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CLINICAL REPORT

Oral Lesions in Four Cases of Subacute Cutaneous Lupus Erythematosus

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Patients with subacute cutaneous lupus erythematosus (SCLE) present with intense photosensitivity. Clinical patterns comprise papulosquamous or annular lesions on sun-exposed areas; although the face is usually spared. Intraoral lesions have not been reported in most case series of SCLE, but are well-documented in other forms of lupus erythematosus. This study included four female patients diagnosed with SCLE, who presented with specific oral involvement consisting of palatal patches (three cases), buccal mucosal patches (one case), gingival keratotic erythema (one case), and lip lesions (one case). All patients presented with exuberant facial lesions, a condition not often observed in SCLE. Our findings suggest that oral involvement in SCLE may not be as rare as once thought, and that patients with intense facial lesions are at particular risk of developing oral lesions. ***Key words: subacute cutaneous lupus erythematosus; oral lesions*****.**

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The term subacute cutaneous lupus erythematosus (SCLE) defines a subgroup of lupus erythematosus (LE) patients with well-characterized cutaneous and serological features (1, 2). Patients with SCLE typically present with marked photosensitivity, and their cutaneous lesions consist of papulosquamous or annular plaques on exposed areas of the trunk and arms; the face is often spared. The serological hallmark of SCLE is the positivity of anti-Ro/SS-A and anti-LA/SS-B antibodies in approximately 70% of patients (2).

Approximately half of SCLE patients will develop symptoms and signs of systemic LE (SLE) (usually non-severe), but the presence of other autoantibodies associated with the detection of LE activity in internal organs, such as anti-Sm, anti-dsDNA is rare. Studies have revealed that only approximately 10–15% of patients whose presenting illness includes SCLE skin lesions go on to develop severe clinical manifestations of SLE (1, 2).

No attention has been paid to the occurrence of mucosal lesions in patients with SCLE in previously published series. Since SCLE is markedly photosensitive, it may be tempting to assume that intraoral compromise is rare in this setting. On the other hand, it is possible that dermatologists and clinicians miss their occurrence, given the exuberance of the cutaneous lesions. Our group has been dealing with LE in the oral mucosa (3–7), and has observed a surprisingly high number of SCLE patients with oral lesions. This report concerns this subset of patients, describing their clinical, histopathological and immunological features.

METHODS

This study included 4 patients with SCLE who presented with specific intraoral LE lesions examined in the Oral Diseases Clinic and in the Collagen Diseases of the Department of Dermatology, University of São Paulo, Brazil. Oral candidiasis was ruled out by negative potassium iodide scrapings prior to biopsy procedure. Cutaneous, as well as mucosal, lesions were photographed and biopsied for histopathological and immunofluorescence studies.

RESULTS

The clinical features of the 4 patients are shown in Table I. All patients were women, in the age range 20–45 years. Two patients presented with papulosquamous SCLE, and two had annular lesions. Besides typical lesions on the chest and arms, all 4 patients presented with facial lesions. Oral lesions consisted of oval non-scarring patches with different degrees of erosion, keratosis or purpura on the palate on 3 patients, asymmetrical lesions on the buccal mucosa in one patient, and linear erythema with keratosis in the upper palatal gingival in one patient. Patches on the vermilion were present in one patient.

Histopathology of all biopsied lesions revealed variable degrees of hyperkeratosis with areas of atrophy or acanthosis, vacuolar alteration of the basal layer, and mostly superficial perivascular and interface lymphocytic mucositis with interstitial mucin. Immunofluorescence findings are depicted in Table I.

DISCUSSION

Oral-specific lesions in LE have long been described. Terminology varies enormously among the published series; a rational classification has not been employed by most authors, unlike with cutaneous lesions. Non-specific terms usually employed include “oral discoid lesion”, “chronic plaque”, “lupus cheilitis”, “acute ulcer”, “oral

Table I. *Characteristics of four female subacute cutaneous lupus erythematosus patients with oral lesions*

Patient	Age (years)	Type and distribution of cutaneous lesions	Oral lesion	Significant additional findings	Direct immunofluorescence of oral lesion	Lupus serology
1 Fig. 1 A–D	23	Annular, face, chest, limbs	Round erythematous and keratotic patches on palate. Linear erythema and keratosis on the upper palatal gingiva. Lips: scaly patches.	Discrete anaemia and leukopenia wbc 3,900	Linear IgM and C3 at BMZ	Anti Ro- + Anti La- – Anti DNA- 200 UI/ml ANA- 1:160
2 Fig. 1 E, F	45	Annular, face, chest, limbs	Round erythematous and erosive palatal patches.	Discrete arthralgia	Linear IgM at BMZ	Anti Ro- + Anti La- –
3 Fig. 1 G, H	22	Papulosquamous, face, chest, limbs	Round erythematous palatal patches with petechiae.	Discrete leukopenia wbc 3,500	Linear IgM at BMZ	Anti Ro- + Anti La- – Anti DNA-1000 IU/ml Anti SM- 100 IU/ml ANA- 1:320
4 Fig. 1 I, J	42	Papulosquamous, face, chest, limbs	Erosive and keratotic plaque on left buccal mucosa.	None	IgM on colloid bodies	Anti Ro- + Anti La- –

C: complement; BMZ: basement membrane zone; rbc: red blood cells/μl; wbc: white blood cells/μl.

ulcer", "red ulcer", "ulcerative plaques", "pebbly red areas", "honeycomb lesion", "keratotic lesion" "white keratotic plaques", "purpuric lesions" and "diffuse palatal petechial erythema". A recent review compared oral lesions to cutaneous lesions, and suggested that intraoral LE lesions simply represent the mucosal counterpart to cutaneous LE lesions (interface dermatitis/interface mucositis), and can be categorized, by analogy, into chronic, subacute and acute forms; variants described include verrucous, bullous and ulcerated presentations (5). This concept is in accordance with studies that demonstrated that oral LE ulcers are histologically specific acute LE lesions (interface mucositis), and do not represent vasculitis as many authors believed (8).

SCLE has been well-characterized clinically and immunopathologically for more than 30 years (1, 2). The 4 patients presented herein fulfil the established clinical and serological criteria for SCLE. Systemic compromise varied between these patients, but their cutaneous lesions were typical for papulosquamous or annular SCLE.

SCLE occurs mostly on light-exposed areas; among all described presentations of cutaneous LE, subacute lesions are considered the most photosensitive (2). In a review, our group reported intraoral lesions in SCLE to be very rare, as oral cavity is not exposed to ultraviolet (UV) radiation (5). These lesions may be not be as rare, as the present series may suggest.

Most descriptions of SCLE stress a tendency of lesions to spare the face, despite marked sun sensitivity (1, 2). The 4 patients presented herein presented exuberant facial lesions, as shown in Fig. 1. This particular feature of the four patients may not be purely coincidental; it might be related to the presence of intraoral lesions.

UV light is believed to worsen cutaneous, as well as systemic, activity of LE (9). The link between photosensitivity and induction of autoimmune disease is explained using a model centred on the apoptotic cell. UV may be an important initiator of apoptosis in keratinocytes. Both apoptosis induction and apoptotic cell clearance can be determined by genetic abnormalities, and result in an increased load of apoptotic cells. Apoptosis may be an important mechanism leading to autoantigen presentation in cutaneous LE (10–14). In addition to promoting cell death and neoantigen generation, UV also induces and modulates immune and inflammatory mediators by increasing levels of both IL-10 and IL-12 (10, 11). IL-10 induces systemic immunosuppression and tolerance by promoting Th2 response. IL-12 seems to promote a Th1 response and can reverse UV-induced IL-10 immunosuppression and tolerance (12, 13). IL-12 may also have a role in controlling UV-mediated apoptosis by suppression of tumour necrosis factor (TNF)-α (13).

Despite of all this evidence, a recent study that compared intraoral and cutaneous LE lesions did not reveal differences in cytokine expression between sun-exposed

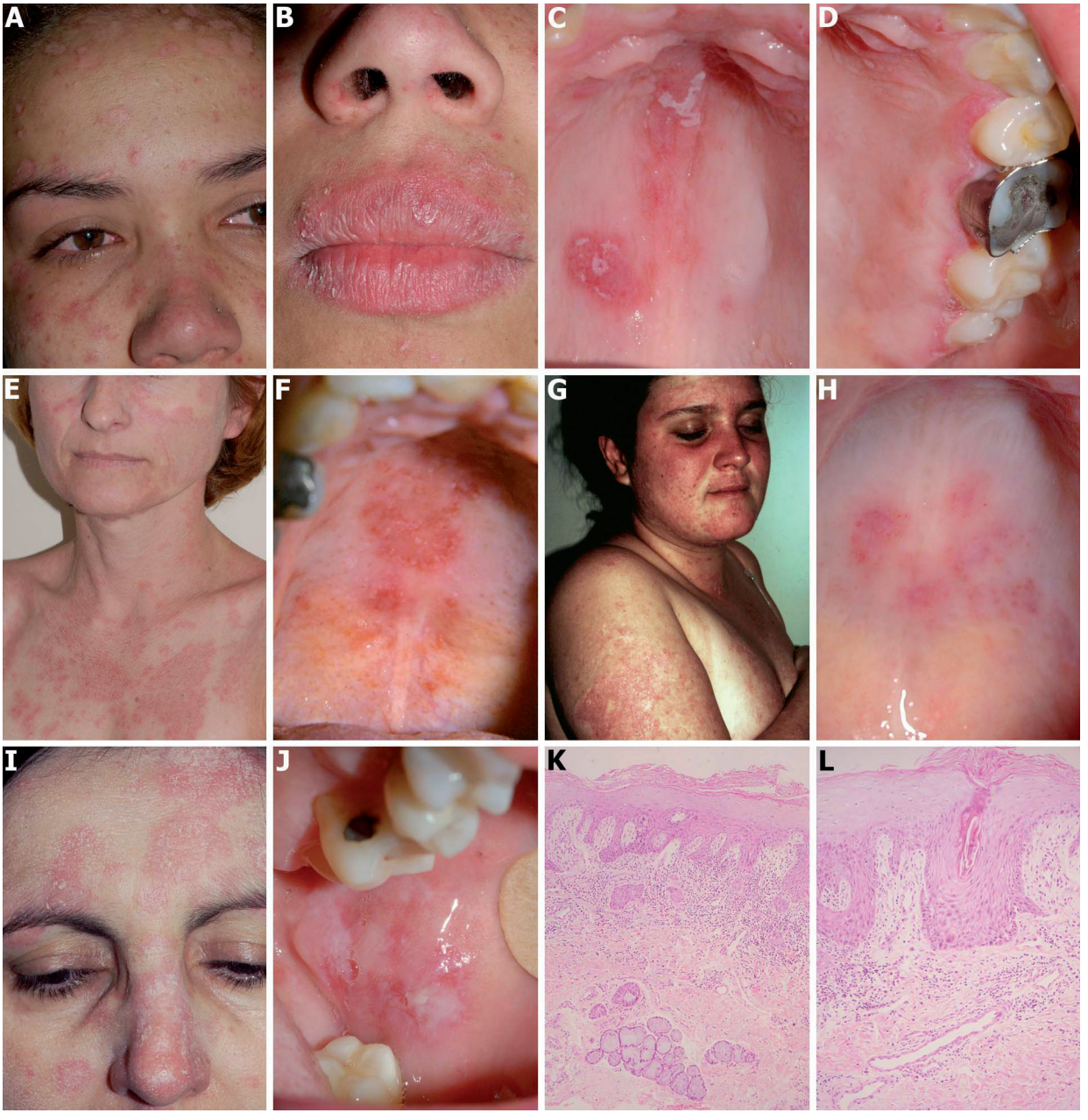

Fig. 1. Clinical and histopathological appearance in patients with intraoral subacute cutaneous lupus erythematosus (SCLE). (A) Annular SCLE on the face in patient 1. (B) Ill-defined scaly papules spreading from vermilion to the skin in patient 1. (C) Palatal erythematous and keratotic patches in patient 1. (D) Linear erythema and keratosis on the upper palatal gingiva in patient 1. (E) Annular SCLE on the face and the trunk in patient 2. (F) Palatal round patches in patient 2. (G) Papulosquamous SCLE in patient 3 (5). (H) Palatal lesions in patient 3. (I) Facial papulosquamous SCLE in patient 4. (J) Buccal erosive and keratotic LE in patient 4. (K) Histopathological aspect of intraoral SCLE: interface and superficial perivascular mucositis associated with hyperkeratosis and areas of vacuolar degeneration of basal layer (patient 1) (haematoxylin and eosin (H&E), original magnification × 40). (L) Detail of interface and superficial perivascular mucositis: presence of apoptotic keratinocytes and oedema of blood vessel walls. Note the hyperkeratosis on the salivary duct (H&E, original magnification × 100).

(lower lip) and sun-covered (intraoral) areas (6). These findings suggest that even though UV light is known to be of great importance in the induction of LE activity, intrinsic mechanisms of mucocutaneous lesions formation may be similar in sun-exposed and sun-covered areas, after the whole process has been initiated. These concepts are in accordance with the hypothesis that oral LE lesions represent the mucosal counterpart to cutaneous LE because they probably arise from the same molecular mechanisms. With these concepts in mind, it is not surprising that intraoral lesions may appear in severely affected SCLE patients.

The lesions described herein were asymptomatic and were found during clinical examination; patients were concerned mainly with the exuberant cutaneous facial picture. Oval palatal patches that presented variably

with erythema, pethechiae, erosions and keratosis were seen in 3 of the 4 patients; we speculate that this is possibly the stereotypical presentation of mucosal SCLE if more cases are observed.

Patient one, besides palatal patches, also presented with a distinctive erythematous and keratotic linear lesion on the upper palatal gingiva. We have not observed this aspect before, and we believe that it represents a specific LE manifestation, since its elements are identical to the ones present on the palate, which proved to be specific on biopsy. This lesion may be of concern, since we do not know whether its persistence might affect periodontal tissues.

The erosive and keratotic lesion on the left buccal mucosa presented by patient 4 is similar to a classic discoid oral lesion, although its borders were more poorly defined. The patient reported that this lesion and her cutaneous flare appeared more or less simultaneously, and their histological features were mostly similar, indicating a possible common origin.

The labial lesions present in patient 1 are typical of labial LE (5). These usually do not spare the limit between the vermilion and the skin. This particular feature is useful in differentiating LE from other forms of cheilitis, such as lichen planus, in cases with localized lesions.

Histopathological findings were similar in all cases, and are in agreement with previous reports (4, 9, 10), although not as intense as in chronic discoid or in acute ulcerated lesions. We observed various degrees of interface mucositis with superficial, or, more rarely, superficial and deep perivascular lymphocytic inflammation with oedema in the lamina propria. The covering epithelium presented slight hyperkeratosis and areas of acanthosis alternated with areas of atrophy. Chronic mucosal LE lesions tend to present intense hyperkeratosis, atrophy, and infiltrate; acute lesions tend to be ulcerated, but the general pathological process is essentially the same (14, 15).

Immunofluorescence findings revealed mostly IgM at the basement membrane zone or at colloid bodies. IgG or IgA were not observed. This is in agreement with previous reports (5).

The treatment of oral LE lesions consists of the same regimen as used to treat the overall LE process. Resistant lesions may benefit from topical or intralesional applications of corticosteroid. Patient 1 was referred to periodontal care for evaluation of the gingival margin.

The percentage of patients with SCLE who present with oral lesions is unknown; this feature should be investigated in future case series. Among many SCLE cases seen at our institution, we collected these four patients who, besides typical papulosquamous or annular lesions, presented with marked facial and intraoral lesions. This presentation is probably uncommon. Intense facial symptoms in the setting of SCLE might be indicative of the simultaneous presence of intraoral lesions. Intraoral lesions in SCLE may not be as important as their cutaneous counterpart in establishing a diagnosis of LE, due to their much less impressive appearance. The occurrence of gingival compromise in one of our patients, a presentation not previously described and with unknown dental risk, highlights the importance of accurate intraoral examination.

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