CONNECTIVE TISSUE DISEASES

Inherited /acquired disorders of connective tissue system

Collagen diseases- unacceptable term
Lupus Erythematosus

Classification

DLE - Localized
- Disseminated

SCLE

SLE Genetically distinct
Somatic mutation
Discoid Lupus Erythematosus

Autoimmune in 50%
Peak age of onset - 40 years
Relatively benign
Mainly affecting face
Characteristic histopathological,
Hematological & Serological changes
ETIOPATHOGENESIS

Genetic factors

3 genotypes according to age of onset
HLA B7, B8, CW7, DR2, DR4, DQW1

Somatic mutations at autosomal loci in lymphoid stem cell
- Forbidden clone of lymphocytes synthesizing cellular autoAB’s
Environmental factors

Trauma, mental stress, sunburn,
Infection, exposure to cold,
Pregnancy,
Drugs - isoniazid, penicillin,
griseofulvin, dapsone
HISTOPATHOLOGY

- Liquefactive degeneration of basal cell layer
- Degenerative changes in connective tissue,
- Hyalinization, oedema, fibrinoid change
- Patchy dermal lymphocyte infiltrate mainly peri-appendageal
Immuno-histology

IgG, IgA, IgM & complement present at DEJ in 80% patients in skin lesions present for more than 6 weeks

Patterns

Homogenous, granular, thready

Unlike SLE

- not in uninvolved skin
Clinical Features

Rash over face, cheeks, nose

Other sites
- Scalp, ears, arms
- Legs & trunk

Variably sized, well-defined erythematous, patches/plaques
Adherent scale - removed
horny plugs in dilated pilosebaceous canals –
‘Tin-tack’/‘carpet tack’ sign
Wide follicular pits in ear
Heals with atrophy & scarring
Annular atrophic plaques
  Face, neck, behind ears

Warty lesions
  Nose, ear, temple, scalp

Hyperkeratotic
  Arms & legs

Tumid type
  Cheek, whole limb

LE telangiectoides
  Face, neck, ears
  Breast, hands
Chilblain lupus

sites- Toes, fingers, neck, Calves, knees, ears, fingers

clinically- Atrophic, spindling 

Hyperextensions of terminal phalanges
Mucus Membranes

Lips - thick, rough, red, superficial ulceration & crusting
Eye lesions
Oedema & conjunctival redness

Eyelids
Infiltrated, scaly, peripheral redness

Nails
Sub ungual hyperkeratosis,
Red-blue colors of nail plate
Lab Abnormalities

↑ S.globulin - most common (55% patients)
Anemia, leucopenia, thrombocytopenia,
↑ ESR
False +ve reactions for syphilis
Anti nuclear Ab’s - 35%
Differential Diagnosis

Lichen planus
PMLE
Seborrheic dermatitis
Lichen sclerosus
Morphea
Chilblains
Sarcoidosis
Prognosis
Untreated - persistant
Complete remission in 50%
Scarring (57%)
Scarring alopecia (35%)
Long duration -
Raynaud’s
Scalp involvement
Chilblains like lesions
Risk of SLE - 6.5% in localised DLE
22% in Disseminated
Treatment

General measures
- Photoprotection

Topical Steroids

Resistant cases - I/L steroids (lips, mouth, ears)
  I/L Interferons
  CO2 laser
  Pulsed dye laser
  Argon laser (telangiectatic type)
Oral therapy

Antimalarials

Chloroquine sulphate 200mg B.D
Reassessed at 6 weeks

Side effects

Corneal deposits, retinopathy, pigmentation of nails & legs, bleaching of hair, Exfoliative dermatitis, Myopathy, neuropathy, mental disturbances
HCQS (Hydroxychloroquine)

400-800mg B.D

75% patients respond

Oral steroids- if antimalarials fail

Prednisolone 5-15mg/day help in joint pains & scalp involvement
Others

B-carotene 50mg TDS
Clofazamine 100mg/day
Dapsone 100mg/day
Etretinate 1mg/kg/day
Methotrexate
Thalidomide (100-200/day)
Cyclophosphamide (50-200mg/day)
Gold salts (6-9mg/day)
Phenytoin 100mg TDS
Subacute cutaneous lupus Erythematosus

10% LE patients
Non scarring papulosquamous (2/3)
Annular polycyclic lesions (1/3)
Resolve with grey-white hypopigmentation & telangiectases
- Follicular plugging & hyperkeratosis not prominent
- Non scarring alopecia & photosensitivity (50%)
- 50% fulfill ARA criteria for SLE (arthritis MC)
- Fever, malaise & CNS involvement frequent
Mild renal disease
Lesional subepidermal Ig deposition (60%)
speckled IgG

Drugs
Hydrochlorothiazide
Griseofulvin
PUVA
Subacute Cutaneous Lupus Erythematosus
Subacute Cutaneous Lupus Erythematosus
Treatment

Sunscreens
Topical steroids
Antimalarials
Oral steroids
Etretinate, Dapsone
Cyclosporine, oral gold
Systemic lupus Erythematosus

- Systemic association of immunological abnormality with pathological changes in various organs
- Particularly Skin, joints & vasculature
- F:M 8:1
- Age of onset - 38 years
Etiopathogenesis

Unknown

Genetic factors

HLA - B8, DR3, A1, DR2, DQ
Auto antibodies

Non organ specific humoral auto AB’s
- hallmark of SLE

Anti ds DNA & Anti Sm Ab’s
- More specific

Antinuclear & Anti Sm Ab’s
- More common
Environmental factors

- Silicone implants, heavy metals, mercury, gold, & trichloroethylene
- Infections, stress, hormonal factors
- UV radiation
- Virus - Myxovirus
- Drugs -n Hydralazine, minocycline
  anticonvulsant, procainamide
Histopathology

Hyperkeratosis without parakeratosis
Liquifactive degeneration of basal cell
Edema in dermis with vesicle formation
at DEJ
Perivascular lymphocyte infiltration
Immuno Histology

Predominantly IgG, IgM, IgA with complement C1, C3 at DEJ in 80% patients
Uninvolved skin from exposed area - 75%
Uninvolved unexposed skin +ve in 50%
Immunofluorescence patterns

- Homogenous
- Stripped
- Thready

Old lesions  Uninvolved skin  New lesions
Internal organs

Characteristic microscopic features
Haematoxylin bodies in heart valves
Periarterial fibrosis
Wire-loop lesions in kidney
Clinical Features

Arthritis
Cutaneous changes
Renal abnormality
Psychiatric disturbance
Serological findings
Pericarditis
Pleurisy
Abdomen pain
PUO, Menstrual disturbances, Raynaud’s
GENERALISED SYSTEMS
Weight loss, Fever, Fatigue, Aching, Weakness

EYE
Retinal exudates, Blindness, Conjunctivitis

CENTRAL NERVOUS SYSTEM
Seizures, Paralysis, Psychiatric Disorders, Neuropathies

SKIN COVERING
Baldness, Discoid L.E., Butterfly rash, Raynaud's Syndrome, Photosensitivity, Mucosal ulcers of Nose, Mouth and Vagina

BLOOD
Decreased platelets, Abnormal Autoantibodies

LINING MEMBRANES
Pericarditis, Pleurisy, Endocarditis

KIDNEY
Renal Failure, Proteinuria, Cedema, Hypertension

LYMPHADENOPATHY
Spleen enlargement

GASTRO-INTESTINAL TRACT
Poor appetite, Vomiting, Diarrhoea

REPRODUCTIVE
Menorrhagia, Amenorrhoea, Prematurity, Stillbirths

MUSCULOSKELETAL
Arthralgias, Arthritis and Myalgias
American Rheumatism Association Criteria for SLE

1. Malar Rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcers - Palate
5. **Non erosive arthritis**
6. Renal disorder (Persistent proteinuria >0.5g/d or cellular casts)
7. Neurological - Seizures/ psychosis
8. Hematological - Hemolytic anemia, leucopenia, thrombocytopenia
9. Immunological - LE cells, anti DNA Ab, anti Sm Ab
10. Antinuclear Ab’s
Lab Investigations

LE cell Test (80%)

LE cells are polymorph with ingested nuclear material from degen. WBC’s (those of an Ab to deoxyribonucleoprotein)
Treatment

Optimal function with minimal disease

General - Photoprotection

Steroids - Prednisolone 60mg/day,

\[ \downarrow 10-15\text{mg/d} \]
Chloroquine/HCQS - Less useful
Immuno suppressives - Azathiophrine, Cyclophosphamide
Plasmapheresis, Cyclosporin, Methotrexate