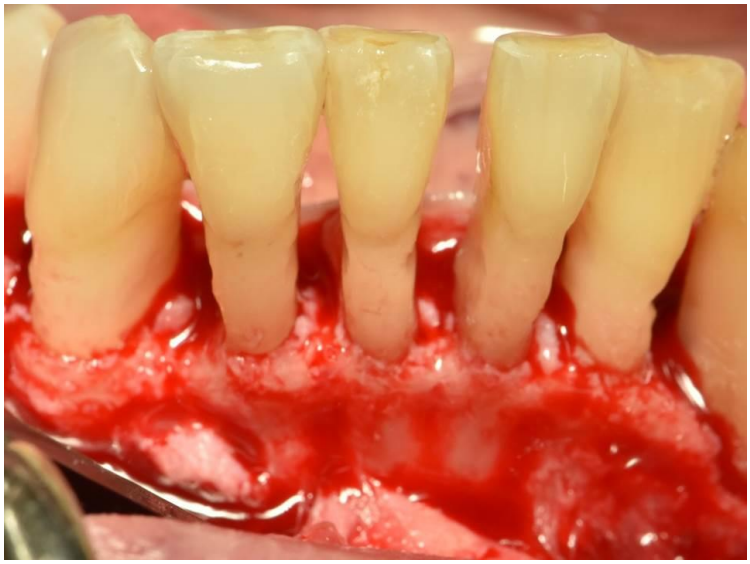

Fig. 6. Periodontal flap was used to remove the overgrowth gingival tissue and to remove the periodontal pockets

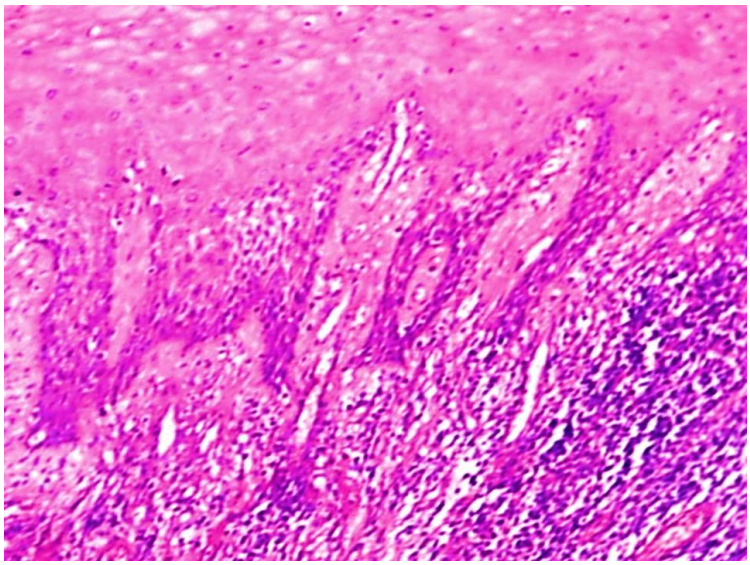

Fig. 7. High power microscopy: H and E staining shows hyperkeratotic epithelium characterized by long, thin interlacing rete pegs. The underlying connective tissue shows the presence of fibroblastic proliferation with abundant collagen fibers and numerous inflammatory cells

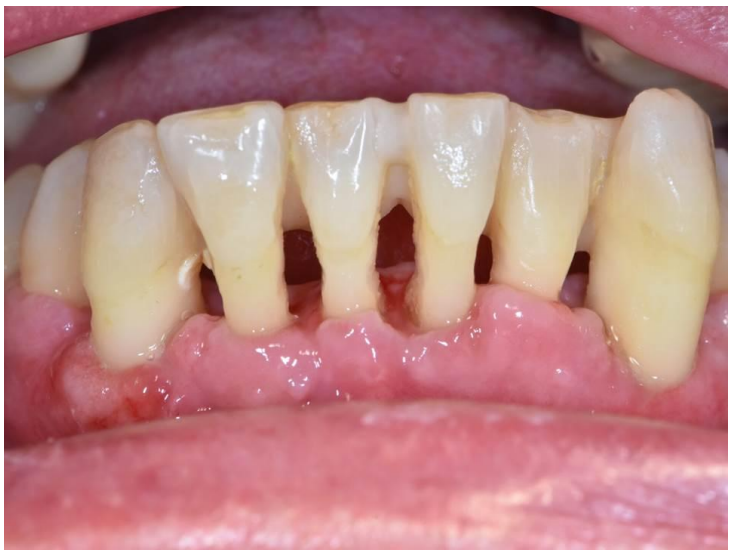

Fig. 8. Clinical situation at the suture removal after 10 days

reported between calcium channel blockers and the production of interleukin 2 by T lymphocytes [2].

The care pathway for these patients generally involves an initial non-surgical approach alongside surgical management as required. However, first of all, the possibility to modify the pharmacological treatment in cooperation with the patient's doctor is to be considered. Replacing the amlodipine with one of the same class or of a different class could lead to an provement of the situation. Non-surgical therapy, including mechanical removal of bacterial deposits associated to antibacterial mouthwashes and/or systemic administration of antibiotic, is aimed at reducing bacterial plaque. A decrease and sometimes-complete remission

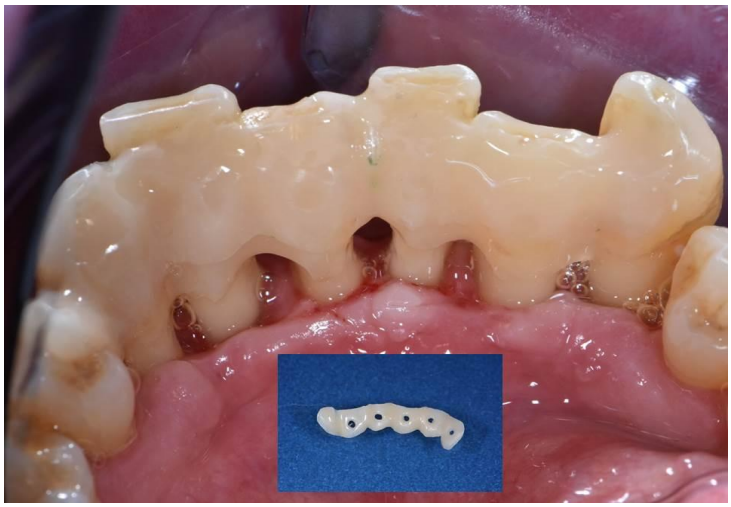

Fig. 9. At the suture removal, a lingual resin adhesive blocking was used to stabilize the teeth from 33 to 43

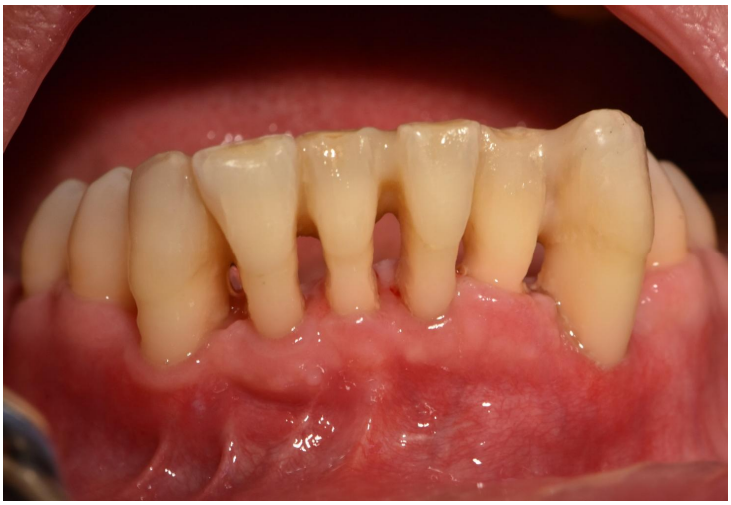

Fig. 10. Clinical situation at the 3-year control visit

of the GO may be observed after non surgical therapy including subgingival instrumentation of tooth and root surface. Consequently, accurate and frequent plaque removal is the basis for the maintenance of the attachment level [14]. Surgical treatment is only advocated when symptoms persist, and where GO is severe or associated with chronic periodontitis [15]. The conventional external bevel gingivectomy is a viable treatment option in small areas (up to six teeth), with no evidence of attachment loss [15]. The internal bevel periodontal flap is indicated in situations with larger areas of GO, or areas where attachment loss is combined with an osseous defect [16] It was found that no difference exists between flap surgery and conventional gingivectomy with respect to recurrence of GO [15]. Meticulous oral hygiene is required in order to maintain a healthy periodontal condition. Poor plaque control is likely to result in recurrence of the GO and thus these patients should be enrolled in a supportive periodontal treatment program. With adequate plaque control, recurrence is less likely, although the patient remains at risk. Presence of conditions such as gingival enlargement may complicate the diagnosis of chronic generalized periodontitis; therefore, diagnosis should always be based on a detailed study of the patient's history and clinical, radiographic and microbiologic findings.

Drug-induced GO must be also differentiated from other drugs induced gingival enlargements, and from other gingival enlargements. In patients taking anticonvulsant agents the gingiva is usually enlarged uniformly without lobulations of the interdental papillae, and severity of the clinical lesions is often greater in the posterior than in as regions [16]. In patients taking agents with immunosuppressive action, often pebbly or papillary lesions are presents on the surface of larger lobulations, which have been associated with the presence of Candida hyphae invading the gingival epithelium [17].

About other gingival enlargements, the differential diagnosis must take into account inflammatory enlargements, idiopathic or familial or hereditary gingival enlargements, neoplastic enlargements or gingival tumors, and systemic diseases induced gingival enlargements. Acute inflamma tory enlargement appears as a localized gingival swelling characterized by acute pain of rapid onset suggesting an abscess. Chronic inflammatory enlargement appears as deep red or bluish red, soft, friable with smooth, shiny surface along with bleeding tendency.[18] In idiopathic or familial or hereditary GO, the attached gingiva, as well as the gingival margin and interdental papillae are generally affected, but the involvement may be limited to either jaw. The enlarged gingiva is pink, firm, and almost leathery in consistency and has a characteristic minutely pebbled surface.[19] Neoplastic enlargement or gingival tumors appear as slowly growing spherical mass that tends to be firm and nodular or hard, wart-like protuberance from gingival surface, while GO associated with systemic diseases, such as, leukemia, sarcoidosis, tuberculosis, and other granulomatous require hematological and histopathological examinations in establishing the differential diagnosis (leukemic infiltrate in leukemia, foreign body giant cell in sarcoidosis, tu berculosis) [20]

4. CONCLUSIONS

Presence of gingival overgrowth or gingival enlargement in cases of chronic periodontitis may complicate the diagnosis, which should be based on the study of a patient's history, clinical, and radiographic findings. A step wise approach inclusive of physician consultation, non-surgical therapy, surgical periodontal therapy, followed by supportive periodontal therapy is essential for management of these cases.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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