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skin manifestation in systemic lupus erythematosus

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Sixth stage

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2020-2021

Abstract

Systemic lupus erythematosus is multiorgan autoimmune disease of unknown causes with many clinical manifestation. The skin is one of the most variably affected by the disease. The American College of Rheumatology established 11 criteria as diagnosis of SLE. Cutaneous lesions account for four of those 11 revised criteria of SLE. Skin lesions in patients with lupus could also be specific or nonspecific. The systemic lupus erythematous specific cutaneous change : malar rash, discoid rash, photosensitivity, and oral mucosal lesion.

The SLE nonspecific skin manifestations are include:Alopecia, lupuspanniculitis, lupusprofundus ,lichenoid lichen overlap,small vessel cutaneous leukocytoclastic vasculitis,urticarial vasculitis,atrophic blanche, periungual telegiectasias, live doreticularis, Raynauds phenomenon and bullous lessions.

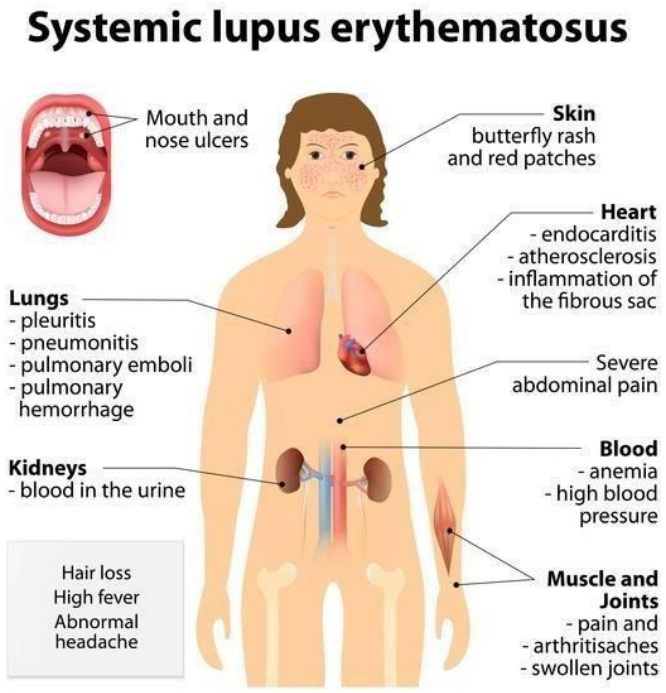


Fig (1) systemic lupus Erythematosus

Introduction

Systemic lupus erythematosus is an autoimmune disorders which the immune system attacks its own tissues, causing wide spread inflammation and tissue damage in the affected organs. It can affect the joints, skin, brain, lungs, kidneys, and blood vessels.It is prototype of a multiorgan autoimmune disease and still considered as a disease with an ambiguous etiology. The diseasepredominantly affect women during the reproductive ages at a ratio of eight women per one man. Its pathogenesis is multifactorial lying on genetic and environmental factors during which it occurs in genetically to individuals who have experienced certain environmental triggers leading to an irreversible loss of immunologic self tolerance.(1)

The strong genetic contribution to the development of SLE supported by the high heritability of the disease (>66%), a higher concordance rate for SLE in monozygotic twins than in dizygotic twins or siblings (24–56% versus 2–5%, respectively).(2) The nature of these environmental triggers is largely unknown. It is possibly that it requires variety of environmental triggers occurring together or sequentially over a limited period of your time. The concept emerged of 'threshold liability' during which disease develops when a threshold of genetic and environmental susceptibility effects is reached. the control of gene packaging and expression independent of alterations in the sequence of the DNA , is providing new directions linking genetics and environmental factors. It has become clear that genetic, epigenetic plays a serious role in complex diseases with complex immunological pathogenesis like lupus. Convincing evidence indicates that epigenetic mechanisms, and in particularly impaired T cell DNA methylation, provide a further factor.(3) Interpreting the precise contribution of epigenetic factors to autoimmunity, and in particular to SLE, has become a lively research area. This complex autoimmune disordeers result from defect of multiple immunologic components of both the innate immune system and the adaptive immune system including altered immune tolerance mechanism, hyperactivation of T and B cells, decreased ability to clear immune complexes and apoptotic cells, and failure of multiple regulatory networks.(4)

In 1982, the diagnosis criteria for SLE published by the (ACR) which were revised in 1997 and currently used in clinical practice, undoubtedly useful, mainly for diagnosis between systemic LE and other rheumatologic disorders; such criteria commonly inadequate for LE subsets , the ACR criteria include malar rash, discoid rash, and oral ulcers.

The 2012 Systemic Lupus International Collaborating Clinics classification criteria addressed many of these issues. Mucocutaneous and neuropsychiatric manifestations provided as were hypocomplementemia and new antiphospholipid antibody tests; and criteria definitions were refined. The SLICC criteria confirmed that Systemic LE primarily an autoantibody, requiring at least one immunological criterion to be present, and categorised histology-proven nephritis compatible with SLE as sufficient for classification, if antinuclear antibodies (ANAs) or antibodies double-stranded DNA (dsDNA) were present. While achieving their goal of accelerating sensitivity, the SLICC criteria have lower specificity than the 1997 ACR criteria.[1]

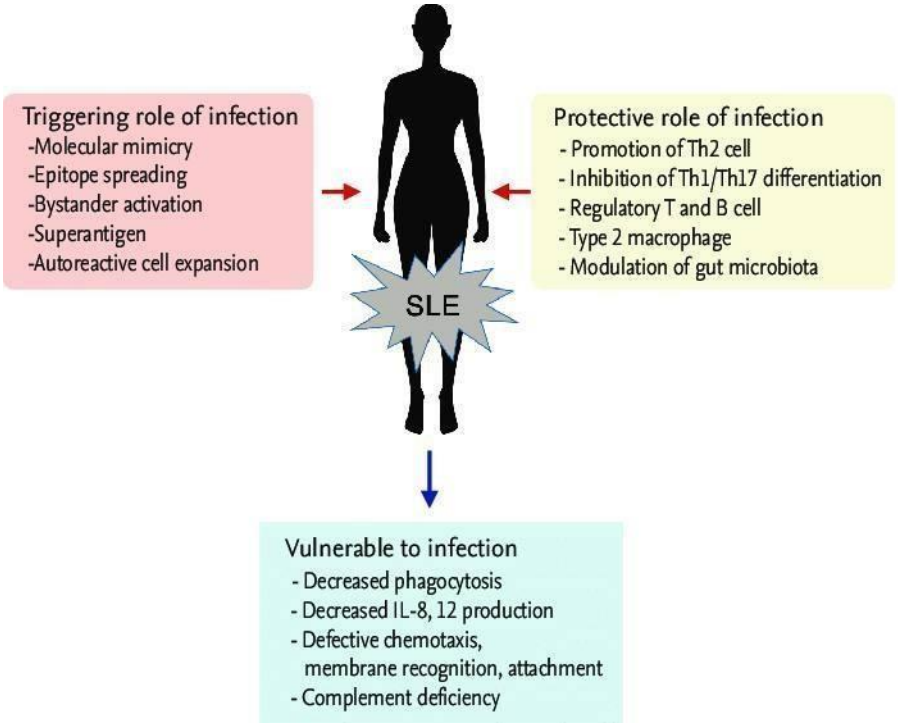


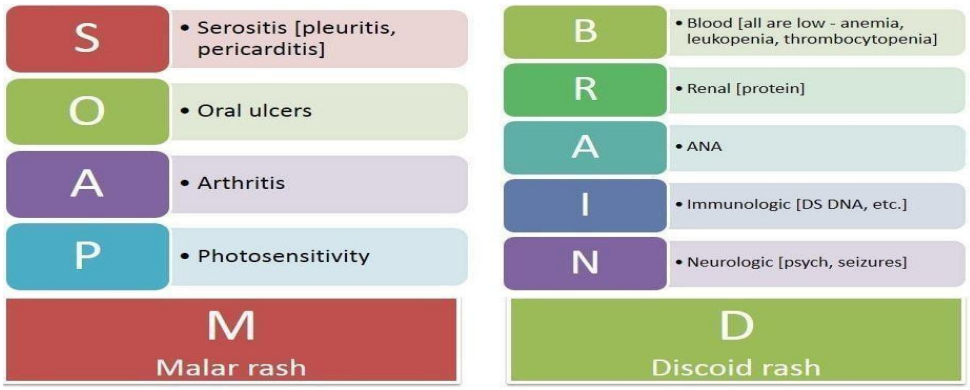
Fig (2) Interaction of infection and systemic LE

.Th, T-helper; IL, interleukin

American College of Rheumatology criteria for the diagnosis of SLE are mucocutaneousfinding. The diagnostic criteria are

1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcers (21%)
5. Arthritis
6. Proteinuria >0.5 g/day or casts
7. Neurologic disease
8. Pleuritis/pericarditis
9. Blood abnormalities
10. Immunologic disease, including anti-dsDNA antibody, anti-Sm, APLAs
11. Positive ANA blood test.[5]

American College of Rheumatology Criteria for diagnosis SLE:



Aim of the study

The skin is one of the target organ most variably affected by the systemic lupus erythematoses. This article covers the SLE - specific cutaneous changes: malar rash, discoid rash, photosensitivity, and oral mucosal lesions these lesions account for four of these 11 criteria of SLE. as well as SLE non specific skin manifestations, their pathophysiology, and percentage of cutaneous manifestations in patients with SLE and if it present in initial of disease or during course of diseases and its role in prognosis of diseases.

Cutaneous manifestations of SLE

The diagnosis of the cutaneous manifestations of Lupus erythematous`1 relies on clinical, histopathology, and immunohistology of skin lesions. In addition, serum autoantibodies considered immunologic markers for distinct clinical types of the illness. [5]

Classification of cutaneous manifestations of lupuserythematosus

I. Chronic cutaneous LE

A. Discoid LE

1. Localized

2. Disseminated

B. Verrucous (hypertrophic) LE (Behçet): usually acral and sometime lichenoid

C. Lupus erythematosus–lichen planus overlap

D. Chilblain LE

E. Tumid lupus

F. Lupus panniculitis (LE profundus)

1. With no other involvement

2. With overlying discoid LE

3. With systemic LE

II. Subacute cutaneous LE

A. Papulosquamous

B. Annular

C. Syndromes commonly exhibiting similar morphology

1. Neonatal LE

2. Complement deficiency syndromes

3. Drug induced

III. Acute cutaneous LE:

Localized or generalized erythematous Or bullus , Generally associated with SLE.

Clinical cutaneous manifestation of SLE:

1- Maler rash

2- Discoid lupus erythematoses DLE

A-Localized DLE

B-Generalized DLE

3- Photosensitivity

4- Mucosal DLE

A-Oral DLE

B-Conjunctival DLE

C- Nasal DLE

D- Genital DLE

5- Subacute cutaneous lupus erythematosus

6- Alopecia

7- Lupus panniculitis/lupus profundus

8- Lichenoid DLE (LE/lichen planus overlap)

9- A small vessel cutaneous leukocytoclasticvasculitis secondary to LE

A- Dependent palpable purpura

B- Urticarial vasculitis

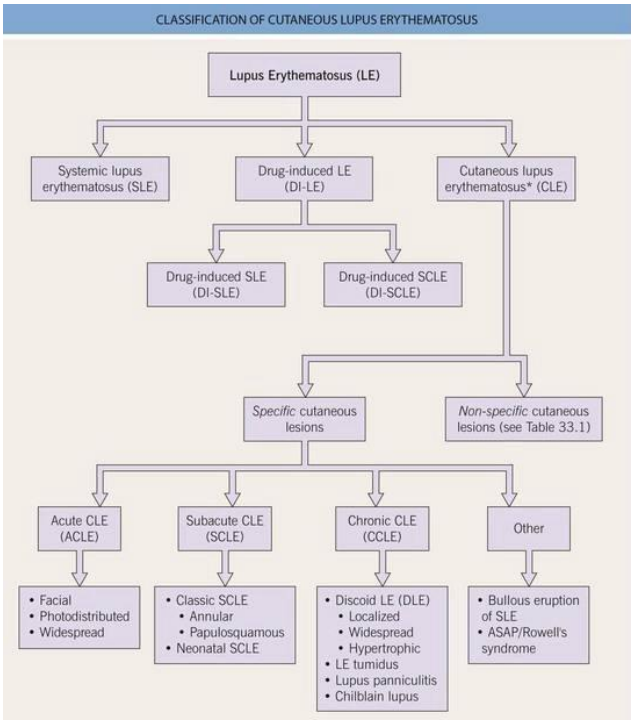
10- Secondary atrophieblanche

11-Periungual telangiectasias

12-Livedo reticularis

13-Raynaud's phenomeno

14-Bullous lesions



Malar Rash

Is the first criteria of the ACR, which characterized by erythematous rash over the cheeks and nasal bridge. Malar rash fixed erythema that typically spread to the nasolabial folds. It is butterfly shaped that can flat or raised over the cheeks and bridge of the nose. It issue from days to weeks and is occasionally painful or pruritic.[6]

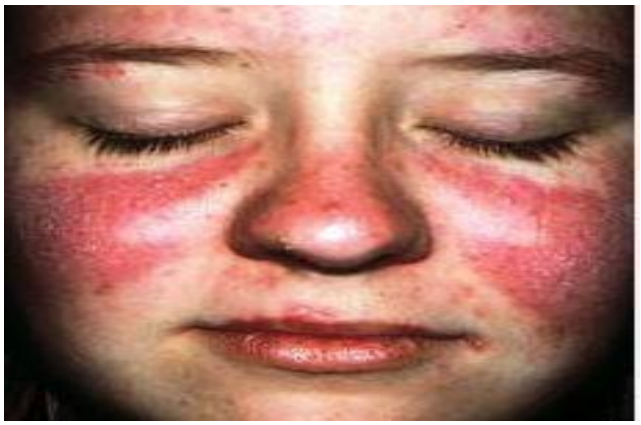


Fig (3) malar rash of SLE

Photosensitivity

The second criteria is photosensitivity (sensitivity 43%; specificity 96%). Exposure to ultraviolet causes rash or other symptoms of SLE flareup. A macular or a diffuse erythematous rash occurs in sun-exposed areas, because the face, arm, or hand which generally persists for over one day. Sometimes erythematous papule or macule on the dorsal of the hands classically sparing the knuckles are observed.[7]

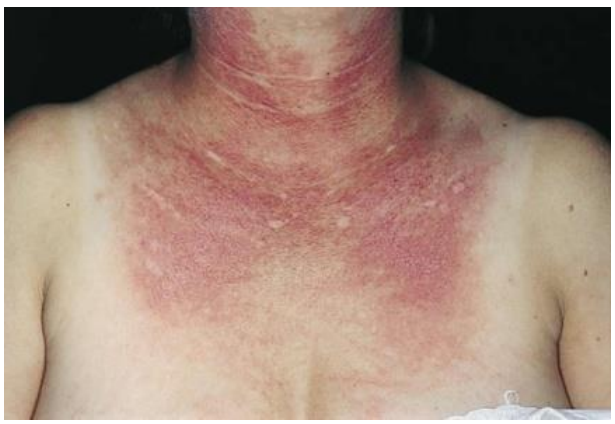


Fig (4) photosensivity of SLE

Discoid Rash

The third criteria may be discoid rash (sensitivity 18% specificity 59%). Discoid Lupus erythematous (DLE), a chronic dermatological disease, is that the commonest sort of chronic CLE. Lesions could also be a part of systemic lupus or may represent discoid lupus without organ involvement, which may be a separate diagnostic entity.The shaped of Lesions are disc like erythematous plaques of varying sizes, and contain areas of follicular hyperkeratoses, which are painful if lifted manually. Disease progression result in pigmentary change, permanent, depressed scarring, atrophy, and alopecia. Lesions spread centrifugally and may merge. Although most patients' manifest lesional confinement to the head area.

for which minimum criteria is the presence of DLE lesion above and below the neck. Mucosal surfaces also be suffering frome lesions that appear just like DLE of the skin or by lesions that may simulate lichen planus. Palms and soles can involved

DLE may occur in patients with SLE, and soma few e patients (<5%) with DLE progress to SLE. Patients may complain of mild pruritus or occasional pain within lesions, but most patients are asymptomatic. Patients with widespread involvement often have hematologic and serologic abnormalities, are more likely to develop SLE, and are more difficult to treat.[8]

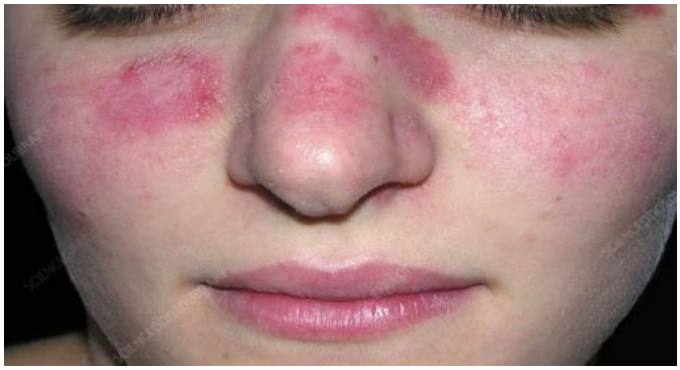


Fig (5) Discoid Rash of SLE

Oral Ulcers

The fourth criteria of ACR is oral ulcers (including oral or nasopharyngeal ulcers). Lupus should considered in patient who experience painless or painful oral (or less frequently nasal or vaginal) ulcers. Palatal ulcers are most specific for SLE. The prevalence of oral lesions is reported to be 7–52% of patients with SLE .The relationship between mucosal lesions and systemic disease activity is additionally nonconsensual. The buccal mucosa, hard palate surface, and vermilion border are the locations most often involved by lesions , which may be three types (discoid lesions, erythematosus, and ulcers) and should coexist [(9)]

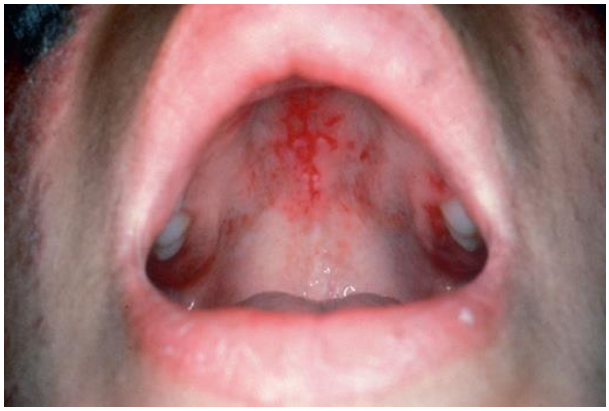


Fig (6) Oral Ulcers of SLE

Alopecia

Alopecia is an often less specific cutaneous criteria of SLE, occurring in about 45% of people with lupus at while during the course of the disease. It affects the temporal regions or creates a patchy pattern of hair loss. Most often, the hair loss occurs at the onset of illness and should be one of the primary symptoms of the disease. When the disease under control, the hair should grow back. Sometimes there a rash in the scalp, usually subacute or chronic discoid that interferes with the follicle of the hair. During this situation, the patient is left with a permanent area of cicatricial alopecia.[(10)]

Lichen Planus in LE

LE in lichen planus are usually seen as individual entity. Their overlap comprises patients who have clinical, histological, and immunopathological characteristics of both diseases simultaneously. The clinical presentation may be a pruritic papular eruption characterized by its violaceous color polygon shape and, sometimes, fine scale. It most ordinarily found on the flexor surfaces of the upper extremities, on the genitalia, and on the mucous membranes. Pruritus is common in lichen planus but varies in severity dcounting on the sort of lesion and therefore the extent of involvement.

Hypertrophic lesion is extremely pruritic while oral lesions is also asymptomatic or have a burning sensation, or they may even be painful if erosions are present. Large, annular, hypertrophic lesions and mucous involvement are more likely to chronic.[11]

Cutaneous Vasculitis

Cutaneous vasculitis is presented during a multivariety of morphological lesions like punctuate lesions, palpable purpura, urticaria, ulcers, papules, erythematosus plaques or macules, and erythema with necrosis which will be self-limiting or relapsing . Cutaneous lesions could also be the only manifestation of the vasculitis or could also be part of a systemic involvement.[12]

Urticarial Vasculitis

Urticarial vasculitis is eruption of erythematous wheals that resemble urticarial but histologically shows changes of leukocytoclastic vasculitis. Inversely to urticaria it usually painful nonpruritic and typically persists for quite 24 hours.[12]

Lichenoid DLE (LE/lichen planus overlap)

Clinical presentations of LE-LP overlap syndrome vary, starting from typical, flat-topped papules, as seen in lichen planus, to atrophic scaling plaques, more like discoid LE (DLE). Although some reported to coexist with DLE, LE-LP overlap syndrome has also been reported that occur with subacute cutaneous LE, clinically represented by hyperkeratotic annular and polycyclic laques.[13]

Subacute cutaneous lupus erythematosus

Subacute cutaneous LE may be a clinically distinct subset of cases of LE that most frequently present in white women aged 15 to 40, consisting of skin lesions that are scaly and evolve as poly-cyclic annular lesions or plaquesalmost like those of plaque psoriasis

Characteristically the lesions appear in sun-exposed areas like the vee of the \ckline or the forearms.[14]

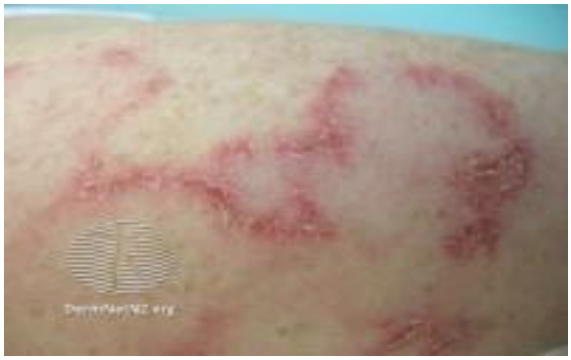


Fig (7) Subacute cutaneous lupus erythematosus

Lupus panniculitis/lupus profundus

Lupus erythematosus panniculitis (LEP), also called lupus erythematosus profundus, may be a rare variant of chronic cutaneous LE (CCLE).LEP commonly presents within the third-to-sixth decades of life, with female predilection. Foremost frequent cutaneous manifestations are indurated plaques or subcutaneous and sometimes ulcerations. The lesions occur predominantly on the face, upper arms, upper trunk, breasts, buttocks, and thighs.LEP not a typical cutaneous manifestation of systemic Alupus erythematosus (SLE), but individuals with LEP developing finally into SLE are reported.[15]

Raynaud syndrome

Due to vasospasm within the fingers and toes causes characteristic blanching and cyanosis .[16]

Telangiectasias

Telangiectasias, describe as spider veins, are small dilated blood vessels which will occur near the surface of the skin or mucous membranes. Telangiectasia of the nailfolds occur in individuals with lupus and correlate with systemic disease activity and Raynaud's phenomenon. Telangiectasias may also be found on the sides of lesions of discoid lupus.(7)

Livedoreticularis

Livedoreticularis is a common skin finding consisting of a mottled reticulated vascular pattern that appear as a lace-like purple discoloration of the skin. 78% consecutive patients with systemic LE assessed for the presence of livedoreticularis.(16)

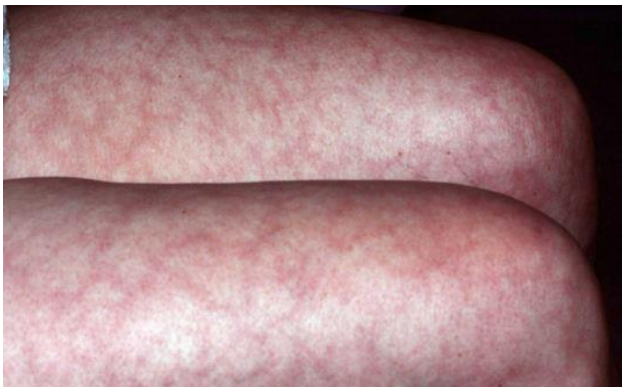


Fig (8) Livedoreticularis

Atrophie Blanche

Atrophie blanche is a particular sort of scar arising on the lower legs that happens after a skin injury when blood supply is poor. The clinical presentation painful petechial, itchy papules, or hemorrhagic bullae. This last one become, necrotic and forms ulcer, which successively become atrophic angular scars with hyperpigmented of the encompassinging skin usually on the lower extremities.(17)

Bollous lesions in SLE

Bullous systemic LE is autoantibody-mediated subepidermal blistering disease which happens in pts with SLE. Blisters and vesicules may arise on erythematous or normal area skin and nonscarring. Lesion occur on sun-exposed or flexural skin. Blistering often parallel flares of SLE involving other organ system, especially kidney.[6]

Lupus Band Test

The lupus band define as deposition of immunoglobulin and/or complements at the dermoepidermal junction which is a histological feature of LE. Examination of tissue could also be done either on lesional skin or on nonlesional skin. Nonlesional skin biopsies may be from sun-exposed or non exposed areas.

Testing of nonlesional, nonexposed skin is termed the lupus band test, approximately 70% of patients with various subtypes of LE show a positive lupus band test when skin biopsies are performed in normal appearing skin. The normal appearans of skin patients showing the diagnosis of chronic cutaneous Lupus erethymatous, are nearly always negative for lupus band test; however, when performed withinin the cutaneous lesions, lupus band test is positive in about 80% of patients.

Other cutaneous manifestations

Multiple eruptive dermatofibromas have been described in SLE. Leg ulcers, typically deeply punched out and with very little or no inflammation, could also be seen on the pretibial or malleolar areas. Many of those patients present with a livedoid pattern, and a lot of have an antiphospholipid antibody. Sneddon syndrome consist of livedoreticularis and strokes associated with a hyalinizing vasculopathy.

Calcinosis cutis is uncommon but may be dramatic. Also seen as plaquelike or papulonodular depositions of mucin. These reddish purple to skin-colored lesions often present on the trunk and arm or head and neck Last, a symmetric papular eruption of the extremities may occur. These skin-colored to erythematous lesions smooth, ulcerated or umbilicated surface show vasculitis or, in older lesions, a palisaded granulomatous inflammation.

Conclusion

Systemic LE is chronic inflammatory disease with a good spectrum of clinical and serological manifestations caused by autoantibody production,complement activation, and immune complex deposition.The etiopathogenesis of SLE not entirely clear,but it believed that it results from the complex interaction between genetic and hormonal factors, and environmental exposures. Abnormalities of the skin, hair or mucous membranes are second most common manifestation of SLE and are seen in 72–85% of patients, they occur at any stage of the disease, regardless of disease activity, and indeed are the primary sign of disease in 23–28%. In addition to discoid lesions, which are included in the ACR criteria for diagnosing Systemic lupus erythematous.

The skin is involved in most systemic lupus erythematosus (SLE) cases and may be the only organ involved in cutaneous lupus erythematosus.The 11 criteria developed by the ACR in 1982 are often helpful in distinguishing CLE from SLE, but considering the overestimation of dermatological criteria (butterfly rash, photosensitivity, discoid lesions, and oral ulcers) 4 criteria for a diagnosis of SLE are fulfilled too often.The most common skin manifestation is that the classic malar butterfly rash, an erythematous rash covering both cheeks and therefore the bridge of the nose, with sparing of the nasolabial folds. The second commonest skin manifestation is maculopapular rush which will be located anywhere on the body. Also are present: nasal/genital ulcer, panniculity, alopecia and purpura.

Most patients with systemic LE report photosensitivity or butter fly lesions, sunlight may precipitate systemic disease de novo or aggravate existing disease. In most recent studies show that cutaneous manifestations are more common in the summer months, These observations suggest that summer UV light exposure may lead to flares of the disease . Therefore, consequent protection against sun light also as other physical and mechanical injuries are of significant value for the course and prognosis of the disease. The lupus band test as an immunologic test for Lupus patients can also be a helpful instrument for diagnosis and differentiate the cutaneous disease from systemic.A understanding of the cutaneous manifestations of Systemic lupus erythematous is important for diagnosis, prognosis of disease. dermatologists should cooperate with other specialties to supply optimal care of SLE patient.

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