Systemic Lupus Erythematosus

3

Overview

- Definition
  - Chronic, multisystem, autoimmune disease characterized by the production of numerous autoantibodies, mostly targeted against components of the cell nuclei
  - Damage is mediated by immune complex deposition in tissues (lupus nephritis and arthritis) or by direct effects of auto-Ab on cell surface molecules or serum components (hemolytic anemia, thrombocytopenia, antiphospholipid syndrome)
  - Disease severity and prognosis vary widely depending on the extent of organ involvement
- Symptoms
  - May precede systemic presentation
  - Wide ranging from dry eye symptoms, ocular pain and photosensitivity, to severe loss of vision
- Laterality
  - Can present unilaterally or bilaterally
- Course
  - Relapsing and remitting
- Age of onset
  - Typically late teens to early 40s, but 15% have late onset (late 50s–early 60s)
- Gender/race
  - F:M = 9:1
  - African Americans, Asians, and Hispanics are more affected
- Systemic association
  - Skin, joints, and kidneys are classically involved, but practically all organs can be affected, as the autoantibodies target all cellular nuclei
  - Skin (85% of patients): butterfly rash across the nose and cheeks, known as malar flush, is the most common finding. Other findings include discoid rash (erythematous raised areas with adherent keratotic scaling and follicular

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Table 3.1 The American College of Rheumatology Criteria for SLE

Malar rash
Discoid rash
Photosensitivity
Oral ulcers
Arthritis (nonerosive, 2 or more peripheral joints)
Serositis (pleuritis, pericarditis)
Renal disorders (proteinuria, nephritis)
Neurologic disorder (seizures, psychosis)
Hematologic disorder (hemolytic anemia, leukopenia, lymphopenia, thrombocytopenia)
Immunologic disorder (positive LE cell prep, anti-native DNA, anti-Sm, false-positive test for syphilis)
Antinuclear antibody in the absence of drugs associated with drug-induced lupus

plugging), cutaneous ulcers, splinter hemorrhages, purpuric skin lesions, and alopecia
- Musculoskeletal (85%): painful peripheral joints, non-deforming migratory polyarthritis, myalgia, and myositis
- Renal (50%): the major cause of morbidity and mortality in SLE patients; manifest as nephrotic syndrome, mesangial disease, focal or diffuse proliferative nephritis, and membranous glomerulonephritis
- Painless oral ulcers (30–40%)
- Neuropsychiatric (30%): seizures, organic brain syndrome, psychosis; transverse myelitis is rare (4%) but is associated with optic neuritis
- Raynaud's phenomenon (20%)
- Cardiac (20%): pericarditis, myocarditis, Libman-Sacks endocarditis (also known as nonbacterial thrombotic endocarditis + phospholipid antibody)
- Pulmonary: pleuritis and pneumonitis
- Hepatosplenomegaly and adenopathy are common despite not being part of diagnostic criteria (see Table 3.1)
- Hematologic: chronic anemia, hemolytic anemia, leukopenia, lymphopenia, thrombocytopenia, and increased thrombotic risks
- Secondary antiphospholipid syndrome (APL): deep vein thrombosis, cerebral arterial thrombosis, pulmonary embolism, thrombocytopenia, and recurrent fetal loss (typically in second and third trimesters) in the presence of APL antibodies

Exam: Ocular

External

- Discoid rash: erythematosus rash over the eyelids characterized by keratotic scaling and follicular plugging (may coexist with blepharitis and thus be overlooked)
- Strabismus due to cranial nerve or muscle involvement

Anterior Segment

- Keratoconjunctivitis sicca
- Episcleritis: generally benign and self-limiting
- Scleritis: anterior diffuse or nodular scleritis; necrotizing is rare
- Recurrent corneal erosions, peripheral keratitis (ulcerative or not), interstitial keratitis, endotheliitis
- Anterior uveitis is rare, non-granulomatous, and typically mild

Posterior Segment

- Retinopathy is the most well-recognized ocular manifestation of SLE, observed in 1 out of 10 patients
  - Microangiopathy is an extremely accurate barometer of systemic disease activity: cotton-wool spots (most common), arteriolar attenuation, retinal hemorrhage, microaneurysms
  - Retinal findings are compounded by systemic hypertension as a sequelae of SLE nephropathy: AV nicking, hard exudates, papilledema, and multifocal choroidal infarctions (Elschnig's spots)
  - Occlusive vasculitis affects the arterioles primarily, causing vascular sheathing and retinal opacification; diffuse non-perfusion leads to neovascular complications such as vitreous hemorrhage, tractional retinal detachment, and glaucoma
  - Venous occlusion is less common and may be due to venous stasis secondary to arterial occlusion
- Choroidopathy is uncommon
  - Present as single or multifocal serous retinal detachment
  - Associated with CNS vasculitis, nephropathy, and uncontrolled hypertension
  - Very responsive to systemic therapy
- Vitritis is rare
- Optic nerve involvement
  - Papillitis due to optic nerve vasculitis
  - Optic neuritis with resultant ischemic optic neuropathy; transverse myelitis is seen in more than half of these patients
  - Papilledema from rare pseudotumor cerebri

Exam: Systemic

- For clinical research, at least 4 of 11 ACR diagnostic criteria need to be met (Table 3.1). However, in practice, patients with fewer than 4 can still be diagnosed with SLE

Imaging

- OCT
  - Macular edema
  - Subretinal fluid in choroidopathy
- FA
  - Microaneurysms
  - Retinal non-perfusion with retinal neovascularization
  - Macular leakage
  - Optic nerve leakage
- ICG
  - Early, transient hypofluorescence followed by late hyperfluorescence in areas of choroidopathy
  - Multifocal hyperfluorescence during intermediate phase possibly indicative of immune complex staining

Laboratory and Radiographic Testing

- BMP, CBC, LFTs, and complete urinalysis
- ANA: nonspecific but present in almost all patients (97–98%); diffuse, peripheral or speckled pattern
- Anti-dsDNA and anti-Smith antibodies are most SLE-specific
  - Anti-dsDNA Ab: present in 30% of SLE patients, tends to represent a more serious disease state such as nephritis; however, its level cannot be used to monitor disease activity
  - Anti-Sm Ab: present in 20% of SLE patients; does not reflect disease severity
- Less SLE-specific antibodies: anti-Ro/SSA and anti-La/SSB (30–40%), anti-U1RNP (25%), APL (17%)
- Anti-histone Abs typically suggests drug-induced SLE, but may also be found in primary SLE
- Total complement (CH50), C3, C4 can be low due to complement consumption
- Chest X-ray
- Echocardiogram

Differential Diagnosis

- Adamantiades-Behcet's disease
- Polyarteritis nodosa
- Takayasu's disease
- Granulomatosis with polyangiitis (Wegener's)
- Syphilis

Treatment

- Oral NSAIDs and aminoquinolines, including chloroquine and hydroxychloroquine, may be appropriate for cutaneous lupus, arthritis, and serositis
- Systemic corticosteroids are reserved for hematologic, renal, and CNS diseases; long-term steroid-sparing immunosuppression may be necessary in systemic and ocular lupus (ocular flare-up can occur despite systemic quiescence)
- Plasmapheresis in combination with immunosuppressive therapy has been used in a few severe, recalcitrant cases
- Laser photocoagulation +/− intravitreal anti-VEGF are used in severe vaso-occlusive disease to prevent ischemic complications

Referral/Co-management

- Rheumatology
- Nephrology
- Other specialists per systemic involvement