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Lupus Erythematosus Profundus: A Case Series and Review of Literature

Deeptara Pathak Thapa[1*], **Raj Kubba**[2] **and Asha Kubba**[2]

[1]*Department of Dermatology, Nepal Medical College and Teaching Hospital, Kathmandu, Nepal*

[2]*Delhi Dermatology group, Kubba Clinic, New Delhi, India*

[*]**Corresponding Author:** Deeptara Pathak Thapa, Assistant Professor, Department of Dermatology, Nepal Medical College and Teaching Hospital, Kathmandu, Nepal, Tel: 00977-9843125706; E-mail: drdeeptarapathak@yahoo.com

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Abstract

Objective: Lupus Erythematosus Profundus (LEP) is a rare subset of Lupus erythematosus and clinically presents as indurated subcutaneous painful nodules and plaques. The objective of the study was to evaluate clinical, histopathological and supplementary laboratory parameters to diagnose Lupus erythematous profundus.

Methods and materials: This was a retrospective study, a clinical series of histo-pathologically proven cases of 11 patients. Data were collected from clinic records from 1996 to 2010. A detailed history including onset of disease, age, sex, residence, hospital ID number and clinical examination, association with Discoid lupus erythematosus (DLE) or Systemic lupus erythematosus (SLE), laboratory workup, histopathological evaluation and Direct Immuno-fluorescence data was taken from the records.

Result: There were total of 11 patients, with mean years of presentation of 26 years. Male to female ratio was 3:8. Face was the commonest site of distribution. Exclusively LEP presentation was seen in 83% and in 18% associated with DLE and 9% with SLE. Clinically lesions varied from nodules, indurated plaques, atrophy and ulcer. In laboratory work up ANA was positive in 9% of the cases, others baseline investigations were within normal limits. On histopathological evaluation, lobular panniculitis and hyaline fat necrosis was seen in all patients. The infiltrates were predominantly lymphohistiocytic. Direct immunofluorescence (DIF) could be done in 3 out of 11 cases. Lupus band at basement membrane zone was seen in all the 3 cases. Deposition of predominantly IgG followed by IgM, IgA and C3 were seen. Two of the three cases with positive DIF findings had no interface pathology.

Conclusion: Diagnosis of LEP is based on clinico-pathological correlation. An early diagnosis and prompt treatment may help prevent disfigurement.

Keywords: Direct Immuno-fluorescence; Discoid lupus erythematosus; Histopathology; Lymphocytic infiltrates; Hyaline degeneration; Lupus erythematous profundus; Systemic lupus erythematosus

Introduction

Lupus erythematosus (LE) is a group of autoimmune disorder with spectrum of clinical manifestations ranging from localized discoid LE lesions to life threatening systemic manifestations involving renal, pulmonary, central nervous system, musculoskeletal, hematologic and cardiovascular system in SLE (systemic lupus erythematosus). The etiopathogenesis of SLE is complex depends on complement system activation triggered by the presence of immune complexes, leading to inflammation and complement proteins consumption. Interaction of genetic background with environmental factors makes SLE one of the most complex diseases. Lupus erythematous profundus (LEP) is a rare subset of Lupus erythematous (LE) predominantly involves subcutaneous tissue. Kaposi in 1883 had first described this condition. Incidence is supposed to be between 1% and 3% of the total LE cases [1]. It is more common in females with females being affected twice more commonly than males [2]. The clinical presentation can be panniculitis only or can be associated with Discoid lupus erythematosus (DLE) or Systemic lupus erythematosus (SLE) [3]. The characteristic histopathologic changes in LEP are lymphocytic panniculitis, hyaline degeneration, calcification etc. Direct immunofluorescence can be an additional diagnostic supplemental tool with histopathology to aid diagnosis of LEP. We present a retrospective study of clinico-histopathological case series of lupus profundus erythematous.

Methods and Materials

This was a retrospective study, a clinical series of histopathologically proven cases of 11 patients. All patients who fulfill the histopathologic criteria of Lupus erythematosus profundus were included in the study. Data were collected from clinic records from 1996 to 2010 which was maintained in the clinic. A detailed history including onset of disease, age, sex, residence, hospital ID number and clinical examination was obtained from the records. Association with SLE or DLE either occurrence prior to LEP lesion or later during follow up of these patients was also ascertained. Baseline laboratory workup like complete blood count, ESR, liver function test, renal function test and urine routine microscopy was taken from the records. In histopathological evaluation, all the microscopic slides preserved in the clinic were reevaluated for each patient and findings were noted. Direct immunofluorescence data was taken from the records.

Results

There were total of 11 patients, age of presentation ranged from 14 to 38 years with mean years of presentation of 26 years. Male to female ratio was 1:3. Face was the commonest site of distribution of the lesions accounted for 64% followed by extremities and scalp 18% each. Exclusively LEP presentation was seen in 83% and in 18% associated with DLE and 9% SLE. Clinically lesions varied from nodules, indurated plaques, atrophy and ulcer; few lesions were associated with hyperpigmentation, scaling, telangiectasia, erythema, follicular plugging (as shown in Figures 1-6).

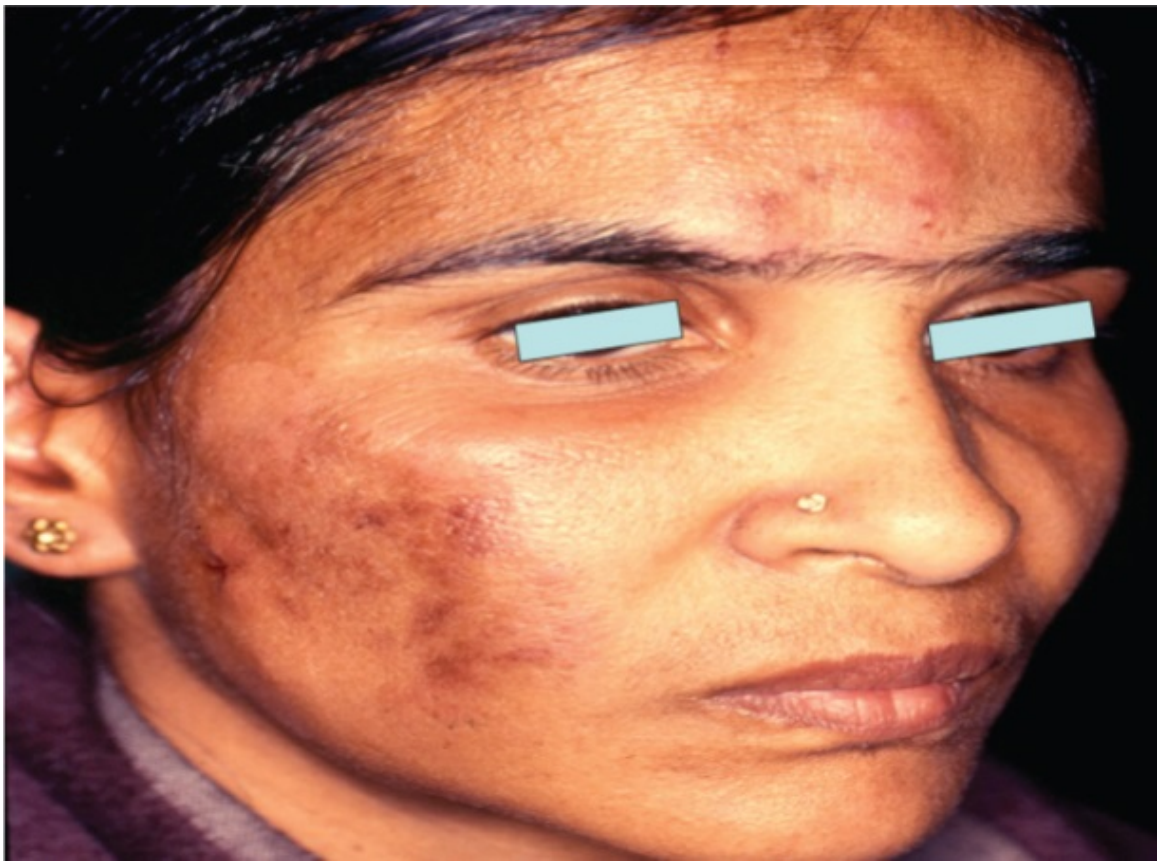

Figure 1: Subcutaneous nodules with hyper pigmentation on cheek of a female.

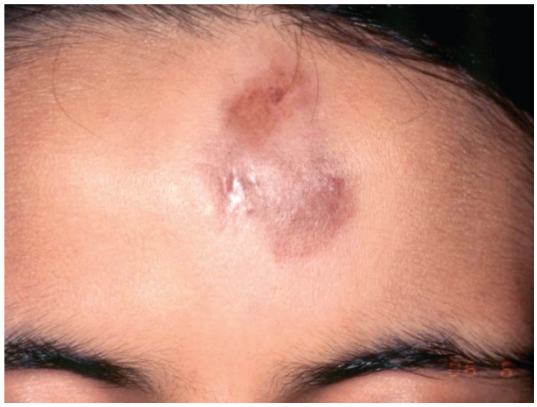

Figure 2: Indurated plaque on forehead of a female.

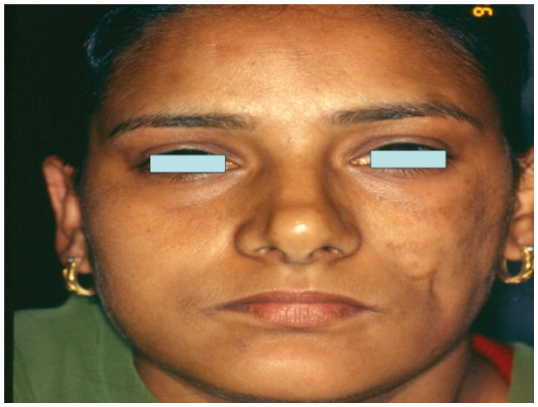

Figure 3: Atrophy of left side of face.

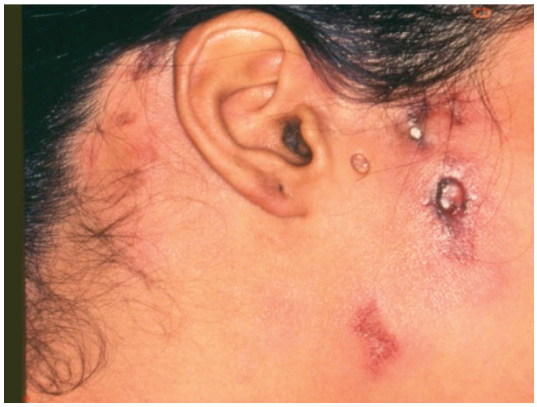

Figure 4: Ulcer on pre-auricular area on right side of a female.

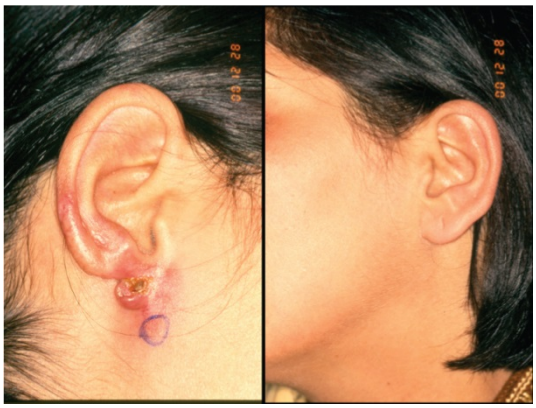

Figure 5: Destruction of right ear lobe in contrast with left side normal ear of same patient.

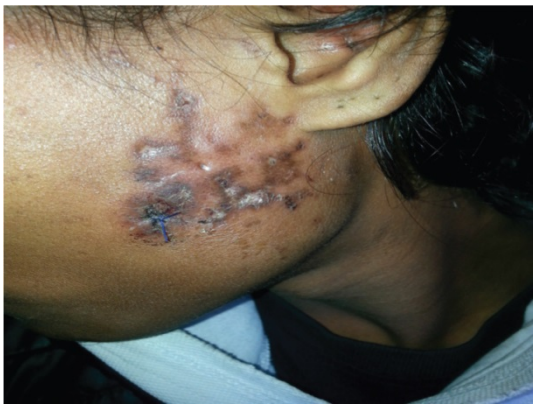

Figure 6: DLE like lesion on left cheek with scaling and hyper pigmentation of a male patient.

In laboratory work up ANA was positive in 9% of the cases, others baseline investigations were within normal limits. In histopathological evaluation, lobular panniculitis was seen in 100%, hyaline fat necrosis in 100% and inflammatory infiltrates in 100% (as shown in Figure 7 and 8).

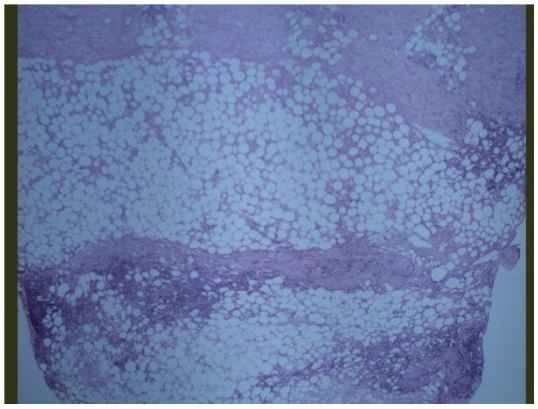

Figure 7: Microphotograph showing Lobular panniculitis with inflammatory infiltrate in 10 x 10 magnifications.

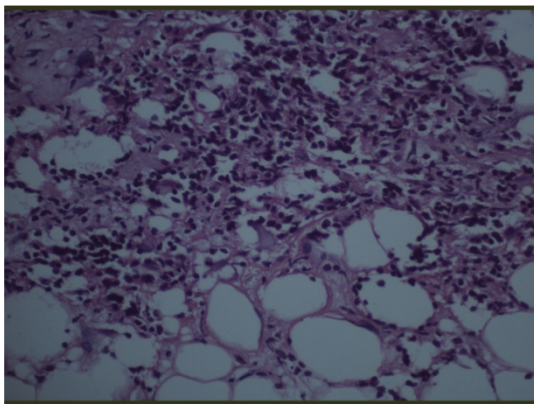

Figure 8: Microphotograph showing Lobular panniculitis with predominantly lymphocytic infiltrate in 40 x 10 magnifications.

The infiltrates were predominantly lymphocytes and histiocyte followed few plasma cells, neutrophils and eosinophils. Dermal mucin was found in 45% and interface pathology was seen in 55%. Direct immunofluorescence (DIF) was done in 3 out of 11 cases. Lupus band at basement membrane zone was seen in all the 3 cases. Deposition of predominantly IgG followed by IgM, IgA and C3 were seen. Two of the three cases with positive DIF findings had no interface pathology.

Discussion

Lupus erythematosus profundus is a unique subset of LE which is associated with panniculitis. In literature review it is more common in females as similar to our study [3]. In western literature it is common in elderly and middle aged people [3,4] while in our scenario we found it more common in young patients which has been supported by findings in Asian literature [2,5,6].

LEP also known as Lupus panniculitis or lupus erythematous panniculitis occurs twice more frequently as a distinct disease than in association with SLE or DLE. Incidence of 1%-3% of patients suffering

from SLE and up to 10% of those suffering from DLE develop lupus panniculitis [7,8].

The association of LEP with discoid LE (DLE) varies from 33% to 60%. Although 10%-42% patients may have associated systemic lupus erythematosus (SLE) [3,7,8].

LEP is not a typical cutaneous manifestation of systemic lupus erythematosus (SLE), but individuals with LEP finally developing into SLE have been reported in literature, almost 10 patients till date have been mentioned in the searchable literature till date [1,4,6,9-11]. In our study we did find association of LEP with SLE in 9% who had LEP initially and later developed SLE. Similar low incidence was seen in studies by Merten et al. and Ng et al. [4,6]. However higher incidence of association had also been cited in literature (50%-83%) [3,12].

The most common cutaneous clinical presentation are tender indurated plaques or subcutaneous nodules with overlying normal skin or from erythematous to those of features of chronic cutaneous lupus erythematous (CCLE) features like scaling, follicular plugging, dyspigmentation, telangiectasia or atrophy and sometimes ulcerations [9]. Skin ulceration is seen in 28% in all of the LEP patients as per Martens et al. [4]. In our study we have seen varied type of clinical presentation ranging from indurated plaque, subcutaneous nodules, atrophy and features of CCLE. In about 18% ulcers were present. Lesions occur predominantly on the face, upper arms, upper trunk, breasts, buttocks, and thighs. In our study we found face was the commonest presentation. Similar findings have been found in studies by Watanabe et al., Ng et al. and Arai et al. [5,6,10].

There are reports of some unusual presentation like involvement of breast, parotid gland, submandibular gland, periocular tissue and scalp as alopecia [13-17].

A linear configuration of LE panniculitis has been reported with rare reports describing the coexistence of different forms of cutaneous LE and localized morphea. Elbendary et al. reported a case of linear sclerodermoid LE profundus [18].

The key histopathological criteria proposed for the diagnosis of LEP include major (important for the diagnosis) and minor criteria. The major criteria are: (1) hyaline fat necrosis, (2) lymphocytic aggregates and lymphoid follicle formation, (3) periseptal or lobular lymphocytic panniculitis, and (4) calcification. The minor criteria are: (1) changes of DLE in the overlying skin, (2) lymphocytic vascular inflammation, (3) hyalinization of sub-epidermal zone, (4) mucin deposition, (5) histiocytes and small granulomas, and (6) infiltrates of plasma cells and eosinophils [19,20].

In practice, both patterns of panniculitis (lobular and septal) occur in the majority of patients simultaneously as the inflammatory infiltration is not strictly separated [21].

In histopathological evaluation we found lobular panniculitis, hyaline fat necrosis and inflammatory infiltrates in all the cases with predominantly of lymphohistiocytic infiltrates similarly in few case series in literature [1,10]. Mucin was seen in 45% in our study but in a study by Arai et al. it was found in 73%.

The percentage of DIF-positive basement membrane can vary from 36% to 90.5%, and 27% to 95.4% of patients with LEP have elevated ANA titer [6,10]. Overlying dermo-epidermal findings of DLE may be present in 50%-75% cases even without clinical evidence of DLE. Direct immunofluorescence may show granular deposition of IgG, IgM, and C3 at the dermal-epidermal junction and blood vessels of deep dermis and sub-cutis in 50%-70% cases, particularly when there is concomitant DLE [20,21]. Lupus band test is yet another tool useful for diagnosing the disease the test is carried out upon non-lesional skin biopsy and the positive result, which indicates the deposits of IgG, IgM and C3 antibodies, is obtained in 36%-70% of cases. In our study we found these to be positive in all the 3 cases tested [22].

Clinico-pathologic correlation helps aid diagnosis of LEP. The differential diagnosis includes erythema nodosum and erythema induratum of Bazin which can be distinguished with routine histology, immunofluorescence, and ANA test. One of the difficult differential diagnoses is subcutaneous panniculitis-like T-cell lymphoma (SPTCL) which has atypical CD3+ and CD8+ T lymphocytes expressing clonal α/β T-cell receptor and arranged in a rim-like fashion around the individual adipocytes. The absence of plasma cells in SPCTL could distinguish it from LEP [23].

Subcutaneous lymphoid dyscrasia, a term has been proposed to include atypical cases of LEP, SPTCL and indeterminate lymphocytic lobular panniculitis.

Histopathological changes like vacuolar interface dermatitis and dermal mucinosis has been reported in SPTCL, thereby pointing to an overlap between the two entities. Lymphoid follicles with reactive germinal centers and mixed infiltrate comprising of plasma cells may favor LEP over SPTCL as suggested by Pincus et al. Patients with LEP should be followed up regularly, lest they develop SLE. Repeat biopsy with immunohistochemistry and the T-cell receptor gene rearrangement studies may be required in refractory cases to rule out subcutaneous panniculitis-like T-cell lymphoma (SPTCL). LEP presents with a spectrum of features including small, mature lymphocytes showing polyclonality on one hand and pleomorphic lymphocytes with hyper-chromatic nuclei demonstrating deletion of pan T-cell markers and monoclonal T-cell receptor gene rearrangement on the other [19,24,25].

Treatment options are variable like steroids, Antimalarials, Quinacrine, Immuno-modulators, Immunosuppressive, Intravenous immunoglobulin, biologicals and autologous fat transfer or dermal filler for atrophy. Most of our patients were treated with steroids and Antimalarials. Patients who develop ulcers had presented late in the disease process, hence treatment could not prevent its cosmetic disfigurement.

Conclusion

In this case series, younger age groups were affected with females being more commonly involved. Facial involvement was the commonest presentation. Diagnosis of LEP is based on clinico-pathological correlation and DIF study. Early diagnosis and therapeutic intervention may prevent disfiguring sequelae and reduce risk of systemic disease like SLE. Further prospective long term follow up studies should be carried out to know its varied clinical manifestation, progression and systemic involvement.

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