Lupus Erythematosus Profundus: Clinical and Histopathological Study

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Background **: Lupus erythematosus profundus (LEP) is an unusual clinical variant of lupus erythematosus (LE). It is unclear which part LEP occupied in the disease spectrum of LE.**

Objective **: Clinical and histopathological studies were performed on 19 patients with LEP in order to further define the clinical patterns, know the various serological findings, and review the histopathological features.**

Methods **: A retrospective review was carried out of the clinical records and histopathological specimens of 19 patients with LEP.**

Results **: The most common clinical features were indurated nodules or plaques on the cheek. There was a 37% positivity in the ANA test. Histopathogically epidermal changes as well as subcutaneous involvements were common. There were no cases of newly developed SLE during the follow up period of 41 months.**

Conclusion **: Most patients with LEP have a relatively benign disease course, although a few develop systemic abnormalities and have abnormal laboratory findings.**

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Key Words : Lupus erythematosus profundus

Lupus erythematosus profundus (LEP or lupus panniculitis) is a rare variant of lupus erythematosus (LE) in which pathologic changes occur primarily in the deeper portions of the corium and subcutaneous tissues. LEP may develop in association with discoid lupus erythematosus (DLE) or systemic lupus erythematosus (SLE) or may occur as an isolated phenomenon. The diagonosis is especially difficult when other features of LE are absent. We reviewed 19 cases of LEP and studied clinical and histopathological characteristics of LEP.

PATIENTS AND METHODS

A search through the records of Asan Medical Center between June 1989 and August 1998 found 19 patients with LEP. For all patients, clinical records and histopathological specimens were reviewed. Typically the lesions of LEP appeared as indurated nodules or plaques chiefly located on the cheek, upper arms, trunk, and other sites of body. The histopathologic diagnosis was confirmed based on the following findings: lymphocytic panniculitis, hyaline degeneration of fat, lymphoid nodular structures in the lower dermis or subcutaneous tissues, and epidermal changes. At the first examinations, serologic tests included antinuclear antibodies, anti-ds-DNA antibody, extractable nuclear antigen (ENA) series were done in the selected instances.

RESULTS

The study was comprised of 19 cases(Table 1). 14 cases were females and 5 were males. The female to male ratio was approximately 2.8:1. The age of the patients at the onset of the lesions varied

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Table 1. Clinical data on the 19 patients

Age on onset	4-74 (mean, 35.1)
Sex (M/F)	5/14
LE association	
DLE	9
SLE	3
LEP alone	7
Duration of disease	5 days-4 years(mean, 33months)

Table 3. Laboratory studies of the 19 patients

	No. done	No. abnormal
CBC	19	5 (26%)
Antinuclear antibody	19	7 (37%)
Extractable nuclear antigen	11	0
Anti-ds-DNA	6	3 (all SLE)

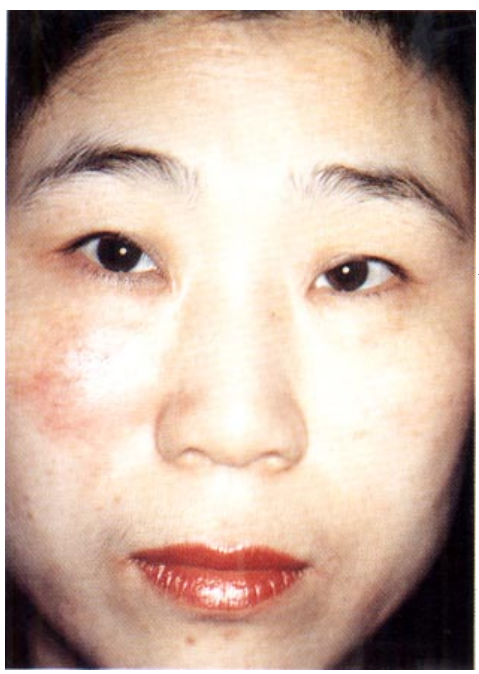

Fig. 1. Erythematous indurated nodules or plaques on the cheek.

from 4 to 74 years. The mean age of onset was 35.1 years. The diseases durations varied from 5 days to 4 years, with a mean of 33 months. There were 9 cases (47%) of LEP associated with DLE in the overlying epidermis or in other sites : 7 were localized (one site above or below the neck) and 2 were disseminated (above and below the neck). Three cases associated with SLE fulfilled the criteria

Table 2. Clinical features of the 19 patients

Chief complaints		
	Nodules	6 (32%)
	Plaques	8 (42%)
	Alopecia	2 (11%)
	Lipoatrophy	1 (5%)
	Eyelid swelling	1 (5%)
	Linear patch	1 (5%)
Location		
	Face	8 (33%)
	Upper arms	5 (21%)
	Lower legs	4 (17%)
	Scalp	3 (13%)
	Shoulder	2 (8%)
	Back	2 (8%)

Table 4. Histopathologic findings in the 19 patients

Findings	No (Percent)
Mucin Infiltration	13 (68%)
Lymphocytic Panniculitis	11 (63%)
Epidermal changes	11 (63%)
Hyaline Fat Necrosis	7 (35%)
Lymphoid Nodule	2 (10%)
Onion-skin like vessels	2 (10%)
Lipomembranous Fat Necrosis	2 (10%)

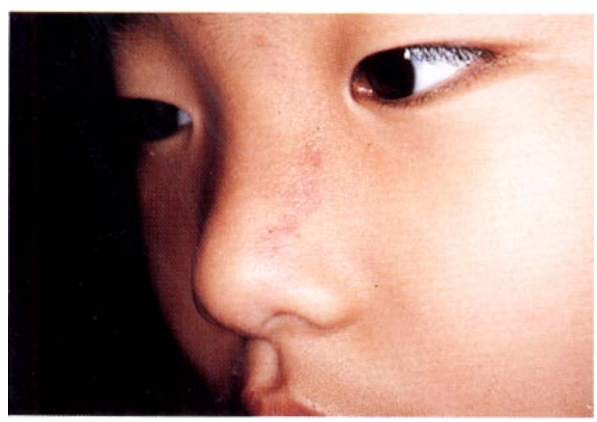

Fig. 2. Linear telangiectatic atriphic patch on the nose.

by American Rheumatism Association(ARA) in 1952. The onset of LE and LEP might be simultaneous or sequential.

The clinical features are listed in Table 2. The initial presentations were nodules in 6 cases and

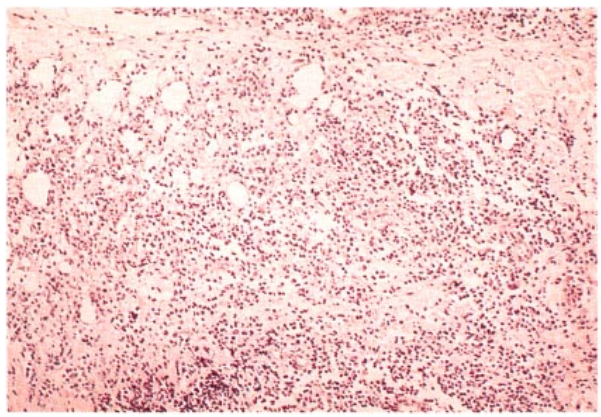

Fig. 3. Lymphocytic cell infiltrations in the fat lobules (H&E, ×100).

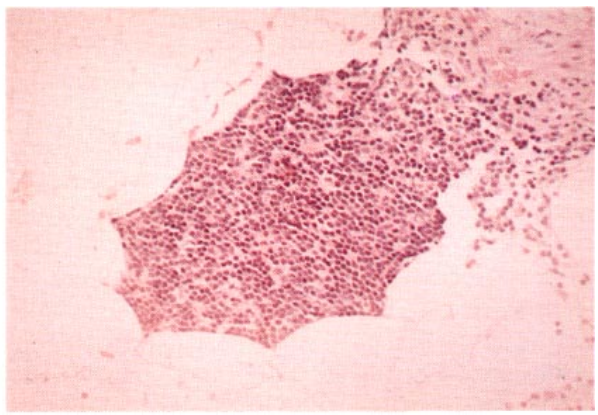

Fig. 4. Lymphoid nodule formation in subcutaneous fat layer (H&E, ×100).

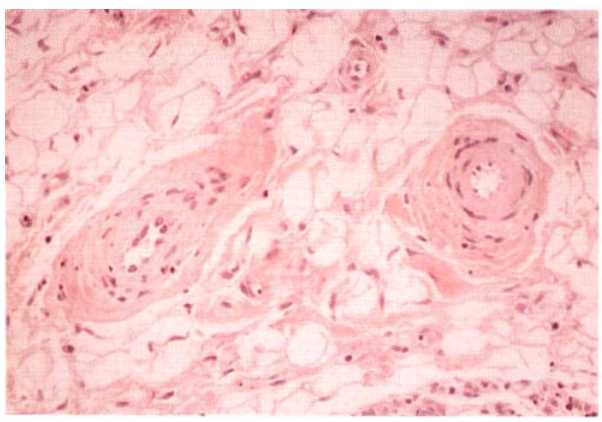

Fig. 5. Blood vessels within fat lobules illustrate perivascular lymphocytic inflammation and hyalinization (H&E, ×200).

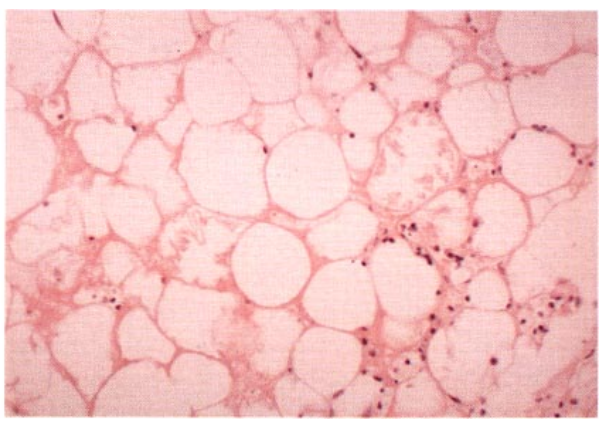

Fig. 6. Lipomembranous fat necrosis showing pseudopapillae formation (H&E, ×200).

plaques in the other 8 cases. They are firm, persistent and sometimes painful. The face was involved in eight cases, upper arms in five, lower leg in four, scalp in three, back in two, and shoulders in two. The most common clinical features were subcutaneous nodules or indurated plaques on the cheek (Fig. 1). One case complained of multiple atrophic depressed scars on the face as the sequele of LEP. A 4-year-old girl showed linear telangiectatic patches on the nose (Fig. 2). And in the three cases of scalp involvement, the chief problem was scarring or nonscarring alopecia. One case showed eyelid swelling.

The laboratories studies are listed in Table 3. There were 7 positive cases (37%) in ANA test, and all positive cases showed speckled patterns. The four DLE associated LEP and two SLE associated LEP revealed positive ANA test. Only one case had a positive ANA test among the LEP alone cases. In LEP alone two cases showed anemia or mild leukocytosis and three SLE associated cases showed pancytopenia or anemia. One SLE case had lupus nephritis.

Histopathologic findings are listed in Table 4. 11 cases showed variable epidermal changes such as epidermal atrophy, follicular plugging, basal cell degeneration regardless of whether the sites of biopsy exhibited discoid skin lesion. The examinations of dermis revealed edema, perivascular and periappendageal lymphohistiocytic cell infiltrations, dermal lymphoid nodules in some cases. The inflammatory cell infiltrates in panniculus were predominantly lymphocytic, patch and lobular (Fig. 3). Some specimens showed hyaline fat

necrosis (35%), lymphoid nodules (10%) (Fig. 4) or onion-skin like vessels (10%) (Fig. 5) in the subcutaneous fat layer. Two cases showed lipomembranous fat necrosis (Fig. 6).

Most of the cases (10/19) were effectively treated with hydroxychloroquine and some cases (6/19) were treated with combined oral corticosteroid and hydroxychloroquine. Two cases with alopecia were treated with intralesional triamcinolone injections. A case with single subcutaneous nodule on the arm was applied with topical corticosteroid (Diflucortolone valerate®) only for 7 months and the skin lesion was cured. Usually the LEP lesions were controlled about two or three months after the medications. The cases were followed up for 41 months of mean duration. 8 cases were cured with depressed scars and the remaining cases showed multiple recurrences. No cases developed SLE during the follow-up period of 41 months.

DISCUSSION

LEP is an unusual but distinctive clinical variety of LE. It is important to recognize this clinical subtype because the diagnosis may otherwise be missed, especially when there is no laboratory evidence of LE. The age of onset is usually in the second to sixth decade of life with a female preponderance of 2:1[1]. Our study showed similar results. LEP is rare in childhood[2]. Only about ten cases have been reported in children younger than 10 years old. Interestingly, there was a 4-year-old girl who had a linear telangiectatic atrophic patches on her face (Fig. 2). The linear LEP such as our case was reported in a 9-year-old Japanese boy[2]. She may have linear DLE and may develop LEP as its sequel. Our child's case had no ANA or other abnormal laboratory findings. But childhood LEP has been reported to be associated with partial genetic deficiency of C2 and C4[3-5].

Clinically LEP is usually characterized by the appearance of persistent, firm, well-defined nodules or plaques[1,6]. Sites of predilection are the scalp, face, upper and outer part of the arm, chest, back, and the buttock[1,6]. The overlying epidermis is often unchanged, but it may be erythematous, atrophic, and poikilodermatous[1]. Patients may have periodic flares that produce lipoatrophy and result in depressed atrophic scars which lead to a serious cosmetic defect[7]. LEP may also develop in unusual locations. LEP on the breast, so called lupus mastitis may cause ductal calcification and affect either sex[8,9]. Clinical and mammogram findings may resemble those of cancer. The erroneous diagnosis may be made in rare cases. Proptosis, or eyelid edema as the initial manifestations of LEP described in three patients[10]. Parotid, periparotid mass mimicked neoplasm, infection, or inflammatory process[1].

The cause of LEP is not clear. Tuffanelli[6] described six cases of LEP in which four cases noted the relation to minor trauma. It has been reported LEP may be precipitated by local trauma, injection, drugs such as iodide, and exposure to the ultraviolet light[7]. The mechanism by which trauma can induce immunological injury is unknown. However there does occur a localized inflammatory response in a susceptible individual. This may be sufficient under certain circumstances to initiate the complex immunological events which follow[6]. Two cases had traumatic precipitants (slipping down and contact to rope) in our study.

No significant correlation of specific autoantibodies and LEP has been proved[11]. The ANA test and other laboratory findings depend on the associated subsets of LE. There was a 37% positivity in our study. Only one case had a positive ANA test in LEP alone and most LE associated cases had positive ANA tests. SLE associated cases had other abnormal laboratory findings.

Although there are some debates about specificity of the pattern, the histologic features appear to be characteristic. The inflammation primarily involves the fat lobules but also the fibrous septal around the lobules[12]. A particular important and constant feature is the hyalinization of the fat lobules with a homogeneous glassy-appearing fat necrosis, which is associated with a lymphocyte infiltration and lymphocytic nuclear dust[12]. Vessels may be involved and show thick hyalinized walls that in some cases have a laminated onion skin-like appearance[12]. In many cases, lymphoid nodules with germinal centers can also occur in the perilobular septal area[12],. Calcification, mucin depositions may be present[12]. One case in our study showed lipomembranous fat necrosis which was most likely a nonspecific form of ischemic fat degeneration[13]. Our study showed similar findings of the fat layer but also 11 cases showed variable epidermal changes such as atrophy, hyperkeratosis, follicular plug-

gings, and basal cell degeneration. So for the diagnosis of LEP epidermal changes as well as subcutaneous changes may be important[12,14].

The histopathologic differential diagnosis includes lipodystrophy, connective tissue panniculitis (morphea, dermatomyositis), lymphocytoma cutis, Weber-Christian disease, Jessner's lymphocytic infiltration, erythema nodosum, and factitial ulceration[8]. Although the number of reports of LEP studies by immunofluorescent test is relatively small, the direct immunofluorescent testing can be important in supplementing the histopatholgic study of LEP[6,12]. Immunoglobulin or C3 deposits at the basement membrane or the blood vessels[6,12].

LEP has a chronic course and recurrence is common[1,6]. The systemic medication of choice is antimalarials, particularly hydroxychroloquine with oral dosage of 200 to 400mg/d[15]. There is a usually clinical response by 6 to 8 weeks and the dosage can be tapered at that point. The high rates of intestinal absorption of antimalarials give rise to gastric irritation with nausea and vomiting in younger children[15], but this was not seen in our 4-year-old girl during the medication which lasted 21 months. Systemic corticosteroid may be useful in the initial therapy for extensive inflammation[16]. Dapsone and thalidomide could be helpful[17]. There was a report[18] treated with topical clobetasol propionate (Dermovate®) under the hydrocolloid dressing similar to our one case . Transplantation of autologous dermal graft often provides satisfactory cosmetic results in patients with circumscribed atrophic depression[7].

No cases developed SLE again during the follow up period. According to the Izumi's review[19], 12 of the 34 cases of LEP reported in the literature had SLE, 11 cases had DLE and 11 cases had LEP alone. Although some of the patients with LEP fulfilled the ARA criteria for SLE, systemic involvement tended to be relatively mild, and the relatively low incidence (4/34) of renal diseases in reported LEP cases. The study of Watanabe[14] et al demonstrated that more than 50% of cases with LEP were initially classified as intermediated LE (ILE) that had more than one extracutaneous manifestation but did not include in the SLE, and except for minor instances, remained as having ILE during the 10 year follow-up period. Studies by Prystowsky[20] et al. demonstrated the patients with active discoid skin lesions rarely develop severe renal diseases. These group studies suggested that discoid skin lesions had a protective effect against the development of SLE. LEP may be closer to the DLE than to the SLE and a similar effect could be proposed in LEP.

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