REVIEW ARTICLE

A Systematic Approach to the Diagnosis of Gingival Enlargements

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Abstract

Aim: Gingival enlargement (GE) is a very frequent condition to be witnessed in routine clinical practice. With a wide array of factors responsible for this clinical situation, it is imperative to identify the precise nature of the causative factor and underlying disease process.

Background: Continuous lifestyle alterations and clinical dental practice over a period of time have seen many new behaviors, disease conditions, and dental treatment options associated with GEs. The existing classification system for the assessment and treatment planning of GEs essentially has been proposed almost half a century ago and thus does not accommodate the newer variants reported by the authors in the form of case reports. Largely all such conditions, which do not fall under the major categories, are grouped under the broad heading of "idiopathic GEs." This grossly affects the clinicians' acumen to comprehend the subtle differences in etiology and pathogenesis of GEs and to provide precise personalized patient care to these patients.

Review results: This article showcases the newer variants of GEs as published in the literature over the last 60 years.

Conclusion: This review provides a contemporary comprehensive update to include the variants as novel categories or subcategories for better identification, diagnosis, and management of these cases.

Clinical significance: With the continuous surge of advances in knowledge of periodontal disease pathogenesis and novel diagnostic/therapeutic methods, a multitude of variants of GE conditions have been witnessed in recent clinical practice. There is a significant need for periodic expansion and update of the variants for GE conditions for precise identification and management of these conditions.

Keywords: Classification, Differential diagnosis, Gingival enlargement, Hereditary.

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Introduction

Gingival enlargement (GE) is a clinical condition of an increase in the size of the gingiva and a very common feature of gingival and periodontal disease. It is characterized by evident growth of the gingiva vertically toward the incisal edge of the clinical crown and/or horizontally in the buccolingual dimension. Several studies have demonstrated that gingival hyperplasia affects different populations and is associated with multiple causes. The most common and recognized type is the drug-induced GE, which is mostly a combined enlargement owing to plaque-induced inflammation and the usage of certain specific systemic drugs. Furthermore, congenital GE (hereditary and metabolic disorders) associated with hormonal factors have also been reported.[1–5] This condition is not a sudden-appearing pathology but progresses from mild-to-severe forms. Though the clinical condition is highly prevalent and morbid in terms of pain, speech, feeding, and esthetic problems, its clinical identification and categorization have not been adequately addressed. In fact, maintenance of proper oral hygiene by plaque removal using toothbrushes becomes very difficult and may further aggravate the progression of periodontal disease.[6] As GE is a clinical entity of differential distribution, degree, and localization in dental and other patients, it needs a thorough and systematic method for precise identification and appropriate clinical management.

Gingival enlargements have been considered in the most widely used 1999 American Academy of Periodontology Classification of Periodontal Disease, that is, but very vaguely. Only hereditary gingival fibromatosis (HGF) and drug-influenced GEs have been incorporated as subcategories under gingival diseases of genetic origin and modified by medications, respectively, rest all types of enlargements have been just put under a single broad head subcategory of GEs under mucogingival deformities and conditions around the teeth.[7,8] Even in the most recent classification system of periodontal diseases, different categories of enlargements have been considered under different periodontal pathologic conditions, that is, drug-induced enlargement (gingivitis–dental biofilm induced), genetic/developmental, reactive processes, neoplasia (gingival disease–non-dental biofilm induced), etc.[9] Such categorization fails to provide a clear view of the features associated with individual cases of GEs and a precise approach

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Table 1: Glickman classification of GE according to underlying histopathological changes and etiology

I. Inflammatory
A. Chronic inflammatory GE
1. Generalized or localized
2. Discrete (Tumor-like)
B. Acute inflammatory GE (Gingival abscess)
II. Non-inflammatory hyperplastic GE (gingival enlargement)
A. Marginal
B. Diffuse
III. Combined GE
IV. Conditioned GE
A. Hormonal
1. The GE of pregnancy
2. The GE of puberty
B. Leukemic GE
C. The GE associated with vitamin C deficiency
V. Neoplasms
VI. Developmental gingival enlargement

Courtesy: See Ref. 10

Table 2: Classification of types of GE

I. Inflammatory enlargement	A. Chronic B. Acute
II. Drug-induced enlargement	A. General information B. Anticonvulsants C. Immunosuppressants D. Calcium channel blockers
III. Enlargements associated with systemic diseases or conditions	A. Conditioned enlargement 1. Pregnancy 2. Puberty 3. Vitamin C deficiency 4. Plasma cell gingivitis 5. Non-specific conditioned enlargement (pyogenic granuloma) B. Systemic diseases that cause GE 1. Leukemia 2. Granulomatous diseases (e.g., Wegener's granulomatosis; sarcoidosis)
IV. Neoplastic enlargement (gingival tumors)	A. Benign tumors B. Malignant tumors
V. False enlargement	

for differential diagnosis. and management. As an individual clinical entity, GEs are classified according to the etiologic factors associated with and/or the pathologic changes in the tissue. Till today, we have only one systematic classification of GEs, which was given by Sir Irving Glickman in 1950 and had been the basis of our contemporary diagnostic and therapeutic management of this clinical entity characterized by huge diversity[10] (Table 1). Although certain attempts for detailed categorization of GEs caused by a single cause, for example, genetics have been made in the recent past. yet there have been no specific modifications or emergence of any novel systematic approach for diagnosis.[5] The contemporary classification system identifies categories of GEs (Table 2).[11] There is an addition of a lot of new knowledge about etiologic factors and much deeper insights into the pathogenesis of periodontal disease. Along with this, there is a rapid increase in science and technology and a constant flow of published literature providing evidence of diverse and a multitude of new factors associated with GEs, for example, systemic diseases or hereditary conditions. So, there is definitely a strong need for expansion and revision of our current diagnostic approach system for GEs. This article attempts to list some novel or lesser-known GE conditions based on the available contemporary published literature. Keeping in view these salient situations under different GEs categories shall help the clinician to better diagnose, differentiate and manage this widely prevalent clinical entity.

Review Results

Inflammatory Gingival Enlargements

Both acute and chronic GEs have been documented as separate categories in basic classification. From a diagnostic standpoint, acute inflammatory GEs are generally easy to recognize owing to their relatively clearer or obvious clinical features and history. Mostly a localized enlargement with severe redness, and sharp pain of short duration, occasionally accompanied by pus formation are typical presentation signs, thus gingival abscess and periodontal abscesses are both included in acute GEs. Chronic GEs have varied presentations ranging from sessile or pedunculated masses to generalized involvement of gingiva in the mouth. Characteristically, chronic enlargements limited to maxillary anterior teeth are generally associated with mouth breathing.

From the outset, the term "gingival enlargements" have been reserved for lesions limited only to gingiva. It is important to define or delineate the extension of inflammation in tissue in the continuum of periodontium, that is, periodontal ligament, cementum, and alveolar bone, as total periodontium is a composite unit physiologically, biologically, and functionally. The component tissues are interdependent on each other in health, function, and disease and do not exist in isolation from each other. Periodontal inflammation in a number of cases may progress to further bone loss, tooth mobility, and eventually tooth loss. The disease process may result from a direct extension of inflammation, a coexisting inflammatory lesion, or a combination of both. Extension and severity of inflammation and tissue destruction is a significant factor for the selection of treatment procedures for the corrective management of GE and restoration of the health of periodontium. A large body of peer-reviewed published literature has documented GEs associated with chronic[12–15] and aggressive periodontitis.[16–19] Most cases of aggressive periodontitis associated with enlargements were found to be generalized aggressive periodontitis.[16–19] Specific management strategies, for example, chemotherapeutic agents, host modulatory agents, regenerative periodontal surgical procedures, etc. focusing on the control of periodontal ligament destruction and bone loss need to be adopted for such cases, in addition to standard surgical resection of GEs.

Gingival Enlargements Associated with Hereditary Syndromic Conditions

The category "Gingival enlargements associated with hereditary syndromic conditions" can be further extended according to etiology, clinical presentation, and histopathological features.[20,21]

Table 3: Hereditary gingival fibromatosis

Hereditary gingival fibromatosis	
Gingival fibromatosis	2p21, 5q, 11p (AR) gene loci
Zimmermann–Laband syndrome	3p14.13 gene locus (AD) Abnormalities of soft cartilages of nose, and/or ears, abnormal fingers, and nails.[26]
Ramon syndrome	Characterized by Cherubism, epilepsy, mental retardation stunted growth, and hypertrichosis.[27]
Systemic hyalinosis	Mutation in *CMG 2* or *ANTRX 2* gene with widespread deposition of hyaline material in all body tissues (AR)[28,29]
Jones syndrome	autosomal dominant syndrome inherited by sensorineural deafness.[30]
Rutherfurd syndrome	Characterized by corneal opacity, mental retardation with failure of tooth eruption (AD).[31]
Cross/Kramer syndromes	Characterized by hypopigmentation, mental retardation.[32]
Gingival fibromatosis, hypertrichosis, and mental retardation	An AR disorder with epilepsy, hirsutism and finger abnormalities.[33]
Neurofibromatosis type 1	Neurocutaneous disorder caused by mutation in *NF 1* gene and 17q11.2 gene map locus (AR).[34]
Schinzel–Giedion syndrome	Gene map locus 18q21.1involved and characterized by progressive neurodegeneration and respiratory failure (AR).[35]
Costello syndrome	Characterized by fetal and neonatal macrostomia, coarse facial dysmorphism, and mental retardation (AD).[36]

AR, autosomal recessive; AD, autosomal dominant

- Hereditary gingival fibromatosis
- Lysosomal storage disorders
- Vascular disorders
- Disorders associated with dental abnormalities

Hereditary gingival fibromatosis was first reported by Goddard and Gross in 1856. Also, HGF is a benign gingival condition with a prevalence of about 1:75,000 with a 1:1 ratio of males and females. Furthermore, HGF can be isolated or it can be diffused with syndromic components.; HGF usually shows an autosomal dominant pattern but autosomal recessive or X-linked inheritance can also be seen in syndromic involvement. Chromosomes 2, 4, and 5 with genetic loci such as 2p21-p22 (GINGF), 2p13-p16, 2p22.3-23 5q13-q22 (GINGF2), 4q21, and 4q are involved with mutations, duplications, deletions, and other genetic anomalies. Genetic loci such as 8, 14q, 19p, 19q, and Xq are also related to syndromic gingival fibromatosis.[22,23]

Hart et al.[24] identified a mutation in the *Son of Sevenless-1 (SOS-1)* gene located on chromosome 2p21. The *SOS-1* gene mutation is thought to cause HGF by upregulation of the activity of type-I collagen, transforming growth factor- β (TGF-β), and tissue inhibitors of metalloproteinases (TIMPS) and by downregulation of the expression of matrix metalloproteinases (MMPS).[25]

Lysosomal storage disorders are a heterogeneous group of disorders caused by lysosomal enzyme dysfunction which includes mucopolysaccharidosis (MPS), mucolipidosis, and others. Mucopolysaccharidoses involve partial catabolism of several GAGs. Depending on the particular deficient enzyme, mucopolysaccharidosis (MPS) syndromes are divided into MPS types I through VII.

A brief description of all these categories have been summarized, including some of the additions to these categories[26–60] (Tables 3 to 6).

Gingival Enlargements Associated with Systemic Granulomatous Diseases

In the original classification of 1940, this category did not exist at all. Only type of enlargement when the systemic condition of the patient is involved in a way to exaggerate or distort the usual gingival response to local irritation was categorized as "conditioned gingival enlargement." This included only three variants at the outset, as follows:

- Hormonal
  - The GE of pregnancy
  - The GE of puberty
- Leukemic GE
- The GE associated with vitamin C deficiency

Over a period of time, enlargements associated with systemic conditions have been expanded and the current classification for this category contains two separate classes for systemic conditions and diseases.

Systemic Diseases Causing Gingival Enlargement

Such enlargements present as variable clinical picture depending upon the mechanism of the implicating systemic disease. The GEs associated with leukemia has been known for a long and may appear as a diffuse or marginal affecting all or a group of teeth. Gingiva shows bluish red hue, with a shiny surface mostly in association with chronic leukemias, and mimics the features of chronic inflammatory enlargements. True leukemic GEs are seen in cases of acute and subacute leukemia with infiltration of leukemic cells in the connective tissue of the gingiva. Wegener's granulomatosis may manifest as purplish enlargement usually confined to the interdental papilla and bleeds on the slightest provocation. Sarcoidosis, a chronic granulomatous disease of

Table 4: Lysosomal storage disorders and MPS

Lysosomal storage disorders	
Hurler syndrome	Gene map locus 4p16.3 involved caused by mutation in gene encoding for enzyme α-L-iduronidase (AR).[37] Accumulation of GAGs (heparan sulfate and dermatan sulfate) and deficiency of enzyme in various tissues. H/F: Hurler cells in gingival tissues. O/F: Gingival hyperplasia, macroglossia.[38]
Maroteaux–Lamy syndrome (type 4)	Gene map locus 5q13 involved caused by deficiency of arylsulfatase B enzyme resulting in accumulation of dermatan sulfate in tissues and excretion in urine (AR). O/F: Gingival hyperplasia, hypertrophy of maxillary alveolar ridges, peg-shaped and calcified teeth with delayed eruption and anterior open bite, macroglossia.[39,40] H/F: Metachromatic inclusions in leukocytes.
Hurler–Scheie syndrome	Mildest form with gene map locus 4p16.3 is involved and corneal clouding.[41]
Hunter syndrome/mucopolysaccharidosis 2	The X-linked autosomal recessive disorder (gene map locus Xq28) characterized by deficient enzyme is Iduronate 2 sulfatase (12S), accumulation of dermatan sulfate and heparan sulfate. It has same features as Hurler's syndrome.[37,38]
Sly syndrome/mucopolysacharidosis type VII	Autosomal recessive disorder (gene map locus 12 q 23.3) caused by deficiency of beta glucuronidase enzyme. O/F: Thickening of alveolar ridges rarely gingival hyperplasia is seen.[42]
I-cell diseases/mucolipidosis	Autosomal recessive disorder (gene map locus 12 q 23.3) with deficiency of enzyme *N*-acetylglucosamine 1 phosphotransferase which leads to accumulation of mucopolysaccharides and mucolipids. H/F: Known as I-cell disease because of macromolecules that accumulate inside cell and form characteristic cytoplasmic inclusions.[43]
Aspartyl glucosaminuria	Autosomal recessive storage disorder (gene map locus 4q33-4q35) characterized by deficiency of aspartyl glucosaminidase enzyme leading to the accumulation of glycoasparagines in lysosomes. Leukoedema and gingival fibromatosis are common feature. H/F: Fibroepithelial hyperplasia is seen.[44]
Alpha mannosidosis	There is deficient alpha mannosidase enzyme leading to abnormal collection of mannose-containing residues (AR). H/F: Cytoplasmic vacuolization of lymphocytes and monocytes is seen. O/F: Macroglossia, firm hyperplastic gingival nodules are seen in oral findings.[45]
Niemann–Pick diseases	Autosomal recessive disorder (gene map 18 q11-12 type c-11p15) caused by deficient acid sphingomyelinase enzyme with accumulation of sphingolipids in cells. The GE is not a constant feature. Thick lips macroglossia and widely spaced teeth are seen.[46] H/F: There is infiltration with foamy histocytes. Cytoplasmic vacuolization of lymphocyte and monocytes.
Anderson–Fabry diseases	The X-linked recessive inherited disorder gene map locus (Xq21-Xq22) with deficiency of enzyme ceramide trihexosidase and intracellular accumulation of glycolipid ceramide trihexoside in vascular endothelial cell, pericyte, fibroblast, macrophage, etc. Angiokeratoma of skin and oral mucosa membrane. H/F: Ceramide inclusions in connective tissue, oral epithelial cells.[47]
Menkes kinky hair diseases	A rare (gene map Xq 13) X-linked recessive neurodegenerative disorder caused by defect of copper transport and metabolism. O/F: There is delayed dentition and gingival hyperplasia.[48]
Ligneous periodontitis (plasminogen deficiency)	It is characterized by gingival swelling covered with tough yellowish white thin pseudomembrane that could be wiped away.[49] H/F: Epithelial hyperplasia and fibrin deposition underneath epithelium and around blood vessels is present. Dermis shows edema and perivascular mixed cellular infiltrate.
Cowden syndrome/multiple hamartoma	Mutation in PTEN tumor suppressor gene (gene map locus 10 q 23,31) (AD). It may be because of methylation of *KILLIN* gene or mutations in certain subunits of succinate dehydrogenase.[50] O/F: Cobblestone such as papules of gingiva and buccal mucosa are seen.[51]

H/F, histologic features; O/F, oral features

Table 5: Vascular disorders

	Vascular disorders
Sturge–Weber syndrome	The AR or the AD, characterized by intracranial vascular anomaly and calcification, leptomeningeal angiomatosis. Unilateral cutaneous nevi along trigeminal nerve sensory distribution, unilateral vascular hyperplasia of oral mucosa and gingiva, neurological manifestations, and oral complications.[52,53]
Klippel–Trenaunay syndrome	Paradominant inheritance (gene map locus 8q 22.3). Triad of features like vascular nevi, venous varicosities, hyperplasia of hard and soft tissues in affected area.[52,54,55]

Table 6: Disorders associated with characteristic dental abnormalities

Wilson syndrome (hepatolenticular degeneration)	Gene map locus (13q14.3-q21.1) involved with mutation in ATP7B gene is present (AR). There is low ceruloplasmin content. Basal ganglia and liver undergo changes.[56] O/F: Multiple small red papules of lips with GE. Early onset periodontitis with repeated oral candidiasis and enamel hypoplasia is present. H/F: Granulomatous inflammation with thick irregular clumps of tortuous red staining abnormal elastic fibers.[57]
Goltz syndrome	The X-linked dominant inheritance with *PORCN* gene mutation (gene map locus Xp11.23) O/F: partial anodontia, lip papilloma, GE, hypoplastic teeth and multiple papillomas of mucous membranes. H/F: Deposits of fat cells or adipose tissue in dermis.[58]
Regional odontodysplasia	Genetic predisposition has been proposed but local factors play a major role. Affect both primary and permanent dentition. Enamel and dentin show lack of contrast with decreased radiopacity and tooth has a ghost-like appearance.[59] Gingival enlargement is commonly seen with regional type.[60] H/F: Odontogenic tissue in the epithelium and intramesenchymal calcification is present.

unknown causation also presents as a smooth surfaced GE in some cases.

The emerging evidence of many new systemic granulomatous diseases affecting the size of the gingiva has been documented in the literature. There are anecdotal reports of orofacial granulomatosis (OFG) displaying enlargement of the gingiva. Orofacial granulomatosis is a non-specific granulomatous inflammation presenting as facial or lip swelling, cheilitis, ulcerations, GE, mucosal tags, and sometimes lymphadenopathy. The term "orofacial granulomatosis" introduced by Wiesenfield in 1985 is used to encompass a variety of possible conditions including Sarcoidosis and Melkersson–Rosenthal syndrome, but essentially OFG occurs mainly in isolation or as a manifestation of Crohn's disease (CD).[61] When the precise etiology is unknown it is referred to as idiopathic OFG.[62,63] Another clinical situation can be GEs associated with tuberculosis. Primary oral tuberculous lesions are extremely rare and generally occur in young adults. It usually involves gingival and is associated with caseation of the dependent lymph nodes; the lesion itself remains painless in most cases.[64] In contrast, secondary oral tuberculosis is common and is usually seen in older adults.[65,66] With the developments in diagnostic science and technology, many new disease entities may now be identified for gingival conditions, where the cause of enlargement had been obscured earlier.

Gingival Enlargements Associated with Systemic Conditions

Plasma Cell Gingivitis

Plasma cell gingivitis is an uncommon condition marked by an intense and diffuse infiltration of the plasma cells into the subepithelial gingival tissue.[67] It has been hypothesized that the immunologic reaction to some allergic antigens might be the possible causative agent. Mint in toothpaste and chewing gum,[68] cinnamon aldehyde,[69,70] strong spices (pepper, cardamom)/chilies, chewing of khat,[71,72] and certain constituents of the herbal toothpaste have been documented as the reported allergens in the literature.[67] A historical perspective of this condition dates back to the year 1952 when Zoon referred to the term "plasma-cell infiltrate." In such cases, the specific allergen need to be identified and ruled from the history of the patient.[73] The lesion is marked with dense infiltration of the plasma cells (chronic inflammatory cells), which provides the basis for the inclusion of this entity in the mentioned category.

Neoplastic Enlargement

This category needs a detailed description from the differential diagnosis standpoint as most benign GEs present themselves as isolated/localized growths or tumors originating from gingival tissue per se. The most prevalent among the benign tumors of gingiva is a fibroma. Fibromas may present as sessile or pedunculated enlargements depending upon the part of the gingiva initially involved.[74] This lesion is usually discrete involving single or two teeth or presents itself as a regional enlarged mass involving three or more teeth in the anterior maxilla (around 80%). Differential diagnoses include pyogenic granuloma, ossifying fibromas, lipoma, peripheral giant cell granulomas, papillomas, neurofibromas. It may be delineated on the basis of specific clinical and histological features. Hyperplastic stratified squamous epithelium with chronic inflammatory cell infiltrate is pathognomonic to its histopathology.[75] A lipoma is a slow-growing

benign neoplasm that rarely presents itself on the gingiva. Clinically it is usually present as a solitary mass near the mucogingival junction and histologically presents cells similar to normal fat tissue with adipocytes surrounded by mature dense connective tissue and adipose cell hyperplasia.[76] Lipomas are delineated differentially from traumatic fibromas and mucoceles based on their clinical presentation and specific histology.

Benign growths originating from gingiva may mimic reactive lesions such as peripheral giant cell granulomas or pyogenic granulomas. Pyogenic granulomas are the most common reactive enlargements in the gingival tissue and may present themselves at any age. These reactive lesions present typical clinical features such as young lesions in pyogenic granulomas that are highly vascular and present as red or purple color enlargement in the anterior maxilla or mandible. The chief clinical feature distinguishing the lesion from a fibrous GE is its color and tendency to bleed.[77] It presents a characteristic smooth shiny surface and has a tendency to bleed profusely with little or no trauma. The distinct histopathology also helps in diagnosis and it exhibits multiple capillaries with neutrophil infiltrate and necrotic tissue.

Another enlargement that needs to be differentiated, though rare in occurrence is papilloma (gingival wart), which is usually a benign proliferation of the skin. Risk factors for these lesions include immune-compromised conditions such as HIV infection and renal transplantation, or AIDS patients undergoing highly active antiretroviral therapy [highly active antiretroviral therapy (HAART)] regimen.[78] Usual presentation of warts is either single or multiple and blunt with cauliflower-like appearance. Human papillomavirus has been identified with increasing frequency in premalignant oral lesions benign leukoplakia and other malignancies.

Histopathologically, there is dyskeratosis with underlying keratinocyte hyperplasia of the gingival epithelium along with inflamed, edematous and vascularized stroma with a thicky, spongy squamous epithelium layer.

Peripheral ossifying fibromas appear as growths originating from peripheral periodontal tissues and are clinically similar to focal fibrous fibromas of the gingiva. It often exhibits cauterization or cupping resorption which may not be seen in fibromas and differentiates it from these benign growths. The histology presents multinucleated giant cells with spindle-shaped mesenchymal cells along with hemosiderin deposition on the borders.[79]

Rare benign enlargements originating from gingival tissue are lymphangiomas. These may be distinguished from benign fibrous growths histologically. These are benign malformations of the lymphatic channels usually presenting as solitary lesions. Lymphangioma of gingiva is very rare and exhibits typical histopathology with lymphatic vascular cavities of various sizes, lined by a flat endothelium and filled with lymph that may occasionally contain erythrocytes.[80]

Ameloblastomas are among the rare benign growths in gingiva that present the pathognomonic clinical feature that they are often associated with unerupted teeth and will also have a tendency to expand the cortices and distinct histopathology of epithelium proliferating in a cord-like fashion.[81]

Benign neoplastic enlargement that may challenge the diagnosis of a growth in gingiva also includes rare presentations such as neurofibromatosis type 1 which presents a diffuse plexiform variant or a part of generalized syndrome known as neurofibromatosis. It is a nerve sheath tumor that rarely presents itself in the gingival (about 2% of all neurofibromas in the oral cavity).[82]

Oral squamous cell carcinomas, in spite of being the most prevalent oral malignancy rarely present on gingival tissue. It may need to be histologically examined for early diagnosis and staging.[83] Neoplastic malignant growths in gingival may mimic inflammatory, reactive lesions, and non-neoplastic benign growths. A keen evaluation of the underlying risk factors such as smoking, radiation exposure or AIDS, or any immunocompromised state can help in the accurate delineation of squamous cell carcinoma from non-malignant or inflammatory growths. The final diagnosis is always based on confirmatory cytological findings, following fine needle aspiration cytology (FNAC) or tissue biopsy. The confirmation of histologic diagnosis is challenging because the cells tend to be well differentiated and lack nuclear atypia resulting in false negative results.[84,85]

Another malignant lesion prevalent in gingiva is a malignant melanoma which presents as an aggressive tumor of melanocytic origin. Frequently affected oral sites include the palate and maxillary gingiva. Initially, it presents as a swelling that is usually pigmented. Histopathologically, it shows characteristic features such as spindle cells and malignant or dysplastic melanocytes.[86] Malignant cells are often present in nests/clusters or groups. These may be differentiated from squamous cell carcinoma and less prevalent Kaposi's sarcoma based on histology.

Hyperplastic leukoplakia in the gingival tissue is a slow-growing lesion and also needs to be differentiated when diagnosing a malignant growth in the gingival as initially, it may present as an asymptomatic benign-appearing solitary white patch that may have a flat papillary or verrucous architecture. Proliferative verrucous leukoplakia of gingiva may present as a solitary reoccurring progressive white patch. Histopathologically may also present as solitary regional flat or papillary or verrucous leukoplakia in the free and attached gingiva (tooth bearing areas).[87]

Conclusion

Gingival enlargements are common clinical findings seen in a periodontal clinic and are characterized by etiological heterogeneity. Additionally, they may present as a typical symptom of diverse genetic syndromes or may occur sporadically in several other syndromes and diseases, as documented in previously published literature. In addition, these may be associated as an adverse effect of a variety of drugs and neoplastic conditions. Identification and diagnosis are made based on medical history, clinical examination, blood tests, and histopathological evaluation of affected gingival tissue.

With the increasing scientific knowledge and diagnostic technologies, many novel conditions have emerged in the periodontal literature, where GEs have been documented as a part and parcel of the disease. Although the disease conditions need to be identified and differentiated on the basis of etiology, the names of disease are a convenient way of stating briefly the endpoint of a diagnostic process that progresses from the assessment of symptoms and signs toward knowledge of causation. Since GEs are conditions of a complex etiology, a systematic approach to clinically diagnose and differentiate the GEs is needed. Based on the contemporary available periodontal literature on GEs, an attempt has been made to provide a clinical update on different varieties of the GEs, which may help to properly identify and differentiate a specific GE from other periodontal disease entities.

Clinical Significance

With the continuous surge of advances in knowledge of periodontal disease pathogenesis and novel diagnostic/therapeutic methods, a multitude of variants of GE conditions have been witnessed in recent clinical practice. There is a significant need for periodic expansion and update the variants for GE conditions for precise identification and management of these conditions.

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