CASE REPORT

Oral and Cutaneous Manifestations of Disseminated DLE: A Case Report with Literature Review.

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Abstract

Introduction: Discoid lupus erythematosus (DLE) is a chronic inflammatory disorder of autoimmune origin. It has got both oral and cutaneous manifestations.

Case presentation: We present here one case of disseminated DLE with both skin and oral manifestations, along with an exhaustive discussion of the clinical, histological and immunological features to rule out the differential diagnoses.

Management: The oral manifestations of lupus erythematosus are very similar to other oral lesions such as lichen planus, lichenoid reactions, GVHD, chronic junctional stomatitis and squamous cell carcinoma. Hence, a biopsy is needed to accurately establish the diagnosis and start appropriate treatment.

Conclusion: Definitive diagnosis is arrived based on the information compiled from clinical, histopathological assessments, serum and urine tests, rheumatological evaluation and advanced diagnostic modalities like direct immunofluorescence tests.

Keywords: Anti Nuclear Antibody, Auto-immune, Discoid lupus erythematosus, Keratotic striae, Para-keratotic plugging

Introduction

Discoid lupus erythematosus (DLE) is a chronic inflammatory disorder of autoimmune origin. The disease involves mainly the sun-exposed areas of the body, especially the face and scalp, with variable clinical presentations as usually characterized by scaly, well-defined erythematous plaques healing with scarring and pigmentary changes.[1] The disease is broadly categorized into two groups: 1. localized variant involving mainly the face and scalp areas and 2. disseminated form with widespread extension beyond the neck area.[2] It is more common in women than in men, with common age of occurrence between 30 to 40 years[3,4]. The pathogenesis of cutaneous lupus erythematosus is multifactorial, with an interplay between genetic and environmental factors. Some contributing environmental factors include ultraviolet radiation (UVR), medications, cigarette smoking, and possibly, viruses.[5]

Lupus erythematosus is an inflammatory, connective-tissue disease of generalized autoimmunity characterized by pathogenic autoantibodies and immune complexes, attributed to a loss of immune tolerance. It was first described by Biett in 1828 and Kaposi in 1872. It can manifest as different clinical forms: systemic lupus erythematosus (SLE), chronic cutaneous lupus erythematosus (CCLE) and subacute cutaneous lupus erythematosus (SCLE). Systemic lupus erythematosus (SLE) is a serious multisystem disorder chiefly involving kidneys, liver, lungs and brain as well as variety of cutaneous and oral manifestations. Chronic cutaneous lupus erythematosus (CCLE), also termed as Discoid lupus erythematosus, primarily affects the skin and oral mucosa but has better prognosis. Subacute cutaneous lupus erythematosus

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(SCLE) lesions chiefly affect sun-exposed areas of the skin.[6] This type can also be initiated by certain drugs, and it has clinical manifestations intermediate between the two other types.

The cutaneous manifestations of DLE usually begin as scaly, erythematous patches that are frequently distributed on sun-exposed skin, especially in the head and neck area. The oral discoid lesions appear as central atrophic area with small white dots and fine white radiating striae. Clinically, the oral manifestations of DLE may resemble those of erosive lichen planus, Graft versus host disease (GVHD), lichenoid reactions, chronic junctional stomatitis and squamous cell carcinoma. Therefore, a biopsy is needed to accurately establish the diagnosis and start appropriate treatment.[7]

We present here one case of disseminated DLE with both skin and oral manifestations, along with an exhaustive discussion of the clinical, histological and immunological features to rule out the differential diagnoses.

Case Report

A 68-years-old female patient from urban area presented with the chief complaint of mouth ulcers and burning sensation since last 01 month. Her history revealed that she had similar episodes of ulcerations for almost 10 years along with ulceration and crustation on the skin of forehands. Skin biopsy was performed at that time elsewhere, but the reports and relevant documents were not available with her. The symptoms re-appeared 06 months ago, this time more predominantly on the skin of back of the trunk and hands, which exacerbated with sun exposure. She has been recently diagnosed with hypothyroidism and has been under medication since last month.

Extra-oral examination revealed the presence of multiple, erythematous or blackish-brown patches with crustations on the skin of forehands and back of the trunk (Figure 1). There was presence of focal white and red spots on the vermilion zone of upper and lower lips. Intra-orally, there was presence of erythematous areas with white patches in haphazard fashion predominantly on the hard palate, buccal mucosa and retro-molar region on right side (Figure 2). These clinical manifestations along with negative Nickolsky's sign led to an initial diagnosis of Lupus Erythematosus or Lichen Planus.

The patient was advised to undergo routine hematological and certain biochemical and serological investigations. The results are given below in the tabular form.

Blood parameters	Values
R.B.C. count	2.93 mill/cu mm
Hb%	9.3 gm/dl
PCV	25.4%
TLC, DLC	Within physiological limits
ESR	Within Normal Limits
Blood sugar level	Within normal limits
Liver function tests	Within normal limits
Serum urea-creatinine	Within normal limits
ANA (Anti Nuclear Ab)	Positive (1.74)
Anti ds DNA Ab	Negative
Anti SmithAb	Negative

An incisional biopsy was performed from a perilesional site on the right buccal mucosa on the retro-molar region under local anesthesia and two bits of tissue were taken. One bit was submitted for routine histopathological examinations in buffered formalin. The other bit was stored in Michel's solution for

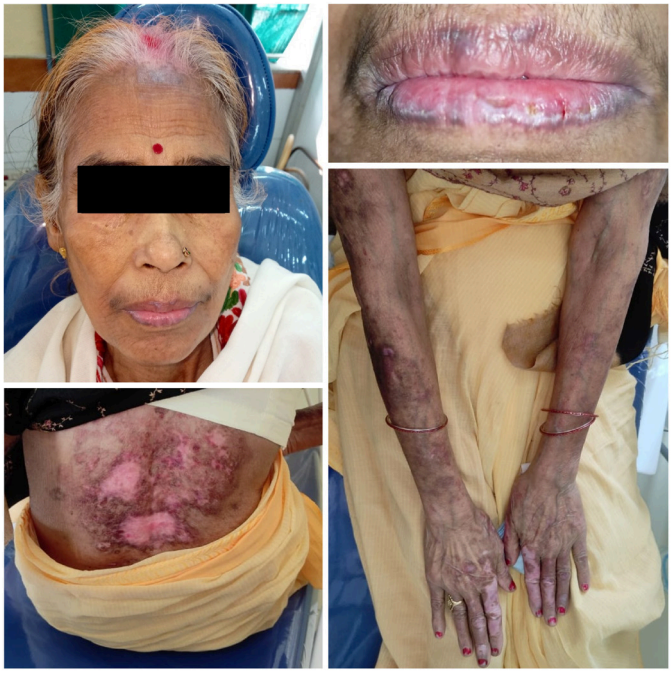

Fig. 1: Photographs showing extra-oral and cutaneous manifestations of the lesion

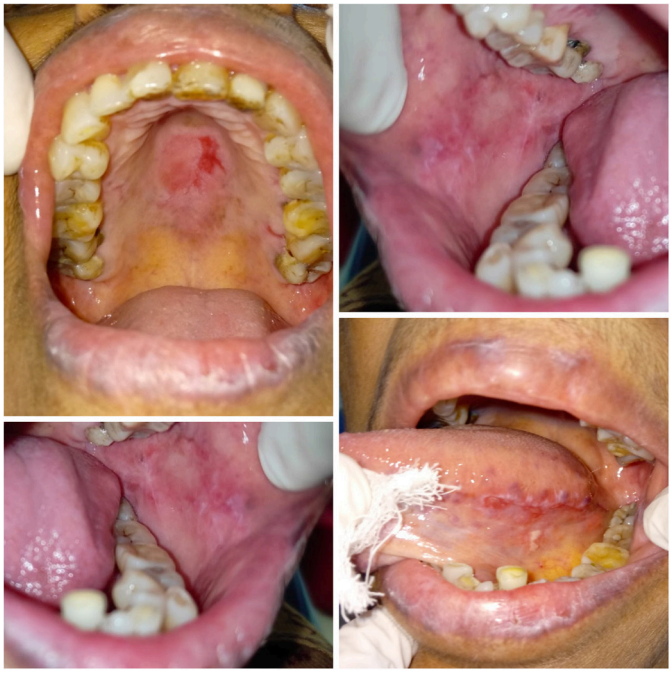

Fig. 2: Photographs showing lesions at various intra-oral sites

immunofluorescence studies. H and E stained sections revealed stratified squamous epithelium with irregular rete ridges and focal atrophic areas along with basal keratinocyte degeneration chiefly in the basal cell layer and spongiosis at places in the spinous cell layer. There was an intense but diffuse chronic inflammatory cell infiltrate in the superficial and deep connective tissue. The connective tissue stroma also revealed multiple capillary proliferations, some of which showed perivascular infiltration of inflammatory cells (Figure 3). The section, when stained with Periodic Acid Schiff (PAS), clearly demonstrated the thickening of basement membrane too (Figure 3). Direct immunofluorescence examination revealed positivity for C3, IgG and IgM as granular deposits at the basement membrane zone, which went in favor of DLE.

The patient was then sent for opinion to the Department of Dermatology of Medical College and Hospital. Considering the oral and generalized cutaneous manifestations of the disease, the case was diagnosed as "Disseminated DLE". Treatment was initiated with Hydroxy chloroquine 200 mg BD for 15 days and Clobetasol ointment for topical application to affected skin areas. Triamcinolone 0.1% ointment was advised for oral application. The acute symptoms subsided after 15 days. After that, the patient did not turn back to our department.

Discussion

Discoid lupus erythematosus (DLE) is one of the most common types of chronic cutaneous lupus erythematosus (CCLE). It has different clinical presentations. Globally, the male: female ratio is noted to be 3:1. The most common age group affected was 14 - 40 years of age with a mean age of onset at 29.4 years.[5] The patient in our case is also a female, though in sixth decade of life.

In LE, the humoral response is increased leading to formation of numerous auto-antibodies and circulating immune complexes. Furthermore, cellular immunity is often impaired.[8] Tissue injury in LE is believed to be mediated by adequate deposition or local formation of immune complexes and participation of complements.[9] Ultraviolet lights may also enhance the humoral response and disrupt the natural tolerance to DNA.[8] Recent evidence also suggest that LE may arise from interplay between environmental factors such as drugs, hormones and viruses in genetically predisposed persons. However, in contrast to SLE, Th17 cells dominate the cutaneous inflammatory infiltrates in DLE instead of Th1.[10]

DLE is a chronic disease which is limited to the skin and/or mucous membranes.[11] The disease is broadly categorized into a localized variant involving mainly the face and scalp areas and a disseminated form which is widespread extending below the neck area.[5] Discoid skin lesions are clinically well-defined, raised, erythematous lesions, which spread slowly with an irregular outline while the center of the lesions heal with scaling, atrophy and scarring[12]. Other variants include chilblain lupus which is characterized by red to violaceous lesions on the acral parts of the body induced by cold, leading to ulceration and scarring, and lupus profundus characterized by painful subcutaneous nodules and plaques followed by atrophy of fat.[5] Discoid oral lesions (i.e. oral DLE, oral discoid lesions) are chronic keratinizing lesions of the oral mucosa or vermilion border, showing a central atrophic red area with small white dots surrounded by radiating white striae. Petechiae, echhymosis like telangiectatic changes are noted too.[13] The patient in our case had similar cutaneous and oral manifestations.

Nevertheless, lichen planus can exhibit similar features,

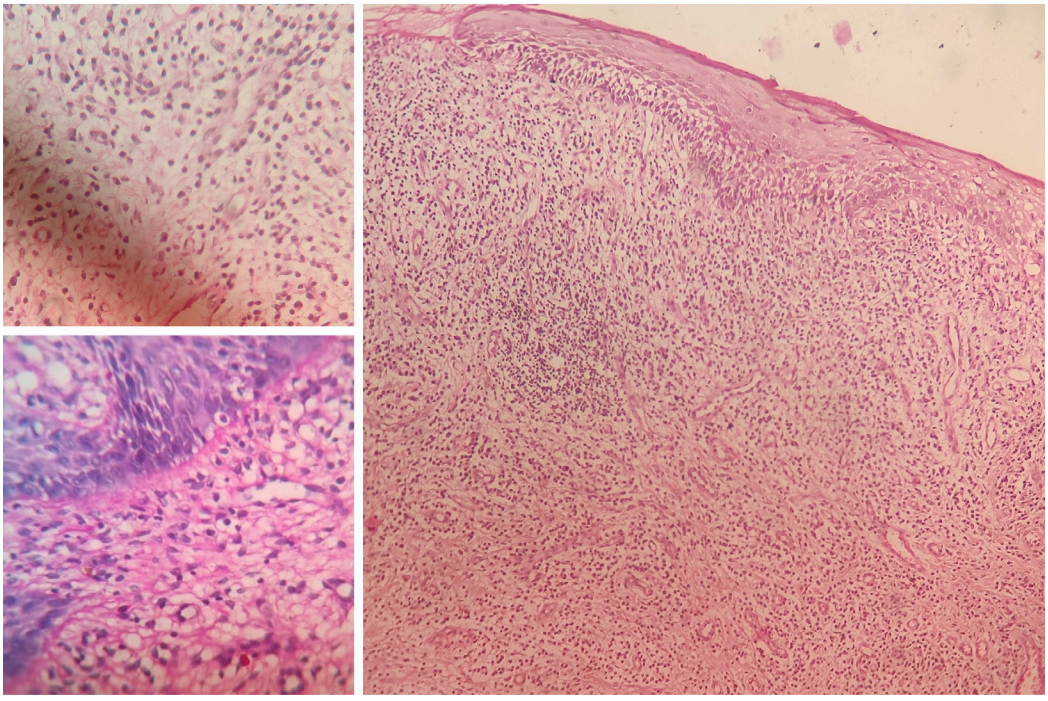

Fig. 3: (A) The connective tissue stroma revealed multiple capillary proliferations, B) Periodic Acid Schiff (PAS), demonstrated the thickened basement membrane

which demands a careful diagnosis considering the different behavior and prognosis of the two diseases. The lesions in both diseases show an erythematous central ulcerated or atrophic area surrounded by fine white radiating striae. Even though the keratotic striae are common to both diseases, in lupus erythematosus, they are more delicate than the Wickham striae of lichen planus.[15]

The diagnosis of DLE is usually made clinically. For confirmation of diagnosis, serological and histopathological analysis with immunofluorescence are done. On histopathological examination by H and E, lupus erythematosus shows hyperkeratosis, para-keratotic plugging, basal cell layer degeneration, chronic inflammatory infiltrate in the connective tissue with diffuse, deep and perivascular distribution. The case under discussion had similar histological features. Lichen planus also shows the same features, with the exception of its inflammatory infiltrate, which has a band-like distribution subjacent to the epithelium and is mainly, composed of T cells.[16] PAS staining reveals thickening of basement membrane in DLE which was noticed in our case also.

Direct immunofluorescence test of lupus erythematosus reveals positive result in the basement membrane zone for one or more immunoglobulins, especially IgM, IgG as well as for C3. For lichen planus, direct immunofluorescence is positive in the basement membrane region for fibrinogen in a shaggy fibrillar pattern and negative for other immunoglobulins other than colloid bodies.[17] Presence of antinuclear antibodies (ANA), as revealed by indirect IF staining, is a sensitive but non-specific test for SLE. High titred Ig G ANA and/or highly increased anti-DNA antibodies have a high specificity for SLE in patients with oral discoid lesions. Slightly increased anti-DNA antibodies and increased serum levels of Ig have some diagnostic value for DLE compared to LP.[18] The immunofluorescence results in our case were in accordance with the findings of previous authors. There are no other specific auto-antibodies to differentiate the subtypes of CLE that are routinely used in practice. One further possible target of auto-antibodies is annexin-1, which has been suggested to play an important role in preventing autoimmune diseases. A recent study found a significantly higher level of anti-annexin 1 antibodies in DLE patients, suggesting that anti-annexin 1 antibodies might be a new diagnostic marker for DLE.[19] However, this test was not advocated in our case due to lack of available infrastructure.

Recent studies indicate the first-line treatment for DLE to be photo-protection in conjunction with topical or intralesional corticosteroids and topical calcineurin inhibitors. When DLE is refractory to these measures, other agents with varying degrees of proven efficacy are used. Acute exacerbations of DLE are treated with the application of a high potency topical corticosteroid. Clinical improvement is usually observed within 2 weeks of treatment. Systemic therapy includes Antimalarials like Hydroxy chloroquine (HCQ) and Chloroquine with or without Quinacrine. Other treatment modalities, such as retinoids, vitamin A analogs with anti-keratinizing and anti-inflammatory effects, are sometimes used in CLE, but documentation in the literature is limited. Lupus is best managed by an inter-professional team of healthcare workers. Besides physicians, the role of the nurse, pharmacist, therapist, social worker, and mental health counselor is vital. The key is to stress the importance of medication compliance. Patients should be told to avoid sunlight, stop smoking, eat healthily and remain active.[20] The patient reported here showed improvement of symptoms with systemic Hydroxychloroquine therapy and topical corticosteroids and was advised periodic follow-up.

Development of SLE occurs in about 6% of patients with DLE of the skin. DLE and progression to SLE are associated with complications like Cicatricial alopecia, Pancytopenia, Thromboembolism, Arthritis, Myositis, Hypertension and Renal failure. Thus, periodic surveillance of DLE lesions and therapy-related side effects is crucial to avoid complications and promote clinical resolution.[20] Squamous cell carcinoma may also arise in long-term DLE, primarily in males, in 2 to 3 percent cases, in scars of the scalp, nose, auricular conchae, cheeks or the lips (vermilion border).[18] Therefore, careful follow-up is important, with regular clinical assessments and laboratory investigations.

Discoid lupus is an unpredictable and highly variable disorder which frequently waxes and wanes. While the condition is benign, it can cause devastating complications, often leading to high morbidity and a poor quality of life. The outcomes are worst for patients with CNS and renal involvement. Today, with treatment, there is 80% survival at ten years, but failure to comply with treatment may lead to complications and early death.[21]

Conclusion

The clinical features alone are not sufficient to establish the diagnosis of DLE because oral manifestations of lupus erythematosus are very similar to other oral lesions such as lichen planus, lichenoid reactions, GVHD, chronic junctional stomatitis and squamous cell carcinoma. Hence, definitive diagnosis is arrived based on the information compiled from clinical, histopathological assessments, serum and urine tests, rheumatological evaluation and advanced diagnostic modalities like direct immunofluorescence tests. Differential diagnosis is important as these diseases have different behaviors and prognoses as well as differs in terms of their treatment. In many cases, manifestation of skin diseases may be preceded by oral lesions. Therefore the dentist may be in an important position to establish the diagnosis with the aid of clinical and histopathological findings before the cutaneous lesions become apparent.

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