Oral manifestations of systemic and cutaneous lupus erythematosus in a Venezuelan population

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BACKGROUND: The aim of this study was to characterize oral lesions in patients with systemic and cutaneous lupus erythematosus (LE) in a Venezuelan group.

METHODS: Ninety patients with LE were studied. Oral biopsies were taken from patients who showed oral mucosal involvement. Tissue samples were investigated with histology and direct immunofluorescence techniques for the presence of immunoglobulins G, M, A and complement factor C3.

RESULTS: In 90 patients with LE, 10 patients showed oral lesions related to the disease. Sixteen lesions were investigated. Oral ulcerations accompanied by white irradiating striae occurred in five patients, erythema was observed in five patients and a white homogeneous plaque in one patient. Fifteen lesions demonstrated vacuolar basal degeneration and 12 thickening of the basement membrane histologically. Direct immunofluorescence was negative in three samples.

CONCLUSIONS: These findings corroborated that ulcers are not the only manifestation of LE in the oral mucosa. Clinical and histological examinations are significant as immunoproteins are not always found on the oral sample.

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Keywords: lupus erythematosus; oral lesions; oral mucosa; systemic and cutaneous lupus erythematosus

Introduction

Lupus erythematosus (LE) is a multisystem autoimmune disease associated with significant morbidity and mortality. Lupus erythematosus occurs most commonly in young women and ranges from mild cutaneous lesions

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and/or arthritis to renal failure or intense nervous, cardiac and haematological disturbances (1).

The basic manifestations of LE occur in the connective tissue and blood vessels, but depending on the anatomical location and course of the disease, LE has been classified as systemic LE (SLE) or cutaneous LE (CLE). Cutaneous lupus erythematosus includes variety of LE-specific skin lesions that are subdivided into three categories: chronic CLE (CCLE), subacute CLE (SCLE) and acute CLE (ACLE) based on clinical morphology and histopathologic examination (2–4).

Patients with SLE frequently show cutaneous manifestations during the course of the disease. Moreover, 4 of the 11 criteria formulated by the American College of Reumathology (ACR) classification for the diagnosis of SLE are cutaneous and oral (4). These criteria are malar rash, discoid rash, photosensitivity and oral ulcers (5).

Oral mucosal ulceration occurs in more than 40% of patients with SLE (6–8); however, reticular, red and white plaques have also been observed in patients with SLE (6, 9, 10). The majority of these lesions showed histopathological changes specific to SLE; however, histological and immunological patterns might be unspecific (11–14).

The aim of this study was to describe the clinical, histological and immunological manifestations of SLE and CLE in the oral mucosa.

Patients and methods

Ninety patients with LE, attending the Dermatology Unit, were evaluated after filling an informed consent. All patients were under immunosuppressive therapy. A careful examination of the oral cavity was performed in each patient. Clinical recognition of oral lesions related to LE was assessed according to previous observations (6, 8, 9).

Biopsies of oral lesions were taken and immediately fixed in 10% formalin. Samples were stained with haematoxylin and eosin and periodic acid-Schiff (PAS) prior microscopic analysis. Biopsies of adjacent mucosa (clinically normal appearance) were also taken and

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Detiont	C	1000	LE alaceifaction	Our Locion	Location	Histored balaniad above astroniation	Direct immunofluorescence
r unent	Vac	Age	cussification	Oral lesion	FOCULION	n is to purify the characteristics	1620113
_	ц	16	SLE	Red macula	Hard palate	Hyperkeratosis, basal layer degeneration, thickening of the basement membrane zone, subepithelial lymphocytic infiltrate and deep perivascular infiltrate, edema	Granular band at the basement membrane zone
2	ц	29	SLE	Red macula	Hard palate	Basal layer degeneration, deep perivascular lymphocytic	Cytoid bodies
				Ked plaque Ulcer surrounded by white irradiating striae	Lower lıp Buccal mucosa	inhitrate	
ŝ	ц	32	SLE	Red plaque	Upper lip	Basal layer degeneration, thickening of the basement membrane zone and deep perivascular infiltrate	Discontinuous lineal band at the basement membrane zone
4	Ц	36	CLE	Red plaque	Hard Palate	Hyperkeratosis, basal layer degeneration, thickening of the basement membrane zone, subepithelial lymphocytic infiltrate and deep perivascular infiltrate	Negative
5	ц	38	SLE	Red macula Ulcers	Hard palate Buccal mucosa	Hyperkeratosis, basal layer degeneration, thickening of the basement membrane zone subepithelial lymphocytic infiltrate and deen menivascular infiltrate cotoid bodies	Granular band at the basement membrane zone
9	Ц	36	SLE	Ulcer surrounded by white irradiating striae	Buccal mucosa	Hyperkeratosis, basal layer degeneration, thickening of the basement membrane zone subepithelial lymphocytic	Granular band at the basement membrane zone
٢	Ц	34	SLE	Red plaque Red plaque Red macula	Lower lip Lower lip Hard palate	infiltrate and cytoid bodies Hyperkeratosis, basal layer degeneration, thickening of the basement membrane zone subepithelial lymphocytic	Continuous lineal band at the basement membrane zone and evioid hodies
~	ц	29	CLE	Ulcer surrounded by white irradiating striae	Buccal mucosa	Basal layer degeneration and deep perivascular infiltrate	Negative
6	Ц	49	CLE	Red plaque comession of the second se	Upper lip Buccal mucosa	Hyperkeratosis, basal layer degeneration, subepithelial lymphocytic infiltrate and deep perivascular infiltrate	Continuous lineal band at the basement membrane zone
10	Ц	52	CLE	Ulcer surrounded by white irradiating striae	Buccal mucosa	Basal layer degeneration, thickening of the basement membrane zone, subepithelial lymphocytic infiltrate and deen perivascular infiltrate	Negative

Table 1 Distributions of LE patients by gender, age, oral manifestation, histological appearance and immunopathological results

embedded in OCT compound (Miles Scientific, USA), snap-frozen in liquid nitrogen and stored at -70° C prior to immunostaining. Direct immunofluorescence technique was used in order to determine the expression of immunoglobulins (Ig) G, M, A and complement protein C3 on the tissue, using fluorescein isothiocyanate conjugated rabbit anti-human anti-sera to IgG, IgM, IgA and C3.

Results

The group of LE patients was composed of 8 males and 82 females with a mean age of 36.39 ± 8.42 years. Thirty-eight patients (42.22%) met the ACR criteria for diagnosis of SLE and 52 patients (57.78%) were diagnosed as CLE. All patients showed cutaneous lesions regardless of LE classification.

Of the 90 patients diagnosed with LE, 10 patients (11.1%), all women, showed oral mucosal lesions. Six patients were classified as SLE and four had the cutaneous form. Patient details are summarized in Table 1. None of the patient was receiving oral topical therapy.

Oral lesions ranged from a red macula or plaque, ulcerations surrounded or not by white irradiating striae to a white plaque on a pigmented mucosa (Fig. 1). Clinical features varied according to the anatomical location. Lesions of the hard palate were red maculae or plaque, in contrast, white lesions (plaque and lichen-like striae) were found only in buccal mucosa. Lesions of the lips were either red plaques or ulcers.

Microscopic analyses of 16 biopsy specimens were performed (Table 1) (Fig. 2). All cases showed epithelial changes. Hyperparakeratosis was observed in 13 biopsies and orthokeratosis in three. Acanthosis was found in 10 lesions while epithelial atrophy was observed in two red maculae. Vacuolar degeneration of the basement membrane with necrosis of basal keratinocytes was



Figure 2 Histopathological micrograph showing hyperkeratosis, basal layer degeneration and subepithelial lymphocytic infiltrate.

observed in all cases (16 lesions) and thickening of the basement membrane in 12 lesions. Lichenoid inflammatory mononuclear infiltrate was a common finding (15 biopsies), and although vasculitis in the deeper connective tissues is a common feature of LE, it was only found in six cases. Periodic acid-Schiff staining did not demonstrate fungal colonisation in any of the specimens.

Ten biopsies of apparent normal mucosa, adjacent to oral lesions, were obtained. Immune deposits were observed at the basement membrane zone in six biopsies. The pattern consisted of either a discontinuous or continuous lineal band or a granular band (Table 1). Positive cytoid bodies were observed in two samples. Three biopsies were completely negative.

Discussion

In the present study, oral lesions of patients with SLE and CLE were characterized. This is the first Venezuelan



Figure 1 Different oral manifestations of LE. (A) Discoid lesion, (B) white plaques on a pigmented mucosa, (C) red plaques on the lips and (D) various erythematous maculae on the palate.

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study, and indeed, the first South-American series. The prevalence of oral lesions in patients with SLE is variable and might depend on the state of the disease and the treatment received. Oral manifestations of LE do not represent a constant finding and may vary from the systemic to the cutaneous pole. In our study, the major percentage of oral lesions was found in SLE consistent with previous works (15). High prevalence of oral lesions in SLE is probably because of the fact that all tissues are potentially affected in this pole of the disease (16).

Ulcerations are usually associated with SLE because they are an ACR criterion for the disease diagnosis. However, other lesions can also appear as SLE and CLE manifestation. Red maculae on the hard palate and Lichen planus-like lesions, observed in this study, has been described previously (6, 8, 17). A white plaque on pigmented mucosa was also observed in this study. Slightly brownish pigmentation has been described in oral mucosa of patients with SLE receiving antimalarials (18). Oral lesions were found in patients with less than 2 years of diagnosis. Immunosuppressive treatments probably maintain patients free of mucosal alterations.

Despite clinical appearance, all lesions showed homogeneous histopathological features. Hyperkeratosis and acantosis were common findings, possibly produced as a response of the epithelia to the chronic aggression. Basal stratum degeneration and thickening of the basal membrane were also noticed in the majority of the cases. Histological characteristics, observed in this study, are congruent with previous studies (6, 19–21); however, differences with entities as oral lichen planus were difficult to assess.

This study also confirms findings of previous immunopathological studies (13, 22). Expression of immunocomplex in almost all cases emphasises the importance of the direct immunofluorescence, differentiating LE with other diseases as oral lichen planus. However, as some cases were negative to any immunological marker, diagnosis should not be relying on immunofluorescence results alone. Clinical, histopathological and immunopathological correlation is imperative in order to accomplish a correct diagnosis.

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