Review

Desquamative Gingivitis - A Clinicopathological Review

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ABSTRACT: This article aims to review the etiology, clinical features and diagnosis of desquamative gingivitis in order to outline all the aspects necessary to increase the efficiency of patient management. Because of the polymorphic etiology, dental practitioners may elude the correct diagnose. Consequently, we find it important to underline all the clinical features that desquamative gingivitis may have as well as the associated oral lesions. Also we shortly review the systemic disorders that frequently associate desquamative gingivitis. It is important to know that the muco-cutaneous disorders frequently involved can have an abrupt onset with lesions sometimes confined to the gingiva. In evolution these diseases can be life threatening and a quick treatment can assure not only a more favorable evolution but also a better life quality. Laboratory analyses are mandatory in order to correctly diagnose the main systemic disorder. Histology and direct immunofluorescence investigations are the most accurate. Remission of the underlining disease brings improvement or even resolution of the oral lesions.

KEYWORDS: *Desquamative gingivitis, systemic disease, oral lesions, differential diagnosis*

Introduction

Desquamative gingivitis is a descriptive clinical term for desquamation, erosions, ulcers, vesicles and bullas that involve both free and attached gingival [1,2].

It is usually associated with autoimmune blistering disease like, pemphigus vulgaris, pemphigoid and bullous form of oral lichen planus, but also other systemic disorders.

We find it appropriate make a short review of these autoimmune disease in order to facilitate recognition and diagnoses.

Desquamative gingivitis is considered to be a clinical sign of an associated systemic disease more than a disease itself.

History

Desquamative gingivitis was first described in 1894 by Tomes and Tomes [1], but it was Prinz in 1932 who established it was a descriptive term used to define the presence of erythema, desquamation, erosions, and blistering of the attached and marginal gingiva [2].

Mc Carthy&co were the first to suggest in 1960 that desquamative gingivitis is not an entity but a gingival response to a variety of systemic disturbances of different etiologies [3].

At that time desquamative gingivitis was also referred to as "gingivosis". In 1964 Glickman and Jerome demonstrated furthermore that this alteration of the gingiva was secondary to other systemic conditions [4].

Etiopathogenesis

The oral mucosa consists of a stratified epithelial layer and connective tissue underneath. Some areas are keratinized and some are non-keratinized.

The gingiva is keratinized in order to resist the trauma caused by masticatory forces.

The oral mucosa consists of three layers: stratified squamous cell epithelium, lamina propria, and the basement membrane that separates them.

Electron microscopy studies have shown that the basement membrane consists of the following layers, see Table 1 [5].

Table 1. Electron microscopy findings, modified after [5]

Layer	Constituents
Basal keratinocyte layer:	Hemidesmosomes Keratin filaments Integrines Collagen Type XVII CD 151
Lamina lucida	Anchoring filaments-laminin 332
Lamina densa	Collagen Type IV Laminin 332/311/511 Nidogen Perlecan
Sublamina densa	Anchoring fibers-collagen Type VII

Some of the epithelial proteins assure inter-cell and cell-membrane integrity. The autoimmune diseases target these proteins (considered to be antigens) and auto-antibodies are formed against them (Table 1).

In patients with pemphigus develop autoantibodies directed toward a glycoprotein adhesion molecule (ICAM-intercellular adhesion molecule) named desmoglein (DSG 1 in primarily found in the skin and DSG 3 is usually detected in mucosal epithelium).

In bullous pemphigoid patients the antigen is a normal protein, constituent of the hemi desmosomes-basement membrane complex. They are called bullous pemphigoid antigen (BP). The initial defect is found in the Lamina Lucida region of the basement membrane.

Table 2. The epithelial proteins targeted in oral autoimmune blistering diseases, after [5]

Blistering oral disease	Targeted protein
Pemphigus vulgaris	Desmogleine 1 and 3
Pemphigus foliaceus	Desmogleine 1
Paraneoplastic pemphigus	Desmogleine 1 and 3
Cicatricle pemphigoid	Laminin V/VI; Integrine; collagen VII; BP
Bullous pemphigoid	BP
Epidermolysis bullosa aquisita	Collagen Type VII
Epidermolysis bullosa simplex	Keratin
Epidermolysis bullosa junctional	Laminin; collagen Type XVII
Epidermolysis bullosa dystrophic	Collagen Type VII
Erythema multiforme	Desmoplakins

Based on etiologic conditions correlated with the findings of histopathology and immunofluorescence studies the following classification was proposed: [3,6,7]

- Dermatological diseases
  - Cicatricial pemphigoid
  - Lichen planus
  - Pemphigus
  - Psoriasis
  - Bullous pemphigoid
  - Epidermolysis bullosa acquisita
  - Contact stomatitis.
- Endocrine disturbances
  - Estrogen deficiencies following oophorectomy and in postmenopausal stages
  - Testosterone imbalance
  - Hypothyroidism.
- Aging
- Abnormal response to bacterial plaque
- Idiopathic
- Chronic infections
  - Tuberculosis
  - Chronic candidiasis
  - Histoplasmosis.

Mucous membrane pemphigoid (MMP), oral lichen planus and pemphigus vulgaris have emerged as the most common causes of desquamative gingivitis, with the first two accounting for about 80% of cases [8].

The degree of oral, periodontal, and systemic involvement determines the overall morbidity and, sometimes, the mortality of these autoimmune disorders [9].

Diagnosis

In most cases of gingival trouble, patients seek out advice from their dental provider and not from the family physician, especially if oral discomfort is the only sign.

Therefore, it is absolutely impetuous that dental practitioners recognize and correctly diagnose desquamative gingivitis.

Especially because the systemic disorders that generate it are rare, aggressive and need immediate treatment.

A correct diagnosis when the lesions are located to the oral mucosa (which in most cases means that the onset of the systemic disease) permits readily treatment. This means a better prognosis of disease evolution and also an improved life quality for patients.

Because desquamative gingivitis is a sign not a disease “per se” the diagnosis is that of the underlining disease.

Age is an important factor not only for diagnosis but also for evaluating treatment and evolution. It is also a differential parameter, considering that some diseases have their onset in a specific age group.

Smoking, alcohol consumption and drug abuse must be taken into consideration.

A detailed analysis of both family and personal medical history is required. Also all comorbidities must be known as well as current medication. Photographs are used to record the clinical aspect at presentation and in evolution.

Since desquamative gingivitis is a distinctive sign of a systemic disease, we find it appropriate to outline all type of lesions that involve gums, in order to facilitate a proper diagnostic.

The most common clinical features are: keratosis (Fig.1), atrophy, erosions, vesicles, bullas and ulcers (Fig.2). Usually the lesions are associated (Fig.3).

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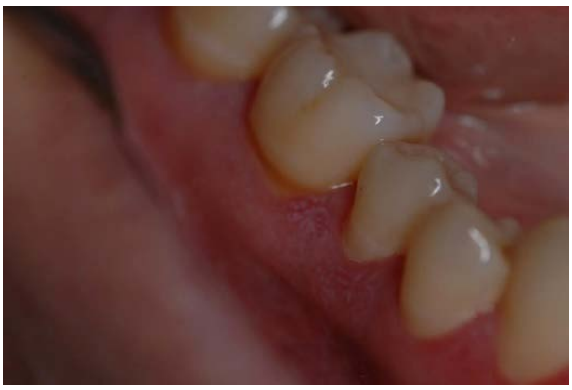

Fig.1. Reticular keratosis

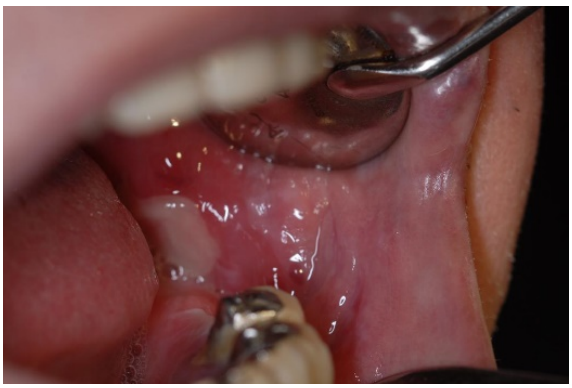

Fig.2. Ulcer after bullae ruptured

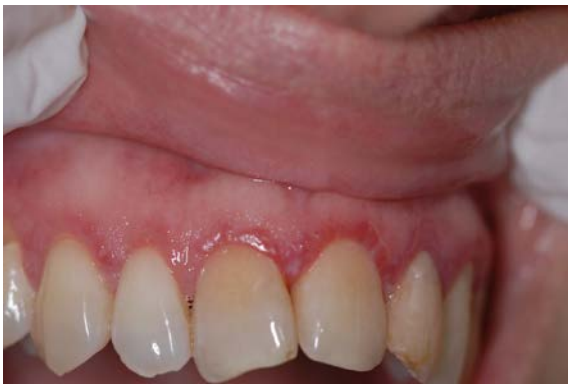

Fig.3. Erosion, keratosis, atrophy

Symptomatology depends on the type and extent of lesions.

Discomfort or mild pain is usually reported with keratosis and atrophy lesions.

Patients usually notice the discomfort while brushing their teeth.

Moderate pain when erosions are present, or vesicles are formed but aren't ruptured.

Patients usually avoid spicy food, sparkly drinks and alcohol because they exacerbate the pain.

Severe pain is associated with ulcers, ruptured bullas and vesicles that leave large denuded areas.

In some cases eating and drinking are impossible.

Dehydration is a severe complication due to pain and admittance into a hospital is required.

A correct diagnosis is hard to achieve in the absence of laboratory investigations.

For a certain diagnosis a biopsy of the altered tissue is made. Histopathology and direct immunofluorescence analyses have proven to be the most relevant.

Some autoimmune disease are frequently associated with desquamative gingivitis.

In Table 3 are presented the results of direct immunofluorescence studies in these blistering diseases.

Table 3. Autoimmune blistering diseases and direct immunofluorescence detected autoantibodies after [5]

Blistering oral disease	Detected autoantibodies
Pemphigus vulgaris	IgG, IgA, IgM in intraepithelial layer
Bullous pemphigus	IgG, C3c in epidermal basal layer
Mucous membrane pemphigoid	IgG, C3c in epidermal basal layer
Paraneoplasic pemphigus	IgG, C3c in intraepithelial layer and basement membrane
Linear IgA disease	Linear IgA along the epidermal-dermal border
Erythema multiforme	IgM, C3 in blood vessel walls
Erosive lichen planus	IgM in colloid bodies in papillary dermis
Lupus erythematosus	IgG, IgM in basement membrane

Oral Lichen Planus

Oral lichen planus is an inflammatory disease that affects both the skin and the oral cavity [10].

The etiology is unclear, stress is thought to be one of the causes but a definite cause-effect relationship hasn't been demonstrated.

Some drugs and dental restorations may cause lichen-like reactions that can be clinically indistinguishable from idiopathic lichen planus.

Penicillamine, hidroclorothiazide and angiotensin-converting enzyme inhibitors are the drugs most common associated with acute lichen planus lesions [11].

Usually the onset is among middle-aged people, with a bit higher frequency among women than men [12].

Oral lesions are usually present in the onset. Clinical features include keratotic lesion (Wickham's striae), erosions, atrophy, vesicles, bullas and ulcers.

Their distribution is usually bilateral and symmetrical.

When erosive lesions involve the gums this is clinically described as desquamative gingivitis [10].

Symptomatology depends on type and extent of lesions, it may vary from slight discomfort to severe pain, in rare cases interfering with eating and drinking.

Because of the specific distribution of lesions diagnose is mostly clinical.

Histological analysis (Fig.4) and direct immunofluorescence (Fig.5) are recommended in order to rule out other oral diseases.

The evolution of this chronic disease is cyclic, periods of remission alternate with exacerbation times.

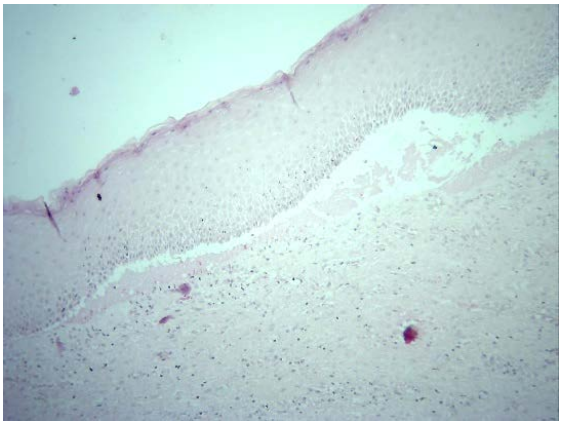

Fig.4. Bullous oral lichen planus-histological image showing a dense inflammatory infiltrate band-like in the lamina propria-Hematoxylin-eosin stain, 4x

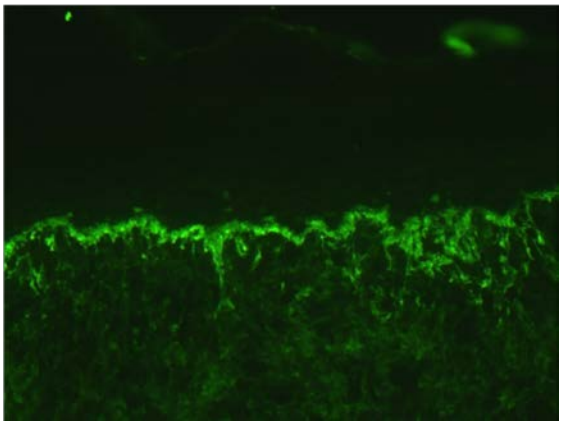

Fig.5. Oral lichen planus. Direct immunofluorescence. Fibrinogen deposits in the lamina propria

Pemphigus

Pemphigus is an autoimmune blistering disease characterized by formation in intraepithelial bullas.

Lesions are vesiculo-bulous and appear on both skin and mucous membranes.

Patients with pemphigus develop auto-antibodies toward an antigen on the surface of squamous epithelial cells destroying the intercellular attachments, generating an intraepithelial bulla [10].

Pemphigus groups consist of 4 major groups: pemphigus vulgaris, pemphigus foliaceus, paraneoplastic pemphigus and drug-related pemphigus.

Pemphigus vulgaris is the most common form of pemphigus, encountered in 80% of cases [11].

Oral involvement is very frequent, more than 90% of patients develop at some time during the course of the disease oral lesions [10].

The onset of the disease is insidious, oral lesions evolve slowly and sometimes it takes months to make a correct diagnose. Patients experience severe weight loss. Nikolsky sign is a characteristic feature. It means that upon applying firm pressure on an area of apparently normal mucosa a bullae will form.

The clinical aspect of oral lesions varies from vesicles, to bullas (rarely seen intact), wide-spread ulcers and erosions. Symptomatology is severe, patients can barely drink or eat. In some cases hospitalization is recommended. Oral hygiene is absent, leading to an increased risk of associated bacterial infection.

Treatment usually consists of systemic corticotherapy.

Local elixirs with coating agents and anesthetics are used to alleviate oral pain and facilitate hydration.

Immunofluorescence studies together with histology analysis are needed in order to make a correct diagnose. Histology analyses show the acantholysis described as intraepithelial cleavage with bulla formation (Fig.6).

Direct immunofluorescence studies show the presence, in different degrees, of IgG and C3 in the epithelial layer (Fig.7,8).

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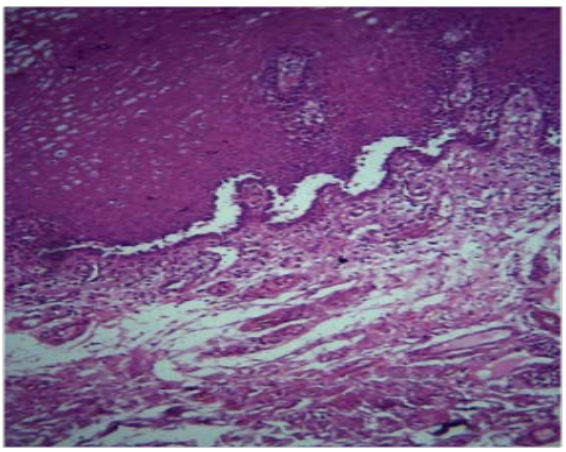

Fig.6. Pemphigus vulgaris: histological image showing intraepithelial bulla formation (Haematoxylin-Eosin stain, 4x)

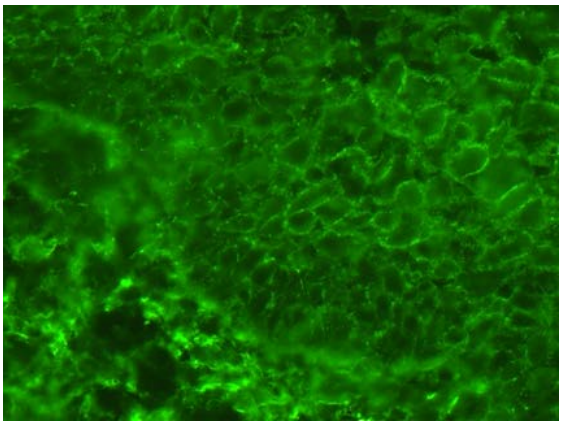

Fig.7. Pemphigus vulgaris. Direct immunofluorescence analyze-IgG positive with net-like (honey comb) disposition

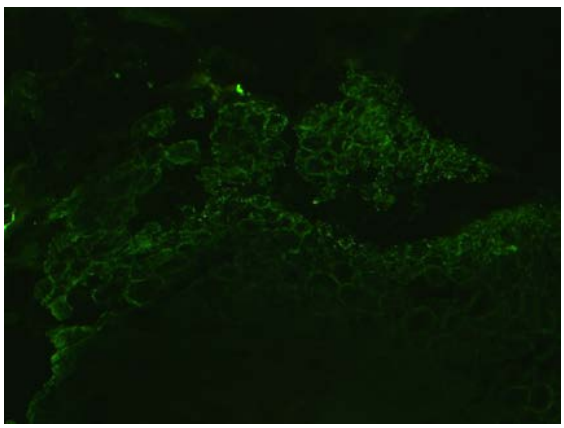

Fig.8. Pemphigus vulgaris. Direct immunofluorescence studies-intraepithelial C3c moderate presence

Differential diagnosis

The differential diagnosis of desquamative gingivitis must be made with other forms of gingivitis:

- Plaque induced gingivitis
- Gingivitis in viral infections (ex.: Herpetic gingivitis)
- Gingivitis in hematological diseases (ex.: leukemic gingivitis)
- Diabetes induced gingivitis

Differential diagnosis of the underlining disease is just as important.

Table 4. Differential diagnosis of systemic disease

Systemic disease	Differential diagnosis
Differential diagnosis for pemphigoid:	Cicatricial pemphigoid from mucous membrane pemphigoid Herpetiformis dermatitis Drug-induced bullous disease Erythema multiform Linear IgA disease Epidermolysis Bullosa
Differential diagnosis for Pemphigus Vulgaris:	Bullous pemphigoid Erythema multiform Linear IgA disease Pemphigus erythematosus Pemphigus foliaceus Paraneoplastic pemphigus Drug-induced pemphigus Mucous membrane pemphigoid
Differential diagnosis for oral lichen planus:	Pemphigus vulgaris Bullous pemphigoid Cicatricial pemphigoid Linear IgA disease Erythema multiform Lupus erythematosus

Management

Dental practitioners must educate their patients about their disease. It is their responsibility to help patients manage their suffering by adequate medication to alleviate the symptoms, proper oral hygiene practices to avoid secondary bacterial infection and adequate nutrition in order to prevent dehydration.

Local treatment can be a viable option if lesions are confined to the gingiva or at least to the oral mucosa. It is also an option for symptomatic lesions. Pain management may be achieved by usage of topic coating agents that form a protective pellicle, as well as local use of elixirs with anesthetic. They are recommended to alleviate pain in order to permit proper nutrition and hydration.

In most cases patients are referred to the adequate specialists (Dermatology, Endocrinology, etc.) in order to treat the systemic disease. The remission of the underlining disease brings resolution of the oral lesions.

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10.12865/CHSJ.44.04.01