A STUDY OF MUCOCUTANEOUS MANIFESTATIONS IN AUTOIMMUNE CONNECTIVE TISSUE DISORDERS AT TERTIARY CARE CENTRE

Manisha Jethwa[1], Hita Mehta[2]

[1]Senior Resident Doctor, Department of Dermatology, Venereology and Leprosy, Government Medical College, Bhavnagar.
[2]Professor and HOD, Department of Dermatology, Venereology and Leprosy, Government Medical College, Bhavnagar.

ABSTRACT

BACKGROUND

Our aim was to study the clinical and immunological profile of patients with newly detected connective tissue disease presented to a tertiary care centre.

MATERIALS AND METHODS

The study involved 51 patients with newly-detected Systemic Lupus Erythematosus (SLE) (fulfilling the revise SLICC criteria for SLE) and Systemic Sclerosis (SS), Mixed Connective Tissue Disease (MCTD), etc. attending Sir. T. Hospital, Bhavnagar, between January 2013 and December 2016. All patients were assessed for clinical features and immunological profile.

RESULTS

Out of the 51 patients, 30 having SLE, 10 having SS, 9 with MCTD, 1 with dermatomyositis and 1 with Rowell's syndrome. Among them, 47 were females and 4 were males. The mean age at presentation was between 15-25 years. The LE-specific skin lesions were noted as malar rash in 25 patients (83%), subacute and acute lupus rashes (80%) and discoid rash (13%). Among LE-nonspecific lesions, non-scarring alopecia was most common followed by oral ulcers, Raynaud's phenomenon, joint pain, scarring alopecia, erythema multiforme, livedo reticularis, vasculitic lesions, urticaria and calcinosis cutis were seen. In MCTD, muscle weakness was common finding. In systemic sclerosis, hide-bound skin and decreases mouth opening were seen in all cases and Raynaud's phenomenon, joint pain, hair loss, calcinosis cutis and respiratory system involvement were other features. Serum ANA was positive in 76% while negative in 3.8% of individuals. The most common pattern observed in ANA profile was speckled (56%) followed by homogenous (32%) and nucleolar (28%).

CONCLUSION

There is diversity in clinical presentation of autoimmune connective tissue disease with regards to their genetic and environmental backgrounds. Cutaneous features are utmost important having diagnostic and prognostic value as well.

KEYWORDS

Autoimmune Connective Tissue Diseases, SLE- Malar Rash, Photosensitivity, Systemic Sclerosis.

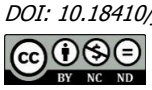
HOW TO CITE THIS ARTICLE: Jethwa M, Mehta H. A study of mucocutaneous manifestations in autoimmune connective tissue disorders at tertiary care centre. J. Evid. Based Med. Healthc. 2017; 4(44), 2701-2705. DOI: 10.18410/jebmh/2017/537

BACKGROUND

Autoimmune Connective Tissue Diseases (CTD) are heterogeneous group of disorders marked by diverse patterns of autoantibody production with multiorgan involvement. It includes spectrum of diseases like Systemic Lupus Erythematous (SLE), Systemic Sclerosis (SS), Polymyositis-Dermatomyositis (PM-DM), Primary Sjogren's Syndrome (SS), Mixed Connective Tissue Disease (MCTD), Rheumatoid Arthritis (RA), etc. Variation in clinical presentation of all CTD is seen, which depends upon several factors like individual's genetic and ethnic background, environmental changes, sex and age of individuals, etc. for example in SLE oral ulcers were more common in patients from east India while lower CNS involvement was seen in North India.[1]The spectrum of disease ranges from minor organ involvement (e.g., cutaneous lesions) to life-threatening major organ involvement (e.g., renal, nervous system). Skin is one of the commonly involved organ in CTDs and sometimes earliest and only to be involved.[2]

Cutaneous features in SLE like malar rash, discoid rash and photosensitivity, oral ulcers and non-scarring hair loss are included in modified SLICC criteria for diagnosis of SLE signifies importance of cutaneous manifestations.[3] Cutaneous features in SLE could also be classified as LE specific and LE nonspecific skin lesions as per Gillian's classification.[4] Similarly in other CTDs, cutaneous features can help in early diagnosis and management of diseases. Thus, a thorough understanding of cutaneous lesions is required. Lupus-specific skin lesions serve primarily as an important diagnostic clue, whereas lupus nonspecific skin lesions are associated with more active disease and thus require more aggressive therapy and disease monitoring.[5]

Financial or Other, Competing Interest: None.
Submission 07-05-2017, Peer Review 17-05-2017,
Acceptance 25-05-2017, Published 01-06-2017.
Corresponding Author:
Dr. Manisha Jethwa,
No. 8/5124, Nandanvan Society,
Kalvibid, Bhavnagar-364002.
E-mail: manishajethwa3333@gmail.com
DOI: 10.18410/jebmh/2017/537



AIM

Aim of our study is to look for variations in clinical features and immunological profile in CTDs in our geographical location. We emphasise here on most common clinical manifestation in SLE and SS.

MATERIALS AND METHODS

The study involved 51 patients attending Sir. T. Hospital, Bhavnagar, between January 2013 and December 2016, selected consecutively. Individuals with newly-detected Systemic Lupus Erythematosus (SLE) (fulfilling the revise SLICC criteria for SLE), Systemic Sclerosis (SS), Mixed Connective Tissue Disease (MCTD), dermatomyositis and Rowell's syndrome were enrolled.

Detailed clinical history was taken, which includes age, gender, history of malar rash, discoid rash, oral ulcers, photosensitivity, scarring and non-scarring alopecia, Raynaud's phenomenon in SLE, history of hidebound skin, difficulty in mouth opening, Raynaud's phenomenon, joint pain, calcinosis cutis, sclerodactyly in SS, history of muscle weakness with hair loss, joint pain in MCTD, history of periorbital rash, Gottron's papules and rash in dermatomyositis were recorded in proforma with written consent for clinical photograph. Antinuclear Antibody (ANA) profile was carried out in 40 patients either by Indirect Immune Fluorescence (IIF) or Enzyme Immunoassay Method (ELISA).

We enrolled both male and female patients of all age groups having clinical features of CTDs. Individuals with critical illness and pregnant females were excluded.

RESULTS

Total 51 patients were enrolled in our study. Among them, 47 (92%) were females, while 4 (7.8%) were males with mean age of presentation was 20.5 years, average duration of complaint was 1.5 years and female-to-male ratio was 11.7:1. The youngest female was of 10 years, while oldest was of 65 years. Most common disease we encountered in our study was SLE (58%) followed by SS (19%), MCTD (17%), dermatomyositis (1.9%) and Rowell's syndrome (1.9%) (Table 1).

Among SLE patients, most common clinical feature was malar rash (83%) and other typical features were described in Table 2. Few rare clinical features like erythema multiforme (6%), livedo reticularis (3%), cutaneous vasculitis (6%), urticaria-like lesions (6%), calcinosis cutis (3%) and pyoderma gangrenosum (3%) was seen.

In patients with SS, out of 10, all had positive history of hidebound skin and decreased mouth opening (Table 3).

Among MCTD group, all had history of muscle weakness followed by joint pain (55%), Raynaud's phenomenon (55%) and hair loss (44%). In one patient with dermatomyositis clinical feature of heliotrope rash, Gottron's papule and rash was seen and in Rowell syndrome positive finding of SLE with erythema multiforme like lesions was present.

Serum ANA and ANA profile was done in 40 cases and among them it was positive in 92% while negative in 7.5% of individuals. The most common pattern observed in ANA profile was speckled (56%) followed by homogenous (32%) and nucleolar (28%). In SLE patients, antibodies like dsDNA (40%), antihistone (25%), smith (15%), SS-A (10%), SS-B (10%) in scleroderma patients Scl-70 (60%), U1SnRMP (30%), Ro-52 (10%) antibodies and in MCTD patients U1SnRMP antibody was commonly seen.

Disease	Number of Patients
SLE*	30
SS†	10
MCTD≠	9
Dermatomyositis	1
Rowell's syndrome	1

Table 1. Disease Distribution in Our Study Group

*=Systemic Lupus Erythematous, †=Systemic Sclerosis, ≠=Mixed Connective Tissue Disease.

Clinical Feature	No. of Patients (%)
Malar rash	83
Subacute and acute lupus rash	50
Non-scarring hair loss	66
Oral ulcers	56
Raynaud's phenomenon	56
Scarring hair loss	23
Discoid rash	13

Table 2. Clinical Features in SLE Group

Clinical Feature	No. of Patients (%)
Hidebound skin with salt-pepper de-pigmentation	100
Decrease mouth opening	100
Joint pain	90
Sclerodactyly	70
Raynaud's phenomenon	90
Hair loss	60
Calcinosis cutis	30

Table 3. Clinical Features in Systemic Sclerosis Group

	Our Study (n=30)	%	Malaviya et al (n=315) N. India	%	Renu Saigal et al (n=60) W. India	%
Age of onset	20 yrs.		31 yrs.		30 yrs.	
F:M	12:1		8:1		11:1	
1.	Malar rash	86	Skin rash	81	Photosensitive dermatitis	75
2.	Photosensitivity	82	Alopecia	53	Alopecia	65
3.	Non-scarring alopecia	20	Oral ulcers	41	Oral ulcers	61
4.	Raynaud's phenomenon	17	Photosensitivity	24	Malar rash	43
5.	Oral ulcers	17	Raynaud's phenomenon	14	Raynaud's phenomenon	21

Table 4. Comparison of SLE Features with Other Studies

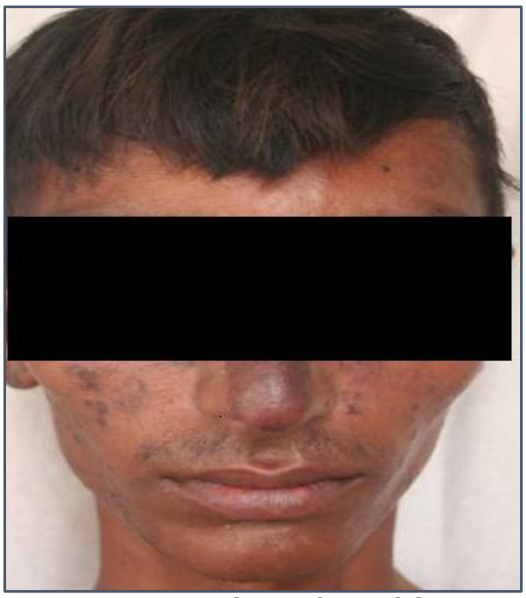


Image 1. Malar Rash Involving Bridge of Nose in SLE Case

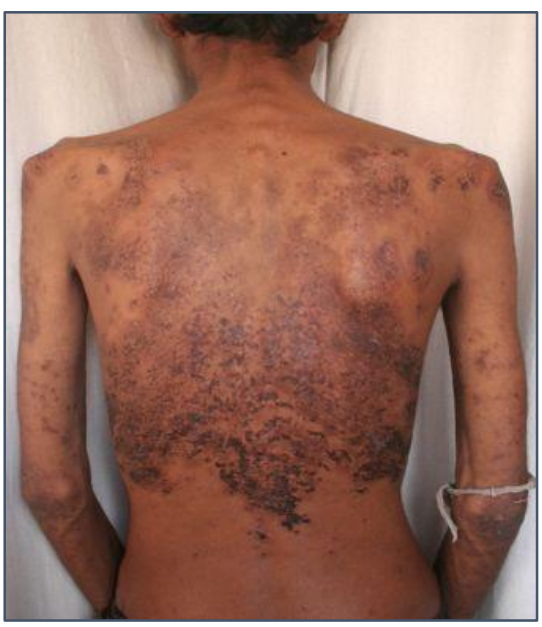


Image 2. Asymmetrical Hyperpigmented Acute Lupus Rash

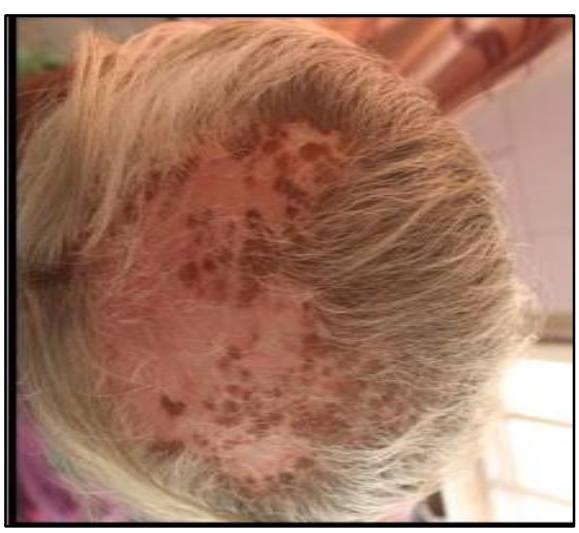


Image 3. Depigmented Patch with Scarring Alopecia in Discoid Lupus

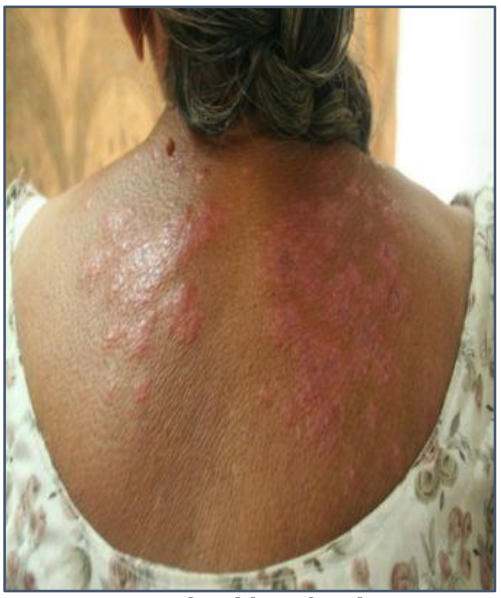


Image 4. Discoid Rashes in Lupus

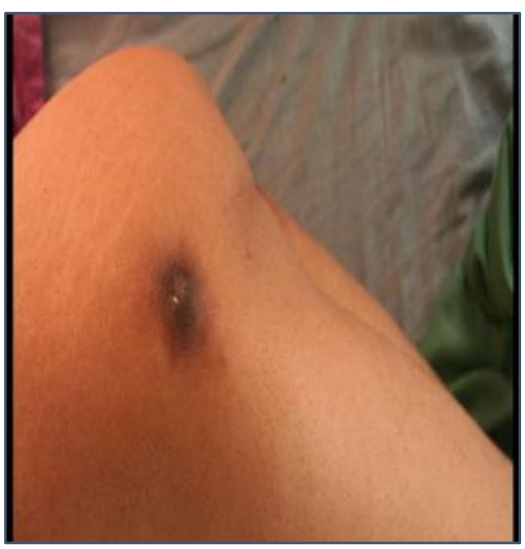


Image 5. Hard Indurated Lesion with Chalky White Discharge in Calcinosis Cutis

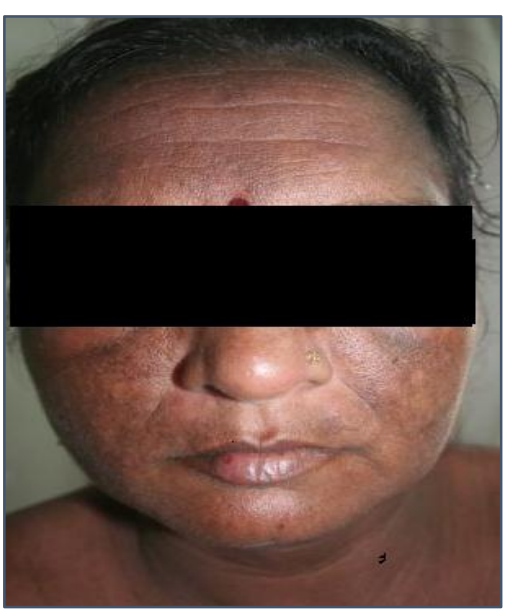


Image 6. Periorbital Oedema with Thickening of Skin in SS Case

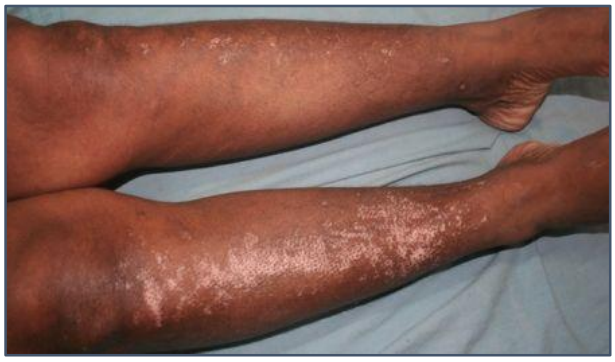


Image 7. Salt and Pepper Depigmentation on Both Legs In SS Case

DISCUSSION

CTDs have vast range of clinical presentation, which differs as per individual's age, sex, geographical and ethnic background.

In our study, female outnumbered male patients with female-to-male ratio was 11.7:1. The corresponding female-to-male ratios in Indian studies by Malaviya et al, Renu et al and Binoy et al were 8:1, 11:1 and 19:1, respectively.[1,6,7] Females are more prone to develop CTDs because of hormonal influences.[8]

The average disease duration of disease noted in the present study was 1.5 years, which is comparable to the study done by Renu et al (2 years) and Malaviya et al (17 months).[1,6]

Age of presentations in both sexes was quite younger 20.5 years, mostly in 2nd decade of life. Similar findings have been observed in other Indian studies.[4,5,6]

Comparison of the clinical features in SLE with other studies are shown in Table 4.

In the present study, among LE specific skin lesions, malar rash (83%) was most common followed by subacute and discoid rashes, which correlate with findings by Renu et al and by Malaviya et al where malar rash was seen in 75% and 81% of cases, respectively (Image 1, 2).

Among LE nonspecific lesions, non-scarring hair loss (66%) was the commonest clinical finding in our study and also in other studies like 86.67% by Kole AK et al,[9] 82% by Malaviya et al and 65% Renu Saigal et al. Discoid rash and scarring alopecia were less common in our study group (Image 3, 4).

Oral ulcers (17%) were the second most common LE nonspecific lesion we found, while it was 41% and 65% by Malaviya et al and Renu Saigal et al. Raynaud's phenomenon is usually less prevalent in SLE cases. However, here we reported it in 56% of our patient, while it was quite less in other studies. Variation could be possible because of climatic change in geographic places.[1]

We have seen some interesting findings like one case of pyoderma gangrenosum in SLE patient; it is a rare skin lesion and maybe the initial presentation of the disease.[10] Urticaria-like skin lesions are uncommon in patients suffering from SLE, but we had noted such lesions in 2 of the cases and one should look for active systemic disease in such cases.[11] Other less common features were vasculitis skin lesions (6.6%), livedo reticularis (3.3%) at the time of presentation and in one female with DLE, there were multiple calcinosis cutis lesions. Calcinosis cutis usually associated with SS, here we found quite unusual presentation (Image 5).

In ANA profile, smith antibody is considered more sensitive while dsDNA is more specific for diagnosis of SLE. However, ANA could be negative despite of other clinical features of LE as we found in 3.8% of our cases. The most common pattern we observed in ANA profile was speckled (56%) followed by homogenous (32%) and nucleolar (28%). In SLE group, anti-dsDNA and in SS group anti-SCL70 antibody was commonly present.

We also noted more prevalence of constitutional symptoms like fever, lethargy, malaise along with neuropsychiatric manifestations, leukopenia, thrombocytopenia, cardiovascular and renal involvement.

In SS, we found hidebound skin and decrease mouth opening in all patients followed by Raynaud's phenomenon (90%) and sclerodactyly (70%) similarly noted in study of Sudip Ghosh in eastern India.[12] In MCTD cases, all had given history of muscle weakness and pain followed by history of hair loss, joint pain and Raynaud's phenomenon (Image 6, 7).

Rowell's syndrome is entity where LE is associated with erythema multiforme like lesions, noted in our one patient. One case presented with classic Gottron's papule and rash on hands, heliotrope rash around eyes with anti-Jo1 antibody profile.

Number of our cases could be increased more and we are not able to carry out ANA profile in all of the individuals because of financial issue.

CONCLUSION

SLE is a multisystem disorder in which cutaneous manifestations can yield valuable diagnostic as well as prognostic information. Skin lesions are responsible for increased morbidity, hence early diagnosis of skin lesions are required. Diversity in clinical presentation in all CTDs are seen and its correlation with systemic involvement should be looked for.

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