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ORIGINAL ARTICLE

Desquamative gingivitis: retrospective analysis of disease associations of a large cohort

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BACKGROUND: Desquamative gingivitis (DG) is usually a manifestation of immunologically mediated mucocutaneous disorders, although it was previously suggested to be hormonally related.
METHODS: One hundred and eighty-seven Caucasian UK residents with clinical features of DG (126 female, median age of 51 years, range 23–93 years) were retrospectively evaluated.
RESULTS: It was established that, in this population, the largest cohort yet reported, oral lichen planus was most common (70.5%) while mucous membrane pemphigoid (14%), pemphigus vulgaris (13%), linear IgA disease (1.6%), dermatomyositis (0.5%) and mixed connective tissue disease (0.5%) were less common.
CONCLUSION: Oral lichen planus is the main disorder associated with DG. However, DG may be a feature of bullous disease and connective tissue disease.
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Keywords: desquamative gingivitis; oral lesions; immunologically mediated diseases

Introduction

Desquamative gingivitis (DG) manifests mainly as painful erosions or ulceration of the attached and free gingivae, unrelated to, but aggravated by, local plaque accumulation. Originally considered to be related to hormonal changes at the menopause (as many of the affected patients are middle-aged women), DG is now recognized principally to be a manifestation of a number of disorders ranging from vesiculobullous diseases to adverse reactions to a variety of chemicals or allergens (Scully and Porter, 1997; Stoopler *et al*, 2003).

In particular, it is suggested that DG is usually a manifestation of oral lichen planus (OLP) (Figures 1a and 1b) or mucous membrane pemphigoid (MMP) (Figure 2) – and may be the only clinical presentation of these disorders (Rogers *et al*, 1982).

A variety of other mucocutaneous disorders such as erythema multiforme (Arteaga and Eisenberg, 1990), discoid lupus erythematosus (Blanco *et al*, 2000), linear chronic IgA disease (Porter *et al*, 1992), dyskeratosis congenita (Anil *et al*, 1994), epidermolysis bullosa (Kossard *et al*, 1979), pemphigus vulgaris (Navarro *et al*, 1999), paraneoplastic pemphigus (Yih *et al*, 1998), psoriasis (Jones and Dolby, 1972), ulcerative colitis and Kindler syndrome (Ricketts *et al*, 1997) may give rise to DG, but the exact frequencies of these disease associations are unclear (Sklavounou and Laskaris, 1983). Drugs or chemicals implicated include various oral health care products (Kuttan *et al*, 2001), sodium lauryl sulphate (Herlofson and Barkvoll, 1993; Ahlfors and Lyberg, 2001) and magnesium monoperoxyphalate (Scully *et al*, 1999a).

There has been no recent detailed analysis of the clinical associations of DG in patients from Northern Europe, and hence the aim of the present study was to examine retrospectively a large cohort of UK patients with DG for associated diseases.

Materials and methods

The study group comprised 187 (126 female, median age of 51 years, range 23–93 years) Caucasian UK residents consecutively referred with clinical features of desquamative gingivitis.

The past medical history of each patient was reviewed carefully. Each patient received a detailed orofacial examination and, where appropriate, the patients were referred for ophthalmological, gastrointestinal and/or dermatological consultations.

Most of the patients had venous blood collected for estimation of full and differential blood cell counts, haemoglobin indices, levels of red cell folate concentration, and serum levels of ferritin and vitamin B12. Serological estimation of liver function was also undertaken.

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Gingival biopsies, obtained from all patients, were undertaken on perilesional tissues and then divided into two pieces; half was fixed in formalin and the other half snap frozen in liquid nitrogen and stored at −70°C until required for immunostaining when indicated. For indirect immunofluorescence, patient serum was incubated with cryostat cut frozen sections (5 μm) of guinea pig lip.

The diagnoses of oral lichen planus (Scully *et al*, 1998), MMP (Alkan *et al*, 2003), pemphigus vulgaris (Scully *et al*, 1999b), dermatitis herpetiformis (Chorzelski and Jablonska, 1975; Egan *et al*, 1997) and linear IgA disease (del Valle *et al*, 2003) were based upon recognized relevant clinical, histological, immunostaining and serological criteria.

Results

Symptoms

All patients complained of oral discomfort, soreness or burning sensation of the gums (Table 1). Indeed gingival soreness was the main complaint of 92% of the patients (n = 172). Fifteen of the patients (8%) also complained of ocular symptoms such as conjunctival grittiness, soreness and/or dryness, or altered vision, but perhaps surprisingly none of the patients had any complaint regarding genital mucosa involvement.

Duration of disease

The average duration of DG often could not be precisely determined, but ranged from 2 months to 25 years. In some patients, the first consultation with the Oral Medicine clinic was as a direct consequence of their initial oral lesions.

Clinical signs

One hundred and thirty-four patients (73%) had localized areas of gingival desquamation (Table 2). At least one-third of the patients had other oral mucosal lesions such as ulcerative and non-ulcerative types of OLP or mucosal vesicles and bullae. Additionally, 26 patients had gingival erythema with white striae (all were ultimately found to have oral lichen planus) and two had gingival bullae (both patients were found to have MMP). Seven patients (five MMP, two pemphigus vulgaris) developed extra-oral vesicles or bullae during the course of their disease.

Table 1 Principal gingival symptoms of 187 UK patients with desquamative gingivitis

Gingival features	*No. of patients*	*% of total*
Soreness alone	172	92
Soreness and blistering	3	1.6
Soreness and oral mucosal blistering	2	1
Soreness and oral mucosal ulceration	10	5

Table 2 Principal clinical signs in 187 UK patients with desquamative gingivitis

Clinical signs	*No. of patients*	*% of total*
Localized desquamative gingivitis	134	72
Generalized desquamative gingivitis	53	28
Striae involving gingival and oral mucosa	26	14
Oral mucosal vesicles/bullae	12	6.4

Underlying pathology

Patients could be separated into four main groups according to clinical history, clinical features and histopathological, and immunological findings – namely OLP (n = 132) (Figure 1a and 1b), MMP (n = 26) (Figure 2), pemphigus vulgaris (n = 24), linear IgA disease and other (rare) disorders (n = 5) (Table 3). There were no notable differences in the age or gender distribution of patients with the different disorders, although all the three patients with linear IgA disease were male.

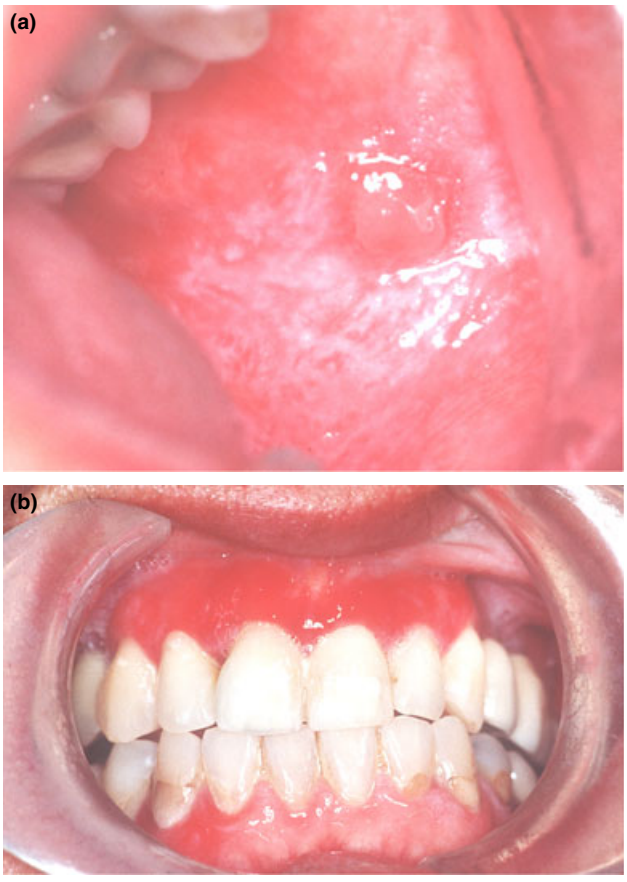

Figure 1 Ulcerative oral lichen planus on the left buccal mucosa (**a**) and desquamative gingivitis of the upper gingival region (**b**)

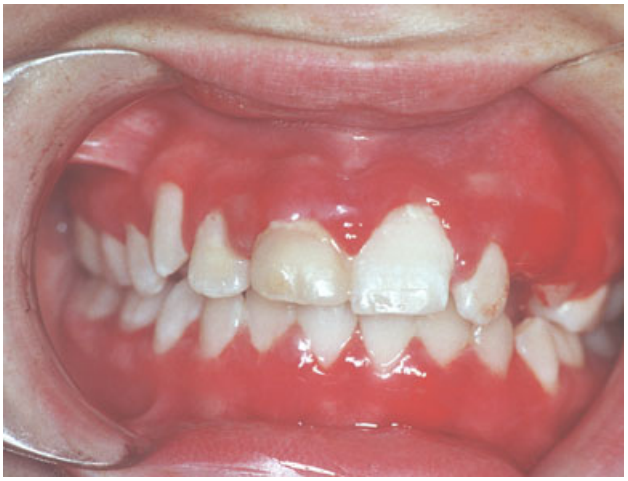

Figure 2 Desquamative gingivitis affecting both upper and lower gingiva in mucous membrane pemphigoid

Haematology/serology

No consistent or significant changes in haematological or serological markers were observed, in particular, no patient had evidence of chronic hepatic disease. Elevated levels of antibodies to epithelial components were only detected in 22 of the 24 patients with pemphigus vulgaris, 10 of these patients had serum titres of anti-epithelial antibodies >1:64. The patient with dermatomyositis had elevated serum levels of creatinine phosphokinase.

Discussion

The present series of 187 patients with DG is the largest cohort reported (Markopoulos *et al*, 1996; Nisengard and Neiders, 1981; Rogers *et al*, 1982; Vaillant *et al*, 2000) and is the first to detail the features of a large group of patients from Northern Europe. In the present series, DG appears to affect more frequently female patients later in life, reflecting the epidemiology of the underlying diseases (Laskaris *et al*, 1982; Eisen, 2002).

Desquamative gingivitis was originally believed to represent a hormone-mediated process (Belding and Anderson, 1968). But there are few, if any, detailed studies demonstrating that DG is caused by any lack of estrogen or progesterone. The human gingiva can metabolize estrogens and contains specific high-affinity estrogen receptors (Yih *et al*, 2000), but there appears to be no correlation between any local disease and the production of estrogen, or the expression of its receptor. Estrogen receptor expression in the gingiva is probably not related to the presence or absence of estrogen supplementation, and therefore the use of estrogen in the treatment of DG is likely to be of limited benefit, aside from the increased risk of adverse affects associated with such hormonal supplementation (Chlebowski *et al*, 2004; Stahlberg *et al*, 2004).

Alterations in female sex hormones do not play a major role in the etiology of OLP (Scully *et al*, 1998), MMP or pemphigus vulgaris (Oostingh *et al*, 2002; Hacker-Foegen *et al*, 2003; Slomov *et al*, 2003), the diseases being more frequently associated with DG. Thus, the notion of DG having such a hormonal basis should be dismissed.

Table 3 Age and gender of patients with desquamative gingivitis *vs* underlying pathology

Confirmed diagnosis	*Females*	*Males*	*Total no. of patients*	*% of total*	*Median age (years)*	*Age range (years)*
Oral lichen planus	83	49	132	70.5	50	23–85
Mucous membrane pemphigoid	19	7	26	14	54	29–93
Pemphigus vulgaris	22	2	24	13	64	44–85
Linear IgA disease	0	3	3	1.6	44	29–70
Dermatomyositis	1	0	1	0.5	36	36
Mixed connective tissue disease	1	0	1	0.5	53	53
Total	126	61	187	100	51.5	23–93

In contrast to previous published data that have suggested that MMP was the most common underlying cause of DG (Sklavounou and Laskaris, 1983; Markopoulos *et al*, 1996; Vaillant *et al*, 2000) at least in the present population, OLP was the primary disease associated with DG – accounting for just over 70%. The reason for OLP being more commonly associated with DG rather than MMP is not known but probably reflects the epidemiology of these two disorders, and possibly differences in the referral pattern of patients to specialized clinics. The results of the present study also confirm that MMP and pemphigus vulgaris account for a significant minority of DG lesions.

There was considerable delay in the final clinical diagnosis of diseases underlying DG, in some instances taking up to 25 years before a definitive diagnosis was made. It is likely that such delay reflects limited understanding of the cause of DG by primary health care providers and perhaps the assumption that most gingival disease is plaque-related and unlikely to reflect systemic disease. It was previously demonstrated that general dental practitioners do not have an understanding of the clinical significance of common oral mucosal diseases (Yellowitz *et al*, 1998; Warnakulasuriya and Johnson, 1999; Clovis *et al*, 2002), hence it might be expected that there would be some confusion in appreciating that DG is not likely to be plaque-related.

The definitive diagnosis of DG is sometimes complex. It is often difficult to differentiate the causes of DG when there are few symptoms and/or the associated disease is limited to the gingival tissues. Hence, there is a need for histopathological examination of lesional tissue, together mainly with direct, and perhaps indirect immunofluorescence to demonstrate lesional and circulating auto-antibodies respectively (Challacombe *et al*, 2001). Such accurate diagnosis of the cause of DG is important as there can be serious connotations. For example, MMP can affect the conjunctiva (Alkan *et al*, 2003), pharynx (Puranwasi and Naidoo, 2001), larynx (Whiteside *et al*, 2003) and

genitals (Rogers, 2003). Pemphigus vulgaris of the mouth may progress to cutaneous disease, and OLP is considered by some authorities to be a potentially malignant disorder (Manuel Gandara and Diniz, 2003; Mignogna *et al*, 2004; Rodstrom *et al*, 2004). Likewise, linear IgA disease can be associated with celiac disease, albeit in a minority of patients (Egan *et al*, 2001).

In summary, based upon the results of the present study it is concluded that OLP is the main disorder associated with DG. However, more rarely, other immunologically mediated diseases such as MMP, pemphigus vulgaris, linear IgA disease, dermatomyositis and mixed connective tissue disease, may also be associated with this painful gingival disorder.

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