DRUG INDUCED GINGIVAL OVERGROWTH

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INTRODUCTION:

Drug induced gingival overgrowth is associated with a prolonged use of certain drugs. The excess gingival tissues that result from drug interactions is neither a hypertrophy nor hyperplasia and hence best referred to as gingival overgrowth (Goldman, Cohen 1990). A variety of oral manifestations can develop as a result of use of drugs. Earlier one such manifestation was termed as "stomatitis medicamentosa".

Aetiology - It has multifactorial aetiologies. It is frequently associated with inflammatory changes in the gingiva. It may be inflammatory, drug-induced, neoplastic, or enlargement associated with systemic diseases1.

The Drug-induced gingival overgrowth (DIGO) is the adverse effect of systemic administration of: -

1. Anticonvulsant: Phenobartbitone, Phenytoin, valproate and primidone2.
2. Calcium channel blockers: Nifedipine, amlodipine, and verapamil. Isradipidine which is a dihydropyridine derivative does not cause gingival overgrowth and can he used too replace nifedipine3.
3. Immunosuppressants : Often used as an immuno- suppressant in renal transplant patient4.
4. NSAIDS.
5. Hormones: Oral contraceptive Drugs.
6. Miscellanous: Sodium valproate, Erythromycin etc.

Clinical features – appears after 1-3 months of administration of drug. Gingival overgrowth usually starts as painless enlargement mainly in the interdental papilla that extends faclially and lingually which when merge causes difficulty in biting and mastication. Growth is generalized but more severe in anterior areas and is absent in edentulous areas. DIGO can occur even in mouths that have very good oral hygiene and vice versa. DIGO often impairs nutrition and also results in increased susceptibility to oral infection, caries and other periodontal diseases.

The presence of overgrowth makes plaque control more difficult and results in inflammation caused by bacterial challenge. **(Fig- 1)**

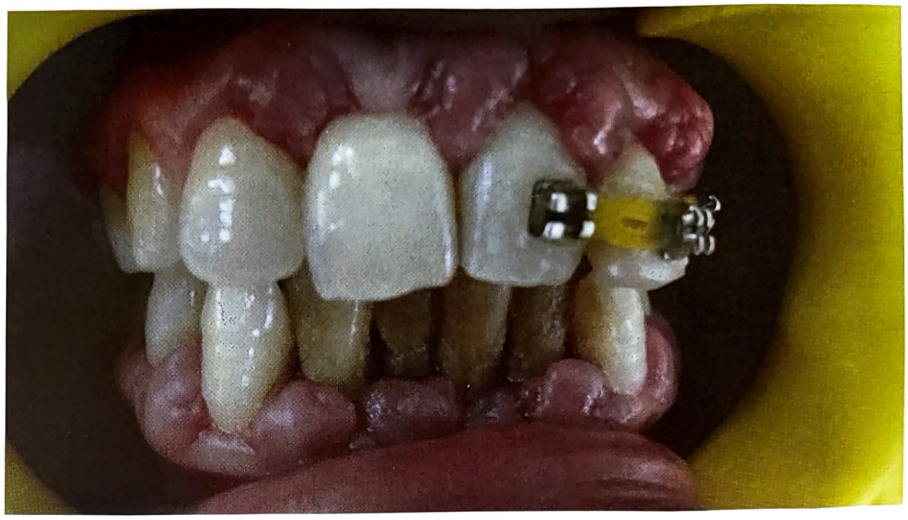

Figure 1

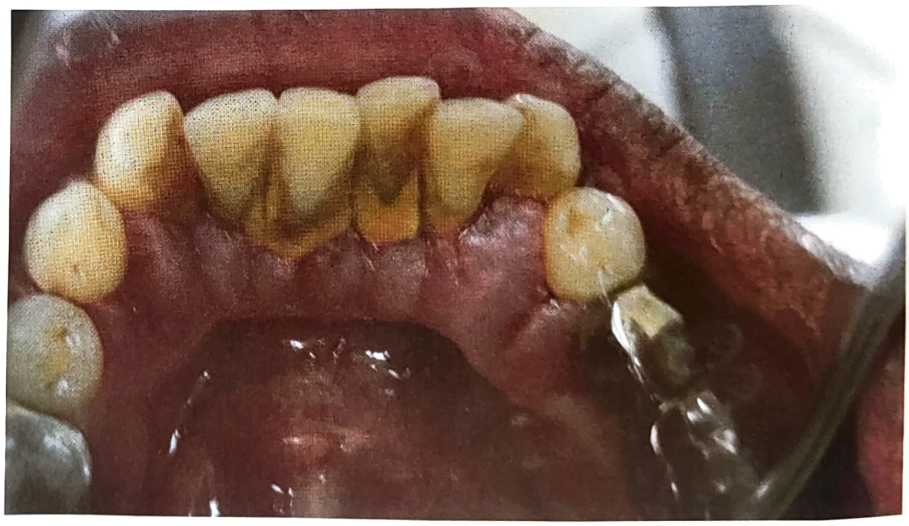

Figure 2

ANTICONVULSANTS

Of these three classes of drugs, phenytoin is the commonest cause and accounts for 50% of cases of DIGO. Patients on phenytoin have low serum level of folic acid. It may reduce the absorption of folic acid from GIT or block it's transport across intestinal epithelium & also inhibit folate reductase, which results in impaired maturation of epithelium, rendering connective tissue more susceptible to inflammation.5 The reduced folate levels have been one of the major factors promoting phenytoin induced gingival overgrowth.

Classification of gingival hyperplasia caused by Phenytoin (James R. Babocks (1974):

- Grade -I - minimal – no hyperplasia
- Grade –II – moderate -Definite hyperplasia of gingiva, with encroachment on the clinical crown of the teeth, but no interference of function.
- Grade III- severe- interfere with function due to overgrowth of tissue

Histological Classification Barak (1987)

- Grade I – Normal Gingiva - Width of epithelium - 0.3-0.5 mm.
- Grade II – Slight Overgrowth - Width of epithelium 0.5-1.5 mm.

- Grade III- Moderate Overgrowth –Width of epithelium 1.5-3 mm.
- Grade IV – Severe Overgrowth- Width of epithelium 3- 4 mm.

IMMUNOSUPPRESANTS

Cyclosporins are responsible for 30% of cases of DIGO.

Cyclosporine- Induced gingival overgrowth has been reported by different transplant centers varying from 7 to 80%. The incidence and severity may be dependent on genetic disposition and local and pharmacological factors.

Tacrolimus causes much less severe gingival overgrowth and is an alterative for cyclosporine.6

Calcium channel blockers

These drugs are the dihydropyridine derivatives (nifedipine), benzothiazine derivatives (diltiazem) and phenyalkylamine dervatives.7 Nifedipine is one of the most often used and cause enlargement in 20%of cases.

Risk factors for DIGO: -

- Age, gender
- Drug (dosage, duration, serum concentration)
- Concomitant medication
- Periodontal variables
- Genetic factor

AGE AND GENDER

It has been studied that age is one of the important risk factors for overgrowth particularly in relation to phenytoin and cyclosporine8,9. Teenagers were at increased risk from DIGO10. Later it was reported that it was the combined effect of young age and poor oral hygiene that led to increased effect11. Age is not considered as a risk factor for calcium channel blockers as their use is limited to middle aged and older age groups.

Hassell 1981 reported that gender and race were not important risk factors. Cyclosporine induced gingival overgrowth was found more commonly in men as organ transplantation invariably seen in them.

DRUG

Drug dosage cannot predict the extent of gingival overgrowth.12, 13. Drug dosage along with body weight can be accounted as a good predictor for gingival changes. Phenytoin and calcium channel blockers serum concentration at any point of time is true predictor of drug's concentration.14

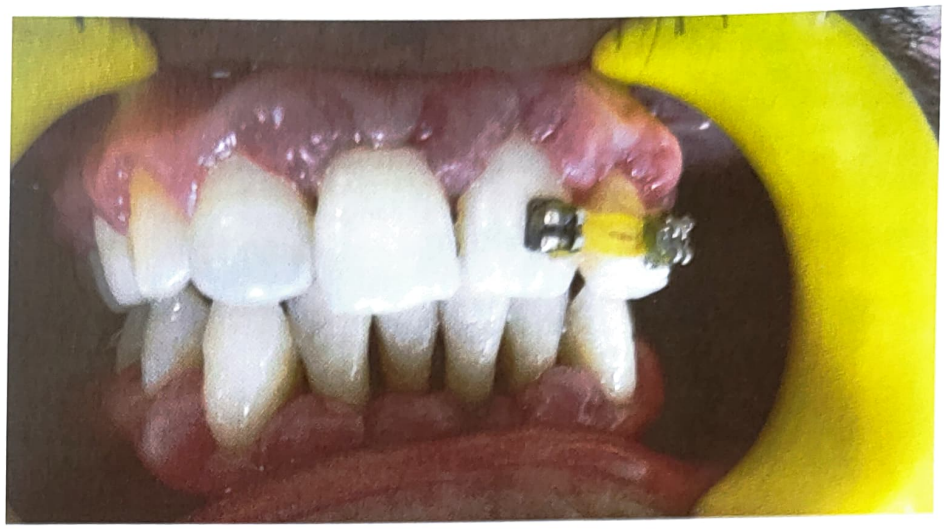

Figure 3

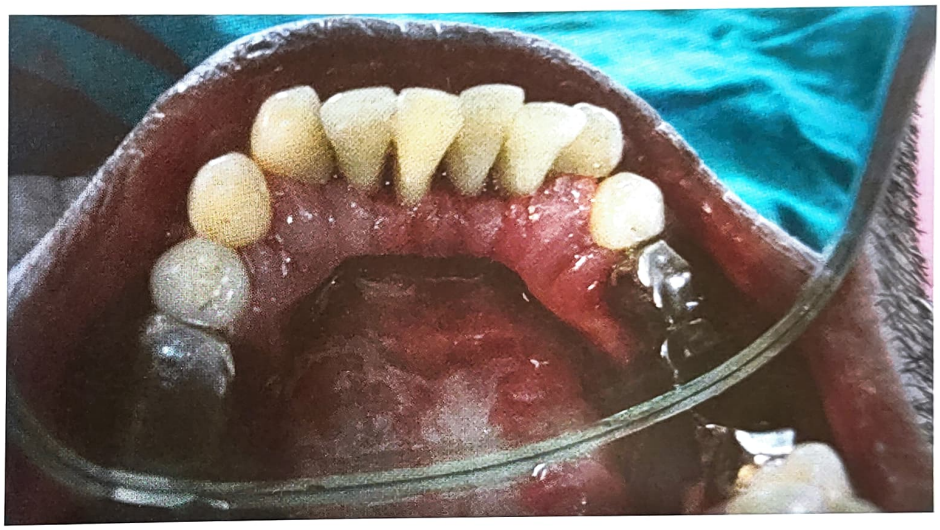

Figure 4

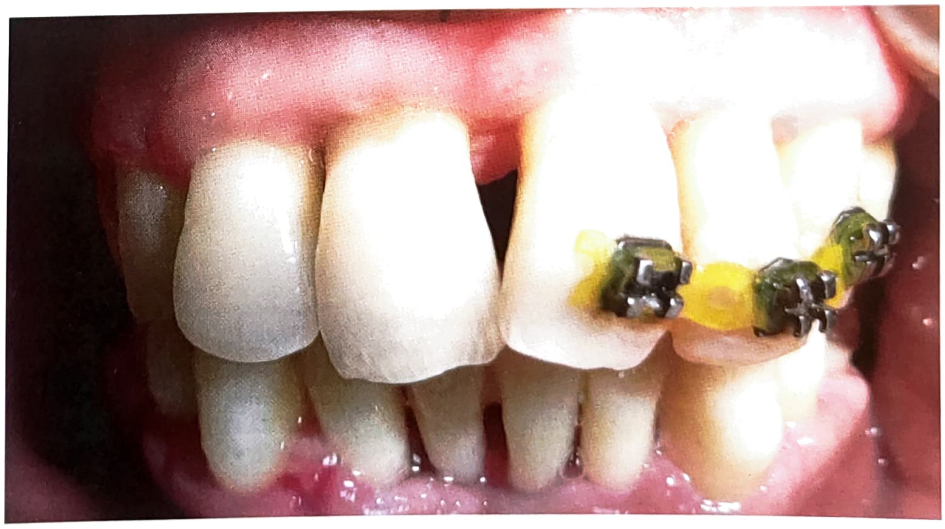

Figure 5

CONCOMITANT MEDICATION

It is very rare to find that only one single medication being prescribed to the patient. There is evidence that when cyclosporine

and nifedipine are prescribed to the patients of organ transplantation there is more gingival growth as compared to when each given alone. 15 Combined therapy may increase the prevalence of the condition but not the severity (Pernu et al 1993)16.

PERIODONTAL VARIABLES

Poor oral hygiene (more plaque scores and gingival inflammation) increase the effect of drugs that cause gingival overgrowth12, 17.

GENETIC FACTOR

One genetic marker that has been found in relation to DIGO is human lymphocyte antigen (HLA). This marker is confined mainly to organ transplantation patients as in them antigen typing is done.18, 19 HLA DR1 provides protection against gingival overgrowth whereas HLA-DR2 increases the undesired effect. 18

TREATMENT

The treatment must focus on the prevention of known predisposing factors such as plaque formation, which is a significant contributing factor for the development of DIGO.

The severity of enlargements is often proportional to the amount of gingival enlargement present. Oral Hygiene and periodic professional maintenance is invariably successful in prevention and/or lessen the severity of the condition. However, it may be insufficient for reversing the process once it is established. Oral Hygiene training and motivation programme of the patients is important5.

The Drug substitution if possible should be done

Topical anti-inflammatory agents are useful in providing symptomatic relief. Chlorhexidine controls both gingival inflammation and dental plaques. Antibiotic therapy where used early, is useful but is not permanent. It is a good adjunct to conventional mechanical treatment.

Surgical infection may be required and can be performed if the general condition of the patient permits.

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