SYSTEMIC LUPUS ERYTHEMATOSIS

See also Lupus Nephritis

Background

1. Definition: Chronic autoimmune disease affecting multiple systems.
    - Secondary to autoimmune complexes and antibodies.
    - Varying courses among different people.

Pathophysiology[1]

1. Pathology of Disease
    - Chronic, antibody-immune complex deposition multi-organ disease with unknown etiology.
        - Possible auto-immune reaction to self-antigens; loss of self-tolerance.
            - Increased cell apoptosis → increased cell antigen presentation
            - Antibodies to DNA, nuclear histones, platelets, WBCs, RBCs, ribosomes, body tissues
            - Polyclonal B-cell activation, specific antigens (HIV, EBV) possible
            - Complement abnormalities: abnormal receptors, clearance, reduced
            - Direct antibody binding, immune complexes → organ destruction
        - Other involved factors
            - Genetic predisposition: HLA-DR2/3
            - Endocrine: lower free androgens, higher FSH, LH in postpubertal pts.
            - **Drug-induced**: hydralazine, isoniazid, procainamide, others
                - Drug metabolized to cross-reacting antigens
                - Positive ANA in 90%
        - Multi-organ system effects
        - Activation of innate immunity (dendritic cells) by CpG
2. Incidence, Prevalence
    - Highest incidence: Native Americans, Latin Americans, Blacks
    - ♀> ♂: up to 13:1
3. Risk Factors
    - Young female
    - Genetic, complement deficiencies
    - More common and severe in African or Asian descent
    - UV light
    - Possible risk factors
        - Infection
        - Epstein-Barr Virus
4. Morbidity / Mortality
    - 5yr survival: >90%; chronic disease: waxes/wanes
    - Mortality: infection, ARF, CNS complications, pulmonary hemorrhage, MI

Diagnostics

1. History[1]
    - Joint pain
    - Fatigue
    - Fever
    - Rash
    - Weight loss
    - Photosensitivity
    - Hair loss
2. Physical Examination[1]
    - Rash: different types
        - Malar ("butterfly") macular rash: both cheeks, nose
            - Erythematous, scaly, or thickened skin
            - Spares nasolabial folds
        - Discoid: erythematous papules/plaques, scaling → follicular plugging, alopecia, scarring
        - Scaling papules/plaques (psoriasis-like) in light exposed areas
        - Macular: distal extremities, fingernails
        - Widespread blistering
    - Mucocutaneous erythema/ulcers on palate/nose
    - Purpura (TTP), Livedo Reticularis
    - LAD, HSM, edema, HTN, Jaccoud arthropathy
    - Pericardial friction rub, murmurs, CHF, endocarditis signs
    - Meningeal signs, retinal changes (cotton-wool exudates), DVTs
3. Diagnostic Testing[1]
    - EKG
    - Echocardiogram if indicated
    - Chest X-ray
    - Biopsy for skin involvement
    - Renal biopsy
    - Lesion biopsy
4. Laboratory evaluation[1]
    -
        - 98% of patients with SLE are positive for ANA
        - 70% of patients with SLE are positive for Anti-dsDNA
        - 25% of patients with SLE are positive for Anti-Sm
        - 40% of patients with SLE are positive for Anti-RNP
        - 90% of patients with drug induced lupus positive for anti-histone antibodies; may also be positive in idiopathic lupus (sensitive, but not specific)
        - ESR increased
        - CRP increased
        - Decreased complement levels
    - General Work-Up
        - CBC
        - UA

        - CMP
        - Amylase, lipase
        - Creatine kinase
        - 24 hr urine for creatine clearance and proteinuria
5. Diagnostic "Criteria" (SOR C)[2] (See https://mospace.umsystem.edu/xmlui/bitstream/handle/10355/7504/WhatRoleLabTestingLupus.pdf?sequence=1)
    - "SOAP BRAIN MD" – at least 4 symptoms
        - Serositis
        - Oral or nasopharyngeal ulcers
        - positive ANA
        - Photosensitivity
        - Butterfly rash
        - Renal involvement
        - nonerosive Arthritis
        - Immunologic disorder
        - Neurologic disorder
        - heMatologic disorders
        - Discoid lupus

Differential Diagnosis

1. Mixed connective tissue dz
2. Systemic sclerosis
3. RA
4. Lyme's dz
5. HIV, CMV, IM
6. Hematologic malignancies
7. Glomerular Nephropathy
8. Chronic fatigue
9. Fibromyalgia

Therapeutics

1. Goal is minimal amount of treatment to control symptoms
    - Acetaminophen; spare opioid use[3]
    - Lifestyle[3, 11]
        - Avoid sun (exacerbates and causes flares)
        - Diet
            - Restrict calories, fat
            - Increase polyunsaturated fat
        - Avoid contraceptives if possible
        - Avoid emotional stress
    - NSAIDS, dose as tolerated; concerns: adverse effects on renal and hepatic function, GI bleeds[3]
    - Hydroxychloroquine (NOTE: Insert link to PEPID drug database) for treatment of joint and mucocutaneous symptoms[6]
        - Start as soon as diagnosed

        - 200 to 400 mg po daily
        - Safe and well tolerated
        - Helps flares and shows some organ protection
        - May take three to four months before it takes effect
        - Concern: retinal toxicity; annual eye exam
    - Methotrexate (NOTE: Insert link to PEPID drug database):
        - 15 mg weekly, and then titrated based upon response
    - Refractory symptoms: topical steroids vs. systemic steroids, as little and as quickly as possible[3]
    - Prednisone in low dose of 10-20 mg per day used
        - Immunosuppressive agents, recommended being dosed by Rheumatology consultant:
            - Azathioprine , in dose of 1.5 – 2.5 mg /kg/ day, for maintenance, lower dose for renal failure
            - Mycophenolate Mofetil (NOTE: Insert link to PEPID drug database)
            - Cyclophosphamide (NOTE: Insert link to PEPID drug database), IV dose - 500-1000 mg/meter square body surface area, given monthly, high toxicities
            - Belimumab – recently approved by FDA[10]
    - Neuropsychiatric symptoms[8]
        - Cyclophosphomide preferred over Methylprednisolone
    - DHEA may improve quality of life[9]
2. Other Types of Therapies[4]
    - Vitamin D supplement
3. Experimental Therapies with no difference[5]
    - Mycopheolate Mofetil (MMF) has similar response as cyclophosphomide[7]
    - Belimumab
    - Rituximab
    - Abatacept
    - Riquent

Follow-Up

1. Return to Office
    - Follow-up is on case by case basis; consider follow-up with nephrology and rheumatologist
2. Refer to Specialist
    - Referral to rheumatology for persistent disease refractory to treatment
    - Nephrology for acute renal failure
    - Eye exams
3. Admit to Hospital
    - Recommendations / urgency

Prognosis[1]

1. 95% survival rate at 5 yrs
2. 90% survival rate at 10 yrs

3. 78% survival rate at 20 yrs
4. Worse prognosis with high serum creatinine levels, hypertension, nephrotic syndrome, male sex, and/or ethnicity

Patient Education

1. http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/lupus.asp

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