433 Teams

DERMATOLOGY

Lecture (5)

Lupus Erythematosus

derm433team@gmail.com

جامعة الملك سعود
King Saud University

Objective:

1. differentiate between the various types of Lupus
2. recognize how Lupus affects the various systems of the body
3. identify all of the current treatment options available for Lupus
4. recognize the psychosocial effects that Lupus has on the patient and their family

Lupus Erythematosus:

Defenition: Chronic inflammatory small vessel vasculopathy that affects the skin in the majority of cases. Cutaneous lesions are a source of disability & ,on many occasions, an indicator of internal disease.

Small vessel Vasculopathy Means that it can be anyware.

Pathogenesis: LE is a multifactorial disease with genetic and immunopathologic abnormalities.

Predisposing Factors:

Genetic predisposition: HLA-B8, -DR2, -DR3…, various polymorphisms: TNF-R gene, CD19 gene…

Complement defects: C1q, C1r, C1s, C4, C2 (skin &renal dis.)

Exogenous factors: UV radiation & medications

Individual factors: hormone status, altered immune status.

Transplacental transfer of maternal autoantibodies (anti-SSA, anti-SSB) can lead to neonatal LE.

Classification:

1- Chronic cutaneous LE: (skin findings)

- Discoid lupus (DLE)
- Lupus tumidus
- Lupus profundus

2- Subacute cutaneous LE (SCLE): (predominently skin finding, mild systemic involvement.)

3- Systemic LE (SLE): (primarily systemic involvement)

Chronic Cutaneous Lupus Erythematosus:

Defenition: Chronic scarring erythematosquamous lesions primarily in sun exposed skin.

Epidemiology:

-Female > male (2-3 :1)

-Age of Onset : 15-60 **(15-45)**

Clinical Features :

- **it heals with scarring**

- Erythematous well-circumscribed persistent plaques with follicular hyperkeratosis, telengiectases, peripheral hyperpigmentation and central hypopigmentation.

- sun exposed areas: scalp, forehead, cheeks, nose, ears, upper lip and chin.

- Common causing of scarring alopecia especially in blacks.

- Small percentage of patients develop SLE.

-Mostly purly Cutaneous without systemic involvement , however leasons could occur in SLE.

-Lesions last for months to years. usually no symptoms, sometimes slightly pruritic orsmarting . no General Symtoms.

- lesions start as bright red papule evolving into plaques , sharply marginated , with adherent scaling .

-"Burned out" lesions may be pink or white macule and scars , but also be hyper pigmented , especially in person with black or brown skin.

Histology:

-Epidermal atrophy with vacuolar degeneration of basal cells, telengiectases, follicular plugs, lymphocytic infiltrate in dermis.

- Shows spines resembling carpet tacks .

Diagnosis:

- Skin biopsy

- Direct immunofluorescence.(deposits of IgG & C3 along the basement membrane in 80 % of affected skin) **nonexposed skin always negative.***

- Labs: negative or low-titer ANA (Because there is no systamic involvment)

- Exclude SLE

*It means that when u do Direct immunofluorescence only the leasion will show changes. i.e : surrounding skin is normal. Unlike boulus Diseases where all skin is affected

Chronic Cutaneous Lupus Erythematosus:

Differential diagnosis:

1- Psoriasis (silver scale)

2- Rosacea (pustules, ears spared)

3- Tinea faciei (KOH examination)

4- Granuloma faciale(brown color, no scarring)

In general : cutaneous lesions are not an indication for systemic corticosteroids in LE.

Therapy:

-Sun avoidance and high potency sunscreens.

-Short term high-potency topical corticosteroids.

-Topical immunomodulators (pimecrolimus, tacrolimus).

-Cryotherapy or IL corticosteroids for stubborn lesions.

Systemic Rx for wide spread, recalcitrant disease:

-Antimalarials: hydroxychloroquine 200-400 mg dailyor chloroquine 250 mg.

-Dapsone 50-100mg daily.

-Thalidomide: 50-200mg daily (watch for neuropathy)

- Management:
  - **Local Glucocorticoids and Calcineurin Inhibitors**: Usually not very effective; topical fluorinated glucocorticoids with caution because of atrophy. Intralesional triamcinolone acetonide, 3–5 mg/mL, for small lesions.
  - **Antimalarials**: Hydroxychloroquine, ≤6.5 mg/kg body weight per day. If hydroxychloroquine is ineffective, add quinacrine, 100 mg three times a day. Monitor for ocular side effects.
  - **Retinoids**: Hyperkeratotic CDLE lesions respond well to systemic acitretin (0.5 mg/kg body weight).
  - **Thalidomide**: 100–300 mg/d is effective. Observe contraindications.

Subacute cutaneous Lupus Erythematosus:

Defenition: Widespread , photosensitive skin disease, mild systemic involvement, charecterictic autoantibody pattern & good prognosis.

Epidemiology:

-Female > male (8 :1)

-Uncomman in blacks or hispanics.

Clinical Features :

- **it heals with NO scarring**

-Symmetrical widepread ***nonscarring*** erythematous patches & plaques.

-Usually light exposed areas: trunk and arms.

-Sometimes annular or targetoid lesions. (3 or 2 Circles merged together)

-Often arthralgia, rarely renal disease.

-Mild fatigue , malaise, fever of unknown origin.

Histology:

-interface dermatitis with vacuolar degeneration & superficial dermal infiltrates.

Diagnosis:

- Skin biopsy

- Direct immunofluorescence.(deposits of IgG & C3 along the basement membrane in lesional lesions 50-60 %; in normal skin in 10-20%.)

- Labs: positive for anti **SSA** & **SSB** and **low titer anti-dsDNA antibodies**, LBT + in 60%.

Differential diagnosis:

1- Tinea corporis

2- Tinea versicolor

Pregnant with +SSA may give birth to baby with neonatal lupas and heart block.

Therapy:

-Same as DLE.

-Emphasis on sun avoidance and sunscreens.

-Antimalarials usually necessary for either skin or arthritis,NSAIDS for joint pain.

- Management: topical glucocorticosteroids, pimecrolimus, and tacrolimus only partially helpful for skin lesions. Systemic thalidomide (100–300 mg/d) very effective for skin lesions but not for systemic disease. Hydroxychloroquine 400 mg/d, quinacrine hydrochloride 100 mg/d. In systemic involvement prednisone ± immunosuppressants.

Systemic Lupus Erythematosus:

Epidemiology:

-Female > male (6 :1)

-In prepubertal 3:1

- African-american > caucasian

-They develop the disaease at an early stage and higher mortality rate.

In SLE Oral Ulcers are PAINLESS.

In Elderly , Butterfly rash could be Rosacea

Clinical Features :

A) Cutaneous lesions

1- Butterfly rash

2- Discoid lesions

3- Alopecia (scarring)

4- nail folds changes : damaged cuticles with telengiectasia

5- oral lesions: palatal erythema or erosions

6- Bullous lesions

B) Systemic lesions:

The ACR criteria: 4 or more , accepted SLE.

Criterion	Definition
1.Malar rash	Fixed malar erythema, flat or raised
2.Discoid rash	Erythematous raised patches with keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3.Photosensitivity	Skin rash as an unusual reaction to sunlight, by patient history or physician observation
4.Oral ulcers	Oral or nasopharyngeal ulcers, usually painless, observed by physician
5.Arthritis	Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion
6.Serositis	a.Pleuritis (convincing history of pleuritic pain or rub heard by physician or evidence of pleural effusion) *or* b.Pericarditis (documented by electrocardiogram, rub, or evidence of pericardial effusion)
7.Renal disorder	a.Persistent proteinuria (> 0.5 g/day or > 3 +) *or* b.Cellular casts of any type
8.Neurologic disorder	a.Seizures (in the absence of other causes) *or* b.Psychosis (in the absence of other causes)
9.Hematologic disorder	a.Hemolytic anemia *or* b.Leukopenia (< 4000/μL on two or more occasions) *or* c.Lymphopenia (< 1500/μL on two or more occasions) *or* d.Thrombocytopenia (< 100,000/μL in the absence of offending drugs)
10.Immunologic disorder	a.Anti–double-stranded DNA *or* b.Anti-Sm *or* c.Positive finding of antiphospholipid antibodies based on (1) an abnormal serum level of immunoglobulin G or M anticardiolipin antibodies, (2) a positive test result for lupus anticoagulant using a standard method, or (3) a false-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test
11.Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any time and in the absence of drugs known to be associated with "drug-induced lupus syndrome"
For identifying patients in clinical studies, a person shall be said to have SLE if any 4 or more of the 11 criteria are present, either serially or simultaneously, during any interval of observation.	

Systemic Lupus Erythematosus

Management:

Table 3

Medications for the Management of SLE

	Medication	Dose Range
NSAIDs, salicylates		Doses toward upper limit of recommended range usually required
	Ibuprofen	400–800 mg 3–4 times/day; maximum dose: 3.2 g/day
	Naproxen	500–1,000 mg/day in two divided doses; may increase to 1.5 g/day of naproxen base for limited time period
	Aspirin	Initial: 2.4–3.6 g/day in divided doses; usual maintenance: 3.6–5.4 g/day; monitor serum concentrations
Antimalarials	Hydroxychloroquine (Plaquenil/Sanofi)	Initial therapy: 400 mg once or twice daily; maintenance: 200–400 mg/day
	Chloroquine	250 mg daily
	Quinacrine	100 mg/day (monotherapy or combination therapy)
Topical corticosteroids	Betamethasone dipropionate	Mild potency for face; mid to high potency for other areas. Apply thin film to affected areas once or twice daily. Maximum dose: 45 g/week
Topical sunscreens		SPF 30 minimum; SPF >30 for highly sensitive patients
Corticosteroids (PO, IV)	Prednisone, prednisolone	Acute: 1–2 mg/kg/day in 2–3 divided doses, maintenance: <1 mg/kg/day as single dose
	Methylprednisolone sodium succinate	High-dose pulse therapy: 1 g/day for 3 days (approved for lupus nephritis)
Immuno-suppressants	Cyclophosphamide IV	Induction: 500–1,000 mg/m^2 monthly for six months, then maintenance: 500–1,000 mg/m^2 every three months for 24 months
	Cyclophosphamide PO	1.5–3 mg/kg/day
	Mycophenolate mofetil (CellCept/Roche) PO	Induction: 2–3 g/day; maintenance: 0.5–3 g/day
	Azathioprine (Imuran/GSK) PO	Initial: 1 mg/kg/day for 6–8 weeks; increase by 0.5 mg/kg every 4 weeks until response or until dose reaches 3 mg/kg/day
	Cyclosporine (Neoral/Novartis)	3–5 mg/kg/day PO
	Methotrexate PO/IM	7.5–15 mg/week, with folic acid
	Immune globulin IV	2 g/kg IV over 2–5 days
	DHEA (prasterone/ dehydroepiandrosterone)	200 mg/day

SLE: systemic lupus erythematosus; NSAID: nonsteroidal anti-inflammatory drug; SPF: sun-protection factor; PO: by mouth; IV: intravenously; IM: intramuscularly. Source: References 7-9, 16, 20, 21, 25-39.

With rare exceptions, cutaneous disease should not be taken as an indication for systemic therapy except for antimalarials.

Drug-Induced Lupus Erythematosus

Defenition: Clinical syndrome resembling LE, induced by various medications, features anti-histone antibodies, usually resolve when drugs are stoppedpattern & good prognosis.

Clinical Features :

Similar to SLE but less severe.

Arthritis most common.

Procainamide causes serositis & pulmonary disease; renal, CNS and skin involvement uncommon.

Responsible Medication:

- Biologicals: IFNa,b , anti-TNF
- antihypertensives: hydralazine, methyldopa
- antiarrhythmic agents: procainamide, quinidine
- anticonvulsants: phenytoin
- others: minocycline, chlorpromazine, isoniazid

Therapy :

STOP MEDICATION

Manage as SLE but expect remission.

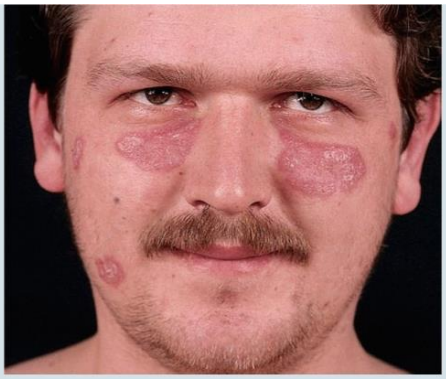

Figure 14-37. Chronic cutaneous lupus erythematosus Well-demarcated, erythematous, hyperkeratotic plaques with atrophy, follicular plugging, and adherent scale on both cheeks. This is the classic presentation of chronic discoid LE.

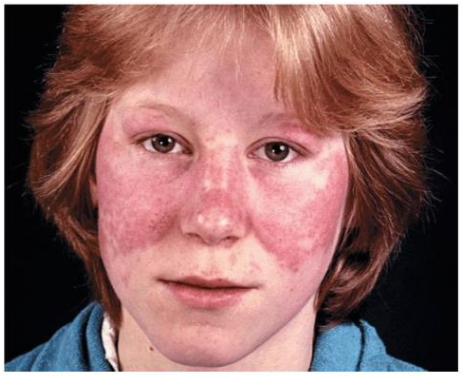

Figure 14-33. Acute systemic lupus erythematosus Bright red, sharply defined erythema with slight edema and minimal scaling in a "butterfly pattern" on the face. This is the typical "malar rash." Note also that the patient is female and young.

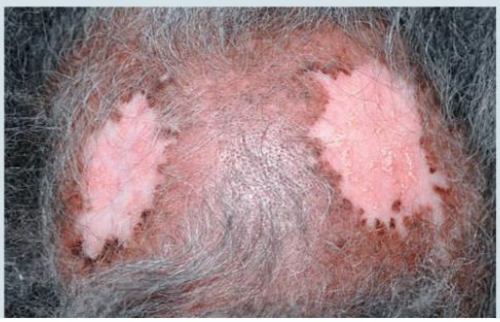

Figure 14-39. Chronic cutaneous lupus erythematosus Involvement of the scalp has led to complete hair loss with residual erythema, atrophy, and white scarring in this black male. Sharp demarcation of the lesions in the periphery indicates that these lesions originally were CDLE plaques.

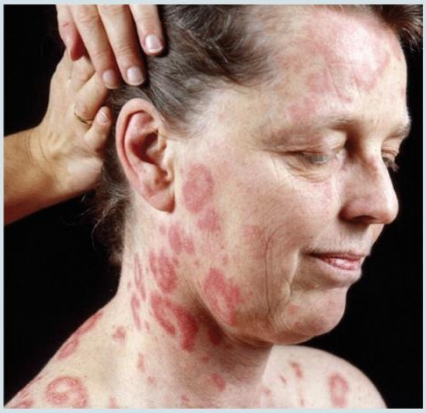

Figure 14-36. Subacute cutaneous lupus erythematosus Round, oval, and annular red plaques on the forehead, cheeks, neck, and upper trunk that show, but minimal, scaling in a 56-year-old woman. The eruption occurred after solar exposure. This is the annular type of SCLE.

Done By:

Abdulaziz Alsudairy	
Musab Almasry	