

A BIZARRE DYSPLASIA OF THE GINGIVA - CASE REPORT WITH REVIEW OF LITERATURE

Authors:

Nadah Najeeb¹
Anoop Mathew²
Nisha U³
Rajesh Raj P⁴
Senior lecturer¹

Department of Oral medicine and Radiology
Indira Gandhi Institute of Dental Sciences
Nellikuzhi P. O., Kothamangalam, Kerala 686 691

Reader²
Department of Oral medicine and Radiology
Indira Gandhi Institute of Dental Sciences
Nellikuzhi P. O., Kothamangalam, Kerala 686 691

Lecturer³
Department of Oral and Maxillofacial Pathology
and Microbiology
Indira Gandhi Institute of Dental Sciences
Nellikuzhi P. O., Kothamangalam, Kerala 686 691

General Practitioner⁴
Karunya Dental Clinic
Pulinknu, Alapuzha

Correspondence Author

Dr Nadah Najeeb
Senior lecturer
Department of Oral medicine and Radiology
Indira Gandhi Institute of Dental Sciences
Nellikuzhi P. O., Kothamangalam, Kerala 686 691
email: nadahsiyad85@gmail.com

ABSTRACT

Gingival enlargement is currently used to describe medication-related gingival overgrowth or hyperplasia, a reactionary phenomenon that occurs with the use of several types of therapeutic agents, chiefly antiepileptic drugs. This disorder was recognized since 1939, shortly after the introduction of phenytoin. Along with the review of literature we are also giving a case report of a female patient with gingival enlargement as an paradigm.

Keywords: Drugs, Gingival enlargement, Phenytoin

INTRODUCTION

Drugs used locally or systematically can induce several changes in the micro and macroscopic tissues.¹ These drugs may be of therapeutic use but may cause adverse effects of other body organs or systems and one such conflicting effect is the overgrowth of the gingival tissues.

“Gingival Enlargement “is a term used to describe medicine - related gingival overgrowth. Gingival hyperplasia is defined as an abnormal growth of the periodontal tissue.² But the latter is discontinued as by histopathology this cannot be accepted now as hyperplasia merely means increase in the number of cells but enlargement is caused due to the increase in the extracellular volume of the cells.

Drug induced gingival enlargement due to the chronic use of phenytoin was first described by Kimball in 1939.² In 1948 Brandon hypothesized that phenytoin had direct effect on the gums. In 1975, Angelopoulos commented that phenytoin induced degranulation of mast cells lead to increased collagen formation. Larmas in 1976 said that phenytoin caused the proliferation of the basal cell layer which increased the epithelial connective tissue interface and this was later confirmed by Hassel et al. Saito et al in 1999 postulated that there is p53 expression in drug induced gingival overgrowth which proved that this is associated with DNA abnormalities.³

Here we are also affixing a case report of a 60 year old female patient affected with this aesthetically, functionally and psychological disturbance seeded due to prolonged use of anti epileptic drugs.

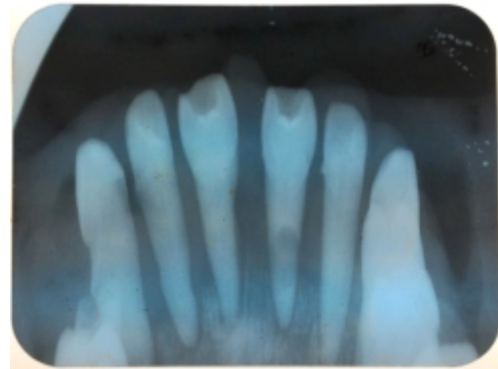
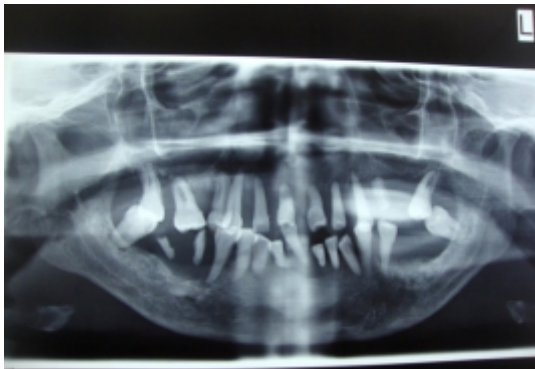
CASE REPORT

A 60 year old female came to our department with a chief complaint of swollen gums in the upper and lower jaws which she had been noticing for the past 1 year. The swelling was initially insignificant which has now increased to the present since the last 2-3 months. She experienced mild pain especially while having food & brushing and also had a unsatisfactory malodor in the last 2 months. She also complained of bleeding while brushing and hence used mouthwashes for cleaning teeth. Since the patient was a psychiatric patient most of the details were given by the bystanders. Patient had a lean built and was malnourished.

She was under psychiatric medication for seizures since the last 35 years. She had been hospitalized several times for the treatment of multinodular goiter, seizure disorder, depression illness, mitral regurgitation and bronchiectasis and was also under various medications. Multiple surgeries were conducted and there was history of hysterectomy, cheiloplasty and surgery for a neck swelling. Drug history revealed that she is allergic to an unknown drug.

Extraoral examination revealed an abnormal face with bimaxillary protrusion and incompetent lips. On intraoral examination there is severe generalized bulbous swelling of the gums which was also edematous. Obliteration of the buccal, labial and lingual vestibule was seen. Almost 2/3 rd of the teeth were covered resulting in the displacement of the teeth with midline shift. On palpation all inspeactory find-





ings were confirmed and there is bleeding present with tenderness. Grade III mobility of almost all teeth was present. Provisional diagnosis was given as leukaemia, granulomatous enlargement and drug induced gingival enlargement.

OPG and Maxillary and mandibular occlusal radiographs revealed severe generalized horizontal bone loss and adequate spacing between the teeth giving a floating teeth appearance. Haemoglobin levels showed that she was anaemic with a value of 10.8 mg. Blood glucose level was 134mg/dl. Biopsy was advised for this patient where the histopathological analysis came as Drug induced Gingival enlargement with inflammatory changes. Later gingivoplasty was also done.

DISCUSSION

The periodontium comprises of tissues that surround and support the teeth.¹The gingiva is a pink or pigmented mucous membrane cover that wrap tightly around the teeth and provides anchorage to the dental arches.² Histologically there is presence of epithelial and connective tissue layer with fibroblasts and the extracellular matrix is predominantly made up of collagen fibres and glycosaminoglycans. The periodontal ligament is a connective tissue layer that surrounds the dental root region and link the cementum to the alveolar bone allocating more functions. The cementum is a hard tissue structure similar to that of the bone. The alve-

olar bone is a supporting structure that provides anchorage to the teeth due to the attachment of the periodontal fibres.⁶

The etiological factors of gingival enlargement comprises of inflammatory factors which include the poor oral hygiene and periodontal diseases¹, idiopathic, various drug induced neoplasias including antiepileptic drugs, genetic changes, hereditary gingival fibromatosis and also the nutritional and hormonal disturbances. These can cause aesthetic changes in an individual with accompanying symptoms like tenderness, pain, bleeding, abnormal tooth movement, problems in speech and in occlusion which further ushers periodontal disorders.² Congenital gingival enlargement includes the fetal valproate syndrome.⁵

But still for gingival enlargement the major causative factor was phynetoin. Currenly, more than 15 drugs have been identified including oral contraceptives, antihypertensives calcium antagonists and immunosupprants chiefly cyclosporins.² One basic factor in all these drugs is that it affects the cellular calcium metabolism. Since the formation of the fibroblasts is modulated by calcium these drugs will affect the collagenase activity leading to inactive forms of collagen thus paving way for increased extracellular matrix.

In one study it was said that a subtype of fibroblasts called “responders” is affected which is highly sensitive to these calcium biased drugs.¹ This decrease in the calcium causes a decrease in the folic acid

uptake causing folate deficiency leading to altered production of collagenase² by the fibroblasts and thus leading to increased over accumulation of collagen causing the increased bulk of the connective tissue.⁵

Phenytoin use is also related to increase in the number of the langerhans cells which can cause a increase in the interleukin 2 and tumor necrosis factor.⁷ But the malignant transformation rate has not yet been reported.

The clinical features of the growth may commence during the first three months after the initiation of the therapy especially the thickening of the pappillary and the marginal gingival of the labial surfaces of anteriors developing to lobules and reaches the maximum severity in the twelfth to eighteenth month.⁸ The enlargement of the gingival tissue ideally begins in the area of interdental papillae which then spreads laterally to the adjacent areas. If there is adequate plaque control then there will be minimal bleeding with firm gingival consistency and healthy colour. But if the enlargement is associated with bacterial inflammation then the colour will turn reddish to purple.⁹ From this can be understood that the bacterial plaque can cause the alterations in the periodontal tissue environment and the systemic factors can enhance the pathological conditions in the underlying connective tissues.¹ The extension of the enlargement depends on the dose, duration of the drug being used. The growth may occur gradually and sometimes in severe cases coverage of the entire tooth is noted with associated displacement of the teeth.² The gingival growth along with the deepening of the sulcus can act as a nidus for the bacterial growth which can aggravate the gingival inflammation.¹ The deepening of the sulcus caused due to plaque can also act as a reservoir for the abused drugs.³

This usually affects the young individuals between the age group of 8 - 13 years who are on dilantin therapy but people of all age groups can be affected.³ Both sexes are affected equally but some studies have shown that males are affected three times more when compared to the females.⁵ Children born to the affected mothers can also be affected.

This can be a serious problem which can aggravate the psychological symptoms of the patients as enlarged gingival can affect the esthetic concern of the patient.⁵

Phenytoin (dilantin) was first introduced in 1930s by Merrit and Putnam, and this has acted as the drug of choice as an anticonvulsant in the treatment of grand mal, temporal lobe, and psychomotor seizures.⁶ The common adverse effect of this drug was gingival hyperplasia of varying degrees. Long term phynetoin use can also cause enlargement of the lips and thickening of the face and scalp.⁷ Incidence rates are found to be 3 - 93 % among the drug users.⁸

Nifedipine a calcium channel blocker commonly used for cardiovascular diseases blocks the influx of calcium into the cardiac muscles.¹ This can cause a decrease in the contractile process of the cardiac muscles thus decreasing the arterial blood pressure. Ramon et al, Heijl et al. and Shaftic et al. reported the prevalence of overgrowth as 0.5 to 83% for nifedipine users. The drug interferes with the calcium metabolism of fibroblast cells and hence reduces the production of the degrading enzyme collagenase. This drug affects the protein synthesis of the fibroblasts.⁵ The prevalence rate is 10%.⁹

Immunosupprants like cyclosporine used for organ transplants also cause gingival enlargement. The prevalence rate is 30%.⁹

Gingival enlargement can be measured by 3 methods.⁸ The cast method, photographic method and the clinical measurement method. According to Bokenkamp⁸ (1994)

Grade 0 - no signs of clinical inflammation

Grade 1 - Enlargement confined to the interdental papilla

Grade 2 - enlargement involves the papilla and the marginal gingiva

Grade 3 - Enlargement covering three quarters or more of the crown of the teeth

Generally Drug induced gingival overgrowth begins as a bead like enlargement of the interdental papilla

affecting the attached gingiva also in the later stages.⁸

The differential diagnosis includes the hereditary gingival enlargement but this is an autosomal dominant trait with a strong family history.¹ Leukaemic infiltration is usually associated with secondary inflammation and so there will be associated bleeding.⁴ Tuberculosis and other granulomatous diseases, including orofacial granulomatosis, Crohn's disease, and sarcoidosis, can also mimic drug-induced gingival enlargement.

The first line in the management is the cessation of the drug but this does not cause a regression of the enlargement.¹ But in long standing cases regression may not take place even on cessation of drug. This had been noticed for 1 year in a study.⁵ Somacarrera et al reported that an alternative of the drug can be given to reduce the symptoms.⁵ Periodontal treatment which includes both the personal and professional care is advised to control the inflammation supplemented with chlorhexidine mouthwashes and folic acid applications.⁶ Mechanical removal of the plaque, calculus can control the inflammation.⁷ A healthy oral environment will help to avert the local microflora eliminating the major focus of infection.⁸ For severe cases surgical excision either by gingivectomy, gingivoplasty or periodontal flap approach is done.⁹ Laser therapy have also proved to be a boon mainly because of its postoperative haemostasis.

Hassan et al suggested that azithromycin toothpaste is an effective, simple and noninvasive treatment for cyclosporine induced GO. Prasad et al. concluded that systemic folic acid prescribed along with phenytoin delays the onset and reduces the incidence and severity of gingival overgrowth.¹ There was a case of relapse in 3 months of the surgical therapy but with proper home care and chlorhexidine mouthrinses the enlargement can be controlled with a 3 month follow up.²

Certain examples of the drugs that cause gingival enlargement.

Anticonvulsants	Phenytoin Mephynetoin Valproic acid Ethosuximide Phensuximide Mesuximide
Calcium channel blockers	Amilodipine Felodipin Nicardipin Nifedipin Nisoldipin Verapamil
Immunosuppressants	Cyclosporin A

CONCLUSION

It is therefore very important that not only neurologists but even the dentists must apprehend the potential conflicting etiology of this aesthetically disfiguring condition and its characteristic features to prevent, diagnose and successfully manage it. Then physicians, general practitioners and dentists must coordinate together for a concise treatment plan that is beneficial to the patients.

REFERENCES

1. Gingival Overgrowth And Drug Association: A Review, M. B. Mishra et al, Indian Journal of Medical Sciences, Vol. 65, No. 2, February 2011
2. Katia Lin (2007), Drug induced gingival enlargement- Antiepileptic Drugs: Not Only Phenytoin is Involved, Clinical, Psychosocial and Scientific Note, Journal of Epilepsy and Clinical Neurophysiology, 13(2):83-88,
3. Drug induced gingival overgrowth, Balasubramanian Thiagarajan (2012), Webmed Central 3(11), Otorhinolaryngology, Article id :WMC003829

4. Moghareh Abed et al, Gingival Enlargement: A Review Article, AJDR 2012; Vol.4, No.2
5. Kumar et al , International Journal of Pharmacology & Toxicology Science vol. 1, Issue 1, 2011, 34-42 , DRUG INDUCED GINGIVAL HYPERPLASIA : AN UPDATED REVIEW
6. Management of Drug Induced Gingival Enlargement, Barbara Ann et al, Australian prescriber, Vol 26 , No 1, 2003, Pg 11-13
7. Drug Induced Gingival Overgrowth and Its Tentative Pharmacotherapy – Review Article, Hirako Matsumoto, Japanese Dental Science Review, 2010,46,Pgs 11-16
8. Smitha rani et al, Unusual Clinical Presentation Of generalized Gingival Enlargement, A Report of 3 cases, Vol 4,No 4,2012, International Journal of Colaborative Research on Internal Medicine & Public Health.
9. William M (1999), Role of Drugs in the pathogenesis of the gingival overgrowth- A collective review of the currant concepts, Periodontology 2000, Vol 21, Pgs 176-195