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E-CONTENT

GINGIVAL ENLARGEMENT

Definition

Many terms have been used to describe gingival overgrowth. The expression gingival hyperplasia ("abnormal increase in the number of normal cells in a normal arrangement in an organ or tissue, which increase in volume") and gingival hypertrophy ("enlargement or overgrowth of an organ or part due to an increase in size of its constituent cells") have been also used, although gingival overgrowth is the general term that better describes this condition.

HYPERTROPHY: There is increase in the size of cells.

HYPERPLASIA: Actual increase in the number of cells.

INFLAMMATORY GINGIVAL ENLARGEMENT: The gingival enlargement is due to edema, vascular engorgement, and inflammatory infiltration

FIBROTIC GINGIVAL ENLARGEMENT: Fibrotic tissue increased due to chronic inflammation or other causes

SESSILE OVERGROWTH: Stalkless and attached directly at the base:

PEDUNCULATED OVER GROWTH: Having or supported on a peduncle**.**

ENLARGEMENT : Increase, expansion

TUMOR : An abnormal growth of tissue resulting from uncontrolled, progressive multiplication of cells

Classification:

According to etiology & pathologic changes:

1. lnflammatory enlargement

   Chronic

   Acute

2. Drug-induced enlargement

3. Enlargements associated with systemic diseases/conditions

    A. Conditioned enlargement

        pregnancy

        Puberty

        Vitamin C deficiency

        Plasma cell gingivitis

        Nonspecific conditioned enlargement

    B. Systemic diseases causing gingival enlargement

        Leukemia

        Granulomatous diseases (Wegener's granulomatosis,sarcoidosis, etc.)

4. Neoplastic enlargement (gingival tumors)

        Benign tumors

        Malignant tumors

5. False enlargement

Using the criteria of location and distribution, gingival enlargement is designated as follows:

• Localized: Limited to the gingiva adjacent to a single tooth or group of teeth.

• Generalized: Involving the gingiva throughout the mouth.

• Marginal: Confined to the marginal gingiva.

• Papillary: Confined to the interdental papilla.

• Diffuse: Involving the marginal and attached gingivae and papillae.

• Discrete: An isolated sessile or pedunculated, tumor like enlargement.

The degree of gingival enlargement can be scored as follows:(Bőkenkamp et al., 1994)

• Grade 0: No signs of gingival enlargement.

• Grade I: Enlargement confined to interdental papilla.

• Grade II: Enlargement involves papilla and marginal gingiva.

• Grade III: Enlargement covers three quarters or more of the crown.

Angelopoulous and Goaz (1972)

Grade 0: none

Grade I: no more than one third of the clinical crown covered

Grade II: any part of the middle third of the crown covered

GradeIII: greater than two third of the crown covered.

INFLAMMATORY ENLARGEMENT

Gingival enlargement may result from chronic or acute inflammatory changes; chronic changes are much more common.

Chronic Inflammatory Enlargement

z Etiology. Chronic inflammatory gingival enlargement is caused by prolonged exposure to dental plaque.

Factors that favor plaque accumulation and retention include

- poor oral hygiene,
- irritation by anatomic abnormalities
- improper restorative and
- orthodontic appliances

Clinical Features:

- originates as a slight ballooning of the interdental papilla and marginal gingiva.
- progresses slowly and painlessly, unless it is complicated by acute infection or trauma.
- Occasionally, a discrete sessile or pedunculated mass resembling a tumor.
- It may be interproximal or on the marginal or attached gingiva.

- The lesions are slow growing masses and usually painless. They may undergo spontaneous reduction in size, followed by exacerbation and continued enlargement.

- Painful ulceration sometimes occurs in the fold between the mass and the adjacent gingiva.

Histopathology:

- . Lesions that are clinically deep red or bluish red are soft and friable
- Lesions have a preponderance of inflammatory cells and fluid, with vascular engorgement, new capillary formation, and associated degenerative changes. Lesions that are relatively firm, resilient, and pink have a greater fibrotic component with an abundance of fibroblasts and collagen fibers.

Gingival Changes Associated with Mouth Breathing.

Gingivitis and gingival enlargement are often seen in mouth breathers. Its harmful effect is generally attributed to irritation from surface dehydration.

Clinical features:

- The labial gingiva of the upper anterior teeth is commonly affected.
- The effected gingiva is erythematous, shiny and enlarged with rolled margins.
- The interdental papillae on the labial aspect are red, edematous and bleed on slightest provocation.
- The effected area is sharply demarcated from the unaffected area and this junction has been referred by Warwick or tension ridge.
- The etiology has been tried to be explained as due to:
    - Irritation caused by passage of air
    - Dehydration of the mucous membrane leading to lowered tissue resistance
    - Saliva about the exposed gingiva becomes viscous, debris collects on the gingival and tooth surface due to lack of salivary flow resulting in enormous increase in bacterial population in the oral cavity.

Drug Induced Gingival Overgrowth/ Enlargement

Drugs commonly associated with gingival overgrowth:

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Category	Drugs
Anticonvulsants	Phenytoin Sodium valproate Phenobarbitone Vigabatrin
Immunosuppressant	Cyclosporine
Calcium channel blockers	
1. **Dihydropyridines**	Nifedipine Felodipine Amlodipine
2. Phenylalkylamine	Verapamil
3. Benzodiazepine	Diltiazem

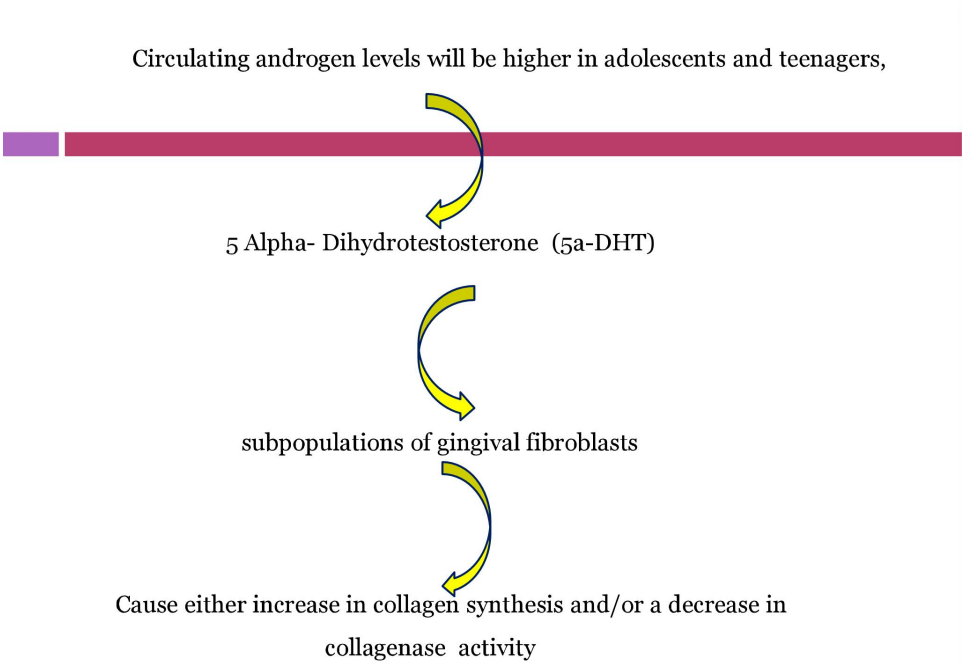
(DIGO)

Risk factors :

- Age
- Drug variables
- Concomitant medications
- Periodontal variables
- Genetic variables

AGE

- ❖ Age has been considered an important risk factor for drug induced gingival overgrowth with particular reference to phenytoin and cyclosporine
- ❖ Age is not an applicable risk factor for the calcium channel blockers since the use of these drugs is usually confined to the middle aged and older adult



DRUG VARIABLES:

The relationship between the extent and severity of gingival overgrowth and a variety of drug variables:

- Dose
- Duration
- Serum and salivary concentrations
- Bioavailability

An overall assessment of drug concentration

CONCOMITANT MEDICATION:

It has been suggested that combined therapy may increase the prevalence of the condition but not the severity.

PERIODONTAL VARIABLES:

Plaque scores and gingival inflammation appear to exacerbate the expression of drug induced gingival overgrowth, irrespective of the initiating drug. (Seymour 1991)

It has been suggest that proper oral hygiene might be expected to minimize the severity of gingival overgrowth, possibly by eliminating the inflammatory component of the lesion.

GENETIC FACTOR:

- Fibroblast heterogeneity remains one of the key factors used to explain the variable response of the gingival tissues to the various gingival overgrowth inducing drugs.
- Genetically susceptible patients on medications will develop GINGIVAL ENLARGEMENT

ROLE OF FIBROBLASTS:

When treated with cyclosporine A, nifedipine and phenytoin, gingival fibroblasts secrete:

- Increased amount of glycosaminoglycans, heparan sulfate.
- increase production of fibroblast cytokines and prostaglandin E_2
- Elevated levels of protein synthesis, most of which is collagen

There is existence of Differential Proportions Of Fibroblast Subsets in each individual which exhibit a fibrogenic response to these medications

- The metabolism of collagen, the most abundant protein in mammals, is precisely balanced by collagen synthesis and degradation to maintain a steady state. Fibrosis is caused by loss of this collagen fiber homeostasis. *Collagen fibrils are degraded via an* extracellular pathway involving secretion of collagenase and *via an intracellular pathway involving phagocytosis in* fibroblasts *Collagen phagocytosis is thought to be an* important pathway for physiological degradation of collagen in gingival connective tissuE. Inhibition of collagen phagocytosis by fibroblasts is one of the mechanisms leading to gingival overgrowth .

ROLE OF INFLAMMATORY CYTOKINES

- ☐ IL-6 may play a role in the fibrogenic responses of the gingiva to these medications.
- ☐ IL-6 is having positive regulation on collagen and glycosaminoglycan synthesis in the connective tissue

Cytokines and growth factors found at elevated levels in human drug-induced gingival overgrowth include:

- ✓ **Interleukin-6 (IL-6)**
- ✓ **IL-1**
- ✓ **Platelet-derived growth factor-B (PDGF-B)**
- ✓ **Fibroblast growth factor-2 (FGF-2)**

- ✓ **Transforming growth factor- β(TGF- β)**
- ✓ **Connective tissue growth factor (CTGF)**

Drug-induced gingival overgrowth is not due to the increased synthesis of type I collagen but the decreased degradation of type I collagen in gingival connective tissue through the reduction of collagen phagocytosis of fibroblasts.

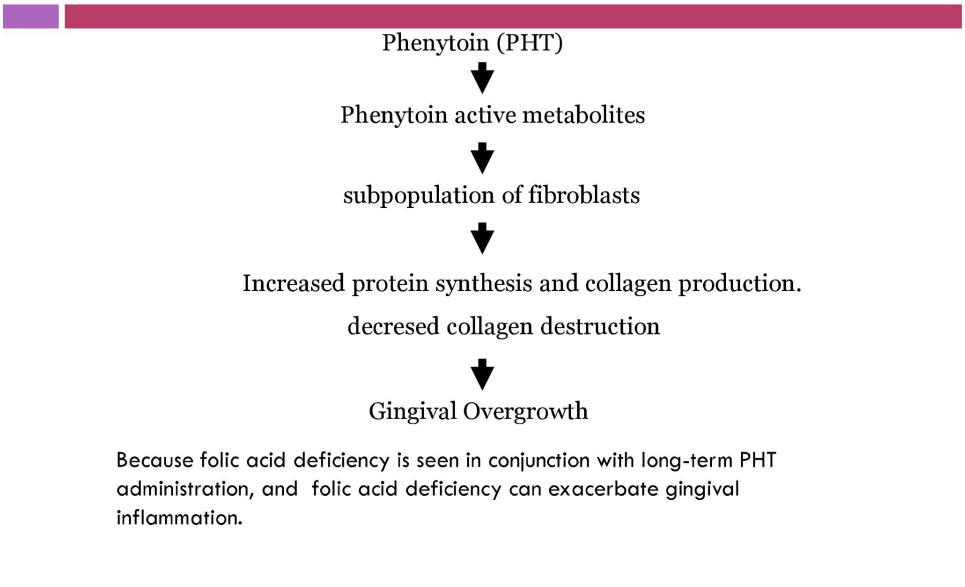
Fibroblasts from patients with phenytoin induced gingival over growth produce an inactive collagenase thus favouring collagen deposition compared to normal fibroblasts.

Phenytoin

It is an hydantoin that was introduced by Merritt and Putnam in 1938 for treatment of epilepsy.

Kimball in 1939 reported the first case of phenytoin induced GO

Possible pathogenesis:



Clinical features

- Gingival overgrowth may occur after the first month of treatment but it usually occurs not earlier than 3 months

- Affect the gingival tissues around the labial surfaces of the anterior teeth
- Begins in the region of the interdental papillae, which gradually increases in size and extends laterally until adjacent papillae coalesce
- If plaque control is good there will be minimal bleeding and the enlarged tissues will be of a firm consistency
- The lesions are mulberry shaped, firm, pale pink, and resilient, with a minutely lobulated surface and no tendency to bleed.
- Active Metabolite : 5-(p-hydroxyphenyl)-5-phenylhydantoin (p-HPPH)

Immunosupressants: cyclosporine A

Clinical Manifestation

- Usually develops within 1-3 months after initiation of treatment with the associated medications before the clinical manifestations of the gingival enlargement may be noted[9,22]
- Enlargement normally begins at the interdental papillae and affects the marginal and papillary tissue[5,9,23]
- Tissues in edentulous areas do *not* seem to be affected[6]

- Gradually, gingival lobulations are formed, and may appear inflamed or more fibrotic in nature depending on degree of local factors inducing the inflammation[13]
- Gingival epithelium is invaded by *Candida* hyphae[24,26]
- Pebbly or papillary lesions that appear on the surface of larger lobulations, sometimes with a cauliflower appearance associated with cyclosporine A[24-26] (see

Pathogenesis:

- The immunosuppressive actions of CsA may allow tissue invasion by micro-organisms, which causes a secondary inflammatory response.
- gingival fibroblasts respond to CsA increasing IL-6 secretion, which itself enhances collagen and glycosaminoglycan synthesis.
- Decreased apoptosis plays a more important role than the increased cell proliferation in the CsA-induced overgrowth.

Calcium channel blockers

Clinical features

- The gingival overgrowth is firm, normal in colour with the surface smooth or lobulated in texture.
- The gingival enlargement usually starts in the interdental papillae and progresses to involve the masticatory mucosa around the dentition.
- Edentulous areas are usually not affected

Mechanism:

- The exact mechanism of NIF-induced gingival overgrowth are still under investigation however several possible hypothesis have been proposed.
- NIF and other calcium channel blockers may directly influence gingival fibroblasts causing increased cell proliferation & matrix synthesis significantly.
- Increased cell proliferation & DNA synthesis have been noted in gingival cells & increased protein and collagen synthesis has been reported in cell cultures
- deficiencies in collagen phagocytosis by fibroblasts have been observed in NIF induced gingival overgrowth.

Histopathology

- A pronounced hyperplasia of the connective tissue and epithelium.

- There is acanthosis of the epithelium, and elongated rete pegs extend deep into the connective tissue
- densely arranged collagen bundles with an increase in the number of fibroblasts and new blood vessels.
- An abundance of amorphous ground substance has also been reported.
- The enlargement begins as a hyperplasia of the connective tissue core.

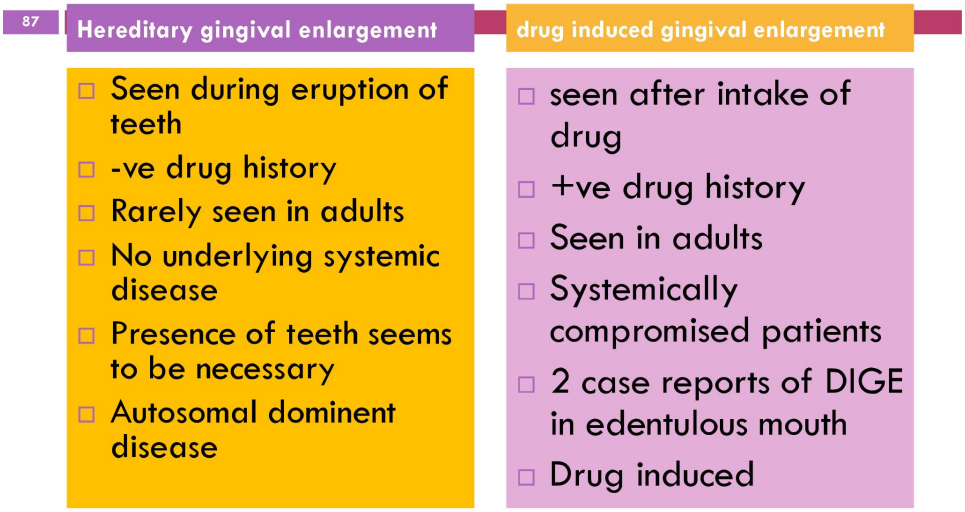
IDIOPATHIC GINGIVAL ENLARGEMENT

Idiopathic gingival enlargement is a rare condition of undetermined cause. It has been designated by such terms as gingivomatosis, elephantiasis, idiopathic fibromatosis, hereditary gingival hyperplasia, and congenital familial fibromatosis.

Clinical Features

- The enlargement affects the attached gingiva, as well as the gingival margin and interdental papillae, in contrast to phenytoin-induced overgrowth, which is often limited to the gingival margin and interdental papillae.
- The enlarged gingiva is pink, firm, and almost leathery in consistency and has a characteristic minutely pebbled surface.
- The jaws appear distorted because of the bulbous enlargement of the gingiva.

Ricardo D. Coletta 2006)



CONDITIONED ENLARGEMENT

- Hormonal
  - Pregnancy associated
  - Puberty associated
- Nutritional
  - Vitamin c associated
- Allergic.
  - Plasma cell gingivitis
- Non specific conditioned enlargements – **pyogenic granuloma**

Conditioned enlargement occurs when the systemic condition of the patient exaggerates or distorts the usual gingival response to dental plaque.

- The three types of conditioned gingival enlargement are hormonal (pregnancy, puberty), nutritional (associated with vitamin C deficiency), and allergic.
- Nonspecific conditioned enlargement is also seen.

<u>Enlargement in Pregnancy</u>

Enlargement may occur as single or multiple tumor-like masses.

The hormonal changes might result in following changes:

1) Microbial changes
   - Increased ratio of anaerobe to aerobe
   - Increased number of prevotella intermedia
2) Vascular changes

- Dilated gingival capillaries
- Increased venule and capillary permeability

3) Cellular changes
   - Stimulated endothelial cells
   - Decreased keratinization
   - Increased epithelial glycogen
   - Altered polymerization of ground substance
   - Inhibited collagen production

4) Immune changes
   - Depressed neulrophil chemotaxis and phagocytosis
   - Depressed antibody response
   - Depressed T-cell response

Marginal enlargement

- It results from aggravation of previous inflammation and does not occur without clinical evidence of local irritation.
- Pregnancy does not cause this condition, the altered tissue metabolism in pregnancy accentuates the response to local irritation.

Clinical Features

- Enlargement is generalized and tends to be more prominent inter proximally than on facial and lingual surface.
- Enlarged gingiva is bright red or magenta, soft and friable having smooth, shiny surface.
- Bleeding occurs spontaneously.

Tumor like Enlargement:

- It is not a neoplasm but an inflammatory response to local irritation and is modified by patients condition.
- It appears after first trimester but may be early also.

Clinical Features

- The lesion appears as discrete, mushroom like flattened spherical mass that protrude from interdental papilla or gingival margin and is attached by pedunculated base.
- It tends to expand laterally and pressure from tongue and check increases it flattened appearance.
- The colour is dusky red or jnagrretg with smooth glistering surface which exhibits numerous deep red, pinpoint markings.

- It is painless.

Management

- The aim of periodontal therapy for pregnant patient is to minimize potential exaggerated inflammatory response related to hormonal alteration.
- Meticulous plaque control, scaling and root planning, polishing should be non emergent periodontal procedures performed.
- Second trimester is safest time in which treatment is performed.
- In conditions like 'supine hypertensive syndrome' which occur during third trimester, in this appointment should be short and patient should change his position frequently.
- Fully reclining position should be avoided as far as possible.

Medication and radiographs are avoided.

- In case of marginal and inter dental enlargement scaling and curettage is done.
- In case of tumour like enlargement, surgical excision is done which is postponed until postpartum.

During pregnancy if it causes problem in mastication, it is removed on patients desire.

Enlargement in puberty

Clinical Features

- Enlargement is seen in marginal and interdental papilla and is characterized by prominent bulbous interproximal papilla.
- Frequently only the facial gingiva is affected, because mechanical action of tongue prevents accumulation of food in lingual surfaces.
- 11 to 7 years shows high prevalence of gingival enlargement.

Management

- Scaling, curettage and oral hygiene instructions.
- Surgical removal in severe cases.

Nutritional, ie Vitamin C deficiency Enlargement:

Acute vitamin C deficiency does not itself cause gingival inflammation but it causes haemorrhage, collagen degeneration and oedema of gingival connective tissue. These changes modify response of gingiva to plaque.

Clinical Features

- Gingival enlargement is marginal, bluish red, soft, friable and have smooth, shiny surface.
- Haemorrhage occurring either spontaneously or on provocation.
- The surface necrosis with pseudo membrane formation is common features.

Plasma Cell Gingivitis.

Plasma cell gingivitis, also referred to as atypical gingivitis and plasma cell gingivostomatitis.

It is thought to be allergic in origin, possibly related to the components of chewing gum, dentifrices or various diet components.

Clinical Features

- It consist of mild marginal gingival enlargement that extends to the attached gingiva.
- Gingiva appears red, friable and bleeds easily. An associated chelitis and glossitis is seen.

SYSTEMIC DISEASES CAUSING GINGIVAL ENLARGEMENT

- **Leukemia :**
  - Bluish red , Firm.
  - The consistency is moderately firm, but there is a tendency towards friability and haemorrhage.
  - True leukaemic enlargement occurs commonly in acute leukaemia

Histopathology

- Immature and proliferating leukocytes
- Engorged capillaries
- Edematous and degenerated connective tissue,
- Isolated areas of acute necrotizing inflammation .

Granulomatous diseases:

Wegner's granulomatosis:

- Acute granulomatous necrotizing lesions of the respiratory tract .

Etiology;

- Unknown/ immunologically mediated tissue injury
- The granulomatous papillary enlargement is reddish purple and bleeds easily on stimulation.

Histology,

- Scattered giant cells.
- Micro abscess.
- Edema
- Engorged blood vessels.

Sarcoidosis

- Unknown etiology
- Affects blacks and can involve any organ
- Gingiva where a red, smooth, painless enlargement may appear.

Histopathology

- Noncaseating whorls of epithelioid cells
- Multinucleated foreign body type giant cells.