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Case Report

Idiopathic Granulomatosis in Gingiva: A Challenging Case Report

Diş Etinde Saptanan İdiyopatik Granülomatozis: Zorlu bir Vaka Raporu

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ABSTRACT

Introduction: Identifying the etiology and pathogenesis of granulomas in the orofacial region can be challenging as a wide range of disorders are associated with granulomatosis. A diverse range of etiologies, including genetic, immunologic, allergic, and infectious mechanisms, have been implicated in granulomatosis. A comprehensive clinical, microscopic, and laboratory assessment may be necessary to ascertain the underlying cause of granulomatous inflammation.

Case Report: This case presents a female adolescent patient with idiopathic granulomatosis in the gingiva, lacking any identifiable causative factors. Intraoral examination revealed granular erythematous gingiva, especially in the anterior regions of the maxillary and mandibular arches, and a biopsy was taken after initial periodontal therapy. A histopathological examination revealed the presence of a non-caseating granulomatous lesion. Further investigations were conducted to rule out potential causative factors. Subsequent analysis showed no abnormalities in the patient's general health.

Conclusion: In the absence of a clear etiological explanation for a given lesion, eliminating the disease and constructing an appropriate treatment plan may prove challenging.

Keywords: Gingival swelling; Granulomatosis; Idiopathic; Inflammation

ÖZET

Giriş: Orofasiyal bölgedeki granülomların etiyolojisini ve patogenezini belirlemek, çok çeşitli hastalıkların granülomatozis ile ilişkili olması nedeniyle zor olabilmektedir. Granülom oluşumunda; genetik, immünolojik, alerjik ve enfeksiyöz dahil olmak üzere çok sayıda etiyoloji öne sürülmüştür. Granülomatöz inflamasyonun altında yatan nedeni tespit etmek için kapsamlı bir klinik muayene ile birlikte, mikrobiyolojik değerlendirme ve laboratuvar değerlendirmeleri gerekebilir.

Vaka Raporu: Bu olgu raporunda, dişetinde idiyopatik granülomatozisi olan ve tanımlanabilir herhangi bir nedensel faktör bulunmayan adölesan dönemdeki kadın hasta sunulmaktadır. Ağız içi muayenede özellikle maksiller ve mandibular arkların ön bölgelerinde granüler eritematöz dişeti saptanmış ve başlangıç periodontal tedavisinden sonra ilgili bölgeden biyopsi alınmıştır. Histopatolojik incelemede, kazeifiye olmayan granülomatöz bir lezyonun varlığı tespit edilmiştir. Potansiyel etiyolojik faktörleri ekarte etmek için ilgili bölümlerde ileri tetkikler yapılmıştır. Devamında yapılan analizler hastanın sistemik durumunda herhangi bir anomali olmadığını göstermiştir.

Sonuç: Granülomatöz lezyonlar için net bir etiyolojik faktör saptanamadığında, hastalığı ortadan kaldırmak ve uygun bir tedavi planı oluşturmak zor olabilmektedir.

Anahtar Kelimeler: Gingival büyüme; Granülomatozis; İdiyopatik; İnflamasyon

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INTRODUCTION

Granulomatous inflammation is a delayed hypersensitivity reaction, known as type IV, that can occur in response to many viral and non-infectious triggers.[1] This inflammatory process can localize within the oral cavity or manifest as part of a systemic pathology. Granulomas are the most characteristic histopathological feature of this condition. They comprise CD4+ T lymphocytes surrounding an area of epithelioid histiocytic macrophages. In certain instances, central caseation may occur within these granulomas, leading to their designation as "caseous granulomas".[1,2] The development of epithelioid histiocytes and the subsequent formation of granulomas can occur due to many causes. Foreign body reactions to dental materials are commonly observed, especially in the oral region. Additionally, granulomas can develop due to infectious agents (such as bacteria or fungi) or indicate the systemic manifestation of several disorders in the oral cavity.[2] Recognizing that granulomatous inflammation may also result from allergic responses to food or pharmacological agents is crucial.[3] Granulomatous lesions within the oral cavity without apparent cause pose considerable diagnostic challenges. The following report details the clinical diagnosis and management of a 17-year-old female adolescent patient who presented at the periodontology clinic for a detailed investigation of gingival hyperplasic areas.

CASE REPORT

A 17-year-old female adolescent was referred to the Department of Periodontology with a chief complaint of difficulty in performing oral hygiene procedures, gingival swelling, and bleeding over the past six months. The patient reported no history of systemic disease, including family history or any medication, drug, or food allergies. She did not have any parafunctional habits. She had not undergone any surgical procedures. The patient reported that she brushed her teeth once a day and did not perform interdental cleaning. An extra-oral examination revealed no abnormalities on or around the lips. There was no paralysis of the facial muscles. Intraoral examination revealed an erythematous gingiva with a granular appearance, particularly in the anterior areas of the maxillary and mandibular arches (Fig.1A, Fig.1B).

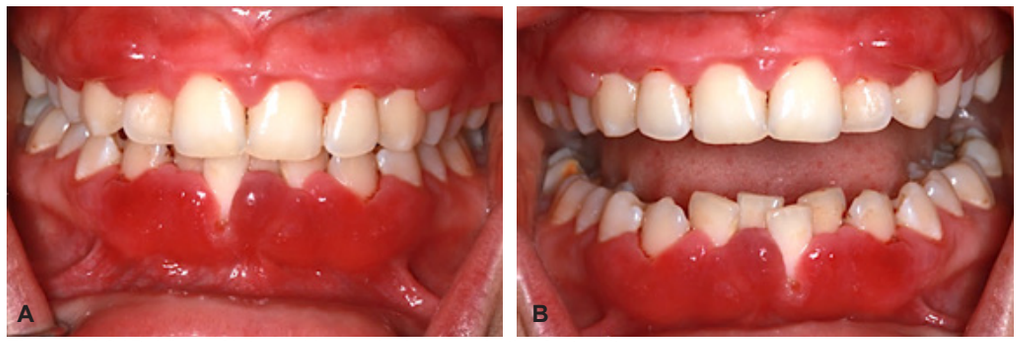


Figure 1A&1B. View of intraoral hyperplasic areas in the first visit.

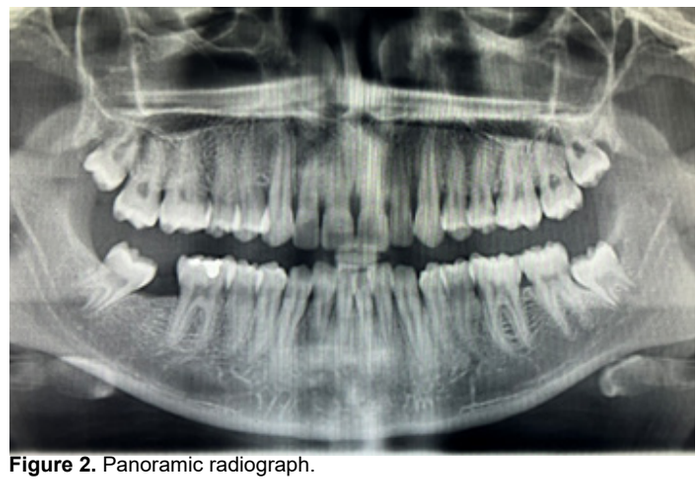


Figure 2. Panoramic radiograph.

Table 1. Baseline periodontal parameters.

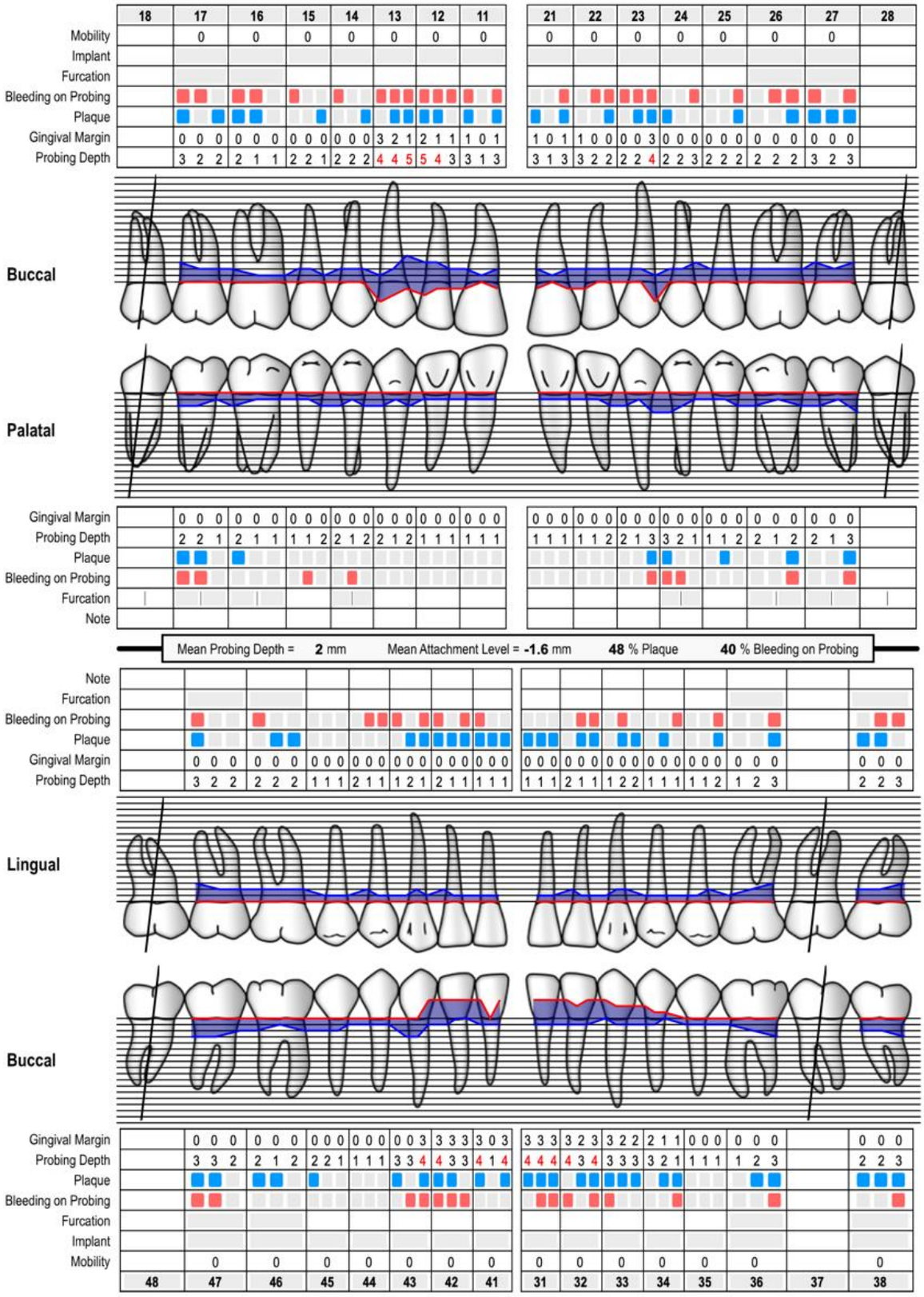
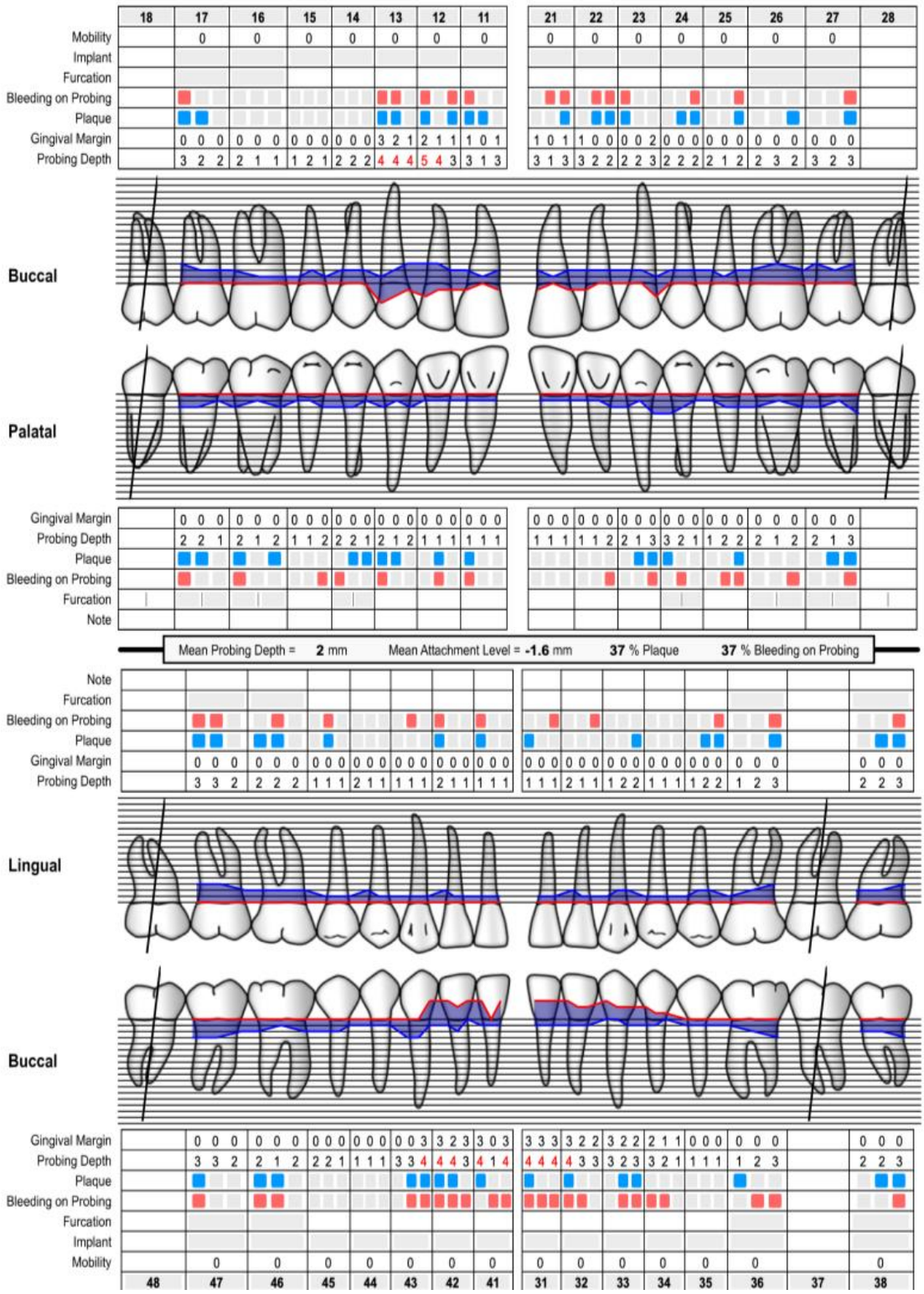


Table 2. Periodontal parameters at the reevaluation session.



There were no apparent changes in the tongue or other parts of the mucosa. The Modified Plaque Score (O'Leary, 1972) was 48%, with 40% bleeding on probing (Ainamo & Bay, 1975) and probing depths ≥ 4 mm due to pseudopockets, and clinical attachment loss on teeth number 12, 13 and 23 (Table 1). A radiographic examination was performed, which revealed evidence of bone loss in the maxillary anterior region (Fig. 2). As stated in the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions, the patient was diagnosed with localized periodontitis, Stage 2, Grade C.[4] Treatment was initiated after obtaining the necessary consent from the patient. In the initial periodontal treatment, supra- and subgingival scaling was performed for all quadrants within one week. The patient was called for follow-up visits to evaluate plaque control at weeks 2 and 4. At the 3-month re-evaluation, no significant improvement was found in the pseudopocket areas (Table 2). In the surgical stage, firstly, surgical removal of the hyperplasic tissue in the lower anterior region was planned. In the surgical stage, under local anesthesia (articaine HCl), hyperplasic tissue was excised using a number 15 scalpel, and gingivoplasty was performed to adjust the contours of the area. Vestibuloplasty was performed to increase the depth of the vestibule in the region of teeth 31,41,42. The procedure was concluded with suturing using a 4/0 resorbable multifilament suture (Fig. 3). The excised specimens were fixed in 10% buffered formalin and sent to the Department of Oral Pathology.

The histological examination revealed the presence of mononuclear inflammatory cells, and the formation of granulomas scattered inside the collagenized connective tissue underneath the keratinized, mature stratified squamous epithelium. Under high magnification, the granulomas were shown to be non-caseating granulomas consisting of epitheloid cells in the center, lymphocytes, and histiocytes in the surrounding area (Fig.4). Polarized light microscopy yielded negative results for foreign bodies, while Periodic Acid-Schiff (PAS) staining showed no evidence of Candida or other fungi. Furthermore, Ziehl-Neelsen staining did not reveal the presence of Tuberculosis bacilli.

A pediatrics consultation was sought to aid in diagnosing granulomatous diseases in the oral region. Additional tests, including a complete blood count, chest radiography, and abdominal ultrasound, were conducted to exclude potential causal factors. Subsequent examination indicated no abnormalities in the patient's overall health. The conclusive diagnosis, drawn from the existing evidence, was a non-specific granulomatous disease.

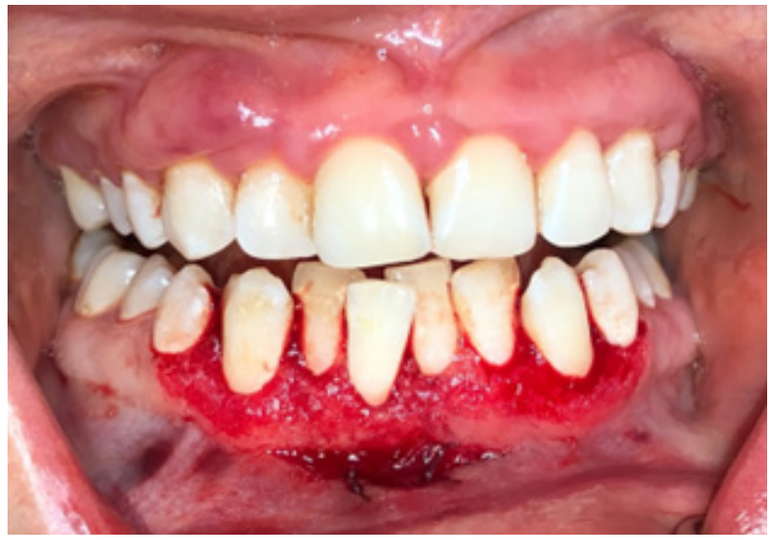


Figure 3. Post-operative view.

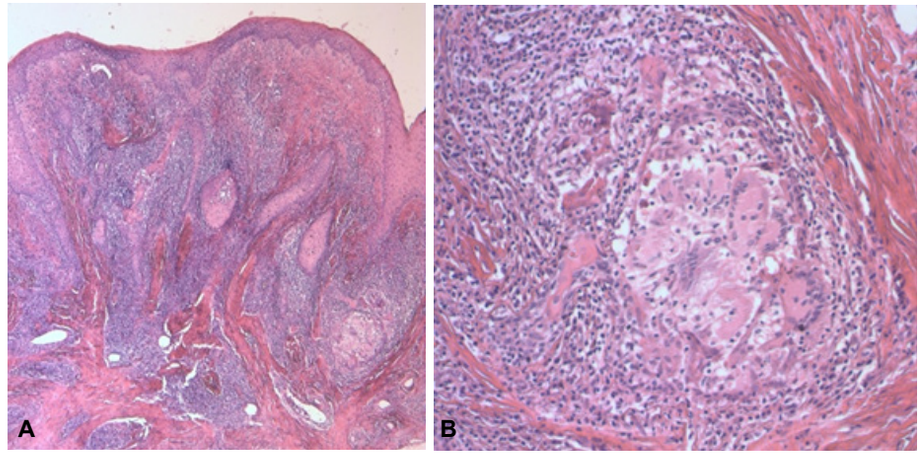


Figure 4. Histopathological characteristics of gingival tissue.
A. Dense inflammation and granulomas in connective tissue beneath mature stratified squamous epithelium, ×40 magnification, Hematoxylin & Eosin. **B.** High-magnification view of a non-caseating granuloma, ×200 magnification, Hematoxylin & Eosin.

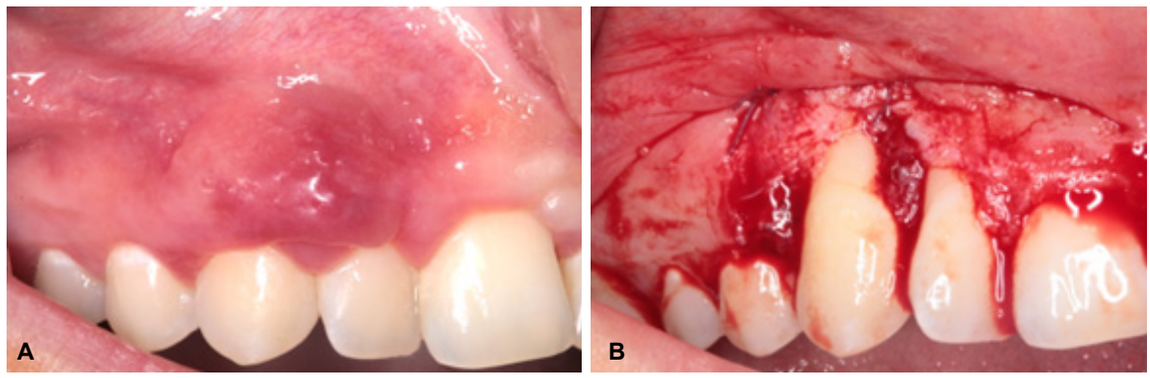


Figure 5. Removal of the second biopsy sample.
A. View of the hyperplasic region with granular structure. **B.** Site view after the surgery.

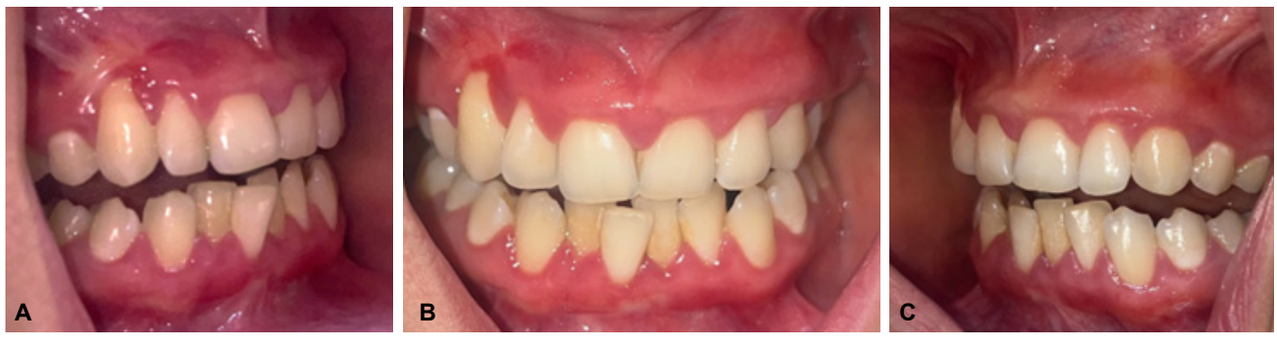


Figure 6A & 6B & 6C. Intraoral view at the one-month follow-up visit after the second biopsy was taken.

In the course of a session conducted to examine the operative site, a decision was made to take a biopsy from the most affected area in the maxilla. The pathology result further supported the initial diagnosis (Fig. 5A, Fig. 5B). Despite the emphasis on the significance of regular periodontal follow-up sessions and the critical role of maintenance treatment, the patient could not be examined at the planned intervals due to socioeconomic constraints. At the one-month follow-up visit following the second biopsy, the patient exhibited an inability to achieve plaque elimination. During the intraoral examination, oedematous areas were identified in the right maxillary canine and mandibular anterior region (Fig. 6A, Fig. 6B, Fig. 6C).

DISCUSSION

The etiologies of erythematous swellings in the gingival mucosa are diverse and may include a range of potential causes.[4, 5] The underlying reason might exhibit significant variability and can provide significant challenges in diagnosis. Among the causes of gingival swelling, granulomatous inflammation is an uncommon reason. Granulomatous inflammation represents a specific form of chronic inflammation.[6] Histopathologically, a granuloma is a distinct structure composed of epithelioid-shaped macrophages, multinucleated giant cells, lymphocytes, and fibroblasts.

Granulomatous inflammation has a multifactorial cause and may arise as a reaction to environmental or genetic factors or infectious organisms, or it may be idiopathic, for which there is no known trigger.[7] The clinical findings associated with granulomatous inflammation are usually variable and often indistinct.[8] It may manifest in the oral cavity, usually with various nonspecific clinical findings. The differential diagnosis includes foreign-body reaction, infectious disease, Crohn's Disease (CD), sarcoidosis, and Orofacial Granulomatosis (OFG).[9] Foreign material, including dental materials and cosmetic fillers, is the most common source of oral granulomatous disorder.[10] Foreign body reactions may develop as a potential consequence of dental materials, including suture material and prosthetic restoration.[11] At this juncture, the patient was queried about their dietary habits, including the consumption of specific foods and spices and the use of cosmetic and dental materials. Despite the change in materials, there was no regression of the lesions. However, as the patient's history did not include anything suggestive of a foreign body reaction, and she did not utilize any prosthetic restoration or intraoral device, a histological analysis ruled foreign body diagnosis out using polarized light microscopy.

In detecting a granuloma in the oral region, it is imperative to consider the possibility of OFG as a potential underlying condition. OFG is a rare condition increasingly recognized by the general medically literate public.[5] No reliable epidemiologic data are available because most case series report small single-center groups of patients.[12] Subepithelial non-caseating granulomas histopathologically characterize it and have a spectrum of possible clinical manifestations ranging from subtle oral mucosal swelling to permanent disfiguring fibrous swelling of the lips and face. Painful oral ulceration and neurologic manifestations in the head and neck region can also occur.[4] In this case, OFG was not considered in the final diagnosis due to the absence of extraoral swelling, particularly in the lips, accompanying OFG, and the lack of facial paralysis.

Crohn's disease (CD) is defined as a chronic granulomatous condition that has the potential to affect any portion of the gastrointestinal tract, including the oral cavity. The clinical presentations of the disease may be highly variable. Up to 60% of patients present with oral lesions, which may be the initial sign of the disease in 5% to 10% of cases. Some studies have indicated a correlation between an earlier onset of the disease and the increased prevalence of oral signs. Abdominal ultrasound was obtained to rule out CD in the differential diagnosis, which was normal. Nevertheless, it is imperative to conduct periodic follow-ups on the case, as CD may still present at a later age.[13]

Sarcoidosis represents a relatively common multisystem disease with an unknown etiology. Several studies suggest that host and environmental factors are essential in developing the disease.[14] While the specific environmental factors or infectious agents that contribute to the development of sarcoidosis remain to be identified, numerous studies have documented the spatial, seasonal, and occupational clustering of sarcoidosis cases. As no specific tests are currently available that can accurately diagnose the disease, sarcoidosis is most frequently diagnosed based on excluding other possible aetiologies. A diagnosis of sarcoidosis can only be made if there is evidence of microscopic granulomatous inflammation. To identify any pulmonary involvement and bilateral hilar lymphadenopathy, chest radiographs are usually employed.[15] In our case, a chest radiography ruled out the diagnosis of sarcoidosis.

If an oral cause for the formation of the granuloma cannot be identified, it is crucial to thoroughly assess systemic factors that could contribute to the development of the granuloma using complete clinical, pathological, and laboratory tests. Once

the cause is correctly identified, the prognosis for the condition is significantly improved.[8] In this particular case, after performing several diagnostic procedures including blood tests, chest radiography, and abdominal ultrasound, no conclusive results were obtained to provide clarity on the potential diagnosis for the formation of granulomas. In this case, generalized hyperplastic areas, as identified through clinical examination, and the absence of systemic findings suggested an idiopathic etiology.

The management of granulomatous lesions depends on the underlying etiology.[2] While various pharmacotherapies, such as topical and intralesional corticosteroid injections and systemic immunosuppressants, are recommended for treatment, it is essential to identify and address the etiological factor. The choice among these different therapies and agents was based on the patient's systemic conditions, preference, and the expertise/experience of the attending clinician.[16] In this case, the absence of knowledge regarding the etiology limited our ability to plan an effective treatment strategy; therefore, regular follow-ups were planned.

The existing literature does not guide the appropriate length of follow-up for cases when idiopathic granulomatous lesions are present. The literature recommends regular follow-up cases with idiopathic granulomas, particularly in young patients, since Crohn's disease may develop symptoms over time.[13] Given the patient's age and the absence of a definitive diagnosis, a comprehensive follow-up strategy, including frequent periodontal control and, if required, further periodontal treatments was deemed appropriate.

CONCLUSION

While it is uncommon, it is advisable to consider granulomatous disease as a possible diagnosis when encountering gingival hyperplasia in the oral region. A comprehensive clinical evaluation, a meticulous anamnesis, scheduled maintenance procedures and periodontal treatment aimed at eliminating biofilm, in conjunction with histopathological examinations are imperative for an accurate diagnosis.

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