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CUTANEOUS LUPUS ERYTHEMATOSUS – CLINICOPATHOLOGICAL SPECTRUM AND ITS CORRELATION WITH ANCILLARY TESTS

Pathology

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ABSTRACT

Context: Cutaneous Lupus Erythematosus of various subtypes, etiologies, and clinical features frequently present with similar clinicopathological features which create a dilemma and diagnostic challenge for experts. Early diagnosis of lesions is of prime concern due to potential social stigma and varying prognosis of the illness. **Aim:** To study the epidemiological and clinicopathological spectrum of Cutaneous Lupus Erythematosus and correlating it with application of special stains. **Methods and Material:** A prospective, hospital based study was carried out at the Department of Pathology, Coimbatore Medical College, over a period of one and a half years(January 2017 – June 2018). Forty clinically diagnosed, untreated Cutaneous Lupus Erythematosus patients were included, their clinical and histological findings were recorded and analyzed and clinicopathological correlation was ascertained. **Results:** In 40 clinically diagnosed patients, 19 were diagnosed as Acute Lupus Erythematosus (47.5%), 6 as Subacute Lupus Erythematosus (15%) and 15 as Discoid Lupus Erythematosus (37.5%). The commonly affected patients were females between 31- 45 years of age. The most common histopathological features in various subtypes of Cutaneous Lupus Erythematosus include basal cell vacuolar degeneration with periadnexal and perivascular inflammation. In DLE patients, additional features such as basement membrane thickening and interstitial dermal mucin were frequently observed with the help of special stain, Periodic Acid Schiff with Alcian blue. **Conclusion:** In our study, histopathological examination of skin biopsy with concurrent use of special stain and clinical correlation helps in diagnosis and subclassification of the disease.

KEYWORDS

Basal cell vacuolar degeneration, Cutaneous Lupus Erythematosus, Dermal mucin, PAS with Alcian Blue.

INTRODUCTION

Lupus Erythematosus is a complex disorder with spectrum of varying prognosis ranging from benign to potentially fatal illness. It is associated with numerous clinical signs and symptoms and a wide range of laboratory abnormalities. Although the etiology is not well characterized, the interplay of genetic factors, autoantibodies and hormones have assumed significance.

The incidence rate in Asian countries ranges from 0.9 – 3.1% per annum. The prevalence of SLE ranges from 14 to 60 per 100,000, which is comparatively low.

Early diagnosis has significantly reduced the mortality rate and improved the overall survival rate. It most commonly affects the middle aged females. Paediatric LE is aggressive, largely due to renal disease. Consequently, the death rate is higher.

Cutaneous manifestations occurs in 70 to 80% of patients, of which specific skin lesions are classified as Acute, Subacute and Chronic (Discoid) based on the clinical features. DLE is the most common subtype encountered and any age group can be affected, most common being third and fourth decade. Widespread disease is often associated with systemic involvement and photosensitivity. LE non specific lesions include Raynaud's phenomenon, Livedo reticularis, Periungual telengiectasias and Leukocytoclastic vasculitis. Antinuclear antibody is present in 90 - 95% of SLE and 30 - 35% of DLE. 10% of normal population can have ANA at low concentration. LE should be distinguished from the other dermatosis with overlapping histopathological features like Lichen Planus and Poikiloderma.

The aim of this study is to analyze the clinical and histopathological features of Cutaneous Lupus Erythematosus (CLE) and to identify the most common and minimum histopathological features in various subtypes of CLE for early diagnosis in patients.

MATERIALS AND METHODS:

The present study is a prospective study conducted in Pathology department, Coimbatore Medical College, over a period of one and a half years (January 2017 to June 2018). Ethical clearance was obtained from the institutional ethics committee, and written consent was obtained from all patients under inclusion in the study.

A 3-4 mm of punch biopsy sent from all clinically diagnosed/suspected cases of isolated CLE or SLE having cutaneous manifestations of all ages and both sexes from the dermatology department in the above mentioned period were included in the study. Treated patients of LE, patients of LE with non-specific skin manifestations and pregnant women were excluded from the study. Clinical data were recorded in a preset proforma. Histological findings were noted from sections stained with haematoxylin and eosin stain. Special stains such as Periodic Acid Schiff and Alcian blue were performed to look for intensity of basement membrane thickening and interstitial mucin deposition in dermis. The recorded data were analyzed and clinicopathological correlation was ascertained.

RESULTS:

Forty cases of clinically suspected CLE comprised the study group which were stained with hematoxylin and eosin stain and PAS with Alcian blue. Female preponderance (n = 27, 67.5%) was observed.

The mean age of occurrence was 41 years and ranged between 17 to 75 years of age. 42.5% (n = 17) of the cases were between 31 -45 years (peak age of occurrence). Acute and DLE lesions were most commonly seen between 31-45 years and SCLE was common between 46 -60 years.

In acute lesion, the incidence of maculopapular lesion was higher(n = 15, 78.9%) as shown in figure 1a. In SCLE and DLE, plaque like lesions were relatively higher (n = 5,83.3% and n = 10, 66.7% respectively) as shown in figure 1b.

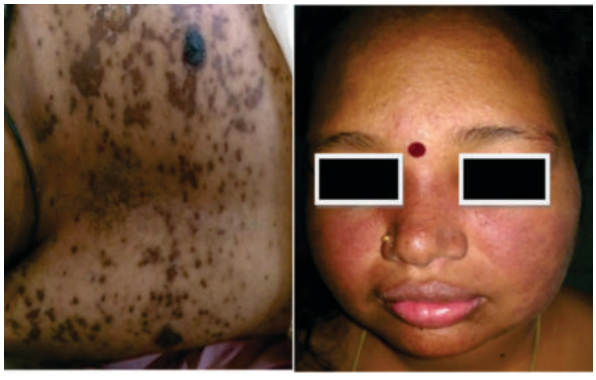

Figure1: (a) Discrete and confluent maculopapular eruptions involving the whole of the upper chest (b) Well defined erythematous plaque sparing the nasolabial fold.

Arthralgia,oral lesions, photosensitivity reactions and other symptoms were observed in certain subtypes of CLE as shown in Figure 2. Majority of the lesions were present over the face and scalp (n = 24, 60%), followed by back and upper extremities. Generalised involvement was observed in 10 cases (25%) and palms and soles in 3 cases only (7.5%).

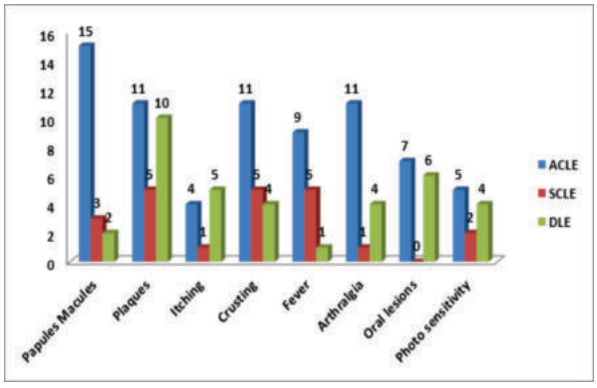

Figure 2 : Clinical features of clinically suspected cases of CLE.

Among the 40 cases, histologically all were confirmed as CLE. The most common subtype diagnosed was Acute LE (n = 19, 47.5%), followed by DLE (n = 15, 37.5%) and SCLE (n = 6,15%) as shown in figure 3.

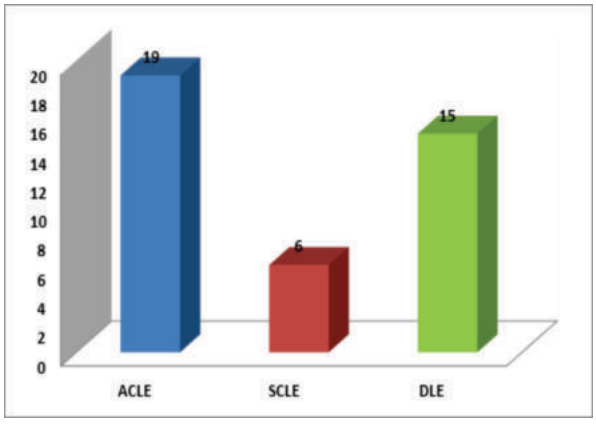

Figure 3: Histopathological subtypes of clinically suspected cases of CLE.

Histologically, the most common feature was basal cell vacuolar degeneration, observed in 12 (63.1%) cases of ACLE, 12 (80 %) cases of DLE and 4 (66.6%) cases of SCLE. Dermal mucin and vasculitis were observed most commonly in DLE and ACLE respectively.

The second most common finding was periadnexal inflammation, followed by epidermal atrophy,follicular plugging and hyperkeratosis.The various histological features in subtypes of CLE were observed as shown in table 1 and figure 4a, b, c and d.

Table 1: Histopathological features of various subtypes of CLE

Histopathological Features	ACLE (19)	SCLE (6)	DLE(15)
Hyperkeratosis	6	3	9
Epidermal atrophy	11	4	9
Basement membrane Thickening	4	0	5
Periadnexal and perivascular inflammation	16	6	15
Follicular plugging	9	2	6
Basal cell vacuolation	12	4	12
Subepidermal edema and dermal mucin	2	3	10
Melanin incontinence	6	1	6
Vasculitis	2	1	0

*ACLE – Acute Cutaneous Lupus Erythematosus, *SCLE – Subacute Cutaneous Lupus Erythematosus, *DLE – Discoid Lupus Erythematosus.

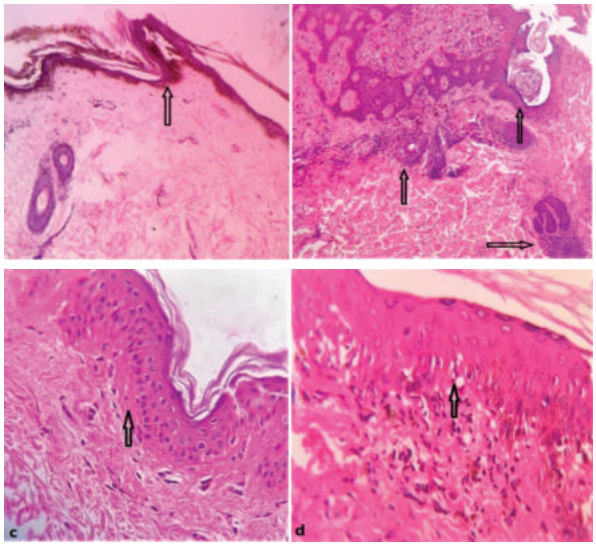

Figure 4: (a) Epidermal atrophy (arrow) and follicular plugging - (H and E, X10).**(b)** Follicular plugging with periadnexal and perivascular inflammation (arrows) – (H and E, X10). **(c)** Hyperkeratosis and basement membrane thickening (arrow) – (H and E, X40). **(d)** Basal cell vacuolar degeneration (arrow) - (H and E, X40).

PAS and Alcian blue stain was performed in all cases. Basement membrane thickening was observed in 30% of CLE patients and dermal mucin was noted more often in DLE (n = 10, 66.7%) as shown in figure 5a and b. All the 6 cases of SCLE did not show basement membrane thickening.

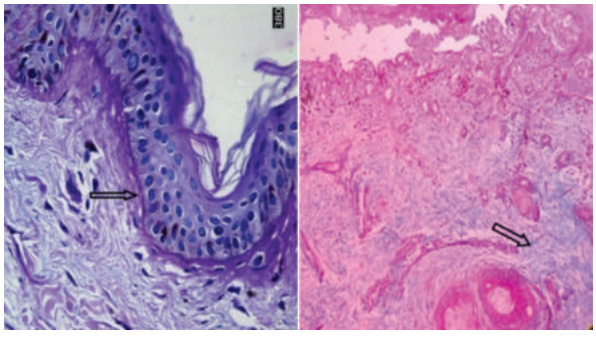

Figure 5: (a) PAS with Alcian blue stain showing basement membrane thickening (arrow) - X40. **(b)** PAS with Alcian blue stain showing interstitial dermal mucin (arrow) -X10.

The clinicopathological correlation of CLE was found to be almost 100% along with the other differential diagnosis given by the clinicians. However, if the subclassification of the disease is considered, it differed to a certain extent.

DISCUSSION:

Connective tissue disorders, present with cutaneous lesions, the biopsy of which is useful in diagnosis and sub-classification of the disease. Lupus Erythematosus is one such disorder which manifests with different skin lesions.

This study was based on clinical features and the spectrum of histopathological findings in different subtypes of CLE. The results obtained were analyzed and compared with literature based on epidemiological, clinical and histological features.

In our study, the biopsy of 40 patients clinically diagnosed as CLE were studied, of which 19 patients were diagnosed as ACLE, 6 as SCLE and 15 as DLE. Karumbaiah et al [3] and Kathleen M et al [4] demonstrated that DLE was the most common type. In our study, ACLE was the most common subtype observed.

The peak age of occurrence was between 31- 45 years in our study. According to Karumbaiah et al, [3] the age group was 21 to 50 years. Aviles- Izquierdo et al,[5] demonstrated that ACLE patients were younger, compared to SCLE and DLE. In our study, the age of onset of

ACLE was between 16 to 45 years. Biazer et al [6] observed that the mean age at disease onset in SCLE, was higher than in patients with ACLE which was similar to our study. Female preponderance (n = 27) observed in our study was similar to Gronhagen CM et al.[7]

In acute lesion, the incidence of maculopapular lesion , arthralgia, crusting and itching were relatively higher. In SCLE and DLE, plaque like lesions were relatively higher similar to David et al [8] and Griffiths et al.[9] Oral lesions and photosensitivity reactions were common in ACLE and DLE. In our study, 60% of patients had face and scalp lesions, then upper extremities, back and generalized body involvement similar to Vera Recabarren et al.[10]

In our study, patients with acute subtype had lesions of < 6 months duration, SCLE patients between 1 to 12 months and DLE of 1 to 5 years of duration. In other studies, the duration of the symptoms were not mentioned.

Basal cell vacuolation, mild periadnexal and perivascular inflammation was observed in most of the cases, followed by epidermal atrophy and follicular plugging as shown in table 2.

Table 2: Comparison of histopathological features of ACLE with karumbaiah et al study:

Histopathological features	Karumbaiah et al [3] – 7 cases	Present study 19 cases
Hyperkeratosis	3	6
Epidermal atrophy	4	11
Basement membrane thickening	-	4
Periadnexal and perivascular inflammation	6	16
Follicular plugging	6	9
Basal cell vacuolation	7	12
Subepidermal edema	6	2
Melanin incontinence	3	6
Vasculitis	-	2

*ACLE – Acute Cutaneous Lupus Erythematosus

In our study, vasculitis was found in 2 cases and basement membrane thickening in 4 cases, which were not observed in any of the cases in the above mentioned study.

Basal cell vacuolar degeneration, epidermal atrophy, periadnexal and perivascular inflammation was commonly observed findings in our study, similar to Karumbaiah et al[3] and Bangert et al studies.[11] Basement membrane thickening was not identified in our study, which contradicts with Bangert et al study, in which 8 cases, demonstrated it as shown in table 3. Dermal mucin was observed in 3 cases in our study, which was not included in the above studies mentioned.

Table 3: Comparison of histopathological features of SCLE in various studies:

Histopathological features	Karumbaiah et al [3] – 4 cases	Bangert et al [11]– 12 cases	Present study – 6 cases
Hyperkeratosis	2	12	3
Epidermal atrophy	2	10	4
Basement membrane thickening	1	8	-
Periadnexal and perivascular inflammation	4	12	6
Follicular plugging	3	2	2
Basal cell vacuolation	3	8	4
Subepidermal edema	3	3	3
Dermal mucin	-	-	3
Melanin incontinence	-	-	1
Vasculitis	-	-	1

*SCLE – Subacute Cutaneous Lupus Erythematosus

Basement membrane thickening was the most common feature observed in DLE in Karumbaiah et al and Bangert et al studies which corroborates with our study as shown in table 4. The intensity of periadnexal and perivascular inflammatory infiltrates was maximum in DLE. Dermal mucin was also commonly found in DLE patients of our study, which was not mentioned in other studies.

4: Comparison of histopathological features of DLE in various studies:

Histopathological features	Karumbaiah et al [3] – 9 cases	Bangert et al[11] – 26 cases	Present study – 15 cases
Hyperkeratosis	5	26	9
Epidermal atrophy	3	11	9
Basement membrane thickening	9	19	5
Periadnexal and perivascular inflammation	9	26	15
Follicular plugging	5	14	6
Basal cell vacuolation	7	19	12
Subepidermal edema	3	3	4
Dermal mucin	-	-	10
Melanin incontinence	-	-	6
Vasculitis	-	-	-

*DLE – Discoid Lupus Erythematosus

The common histopathological changes found in ACLE were basal cell vacuolar degeneration, periadnexal and perivascular inflammation and epidermal atrophy similar to that of SCLE but with lesser degree of inflammation in ACLE. Basement membrane thickening, follicular plugging and vasculitis were rarely observed in cases of SCLE in contrast to ACLE, whereas subepidermal edema and mucin deposition were frequently observed in SCLE than ACLE, in contrast to Karumbaiah et al study.

The frequently observed features in DLE were basal cell vacuolar degeneration, subepidermal edema, dermal mucin followed by epidermal atrophy, hyperkeratosis and less commonly follicular plugging and basement membrane thickening but more compared to SCLE. Dermal mucin and basement membrane thickening are frequently observed in DLE than SCLE, similar to Karumbaiah et al study. The combination of basal cell vacuolar degeneration and epidermal atrophy with clinical correlation are highly suggestive of SCLE, similar to Karumbaiah et al study. BM thickening demonstrated by PAS was observed most commonly in DLE. Dermal mucin deposition highlighted by Alcian blue was found frequently in DLE and SCLE.

The limitations of the study is that, Direct Immunofluorescence could not be performed in all the cases which would provide added information to the various subtypes of cutaneous lesions and for further treatment. Comparison of skin biopsy findings of treated and untreated patients could add more information to the available literature.

CONCLUSION :

The clinical features and distribution of cutaneous lesions in Lupus Erythematosus simulate few other dermatological diseases. Serological tests, though available are sometimes confounding. The skin biopsies,show profound variation in the combination of the actual histopathological features required for the diagnosis which can impede the pathologist from providing a conclusive diagnosis. Factors like age of the lesion, site of biopsy and non specific or atypical clinical presentations can cause variations in the histopathological findings.

In such cases, the histopathological examination along with special stain, PAS with Alcian blue and Direct immunofluorescence helps to subclassify and diagnose, based on the thickening of basement membrane and interstitial dermal mucin deposition along with the clinical features and serological tests. Since, basement membrane thickening and dermal mucin are commonly observed in chronic patients it is advisable to carry out special stain in skin biopsy samples of patients with symptoms of more than 1 year duration. Periodic review and analysis of series of cutaneous lesions of lupus erythematosus will help us to understand the variations in the manifestations of the disease in all aspects.

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