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Case Report

Exploring Gingival Overgrowth Due to Epileptic Medication: A Case Report

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ABSTRACT

Background: Gingival tissue hyperplasia is a condition that affects oral hygiene, aesthetics, and quality of life. Commonly associated with the use of some antiepileptic drugs (AEDs) like phenytoin and sodium valproate, this condition has become a normal occurrence in patients who take ATPs for seizure management because of the side effects that come along with the adverse tissues' growth.

Case Presentation: A 21-year-old female who had been taking sodium valproate to control her seizures developed severe gingival overgrowth. The clinical exam showed significant overgrowth in the anterior gingival area and with the overgrowth came inflammation along with symptoms of bleeding and bad breath (halitosis). The initial intervention of the problem (overgrowth) was some steps to improve oral hygiene with the use of some chlorhexidine mouthwash along with a short course of some antibiotics. But because of the severity of the overgrowth, surgical intervention to excise some of the overgrown tissue was performed. The tissue that was excised had a histopathological exam that confirmed the diagnosis along with giving some information for the changes in the tissue (cellular) to help understand the condition.

Conclusion: This case highlights the importance of a multidisciplinary approach in managing DIGO, which includes regular dental monitoring, improved oral hygiene practices, and surgical interventions when necessary.

Keywords: Antiepileptic drugs, Gingival enlargement, Oral hygiene, Phenytoin, Sodium valproate.

BACKGROUND

Gingival enlargement, commonly known as gingival hyperplasia or hypertrophy, is an increase in the volume of gingival tissue due to either cellular proliferation (hyperplasia) or tissue expansion (hypertrophy) [1]. Gingival enlargement is caused by a variety of factors including adverse drug effects, inflammatory processes, neoplastic changes, and other genetic conditions as hereditary gingival fibromatosis [2]. Among drug-induced cases, the major contributors are anticonvulsants, notably phenytoin [3]. Other drugs include calcium channel blockers, such as nifedipine, and immunosuppressants, including tacrolimus and cyclosporine. The antiepileptic drug phenytoin has a very well-documented association with gingival overgrowth in those patients who rely on the drug for their epilepsy treatment [4]. Epilepsy is a chronic neurological disorder that affects about 1 percent of the world's population. In 1939, Merritt and Putnam introduced PHT, the first effective antiepileptic drug, marking a new era in epilepsy treatment [5]. However, the side effects of the drug, like gingival enlargement, present a major dental health problem. The principal conservative management of drug-induced gingival enlargement is always the maintenance of good oral hygiene, control of plaque, and, if possible, discontinuation of the causative drug. Surgical removal of overgrown tissue can be performed in cases where conservative treatment fails [6].

Pathophysiologically, Seymour et al. (1996) reported that genetic predisposition forms part of the contributing cause in drug-induced gingival overgrowth (DIGO). Drug interactions with gingival fibroblasts cause overgrowth of connective tissues and increase inflammation, thereby leading to increased levels of interleukins such as IL-6, IL- 1, and IL-8 [7]. Mechanistically, the interference with extracellular matrix formation occurs due to the inhibition of calcium and folic acid absorption; hence, phenytoin enhances the synthesis of collagen and the activation of the fibroblast by decreasing collagenase activity [8]. The inflammatory mediators, such as connective tissue growth factor, platelet-derived growth factor, and transforming growth factor-beta, that induce the immune responses and cellular activities associated with gingival overgrowth are increased by the presence of dental plaque [9]. This drug-induced gingival enlargement most often occurs in adolescents and children, and there is a high incidence of the same in the anterior gingival tissues [10]. Of all the drugs involved, it is seen most frequently with phenytoin, cyclosporine, and nifedipine. The highest incidence was, however, noted with phenytoin. As mentioned in different studies, 50% of the drug-induced gingival overgrowth occurs with phenytoin, 30% with cyclosporine, and 20% with nifedipine. This pattern emphasizes oral surveillance and monitoring with management for those on these drugs, especially the younger age group [11-12]. This case report describes the clinical presentation, etiology, and treatment plans for the gingival enlargement caused by antiepileptic drugs, especially those that include phenytoin, and therefore is able to provide an understanding of how the patients are managed.

CASE PRESENTATION

A 21-year-old female patient had been attending the Department of Dentistry, IPGME&R SSKM Hospital with the complaint of swelling in the anterior gingival region accompanied by hemorrhagic gums and halitosis. Her medical background was on sodium valproate for epilepsy for a period of 6-7 years.

Clinical Findings

Intraoral examination revealed a nodular enlargement in the interdental papilla of the lower anterior region covering more than two-thirds of the affected teeth [Figure 1].

The gingival tissue was bluish-red and bled during examination. Initial management consisted of instructions for improved oral hygiene and a prescription for 0.12% chlorhexidine mouthwash. After a week, she was followed up on. Up to then, full-mouth subgingival ultrasonic scaling, along with five days of antibiotics, was done. She was given suturing of the lesion with 3-0 BBS, along with vascularity that was reduced and kept under observation.

Figure 1: Pre-Operative Photograph of the Patient

Surgical Interventions

A complete hematological examination was performed, and the parameters came out to be normal. Local anesthesia was given along with the assessment of the periodontal pockets through a WHO probe. A continuous incision was done with a BP blade no. 15. The hypertrophic gingival tissue was curetted away to ensure a healthy keratinized gingival base for ideal healing. Primary hemostasis was achieved with electrocautery, and a COE pack was applied [Figure 2A, 2B]. The excised tissue was taken in formalin for biopsy, and the patient was advised to return after a week for follow-up. [Figure 3].

Figure 2 A: Primary hemostasis achieved with electrocautery

2B: COE pack applied

Figure 3: Post Op photograph after surgical intervention

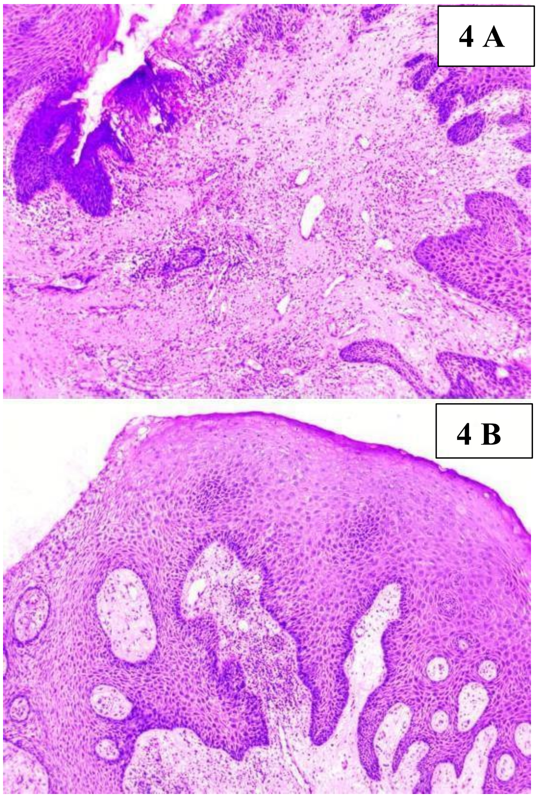

Figure 4 A: Photomicrograph showing hyperplastic squamous epithelium with areas of focal ulceration and inflammation (H&E staining, magnification x100).

Figure 4 B: Higher magnification view of the connective tissue revealing collagen fibers with prominent fibroblasts, plasma cells, and lymphocytes, indicating an inflammatory infiltrate (H&E staining, magnification x200).

Histopathological Examination

The excised tissue was a whitish nodular mass measuring 1 x 1.5 cm. It was subjected to a histological examination. With H&E staining, the presence of hyperplastic squamous epithelium with areas of focal ulceration, inflammation, subepidermal edema, and congestion was detected. The connective tissue revealed collagen fibers with prominent fibroblasts, plasma cells, and predominantly seen lymphocytes [Figure 4A, 4B].

DISCUSSION

The side effect of drug-induced gingival enlargement is well documented with drugs prescribed for angina pectoris and hypertension (calcium channel blockers), for epilepsy (anticonvulsants), and for organ and tissue transplantation (immunosuppressants). Poor oral hygiene, plaque, and other periodontal conditions increase the risk of overgrowth of the gingival tissue. The hyperplasia of the gingiva is caused by changes in the tissue and fibroblast activity of the connective tissue, along with changes in calcium metabolism and metalloproteinases responsible for the alteration of collagen.

The enlargement of the gingiva can negatively affect one's quality of life. The overgrown tissue hampers some routine activities of life such as eating food and talking, and at the same time, it can affect one's facial characteristics, thereby having a psychological impact accompanied by depression. The inflammation of the gingiva caused by drugs can be resolved with the use of some conservative treatments such as the use of antibiotics, chlorhexidine mouthwash and also be coupled with the preventive discontinuation of drugs, if applicable. In the absence of a reduction of the enlargements managed with oral care (i.e., oral hygiene, maintenance of a high standard of oral hygiene), gingivectomy is recommended [12-14].

In managing drug-induced gingival overgrowth, conservative measures are necessary, such as thorough oral hygiene and plaque control, which are often not effective on their own in advanced cases. Mavrogiannis et al. state that in cases with advanced gingival conditions where conservative measures are not sufficient, surgical approaches are required to adequately balance and restore aesthetic and functional gingival health. This is especially relevant in patients that are on antiepileptic drugs for extended periods of time, as medically it is not possible to discontinue these medications.

The mechanisms of actions of these drugs, especially antiepileptics like Phenytoin, are particularly complex at the level of the gingival fibroblasts. Anil et al. describes how these factors contribute to overly active fibroblasts which are associated with excessive connective tissue inflammation hyperplasia and inflammation. Thariny provides a comparison between drug-induced gingival enlargement and hyperplasia caused by dentally related inflammation. Drug-induced cases are unique in that they have distinct histopathological patterns such as excessive proliferation of fibroblasts with inadequate collagen resorption, thus contributing to the enlargement.

Histologically, DIGO/in DIGO displays marked changes in connective tissue, with an increase in fibroblasts and collagen and fibroblasts and collagen deposition, as seen in investigational studies on cyclosporin and tacrolimus [14,15]. This correlates with the findings from this case, in which histopathology revealed hyperplastic epithelium with fibro-inflammatory changes. These findings point to the importance of collaboration across different fields for patients on multi-drug therapies known to induce changes within the gingiva and balance potential health benefits with increased risk of detrimental oral health issues.

CONCLUSION

This case brings to light the importance of multidisciplinary approach to the management of drug related gingival overgrowth. To counter the effects of antiepileptics and promote the the patients well being, regular dental check ups, improved oral hygiene, and, if necessary, dental surgery are recommended. To achieve the best possible quality of life for these patients, the integration of medical care required to manage epilepsy and the oral care required poses a unique challenge.

PATIENT PERSPECTIVE

A 21-year-old woman with an overgrowth of gingiva secondary to sodium valproate use for epilepsy is worried about her oral health and appearance. At first, the swelling of the gingiva and the bleeding, along with the halitosis, caused her serious discomfort and embarrassment. The discomfort and embarrassment were compounded, in her case, because of the changes to her self-confidence associated with the negative impact on the appearance of her smile.

There is relief in knowing that overgrowth is a common side effect of epilepsy medications and that there are available options for treatment.

Certainly, oral hygiene was improved as the patient complied with the prescription of chlorhexidine mouthwash and antibiotics for the control of inflammation. There were overgrown tissues that were to be surgically excised as an integral component of the treatment, and her involvement in the decision was appreciated.

Postoperatively, the patient stated she was much more satisfied with her oral health and was more confident than she was preoperatively. The decrease in swelling and bleeding, and the appearance of her smile, made her feel more comfortable with her smile. The patient was thankful for the collaborative care and the positive change in her health and oral health, and the change in her overall quality of life.

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Ethical Approval: Institutional Review Board approval was not required.

Declaration of Patient Consent: Written informed consent was obtained from the patient prior to initiating the treatment. The patient was fully informed about the nature of the ceramic veneer procedure, the potential risks and benefits, and the expected outcomes. Consent was also obtained for the publication of the case report, including the use of anonymized clinical photographs and information for educational purposes.

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AUTHOR CONTRIBUTIONS:

1. Srimayee Chaudhuri: She was responsible for conceptualizing the study, carried out the clinical examination, and was responsible for the patient management as well as drafting and editing the manuscript. Srimayee also played the most important role in reviewing and coordinating the multidisciplinary collaboration and the treatment strategy.

2. Rahul Sarkar: Had a role in the clinical management of the patient, which also included the surgical procedure, and he did the literature review. In writing the manuscript, he was responsible for the discussion and results parts also.

3. Kaynat Parween: Contributed to the role in the patient care as well as the follow-up which also included assisting the surgical intervention and she also was part of the data collection, the analysis, and the manuscript writing especially in the methodology part.

ABBREVIATIONS USED IN THE STUDY:

a) **DIGO -** Drug-Induced Gingival Overgrowth
b) **PHT -** Phenytoin (anticonvulsant drug)
c) **WHO -** World Health Organization
d) **H&E -** Hematoxylin and Eosin (staining method used in histopathology)
e) **IL -** Interleukin (cytokines involved in inflammation)
f) **COE -** Coe Pack (used for packing the surgical site)
g) **BBS -** Black Silk Sutures (used for suturing the lesion)
h) **PVS -** Polyvinyl Siloxane (material used for impressions)
i) **PB -** Periodontal Blade (used for tissue incision)
j) **CBCT -** Cone Beam Computed Tomography (if applicable)
k) **ECG -** Electrocardiogram (if applicable)

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