Desquamative Gingivitis − Aetiology, Diagnosis and Management

Abstract: The diagnosis and classification of mucosal disease for the busy general dental practitioner can be difficult since many mucosal diseases present with a similar oral appearance. The term desquamative gingivitis (DG) is often used as a descriptive term because the aetiology of the inflammation may originate from multiple oral conditions. In this review article, we discuss oral lichen planus, mucous membrane pemphigoid, and pemphigus vulgaris as the main mucocutaneous diseases associated with DG. The importance of plaque control is emphasized in the initial management of these cases.

CPD/Clinical Relevance: As an oral complaint, patients will likely seek dental advice as their first point of contact for symptoms associated with DG. Therefore, an understanding of potential conditions that are causing their symptoms, as well as some general measures which may help improve their condition, are important.

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Desquamative gingivitis (DG) is a descriptive term, that includes the presence of erythema, desquamation, erosion and blistering of the attached and marginal gingiva. Lesions can be localized (Figure 1), or generalized (Figure 2) and may extend into the alveolar mucosa. Lesions tend to start with diffuse erythema and minimal desquamation. The affected gingival epithelium is very fragile and tends to exfoliate easily, even with the slightest trauma. Intact vesicles/bulla can occur but usually rupture quickly. Almost all the disorders associated with DG can affect different oral sites and have extra-oral involvement. Skin, scalp, nails and mucosa with differentiated epithelium, including laryngeal, oesophageal, nasal, genital and conjunctival, represent possible locations. Desquamative gingivitis is not considered a definitive diagnosis because it is a clinical manifestation of several disorders. Conditions that are associated with the development of DG generally have a peak of incidence in the 4th to 6th decade of life, with a higher incidence in females than in males.

Aetiology

Desquamative gingivitis can be caused by numerous conditions. These include dermatoses such as oral lichen planus (OLP), mucous membrane pemphigoid (MMP), pemphigus vulgaris (PV), epidermolysis bullosa, linear immunoglobulin A disease and dermatitis herpetiformis. Local hypersensitivity responses to various substances, such as dental materials (described as lichenoid contact reactions), mouthwashes, drugs, cosmetics, chewing gum, cinnamon, sodium lauryl sulphate (a common ingredient of toothpaste), may also play a role as causative agents in some patients (Figure 3).

Other likely causes of DG that present with erythematous and ulcerative lesions include plasma cell gingivitis, systemic lupus erythematosus, discoid lupus erythematosus, chronic ulcerative...
Oral lichen planus (OLP)

OLP is a common T cell-mediated, inflammatory disease of unknown aetiology. Other mucous membranes, including the genitalia, oesophagus and conjunctiva, as well as skin appendage areas, such as nails, may also be affected. Cutaneous lesions (Figure 4), are present 12–14% of the time.

Many factors have been proposed as relevant to the aetiology of the lesions, including genetic history, dental materials, drugs, infectious agents such as bacteria and viruses, autoimmunity, associations with other autoimmune diseases, immunodeficiency, food, allergies, stress, habits, trauma, diabetes and hypertension, malignant neoplasms and intestinal diseases.

Oral lichen planus lesions most often present as bilateral lesions with lace-like, white, slightly elevated keratotic lesions (Figure 5). This may progress to DG where there is normally a painful red centre with erosions and/or ulcerations, and a less painful or painless radiating white form with papular or reticular patches over the buccal mucosa. Classically, in OLP lesions the tips of the gingival papillae may be spared (Figure 6). Exclusive gingival involvement is observed in about 10% of patients with OLP.

The World Health Organization (WHO) has classified lichen planus as a potentially malignant condition. Studies show that approximately 1% of patients with OLP may develop a squamous cell carcinoma. It is therefore essential that, once a diagnosis of OLP has been made, arrangements are in place for long-term monitoring of patients. Given how common a diagnosis of OLP can be, care should be taken when informing patients about the potential malignant transformation rate of lichen planus to avoid excess anxiety.

Mucous membrane pemphigoid (MMP)

Mucous membrane pemphigoid is an autoimmune disease which is tissue specific. The initiating factor for the autoimmune response in MMP is usually mucocutaneous diseases associated with desquamative gingivitis.
Eventually, cutaneous blisters and erosions occur which extend progressively, causing fluid loss, electrolyte imbalance and septicaemia. Pemphigus vulgaris may result in death if left untreated.

Diagnosis

Diagnosis of DG-associated disease begins with a detailed history of the presenting complaint, review of past and current medical history, followed by clinical examination. Differentiation of the cause is essential as many will share a similar clinical presentation, but often have different management and prognosis.

Medical history and history of complaint

An appropriate medical history should consider the patient’s systemic disease history and current therapies. This will be of importance in identifying potential conditions which may associate with DG. A history of any extra-oral skin lesions or eye problems is also important to note. This may include any investigation/therapy the patient is undergoing with other relevant specialties, including dermatologists, ophthalmologists, gynaecologists: and ear, nose and throat specialists.

Lesions associated with OLP may be asymptomatic at initial presentation and the patient may not even be aware of their existence. Those presenting as full desquamative lesions can have symptoms that range from mild discomfort on toothbrushing or eating certain foods (spicy or acidic foods in particular), to more significant pain which impacts on the patient’s quality of life. A history of blistering or ulceration is important to note as this may be suggestive of vesiculobullous conditions. The onset and progression of lesions should be carefully investigated. Some conditions can present acutely where others can be more progressive. The history of day or weeks preceding the outbreak of lesions may help identify potential triggering factors such as drugs or infections. A history of what products patients utilize as part of their self-performed oral hygiene regimen is also important to note. Sodium lauryl sulphate is a widely-used detergent added to many

unknown, but occasionally may be drug related, for example furosemide. Patients with MMP have auto-antibody directed against various proteins in the basement membrane zone, and this causes damage resulting in the full thickness of the epithelium lifting off the submucosa. In patients with MMP, oral involvement is most common (in 90% of cases), followed by ocular involvement (in 61% of cases). Ocular involvement of MMP (Figure 7) is considered high risk and carries a poorer prognosis (despite treatment) than when oral mucosa and/or skin alone are affected. Ocular involvement can eventually lead to blindness, and laryngeal lesions can cause airway obstruction. The skin is involved in approximately 15% of cases.

Patients presenting with oral symptoms often have pain, dysphagia and chronic soreness, particularly when eating acidic foods. Desquamative gingival changes can vary from mild small patches to widespread erythema with a glazed appearance. Vesicles or bullae may occur which tend to rupture leaving irregularly-shaped erosions with a yellowish slough and a surrounding inflammatory halo that are persistent but rarely scar (Figure 8).

Pemphigus vulgaris (PV)

Pemphigus defines a group of rare mucocutaneous autoimmune diseases of which pemphigus vulgaris (PV) is the most common. The aetiology and pathogenesis of PV is unclear. However, there is likely to be a genetic susceptibility, with ethnic groups such as Ashkenazi Jews, some Mediterranean populations, and people from India being particularly susceptible. The disease is characterized by blistering that affects stratified squamous epithelium and results in cutaneous or mucosal blistering. Bullae associated with pemphigus are intra-epithelial. Involvement of the oral mucosa, including gingiva (Figure 9), is observed in the early stages of pemphigus in approximately 70% of cases. Bullous lesions initially affect the mouth, but quickly rupture leaving painful erosions with irregular margins (Figure 10).
Figure 11. Histology of mucous membrane pemphigoid lesions shows characteristic sub-epithelial bulla formation with a fibrin net and inflammatory infiltrate. (Image courtesy of Professor PJ Lamey).

Figure 12. Histology of pemphigus vulgaris shows acantholysis in the lower spinous cell layers. Basal layer cells remain attached to the connective tissue with formation of suprabasal clefts giving rise to the characteristic intra-epithelial blistering. (Image courtesy of Professor PJ Lamey).

Figure 13. Direct immunofluorescence of mucous membrane pemphigoid lesion shows characteristic linear deposition of IgG in the basement membrane zone.

Figure 14. Direct immunofluorescence of pemphigus vulgaris lesion shows characteristic intercellular deposition of IgG ('chicken-wire' pattern). (Image courtesy of Professor PJ Lamey).

dental hygiene products. For some patients, its use has been associated with mucosal irritation.

Clinical examination

The purpose of the clinical examination is to look for oral lesions with a specific appearance that can assist in diagnosing different DG-associated disorders.

OLP lesions tend to present with very characteristic features (Figures 5 and 6). They generally involve multiple oral sites and have a keratotic papular or reticular form. When a desquamative type lesion associated with OLP is present in the attached gingivae, it may be difficult to differentiate from other forms of DG, but often there is a keratotic lesion at the margin or interspersed within the desquamative area which can support a provisional diagnosis.

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A careful note should also be made of the position of dental restorative materials and their approximation to lesions (Figure 2). Some restorative materials (amalgam, composites, nickel and cobalt) have been reported to induce lichenoid type reactions. Lesions are similar to OLP lesions in presentation, but may resolve when the dental material is replaced with an alternative. Referral for patch testing may be of use in some of these patients to identify hypersensitivity reaction.

As previously discussed, MMP and PV lesions may present with widespread erythema and blister formation, with subsequent breakdown leading to areas of ulceration.

Definitive diagnosis – specialist referral

Usually, specialist referral to an Oral Medicine or Periodontology unit is required for further investigation and definitive diagnosis. This will normally include indirect immunofluorescence on a blood sample, and examination of a tissue sample using H&E staining and direct immunofluorescence.

Histological changes of diseases associated with DG generally involve both the epithelium and underlying connective tissue. Changes observed in OLP are usually in the form of epithelial thickness, including reduction (erosive forms of OLP) and increases (hyperkeratosis of OLP). Antibody mediated diseases such as MMP and PV are characterized by blister formation: subepithelial for MMP (Figure 11) and intraepithelial for PV (Figure 12).

In addition to histopathological assessment, pathologic immunoreactants present in DG-associated diseases can be investigated with immunofluorescence studies (Figures 13 and 14). The types of immunoreactants include various immunoglobulin classes (IgG, IgM and IgA), complement cascade factors, fibrinogen and fibrin, and immune complexes. Immunofluorescence studies are of particular use in helping to diagnose DG-associated disease accurately, especially when typical features are not present in histopathological analysis.

Management

From a general dental practitioner’s point of view, management will generally involve a thorough history, examination and appropriate referral for definitive diagnosis as previously discussed. The low incidence rates of some of the diseases associated with the development of DG mean that their presentation in general practice may be quite rare. Nonetheless, as an oral complaint, patients will likely seek dental advice as their first point of contact. Therefore, an understanding of potential conditions that are causing their symptoms, as well as some general measures which may help improve their condition, are important.

General measures

An outline of practical steps and advice that can be offered to patients is displayed in Table 1. Triggering factors such as drugs, local irritants such as spicy foods and overly aggressive toothbrushing habits should be discontinued. Topical analgesics, such
Corresponding improvements were observed using mucosal disease indices at both 4- and 20-week follow-up (p<0.001). The authors concluded that a structured plaque control intervention was effective in improving the oral health-related quality of life and clinically observed gingival lesions. This study highlights that intensive plaque control should be an important initial phase of treatment, which can be delivered pre-referral by general dentists and dental hygienists.

### Specific therapies

**Upon referral, specialist management will be specific to the diagnosis established and may involve a multidisciplinary approach, especially when there is extra-oral involvement. Depending on the definitive diagnosis, treatment of the disease associated with DG is aimed at controlling lesions along with symptoms, and preventing further disease progression.**

#### Oral lichen planus (OLP)

In symptomatic lesions, topical corticosteroids are the drug of choice. Topical corticosteroids are available in different strengths and preparations and provide an anti-inflammatory and immunosuppressant effect. Ointments such as fluticasone mixed with Orabase® are suitable for the management of small isolated accessible lesions such as the buccal mucosa, tongue, gingiva or palate. Application is normally 3–4 times daily. Where multiple lesions exist, corticosteroid mouthrinses, utilizing for example betamethasone 500 mcg soluble tablets or fluticasone 400 mcg nasules can be very effective. The use of vacuum-formed steroid carrier trays have also been advocated as a way of extending drug permanence onto oral lesions. It is important that the use of such custom trays do not themselves cause trauma or irritation to the gingivae.

**Patients should be informed about possible adverse side-effects of using topical corticosteroid preparations; the most common being secondary candidiasis. Antifungals such as miconazole gel and/or chlorhexidine mouthwash may be useful in preventing secondary candidiasis.**

Other drug treatments which further ‘dampen down’ the immune system can be added so that the dose of corticosteroid can be reduced as soon as possible. These include azathioprine and mycophenolate mofetil. In those individuals who are steroid unresponsive, topical calcineurin inhibitors, such as tacrolimus or pimecrolimus, are important treatment options for patients. Side-effects, including transient burning or stinging at the site of application, have been reported.

#### Mucous membrane pemphigoid (MMP)

Therapy for oral MMP may similarly involve high potency topical corticosteroids. However, systemic corticosteroids are generally the first line treatment for patients with severe progressive mucosal lesions associated with immune-mediated diseases. Systemic corticosteroids may be useful for short-term (2–3 week) treatment to achieve improvement in DG lesions, with treatments being further supplemented with, or followed by, topical agents. Potential side-effects of systemic steroid treatment need to be considered (eg adrenal suppression, hypertension, blurred vision, elevated blood glucose, and GI haemorrhage). Secondary systemic immunosuppressants, such as

| 1   | Advise patients to avoid spicy, acidic or salty foods if these make their mouth sore. |
| 2   | If a patient presents with acute pain recommend use of an anaesthetic mouthwash, eg benzylamine hydrochloride (Difflam®). |
| 3   | Advise patients to keep their teeth clean by using a soft brush and interdental brushes. |
| 4   | Perform basic non-surgical periodontal therapy, if indicated. |
| 5   | Perform regular (2–3 monthly) prophylactic periodontal maintenance therapy as part of a structured plaque control programme. |
| 6   | Advise patients to choose a toothpaste with a mild flavour and free from the foaming agent sodium laurel sulphate (SLS). |
| 7   | Advise patients to discontinue use of alcohol-based mouthwashes, and mouthwashes containing SLS. |
| 8   | Advise patients in view of the small risk of cancerous change in OLP. It is important that they ensure that their mouth is checked on a regular basis by a dentist or specialist, so that any early changes can be spotted. |
| 9   | If smoking is a factor, smoking cessation advice should be offered. |
| 10  | Advise patient on safe limits of alcohol consumption (currently 14 units a week for both men and women in the UK). |

Table 1. Practical steps and advice to give to patients presenting with DG in general dental practice.

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As mentioned previously, dental plaque is an important aggravating factor to whatever is the underlying cause, so initial management in these cases should be centred on optimizing plaque control while reducing any associated inflammation through non-surgical periodontal therapy. A recent study aimed to examine the effect of a structured plaque control intervention on clinical and patient-centred outcomes for patients with gingival manifestations of oral lichen planus. Eighty-two patients with a diagnosis of OLP with gingival involvement (confirmed by biopsy and histopathological analysis) were divided into two groups: intervention and control. The intervention was structured plaque control comprising powered toothbrushing and inter-dental cleaning advice. Control subjects continued with their normal dental plaque control regimen. The mean plaque index scores reduced for the intervention group by 39.5% at the 20-week follow-up, compared to a marginal improvement of 4.1% in the control group (p<0.001).
azathioprine and mycophenolate mofetil, may again be required depending on the severity and duration of lesions. Dapsone has been successfully used in MMP patients with both oral and ocular lesions. \(^{27}\) Side-effects to consider include anaemia, shortness of breath and tiredness.

**Pemphigus vulgaris (PV)**

With the risk of mortality in PV, moderate to high doses of systemic corticosteroids are the mainstay of treatment. Other immunosuppressant drugs may again be additionally required. Intravenous immunoglobulins have previously been successfully used in cases of steroid resistant PV. \(^{28}\)

**Conclusions**

The most common conditions associated with the development of desquamative gingivitis are oral lichen planus, mucous membrane pemphigoid and pemphigus vulgaris. Regardless of the cause, plaque is an important aggravating factor and efforts should be made in patients presenting with DG to improve plaque control as part of their overall management. Referral is normally required for definitive diagnosis and specialist treatment. However, ongoing monitoring and surveillance of these patients within the dental setting is essential for signs of relapse, complications, side-effect of the medications, and potential malignant transformation in OLP.

**References**