Drug induced gingival enlargement in a Stroke Patient - A Case Report

Dr Sruthy Prathap

Additional Professor
Department of Periodontology
Yenepoya Dental College

Dr Prathap M.S

Professor and Head
Department of Conservative Dentistry and Endodontics
Yenepoya Dental College

Dr Santhosh Kumar.C

Senior Dentist and General Practitioner

Drug-induced gingival overgrowth (DIGO), also referred to as drug-induced gingival enlargement, and previously known as drug-induced gingival hyperplasia, is a noted side-effect of certain drugs given for non-dental uses where the gingival tissue is not the intended target organ. Drug-induced gingival overgrowth (DIGO) is a pathological growth of gingival tissue, primarily associated with calcium channel blockers and immunosuppressants. The key offending drug classes are anticonvulsants, immunosuppressants, and calcium channel blockers.Consequently, it is mainly seen in cardiovascular and transplanted patients. Gingival overgrowth impedes proper dental hygiene and, apart from the cosmetic damage, causes painful chewing and eating.[1,2,3]

ETIOLOGY

Drugs are the most common reason behind gingival enlargements. DIGO is a side effect seen in patients taking anticonvulsants, immunosuppressants, or calcium channel blockers. It is associated with the patient's genetic predisposition and the presence of existing plaque or gingival inflammation.

Cardiovascular and transplanted patients are at particular risk due to the extensive use of CCBs alone or in combination with immunosuppressants. Significant variability among patients medicated with the same drugs is observed, indicating the importance of additional risk factors involved in the pathogenesis. Genetic factors, male gender, bacterial plaque, and gingival inflammation are associated with increased DIGO risk. Aside from the cosmetic effect, which is the most apparent feature, patients who develop DIGO experience difficulty maintaining oral hygiene, pronunciation, and mastication. Simultaneously, the extensive disease can cause pain and loss of the teeth. As a result, quality of life is reduced significantly. Since this side-effect is not rare in a group of cardiovascular patients, oral health needs to be emphasized and included as part of a care plan for patients treated with the drugs mentioned above.[4,5]

Histopathology

The histopathology for drug-induced GO (DIGO) is consistent, in which the epithelial layers showed elongated rete pegs, proliferation, acanthosis, and parakeratosis. The underlying connective tissue showed an abundance of ground substance, reduced myxomatous changes, pronounced inflammatory cells, and dense collagen bundles with active fibroblasts . In an isolated case report on NIGO, they found marked epithelial hyperplasia, acanthosis, and moderate inflammatory reactions in the lamina propria. In a study involving a 53-year-old hypertensive female on 20 mg of nifedipine daily, the patient presented with generalized GO covering almost all of the clinical crowns. The histopathological report presented stratified squamous epithelium with hyperplasia and acantholysis; the underlying fibrocollagenous connective tissue showed dense mixed inflammatory infiltrate with congested blood vessels. Histopathological observations were similar when comparing the first report of DIGO and the most recent report[6]

Pathophysiology

The exact mechanism behind DIGO has not yet been determined. However, there have been several theories and experimental hypotheses. Two main pathways have been proposed in the literature: an inflammatory and non-inflammatory mechanism. According to the literature, the mechanism for GO caused by CCBs was first proposed by Nyska and co-workers in 1994. Nyska proposed that when CCBs are administered orally, their pharmacotherapeutic effect lowers the blood pressure and, in turn, signals the release of renin and angiotensin-converting enzyme. The angiotensin, which generally would produce aldosterone, is blocked by the calcium ions of the drug, which causes a diversion into another unblocked metabolic pathway. This pathway leads to the overproduction of androgens and adrenocorticotropic hormone (ACTH), which induces hypertrophy of the kidneys. This overproduction in androgens is suggested to act on the gingival tissue and stimulate fibroblast proliferation and collagen production, resulting in GO.[7,8]

The classification of GO has been defined in the literature several times over the last century. The most commonly known classifications are Angelopoulos and Goaz Index (1972), hyperplastic index (1985), Bokenkamp classification (1994), and Ingle classification (1999). These classifications vary in their definitions, whether in the nature of the GO or in the direction of overgrowth. Angelopoulos and Goaz described an index that measured the vertical relationship of gingival tissue on the clinical crown: Grade 0: no GO, Grade 1: overgrowth covering cervical third of clinical crown, Grade 2: overgrowth extending to the middle of the clinical crown, Grade 3: overgrowth covering two-thirds of the clinical crown. As defined by Seymour etal (1994), the hyperplastic index assesses GOs based on their vertical and horizontal relationship with the clinical crown: Grade 0: absent gingival hyperplasia, Grade 1: blunting of margin, Grade 2: hyperplasia less than two-thirds of the clinical crown, Grade 3: hyperplasia more than two-thirds of the clinical crown. The disadvantage with this index is that it is non-specific and vague. Classifying GOs in this index may be confusing. Bokenkamp's 1994 classification is similar to Seymour's hyperplastic index; however, it is more specific and defined: Grade 0: no sign of gingival enlargement, Grade 1: enlargement confined to the interdental papilla, Grade 2: enlargement involving marginal and papillary gingiva, and Grade 3: enlargement diffused and covering almost the entire crown. The most updated and commonly used index in 2021 is Ingle's 1999 classification, which defined GO in a cohesive and precise manner: Grade 0: no overgrowth, slight stippling, and knife-edge papilla; Grade 1: increase in the density with marked stippling, papilla is rounded, and probing depth is equal to or less than 3 mm; Grade 2: moderate overgrowth, size of the papilla is increased and/or rolled margins, gingival enlargement has a buccolingual dimension of up to 2 mm, probing depth is equal to or less than 6 mm; Grade 3: marked overgrowth, the contour of the margin is convex, enlargement has a buccolingual dimension of approximately 3 mm or more, probing depth is greater than 6 mm, the papilla is retractable; Grade 4: severe overgrowth, thickening of the gingiva, large percentage of the crown is covered, the papilla is retractable, probing depth is greater than 6 mm, and buccolingual dimensions are approximately 3 mm.[8]

Case Report

A 65 year old patient reported with a chief complaint of swollen gums with spontaneous bleeding.On medical history patient gave a medical history of stroke 6 months back and patient also revealed a history of hypertension for the last 20 years. Patient was under antihypertensive drugs(Calcium channel blockers) for last 20 years.

General examination: Patient had difficulty in walking , with altered posture and gait. Patient was paralysed partially and needed support for walking.Upperlimbs were also had limited movement.

Oral examination revealed generalized gingival enlargement and spontaneous bleeding while probing. The colour of the gingiva was purplish red. The gingiva presented with both sessile and pedunclated swelling. The teeth showed varying degrees of mobility and presence of deep pockets and associated with attachment loss and bone loss.

The patients had a poor oral hygiene score with abundance of calculus and debri. Severe halitosis was also detected.

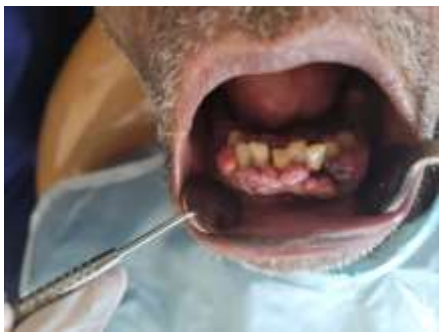

Fig (a)

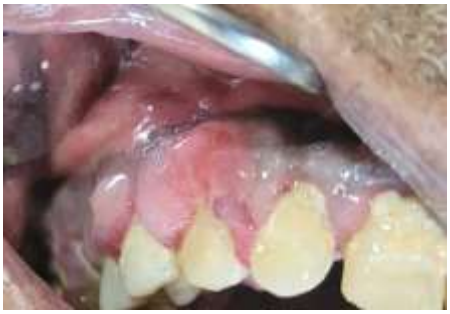

Fig (b)

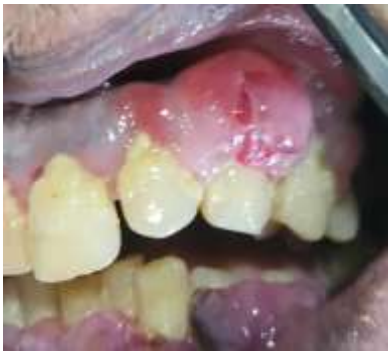

Fig (c)

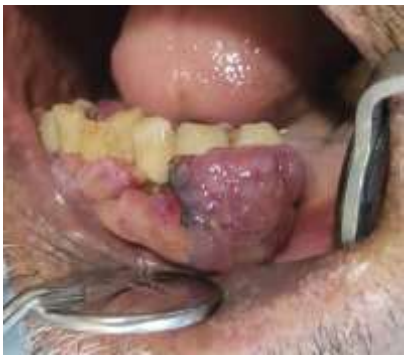

Fig (d)

Treatment Approaches

The primary treatment for GH is simple. CCBs should be discontinued. Often, this is sufficient to reduce the level of hyperplasia. There are instances, however, in which hyperplasia does not decrease after discontinuing medication. In these cases, surgical intervention is recommended with either a gingivectomy or a periodontal flap. If the drug is eliminated, hyperplasia should not recur.Management of DIGO can be conservative or surgical, with the aim to provide a satisfactory cosmetic outcome and minimize discomfort and pain. Non-surgical methods are the treatment of choice, including proper oral hygiene and mechanical removal of dental plaque, together with the mandatory exclusion of the offending drug. Periodontal treatment reduces inflammation and prevents the need for surgical treatment in cyclosporin-treated patients. A rigorous oral hygiene regime has been recommended for patients with DIGO resulting from CCBs use. Since a worse periodontal state has been associated with a higher risk for DIGO, preventive measures targeting oral health could be valuable. Reduction of drug dose or switching to that of a lower potential for side-effects should always be considered, if possible. In that case, complete improvement can be expected in 1-8 wk

Discussion

Calcium antagonists are substances that inhibit the flow of calcium ions through the slow channel membrane. The therapeutic consequences are the inhibition of myocardial contraction, depression of myocardial function, specifically generating potential slow (sinus and atrioventricular node, antiarrhythmic effect, bradycardia) and relaxation of smooth muscle, particularly in the vessels, with vasodilator effect.

The volume of hyperplasia depends on the daily dose (more than 10mg), the time of administration, gender (men are more likely than women) and the presence of plaque and local irritation factors (decays, the incorrectly dental bridges) [3].

The mechanism by which GH occurs is not known, though there are several theories. First, CCBs can induce up-regulation of keratinocyte growth factor. Second, decreased folic acid uptake decreases the secretion of collagenases and may cause collagen to build up in the gingiva. And third, decreased calcium influx reduces T-cell proliferation, impairing immune function and allowing uncontrolled bacterial growth. It is unclear whether these mechanisms are isolated or whether they occur concurrently to cause GH.[10,11]

The true prevalence of GH is not clear. In the literature, there is no reported racial or sexual bias,some believe that the severity of GH is greater in younger patients.[12]

CONCLUSION

This case report adds another example of DIGO to the literature. In some populations, like those without access to dental care, the prevalence may be quite high.

The poorest patients are at the highest risk for DIGO and suffer the greatest injury due to a lack of access to dental care to prevent and treat this condition. By educating our patients about the risk for AIGO, NPs can prevent this iatrogenic disease and reinforce our trustworthiness as stewards of good health.

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