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REVIEW

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Desquamative gingivitis: A sign of mucocutaneous disorders – a review

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Abstract

Desquamative gingivitis is a clinical term to describe red, painful, glazed and friable gingivae which may be a manifestation of some mucocutaneous conditions such as lichen planus or the vesiculo-bullous disorders. It is important to be aware of this rare clinical entity so as to distinguish desquamative gingivitis from plaque induced gingivitis which is an extremely common condition, easily recognized and treated daily by the dental practitioner. This article gives an overview of desquamative gingivitis, its presentation, the possible causes, diagnosis and treatment. Early recognition of these lesions may prevent delayed diagnosis and inappropriate treatment of potentially serious dermatological diseases.

Key words: Gingivitis, lichen planus, pemphigus, pemphigoid, immunofluorescence.

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INTRODUCTION

The term desquamative gingivitis (DG) is used in this paper as a clinical description of the gingiva which may manifest as a result of various underlying conditions to be discussed below. It is characterized by fiery red, glazed, atrophic or eroded looking gingiva. There is loss of stippling and the gingiva may desquamate easily with minimal trauma (Fig 1, 2). As opposed to plaque induced gingivitis, DG is more common in middle-aged to elderly females, is painful, affects the buccal/labial gingiva predominantly, frequently spares the marginal gingiva but can involve the whole thickness of the attached gingiva and its clinical appearance is not significantly altered by traditional oral hygiene measures or conventional periodontal therapy alone (Table 1).[1,2]

The majority of cases of DG are now known to be due to mucocutaneous conditions, in particular lichen planus, pemphigoid and pemphigus.[3-6] Other causes include allergic reactions to toothpastes/mouth rinses (plasma cell gingivitis),[7-9] Crohn's disease,[10] psoriasis,[11] linear IgA disease[12] and chronic ulcerative stomatitis.[13] Desquamative gingivitis can be mistaken for plaque induced gingivitis and this can lead to delayed diagnosis and inappropriate treatment of serious dermatological diseases such as pemphigoid or pemphigus.[14-17] The common mucocutaneous conditions which may manifest as DG are outlined below.

Gingival lichen planus

Desquamative gingivitis as a presenting feature is most commonly noticed in oral lichen planus (OLP).[1,3,6] Lichen planus is a relatively common immunologically mediated mucocutaneous disease of unknown aetiology. It is more common in middle-aged to elderly females. Several forms of OLP are described intra-orally; reticular, papular, plaque-like, atrophic, bullous and erosive forms. The most common site of involvement is the buccal mucosa followed by the tongue and the gingiva. The characteristic features of OLP are its chronicity, symmetrical appearance and multi-site involvement.[18]

The gingiva may be the only site of involvement in about 10 per cent of cases. The atrophic form of OLP presents often on the gingiva giving the classical appearance of DG. The whole thickness of the attached gingiva up to the mucogingival junction may be affected (Fig 3). The gingival tissues appear erythematous with occasional areas of erosions and possibly white striae at the periphery. Patients may complain of persistent soreness of the gums which is made worse by spicy foods or when carrying out daily oral hygiene procedures. The latter may become restricted to the point that plaque induced gingivitis and periodontitis sets in, confusing the clinical picture. However, it is important to note that the immunological reaction occurring in lichen planus does not result in clinical attachment loss and periodontitis.[19-21]

Diagnosis of OLP can be difficult if the gingiva is the only site of involvement. Careful examination of the erythematous gingiva may reveal faint keratotic lines. The rest of the oral mucosa should be examined

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Fig 1. Fiery, red gingiva of desquamative gingivitis. The clinical features are non-specific. This patient has mucous membrane pemphigoid.

Fig 2. Desquamative gingivitis. Note that the patient has relatively good oral hygiene but the attached gingiva have lost their keratinization making them more susceptible to desquamation with trauma.

carefully for evidence of classical lichenoid lesions. The patients should be questioned and examined for the presence of any cutaneous lesions. The most common cutaneous site involved in lichen planus is the flexural surface of the wrist, presenting as intensely pruritic, purple, polyglonal papules. Other sites that can be affected are the nails, scalp, oesophagus and the genital mucosa. In recent years, there have been reports of concomitant involvement of the genital mucosa and the gingiva, especially in females. This association of lichen planus of the vulva, vagina and the gingiva (presenting as classical DG) has been termed the vulvovaginal-gingival syndrome.[22,23]

An incisional biopsy is necessary to confirm the diagnosis of OLP. The biopsy should be taken well away from the marginal gingiva as plaque-induced

Table 1. Clinical features of desquamative gingivitis

Fiery, red, friable gingiva
Painful, desquamates easily
Buccal aspect of anterior attached gingiva affected
Marginal gingiva spared
Not significantly improved by oral hygiene measures alone

Fig 3. Gingival lichen planus showing no pathognomonic gingival features but associated with buccal reticular lichen planus.

gingival inflammation may complicate the histological picture. The specimen taken should have intact epithelium as well. The tissue specimen should be transected; one piece fixed in formalin and examined under light microscopy and the other transported fresh to an appropriate laboratory to be snap-frozen immediately in liquid nitrogen. The latter specimen is then processed for immunofluorescent staining. These tests serve to detect the presence of autoantibodies and other inflammatory proteins within the tissues (direct immunofluorescence). The patient's tissue is incubated with fluorescence labeled anti-sera against human antibodies, complement component 3 (C3) and fibrinogen. The specimen is then examined under ultraviolet microscopy.[24] In OLP deposits of fibrinogen alone are seen along the basement membrane zone. As stated earlier the atrophic form of lichen planus affects the gingiva and the typical light microscopic features of gingival lichen planus are:[25] severe thinning and flattening of the epithelium; basal cell liquefaction degeneration; and a subepithelial, dense, band-like infiltrate of lymphocytes (with a sharply demarcated lower border) hugging the epithelio-mesenchymal junction.

Treatment of gingival lichen planus is as for the other forms of intra-oral lichen planus.[21,26] Effective but atraumatic oral hygiene needs to be instituted as well as professional scaling and root planning.[2,27] Topical corticosteroids are the mainstay of treatment for lichen planus and should be applied directly onto the affected gingiva. Vacuum formed custom trays or gingival veneers can be constructed to achieve this. Patients are instructed to apply the topical steroids on the fitting surface of the splints which can be worn overnight. Additionally, the splints serve to protect the friable gingiva.[28,29] For patchy involvement of the gingiva, localized delivery of corticosteroids can be achieved with a topical beclomethasone spray. Systemic tetracycline[30] and recently topical cyclosporin (mouth wash),[31] has been used for DG as well. For recalcitrant OLP, topical tacrolimus has recently been tried with promising results.[32]

Table 2. Immune-mediated blistering diseases

Intra-epithelial
Pemphigus
Subepithelial
Pemphigoid
Linear IgA disease
Dermatitis herpetiformis
Epidermolysis bullosa
Erythema multiforme

Immune-mediated blistering diseases (vesiculobullous disorders)

These have traditionally been divided into intra-epithelial and subepithelial disorders (Table 2).[33] The most common presentation of mucous membrane pemphigoid intra-orally is DG. The other bullous diseases of which DG is the presenting oral manifestation include pemphigus, linear IgA disease, dermatitis herpetiformis and occasionally erythema multiforme.[3] A detailed review of the above vesiculobullous disorders is beyond the scope of this article. The interested practitioner is referred to recent excellent reviews, cited below.[34-37]

Mucous membrane pemphigoid

Mucous membrane pemphigoid (MMP) as defined in a recent consensus statement,[38] is a 'group of putative autoimmune, chronic inflammatory, subepithelial blistering diseases predominantly affecting mucous membranes, with or without clinically observable scarring'. Antibodies are produced against certain target antigens found in the basement membrane, resulting in the epithelium being detached from the underlying lamina propria. In recent years detailed characterization of the various target antigens have been made and subsets of pemphigoid subsequently identified.[34-36] Mucous membrane pemphigoid chiefly affects the oral cavity, larynx, oesophagus and ocular membranes but rarely the skin. Females in their sixth decade tend to be afflicted more commonly but males and patients in other age groups can be affected as well. The most common presentation intra-orally is DG. The typical appearance of DG as described earlier is seen in MMP. There might be areas of superficial erosions and tags of detached epithelium on the gingiva (Fig 4). Other oral mucosal sites involved are the buccal mucosa, palate, alveolar ridge and tongue. Rarely are intact bulla seen intra-orally (the traditional description of blood-filled bullae on the palate is seldom observed), the more common presentation being fibrin covered superficial erosions with irregular margins. Oral lesions tend to heal over without scarring. Unfortunately this is not so in the other mucosal sites chiefly the conjunctiva. The eyes can be affected in as high as 80 per cent of cases with 15 per cent developing permanent blindness as a result of subconjunctival scarring (Fig 5).[33] Less commonly, strictures may form in the larynx, oesophagus and genital mucosa with serious complications.[35-38]

Fig 4. Desquamative gingivitis in a patient with pemphigoid bulla formation. Mucous membrane pemphigoid was confirmed by immunofluorescence.

Fig 5. Ocular pemphigoid showing scarring which has led to the term cicatricial pemphigoid.

The diagnosis of MMP depends on taking a careful clinical history and performing a thorough clinical examination. The gingiva can be the only site of involvement in MMP and this frequently results in delayed diagnosis as the patient is put through repeated sessions of periodontal therapy and/or prescribed various antimicrobials. The classical features of DG are usually present in the gingiva. The patient usually gives a long history of gingival soreness. Long standing superficial erosions may be present on the gingiva or on other sites and this will help in the diagnosis.[39]

However, the definitive diagnosis depends on histological examination of the gingival tissues. A biopsy needs to be taken from an area with intact epithelium (eroded sites are uninformative). Some advocate inducing a blister by stroking the epithelium (Nikolsky's sign) and then removing the blister intact.[40] The tissue specimen should be transected as before; one piece for routine light microscopy studies and the other for immunofluorescent staining. In MMP, linear deposits of IgG and C3 are most commonly detected in the basement membrane zone. Indirect immunofluorescence involves incubating the patient's serum with normal skin. If antibodies are present in the patient's sera they will bind to the target antigens in the normal specimen and this is then detected by similarly labeled anti-human immunoglobulins. In the past,

circulating antibodies in MMP were rarely detected or were of low titers that did not correlate with disease activity.[41] However, with the use of chemically separated normal human epithelium as substrate, detection rates for circulating autoantibodies in patients with MMP have reported to be between 88 to 100 per cent.[42] Further, recent evidence suggest that serial titers of IgG as well as IgA , detected on salt-split human skin, may correlate with disease activity and severity.[43,44]

To summarize the histological features of MMP are: subepithelial bulla formation; no acantholysis; chronic inflammatory infiltrate in the lamina propria; and linear deposition of IgG, IgA or C3 along the basement membrane.[33,35,36,45]

Once a diagnosis of MMP is made, an ophthalmologic opinion should be sought even if patients do not complain of eye symptoms. Ocular symptoms can be mild initially and then presents as chronic conjunctivitis before more serious scarring takes place. A slit-lamp examination should be carried out by the ophthalmologist early in the disease so that appropriate therapy can be instituted. Glaucoma appears to be more common in MMP patients and this argues for an early ophthalmologic consult as well.[46]

Oral lesions are typically indolent. They can usually be controlled with topical corticosteroids and if DG is present a custom made splint is used for the gingiva as in lichen planus, described earlier. The more potent topical steroids may need to be used initially until symptoms subside. Oral hygiene must be improved and regular professional cleaning should be emphasized. If other mucosal sites or the skin is involved then more potent medication such as systemic corticosteroids, azathioprine, sulphapyridine or dapsone is used.[33,35,38,47]

Pemphigus

Pemphigus is one of the very few potentially fatal mucocutaneous diseases characterized by intra-epithelial bullous formation. It is an uncommon condition and usually affects females in their fourth to fifth decade of life. Pemphigus vulgaris is the most important subtype to occur in the mouth and it can be the initial site of presentation in 50 per cent of cases. In pemphigus vulgaris, antibodies are produced against desmosomes (adhesion proteins), in particular, desmoglein 3. The latter is one of the components of desmosomes responsible for holding the spinous cell layer of the epithelium together. The intercellular adhesion between the spinous cells is disrupted resulting in bulla formation immediately suprabasal.[33,34,48] In pemphigus foliaceus, which predominantly affects skin, autoantibodies are produced against desmoglein 1.[49] It has been shown that a subset of patients with pemphigus vulgaris may have antibodies against desmoglein 1 as well.[50] The clinical significance of this will be explained later.

Oral pemphigus vulgaris presents as bullae that break down rapidly to leave persistent irregular ragged edged painful erosions. Any site subjected to trauma may be involved especially the palate, tongue and buccal mucosa. Gingival involvement may manifest as DG though less commonly than pemphigoid. There is severe desquamation of the gingiva more so than other vesiculobullous diseases. Bullae on the gingiva rupture leaving painful eroded areas. Gentle pressure on the epithelium may result in its separation and normal activities such as oral hygiene procedures and having meals becomes extremely painful for the patient.[17,51] Other sites that can be involved include the oesophagus, pharynx, larynx, nasal and genital mucosae. Although ocular lesions can occur in pemphigus, they are uncommon and tend to be transient and heal completely without scarring. Skin lesions present as flaccid fluid filled blisters on sites exposed to trauma. The blisters break to form large denuded areas of skin. In the past before the use of steroids the mortality was 30 per cent as a result of electrolyte loss and sepsis.[33,52]

Definitive diagnosis depends on taking a biopsy specimen with an intact epithelium. This can be difficult in pemphigus as the epithelium is very friable. Again a fresh and a formalin-fixed specimen is needed. Direct immunofluorescence demonstrates deposition of IgG and C3 intercellularly in a fish-net pattern. Circulating autoantibodies can usually be detected by indirect immunofluorescence and the titers of such antibodies usually correspond to disease activity and severity.[24,33,40,50] Specific enzyme-linked immunosorbent assays (ELISA) are now available for detecting desmoglein 3 and desmoglein 1 autoantibodies.[53] As stated earlier, patients with pemphigus vulgaris have autoantibodies mainly against desmoglein 3. Recent data suggest that the detection of desmoglein 1 antibodies in patients with oral pemphigus vulgaris signifies a more severe course of the disease and heralds the involvement of cutaneous sites as well.[50,54]

Conventional histology demonstrates:[45] acantholysis; suprabasal bulla formation; free-floating acantholytic cells within the vesicle fluid (Tzanck cells); intact basal cell layer, still attached to basal lamina; and mild inflammatory infiltrate.

Early diagnosis of pemphigus vulgaris is important as it is a serious condition. Lesions present initially in the mouth. It can then rapidly spread to skin or other mucosal sites. Alternatively the mouth may be the only site of involvement for about six months to a year before the skin is involved. The key here is early diagnosis and institution of therapy before skin and other sites are involved.[14,17,55] Referral to a dermatologist is advised.

Systemic corticosteroids are the mainstay of treatment. These are given initially in high doses orally or if the disease is severe and rapidly progressing, in the form of pulse therapy with megadoses of corticosteroids (intravenously). Once the disease is under control, the steroids can be tapered off and 'steroid-sparing' adjuncts added. These include azathioprine, cyclosporin, cyclophosphamide and

methotrexate. Other therapies include photopheresis and plasmapheresis. The progress of therapy is evaluated by clinical response as well as a falling circulating antibody titer. Desquamative gingivitis in pemphigus is treated additional with topically steroids as described earlier. It must be appreciated that pemphigus is a systemic autoimmune disease with a potentially rapid progressive course and so topical steroids alone are insufficient to treat the condition. Treatment may need to be lifelong as stopping therapy may result in exacerbation of the disease. The mortality of pemphigus is currently around 6 per cent and is due to the effects of immunosuppressive therapy.[56-58]

Others

Linear IgA disease

This is a rare subepithelial vesiculobullous disease characterized by deposition of IgA autoantibodies in a linear pattern along the basement membrane zone. Oral lesions can mimick those seen in mucous membrane pemphigoid. The gingiva can exhibit a typical diffuse DG. Non-specific oral ulcerations also occur on the palate, tongue and buccal mucosa. This disease, as opposed to dermatitis herpetiformis, is not associated with a gluten sensitive enteropathy. Treatments include topical or systemic steroids, dapsone or sulphapyridine.[12,59]

Chronic ulcerative stomatitis

This is a new entity characterized by unique immunostaining properties.[60] It mimics oral lichen planus both clinically and histologically. Desquamative gingivitis can be its presenting feature as well. Direct immunofluorescence studies of lesional and clinically normal mucosa reveals nuclear deposits of IgG in the basal one-third of the epithelium. Circulating anti-nuclear antibodies are also detectable. Treatment is with potent topical steroids or hydroxychloroquine, the latter reportedly bringing about complete and long lasting remission.[13,40,61,62]

Plasma cell gingivitis

This is an uncommon condition that presents as DG. It is generally believed to represent a hypersensitivity reaction to exogenous substances such as toothpastes, chewing gum, flavored mints, mouth washes or cinnamon flavoring products. However, in other cases no agent can be identified. Histological features of this lesion include spongiform pustules in the epithelium and a dense infiltrate of normal polyclonal plasma cells in the underlying lamina propria. Treatment consists of identification of the possible inciting agent by taking a careful clinical history (patch testing is usually negative). Removal of the offending agent results in resolution of symptoms.[7-9,63]

CONCLUSIONS

The clinical features of dermatoses or mucocutaneous disorders where DG is a presenting manifestation have been described. Correct identification of these conditions entails taking a careful history and performing a thorough intra-oral examination. Presence of cutaneous, nasal, ocular and genital lesions should be carefully elicited from the patient. A definitive diagnosis depends on taking an incisional biopsy from a peri-lesional site (with intact epithelium) and sending a fresh specimen for immunostaining. If a blistering condition is diagnosed, referral to an appropriate specialist is advised. The gingival lesions are usually treated by improved oral hygiene measures and occlusive topical corticosteroid therapy.

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