

Gingival Enlargement: A Review

Dr.ABHIJITH SHETTY, Dr. NANDINI N KRISHNAMURTHY, Dr. ABRAHAM DAVIS, Dr. DISHA RAI,
Dr.MISHA ROSE MATHEW, Dr.CHRISTY GEORGE

Abstract:- Gingival enlargement or overgrowth is a common disease of gingiva. The causative factors may range from inflammation due to local factors to conditioned enlargement and neoplastic enlargements. They commonly present as bulbous interdental gingival, diffuse swelling of gingival. The care of these lesions and the prevention of their recurrence are entirely contingent on a correct diagnosis. Furthermore, in some circumstances where gingival enlargement is the primary symptom of potentially fatal systemic disorders, a precise diagnosis of these enlargements could save the patient's life or, at the very least, start treatment early and enhance their quality of life. Due to the unaesthetic appearance of the overgrown gingiva, treatment becomes inevitable. This results in excision of overgrowth known as gingivectomy. The first gingivectomy procedure was explained by Robicsek in 1884 and later by Zentler (1918). Grant (1979) defined gingivectomy as excision of soft tissue wall of pathologic periodontal pocket. Gingivectomy procedures can be done by means of scalpel, laser, electrosurgery and chemosurgery. The ultimate result remains the same indifferent of the method used. However the amount of remaining keratinized gingival and esthetic appearance is of supreme importance. The goal of this review paper is to highlight key data from various forms of gingival enlargement in order to help clinicians distinguish between them.

Keywords:- gingival enlargement, Gingival hyperplasia, Gingival overgrowth, Gingival diseases, anticonvulsants.

I. INTRODUCTION

Gingival enlargement, also known as gingival overgrowth, is a typical symptom of gum disease that is marked by an increase in the size of the gingiva. Effective treatment requires a correct diagnosis of the cause of the growth. When identifying a precise diagnosis among the various gingival enlargements that can be classified based on etiologic origins and pathologic changes, location and distribution, and/or degree of enlargement, a clinician's abilities are put to the test. Depending on the etiopathogenesis, enlargements might be inflammatory, drug-induced, linked to systemic illnesses or disorders, malignant, or fake. According to their location, enlargements might be marginal, papillary, or diffuse, and their dispersion

can be limited or extensive. Three forms of localised enlargements exist: "isolated, discrete," "regional," and "isolated, discrete." "Isolated" enlargements (e.g., gingival/periodontal abscess) are gingiva enlargements that are restricted to the gingiva next to one or two teeth. "Discrete" lesions are solitary, sessile, or pedunculated tumor-like enlargements (e.g., fibroma/pyogenic granuloma). "Regional" enlargements are gum involvement around three or more teeth in one or more areas of the mouth (e.g., inflammatory enlargement associated with mouth breathing in maxillary and mandibular anterior region).

The term "generalised" enlargement refers to gingiva involvement next to nearly all of the teeth present (e.g., drug influenced gingival overgrowth). Ingle et al.(1) analysed numerous methods for assessing the extent of gingival enlargements and reported their clinical index. The purpose of this article is to highlight significant features of distinct types of gingival enlargement in order to help doctors differentiate between them.

II. ISOLATED REACTIVE LESIONS OF THE GINGIVA

Edulis(2), also known as solitary/discrete, pedunculated, or sessile gingival swellings with no histologic characterization, is a word used to describe any solitary/discrete, pedunculated, or sessile gingival swellings with no histologic characterization. The term "reactive lesion of the gingiva"(3) seems to be more accurate for these types of swellings. The most prevalent diagnosis in this category is angiogranuloma/pyogenic granuloma, fibrous epulis/peripheral fibroma, and peripheral giant cell lesion/granuloma.

A. Fibrous epulis/peripheral fibroma

This lesion grows from the free gingival margin/interdental papilla in adults and appears as a firm, pink, non-inflamed mass (Figure 1A). In the vast majority of cases, the lesion is painless. Secondary traumata, which can cause pain, can be caused by brushing, flossing, or chewing. The fibroma may have more calcification foci (peripheral calcifying fibroma, Figure 1B), cementicles foci (peripheral cementifying fibroma, Figure 1C), or bone trabeculae (peripheral ossifying fibroma, Figure 1C) on histological examination.



Fig. 1:Fibrous epulis and its subtypes

A: Peripheral fibroma, which appears as a pink firm, non-inflamed mass emerging from beneath the gingiva;
 B: Peripheral cementifying fibroma, which has additional foci of cementicles;
 C and D: Surgical exposure of the lesion, which shows substantial bone development in the centre of the lesion. Histological examination revealed the presence of bone trabeculae.

B. Angiogramuloma/pyogenic granuloma

In adults, it manifests as a smooth-surfaced, ulcerated tumour that extends beyond the gingival edge. The vascular, compressible, and bleed-prone masses are reddish/bluish in colour. They usually grow quickly over the first few weeks, then slow down. The mass may extend between the teeth and appear as a bilobular (buccal and lingual) mass connected through the col region, however bone loss is rare (Figure 2A). Pregnancy epulis/tumor or granuloma

gravidarum are terms for angiogramuloma that occurs during pregnancy (Figure 2B). Thicker stratified squamous epithelium with conspicuous rete pegs and some intracellular and extracellular edoema, considerable intercellular bridges, and leukocytic infiltration are revealed on histological inspection.



Fig. 2: Angiogramulomas can manifest themselves in a variety of ways, as seen in Figure 2.
 (A)Pyogenic granuloma, a bilobular mass joined through the col region, (B) and similar lesions that arise during pregnancy are referred to as "pregnancy epulis."

C. Peripheral giant cell granuloma

They're more abundant in the front of a child's mouth, as well as in the back of an adult's mouth during the mixed dentition period. They're virulent lesions with a lot of room to grow. Due to their purplish-red colour and proclivity for

bleeding, these lesions have a high vascularity. They're also prone to piercing between teeth, resulting in bone loss and the loss of nearby teeth (Figure 3).



Fig. 3: A peripheral giant cell granuloma lesion. Purplish crimson colour and a tendency to haemorrhage characterise this extremely vascular lesion.

D. Gingival cysts

Gingival cysts are a very uncommon kind of odontogenic cyst. They are more common among women in their 50s and 60s. The labial connected gingiva of the mandibular anterior teeth has a higher number of them. They may have a bluish colour due to the presence of fluid, and they may stimulate labial bone resorption as a result of pressure. Its radiolucency can be mistaken for a lateral

periodontal cyst on radiography. The best treatment for these lesions is excisional biopsy. ⁽⁴⁾



Fig. 4: Other unusual localised gingival enlargements that could be misinterpreted as epulis are shown in **Figure 4**. A: A hemangioma in the right quadrant of the mandible; B: A mucocele linked with the palatal minor salivary gland; C and D: A lateral periodontal cyst extending labially and creating localised gingival hypertrophy.

E. Neoplastic

It is also possible to determine if distinct epulis-like lesions are benign or malignant. Fibroma, peripheral giant cell granuloma, central giant cell granuloma, papilloma, leukoplakia, nevus⁽⁵⁾, myoblastoma^(6,7), hemangioma (Figure 4A)^(7,8), neurilemoma⁽⁹⁾, neurofibroma⁽¹⁰⁾, and ameloblastoma⁽¹¹⁾ are benign masses. Malignant tumours include squamous cell carcinoma and melanoma. Kaposi's sarcoma⁽¹²⁾ is the most frequent sarcoma, while fibrosarcoma, lymphosarcoma, and reticulum cell sarcoma are less prevalent⁽¹³⁾. Angioma, osteofibroma, myxoma, fibropapilloma, adenoma, and lipoma⁽¹⁴⁾ are all rare tumours that affect fewer than 2% of people.

Some other localized Chronic lesions that can be misdiagnosed as epulis would be palatal mucocele (Figure 4B), a lateral periodontal cyst projecting on labial/lingual surface (Figure 4C and D), etc

F. Acute

Solitary gingival enlargement can be caused by gingival, periodontal, periapical, or pericoronal abscesses. Their position and the life of the tooth with which they are associated can be used to distinguish them. It could be localised (gingival abscess) around the gingival border or papilla (Figure 5A), or it could be diffuse (periodontal abscess) and cover a significant region of the linked gingiva (Figure 5B) (Figure 5B). The lesion could be the result of an

endodontic problem if the attached tooth is no longer living. m (endo-perio lesion/periapical abscess) (Figure 5C).

Irritation and swelling of the pericoronal flap, which covers the distal-most mandibular teeth, is prevalent. If the inflammation persists, an abscess of these pericoronal flaps may develop (Figure 5D). Gingival/periodontal/pericoronal abscesses may have a purulent centre in the connective

tissue surrounded by diffuse infiltration of polymorphonuclear leukocytes, edematous tissue, and vascular engorgement, according to histological examination. The surface epithelium shows intracellular and extracellular oedema, leukocyte infiltration, and ulceration in various degrees.



Fig. 5: Gingival hypertrophy due to an abscess. A:Gingival abscess, at gingival border or papilla; B: Swelling is generalised in periodontal abscess; C: Periapical abscess, near apex of concerned tooth; D: Abscess of pericoronal flap

G. Characteristic features of generalized gingival enlargement

Gingival disease is most typically manifested as localised or widespread gingival enlargement, which can be classified into one of several kinds.

H. Inflammatory gingival enlargement

These are symptoms of an inflammatory response to a localised gingival irritation. Microbial deposits (plaque and calculus) (Figure 6A), broken teeth, overhanging restorations, ill-fitting prosthesis (Figure 6B), orthodontic brackets (Figure 6C), and other irritants are possible causes. The presentation starts with a little inflating of the papilla or marginal gingiva, depending on the location of the irritant. Over time, the bulge may expand in size and scope, finally becoming widespread. They may seem bluish or deep red in clinical settings. They're usually soft and friable, having a smooth, lustrous surface that bleeds easily. On histology, chronic inflammatory enlargement can look like a firm,

resilient, pink, and fibrotic enlargement with an abundance of fibroblasts and collagen fibres.

I. Gingival enlargement in mouth breathers

Despite the fact that enlargement in mouth breathers is thought to be inflammatory, the exact mechanism is unknown. The cause is thought to be the gingival surface's alternate soaking and drying. With a diffuse shiny surface, the gingiva appears red and edematous. The appearance of significant enlargement in the maxillary and mandibular anterior areas without any involvement of the posteriors is a diagnostic feature of this type of enlargement. The palatal aspect of the maxillary anteriors and the labial aspect of the mandibular anteriors will be extended in a typical bimaxillary protrusion condition. Mouth breathing is a common complaint among patients, and it can be caused by a short upper lip, hyperactive labii superioris, proclined incisors, rhinitis, or other causes.



Fig. 6: Gingival enlargement. Plaque and calculus, ill-fitting prosthesis, and orthodontic brackets are all examples of A, B, and C respectively.

Table 1 Different drugs known to predispose to gingival enlargements			
Anticonvulsants ^[15,16]		Immunosuppressants ^[17]	Calcium channel blockers ^[15]
Phenytoin	Vigabatrin	Cyclosporine	Nifedipine
Ethotoin	Ethosuximide	Tacrolimus	Diltiazem
Mephenytoin	Topiramate	Sirolimus	Felodipine
Phenobarbital	Pyrimidinone		Nitrendipine
Lamotrigine			Verapamil
			Amlodipine



Fig. 7: Drug influenced gingival overgrowth. A: Superimposed with secondary inflammation; B: Fibrotic and leathery.

III. FIBROTIC

A. Drug induced gingival enlargement:

Anticonvulsants, immunosuppressants, and calcium channel blockers are just a few of the drugs that might induce gingival development (Table 1 and Figure 7). Gingival enlargement indications and symptoms emerge within 2-4 months of starting the medication.

During the initial presentation, there is usually little discomfort. The interdental papilla enlargement begins as a beadlike extension and proceeds to include the marginal gingiva. The enlargement has a mulberry shape, is firm,

pink, and durable, with minute lobulations and minimal bleeding when probed when it is not affected by secondary inflammation. It can damage the gingiva surrounding any tooth, however it is most frequent in the maxillary and mandibular teeth's anteriors. It will be lacking in edentulous areas and will vanish in areas where teeth have been extracted. The existing enlargement expands in size and takes on the characteristics of inflammatory enlargement when infected subsequently. The vascularization of drug-induced gingival enlargement (DIGO) generated by

immunosuppressive medications like cyclosporine appears to be greater than that of phenytoin-induced DIGO⁽¹⁷⁾.

It's difficult to say which of two or more medicines known to produce gingival enlargement should be blamed for the DIGO diagnosis when patients are on combination treatment. In such cases, consulting the patient's physician and making a request is one approach for determining a diagnosis.

To begin, he should substitute/stop one drug at a time, causing as little disruption to the patient's daily routine as possible. The patient frequently states that he or she has been taking relevant medications (antihypertensives, anticonvulsants, immune suppressants) for a long time but that the enlargement has only recently manifested. It's impossible to link the duration of the enlargement's recurrence to a drug history in these conditions. A precise enquiry about a recent change in medicine type/dose will help connect the dots.

B. Genetic disorders associated with gingival enlargement:

They are classified into four groups based on their origins, clinical characteristics, and histology. Idiopathic gingival hypertrophy, lysosomal storage disorders, vascular illnesses, and those linked to frequent dental abnormalities

are only a few examples (Table 2). Gingivomatosis, idiopathic fibromatosis, elephantiasis, and hereditary gingival hyperplasia are all terms used to describe idiopathic gingival hyperplasia. It shows up as a strange fibrotic gingival enlargement that might be localised or widespread. It could manifest as a separate entity or as a symptom of another ailment.

Gingival hypertrophy runs in the family, thus a positive family history can assist confirm the diagnosis. The first step is usually the eruption of the main or permanent teeth. The presence of hard bulky gingiva enlargement restricted to the maxillary and mandibular second and third molar locations is a common occurrence. When palpated, the enlarged mass may be pink or reddish in colour and firm/nodular. Although the alveolar bone is rarely impacted, periodontal issues can result from the formation of pseudo-pockets and a lack of dental hygiene. Extensive overgrowths can have a negative impact on a patient's look and ability to function (Figure 8).



Figure 8: Unusual firm fibrotic gingival enlargements in a patient with hereditary gingival fibromatosis.

Table 2 Gingival enlargement associated with syndromes in different types of genetic disorders	
Syndromes associated with hereditary gingival fibromatosis	
Zimmerman-Laband syndrome ^[19]	Abnormal fingers, nails, nose and ears, splenomegaly, hepatomegaly, hyperextensible metacarpophalangeal joints
Ramon syndrome ^[19]	Cherubism, seizures, mental deficiency, hypertrichosis, stunted growth, juvenile rheumatoid arthritis
Systemic Hyalinosis ^[20]	Painful joint contractures, diffuse thickening of the skin with pearly papules and fleshy nodules and failure to thrive
Jones syndrome ^[21]	Progressive sensorineural deafness
Rutherford syndrome ^[22]	Corneal opacity, mental retardation and aggressive behavior, failure of tooth eruption
Cross syndrome ^[23]	Hypopigmentation, mental retardation and writhing movement of hand and legs
Schinz-Giedion syndrome ^[24]	Severe mid face retraction, severe mental retardation and congenital heart defect, patient usually die under 10 yr of age
Costello syndrome ^[25]	Macrostomia, redundant skin of neck, hands and feet, nasal and perioral papillomas, enlargement within first years of life
Syndromes associated with lysosomal storage diseases	
Hurler syndrome ^[26]	Dwarfism, flexion contractures, hernias, corneal clouding, macroglossia, short mandibular rami, peg-shaped teeth
Maroteaux-Lamy syndrome ^[27]	Enlargement of skull, corneal opacities, short peg-shaped poorly formed teeth, hypertrophy of alveolar ridges, anterior open bite
Neimann-Pick disease ^[28]	Thick lips, macroglossia and widely spaced teeth
Anderson-Fabry disease ^[29,30]	Painful crises on extremities and abdomen, angiokeratomas of skin, labial mucosa and buccal mucosa
Cowden syndrome ^[31]	Cobblestone papules of gingiva and buccal mucosa, macrocephaly, multiple hamartomas, learning disabilities, autism
Gingival enlargement associated with vascular disorders	
Sturge-Weber syndrome ^[32]	Unilateral cutaneous nevi, unilateral vascular hyperplasia, neurological manifestations and ocular complications
Klippel-Trenaunay syndrome ^[33]	Capillary hemangiomas, increased size of lips, tongue, teeth malformations, delayed exfoliation of teeth, calcified roots
Gingival enlargement associated with characteristic dental abnormalities	
Wilson syndrome ^[34]	Enamel hypoplasia, multiple small red papules of lips, early onset periodontitis and repeated oral candidiasis, signs of cirrhosis
Goltz-Gorlin syndrome ^[35]	Partial anodontia, hypoplastic teeth, atrophy and linear pigmentation of skin, herniation of fat, multiple papillomas, digital anomalies

C. Conditioned gingival enlargement

Hormonal: During pregnancy and puberty, hormonal changes that impact the response to local irritants increase generalised gingival hyperplasia. The facial and/or lingual surfaces have a smaller diameter than the interproximal gingiva (Figure 9). Gingiva that has grown in size is often

soft and friable, with a bright appearance. possessing a smooth, glossy red or magenta surface. Bleeding can occur naturally or as a response of a little trigger. The enlargement may go away on its own after a while. However, removal might be necessary.



Fig. 9: A pregnant woman with several interproximal enlargements.

D. Vitamin C deficiency:

A blood ascorbic acid content of less than 2 g/mL indicates vitamin C insufficiency. Diabetes, stress, and smoking are the most common diagnosis. A variety of factors can lead to vitamin C deficiency. Vitamin C insufficiency is connected to enlargement of the gingiva, or gums, which are soft and friable with a smooth, shiny surface and a bluish red colour. Bleeding can occur spontaneously or as a result of a small irritant. Surface

necrosis is classified as either surface necrosis or pseudomembrane development. Also seen a lot⁽³⁶⁾. High-sensitivity C-reactive protein (hs-CRP) levels are inversely related to serum vitamin C content, according to Kubota et al.⁽³⁷⁾, implying that hs-CRP blood levels may be elevated in these patients..

E. Plasma cell gingivitis:

Although the cause of this sickness is unknown, histology studies indicate that it is most likely a hypersensitivity reaction involving affluent plasma cells. Toothpaste, khat, culinary items, especially cinnamon, chewing gum, and unknown sources are all known allergens linked to this condition. It may bleed if provoked. After eating hot and

spicy foods, patients usually experience a burning sensation. The gingiva is nearly entirely adhering and the surface is slightly gritty, giving it a reddish look (Figure 10).



Fig. 10: Appearance of gingiva in patient with plasma cell gingival enlargement. The color is reddish and involves almost complete attached gingiva and slightly granular appearance.

F. Gingival enlargement associated with systemic disease Leukemia:

In persons with leukaemia, significant infiltration of leukemic cells in the gingival connective tissue induces generalised gingival hypertrophy. It's possible that it's misdiagnosed as an inflammatory illness. Oral ulceration, spontaneous gingival bleeding, petechiae, mucosal pallor, herpetic infections, and candidiasis have all been connected to gingival hypertrophy. On rare circumstances, unusual symptoms such as chin numbness and/or toothache have been noted. ⁽³⁸⁾. In this category, acute myeloid leukaemia is the most dangerous disease associated with gingival hypertrophy. Ecchymosis, night sweats, recent infections, and tiredness are all signs and symptoms of bone marrow depletion. A rapid diagnosis can be made using a basic whole blood count. There was also a case of gingival hyperplasia induced by acute lymphoblastic leukaemia⁽³⁹⁾.

G. Wegener's Granulomatosis:

Wegener's granulomatosis causes strawberry gingivitis, a reddish-purple exophytic gingival hypertrophy with patchialhaemorrhages. Because oral lesions linger for a long period before involving other organs (Figure 11)^(40,41), they may be valuable in diagnosing this potentially deadly condition early. At least two of the following conditions must be present in order to be diagnosed with Wegener's granulomatosis: Oral mucosa ulcers, nasal haemorrhage, or inflammation; chest radiographs showing nodules, fixed infiltrates, or cavities; abnormal urine sediment; and biopsy granulomatous inflammation ⁽⁴⁰⁾.



Fig. 11 : Gingival condition in patient with Wegenersgranulomatosis, presents as reddish purple, exophytic gingival overgrowth

H. Crohn's disease:

In Crohn's disease, gingiva is pink, rigid, and leathery in appearance, with a distinctive minutely pebbled surface. In these patients, the signs and symptoms of these illnesses must be closely monitored. Symptoms include lip swelling, gastrointestinal issues, fever, and ulcers. A trip to the doctor

for a consultation with a gastroenterologist may be beneficial.

I. Sarcoidosis:

Sarcoidosis is an inflammatory illness that affects a variety of organs. The most common symptoms are pulmonary infiltration and hilar lymphadenopathy, as well as cutaneous and ocular lesions⁽⁴²⁾, but oral involvement is uncommon. There is no specific test for sarcoidosis. Other laboratory testing and the exclusion of other non-caseating granuloma-forming disorders are utilised to identify sarcoidosis^(42,43). The quantity of eosinophils in the blood (normal range 0-4 percent) and serum angiotensin converting enzyme levels (normal range less than 670 nkat/L) may be significantly higher.

J. Tuberculous gingival enlargement:

Primary tuberculous lesions in the mouth are rare, but when they do occur, they usually afflict youngsters. The lesions are usually asymptomatic, however they may be accompanied with caseation of the dependent lymph nodes^(45,46). Furthermore, primary tuberculosis with only gingival enlargement is extremely unusual, and can be detected by a history of fever, weakness, appetite loss, and weight loss. To confirm the diagnosis, histopathology, full blood count, and polymerase chain reaction can all be employed⁽⁴⁷⁾. Secondary oral TB, on the other hand, affects 0.05 percent to 1.5 percent of people and is more common in the elderly^(48,49).

K. Unusual presentations:

Amelogenesis imperfect⁽⁵⁰⁾, Hashimoto's thyroiditis⁽⁵¹⁾, I-cell disease⁽⁵²⁾, and Multiple myeloma⁽⁵³⁾ have all been linked to generalised gingival enlargement in the past.

L. False enlargement:

False enlargements occur when underlying osseous (tori, exostosis, Paget's disease, cherubism, osteoma, etc.) or dental tissues grow larger (during tooth eruption). Except for the massive increase in size of the area, the overlying gingiva has no abnormal clinical features (Figure 12).

M. Decision:

A full dental and medical history, a careful examination of the nature, origin, and extent of the enlargement, and the identification of causal or predisposing variables are all required for differential diagnosis of gingival enlargement. A decision tree (Figure 13) is designed to give you a broad picture of many different gingival enlargement diagnoses, whether they're localised or extensive. This comprehensive presentation would be extremely helpful to clinicians in arriving at a specific diagnosis.

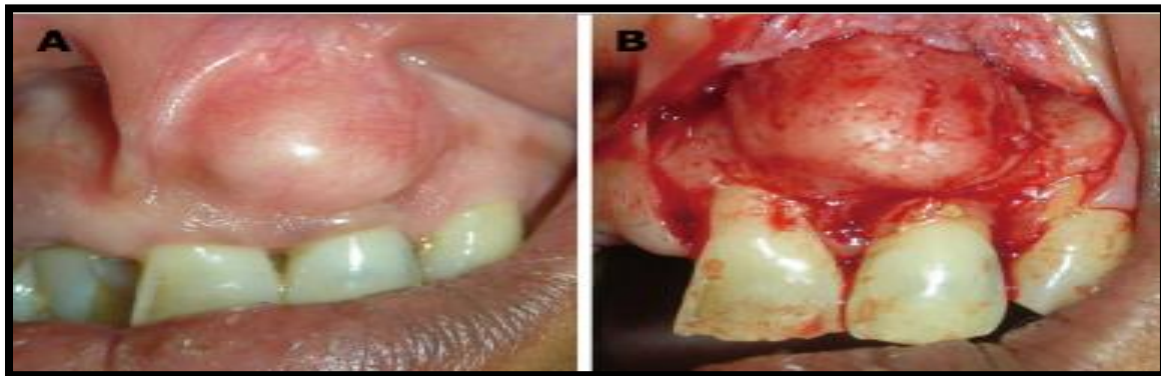


Fig. 12: Case of false enlargement wherein. A: The overlying gingiva presents with no abnormal clinical features except the massive increase in size of the area; B: Formed completely by underlying bone.

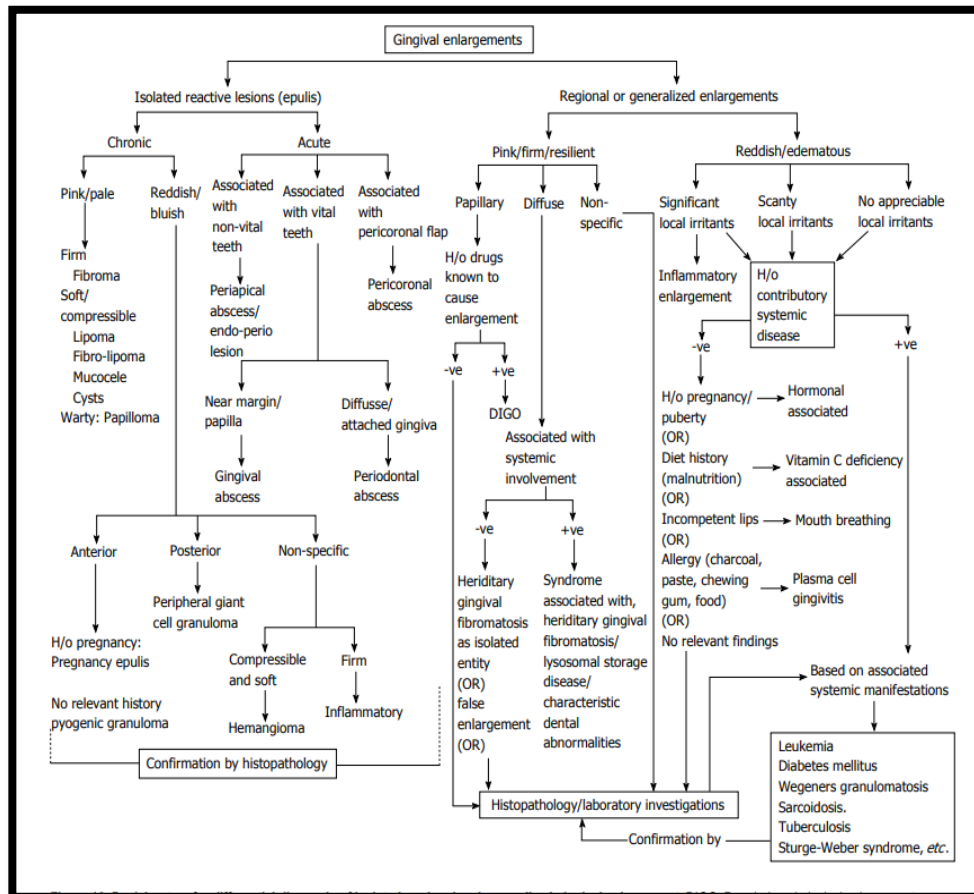


Fig. 13: Decision tree for differential diagnosis of isolated, regional and generalized gingival enlargement. DIGO: Drug induced gingival enlargement

In addition, laboratory tests and/or biopsy specimens may be needed to confirm the diagnosis or make an exclusionary diagnosis.

IV. CONCLUSION

Despite a wide range of etiologies, gingival enlargements can be diagnosed by a detailed history (e.g., drug- or hormone-induced gingival enlargement), location (e.g., mouth-breathing enlargement around anterior teeth), or clinical presentation (e.g., strawberry gingivitis). The presence of local irritants could cause gingival enlargements (plaque and calculus). As a result, plaque management is a critical component of all patients' treatment plans. An excisional/incisional biopsy and/or a hematologic/histologic examination may be required on occasion to appropriately characterise the infrequent occurrences of gingival hypertrophy. The doctor should have an open mind and explore all possibilities before making a final diagnosis of the illness at hand.

REFERENCES

- [1.] Inglés E, Rossmann JA, Caffesse RG. New clinical index for drug-induced gingival overgrowth. *Quintessence Int* 1999; 30: 467-473.
- [2.] Lee KW. The fibrous epulis and related lesions. Granuloma pyogenicum, 'Pregnancy tumour', fibro-epithelial polyp and calcifying fibroblastic granuloma. A clinico-pathological study. *Periodontics* 1968; 6: 277-292.
- [3.] Kfir Y, Buchner A, Hansen LS. Reactive lesions of the gingiva. A clinicopathological study of 741 cases. *J Periodontol* 1980; 51: 655-661.
- [4.] Giunta JL. Gingival cysts in the adult. *J Periodontol* 2002; 73: 827-831.
- [5.] Allen RR, Bruce KW. Nevus of the gingiva; report of case. *J Oral Surg (Chic)* 1954; 12: 254-256
- [6.] Hagen JO, Soule EH, Gores RJ. Granular-cell myoblastoma of the oral cavity. *Oral Surg Oral Med Oral Pathol* 1961; 14: 454-466.
- [7.] Sznajder N, Dominguez FV, Carraro JJ, Lis G. Hemorrhagic hemangioma of gingiva: report of a case. *J Periodontol* 1973; 44: 579-582.

- [8.] Rashmi MS, Alka KD, Seema C. Oral hobnail hemangioma--a case report. *Quintessence Int* 2008; 39: 507-510.
- [9.] Fowler CB. Benign and malignant neoplasms of the periodontium. *Periodontol* 2000 1999; 21: 33-83
- [10.] Pollack RP. Neurofibroma of the palatal mucosa. A case report. *J Periodontol* 1990; 61: 456-458.
- [11.] Stevenson AR, Austin BW. A case of ameloblastoma presenting as an exophytic gingival lesion. *J Periodontol* 1990; 61: 378-381.
- [12.] Lager I, Altini M, Coleman H, Ali H. Oral Kaposi's sarcoma: a clinicopathologic study from South Africa. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003; 96: 701-710.
- [13.] Ponnampal SR, Srivastava G, Jampani N, Kamath VV. A fatal case of rapid gingival enlargement: Case report with brief review. *J Oral Maxillofac Pathol* 2014; 18: 121-126.
- [14.] Bernick S. Growths of the gingiva and palate; connective tissue tumors. *Oral Surg Oral Med Oral Pathol* 1948; 1: 1098-1108.
- [15.] Hallmon WW, Rossmann JA. The role of drugs in the pathogenesis of gingival overgrowth. A collective review of current concepts. *Periodontol* 2000 1999; 21: 176-196.
- [16.] Bologna JL, Jorizzo JL, Rapini RP, editors. *Dermatology*. 2nd ed. St. Louis: Mosby, 2007.
- [17.] Seymour RA, Smith DG, Rogers SR. The comparative effects of azathioprine and cyclosporin on some gingival health parameters of renal transplant patients. A longitudinal study. *J Clin Periodontol* 1987; 14: 610-613.
- [18.] Hoogendijk CF, Marx J, Honey EM, Pretorius E, Christianson AL. Ultrastructural investigation of Zimmermann-Laband syndrome. *Ultrastruct Pathol* 2006; 30: 423-426.
- [19.] Suhanya J, Aggarwal C, Mohideen K, Jayachandran S, Ponniah I. Cherubism combined with epilepsy, mental retardation and gingival fibromatosis (Ramon syndrome): a case report. *Head Neck Pathol* 2010; 4: 126-131.
- [20.] El-Kamah GY, Fong K, El-Ruby M, Affifi HH, Clements SE, Lai-Cheong JE, Amr K, El-Darouti M, McGrath JA. Spectrum of mutations in the ANTXR2 (CMG2) gene in infantile systemic hyalinosis and juvenile hyaline fibromatosis. *Br. J. Dermatol.* 2010 ;163(1):213-5.
- [21.] Kasaboglu O, Tümer C, Balci S. Hereditary gingival fibromatosis and sensorineural hearing loss in a 42-year-old man with Jones syndrome. *Genet Couns* 2004; 15: 213-218.
- [22.] Raja TA, Albadri S, Hood C. Case report: Rutherford syndrome associated with Marfan syndrome. *Eur Arch Paediatr Dent* 2008; 9: 138-141.
- [23.] Witkop CJ. Heterogeneity in gingival fibromatosis. *Birth Defects Orig Artic Ser* 1971; 7: 210-22.1
- [24.] Kondoh T, Kamimura N, Tsuru A, Matsumoto T, Matsuzaka T, Moriuchi H. A case of Schinzel-Giedion syndrome complicated with progressive severe gingival hyperplasia and progressive brain atrophy. *Pediatr Int* 2001; 43: 181-184.
- [25.] Digilio MC, Sarkozy A, Capolino R, Chiarini Testa MB, Esposito G, de Zorzi A, Cutrera R, Marino B, Dallapiccola B. Costello syndrome: clinical diagnosis in the first year of life. *Eur J Pediatr* 2008; 167: 621-628.
- [26.] Thomas S, Tandon S. Hurler syndrome: a case report. *J Clin Pediatr Dent* 2000; 24: 335-338.
- [27.] Guimarães Mdo C, de Farias SM, Costa AM, de Amorim RF. Maroteaux-Lamy syndrome: orofacial features after treatment by bone marrow transplant. *Oral Health Prev Dent* 2010; 8: 139-142.
- [28.] Kaisare S. Gingival enlargement in Niemann-Pick disease: a coincidence or link? Report of a unique case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007; 104: e35-e39.
- [29.] Young WG, Sauk JJ, Pihlstrom B, Fish AJ. Histopathology and electron and immunofluorescence microscopy of gingivitis granulomatosa associated with glossitis and cheilitis in a case of Anderson-Fabry disease. *Oral Surg Oral Med Oral Pathol* 1978; 46: 540-554.
- [30.] Young WG, Pihlstrom BL, Sauk JJ. Granulomatous gingivitis in Anderson-Fabry disease. *J Periodontol* 1980; 51: 95-101.
- [31.] Tan MH, Mester J, Peterson C, Yang Y, Chen JL, Rybicki LA, Milas K, Pederson H, Renzi B, Orloff MS, Eng C. A clinical scoring system for selection of patients for PTEN mutation testing is proposed on the basis of a prospective study of 3042 probands. *Am J Hum Genet* 2011; 88: 42-56.
- [32.] Bhansali RS, Yeltiwar RK, Agrawal AA. Periodontal management of gingival enlargement associated with Sturge-Weber syndrome. *J Periodontol* 2008; 79: 549-555.
- [33.] Pereira de Godoy JM, Fett-Conte AC. Dominant inheritance and intra-familial variations in the association of Sturge-Weber and Klippel-Trenaunay-Weber syndromes. *Indian J Hum Genet* 2010; 16: 26-27.
- [34.] Tovar S, Parlatescu I, Dumitriu AS, Bucur A, Kaplan I. Oral complications associated with D-penicillamine treatment for Wilson disease: a clinicopathologic report. *J Periodontol* 2010; 81: 1231-1236.
- [35.] Maas SM, Lombardi MP, van Essen AJ, Wakeling EL, Castle B, Temple IK, Kumar VK, Writzl K, Hennekam RC. Phenotype and genotype in 17 patients with Goltz-Gorlin syndrome. *J Med Genet* 2009; 46: 716-720.
- [36.] Omori K, Hanayama Y, Naruishi K, Akiyama K, Maeda H, Otsuka F, Takashiba S. Gingival overgrowth caused by vitamin C deficiency associated with metabolic syndrome and severe periodontal infection: a case report. *Clin Case Rep* 2014; 2: 286-295.
- [37.] Kubota Y, Moriyama Y, Yamagishi K, Tanigawa T, Noda H, Yokota K, Harada M, Inagawa M, Oshima M, Sato S, Iso H. Serum vitamin C concentration and hs-CRP level in middle-aged Japanese men and women. *Atherosclerosis* 2010; 208: 496-500.
- [38.] Cetiner S, Alpaslan C, Gungor N and Kocak U. Tooth pain and numb chin as the initial presentation of systemic malignancy. *Turk J Med Sci* 1999; 29: 719-722.

- [39.] Patil S, Kalla N, Ramesh DNSV, Kalla AR. Leukemic gingival enlargement: a report of two cases. *Arch OrofacSci* 2010; 5: 69-72.
- [40.] Stewart C, Cohen D, Bhattacharyya I, Scheitler L, Riley S, Calamia K, Migliorati C, Baughman R, Langford P, Katz J. Oral manifestations of Wegener's granulomatosis: a report of three cases and a literature review. *J Am Dent Assoc* 2007; 138: 338-348; quiz 396, 398.
- [41.] Shiboski CH, Regezi JA, Sanchez HC, Silverman S. Oral lesions as the first clinical sign of microscopic polyangiitis: a case report. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod* 2002; 94: 707-711.
- [42.] Samtsov AV. Cutaneous sarcoidosis. *Int J Dermatol* 1992; 31: 385-391.
- [43.] Newman LS, Rose CS, Maier LA. Sarcoidosis. *N Engl J Med* 1997; 336: 1224-1234.
- [44.] Kadiwala SA, Dixit MB. Gingival enlargement unveiling sarcoidosis: Report of a rare case. *Contemp Clin Dent* 2013; 4: 551-555.
- [45.] Nwoku LA, Kekere-Ekun TA, Sawyer DR, Olude OO. Primary tuberculous osteomyelitis of the mandible. *J Maxillofac Surg* 1983; 11: 46-48.
- [46.] Smith WH, Davies D, Mason KD, Onions JP. Intraoral and pulmonary tuberculosis following dental treatment. *Lancet* 1982; 1: 842-844.
- [47.] Karthikeyan BV, Pradeep AR, Sharma CG. Primary tuberculous gingival enlargement: a rare entity. *J Can Dent Assoc* 2006; 72: 645-648.
- [48.] Weaver RA. Tuberculosis of the tongue. *JAMA* 1976; 235: 2418.
- [49.] Woolfe M. Secondary tuberculous ulceration of the tongue. A case report. *Br Dent J* 1968; 125: 270-271.
- [50.] O'Connell S, Davies J, Smallridge J, Vaidyanathan M. Amelogenesis imperfecta associated with dental follicular-like hamartomas and generalised gingival enlargement. *Eur Arch Paediatr Dent* 2014; 15: 361-368.
- [51.] Fisekcioglu E, Dolekoglu S, Ilguy D. Idiopathic gingival hyperplasia: clinical features and differential diagnosis. *J Can Dent Assoc* 2011; 77: b148
- [52.] Lee W, O'Donnell D. Severe gingival hyperplasia in a child with I-cell disease. *Int J Paediatr Dent* 2003; 13: 41-45.
- [53.] Jain S, Kaur H, Kansal G, Gupta P. Multiple myeloma presenting as gingival hyperplasia. *J Indian Soc Periodontol* 2013; 17: 391-393.