LUPUS TREATMENT

By: sh.assar MD

Assistant professor of rheumatology

NONPHARMACOLOGIC AND PREVENTIVE INTERVENTIONS

- Sun protection
- Diet and nutrition and Exercise
- Smoking cessation
- Immunizations:

Live attenuated vaccines (eg, measles, mumps, rubella, polio, varicella zoster, and vaccinia [smallpox]) can lead to complications in patients on immunosuppressive

- Treating comorbid conditions: Accelerated atherosclerosis, pulmonary hypertension, and APS syn.,osteopenia or osteoporosis

Drugs associated with SLE exacerbations

- Sulfonamide-containing antimicrobials
- minocycline

PHARMACOLOGIC THERAPIES

The choice of therapy is highly individualized depends on the :

- Predominant symptoms
- Organ involvement
- Response to previous therapy
- Disease activity and severity
- Adverse effects of individual therapeutic agents
- Patient preferences

GENERAL PRINCIPLES OF DRUG THERAPY

- In general, all patients with SLE with any degree and type of disease activity should be treated with **hydroxychloroquine or chloroquine**, unless these agents are contraindicated

- relief of constitutional symptoms, musculoskeletal manifestations, and mucocutaneous manifestations

- mostly observational evidence suggest that hydroxychloroquine may reduce flare rates, thrombotic events, organ damage accrual, and mortality

Predictors of SLE flare

- The most useful laboratory tests to predict an SLE flare (particularly lupus nephritis: ↑anti-dsDNA and a ↓ complement levels (especially CH50, C3, and C4) .Persistently ↓C1q are also associated with activity of lupus nephritis.

- Not all patients with these serologic markers have active disease, and these markers do not necessarily predict disease exacerbation

- Increased risk of SLE flare: SLE before age 25 ,patients who have renal, vasculitic, or neurologic involvement

- Almost any organ system can be involved in a lupus flare
- ●**Mild SLE flare :** new onset low-grade fevers, a malar rash, and arthralgias, and who also feels increasingly fatigued. Laboratory evaluation is notable for a mild leukopenia. This patient may require no treatment. Alternatively, the patient may require the addition of hydroxychloroquine or the equivalent of prednisone 7.5 mg per day or less.

- ●**Moderate SLE flare** : pleuritic chest pain ,arthritis. Laboratory : acute phase reactants. A CXRay is notable for a pleural effusion. The patient may require a short course of prednisone.

- ●**Severe SLE flare** : new onset renal insufficiency and significant proteinuria due to lupus nephritis. Laboratory :↓C3, C4, ↑ AntidsDNA , and ↑acute phase reactants. The patient may require high doses of glucocorticoids (eg, 1 to 2 mg/kg/day of prednisone or equivalent or "pulses" of methylprednisolone), additional immunosuppressive therapy (eg, cyclophosphamide, azathioprine, or mycophenolate mofetil), and/or hospitalization

MILD LUPUS MANIFESTATIONS

- Skin, joint, mucosal involvement
- Hydroxychloroquine or chloroquine, with and without NSAIDS, and/or short-term use of low-dose glucocorticoids (eg, ≤ 7.5 mg prednisone equivalent per da

MODERATE LUPUS INVOLVEMENT

- significant but non-organ-threatening disease (eg, constitutional, cutaneous, musculoskeletal, or hematologic

- hydroxychloroquine or chloroquine plus short-term therapy with 5 to 15 mg of prednisone (or equivalent) daily. Prednisone is usually tapered once hydroxychloroquine or chloroquine has taken effect.

- A steroid-sparing immunosuppressive agent (eg, azathioprine or MTX) is often required to control symptoms.

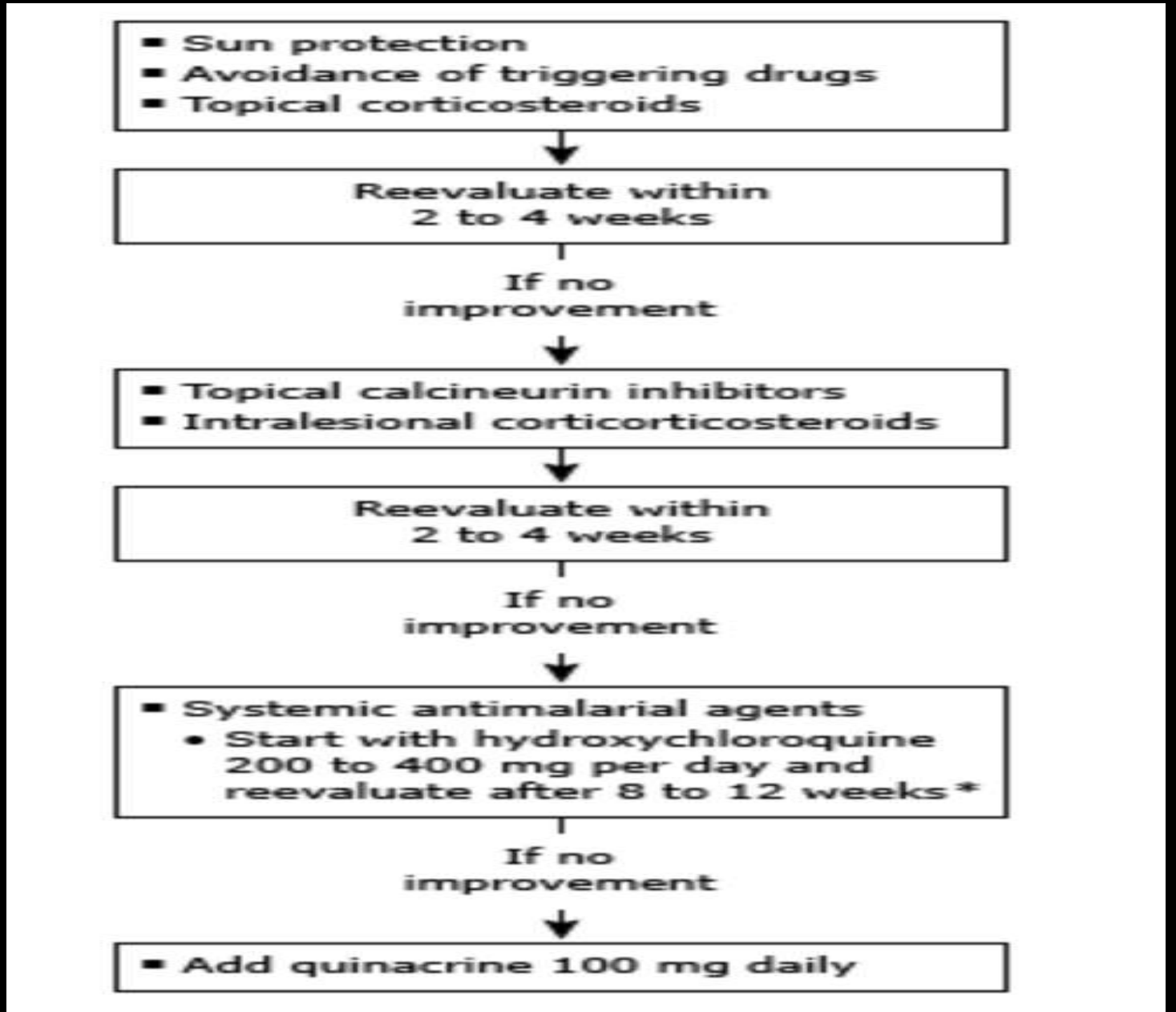
SEVERE OR LIFE-THREATENING LUPUS

- manifestations of major organ involvement (eg, renal and CNS)

- **induction therapy :** IV "pulses" of methylprednisolone, 0.5 to 1 g/ 3day, or 1 to 2 mg/kg/day in more stable patients) used alone or in combination with other immunosuppressive agents include mycophenolate, azathioprine, cyclophosphamide, or rituximab

- **maintenance therapy:** to consolidate remission and prevent flares. During this phase of treatment, the dose of prednisone or equivalent is reduced while monitoring clinical and laboratory measures of disease activity

Discoid Lupus And Subacute Cutaneous Lupus



Discoid Lupus And Subacute Cutaneous Lupus

- Patients with DLE or SCLE who have failed topical, intralesional, and antimalarial therapy can be treated with MTX , systemic retinoids, MMF, or dapsone

- When one or more of the above agents is unsuccessful:
- Thalidomide, IVIG, azathioprine, rituximab, Belimumab,and other immunomodulatory agents

- Clofazimine has also been used for the treatment of refractory cutaneous LE, but the availability of this drug is limited

Drugs implicated in the development of SCLE

ACE inhibitors (captopril, cilazapril)
Antiarrhythmics (procainamide)
Anticonvulsants (phenytoin, lamotrigine)
Antifungals (griseofulvin, terbinafine)
Antihistamines (cinnarizine/thiethylperazine)
Antineoplastics (docetaxel, paclitaxel, anastrozole, gemcitabine, doxorubicin, tamoxifen, leuprorelin)
Beta blockers (acebutolol, oxprenolol)
Calcium channel blockers (diltiazem, nifedipine, nitrendipine, verapamil)
Diuretics (hydrochlorothiazide, spironolactone)
Immune modulators (leflunomide, interferon-alpha, interferon-beta)
Lipid-lowering agents (pravastatin, simvastatin)
NSAIDs (naproxen, piroxicam)
Proton pump inhibitors (omeprazole, lansoprazole, pantoprazole)
Sulfonylureas (glyburide)
TNF-alpha inhibitors (etanercept, infliximab, adalimumab, golimumab)
Others (D-penicillamine, bupropion, ticlopidine, ranitidine*)

ARTHRITIS AND ARTHRALGIAS

- usually responds to the use of hydroxychloroquine and NSAIDs
- Short courses of low doses of glucocorticoids may be required to treat the arthritis in patients also having a systemic disease flare. For patients with persistent arthritis, additional DMARDs may also be used in a manner largely based upon the treatment of RA

- For patients with persistent arthritis unresponsive to methotrexate or leflunomide after three to six months of therapy, azathioprine may be substituted for these DMARDs.

- For persistent arthritis that has not responded to the therapies described above (including hydroxychloroquine, methotrexate, leflunomide, and azathioprine), we may try **belimumab**
- **avoid using tumor necrosis factor-alpha inhibitors to treat arthritis associated with lupus**

- refractory arthritis unresponsive to any of the therapies discussed above, rituximab may be used.

Management Of Thrombocytopenia

- **Isolated, mild thrombocytopenia:**
- review of the CBC,vitamin B12 and folate deficiencies, liver disease, and coagulation abnormalities, especially antiphospholipid antibodies

- **Acutely ill, severe thrombocytopenia, or other cytopenias:**
- review of medications; review of PBS for schistocytes or other abnormal cells, coagulation testing, and testing of renal and hepatic function. Disorders to be considered include thrombotic microangiopathies, CAPS, severe infections, HLH/MAS, and severe drug reactions

Management Of Thrombocytopenia

- Glucocorticoids are typically used as first-line therapy
- IVIG can also be used if there is a need to raise the platelet count more rapidly (eg, for surgery or an invasive procedure)
- Rituximab
- Romiplostim(Nplate): TPO mimetic
- splenectomy response may be less durable in the setting of SLE

Lupus nephritis

- Immunosuppressive therapy for focal (class III) or diffuse (class IV) lupus nephritis (LN) consists of initial and subsequent phases:

- Initial therapy with MMF or cyclophosphamide — For patients with diffuse or focal LN, we suggest initial therapy consisting of glucocorticoids in combination with either MMF or IV or oral cyclophosphamide.

- **We do not use rituximab as initial therapy**

- Monotherapy with glucocorticoids is not given

Lupus nephritis

- Although pulse IV cyclophosphamide has been best studied for initial therapy in diffuse LN and is most widely used, daily oral cyclophosphamide has also been used including in a short-course regimen followed by azathioprine or cyclosporine subsequent therapy.
- Alternative combination regimens for initial therapy:
- Belimumab plus mycophenolate or cyclophosphamide
- Belimumab in combination with standard initial therapy
- Calcineurin inhibitors plus mycophenolate: (include tacrolimus and voclosporin).

Lupus nephritis

- Rituximab is not used as initial therapy based upon data from a randomized trial that found **no statistically** significant difference in rates of complete or partial remission with rituximab plus MMF versus MMF alone.

- Rituximab may be used in the management of patients with resistant or relapsing LN, which is discussed separately

Subsequent therapy

- In most patients ,suggest MMF rather than azathioprine for subsequent therapy
- Although RCTs have shown that the mortality and rates of ESRD are similar for MMF and azathioprine, the risk of relapse appears to be higher for azathioprine
- Patients who are intolerant to both MMF and azathioprine can be treated with cyclosporine or tacrolimus

LUPUS PSYCHOSIS & MYELITIS

- high-dose IV ("pulse") glucocorticoids along with an evaluation for non-SLE causes.
- After non-SLE diagnoses have been excluded, immunosuppressive agents such as cyclophosphamide or mycophenolate can be added as steroid-sparing therapies.
- IVIG and rituximab have also been used in refractory cases
- Plasma exchange for severe myelitis or who do not respond to glucocorticoids

PULMONARY MANIFESTATIONS

- **Pleuritis (with or without a pleural effusion) :**

- NSAIDs unless contraindicated by GI or renal disease or heart failure
- naproxen 250 to 500 mg every 12 hours prefred , but other NSAIDs are acceptable
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- If there is no response within 1-2 weeks, systemic glucocorticoids (eg, prednisone 20 mg/day followed by a taper over 2-3 weeks

- oral glucocorticoids are used as initial therapy to achieve a more rapid response. Other immunosuppressive agents are rarely indicated.

ACUTE PNEUMONITIS

- Broad spectrum antibiotics, including coverage of encapsulated organisms, should be given while awaiting
- The mainstay of therapy is systemic prednisone (1 to 1.5 mg/kg per day orally in divided doses or equivalent IV dosing).
- If no response is seen within 72 hs or if the patient declines clinically IV pulse glucocorticoids
- In addition, immunosuppressive therapy (eg, cyclophosphamide, rituximab, IVIG) is usually initiated.

PULMONARY HEMORRHAGE

- IV pulses of methylprednisolone, 0.5 to 1 g/day for three days, in acutely ill patients or prednisone, 1 to 2 mg/kg/day, in more stable patients) with another immunosuppressive agent (eg, cyclophosphamide, rituximab, mycophenolate, azathioprine

- Cyclophosphamide or rituximab may be preferred when a rapid onset of effect is needed

- Plasma exchange and IVIG are considerations as additional therapy for refractory disease, although supportive data are limited

Refractory lupus

- Haemopoietic stem cell transplantation in Systemic lupus erythematosus