

Which Skin Lupus Criteria are of More Value in Determining the Disease: A Greater View with the Help of Direct Immune Fluorescent (DIF)

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Abstract

Background: Lupus erythematosus (LE) includes a spectrum of auto immune disorders, involving whole body (systemic LE) in one end and is cutaneous limited LE on the other side. Cutaneous LE mainly diagnosed via clinical manifestations as well as histopathologic examination. According to different pathologic specifications, the aim of present study was to determine which histopathologic criterion is more accurate and practical in diagnosing cutaneous LE.

Material and Methods: The Samples which have been taken were from the patients with clinical manifestations of Cutaneous LE with pathologic confirmation. All patients had direct immuno fluorescent (DIF) samples that recorded. Histopathologic findings are categorized into three groups: group 1 contains epidermal changes, group 2 includes interface changes and group 3 contains dermal changes. Different histopathologic finding such as prevascular infiltration, follicular atrophy, follicular plaque, and basements membrane thickness and other changes, as well as DIF patterns, were recorded in designed questionnaires. Further analysis had been done with SPSS software version 22.

Results: Of 145 patients (61.4% female and 38.6% male) in 58.6% DLE was the first clinical diagnosis, 23% was the second and in subsequent 4.1%, 1.4% and 0.7% was third, fourth and fifth diagnosis respectively. In 11% of caeses DLE was not among clinical impressions. DIF was positive in 49%. As a whole, superficial perivascular and perifollicular infiltration were observed in 99% of the cases and was the commonest pathologic feature followed by basal vacuolization, peri follicular infiltration and epidermal atrophy. Other pathologic changes were observed with variable rates.

Discussion: By grouping histopathologic criterion, it seems that hyperkeratosis and thickening of Basement membrane may be major histologic criterion and peri vascular infiltration, peri follicular infiltration and eccrine gland infiltration, may be minor.

Keywords: Skin; Immune; Fluorescent; Lupus erythematosus

Abbreviations: SPVIL: Superficial perivascular infiltrate of lymphocyte; DPVIL: Deep perivascular infiltrate of lymphocyte; PFIL: Perifollicular infiltrate of lymphocytes; PEIL: Perieccrine infiltrate of lymphocytes

Introduction

Genetic, hormones, and environment play altogether to give birth to lupus erythematosus (LE); a disease of autoimmune features with a more frequency in women especially in childbearing age which can present variously in different involved organs. The aforesaid disease could be manifested from a skin lesion (cutaneous lupus) to a fatal diffused type (systemic lupus erythematosus [SLE]). LE is clinically divided to three classes: systemic lupus with acute onset, sub-acute cutaneous type, and a chronic discoid form (discoid lupus erythematosus [DLE]). Occurring two to three times more often than SLE, cutaneous lupus is a variant of LE being able to bother the patients' daily life [1-15].

On the other side, DLE is characterized by well-defined erythematosus scaly patches mostly seen on face and other sun exposed areas; palmoplantar lesions are rarely seen in DLE and can be disabling to the patients especially when we know they are refractory to the conventional treatments [16-19]. There is a variant of DLE called tumid lupus erythematosus (TLE) which is recognized by excess production of mucin in derma giving the skin a brawny appearance with indurations. Interface dermal infiltration of lymphocytes involving superficial and

deep perivascular areas, periappendageal sites, follicles, and epidermis are histopathological changes in DLE [20]. Lupus band test by using immunofluorescence also shows how autoantibodies of IgG, IgM, and IgA type have deposited over the dermoepidermal junction (DEJ); it is notable that its definition from a test confined to the skin lesions have expanded to all the areas on the skin of peoples with LE whether in the sun exposed or protected areas of the body [21-28].

It is mentioned that the diagnosis will come out when clinical manifestations (symptoms), serology (auto antibodies detected by sensitive rather than specific enzyme-linked immunosorbent assay [ELISA]), and pathology (histopathological changes in the skin lesions' sampling) all are correlated to each other [29]. Our study here aims to

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find out the prevalence of each pathologic criterion and to determine the benefits of these criteria over the other ways with a special attention to the direct immunofluorescence (DIF) test to reach a more accurate diagnosis on cutaneous lupus erythematosus particularly DLE.

Methods

The current survey has retrospective design which had been held in Razi Hospital, which is affiliated with Tehran University of Medical Sciences. All the patients with a pathologically confirmed diagnosis of skin lupus referring to Razi hospital were included in the study between 2008 and 2010. Another inclusion criterion was patients consent to enroll in the study. Pathologic samples were extracted from the medical records of patients and assessed by the faculties under the light microscopy for the histopathological features of the DLE; lupus band test was also evaluated on these and recorded as positive or negative result based on the pattern of antibodies, complement, and membrane attack complex deposition in dermo-epidermal junction to see if it is of any benefit over the other pathologic criteria in confirming a clinical diagnosis of DLE.

Data were analyzed by Statistical Package for the Social Sciences version 22 (SPSS) and cross tab software to find the relationship between each criterion; of all histopathologic features, hyperkeratosis, follicular atrophy, follicular plugging, and basements membrane thickness increasing were in a single group (group 1); superficial and deep perivascular infiltration in another category (group 2), and perivascular, perifollicular, and perieccrine were included in a separated one (group 3). Overall results were used in bringing out a series of pathologic criteria for accurate diagnosis of cutaneous lupus. Differential diagnoses similar clinically to cutaneous LE were also assessed to find out the prevalence of their histopathological differences. Test results from DIF were also another aspect of the study which was evaluated for its prevalence to see the efficacy.

Result

Of 145 cutaneous lupus samples, 61.4 % and 38.6% were belonged to the females and males, respectively. In 58.6% of the patients, DLE had been the first diagnosis associated with 23.4% in the second rank, 4.1% in the third, 1.4% fourth, 0.7% fifth, and in 11% of the cases, it had not been among the diagnoses. Also DIF was reported positive in 49% of the cases with 25% IgG, 33% IgM, and 42% C3 all deposited in the dermo-epidermal junction Table 1. The differential diagnoses are shown in table 2. Also in 36.6% of the cases, the presenting symptom was plaque, 16.6% papule, 15.9% erythematosus lesion, 10.3% patch, 5.5% alopecia, 4.8% pigmentation, 2.1% nodule, and other 0.7% scar, rash, blister, macula, erosion, hypopigmentation, and vesicles (Table 2).

The frequency of histopathologic features in three histopathologic groups is summarized in Tables 3-5 regardless of the sequence they have appeared at the field. The most common finding of histopathology in our study was SPVIL that was the same with other articles.

Demographic data	No. of cases (%)
Sex	
Man	56 (38.6)
Woman	89 (61.4)
Age	
Range	23
Mean	24
Site	1

Table 1: Demographic data of different cases.

Type of antibody	No. of cases (%)
IgG	71/145 (49)
IgM	48/145 (33)
C3	60/145 (42)

Table 2: Amount of antibody.

Epidermal changes	No. of cases (%)
Epidermal atrophy	107 (73.8)
Hyperkeratosis	91 (62.8)
Follicular plugging	84 (57.9)
Parakeratosis	45 (31)
Spongiosis	31 (21.4)
Epidermal hyperplasia	19 (13.1)
Lymphoexocytosis	18 (12.4)

Table 3: Epidermal changes data.

Dermoepidermal changes	No. of cases (%)
Basal vacuolation	120 (83.4)
Lichenoid infiltration	95 (65.5)
Melanin incontinuity	80 (55.2)
Civatte bodies	26 (17.0)
BM thickening	17 (11.7)

Table 4: Dermoepidermal changes data.

Dermal changes	No. of cases (%)
SPVIL	137 (94.5)
PFIL	117 (80.7)
DPVIL	104 (71.7)
PEIL	101 (69.7)
Follicular atrophy	67 (46.2)
Mucin deposition	45 (31)

Table 5: Dermal changes data.

Histopathology combination (%)	Percentage
SPVIL (94.5) + BM thickening (11.7)	100%
SPVIL (94.5) + PFIL (80.7)	99%
SPVIL (94.5) + F. plugging (57.9)	96.4%
DPVIL (71.7) + PEIL (69.7)	95%

Table 6: Histopathology combination (%) data.

We analyzed data using SPSS and cross tab software to connect the features of three groups to each other to see which combination can bring a more accurate diagnosis. The most powerful associations of histopathologic findings were SPVIL and BM thickening (100%), SPVIL and PFIL (99%), follicular plugging and SPVIL (96.4%), DPVIL and PEIL (95%), PFIL and PEIL (90%). These data are summarized in Table 6.

Other analysis was done to find out the relations between these categories; it showed that hyperkeratosis and superficial perivascular infiltration are seen in 94.5%, follicular atrophy and superficial perivascular infiltration in 79%, follicular plaque with superficial perivascular infiltration in 96.4% while with reflective in 89.2%, superficial perivascular infiltration and basements membrane thickness increasing in 100%, basements membrane thickness increasing and deep perivascular infiltration in 88%, and deep perivascular infiltration with superficial perivascular, perifollicular, and paracrine infiltration in 95.10%, 87.5% and 90.9% respectively. Deposition of C3 in dermo-epidermal junction in combination with basements membrane thickness increasing, were associated with the highest rate of positive predictive value for the diagnosis of SLE.

Discussion

Our results showed a different proportion of gender in the evaluated cases; 61.4% of female to 38.6% male in comparison to a 83% to 17% proportion in other sources. The most prevalent finding was perivascular infiltration which is in absolute correlation with other studies. When looking from one aspect to the frequency of the histopathologic features and consider them with one direction, hyperkeratosis and basement membrane thickness increasing altogether in association with one or two other features of this category, superficial and deep perivascular infiltration in association with one or two other features of other categories, and superficial perivascular, perifollicular, and paracrine infiltration have all more sensitivity to determine cutaneous lupus pathologically; while, another analytical look told a different story.

The research which has been done by Tiao et al tried to use the American College of Rheumatology (ACR) and Systemic Lupus International Collaborating Clinics (SLICC) criteria to determine the diagnosis of systemic lupus erythematosus in patients with subacute cutaneous lupus erythematosus. They concluded that most patients with cutaneous SLE who formally meet criteria for SLE do so based on the laboratory and mucocutaneous criteria. Neither the ACR nor SLICC criteria distinguish patients with subacute cutaneous lupus erythematosus (SCLE) and major internal disease from patients with SCLE without major internal disease. They concluded that renal disease and central nervous system disease were no more frequent in patients with SCLE who met SLE criteria than in patients with SCLE who did not. Most patients with SCLE who formally meet criteria for SLE do so based on the laboratory and mucocutaneous criteria. Neither the ACR nor SLICC criteria distinguish patients with SCLE and major internal disease from patients with SCLE without major internal disease [30].

Most previous studies comparing patients with SCLE versus those with only SLE have demonstrated that patients with SCLE are less likely to have severe renal and central nervous system disease, suggesting that SCLE differs from SLE by involving less internal organ disease [31-35].

In the survey which has done by Merklen et al, they analyzed 22 SLE patients with epidermal detachment. They revealed two main pathomechanisms: a classic SLE interface dermatitis, which can be hyperacute and lead to toxic epidermal necrolysis (TEN)-like skin detachment; and a neutrophilic dermatosis, with tense vesicles and/or blisters, including classic bullous SLE [36].

We can concluded from the previous researches that in patients with LE, we should definitely separate bullous lesions/loss of epidermis occurring in the setting of an interface dermatitis, from those occurring as a consequence of a neutrophilic dermatosis. The latter usually respond to dapsone, and can or cannot be immunopathologically characterized, whereas the former can either be a bullous variant of classic lupus lesions or, rarely, a life-threatening TEN-like acute dermatosis. Classic "bullous LE" is a dapsone-sensitive neutrophilic dermatosis, which probably encompasses different autoimmune bullous diseases. In the series reported here, the patients with neutrophilic bullous LE were those who had most frequently experienced associated significant renal involvement [36].

As these analytical combinations show, we can mention that superficial perivascular infiltration along with hyperkeratosis, and basements membrane thickness increasing and deep perivascular infiltration, perifollicular infiltration and paracrine infiltration could be considered as cutaneous lupus diagnostic criteria.

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