REVIEW ARTICLE

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Gingival involvement of oral non-tumoral mucosal diseases

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Abstract: *Gingival conditions are frequently encountered in dental clinical practice and they can raise diagnosis and treatment problems. The diagnostic is variable from normal conditions to autoimmune diseases or even malignancy. Some of them cause disturbances such as pain, burning sensation and have an impact on patient's quality of life.*

INTRODUCTION

Although oral cavity is an area easy to explore by visual exam, there is a large variety of conditions and disorders which can be encountered. We present a general overview of gingival lesions frequently associated with oral mucosal diseases. Dental plaque-induced gingivitis and all gingival enlargements (reactive or tumorous with benign, cystic or malignant variants) are not the subject of this article.

DEFINITION OF SPECIFIC TERMS AND LESIONS

The gingiva is a "first line" mechanical barrier defined as the keratinized mucosa that covers the teeth and the alveolar bone. The periodontium is made of gingiva with the alveolar bone, periodontal ligament and cementum. The mucogingival junction separates the gingiva from alveolar mucosa [1]. In healthy persons the gingiva has a pink color (Figure 1), or it can have pigmented areas depending on the individual skin color (Figure 2).

Histologically, gingiva is composed of a thick stratified, keratinized epithelium and the underling connective tissue made of collagen and elastin fibers, fibroblasts, melanocytes and immune cells [2]. The epithelium cell-to-cell adhesion is done through desmosomes and adherence junctions while the adhesion to the basement membrane is done by hemidesmosomes and focal contacts [3].

Superficial lesions affect epithelium and underlying connective tissue. Depending on the clinical appearance, evidenced by visual examination, they can be divided into: keratosis or white lesion (Figure 3A and 3B), atrophic (Figures 4A, 4B, 4C), ulcers resulting from vesicles (Figure 5A) or bulla (Figure 5B).

The gingival diseases are presented in the periodontal diseases classification elaborated by Armitage in 1999 [4] which is universally

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accepted for both periodontal and gingival conditions.

Figure 1. Normal gingiva

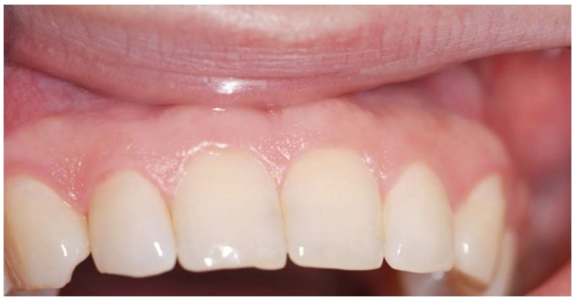


Figure 2. Pigmented gingiva

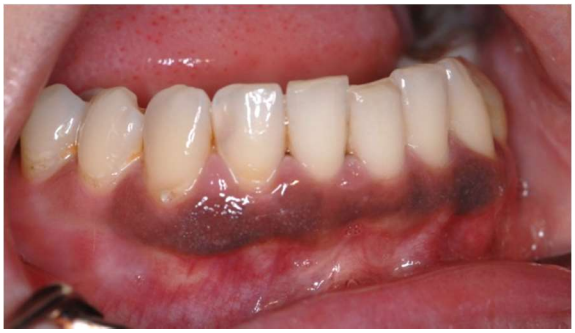


Figure 3A. Gingival white lesion. Extended homogenous plaque of unknown etiology. Diagnosis: leukoplakia

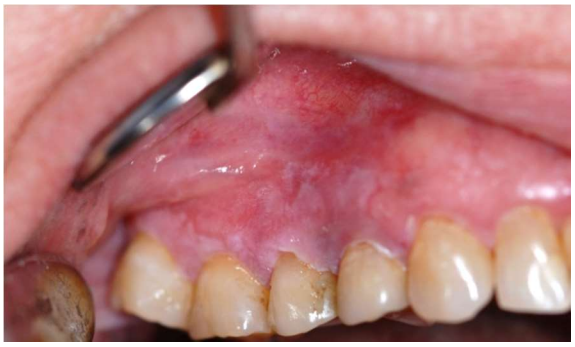


Figure 3B. Gingival white lesion. Diagnosis: traumatic keratosis (associated with aggressive tooth-brushing technique)

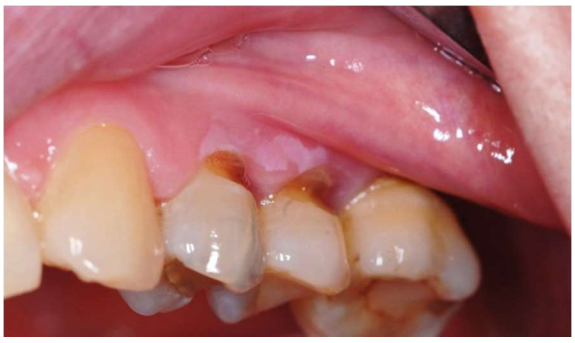


Figure 4A. Mild atrophy. Diagnosis: desquamative gingivitis in oral lichen planus

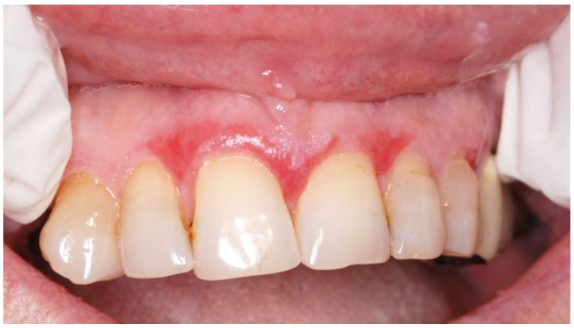


Figure 4B. Moderate atrophy. Diagnosis: desquamative gingivitis in oral lichen planus

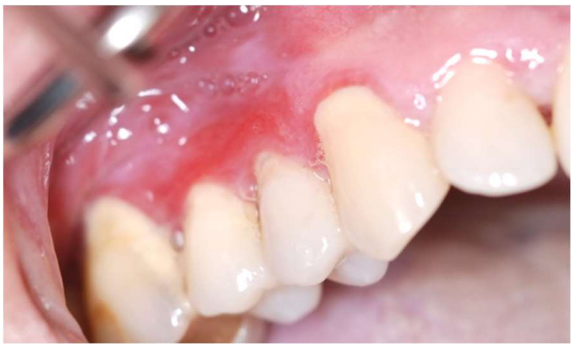


Figure 4C. Severe atrophy and reticular keratosis. Diagnosis: desquamative gingivitis in oral lichen planus

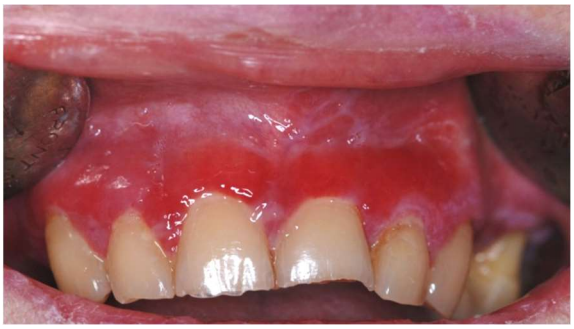


Figure 5A. Small gingival ulcers following vesicles. Diagnosis: primary herpetic gingivitis

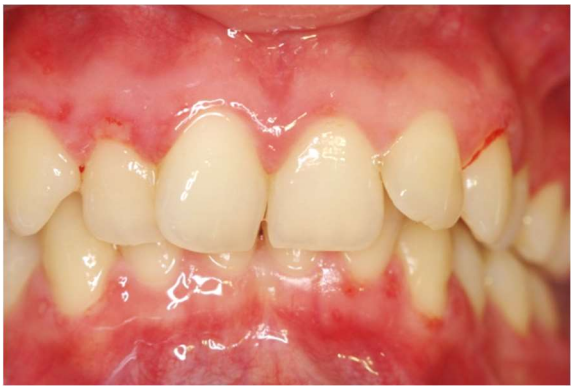
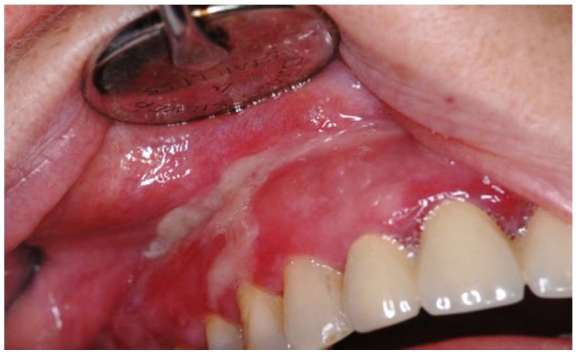


Figure 5B. Extended ulceration after bullae rupture. Diagnosis: desquamative gingivitis in bullous dermatosis



The gingival disorders are presented in Table 1.

CLINICAL FEATURES AND THE BASIC THERAPEUTICALLY APPROACH OF ORAL MUCOSAL DISEASES WITH GINGIVAL INVOLVEMENT

We reviewed and summarized the clinical characteristics of the most frequent oral diseases. The oral manifestations of general diseases cover a large range of conditions (Table 2). The mainly local signs usually affects more than one mucosal area, so the gingival lesions must be interpreted in the whole context.

Table 1. The gingival diseases classification [4]

Periodontal diseases classification. Section gingival diseases		
A. Dental plaque-induced gingival diseases	1. Gingivitis associated with dental plaque only 2. Gingival diseases modified by systemic factors 3. Gingival diseases modified by medications 4. Gingival diseases modified by malnutrition	
B. Non-plaque-induced gingival lesions	1. Gingival diseases of specific bacterial origin 2. Gingival diseases of viral origin 3. Gingival diseases of fungal origin	
C. Gingival lesions of genetic origin	1. Hereditary gingival fibromatosis 2. Other	
D. Gingival manifestations of systemic conditions	1. Mucocutaneous disorders	1) lichen planus 2) pemphigoid 3) pemphigus vulgaris 4) erythema multiforme 5) lupus erythematosus 6) drug-induced 7) other
	2. Allergic reactions	
E. Traumatic lesions (factitious, iatrogenic, accidental)	1. Chemical injury 2. Physical injury 3. Thermal injury	
F. Foreign body reactions		

Oral lichen planus is a disease with chronic evolution and immune mediated pathogenesis [5]. The clinical signs and symptoms are variable depending on the lesions associated [2]. The lesions are multiple, associated, merged and coexist and symmetrically distributed. The gingival involvement, commonly encountered in these patients is described as desquamative gingivitis. This shows various lesions from white, keratotic to atrophy, ulcerations and bullae. The diagnostic criteria universally accepted includes the histological confirmation (with hydropic degeneration and band-like T-cells infiltrate), although there are microscopic features similar to other mucosal diseases [6].

The therapy is not curative but it intends to control acute lesions and symptoms. The agents used cover a large spectrum of drugs: topical or systemic corticoids, hydroxychloroquine, azathioprine, mycophenolate mofetil, methotrexate, dapsone, thalidomide, biological agents etc. [6].

Mucous membrane pemphigoid is a chronic

autoimmune blistering disease which presents subepithelial vesicles and bullae. Any area of the oral mucosa can be affected. The gingival lesions present as desquamative gingivitis which simulates oral lichen planus and are noticed in 60% of cases [6]. The diagnosis is established by histopathological analysis and direct immunofluorescence which shows along the basal membrane linear deposits of immune-globulin IgG, IgM, IgA and complement [6]. The therapy is mainly long-term immunosuppressive treatment used local and systemic.

Table 2. General data on oral mucosal diseases, clinical features [1-3]

Oral conditions	Disease	Oral mucosa manifestations
Autoimmune diseases	Oral lichen planus	Variable presentation, generally symmetrical lesions (reticular, popular, plaque form, atrophy, ulcers, bulla)
	Pemphigus vulgaris	Small intraepithelial bulla and secondary erosion
	Mucous membrane pemphigoid	Desquamative gingivitis, shallow ulcer after multiple blisters affecting the oral mucosa
	Linear IgA dermatosis	Annular vesicular-bullous lesions
	Allergic reaction to dental materials and/oral health products	Variable clinical features: inflammation, reddish or white areas
Infectious diseases		
Viral	Primary herpetic infection	Ulcerative lesions following short duration vesicles
	Secondary herpetic infection	
	Herpes zoster	Unilateral ulcers following vesicles, located along nerve distribution, mainly in older patients
Bacterial	Necrotizing ulcerative gingivitis	Painful, purulent ulcers of the gingival papillae; mostly in teenagers and young adults
Traumatic lesions	Caused by excessive tooth brushing	Ulcers, atrophy and keratosis
	Mucosal burn caused by substances held in close contact for a long period of time	
	Local radiotherapy	
Pigmented lesions	Rasial pigmentation	Pigmented areas on the gingiva
	Melanotic macule	
	Metallic tattoo	
White lesions	Leukoplakia	Predominantly white lesion of unknown or tobacco etiology

Oral pemphigus vulgaris is a lifelong autoimmune bullous disease which affects the epithelium with autoantibodies directed against the desmosomal cadherine – desmoglein 3 causing acantholysis and blistering [7]. Oral mucosa is the initial site of the lesions in 80% of the patients [7]. The painful, irregular-shaped erosions and blisters affect the buccal mucosa, the tongue and gingiva. In these patients the desquamative gingivitis shows ulcers following bullae. The diagnosis is established by clinical features, histopathology, immunopathology, and serology. Direct immunofluorescence shows intercellular deposition of immunoglobulin G and complement 3 [7]. Treatment is complex and includes a variety of immunosuppressive and anti-inflammatory steroids in order to get disease control.

In patients with desquamative gingivitis there is an increased risk periodontal tissue breakdown mainly caused by the plaque deposits and the pain associated with tooth-brushing [8].

Herpetic oral viral infection is caused by two types of herpes simplex virus. The primary infection which affects mainly children or young adults shows a wide range of manifestations varying from an extended oral vesicular-ulcerative eruption to a reduced, asymptomatic condition [2, 9]. The primary eruption may be associated with general signs and symptoms such as fever, malaise, lymphadenopathy and dysphagia. The secondary infective episode usually involve gingival mucosa and the hard palate. The lesions are vesicles which break quickly and leave painful ulcers. These heal in 7-10 days without scars [9] in healthy and immunologically competent patients. Infections diagnosed early show a good response to antiviral medication. Also local symptomatic suspensions will ease the discomfort in both primary and secondary herpetic eruption.

For **pigmented lesions of the oral cavity**, more than for other conditions the diagnosis is challenging even for an experienced clinician [10]. On the gingiva the physiological pigmentation and the melanotic macules are frequently seen but this does not exclude a melanoma or Kaposi sarcoma diagnosis. The physiological pigmentation is caused by an increased melanin pigmentation of the basal layer or incontinent melanin and/or melanophages in the superficial lamina propria and the melanotic macules are a result of a increased melanin production from the basal melanocytes. In these cases, the diagnosis is appreciated after size, shape, or color, location together with the anamnestic data [10]. Generally a biopsy is needed to determine a definitive diagnosis and to exclude risky conditions.

Oral leukoplakia is defined as a predominately white lesion of the oral mucosa, lesion of questionable risk having excluded (other) known diseases or disorders that carry no increased risk of cancer [11]. It can be met in any area of the oral mucosa, including gingiva. At present about this lesion, the literature states that neither histology nor clinical factors can reliably predict the behavior [12]. Proliferative verrucous leukoplakia is one of the most aggressive form described which shows a predominant gingival involvement.

CONCLUSIONS

These gingival conditions can share similar clinical features which may lead to misdiagnosis or underdiagnosed situations. Dentists and general practitioners need to be familial to the gingival disorders. In general a definitive diagnosis is based on biopsy of the lesional tissue but also the anamnestic data should be taken to account.

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