Definitive and Differential Diagnosis of Desquamative Gingivitis Through Direct Immunofluorescence Studies

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Background: Desquamative gingivitis (DG) is a common clinical manifestation of oral autoimmune vesiculobullous diseases (VBDs). Their polymorphous clinical presentations coupled with similar histologic features make diagnosis indistinguishable among the different VBDs. Direct immunofluorescence (IF) studies are valuable gold-standard diagnostic tests that allow for discrimination among the various VBDs that present with DG. There have been no recent detailed analyses done that have used conventional light microscopy and direct IF in diagnosis to document the clinical associations of DG with various autoimmune oral diseases. The aim of this study is to examine retrospectively a large cohort of patients with DG for associated diseases and to determine the utility of direct IF and conventional light microscopy in establishing a definitive diagnosis.

Methods: During a 14-month period, our laboratory in Buffalo, New York, received 239 consecutive archival cases of gingival biopsy with a clinical diagnosis of DG. These specimens were submitted to establish or rule out a diagnosis of a direct IF–positive VBD. The demographic, clinical, and microscopic findings were tabulated using established inclusion and diagnostic criteria.

Results: Approximately half the number (48.1%) of biopsies received for direct IF studies were submitted by periodontists. Slightly more than half of the patients (53%) previously had biopsies submitted for both hematoxylin and eosin (H & E) and direct IF testing. There was a female predilection for all the diseases studied except for pemphigus and linear immunoglobulin A disease. Oral lichen planus was the most common disease presenting as DG, followed by pemphigoid. The clinical diagnosis of lichen planus correlated with the biopsy findings in 80% of the cases and with pemphigoid in 60%. Definitive diagnosis was rendered to ≈80% of the gingival biopsies submitted. Negative cases of direct IF presenting as DG had significant pathology, such as dysplasia and carcinoma, which would have been otherwise missed if H & E studies had not been performed.

Conclusions: This study has the largest cohort of patients with DG suspected of VBD reported in the literature. The patients were predominantly females who had most often been seen by a periodontist. The definitive diagnosis of DG was most accurately achieved when H & E along with two biopsies for direct IF studies were submitted for testing. H & E studies were particularly important for definitive diagnosis of negative cases. Oral lichen planus was the most common disease presenting as DG, which is consistent with recent studies. Systemic connective tissue disorders that present as DG at initial clinical examination require direct IF and serum studies for a conclusive diagnosis. Clinical pathologic correlation, including history, presentation, H & E, and direct IF studies, are essential in establishing a definitive and differential diagnosis for cases presenting with DG. *J Periodontol 2012;83:1270-1278.*

KEY WORDS

Autoimmune diseases; clinical laboratory techniques; fluorescent antibody technique, direct; gingivitis; lichen planus, oral; skin diseases, vesiculobullous.

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Desquamative gingivitis (DG) is a general descriptive term that indicates the presence of diffuse desquamation, erythema, erosion, and blistering of the attached and marginal gingiva. The term DG was introduced by Prinz in 1932.[1] DG is not a definitive diagnosis. It encompasses a broad clinical spectrum of mucocutaneous disorders ranging from immune-mediated vesiculobullous diseases (VBDs) to allergic reactions to various chemicals or allergens.[2] This group of diseases is considered to be non-plaque-induced gingival disorders according to the current classification system for periodontal diseases and conditions.[3] These diseases include oral lichen planus (OLP), oral lichenoid lesions, mucous membrane pemphigoid (MMP), pemphigus vulgaris (PV), erythema multiforme, graft versus host disease, paraneoplastic pemphigus, epidermolysis bullosa acquisita, linear immunoglobulin A (IgA) disease, chronic ulcerative stomatitis (CUS), plasma cell gingivitis, dermatitis herpetiformis, foreign body gingivitis, and various immune-mediated systemic connective tissue diseases (SCTDs), including lupus erythematosus, scleroderma, and mixed connective tissue disease.[4] Most of these conditions present with a similar clinical appearance of DG in the gingiva and non-specific or similar histologic presentation, which make them indistinguishable from one another.[5] This problem is illustrated in Figure 1. Making a definitive diagnosis by differentiating these disorders from one another is important because management and prognosis may differ among the disorders.[4,5]

Direct immunofluorescence (IF) studies are valuable diagnostic tests that allow the discrimination of VBD and allergic reactions presenting as DG that may be histologically indistinguishable on conventional hematoxylin and eosin (H & E) microscopy examination. Direct IF is the gold standard used to diagnose many of the VBDs presenting as DG and is required for a definitive diagnosis.[5]

There has been no recent detailed analysis of clinical associations of DG and utility of direct IF in the diagnosis of VBD. Moreover, there are differences in data between older and newer literature concerning the frequency of various VBDs presenting in oral mucosa. The aim of the present study is to examine retrospectively a large cohort of patients with DG for associated diseases and determine the utility of direct IF in the definitive diagnosis.

MATERIALS AND METHODS

Selection and Processing of Tissue Specimens

This is a retrospective study of consecutive cases submitted with gingival biopsy specimens for histopathologic studies that were received by IMMCO Diagnostics in Buffalo, New York, from November 1, 2009 to January 31, 2011. The cases were submitted to us for identification or elimination of a specific immune-mediated oral disorder. Our test request form instructs the clinician to submit three biopsy specimens for each case to establish a diagnosis. Two biopsies are requested for direct IF studies, one from a perilesional site and the other from normal-appearing mucosa. One perilesional biopsy is requested for H & E studies. Demographic data, clinical diagnosis, and location of the biopsy site were also requested.

The inclusion criteria were complete demographic data and a suspected clinical diagnosis of DG, including pemphigus, pemphigoid, lichen planus, and other systemic connective tissue disorders. Cases submitted to rule out VBDs were also included. Only biopsies taken from the gingiva were included in the study. All cases with positive direct IF findings were included in the study, irrespective of concomitant H & E submission or diagnosis.

Direct IF Testing

Biopsies were received in Michel's transport media.[6] The biopsies were snap-frozen on dry ice and cut to obtain 4-μm-thick sections. The sections were then stained for immunoglobulins IgG, IgG4, IgA, IgM, fibrin, and complement C3 using fluorescein-labeled goat anti-human conjugates.‡ The details of the technique have been described previously.[7] Interpretation was made using a fluorescence microscope§ at ×200 magnification.

H & E Testing

Specimens submitted for H & E testing were received in 10% buffered formalin. The formalin-fixed tissues were processed overnight in a tissue processor. The processor used alcohol to dehydrate, xylene to clear, and paraffin to infuse the tissues. The processed tissues were paraffin embedded, and 4-μm-thick sections were obtained. The sections were stained with H & E, dried, coverslipped, and viewed under a light microscope.

Diagnostic Criteria and Diagnosis

The diagnosis for each case was established through the assessment of microscopic and direct IF characteristics of the biopsy specimen. Diagnosis of the cases was rendered by either an oral and maxillofacial pathologist (LS) or an immunopathologist (MN).

Pemphigus

A diagnosis of pemphigus was dependent on direct IF findings of an epithelial intercellular deposition of IgG, IgG4, and complement C3 individually or in varying combinations (Fig. 2A).[8,9]

‡ Conjugates, Sigma-Aldrich, St. Louis, MO.
§ Eclipse 50i, Nikon, Melville, NY.

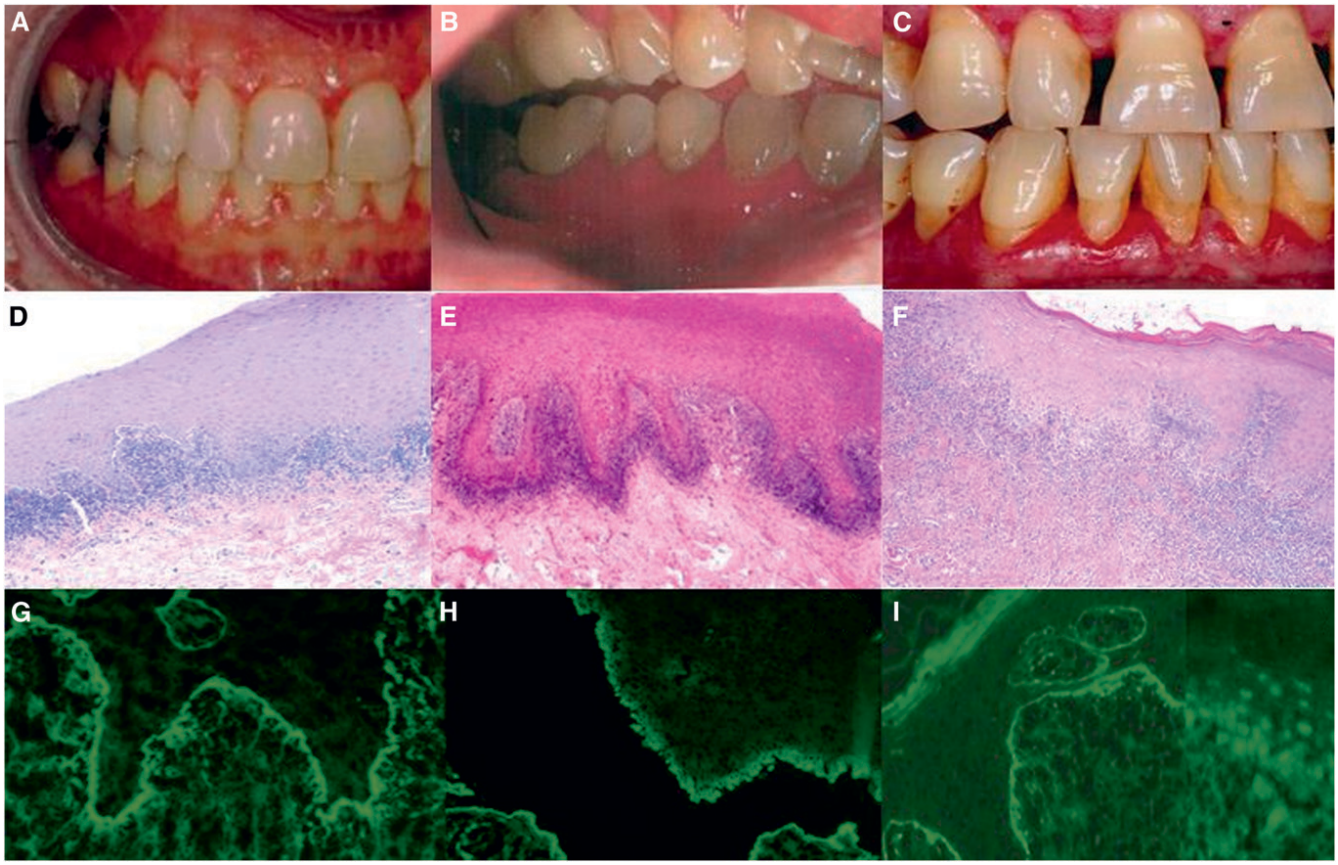

Figure 1.
A, B, *and* ***C)*** *Similar clinical presentations of three cases with generalized DG.* ***D, E,*** *and* ***F)*** *Similar histologic presentations in H & E studies (original magnification ×100) of chronic inflammation in lamina propria, making them indistinguishable from one another.* ***G, H,*** *and* ***I)*** *Direct IF findings (original magnification ×100) helping in the definitive diagnosis of the three cases: G) OLP, with shaggy fibrin deposits at BMZ; H) MMP, with linear complement C3 deposits at basal cells; I) CUS, with fibrin at BMZ and IgG nuclear deposits in the epithelial cells.*

MMP

A diagnosis of MMP was dependent on direct IF findings of linear deposits IgG, IgG4, and complement C3 in the basement membrane zone (BMZ).[10,11] The immunodeposits could occur singly or in varying combinations of IgG, IgG4, and complement C3 (Fig. 2B). The immunodeposits were localized to the basal cells of the epithelium or seen in both epithelium and the superficial connective tissue with a linear pattern.

Epidermolysis Bullosa Acquisita

Cases with immunodeposits of IgG, IgG4, and complement C3, singly or in varying combinations only on the superficial connective tissue, were considered as epidermolysis bullosa acquisita.

Dermatitis Herpetiformis or Oral Manifestation of Celiac Disease

Cases with granular deposits of IgA in the lamina propria with or without complement C3 and/or fibrin were diagnosed as dermatitis herpetiformis or oral manifestation of celiac disease (Fig. 2C).

Linear IgA Disease

Biopsies showing exclusive IgA deposits in the BMZ with a linear pattern on direct IF constituted linear IgA disease (Fig. 2D).[12]

OLP

The histopathologic criteria for a diagnosis of OLP on examination of the H & E sections included a finding of a band-like lymphocytic infiltrate at the superficial part of connective tissue; basal cell layer degeneration; shortened rete ridges, some of which showed a saw-tooth configuration; and absence of epithelial dysplasia (Fig. 1D).[13,14] Direct IF findings for lichen planus consisted of linear-to-fibrillar shaggy deposition of fibrin along the BMZ (Fig. 1G).

CUS

CUS is a rare autoimmune mucocutaneous disease that is characterized by the presence of oral erosive or ulcerative lesions that display unique direct and indirect IF patterns.[15-17] Diagnosis is usually confirmed by serology studies.[16,17] Light microscopy demonstrates that CUS histologic features are similar to

OLP and show basal cell degeneration with a mononuclear inflammatory cell infiltrate in the lamina propria that displays a "band-like" pattern (Fig. 2A). Direct IF studies show linear-to-fibrillar shaggy deposition of fibrin along the BMZ (Fig. 2C) and a speckled, finely granular pattern of IgG deposition in the nuclei of keratinocytes that is confined to the basal cells and lower third of the spinous layer (Fig. 3C). Serum studies for indirect IF studies are considered diagnostic of CUS and show stratified epithelial antinuclear antibodies limited to basal and parabasal epithelial cells using monkey and guinea pig esophagus.

The direct IF finding of speckled, finely granular pattern of IgG deposition in the nuclei of keratinocytes seen in CUS can also be observed in SCTDs such as lupus and Sjogren's syndrome.

CUS also shares similar conventional histology findings and direct IF findings of shaggy and fibrillar fibrin along the BMZ with OLP. In addition to conventional histology and direct IF, serology studies for indirect IF studies need to be performed to differentiate among CUS from various SCTDs and OLP. Because we did not include serology studies in our study, we could not definitively conclude that cases showing the established histologic features in conventional and direct IF studies were definitively CUS. These cases could represent CUS or OLP coexisting with various SCTDs, including lupus erythematosus, scleroderma, and/or mixed connective tissue disease.

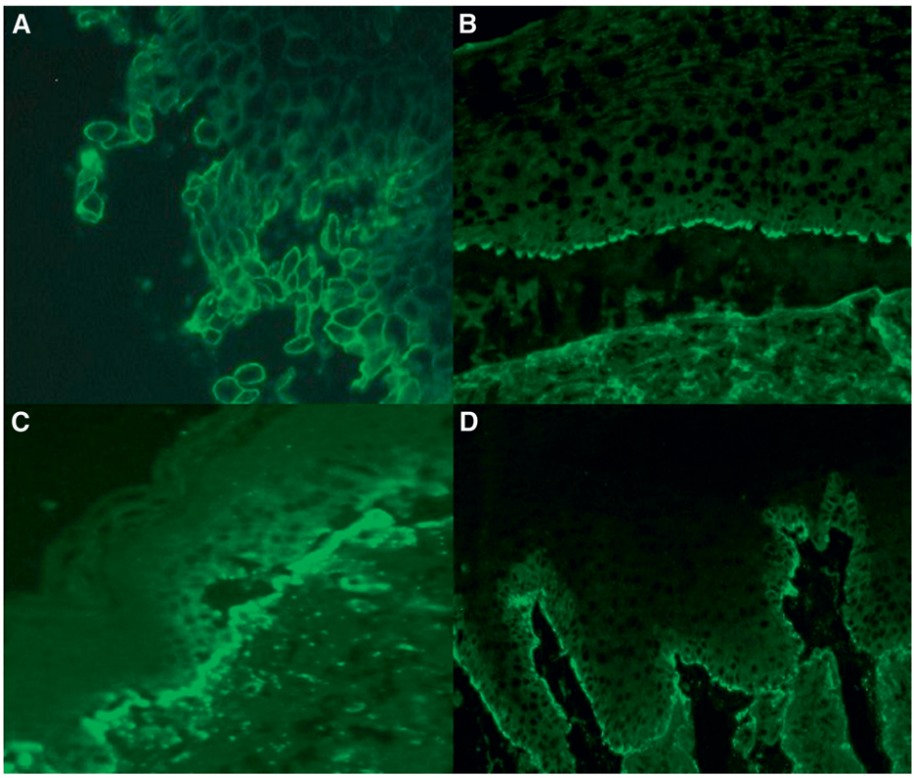

Figure 2.
Direct IF findings of pemphigus, MMP, dermatitis herpetiformis, and linear IgA disease (immunoglobulin IgG, IgA and complement C3 stains; original magnification ×200). ***A)*** *Pemphigus direct IF findings of an epithelial intercellular deposition of IgG.* ***B)*** *MMP direct IF findings of a linear deposit complement C3 in the epithelial side of the BMZ.* ***C)*** *Granular deposits of IgA in the lamina propria diagnostic of dermatitis herpetiformis.* ***D)*** *IgA deposits in the BMZ with a linear pattern on direct IF diagnostic of linear IgA disease.*

SCTDs

Our diagnostic criteria for various SCTDs, such as lupus erythematosus, Sjogren's syndrome, scleroderma, and mixed connective tissue disease, were based on the following direct IF findings.[18] 1) The presence of nuclear or cytoplasmic deposits in the epithelium with a homogeneous, speckled

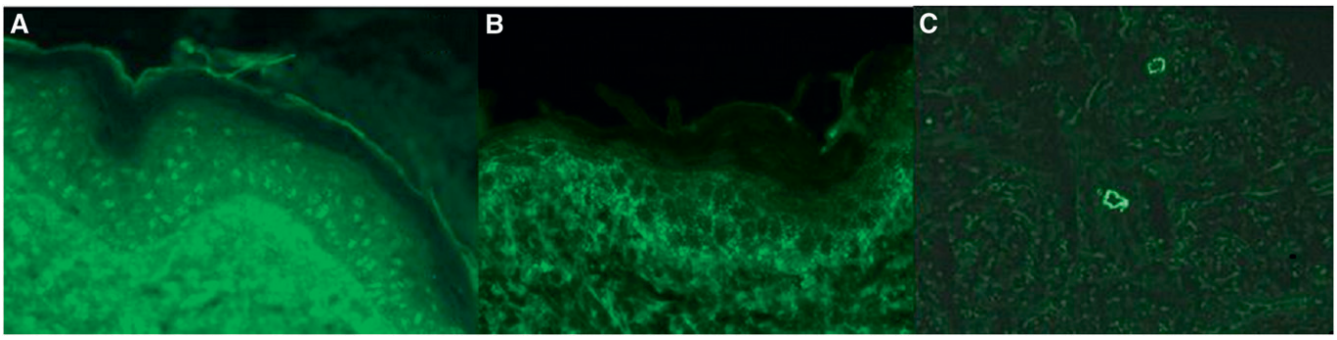

Figure 3.
Direct IF findings of systemic connective tissue disorders (immunoglobulin IgG and complement C5b9 stains; original magnification ×200). ***A)*** *The presence of IgG nuclear deposits in the epithelium.* ***B)*** *The presence of IgG cytoplasmic deposits in the epithelium.* ***C)*** *The deposits of complement membrane attack complex C5B9 around the vessels walls.*

(Fig. 3A), and dust-like pattern (Fig. 3B) represented lupus erythematosus, Sjogren's syndrome, scleroderma, and mixed connective tissue disease. 2) The presence of IgM at the dermal–epidermal interface with a granular pattern was considered a positive lupus band test and was diagnostic for lupus. 3) The deposits of complement membrane attack complex C5B9 around the walls of the vessels (Fig. 3C) in the absence of the lupus band were considered diagnostic of mixed connective tissue disease.

Biopsy specimens lacking surface epithelium were considered non-diagnostic. If there was a lack of immunodeposits and complement C3, it was considered to be negative.

Diagnosis of SCTDs cannot be established based solely on direct IF findings. Clinical history, presentation, conventional histopathology and serology, and especially indirect IF findings must be correlated with direct IF findings to establish a definitive diagnosis.

RESULTS

Oral biopsies were submitted for 594 cases in the time period selected for the study. A total of 239 cases had been biopsied from the gingiva and met the inclusion criteria for this study. The specialization of the contributors is listed in Table 1. Forty-six percent of the contributors were periodontists, with oral surgeons representing the second largest group. Contributions from oral pathologists may represent the cases they are managing themselves or include cases that have been submitted to their pathology service.

The type of testing and number of specimens submitted per patient are shown in Table 2. Forty percent of cases consisted of lesional and normal biopsies for direct IF and H & E studies.

Table 1.

Clinical Specialties of the Contributors Submitting Specimens for Direct IF Testing (with or without H & E)

Clinical Specialty	Total n (%)
Periodontics	115 (48)
Oral surgery	67 (28)
Oral pathology	33 (15)
General dentistry	13 (5)
Oral medicine	5 (2)
Medicine	6 (2)

Table 2.

Specimen Contribution for H & E and Direct IF Testing per Patient

Test	Total n (%)
H & E and 2 direct IF biopsies	95 (39.7)
H & E and 1 direct IF biopsies	31 (12.9)
2 Direct IF biopsies	62 (25.9)
1 Direct IF biopsies	51(21.3)

H & E biopsies were submitted for more than half (61%) of the cases submitted. Oral pathologists submitted biopsies for direct IF studies only after H & E studies were performed in their own laboratories. Direct IF biopsies without biopsies for H & E studies were also submitted by periodontists and oral surgeons after recommendation by the pathologists.

Table 3 presents the findings and demographics of the 239 gingival cases. One of the most obvious findings is that almost all entities that showed positive deposits of one or more IgG, IgA, IgM, fibrin, and/or complement C3 were predominantly female. The most common finding was positive staining with antifibrin seen in 106 patients. Sixty-one cases had both H & E and direct IF biopsy submissions and findings consistent with OLP. This group met the most rigid criteria of OLP. The second group of six cases had H & E findings that did not conclusively support OLP diagnosis. In this group, four H & E biopsies were nondiagnostic with a lack of epithelium, and one of each represented hyperkeratosis and chronic non-specific inflammation. The third group of 39 cases was submitted without H & E. Of this group, 16 cases were submitted by oral pathologists who had examined the H & E sections. We do not have data on the remainder of the 23 cases regarding how many in this group were submitted by clinicians on the suggestion of pathologists who were signing out the H & E biopsy reports. MMP represented 25% of the gingival biopsies submitted.

The negative cases in this study constitute 20.5% (49 cases). The majority of cases had a sole clinical diagnosis of lichen planus (15 cases) or included lichen planus in the differential diagnosis (10 cases). The remainder of the cases (24) had an inclusive diagnosis of DG and VBD. Ten of these cases had one direct IF biopsy with H & E, and 10 had two direct IF biopsies with H & E biopsies. The H & E diagnosis for the available 25 cases were as follows: four were diagnosed as lichen planus, two as plasma cell gingivitis, and two cases had no epithelium, whereas one showed mild epithelial atypia, one was diagnosed with

Table 3.

Demographics and Direct IF Findings of the DG Cases

Diagnosis	Male n (%)	Female n (%)	Total n (%)	Age Range (years)	Median Age (years)
OLP	20 (18.9)	86 (81.1)	106 (44.3)	21 to 91	65
MMP	16 (26.7)	44 (73.3)	60 (25.1)	30 to 95	70
Negative	7 (14.3)	42 (85.7)	49 (20.5)	16 to 89	67
SCTD	0 (0)	6 (100)	6 (2.5)	39 to 80	73
Non-diagnostic samples	0 (0)	4 (100)	4 (1.6)	56 to 76	71
CUS/OLP–SCTD overlap	1 (16.6)	5 (83.4)	6 (2.5)	56 to 90	65
Pemphigus	3 (60)	2 (40)	5 (2.1)	37 to 65	61
Linear IgA disease	1 (50)	1 (50)	2 (0.8)	56 to 81	68
Dermatitis herpetiformis	1 (100)	0 (0)	1 (0.4)	67	67

squamous cell carcinoma, and the remaining 15 cases mostly represented non-specific chronic inflammation. The remaining 24 cases lacked light microscopy studies, and hence no definitive diagnosis was possible. SCTDs represented 2.5% (six cases), and the diagnosis included lupus erythematosus (three cases) and scleroderma (three cases). The rest of the 14 cases included CUS (six cases), pemphigus (five cases), linear IgA disease (two cases), and dermatitis herpetiformis (one case).

Direct IF findings with clinical diagnosis for fibrin staining and MMP correlation are shown in Tables 4 through 6. Table 4 shows the clinical diagnosis of those cases with positive fibrin and H & E diagnosis consistent with OLP. Eighty-eight percent of the cases had a clinical diagnosis of OLP (sole clinical diagnosis of OLP in 49.2% and another 38.8% included OLP in the differential diagnosis). Table 5 shows the clinical diagnosis of cases that were fibrin positive on direct IF but did not have H & E to confirm diagnosis. As in Table 4, >87% of the cases gave OLP as the clinical diagnosis (sole clinical diagnosis of OLP in 51.3% and >35% included OLP in the differential diagnosis). The clinical diagnosis with direct IF findings correlated with >80% of cases with MMP (Table 6). Twenty percent of cases gave other clinical differential diagnosis that excluded MMP.

DISCUSSION

Immune-mediated oral VBDs often manifest as DG in the oral cavity.[19] In many cases of DG, gingival lesions represent the onset of the disorder and appear very early during the clinical course.[2] Most cases of OLP, MMP, and PV present initially as gingival lesions. This is reflected by the contribution of the

Table 4.

Clinical Diagnosis of Fibrin-Positive Cases With H & E Biopsy

Clinical Diagnosis	Total Cases	%
Lichen planus (sole diagnosis)	33	49.2
Lichen planus plus other diagnosis	18	26.8
All inclusive terms (DG, VBD)	8	12
Other diagnosis	8	12
Total	67	100

Table 5.

Clinical Diagnosis of Fibrin-Positive Cases Without H & E Biopsy

Clinical Diagnosis	Total Cases	%
Lichen planus (sole diagnosis)	20	51.3
Lichen planus plus other diagnosis	12	30.8
All inclusive terms (DG, VBD)	2	5.1
Other diagnosis	5	12.8
Total	39	100

Table 6.

Clinical Diagnosis of MMP

Clinical Diagnosis	Total Cases	%
MMP (sole diagnosis)	23	38.3
MMP plus other diagnosis	13	21.7
All inclusive terms (DG, VBD)	13	21.7
Other diagnosis (no MMP)	11	18.3
Total	60	100

biopsies for this study, with approximately half of the biopsies submitted by periodontists (Table 1). Another reason for the predominance of periodontists in the biopsy submission could be attributable to the design of the study with inclusion criteria restricted to cases on gingiva with clinical diagnosis of DG. When the disease is confined to gingiva, the diagnosis becomes difficult. Clinical presentation of generalized ulceration or erythema with non-specific symptoms makes the definitive diagnosis of DG more complex. The clinical presentation of DG is polymorphous, and the presence of plaque complicates the diagnosis. Most VBDs share similar clinical and microscopic features as illustrated in Figure 1. Clinical and light microscopy examination and direct and indirect IF testing are often needed to characterize the disease further and to determine the underlying pathology. For most autoimmune-mediated blistering diseases, such as MMP, pemphigus, linear IgA disease, and CCIS, direct IF studies are considered to be the gold standard in diagnosis.[18,20] The direct IF studies are supportive for OLP and SCTDs.

Approximately half the submissions for diagnosis included biopsies for H & E and direct IF studies (Table 2). Oral pathologists tended to submit biopsies only for direct IF studies if they had a previous H & E diagnosis, and this accounted for 15% of the cases (Table 1). There were some cases of direct IF submitted by other contributors in which previous H & E had been performed elsewhere. However, the exact number of these cases could not be ascertained. Approximately 30% of the cases submitted did not include biopsies for H & E studies.

Light microscopy findings were especially important in the diagnosis of OLP and negative cases. The H & E findings did not conclusively support OLP diagnosis in six cases because of lack of epithelium (four cases), indicating that the biopsy had been taken from a completely ulcerated area. The other two cases showed little or no inflammation and represented hyperkeratosis and non-specific inflammation. It could be speculated that the site selection for biopsy in these cases for H & E studies could have been better. There were 39 cases of OLP submitted without H & E. In this group, 16 cases were submitted by oral pathologists who had examined the H & E sections. We do not have data on the rest of the 23 cases and how many in this group were submitted by clinicians on the suggestion of pathologists who were signing out the H & E biopsy reports. The need for routine H & E biopsies is of particular importance in cases that show negative direct IF findings. The H & E diagnosis was available for only 25 of the 49 cases with negative direct IF findings. Significant findings were found in four cases: squamous cell carcinoma (one case), plasma cell gingivitis (two cases), and mild epithelial atypia (one case). Twenty-four cases did not have H & E, and hence no definitive diagnosis could be obtained. Light microscopic examination was not performed in these cases previously and could have helped in establishing a definitive diagnosis. H & E studies are mandatory in any chronic condition for a definitive diagnosis, and conventional microscopic examination will help with the diagnosis of conditions that yield negative direct IF findings. Without H & E studies, a number of significant lesions, such as squamous cell carcinoma and dysplasia, could be missed, which could otherwise be diagnosed by routine light microscopy.

There were four non-diagnostic samples, and all of them lacked surface epithelium (Table 3). Diagnosis for direct IF and H & E testing requires an intact tissue specimen with surface epithelium and connective tissue. Tissue specimens from VBD lesions tend to be fragile because of undermined epithelial attachment attributable to antibodies against the tissue components. Furthermore, areas that are ulcerated are completely denuded of epithelium, lacking the very tissue necessary for diagnosis. Ideally, the best results can be achieved by obtaining three biopsies, two for direct IF studies and one for H & E studies. One biopsy for direct IF should be taken from perilesional tissue found adjacent to an ulcer or vesicle and another from normal intact mucosa. For H & E studies, the biopsy should be from the lesional site, including an area of normal tissue.

To the best of our knowledge, our study of 239 cases is the largest cohort of patients with DG having autoimmune-mediated blistering diseases reported in the literature (Table 7).[4,21-30] Forty-four percent of the cases in this study represent OLP (Table 3). This corresponds to the recently published studies.[4,26] The median age of the patients in this group was 65 years, and the great majority of patients with OLP were females (81%). These demographic data are in accordance with the previous reports.[4,26] The suspected clinical diagnosis of OLP correlated with the direct IF findings in >75% of the cases (Tables 4 and 5). The correlation was similar in the cases with or without H & E biopsy, with minimal difference. Our study also

Table 7.

Literature Review of DG and Direct IF Studies

Reference	Year of Publication	Number of Cases
Present study	2012	239
Lo Russo et al.[4]	2008	125
Yih et al.[21]	2000	24
Yih et al.[22]	1998	72
Rogers et al.[23]	1982	41
Nisengard and Neiders[24]	1981	100
McCarthy et al.[25]	1960	13
Leao et al.[26]	2008	187
Markopoulos et al.[27]	1996	49
Sklavounou and Laskaris[28]	1983	111
Vaillant et al.[29]	2000	33
Laskaris et al.[30]	1982	212

showed that MMP was the second most common presentation of DG, representing >25% of the cases. The median age of the patients in this group was 70 years, and the great majority of patients with MMP were female (71.5%). These demographic data are in accordance with the previous reports.[4,26] In our study, we find a clinical diagnosis of MMP correlating with direct IF findings in more than half of the cases. If an all-inclusive term such as VBD is used, then the clinical correlation rises to 80% (Table 6). As with OLP, 20% of the cases with clinical diagnosis of MMP did not correlate with the direct IF findings. In the older literature, MMP was reported as the most common condition presenting as DG.[23-25,27,28] However, the recent studies[4,2] have shown that OLP is the most common disease associated with DG. Our study supports this, and OLP accounted for >40% of the cases compared to 25% of cases who had MMP. This presentation more accurately reflects the epidemiology of the OLP, which is present in 1% to 2% of the population.

Systemic connective disorders, CTS, pemphigus, linear IgA disease, and dermatitis herpetiformis constituted <10% of the cases of DG. The six cases of SCTD included three cases each of lupus and scleroderma. All the SCTD cases were confirmed by additional serology tests. Interestingly, in one case of scleroderma, DG was the initial clinical presentation. The mean age of onset and predilection to middle-aged females were consistent with the literature. Pemphigus was seen in 2% of the cases, with a mean age at presentation of 58 years.[24,25]

CONCLUSIONS

DG may represent OLP, MMP, other autoimmune disorders, and also diseases that are negative on direct IF. Therefore, both H & E and direct IF studies are required. Because DG may show areas of ulceration, care must be taken to submit tissue from a perilesional area and include an area of normal tissue showing intact epithelium for both direct IF and H & E studies. Diagnosis of DG cannot be established based solely on clinical or microscopic findings. The clinical history and presentation of DG must be correlated with both H & E and direct IF findings to establish diagnosis. For cases of CTS and SCTD, serology testing by indirect IF is required for a definitive diagnosis.

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