

**TITLE: Lupus Erythematosus - A Report of 3 Cases**

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## **ABSTRACT:**

Lupus erythematosus (LE) is an autoimmune disease which may be seen in one of two well recognized forms, systemic lupus erythematosus (SLE) and discoid lupus erythematosus (DLE) both of which may have oral manifestations. We here with reported 3 cases of LE with oral lesions. The clinical presentation, histological features, diagnostic criteria were discussed. Early diagnosis, better treatment protocols and aggressive management of infections all contribute to the improved outcome in this severe disease.

**Key words: Autoimmune disease, Discoid, Erythematosus**

## **INTRODUCTION**

Lupus erythematosus (LE) is a connective tissue disease which includes Discoid Lupus Erythematosus (DLE) confined mainly to the skin & mucosa and the florid disease with systemic involvement of heart, lungs, brain, kidneys and other organs called Systemic Lupus Erythematosus (SLE). In between the two ends of the spectrum is subacute cutaneous lupus<sup>1</sup>. Lupus occurs in all age groups with a mean age varying from 21 years to 50 years and a prevalence of 17 to 48 in 100,000 with a greater prevalence in Afro-Caribbean people. It is reported to occur in 0.1 to 0.4% of general population<sup>2</sup>. LE is an autoimmune disease with other etiological factors such as involvement of certain genetic factors, environmental factors like ultraviolet light, and hormonal factors with antibodies<sup>1</sup>.

SLE, the aggressive form of LE, is most common in women of childbearing age with a prevalence of nearly 15% in children younger than 16 years<sup>3</sup>. Organ involvement in SLE is characterized by periods of relative quiescence and exacerbations<sup>4</sup>. Rates of organ involvement are higher in children compared to adults. Involvement of kidney in the form of Lupus nephritis is one of the main clinical presentations determining the course and outcome in patients with SLE<sup>5</sup>. The prevalence of SLE varies throughout the world<sup>4</sup>.

Discoid Lupus Erythematosus, less aggressive form of LE is a chronic, scarring, atrophy producing, photosensitive dermatosis. It rarely (5%) progresses to SLE. It is most commonly seen in middle aged women. The clinical manifestations includes the appearance of discoid lesions solely on the skin, most commonly on the face, scalp, oral mucous membrane, chest, back and extremities<sup>6</sup>.

Here, we present 2 case reports of systemic lupus erythematosus and 1 discoid lupus erythematosus which come under the spectrum of Lupus Erythematosus.

#### CASE REPORT - 1:

A 23yr old female patient presented with malar erythema, photosensitivity, joint pains, and difficulty in breathing of 3 months duration. Examination revealed butterfly shaped malar rash, multiple erythematous patches all over the face, chest, back, and extremities (Fig 1). These erythematous patches were associated with scaling and itching. She also showed involvement of oral cavity with presence of multiple ulcers and erosions with encrustations on the both the lips, hard palate and buccal mucosa (Fig 1).

Laboratory investigations such as chest radiograph and echocardiogram were advised to evaluate the organ involvement where they showed positive findings of pleural effusion and pericarditis. Incisional biopsy was taken from the intra oral lesion and was sent for histopathological examination which revealed hydropic degeneration and liquefaction degeneration of the basal cell layer with perivascular infiltration of lymphocytes within the connective tissue which was suggestive of SLE (Fig2). Direct Immunofluorescence test of the same was positive with deposition of IgM at the basement membrane zone. (Fig 3). Specific tests like ANA and DSDNA were also advised for the confirmatory diagnosis. In this case both were positive with an end point titre of 1:2560 and 1:640 respectively. Based on the clinical criteria proposed by American Academy of Rheumatologists (AAR), histopathology, Direct Immunofluorescence, ANA, dsDNA report she was finally diagnosed as systemic lupus erythematosus.

#### CASE REPORT: 2

A 30 yr old female patient presented with a history of erythema of the cheeks, bridge of the nose and forehead for the past 5 months. She noticed an exacerbation of the erythema and swelling within 10-15 minutes of exposure to the sun. A history of continuous low grade fever was present since last 3 months. During episodes of exacerbation of skin and oral lesions, the patient developed high grade fever. She developed arthralgia and diffuse hair loss for the past 4 months.

General physical examination revealed generalized scaly erythematous plaques over the cheeks extending to the bridge of the nose and forehead (Fig 4). Some of the plaques were exudative and crusted. Multiple ulcers were seen on lip vermilion zone, upper and lower labial mucosa and hard palate (Fig 5). A complete haemogram revealed mild anemia (Hb- 8 g/dl) while the total leucocyte count and platelet count were within normal limits. The erythrocyte sedimentation rate was 75 mm in first hour. Her renal and liver function test values were within normal limits. A routine chest X-ray and electrocardiogram revealed no abnormality. Serology for antinuclear antibody (ANA) was positive with an end point titre of 1:1280 and DSDNA was positive with an end point titre of 1: 640. Incisional biopsy was taken from the intraoral lesion and sent for routine histopathological examination and immunofluorescence test. Histopathology was suggestive of SLE with the similar appearance to the above. Direct Immunofluorescence test showed shaggy band of deposition of IgG at the basement membrane zone. (Fig 6). With the above clinical features, laboratory findings, histopathology and Direct Immunofluorescence results , she was also finally diagnosed as systemic lupus erythematosus.

### CASE REPORT 3:

A 40yr old female patient came with a chief complaint of ulcerations on the upper lip for the past 1 year. On general examination well demarcated, erythematous, slightly infiltrated discoid plaques were seen over the right arm and chest (Fig 7). Intra oral examination revealed multiple ulcers on the upper labial mucosa (Fig8). Based on the detailed general clinical examination a provisional diagnosis of Discoid lupus erythematosus was given.

Hematological investigations were done which were within the normal limits. Incisional biopsy report of the ulcer, taken from the lower labial mucosa was suggestive of DLE which showed

degeneration of basal cell layer and subepithelial lymphocytic infiltration and PAS positive thickening of basement (Fig 9). The immunofluorescence test of the same was also positive with deposition of C3 at the basement membrane (Fig10). This histopathology report and immunofluorescence report confirmed the diagnosis of Discoid lupus erythematosus.

## DISCUSSION

Systemic Lupus erythematosus (SLE) is a prototypic autoimmune disease that is characterized by the production of antibodies to nuclear molecules in association with clinical manifestations of fluctuating intensity and severity<sup>7</sup>. This disease commonly affects young women of child bearing age with a F: M ratio of 12:1 within the age group of 15-45yr and ratio of 2:1 in children or elderly<sup>8</sup>. In our cases also both were women and fall in the same age group.

Cutaneous manifestations are seen in the form of erythematous patches on the face which coalesce to form a roughly symmetrical pattern over the cheeks across the bridge of the nose in a butterfly distribution which is known as malar rash. Skin over the neck, arms, shoulders and fingers are also affected. They may also be associated with itching or burning sensation, and areas of hyperpigmentation. Involvement of various organs including the kidney (40-50 %), heart (50%-warty vegetations), lungs and CNS occurs. Joint pains and arthritis are common manifestations<sup>9</sup>. In our cases cutaneous involvement was similar to the above description and one case showed involvement of lungs and heart in the form of pleural effusion and pericarditis but both of them showed involvement of joints in the form of arthritis.

Oral lesions are found in approximately 21% of patients with SLE<sup>4</sup> which appear most commonly on palate, buccal mucosa, gingiva in the form of ulcers, erythema or hyperkeratosis<sup>9</sup>. We also reported same kind of oral lesions in both the patients.

The pathogenesis of SLE is multifactorial, involving interactions among multiple genes (HLA-DR and HLA-DQ<sup>4</sup>, C-RP), hormones and several environmental factors like Ultraviolet rays and exposure to tobacco and aromatic amines<sup>4</sup>. Impaired handling of antigen–antibody complexes and subsequent tissue deposition leading to release of inflammatory mediators and an array of inflammatory cells can induce a broad spectrum of clinical manifestation<sup>10,4</sup>.

Histological appearance of SLE is not pathognomic but is suggestive of the disease. It is characterized by the presence of hyperkeratosis with alternating thickness and atrophy of spinous layer, degeneration of basal cells and Connective tissue showing dense aggregates of inflammatory cells. Direct immunoflouresece testing is often used to detect the presence of IgG, IgM, IgA at the basement membrane<sup>6</sup>. A very specific test for SLE is anti-double-stranded DNA but is not very sensitive seen only in 50% of SLE cases. Others tests, like ANA, are sensitive but not specific and is present in 95% of patients with SLE, but the positive predictive value of the test given by only 11% of SLE patients<sup>8</sup>.

For the diagnosis of SLE, patient should fulfill more than 4 of 11 criteria made by **American College of Rheumatology**<sup>11</sup>.

Item	Definition
Malar rash	Fixed erythema, flat or raised, over malar eminences, sparing the nasolabial folds
Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging: Atrophic scarring may occur in older lesions
Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or observed by physician
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
Non erosive arthritis	Involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion
Pleuritis or pericarditis	<p>A. Pleuritis—convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion</p> <p>OR</p> <p>B. Pericarditis—documented by electrocardiogram or rub or evidence of pericardial effusion</p>
Renal disorder	<p>A. Persistent proteinuria &gt;0.5 g per day or &gt;3+ if quantitation not performed</p> <p>OR</p> <p>B. Cellular casts—may be red cell, hemoglobin, granular, tubular, or mixed</p>
Neurologic disorder	<p>A. Seizures in absence of offending drugs or known metabolic derangement (eg, uremia, ketoacidosis, or electrolyte imbalance)</p> <p>OR</p>

	<p>B. Psychosis—in absence of offending drugs or known metabolic derangement (eg, uremia, ketoacidosis, or electrolyte imbalance)</p>
<p>Hematologic disorder</p>	<p>A. Hemolytic anemia with reticulocytosis,  B. Leukopenia &lt;4000/mm<sup>3</sup> on &gt;2 occasions,  C. Lymphopenia &lt;1500/mm<sup>3</sup> on &gt;2 occasions,  OR  D. Thrombocytopenia &lt;100,000/mm<sup>3</sup> in absence of offending drugs</p>
<p>Immunologic disorder</p>	<p>A. Anti-DNA: antibody to native DNA in abnormal titer,  B. Anti-Sm: presence of antibody to Sm nuclear antigen,  OR  C. Positive finding of antiphospholipid antibodies based on  (1) abnormal serum level of IgG  or  immunoglobulin M (IgM) anticardiolipin antibodies,  (2) positive test result for lupus anticoagulant by means of standard method,  or  (3) false-positive test result for at least 6 months and confirmed by <i>Treponema pallidum</i> immobilization or fluorescent treponemal antibody absorption test</p>

Therapy for SLE patients is given according to the severity of the disease which usually involves non steroidal anti inflammatory drugs (NSAIDs), corticosteroids, anti malarial agents, and immunosuppressive drugs in alone or in combination<sup>4</sup>.

Discoid lupus erythematosus (DLE) is the most common form of chronic cutaneous lupus erythematosus. Classic DLE lesions Consists of well demarcated, erythematous, slightly infiltrated, discoid plaques that often show adherent thick scales and follicular plugging<sup>13</sup>. In our case the clinical presentation was similar to the above. Approximately 24% of DLE patients show oral involvement which present as annular leukoplakic areas or erythematous erosions on buccal mucosa tongue, palate, and lips. They may also present as a prominent marginal gingivitis<sup>4</sup>. In our case there was presence of multiple ulcers on the lower labial mucosa.

The pathophysiology of DLE is unknown with a probable role of genetic factors and UV light. It has been suggested that heat shock protein is induced in the keratinocyte following UV light exposure or stress and this protein acts as a target for T cell mediated epidermal cell cytotoxicity<sup>6</sup>.

The diagnosis of discoid lupus is generally made based on clinical features. Histology may be required to confirm the diagnosis. Histopathological features includes, changes at the dermo-epidermal junction that include thickening of the basement membrane (best demonstrated by periodic acid-Schiff staining) and vacuolar degeneration of the basal cells along with perivascular and peri-appendageal inflammatory cell infiltration of a variable degree in the reticular dermis. Hyperkeratosis is more evident and follicular plugging may be seen in more mature lesions<sup>12</sup>. Histopathology of our case was in accordance to the above.

Management of discoid lupus must include sun avoidance and the liberal application of sunscreens (protection from UV light). Topical steroids are the mainstay of treatment of DLE.

## **CONCLUSION**

Lupus is like a puzzle, with genetics, gender, and the environment being important pieces of the puzzle. If all the pieces come together, people develop defective immune regulation and a break in self-tolerance. Early diagnosis, better treatment protocols and aggressive management of infections all contribute to the improved outcome in this severe disease.

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Fig 1: Clinical picture showing characteristic malar erythema, and the erosions with encrustations on the lips

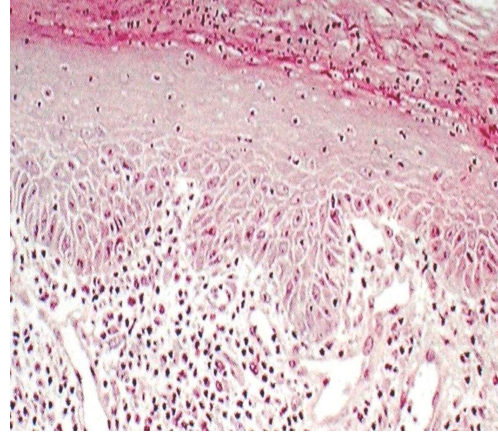


Fig2: 10X view: Showing hydropic degeneration of the basal cell layer

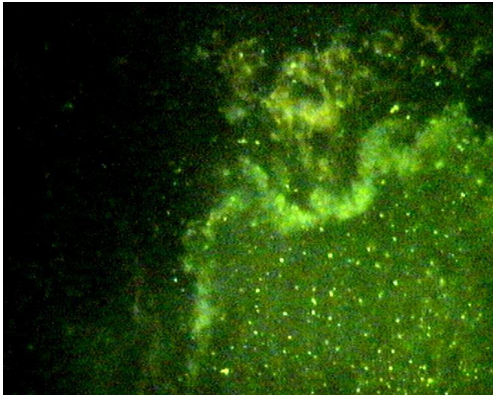


Fig3: Direct Immunofluorescence exhibiting linear deposition of IgM at the basement membrane



Fig4: Clinical picture showing characteristic butterfly rash



Fig5: Intraoral clinical picture revealing ulcerations on the palate

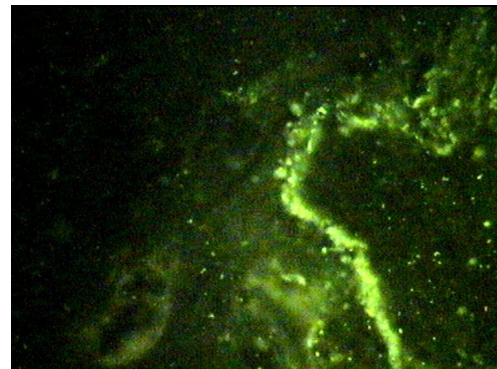


Fig6: Positive Immunofluorescence test demonstrating deposition of IgG at the basement membrane.



Fig7: Clinical picture showing discoid lesion on the right arm

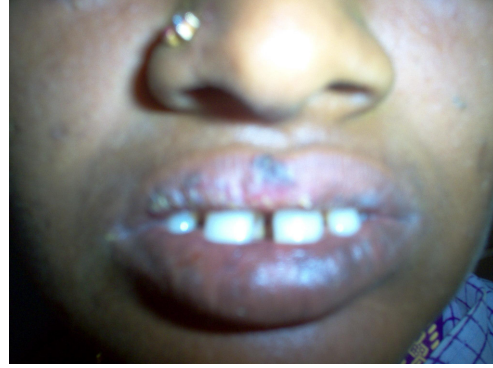


Fig8: Clinical picture showing ulcerated upper lip and labial mucosa

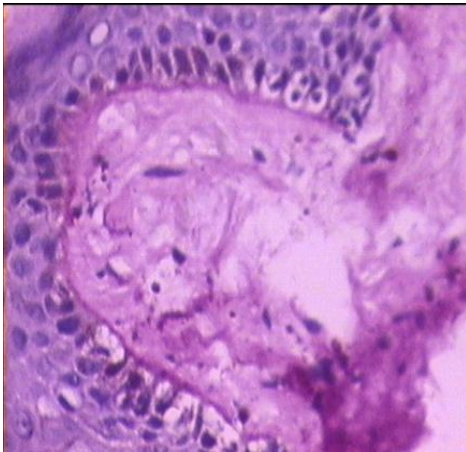


Fig9: 20X view showing PAS positive thickening of the basement membrane

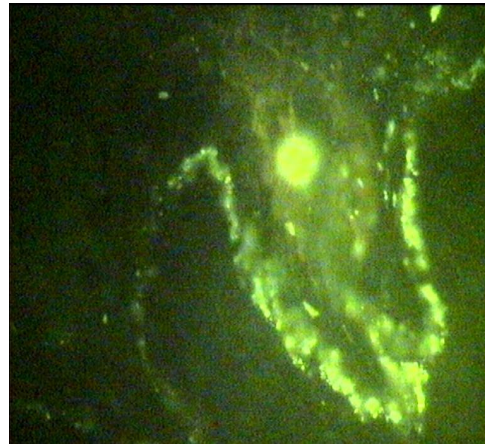


Fig10: Direct Immunofluorescence showing positivity with the deposition of C3 at the basement membrane.