

CONNECTIVE TISSUE DISEASES

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LUPUS ERYTHEMATOSUS (LE)

A spectrum of clinical forms, with chronic cutaneous LE and systemic LE polar expressions of disease activity.

CHRONIC CUTANEOUS (LE)

DISCOID LUPUS ERYTHEMATOSUS (DLE)

Well-defined, erythematous, slightly infiltrated, “discoid” macules, with adherent thick scales, follicular plugging and telangiectasia. Older lesions show atrophic scarring, pigmentary changes, and verrucous hyperkeratosis.

Lesions often limited to the face (malar areas and nose), but scalp, ears, lips, and oral mucosa can also be involved.

In patients with disseminated DLE, further lesions occur on the upper trunk and arms; systemic LE may develop in some.

HISTOPATHOLOGY

- epidermal thinning
- hydropic degeneration of basal layer
- dense lymphocytic infiltrate in upper dermis

TREATMENT

topical

- corticosteroid applications
- intralesional steroids
- sunscreen

systemic

- antimalarials
- corticosteroids

LE PANNICULITIS (LE PROFUNDUS)

Subcutaneous nodules that are firm, sharply defined, and asymptomatic. Especially on proximal extremities. Overlying skin usually normal, but may show DLE. DLE may occur in other sites. Leave depressions, because of loss of panniculus.

SUBACUTE CUTANEOUS LE

9% of LE cases. Extensive erythematous nonscarring lesions in face, neck, upper trunk, arms, and hand dorsa. Severe photosensitivity. Occasional mild systemic manifestations; can progress to systemic LE, usually without renal disease.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Associated with systemic symptoms; leads to death within 10 years in half of patients.

The American Rheumatological Association lists 14 manifestations of SLE; the diagnosis is made if four or more of these signs are present.

The diagnosis can also be made if a patient has three of the following four symptoms:

- skin lesions consistent with SLE
- renal involvement
- serositis
- joint involvement

CUTANEOUS MANIFESTATIONS

- eruption on malar area and bridge of nose (butterfly)
- erythema and telangiectasia of finger- and toe tips, palms and soles
- diffuse hair loss
- mucous membrane lesions
- leg ulcers (severe cases)
- bullae (some cases)

SYSTEMIC MANIFESTATIONS

- arthralgia (earliest, and commonest abnormality)
- thrombosis and thromboembolism
- renal involvement
- myocarditis and pericarditis
- vasculitis in CNS, with convulsions

- idiopathic thrombocytopenic purpura
- hepatitis
- gastro-intestinal involvement
- pleural effusion and interstitial lung disease
- muscle atrophy
- Sjögren's syndrome, Hashimoto's thyroiditis

IMMUNOLOGIC FINDINGS

Multiple antibodies in serum of patients with SLE.

- Antinucleoprotein antibodies used in two diagnostic tests
 - + fluorescent antinuclear antibody (ANA) test
Very sensitive, but not specific for SLE. Good for screening.
 - + LE cell test
Very specific, but time consuming.
- Anti-doublestranded DNA (ds DNA) antibodies
 - + specific; indicates SLE with renal involvement.
- Additional antibodies
 - + anti-singlestranded (ss) DNA antibodies
 - + antinuclear ribonucleic acid protein (anti-nRNP) antibodies
- Occasionally, antinuclear antibodies are absent, and cytoplasmic antigens Ro and La are present. Special subset of SLE with photosensitivity and low incidence of renal involvement. (Subacute cutaneous LE)

LUPUS BAND TEST

Direct immunofluorescence of skin biopsy

- Biopsy of involved skin
IgG, IgM and complement along dermal-epidermal junction in DLE and SLE
- Biopsy of uninvolved exposed skin
lupus band negative in DLE, positive in SLE
- Uninvolved sun-protected skin
correlation between incidence of lupus band, and severity of renal disease

OTHER LAB TESTS

- albumin, red cells, casts in urine
- haemolytic anaemia, thrombocytopenia, lymphopenia, leukopenia
- antiphospholipid antibody
- Coombs test positive
- false positive syphilis serology
- increased levels of IgG
- albumin : globulin ratio reversed

TREATMENT

- bed rest
- nsoids and salicylates
- antimalarials
- systemic corticosteroids
- immunosuppressives (azathioprine, cyclophosphamide)
- renal dialysis

DERMATOMYOSITIS

Dermatomyositis: skin and skeletal muscle affected.

Polymyositis: absence of skin involvement.

Both occur in childhood, or middle age.

CUTANEOUS LESIONS

- erythematous to purple patches with slight oedema
- face: swelling and redness of periorbital skin and eyelids (heliotrope erythema)
- chest, limb extensors: LE-like lesions, or poikiloderma (atrophy, with lines of hyper- and hypopigmentation)
- knuckles: Gottron papules
- cutaneous lesions may precede muscle weakness by months or years

SKELETAL MUSCLE INVOLVEMENT

- weakness, muscular pain, atrophy
- proximal muscles of limbs, and anterior neck, involved first
- pharynx: dysphagia, aspiration
- intercostal muscles: respiratory failure
- calcinosis of subcutaneous and periarticular tissue (children)

NEOPLASIA WITH DERMATOMYOSITIS

- In adults, malignancy frequently associated with dermatomyositis

LABORATORY FINDINGS

- elevated s-creatinine kinase
- elevated aldolase, lactic dehydrogenase, and transaminases
- Fe-deficiency anaemia, leukocytosis
- increased ESR
- positive ANA-test
- direct immunofluorescence of skin: positive in one third

TREATMENT

- systemic corticosteroids (1mg/kg daily)
- adjuvant therapy
 - + methotrexate
 - + mycophenolate mofetil
 - + azathioprine
- cyclophosphamide in severe cases
- intravenous immunoglobulin

SCLERODERMA

Two types: localized scleroderma (morphoea), and systemic scleroderma (progressive systemic sclerosis).

MORPHOEIA

Lesions limited to skin and subcutaneous tissue.

FIVE TYPES

- plaque type: round or oval lesions, indurated, with smooth surface and ivory colour – commonest type
- guttate lesions: small, superficial
- linear type: extremities, or anterior scalp
- segmental: one side of face
- generalized: very extensive, mainly in children

HISTOPATHOLOGY

An early inflammatory and late sclerotic stage exist. In the sclerotic stage, collagen bundles in the dermis are thickened and closely packed. Eccrine glands are atrophic, and fatty tissue reduced or absent.

SYSTEMIC SCLERODERMA

CUTANEOUS LESIONS

- not demarcated, as in morphea; skin diffusely indurated
- acrosclerosis: lesions start on hands and face, and extend centripetally
- mostly preceded by Raynaud's phenomenon
- underlying fat undergoes fibrosis, and skin becomes firmly bound to underlying structures
- skeletal muscles affected, resulting in atrophy
- contractures and ankyloses
- other changes: hypo- or hyperpigmentation; telangiectasia of hands and face; ulcerations of fingertips and knuckles; calcinosis cutis of extremities

INTERNAL ORGANS

- oesophagus: dysphagia
- intestine: malabsorption or ileus
- lungs: dyspnoea, cor pulmonale
- kidneys: uraemia, malignant hypertension (commonest cause of death)
- CREST syndrome often has better prognosis (Calcinosis cutis, Raynaud's phenomenon, Esophagus; Sclerodactyly, Telangiectases); death from visceral involvement, as well as polyarthritis, is scarce

LABORATORY FINDINGS

- Antinuclear antibodies present in nearly all patients

In CREST variant, majority are anticentromere in type
Scl-70 antibody in 20% of patients with systemic scleroderma

- Rheumatoid factor (35%)
- False positive syphilis serology (5%)
- IgG increased (26%)
- Increased ESR (66%)

TREATMENT

Often unsatisfactory, esp regarding cutaneous lesions

- physical therapy to maintain joint mobility
- exposure to cold, and smoking, forbidden
- Raynaud's phenomenon: vasodilating drugs (Ca-channel blockers, angiotensin II receptor antagonists, topical nitrates, prostanoids, sildenafil)
- pulmonary hypertension: sildenafil, IV iloprost
- cyclophosphamide for severe skin and internal lesions
- methotrexate, D-penicillamine
- systemic corticosteroids
- renal crisis: ACE inhibitors