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Systemic Lupus Erythematosus

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DEFINITION AND EPIDEMIOLOGY

Systemic lupus erythematosus (SLE) is the classic systemic autoimmune disease. The cause is unknown. SLE predominantly affects young women of childbearing age but can also afflict young men and older individuals of either sex.

The clinical manifestations are protean, ranging from mild symptoms of fatigue and oral ulcerations to life-threatening renal and neurologic disease. Typically, the disease fluctuates with periods of flares and clinical quiescence. However, recurrent disease flares and their treatment may ultimately lead to irreversible organ damage.

SLE is diagnosed by a thorough history, physical examination, and laboratory testing. A single diagnostic laboratory test for SLE is not available, and the diagnosis is often difficult, requiring many patient visits to numerous doctors.

Although there is no cure for SLE, patients are treated for the many chronic medical conditions associated with the disease with a variety of medications, primarily immunosuppressants. Unique consideration must be given to SLE patients regarding pregnancy, bone health, cardiovascular disease (CVD), and malignancy.

The reported incidence and prevalence of SLE vary greatly, reflecting the heterogeneity of the disease. The incidence of SLE worldwide is estimated at 1.8 to 7.6 cases per 100,000 persons per year and appears to have increased over time. Prevalence rates range from 14.6 to 149.5 cases per 100,000 persons.

During the childbearing years, the female-to-male ratio of SLE prevalence is 10 : 1 to 15 : 1. This gender discrepancy also exists but is less distinct (2 : 1) in young children and older patients. SLE also has a predilection for nonwhite ethnic populations, with greater prevalence rates for African Americans (three times), Afro-Caribbeans (five times), Asians (two times), and Hispanics than for whites. These patients also tend to have more severe SLE disease and worse overall prognoses than those who are white.

PATHOLOGY

Although SLE pathogenesis remains poorly understood, individuals who develop SLE likely have a genetic predisposition in the setting of immune system dysregulation, environmental triggers, and altered hormonal milieu. The genetic contribution to SLE is emphasized by the high concordance rate for monozygotic twins (>20%) and a lower concordance rate among other siblings (<5%). The search for genes involved in SLE pathogenesis is an active area of research. Genes coding for certain human leukocyte antigens, complement system components, immunoglobulin receptors, and various other proteins are being considered as candidate genes for SLE.

The many immune abnormalities in SLE implicate dysregulation of the humoral and cellular immune systems in the pathogenesis of the disease. Dysregulation leads to loss of self-tolerance and autoimmune destruction of healthy tissues, hallmarked by the production of autoantibodies and immune complexes.

Various environmental triggers, including microorganisms and ultraviolet light exposure, may influence the development of SLE and lupus activity. The striking differences in SLE prevalence between genders and the effect of pregnancy on disease activity suggest a role for hormones in SLE pathogenesis.

CLINICAL PRESENTATION

Virtually any organ system may be involved in SLE. Table 79-1 outlines some of the many clinical manifestations of SLE.

Constitutional Manifestations

Fatigue, fever, lymphadenopathy, and generalized arthralgias and myalgias are common in SLE patients. The most common symptom, fatigue (>90%), can also be the most debilitating. Other reasons for fatigue, including anemia, hypothyroidism, and fibromyalgia, should be excluded when attempting to diagnose SLE.

Mucocutaneous Manifestations

Oral ulcerations may be painful or painless and are classically located on the tongue or palate. Skin manifestations of SLE are common and include the classic malar (butterfly) rash, discoid lesions (i.e., permanent scarring and disfigurement), alopecia, and photosensitivity. Subacute cutaneous SLE can manifest with a psoriasiform rash or annular lesions mimicking tinea corporis. Frequently, acne rosacea is mistaken for a malar rash. A key distinguishing feature is that erythema in lupus malar rash does not cross the nasolabial folds.

Musculoskeletal Manifestations

Arthralgias and inflammatory arthritis are common manifestations in SLE (>75%). Lupus arthritis is usually nonerosive (unlike rheumatoid arthritis), but 10% of patients have Jaccoud's arthropathy with reversible hand deformities due to inflammation and joint tendon laxity.

Cardiopulmonary Manifestations

More than 60% of SLE patients have pericarditis and pleuritis during their disease course. Subsequent pericardial or pleural effusions are typically exudative. Valvular thickening and