

Systemic lupus erythematosus (SLE)

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Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple organ systems that is defined clinically and associated with antibodies directed against cell nuclei. Its multisystem manifestations and complications from use of immunosuppressive agents make the diagnosis and management of this entity challenging. In this article, we would like to present most common finding and its treatment plan.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple organ systems that is defined clinically and associated with antibodies directed against cell nuclei. Its multisystem manifestations and complications from use of immunosuppressive agents make the diagnosis and management of this entity challenging.

CAUSES

Although the specific cause of SLE is unknown, immune system deregulation and immune complex tissue damage at sites such as skin and kidneys, as well as direct antibody-mediated cytotoxicity that causes thrombocytopenia and hemolytic anemia, are suspected causes. Multiple immune disturbances may predispose to SLE

Different gene loci are known to increase the risk for SLE.

A genetic predisposition is supported by the 10-fold increase in concordance among monozygotic twins versus dizygotic twins.

Studies of the human leukocyte antigens (HLA) reveal that HLA-DR2 and HLA-DR3 occur more often in people with SLE than in the general population.

The presence of the null complement alleles and congenital deficiencies of complement (especially C4, C2, and other early components) are also associated with an increased risk of SLE.

The multitude of distinct genetic associations suggests a complex genetic predisposition for the disease, perhaps explaining the variable clinical courses and organ system involvement.

PATHOPHYSIOLOGY

Autoantibodies, circulating immune complexes, and T lymphocytes contribute to the expression of disease. Organ systems affected include dermatological, renal, central nervous system (CNS), hematological, musculoskeletal, cardiovascular, pulmonary, the vascular endothelium, and gastrointestinal.

The revised criteria for SLE must include four of the following at any time during a patient's history (specificity 95% and sensitivity 75%)

- Malar rash
- Discoid rash
- Photosensitivity
- Oral ulcers
- Arthritis
- Serositis
- Renal disorder
- Neurological disorder
- Hematological disorder
- Immunologic disorder
- Antinuclear antibody

CLINICAL FEATURES

- Systemic symptoms include a low-grade fever, fatigue, malaise, anorexia, nausea, and weight loss.

Initial presentation may involve one or more organ systems.

- Arthralgia is the initial complaint in many patients. Often, the pain is out of proportion to physical findings.
- Malar, butterfly rash over the cheeks and bridge of the nose with photosensitivity to ultraviolet (UV) light has been reported. It also involves the chin and ears.
- Painful or painless ulcers in the nose and mouth are frequent complaints.
- CNS symptoms may range from mild cognitive dysfunction to a history of seizures. Any region of the brain, meninges, spinal cord, and cranial and peripheral nerves can be involved. CNS events often occur when SLE is active in other organ systems. Intractable headaches and difficulties with memory and reasoning are the most common features of neurological disease in patients with lupus.
- Pleuritic pain, dyspnoea, cough, fever and chest pain are important cardiopulmonary complaints.
- Patients may present with abdominal pain, diarrhea, and vomiting. Intestinal perforation and vasculitis are important diagnoses to exclude.
- A number of other symptoms can be elicited by history which can help in identifying other pathology, including the following:
 - Stroke
 - Pulmonary embolus
 - Deep venous thrombosis (DVT)
 - Acute ischemia
 - Retinal vasculitis

PHYSICAL FINDINGS

- Fever is a challenging problem in SLE. It can be a manifestation of active lupus or a representation of infection, malignancy, or a drug reaction. Temperature higher than 104°F should prompt a search for infection and may be a lower-grade

temperature in patients on immunosuppressive agents.

- Malar rash is a fixed erythema sparing the nasolabial folds. It is a butterfly rash that can be flat or raised over the cheeks and bridge of the nose. It
 - Also often involves the chin and ears.
 - Discoid rash occurs in 32% of patients with SLE and can be disfiguring secondary to scarring. It presents as erythematous patches with keratotic scaling over sun-exposed areas of the skin and may occur in the absence of any systemic manifestations.
 - All patients experience painless or painful oral or vaginal ulcers at some time in their illness, which are helpful in making the diagnosis.
 - Gastrointestinal findings include vague abdominal discomfort, nausea, and diarrhea. Acute crampy abdominal pain, vomiting, and diarrhea may
- Constitutional
- Nonspecific fatigue, fever, arthralgia and weight changes are the most frequent symptoms in new cases or recurrent active SLE flares.
 - Fatigue, the most common constitutional symptom, can be due to active SLE, medications, lifestyle habits, or affective disorders. Fatigue due to active SLE generally occurs in concert with other clinical and laboratory markers.
 - Fever, another common yet nonspecific symptom, may also be due to many causes. Active SLE, infection, and drug fever are the most common etiologies. Careful history taking may help to differentiate these.

- Weight loss may occur with active disease. Weight gain may also be due to corticosteroid treatment or active disease such as nephrotic syndrome anasarca and significant vasculitis of the intestine.
- Renal

- The kidney is the most commonly involved visceral organ in SLE. Although only approximately 50% of patients develop clinically evident renal disease, biopsy studies demonstrate some degree of renal involvement in almost all patients.
- Glomerular disease usually develops within the first few years after onset and is usually asymptomatic.
- Acute nephritic disease may manifest as hypertension and hematuria.
- Nephrotic syndrome may cause edema, weight gain, or hyperlipidemia.
- Acute or chronic renal failure may cause symptoms related to uremia and fluid overload.
- Hematological
 - History of multiple cytopenias such as leucopenia, anemia or thrombocytopenia may suggest SLE, among other etiologies.
 - Leucopenia and, more specifically, lymphopenia are common in SLE
 - Anemia is occasionally overlooked in young menstruating women
- Joint findings
 - Tenderness, edema, and effusions accompany polyarthritis that is symmetric, nonerosive and usually nondeforming. It frequently involves the proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints of the hands, as well as the wrists and knees.
 - Consider avascular necrosis, which is common in patients receiving glucocorticoids.
 - Also consider septic arthritis when one joint is inflamed out of proportion to all other joints.
- Central nervous system findings
 - All types of seizures have been reported, with grand mal being the most common. Sensory or sensorimotor neuropathies are also common.
- Fundus
 - Funduscopic examination is important in patients with visual complaints. Retinal vasculitis can lead to blindness and are demonstrated by sheathed narrow retinal arterioles with white exudates adjacent to the vessels.
 - Renal system - Specific signs and symptoms of renal disease may not be apparent until advanced nephrotic syndrome or renal failure is present; therefore, obtaining a urine analysis and serum BUN and creatinine levels on a regular basis is important.
- Cardiovascular system
 - Atherosclerosis occurs prematurely in patients with SLE and is an independent risk factor for cardiovascular disease.
 - Pulmonary hypertension, vasculitis with digital infarcts, and splinter hemorrhages may be observed.
 - Systolic murmurs are reported in up to 70% of cases. They may be secondary to fever, hypoxia, anemia, or Libman-Sacks endocarditis.
 - Pericarditis is the most common presentation of heart involvement. It is usually associated with small effusions but it may involve larger effusions when uremia is concomitant. Myocarditis can cause heart failure, arrhythmias, and sudden death.

PULMONARY FINDINGS

- Tachypnoea, cough, and fever are common manifestations of lupus pneumonitis. Hemoptysis may signify pulmonary hemorrhage. However,

infection is the most common cause of infiltrates seen on radiographs.

ETIOLOGY

- Many of the clinical manifestations of SLE are caused by the effects of circulating immune complexes on various tissues or to the direct effects of antibodies to cell surface components.
- Whether polyclonal B-cell activation or a response to specific antigens exists is unclear.
- A lack of immune tolerance is observed in animal models.
- A genetic predisposition to the development of SLE exists. The concordance rate in monozygotic twins is approximately 25-70%. Each patient manifests his or her disease differently.
- If a mother has SLE, her daughter's risk of developing the disease is 1:40, and her son's risk is 1:250.
- Photosensitivity is clearly a precipitant of skin disease. The presence of antiphospholipid antibodies in patients dictates a constellation of signs caused by thrombosis.

DRUG-INDUCED LUPUS

Before making a diagnosis of SLE, it is important to rule out drugs, as the cause of the condition is important. Many pharmacological agents associated with a lupus like syndrome. Procainamide, hydralazine, and isoniazid have been studied the best. Many patients receiving these medications have positive antinuclear antibody test results and other serologic findings. Only a few have the clinical manifestations.

Drug-induced lupus differs from SLE by the following features:

- Nephritis and central nervous system features are not commonly present.
- No antibodies to native DNA or hypocomplementemia are present.

When the drug is discontinued, the patient has resolution of clinical manifestations and reverting of abnormal laboratory values to normal

LABORATORY FINDINGS

- Simple laboratory tests may be helpful in making the diagnosis or in evaluating a flare. However, the diagnosis is mostly dependent on the historical and physical findings.
- Rarely should autoantibody tests be ordered in the ED, unless that is done for the assistance of a secured rheumatology follow-up.
- Complete blood count (CBC)
 - Leukopenia, which generally is a good index for disease activity
 - Lymphopenia
 - Anemia of chronic disease
 - Evidence of a hemolytic anemia
 - Cytotoxic therapy (can cause anemia or leukopenia)
 - Thrombocytopenia may be profound secondary to antiplatelet antibodies or to antiphospholipid antibodies
- The partial thromboplastin time (PTT) may be elevated secondary to lupus anticoagulant (antiphospholipid antibody), which is associated with thrombosis.
- Urinalysis
 - Pyuria
 - Hematuria
 - Granular casts
 - Proteinuria
- Blood urea nitrogen (BUN) and creatinine
 - Usually not elevated at the onset of disease. It can be useful for the determination of any progression of renal disease

HISTOLOGIC FINDINGS

Renal biopsy confirms the presence of lupus nephritis, aids classification of SLE nephritis, and guides therapeutic decisions.

The World Health Organization classification for lupus nephritis is based on light microscopy, electron microscopy, and immunofluorescence findings.

IMAGING FINDING

- Chest radiographs
 - Effusion
 - Infiltrates
 - Cardiomegaly
- Echocardiogram may be indicated to evaluate any effusion causing pericardial pain or any valvular pathology and to confirm any signs of pulmonary hypertension.
- Magnetic resonance imaging (MRI) is most useful for assessing brain pathology.
- Computed tomography (CT) is useful to rule out bleeding or mass lesions.

TREATMENT

Conservative management with nonsteroidal anti-inflammatory drugs including salicylates is recommended for arthritis, arthralgias, and myalgias not requiring immunosuppression. Only initiate high-dose glucocorticoids and cytotoxic agents by, or in consultation with, a rheumatologist. Patients with thrombosis require anticoagulation with warfarin for a target international normalized ratio (INR) of 3-3.5. Antibiotics may be required

PREVENTION

Advise patients to use a sunscreen. Exposure to ultraviolet light causes SLE to flare in approximately is appropriate in the treatment of ordinary and opportunistic infections.

COMPLICATIONS

- Vasculitis and its various complications
- Pericarditis
- Myocarditis
- Lupus pneumonitis

- Pulmonary hemorrhage, pulmonary hypertension
- Proliferative glomerulonephritis
- Hemolytic anemia, thrombocytopenia
- Intravascular thrombosis (e.g., stroke and myocardial infarctions)
- Complications of high dose glucocorticoid therapy
- Complications of cytotoxic agents

SPECIAL CONSIDERATIONS

- Whether flares of SLE are more frequent during pregnancy is controversial. The flares do not seem to be exceedingly more serious compared to those in non-pregnant patients. Pre-eclampsia, fetal wastage, prematurity, and intrauterine growth retardation are more frequent. Predictors for fetal loss include active nephritis at conception and the presence of antiphospholipid (aPL) antibodies.
- High-dose aspirin and NSAIDs should be avoided in the last few weeks of pregnancy. Hydroxychloroquine has not been shown to induce congenital malformations. Furthermore, unnecessary discontinuation of hydroxychloroquine during pregnancy may result in lupus flares. Prednisolone and methylprednisolone are the corticosteroids of choice, if necessary, during pregnancy because of their minimal placental transfer.

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