RadioGraphics

Imaging Findings in Systemic Lupus Erythematosus[1]

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CME FEATURE

See the questionnaire on pp 1211–1217.

LEARNING OBJECTIVES FOR TEST 4

After reading this article and taking the test, the reader will be able to:

- Describe the pathogenesis of SLE and the complications of therapy for this disease.
- Recognize the radiologic patterns of disease in SLE.
- Discuss the importance of imaging in the management of SLE.

Systemic lupus erythematosus (SLE) is an unusually complex autoimmune disease that is encountered in every radiology subspecialty because of its multisystem involvement and the wide age range of affected patients. There are no universally accepted diagnostic imaging criteria for SLE, and in fact, many SLE patients present with systemic findings and laboratory abnormalities and do not require imaging. Nevertheless, radiology plays an ancillary role in the diagnosis and management of this often insidious disease, and knowledge of the spectrum of radiologic findings in SLE and its complications is crucial for proper image interpretation. Imaging is often performed in patients with a known diagnosis of SLE to determine the extent and severity of disease, which depend on the extent of organ involvement, and to monitor complications. In addition, imaging may be important in selected patients with diseases such as pneumonia who present with atypical symptoms due to immunosuppressive therapy.

Abbreviations: aPL-ab = antiphospholipid antibody, AVN = avascular necrosis, CNS = central nervous system, SLE = systemic lupus erythematosus, WHO = World Health Organization

Index terms: Antiphospholipid syndrome • Lupus erythematosus, **.612[2]

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[2]**. Multiple body systems

Imaging Findings in SLE

System	Components	Manifestations
Respiratory	Pleura	Effusion, pleuritis, fibrosis
	Parenchyma	Infection, hemorrhage, pneumonitis, fibrosis (mild)
	Pulmonary vasculature	Pulmonary arterial hypertension, pulmonary embolism
	Diaphragm	Diaphragmatic dysfunction
	Lung	Pulmonary infection
Cardiovascular	Myocardium	Myocarditis
	Pericardium	Effusion, pericarditis
	Valves	Valvulitis, Libman-Sacks endocarditis
	Vasculature	Atherosclerosis (arteries), vasculitis
Gastrointestinal	Esophagus	Hypomotility, reflux esophagitis
	Gallbladder	Acalculous cholecystitis
	Pancreas	Pancreatitis
	Bowel	Ischemia, vasculitis, edema
Genitourinary	Kidneys	Glomerulonephritis, nephrotic syndrome
	Vasculature	Renal vein thrombosis
Musculoskeletal	Joints	Arthritis
	Ligaments	Laxity, instability
	Bone	AVN, infarction, insufficiency fracture, osteomyelitis
Neurologic	Cerebral vessels	Vasculitis, dural venous sinus thrombosis
	Brain	Cerebritis, intracranial hemorrhage, infarction, infection

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by inflammation, immune complex deposition, vasculitis, and vasculopathy (1). SLE affects one out of every 700 white females and one out of every 245 black females. In adults, females are affected nine to 13 times more often than males, whereas in children, males are affected two to three times more often. The peak age at onset is the 2nd to 4th decades of life, but individuals of all ages can be affected (2).

SLE affects multiple components of the immune system, including the complement system, T suppressor cells, and cytokine production, resulting in the generation of autoantibodies, which can circulate for many years prior to the development of clinical SLE (1,3). Activation of the complement system manifests as increased plasma levels of complement breakdown products (C3a, C3d), the formation of immune complexes in tissues, and decreased serum levels of factors in both the classic and alternate complement pathways (4). The immune complexes recruit B lymphocytes, resulting in the formation of autoantibodies. The normal immune system does not permit generation of an autoimmune response. In SLE, however, the normal suppressive controls on the immune system are dysfunctional, resulting in an unchecked autoimmune response. In addition, dysfunction of the immune system in SLE results in an increased prevalence of lymphoreticular malignancies and frequent infections (4).

Eleven criteria established by the World Health Organization (WHO) are used in the diagnosis of SLE. These criteria include malar rash, discoid lesions, photosensitivity, oral ulcers, nonerosive arthritis, serositis (pleuritis or pericarditis), renal involvement, seizures or psychosis, hematologic abnormalities, immunologic abnormalities, and a positive antinuclear antibody test. When four or more of these criteria are met, whether serially or simultaneously, the diagnosis of SLE can be established with 98% specificity and 97% sensitivity (5). Because the manifestations of SLE often do not occur simultaneously, the diagnosis is usually not made at initial presentation. A high degree of clinical suspicion and reevaluation over time are crucial to the correct diagnosis of SLE and may suggest the possibility of SLE before clinical criteria are met.

Unlike the WHO criteria, there are no universally accepted imaging criteria for the diagnosis of SLE, and not all SLE patients need imaging because many will present with systemic findings as well as laboratory abnormalities. However, knowledge of the spectrum of radiologic findings in SLE (Table) and of complications related to therapy may help confirm the diagnosis when less than four of the 11 WHO criteria are met and may help direct management when there are complications related to therapy. In a patient with a known diagnosis of SLE, imaging is often performed to determine the extent and severity of disease and to monitor the myriad complications that arise from the disease and its therapy. The severity of disease in SLE is classically defined on the basis of the number of organ systems involved, not on the basis of disease complications or complications of therapy. In addition, in se-

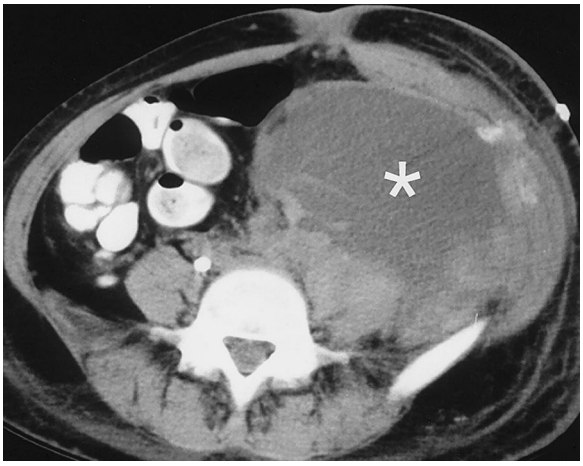


Figure 1. Massive retroperitoneal hemorrhage due to thrombocytopenia in a 21-year-old woman with SLE and aPL-ab syndrome. Contrast material–enhanced computed tomographic (CT) scan shows a large, heterogeneous retroperitoneal fluid collection (*) that represents hemorrhage.

lected patients with diseases such as pneumonia who present with atypical symptoms due to immunosuppressive therapy, imaging may be important for prompt diagnosis of and initiation of therapy for complications of SLE.

In this article, we discuss and illustrate the various radiologic manifestations of SLE that we have encountered in the respiratory, cardiovascular, gastrointestinal, genitourinary, musculoskeletal, and neurologic systems as well as findings in disease complications and complications related to therapy. We also review antiphospholipid antibody (aPL-ab) syndrome, which occurs frequently in SLE patients.

Antiphospholipid Antibody Syndrome

Between 27% and 42% of SLE patients have aPL-ab syndrome, which is characterized by arterial and veno-occlusive disease, thrombocytopenia, and recurrent vascular thromboses and miscarriages (2,4,6–9). These antibodies target cell surface molecules on vascular endothelium and platelets, and their presence often precedes vascular thrombosis by months or even years (4,6). Although the exact cause of aPL-ab syndrome is not known, disruption of the normal coagulant and thrombolytic systems by antibodies reacting with cell membranes has been suggested (10). In addition, an acquired free protein S deficiency, which is seen in patients with aPL-ab syndrome, has also been implicated (8).

Patients with aPL-ab syndrome can present with recurrent strokes, Budd-Chiari syndrome, dural venous sinus thrombosis, ischemic bowel, and recurrent pulmonary embolism. The diagnosis of aPL-ab syndrome is established when at least one clinical criterion (deep venous thrombosis, arterial thrombosis, pregnancy loss, thrombocytopenia) and one laboratory criterion (presence of immunoglobulins [IgG, IgM, IgA] against cardiolipin, presence of lupus anticoagulant) is met. Minor criteria for the diagnosis of aPL-ab syndrome may include heart valve abnormalities, livedo reticularis, migraine, pulmonary hypertension, avascular necrosis (AVN), myelopathy, and chorea. Serum levels of lupus anticoagulant serve as a marker of functional activity of aPL-ab syndrome (2,4,6).

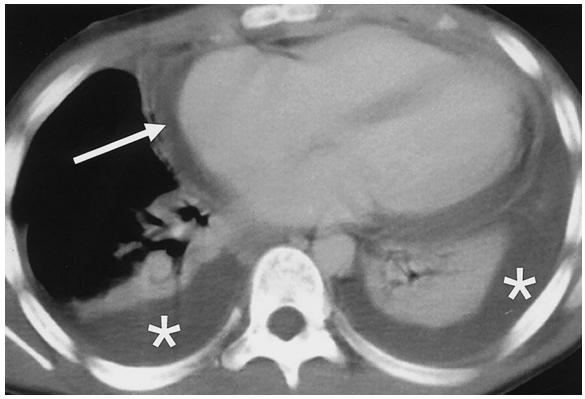


Figure 2. Serositis in a 13-year-old boy with SLE. Contrast-enhanced CT scan shows bilateral pleural effusions (*), cardiomegaly, and a pericardial effusion (arrow). Bilateral lower lobe atelectasis is also present.

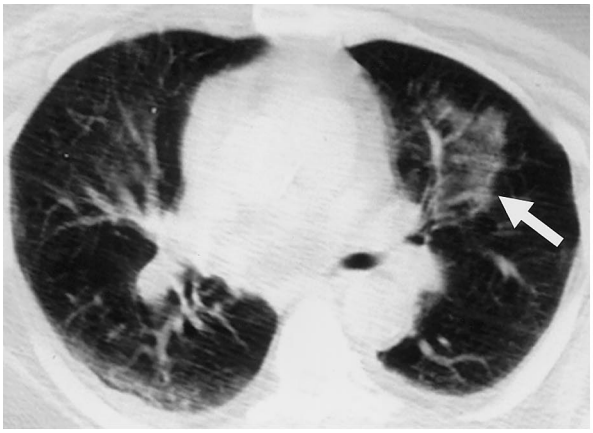
Acute vascular occlusion in aPL-ab syndrome is noninflammatory and may be preceded by endothelial injury, unlike the immune complex–mediated inflammatory vasculitis seen in SLE without aPL-ab syndrome. Inflammatory vasculitis is treated with corticosteroids, whereas vascular occlusion in aPL-ab syndrome is treated with anticoagulants, predisposing patients to life-threatening hemorrhage (Fig 1) (2).

Respiratory Disease

Involvement of the respiratory system in SLE is relatively common. Between 40% and 57% of patients with SLE will have symptoms of dyspnea and poor exercise tolerance (2). These symptoms may arise from primary pulmonary dysfunction, as a complication secondary to infection, or from a disease process in another organ such as renal failure leading to pulmonary edema. SLE can affect the pleura, lung, and respiratory muscles, all contributing to respiratory dysfunction.

Pleura

Pleural effusions (Fig 2) are the most common manifestation of SLE in the respiratory system and are bilateral in approximately 50% of patients



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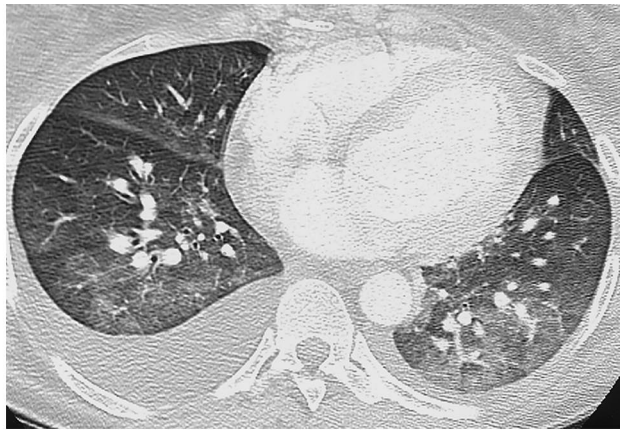

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Figures 3, 4. **(3)** Acute lupus pneumonitis in a 61-year-old woman. Contrast-enhanced CT scan shows a lingular area of patchy increased attenuation (arrow) and small bilateral pleural effusions. **(4)** Acute pulmonary hemorrhage in a 21-year-old woman with SLE. Contrast-enhanced CT scan shows patchy ground-glass attenuation in the posterior lower lobes. Bilateral pleural effusions are also present.

(11). Pleural effusions in SLE are generally small and are exudative, containing lupus erythematosus cells, immune complexes, and anti-DNA antibodies, among other things. Pleuritis and pleural fibrosis are reported in 50%–83% of SLE patients in some autopsy series (11). Although an isolated pleural effusion is a nonspecific radiographic finding, its presence, particularly when chronic, may suggest SLE when clinical evaluation suggests an underlying autoimmune process. Diagnostic thoracentesis under ultrasonographic (US) or CT guidance may aid in differentiating between pleural effusions from SLE and pleural effusions from other causes, especially when they are new or large, enabling prompt initiation of treatment with anti-inflammatory and immunosuppressive agents.

Parenchyma

Over one-half of patients with SLE develop pulmonary disease, with pneumonia, pulmonary hemorrhage, and lupus pneumonitis being the most common manifestations (12–14). Acute pneumonitis (Fig 3), which occurs in up to 12% of patients (12), manifests as unilateral or bilateral patchy consolidation, typically in the lung bases, resulting from alveolar capillary injury leading to edema and hemorrhage. An accompanying pleural effusion is often present (11,12). Focal consolidation from acute pneumonitis may be difficult to differentiate from that due to pneumonia, and, given that infection is more common, it is imperative to exclude an infectious source with both clinical and laboratory evaluation before considering lupus pneumonitis.

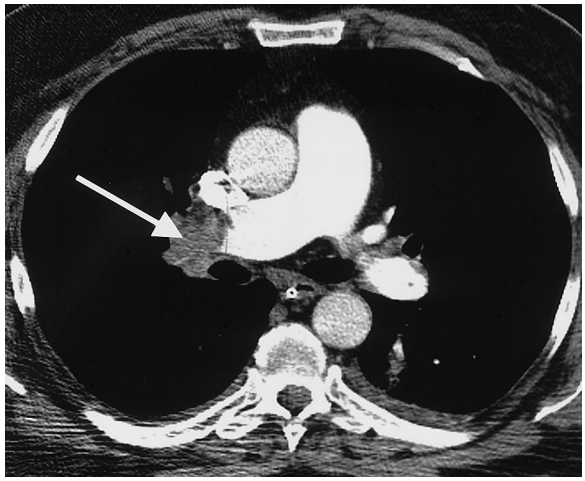
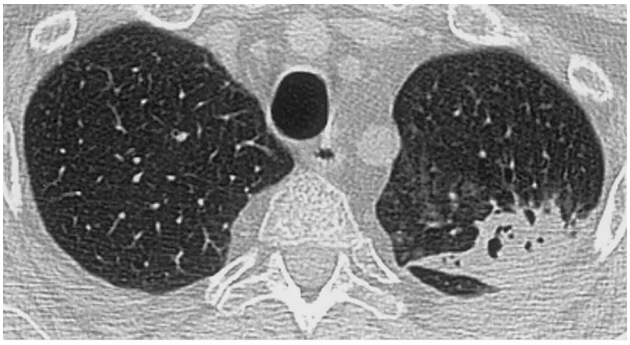


Figure 5. Acute pulmonary embolism in a 66-year-old man with SLE and aPL-ab syndrome. Pulmonary CT angiogram shows a large clot in the central right lung (arrow).

Pulmonary alveolar hemorrhage (Fig 4) is a rare complication of SLE and is either immune mediated or secondary to infection or uremia. Patients are typically acutely ill with hemoptysis, fever, cough, and hypoxemia, and blood loss can be extensive. Mortality rates of 70%–90% have been reported (15). At chest radiography, patchy bilateral and acinar areas of increased opacity, predominantly in the lower lungs, may be present.

Unlike other collagen-vascular diseases such as rheumatoid arthritis and scleroderma, chronic interstitial pneumonitis and pulmonary fibrosis occur in less than 3% of SLE patients and may represent sequelae of acute pneumonitis (11,16–18). Thin-section CT can aid in the evaluation of interstitial lung disease and may show subtle abnormalities when chest radiographic findings are



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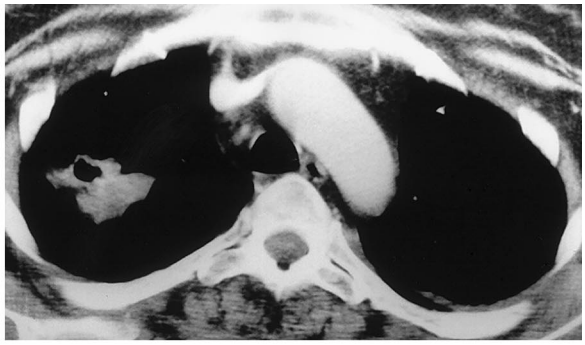

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Figures 6, 7. **(6)** *M tuberculosis* in a 48-year-old woman with SLE. Unenhanced CT scan shows consolidation with cavitation in the left apex. **(7)** *Nocardia* infection in a 32-year-old woman with SLE. Contrast-enhanced CT scan demonstrates consolidation with cavitation in the right upper lobe.

normal and findings are discordant with the patient's symptoms and pulmonary function test results (11,16–18). Irreversible lung disease and pulmonary fibrosis, characterized by architectural distortion, honeycombing, and subpleural thickening, should be differentiated from acute alveolitis, which demonstrates ground-glass opacity and is reversible with corticosteroid treatment. This is an important distinction, because reversible disease, especially parenchymal lung disease, should be treated promptly to prevent long-term sequelae of pulmonary fibrosis and secondary pulmonary arterial hypertension, both of which affect not only quality of life but also the function of other organ systems in SLE.

Pulmonary Vasculature

Pulmonary arterial hypertension is an increasingly recognized complication of SLE and is more common in patients with aPL-ab syndrome (19,20). Pulmonary arterial hypertension occurs in 14% of SLE patients secondary to chronic interstitial disease and in 25% of SLE patients with aPL-ab syndrome (20). The increased prevalence in aPL-ab syndrome is thought to be due to recurrent pulmonary emboli (20). The pathogenesis of pulmonary hypertension in SLE is unknown but has been associated with vasculopathy, recurrent pulmonary embolism (Fig 5), and parenchymal disease (11,16,19,20). There is currently no efficacious therapy for pulmonary hypertension, and prognosis is poor, with steady decline in pulmonary and cardiac function.

Diaphragm

Up to 25% of SLE patients are affected by respiratory muscle dysfunction, which often manifests as elevated hemidiaphragms at chest radiography (11). Patients may exhibit radiologic evidence of linear atelectasis and an ill-defined juxtadiaphragmatic areas of increased opacity (6,11). Pulmonary function tests show decreased static lung volumes and vital capacity, findings that are consistent with a restrictive process; however, unlike in restrictive parenchymal disease, the diffusing capacity is normal. Postmortem evaluations suggest that a primary myopathy of the diaphragm contributes to restriction of respiratory muscle excursion and low static lung volumes (6,11). Thus, diaphragmatic dysfunction should be considered when dyspnea is out of proportion to the severity of chest radiographic abnormalities and when pulmonary function tests show a restrictive pattern. Abnormal diaphragmatic excursions seen at fluoroscopic or real-time US may allow accurate recognition of this entity.

Lung

The risk of pulmonary infection is three times higher in patients with SLE than in the general population due to intrinsic immunologic abnormalities, including diminished phagocyte activity and decreased NK cell activity against pathogens, as well as immunosuppressive therapy (2,4,6,11). Atelectasis, underlying parenchymal disease, and respiratory muscle weakness also predispose SLE patients to respiratory tract infections due to poor clearance of secretions and stasis. Pneumonia can be atypical and advanced at the time of initial presentation. Aside from common organisms in community acquired pneumonia, *Staphylococcus aureus, Mycobacterium* species (Fig 6), and *Pneumocystis carinii* may cause pneumonia in patients with SLE. *Nocardia* species (Fig 7) deserve special mention because the prevalence of *Nocardia* infection is slightly higher in SLE patients than in the general population, and central nervous system (CNS) involvement by *Nocardia* species, which is not uncommon in immunocompromised patients, can be confused with lupus cerebritis (6,11). A high prevalence of pulmonary tuberculosis in patients with SLE has been documented

(21). Recurrent pulmonary infections can lead to bronchiectasis and respiratory compromise (Fig 8).

Cardiovascular Disease

SLE can involve the myocardium, pericardium, cardiac valves, and coronary arteries. Cardiomegaly can be a result of SLE myocarditis, Libman-Sacks endocarditis, subacute bacterial endocarditis, uremia, pulmonary arterial hypertension with right-sided heart failure, or corticosteroid-related cardiomyopathy (6,22–25).

Myocardium

Myocarditis may be clinically silent in up to 50% of patients (2,4,24,25) and is an uncommon manifestation of SLE, consisting of myositis with perivascular infiltration by lymphocytes and neutrophils. Intimal proliferation within the smaller intramyocardial arteries with hyalinization has been reported. SLE myocarditis is not likely to produce major regional wall motion abnormalities but may contribute to global left ventricular dysfunction (24,25).

Transesophageal echocardiography helps define wall motion abnormality (22,24), and newer and faster magnetic resonance (MR) imaging in cine acquisition mode may allow noninvasive evaluation (26). In addition, exercise electrocardiography and myocardial scintigraphy may help define reversible ischemia, typically from accelerated atherosclerosis, that is amenable to surgery or intravascular therapy in SLE patients with symptoms of myocardial disease (6,23).

Pericardium

Exudative pericardial effusions and pericarditis (Fig 9) occur in 17%–50% of patients with SLE (2,6,22–25). Unless pericarditis is accompanied by effusion, echocardiography is insensitive for the diagnosis (24). Clinical symptoms and electrocardiographic findings may be helpful in the diagnosis of SLE pericarditis. Contrast-enhanced chest CT may reveal abnormal thickening and enhancement of the pericardium as well as a pericardial effusion.

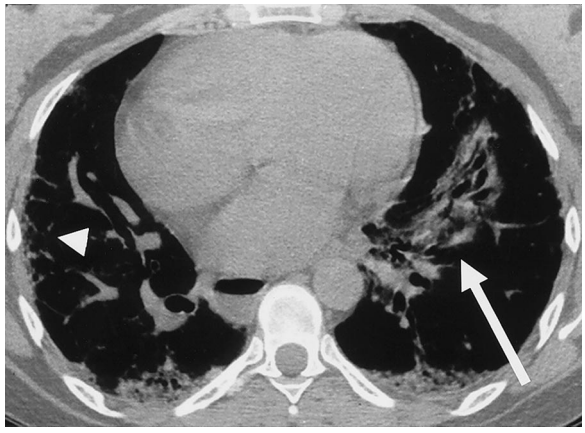


Figure 8. Complications of recurrent pulmonary infection in a 41-year-old woman with SLE. Thin-section CT scan shows bronchiectasis (arrow) and thickening of the interlobular septa (arrowhead). The heart is moderately enlarged.

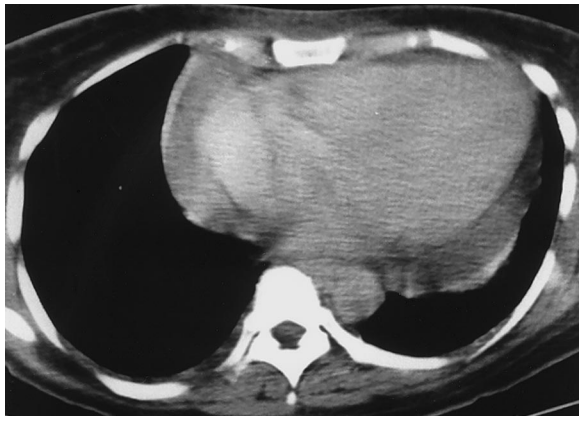
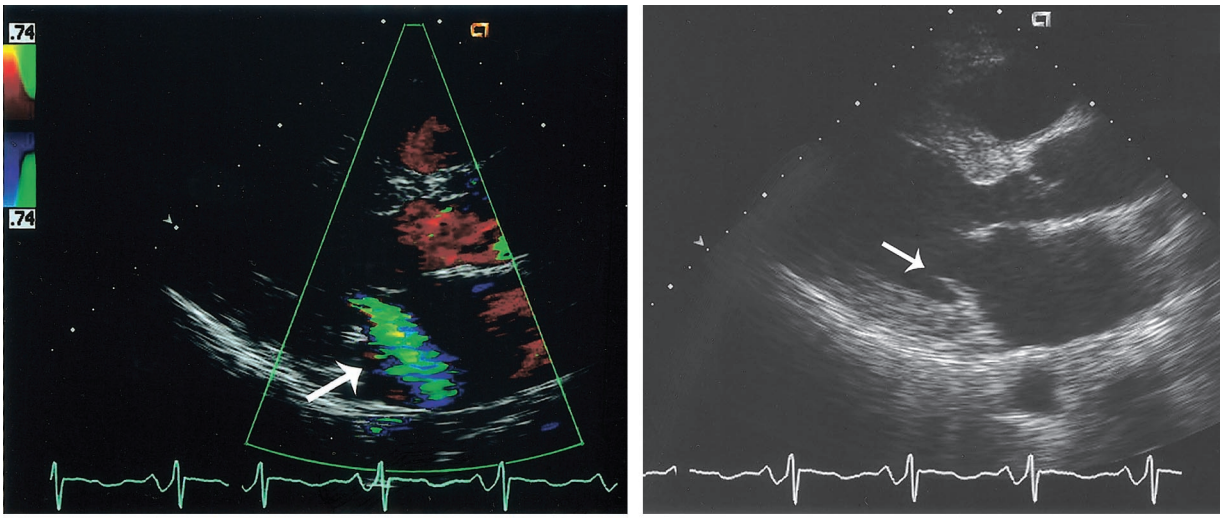


Figure 9. Lupus pericarditis in a 42-year-old woman. Contrast-enhanced CT scan demonstrates cardiomegaly, a thickened and enhancing pericardium, and a pericardial effusion.

Valves

Involvement of the cardiac valves is the most common cardiac manifestation of SLE. Valvular involvement is seen in 18%–74% of SLE patients depending on the duration and severity of disease and the mode of diagnosis (autopsy vs echocardiography) but is more often seen in patients with aPL-ab syndrome (2,6,22,24,27). These lesions are often hemodynamically significant, and prompt recognition of abnormal flow dynamics may lead to timely surgical correction. In



a. b.

Figure 10. Valve leaflet thickening in a 45-year-old woman with SLE-related endocarditis. **(a)** Color Doppler flow echocardiogram shows mitral regurgitation (arrow). **(b)** Two-dimensional echocardiogram demonstrates a thickened mitral valve leaflet (arrow). (Case courtesy of Catherine M. Otto, MD, Department of Cardiology, University of Washington, Seattle.)

addition, antimicrobial prophylaxis can be administered for routine dental procedures (for example) to prevent bacterial seeding of valvular vegetations (2,6,22,24).

The spectrum of valvular disease in SLE ranges from valve leaflet thickening (Fig 10) to Libman-Sacks endocarditis. The latter is characterized by the formation of small single or multiple, sterile, granular pink vegetations ranging from 1 to 4 mm that may be associated with intense valvulitis and lead to valve destruction (28). The pathogenesis is not known; however, fibrinoid degeneration of the valvular cusps, vasculitis, and steroid-related valvulopathy are three postulated mechanisms (22,24). Valvular involvement can vary over time, with some foci of inflammation healing while new ones appear (27). Cine cardiac MR imaging is a useful noninvasive tool for evaluating abnormal flow patterns, ventricular dimensions, stroke volume, and regional myocardial function, but echocardiography is essential for evaluating valvular disease (26).

Vasculature

Atherosclerosis.—Atherosclerosis in SLE patients is a multifactorial problem (29). Traditional risk factors for coronary artery disease such as hypertension, obesity, and hyperlipidemia are seen with greater frequency in SLE patients, possibly due to multiorgan involvement and accelerated deterioration of patients with significant renal disease. In addition, the mortality rate from coronary artery disease for SLE patients is nine times that for the general population (6,22–24). Atherosclerosis may be accelerated by corticosteroid-induced dyslipoproteinemia and secondary hypertension from renal disease as well as vasculitis and circulating immune complexes, the last of which may contribute not only to endothelial injury but also to intracellular cholesterol accumulation (2,6,22–24).

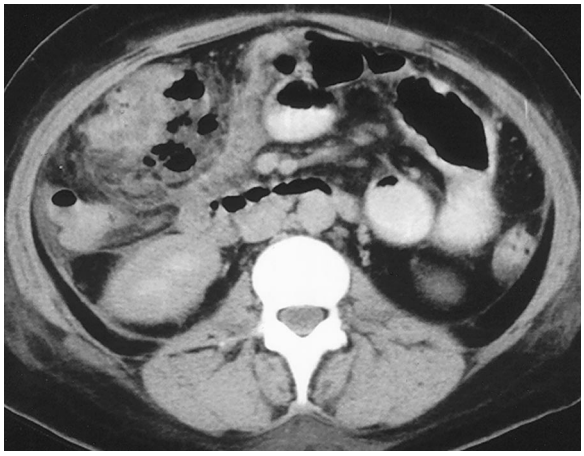


Figure 11. Bowel perforation in a 37-year-old woman with SLE. Contrast-enhanced CT scan shows inflammation and extraluminal gas in the upper right side of the abdomen. Necrosis and perforation were confirmed at laparotomy.

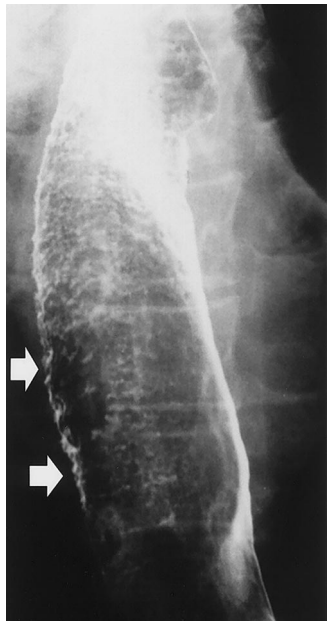


Figure 12. Reflux esophagitis in a patient with SLE. Air-contrast esophagogram shows mucosal granularity (arrows).

Vasculitis.—Typically, vasculitis in SLE patients affects vessels that are less than 100 μm in diameter and is characterized by fibrinoid necrosis with marked wall thickening and minimal infiltration by inflammatory cells (2,4). This entity can occur in any organ system and can result in ischemia. In organs with end arteries such as the bowel, vasculitis can compromise the blood supply to a segment of bowel, resulting in ischemia or hemorrhage into the bowel wall with subsequent perforation and peritonitis (Fig 11).

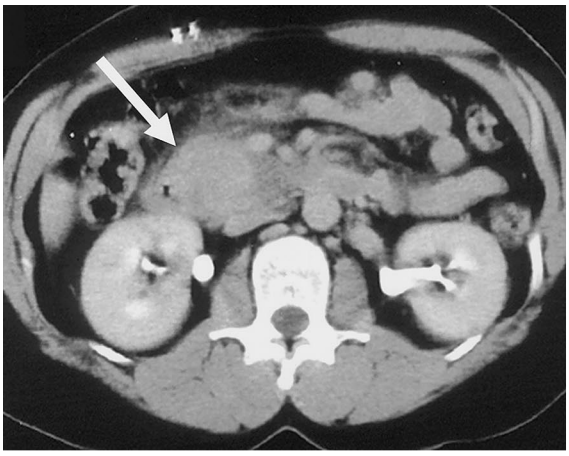
Gastrointestinal Disease

SLE may involve any portion of the gastrointestinal system. Nonspecific and vague abdominal pain is seen in 10%–37% of patients with SLE (2) and may be due to vasculitis, obliterative vascular thrombosis resulting in ischemic bowel, or immune complex deposition of autoantibodies in tissues, eliciting an inflammatory response. Immunosuppressants such as azathioprine and prednisone can also induce abdominal symptoms and have been implicated in pancreatitis. With the use of immunosuppressive medication, the natural immune response to infection is suppressed, and clinical markers of significant infection such as leukocytosis and fever are not fully expressed. Therefore, the diagnosis of perforation, peritonitis, or abscess requires a high degree of clinical suspicion (2,4).

Esophagus

Hypomotility of the distal third of the esophagus is seen in 13%–32% of SLE patients, predisposing them to reflux esophagitis (Fig 12) (2). Most patients present with dysphagia, gastroesophageal reflux symptoms, and atypical chest pain, similar to patients without SLE. The cause of hypomotility in SLE is unclear, but two theories have been postulated. One theory suggests that an inflammatory reaction occurs in the esophageal musculature and thereby directly affects motility; the other states that ischemic damage to the Auerbach plexus affects the intrinsic motility of the esophagus (2). Evaluation of SLE patients who present with gastroesophageal reflux symptoms should include an upper gastrointestinal barium study. Careful investigation may demonstrate mucosal granularity from reflux esophagitis, and, in severe cases, ulceration may also be present.

Often, SLE patients are on multiple drug regimens, including nonsteroidal anti-inflammatory drugs, which can contribute to the development of gastritis and peptic ulcers. In these patients, the stomach and duodenum should also be evaluated using a double-contrast technique.



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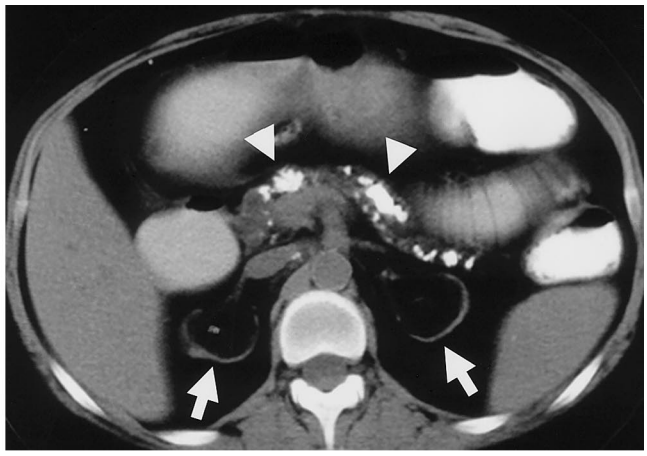

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Figures 14, 15. **(14)** Acute pancreatitis in a patient with SLE. Contrast-enhanced CT scan shows edema and inflammation in the pancreatic head (arrow). **(15)** Chronic pancreatitis and chronic renal failure from SLE in a 28-year-old woman. Unenhanced CT scan shows an atrophic pancreas with calcifications (arrowheads). The kidneys are also atrophic, with cortical thinning and renal sinus lipomatosis (arrows).

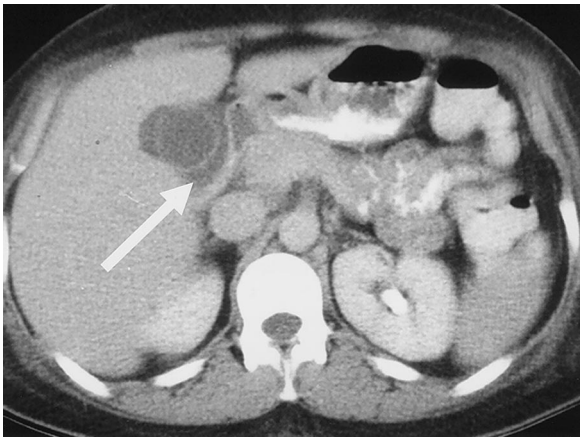


Figure 13. Acute cholecystitis in a 33-year-old woman with SLE. Contrast-enhanced CT scan shows pericholecystic fluid (arrow) and mural thickening.

Gallbladder

The gallbladder is not commonly involved in SLE. Acute cholecystitis (Fig 13), when due to primary SLE involvement, is usually not related to gallstones but rather to periarterial fibrosis and acute vasculitis that occur with elevated levels of circulating immune complexes (2). Imaging findings include gallbladder wall thickening at US and a nonfunctioning gallbladder at hepatobiliary scintigraphy. When left untreated, acalculous cholecystitis in SLE can progress to gangrene, perforation, and sepsis (2).

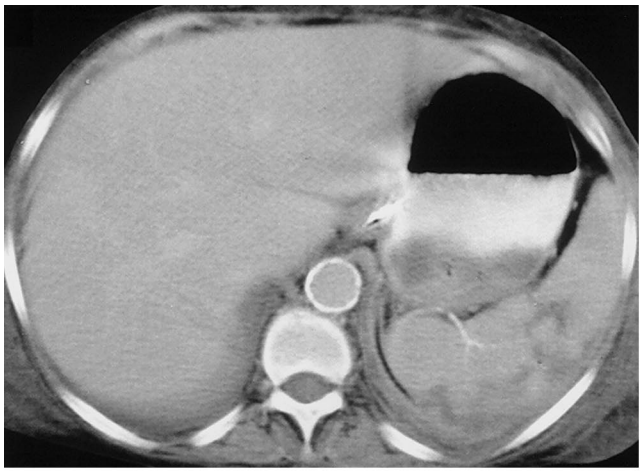
Pancreas

Pancreatitis is seen in 8%–28% of patients with SLE and can be focal or diffuse (30–32). Pancreatitis in SLE may be due to vasculitis, ischemia of small pancreatic vessels, immune complex deposition, or a combination of these entities. In the case of hemorrhagic pancreatitis, a necrotizing vasculitis due to obliterative vascular thrombosis has been implicated (30–32).

Whereas corticosteroids have been implicated in pancreatitis in non-SLE patients, acute pancreatitis is usually related to active multiorgan involvement in SLE patients. Therefore, corticosteroid therapy need not be withheld in a patient with active SLE manifesting as acute pancreatitis (30).

The US and CT features of acute pancreatitis (Fig 14) include peripancreatic edema, phlegmon formation, and mesenteric fatty infiltration around the pancreas, and these findings can be accompanied by glandular enlargement. Changes in parenchymal attenuation and associated peripancreatic edema result in indistinctness of the pancreatic margins.

Chronic pancreatitis (Fig 15) is common and may be asymptomatic. Pancreatic dysfunction in SLE may be related to recurrent episodes of low-grade pancreatitis and chronic vasculitis affecting



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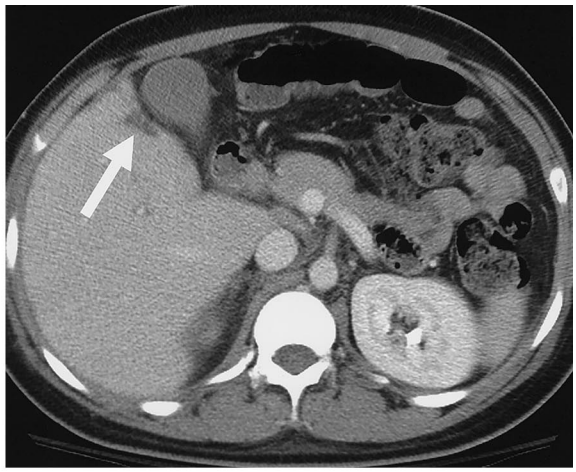


17.

Figures 16, 17. **(16)** Splenic infarctions from lupus vasculopathy in a 30-year-old woman with SLE. Contrast-enhanced CT scan demonstrates peripheral low-attenuation areas within the spleen. **(17)** Hepatic infarction from aPL-ab syndrome in a 20-year-old man. Contrast-enhanced CT scan shows a wedge-shaped low-attenuation area in the liver (arrow) adjacent to the gallbladder. Similar areas were present elsewhere in the liver and proved to be infarctions at percutaneous biopsy.

the small vessels within the pancreas (31,32). With repeated bouts of acute pancreatitis, the gland saponifies with calcium deposition within the ductal system. The pancreas often atrophies, whereas the pancreatic duct becomes alternately strictured and dilated. These chronic changes are best seen at CT but can also be detected with US.

Bowel

Ischemia due to SLE vasculopathy may affect any organ system, but the gastrointestinal tract is particularly susceptible to small vessel vasculitis, particularly in the distribution of the superior mesenteric artery (33). Thrombogenesis in aPL-ab syndrome further increases the risk for ischemia. Regardless of the cause, the result is end organ damage manifesting as bowel ischemia. Bowel ischemia is often difficult to detect at radiography and barium studies, but CT is more sensitive. Radiographs can demonstrate thumbprinting due to bowel wall edema or intramural hemorrhage; in more advanced stages, pneumatosis or portal venous gas, the latter being a poor prognostic sign, can be present. CT may show ascites, dilated bowel, mural thickening, or abnormal wall enhancement as well as abnormalities in the mesentery including edema and vessel engorgement (34). However, the features of ischemic bowel are not specific for SLE and vary depending on the duration of the ischemia. In the spleen and liver, ischemia manifests as small, peripheral, wedge-shaped areas of low attenuation at CT (Figs 16, 17).

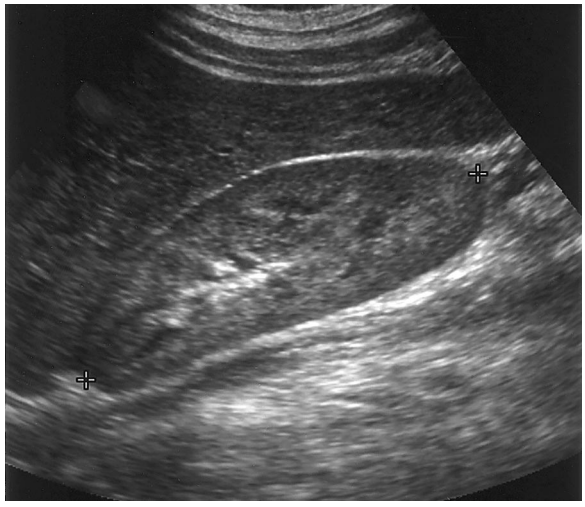
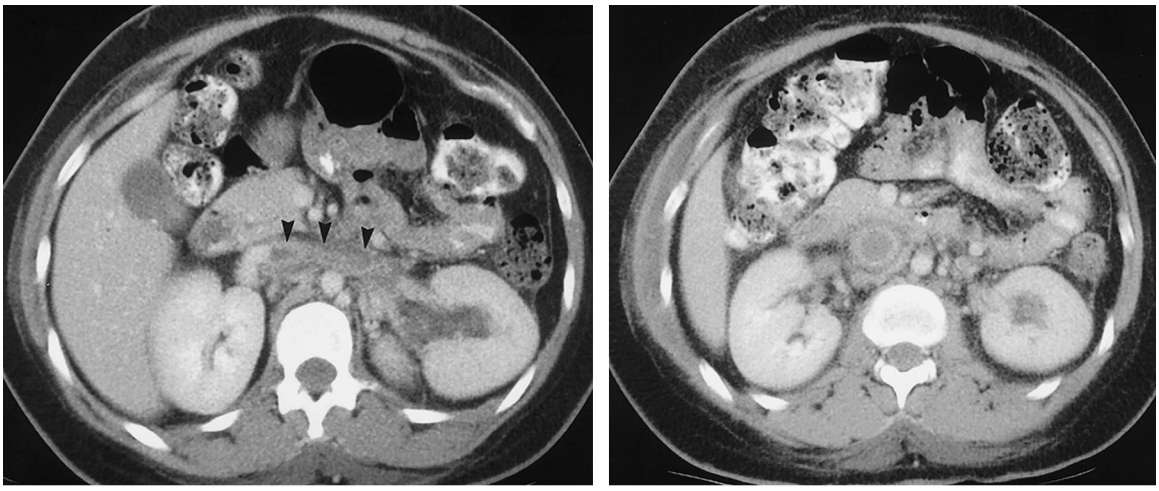


Figure 18. Lupus nephritis in a 21-year-old woman with SLE. Longitudinal US image shows mild echogenicity of the right kidney (cursors) relative to the liver. Results of percutaneous biopsy confirmed nephritis.



a. **b.**

Figure 19. Renal vein thrombosis in a 27-year-old woman with SLE. **(a)** Contrast-enhanced CT scan shows a clot within the left renal vein (arrowheads). **(b)** Contrast-enhanced CT scan reveals that the clot extends into the inferior vena cava.

Genitourinary Disease

Kidneys

The kidney is usually affected in SLE. With the use of immunofluorescence to detect immune complex deposition, nearly all SLE patients who undergo renal biopsy have abnormal microscopic findings of renal disease (2,4,16). The pathogenesis of SLE nephritis (Fig 18) is mediated by autoantibodies crossreacting with glomerular surface antigens, mesangial matrix, or basement membranes, resulting in immune complex deposition in the subepithelial and subendothelial layers of the glomeruli (4,16). Immune complex deposition elicits an intense cell-mediated immune response, resulting in the liberation of cytokines and culminating in glomerular necrosis and fibrosis.

Whereas the pathologic findings in SLE renal disease are specific for entities such as membranous or proliferative glomerulonephritis, the imaging findings in SLE renal disease are generally nonspecific and similar to those in other causes of medical renal disease. At US, the kidneys are generally hyperechoic (Fig 18), and the size of the kidney depends on the duration of renal involvement. However, small and diffusely echogenic kidneys are commonly seen in SLE-related chronic renal failure (2,16).

Vasculature

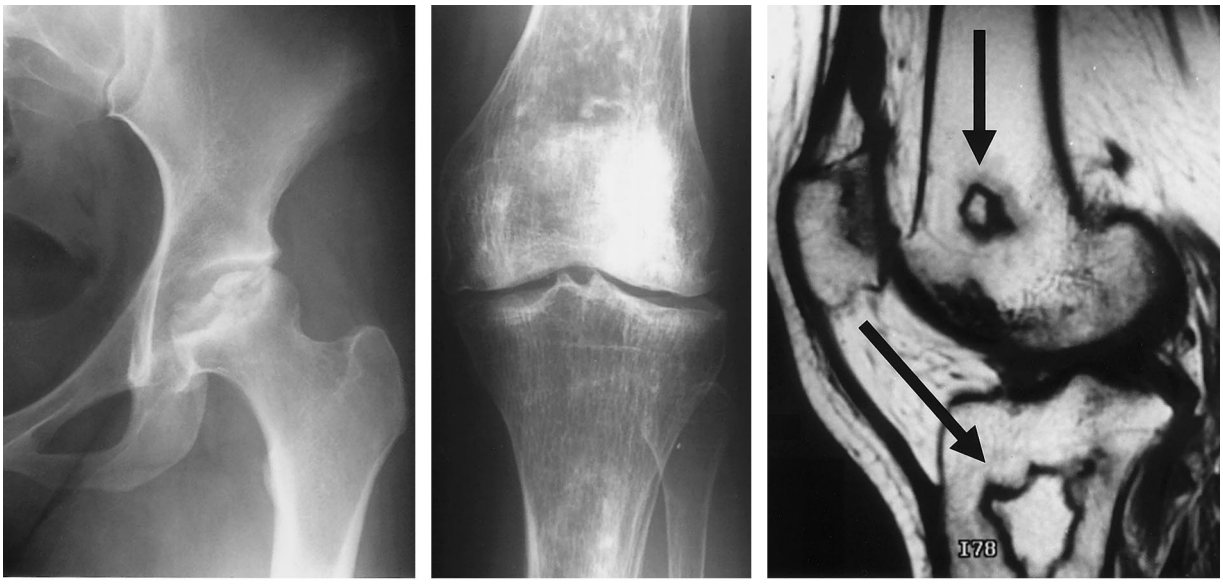
Renal vein thrombosis (Fig 19) is uncommon in SLE patients and is thought to be due to hypercoagulability induced by nephrotic syndrome. Most patients with SLE have glomerulitis but do not have nephrotic syndrome. In the subgroup of SLE patients with aPL-ab syndrome, renal vein thrombosis is more common due to the propensity for thrombogenesis (2).

Musculoskeletal Disease

Joints

Over 80% of SLE patients have symmetric, nonerosive, nondeforming polyarthritis affecting the small joints of the hands, wrists, knees, and shoulders (2). Approximately 10% will have irreversible deformities and ulnar drift at the metacarpophalangeal joints as well as swan neck and boutonniere deformity (Jaccoud syndrome) (2). On radiographs of the hands, pericapsular soft-tissue edema represents synovitis around small joints, and juxtaarticular osteoporosis is seen, appearing similar to rheumatoid arthritis. It is often difficult to distinguish between these two disease processes because they can occur simultaneously in some individuals, with erosive arthritis being a feature of both entities. In such cases, the other diagnostic criteria for SLE will help determine which entity is predominant (2).

In the wrist, carpal instability is seen in 15% of SLE patients (2,35). This condition manifests as increased distance (>3 mm) between the scaphoid bone and the lunate or other carpal bones. Instability of the wrist can be demonstrated with radiographs obtained with the wrist in radioulnar deviation (2).



20. **21a.** **21b.**

Figures 20, 21. **(20)** AVN of the femoral head secondary to SLE. Anteroposterior radiograph of the pelvis shows subchondral fractures and joint surface disruption of the left femoral head. **(21)** Multiple bone infarcts in a 26-year-old woman with SLE and left knee pain. **(a)** Anteroposterior radiograph of the left knee shows sclerosis in the distal femur and proximal tibia. **(b)** Sagittal T1-weighted MR image shows foci of isointense signal encircled by a low-signal-intensity rim in the distal femur and proximal tibia (arrows). The hypointense rim represents reparative granulation tissue surrounding infarcted bone.

Ligaments

Ligamentous instability and laxity of supporting structures make the deformities in SLE reversible. However, with muscle atrophy and contractures, reversible deformity can become fixed, as in Jaccoud syndrome. Corticosteroids usually alleviate the acute inflammation of the joints, but chronic steroid therapy can lead to AVN, osteoporotic insufficiency fractures, and infection.

Bone

Osteonecrosis.—Osteonecrosis or AVN (Figs 20, 21) occurs in 5%–50% of SLE patients and mainly affects weight-bearing joints (35). It may be attributable to SLE itself or intensified by steroid therapy. This situation is confounding because almost all SLE patients are treated with corticosteroids at some point, although they may be receiving cyclophosphamide, azathioprine, or nonsteroidal anti-inflammatory drugs at the time of presentation. The femoral head is most commonly affected, followed by the humeral head, femoral condyle, and tibial plateau (2,35–37). Radiographs are usually normal in early AVN, and late changes of bone sclerosis indicate the presence of irreversible articular damage. With radiography, a grading system is used to denote the severity of AVN according to the sclerosis, flattening of the articular surface, and joint space abnormalities. This scale ranges from stage 0 (clinically suspected AVN) to stage V (obvious joint space narrowing and articular surface disruption) (35).

Two basic factors in bone scintigraphy—hyperemia of the affected bone and osteogenesis—are important in AVN. Unfortunately, hyperemia and osteogenesis are absent in acutely infarcted bone; therefore, early AVN will appear as photopenic areas on technetium-99m methylene diphosphonate bone scans. Within days, recruitment of osteoclasts to resorb necrotic bone and of osteoblasts to build or bridge new bone yields increased radiotracer uptake at the margins of the infarction. In fact, this healing, which occurs gradually, is seen once irreparable articular surface damage has been sustained. Thus, bone scintigraphic findings can be nonspecific as well as reflect more advanced AVN.

Prospective studies have demonstrated that MR imaging is superior to and more sensitive than radiography and scintigraphy for documenting early AVN, and MR imaging has been used to document osteonecrosis in asymptomatic SLE patients receiving high-dose corticosteroids (36,37). The MR imaging appearance of AVN correlates with the pathophysiologic features of the process. Vascular insufficiency leads to necrosis of different cell types, starting with hematopoi-

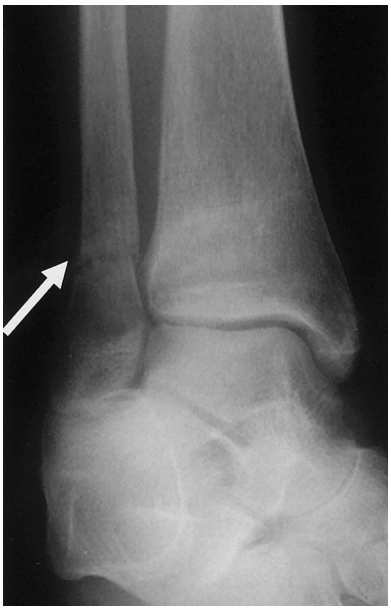


Figure 22. Insufficiency fracture in a patient with SLE. The patient presented with ankle pain but had no history of trauma. Oblique radiograph of the right ankle shows a fracture through the distal fibular diaphysis (arrow).

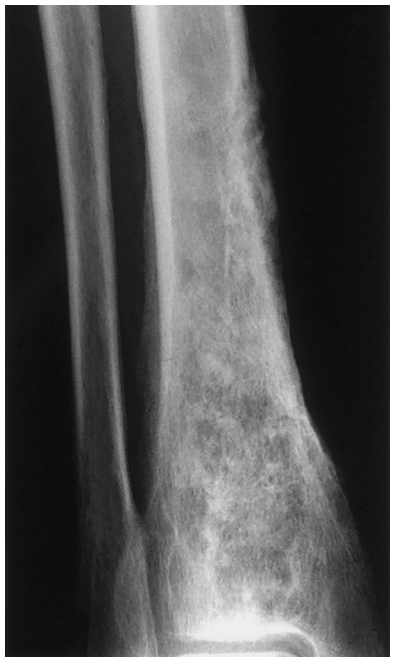


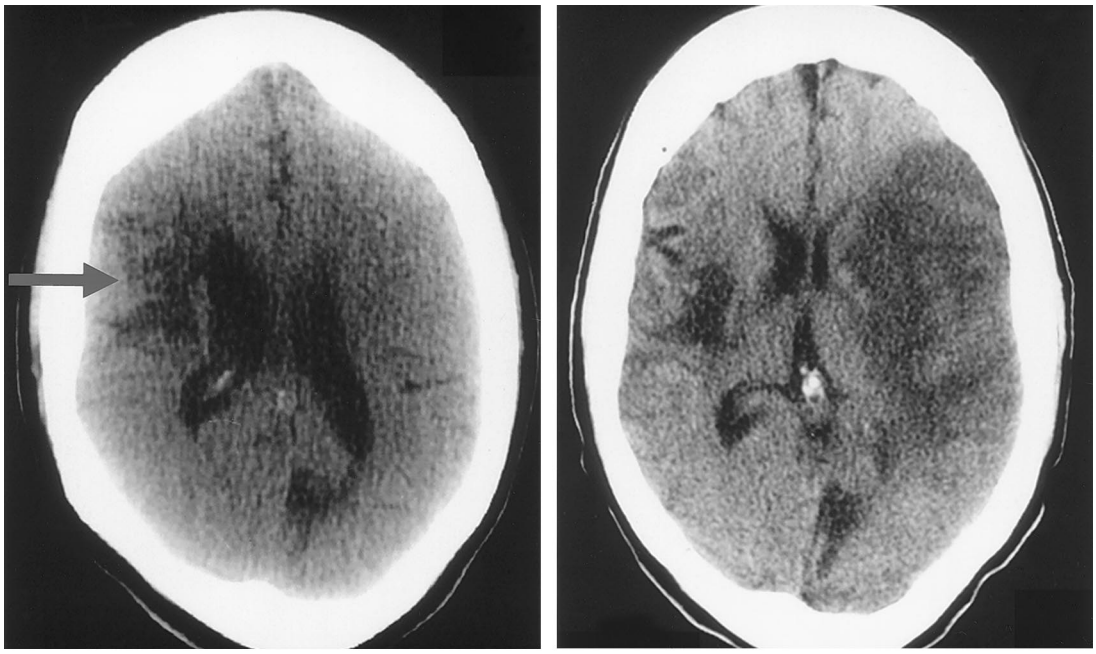
Figure 23. Osteomyelitis in a patient with SLE. Anteroposterior radiograph of the distal right leg shows bone destruction and periostitis involving the lateral aspect of the tibia.

etic cells, followed by adipocytes and, finally, osteocytes. Therefore, the earliest MR imaging examination may be normal due to the lack of edema, hemorrhage, or bone marrow response. At this juncture, gadolinium-enhanced MR imaging may demonstrate lack of enhancement of the devascularized areas when the findings at standard spin-echo and short inversion time inversion-recovery imaging are still normal (35).

Initial abnormalities at MR imaging consist of bone marrow edema, which can be extensive even when the area of infarction is small. Over a period of days, reactive changes at the margins of the infarct become visible and manifest as low-signal-intensity areas on standard spin-echo T1- and T2-weighted images. Vascularized granulation tissue just inside the reactive bone manifests with intermediate to high signal intensity on T2-weighted images, producing a line of low signal intensity with an adjacent high-signal-intensity line. Subchondral fractures manifest with high signal intensity on T2-weighted images and are accompanied by fluid signal intensity or edema. Collapse of the articular surface results in loss of the normal spheric contour of bone and incongruity of the articular surfaces. Such collapse usually has low signal intensity on T2-weighted images, a finding that is compatible with fibrotic changes in the infarcted bone marrow (35–37).

Insufficiency Fracture.—Normal stress on abnormal bone can cause insufficiency fractures (Fig 22). In patients with SLE, the pathogenesis of insufficiency fractures is unclear but may be related to deconditioning, accelerated bone loss due to steroid therapy, or both (2,35). The end result is an insufficiency fracture. MR imaging may depict early or subtle insufficiency fractures, which may be occult on radiographs due to severe osteoporosis. At T2-weighted MR imaging, insufficiency fractures appear as areas of high signal intensity due to bone marrow edema in characteristic stress locations (35–37).

Infection.—Dermatologic factors, corticosteroids, and vasculopathy predispose patients with SLE to septic arthritis and osteomyelitis (Fig 23). Because of steroid therapy, infection can be masked, and chronic indolent disease is often seen (2). The types of organisms seen are *S aureus*, gram-negative bacilli, and *M tuberculosis*. Radiographic findings include progressive bone destruction and cartilage loss, periostitis, and joint effusion (2,35). Indium-111–labeled white blood cell scintigraphy is better suited for acute infections because the neutrophils are labeled.



a. b.

Figure 24. Multiple cerebral infarctions in a 52-year-old woman with SLE. **(a)** Unenhanced CT scan shows a low-attenuation area in the distribution of the right middle cerebral artery (arrow). **(b)** Unenhanced CT scan obtained 3 years later shows encephalomalacia near the right sylvian fissure from the previous infarction and a new region of low attenuation with partial effacement of the left lateral ventricle in the distribution of the left middle cerebral artery.

However, in chronic osteomyelitis, in which lymphocytes are usually the predominant cell type, gallium-67 citrate is more useful. When scintigraphic findings are equivocal, gadolinium-enhanced MR imaging may be helpful in differentiating soft-tissue infection from osteomyelitis.

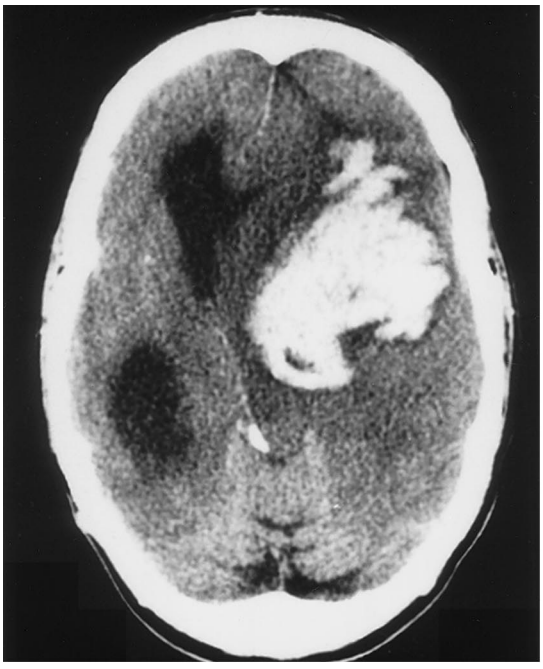
Neurologic Disease

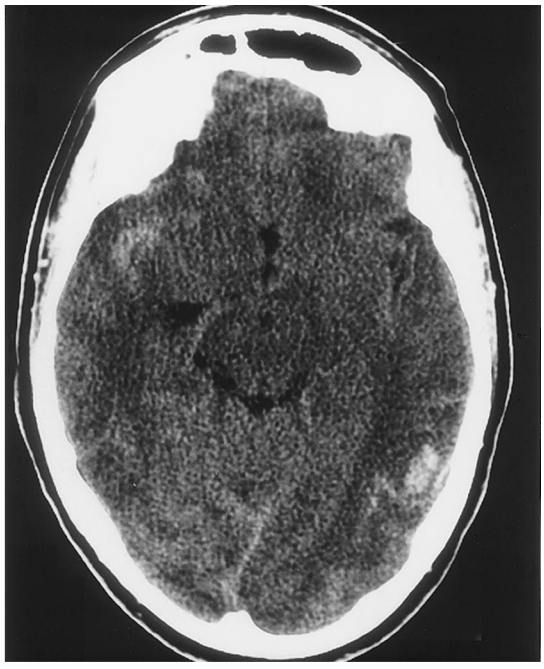
CNS lupus, first recognized by Kaposi in 1872, has a prevalence of 30%–40% and accounts for up to 19% of lupus-related deaths (38). CNS lupus is generally accepted as being angiopathic in origin, although other mechanisms such as direct neural autoimmune damage, demyelination, and thromboembolism can contribute to CNS disease (2,16,39). Cerebral ischemia and infarction (Fig 24) in SLE patients may result from *(a)* coagulopathy secondary to aPL-ab syndrome, *(b)* accelerated atherosclerosis due to corticosteroids, *(c)* vasculitis, or *(d)* cardiogenic thromboemboli in Libman-Sacks disease (2,4,39). The average age of patients with SLE-related stroke is 35 years, with a recurrence rate of 35%–60% in those patients with aPL-ab syndrome (40,41). Children with these antibodies have an unusually high prevalence of cerebral ischemia (~76%) (42,43).

Cerebral Vessels

Large Vessel Disease.—Single artery distribution infarcts are seen with large vessel vasculopathy. The relationship between large vessel disease and aPL-ab syndrome is unclear and may be related to hypercoagulopathy and a history of previous systemic venous or arterial occlusion (44). Approximately one-half of all children with aPL-ab syndrome who present with transient ischemic attack or stroke are found to have occlusion of medium-sized or large vessels at cerebral angiography (42,43). Usual symptoms range from headache and weakness to focal neurologic deficits localized to the side of the ischemia (42,43,45). At CT or MR imaging, a clearly defined arterial territory affected by ischemia is seen, and in younger patients with a diagnosis of stroke, SLE should be considered.

Small Vessel Disease.—Small cortical or deep gray matter infarcts are seen with small vessel disease (40,44,46). The underlying pathogenesis of small vessel disease has not been identified. At histopathologic analysis, there is marked endothelial hyperplasia and obliterative intimal fibrosis in





25. 26.

Figures 25, 26. **(25)** Hypertensive intracranial hemorrhage in a 45-year-old woman with SLE and hypertension secondary to chronic renal failure. Unenhanced CT scan shows massive hemorrhage in the left hemisphere with substantial mass effect. **(26)** SLE vasculopathy in a 55-year-old woman who presented with seizures. Unenhanced CT scan shows subarachnoid hemorrhage tracking in the sulci and basilar cisterns and along the sylvian fissures.

the small vessels of the brain, leading to occlusion (46). This process has been described as lupus angiitis or vasculitis. Fibrinoid degeneration of collagen in arterioles and small arteries produces fibrinoid masses in the vessel walls. The muscular and elastic tissue of the vessel is disrupted, and the vessel becomes occluded. Endothelial proliferation occurs in response to both the necrosis and efforts to repair the vessel, and this proliferation often contributes to vascular occlusion. This may not be the only mechanism; other studies have demonstrated fibrin thrombi in small and medium-sized arterioles at brain autopsy without evidence of vasculitis (47). Thus, several mechanisms may be involved simultaneously in the pathogenesis of small vessel disease in SLE.

Occlusion of Dural Venous Sinuses and Deep Cerebral Veins.—Some series report a 29% prevalence of intracranial venous occlusion in patients with aPL-ab syndrome (2,44,47). Although most of these patients do not have predisposing factors such as dehydration, pregnancy, and hypovolemia, they have abnormally increased coagulability and usually have a history of recurrent venous thrombosis. The imaging findings depend on the site of occlusion and the presence of alternate venous drainage pathways. At unenhanced CT, increased attenuation is seen along the course of the affected sinus, and at contrast-enhanced CT, a "delta" sign representing thrombus in the occluded sinus outlined by contrast material may be present (48,49). In addition, low-attenuation areas representing edema or infarction may be present within the thalamus, basal ganglia, and white matter because these structures are drained by the deep venous system of the brain (49).

On spin-echo T1-weighted MR images, the normal flow void is replaced with increased signal intensity in the sinus. However, slow flow may also manifest as intravascular hyperintensity. In equivocal cases, MR venography with time-of-flight sequences may help depict the absence of flow in the occluded sinus. Cerebral venography, which is more invasive, is rarely used to demonstrate dural venous sinus thrombosis.

Brain

Intracranial Hemorrhage.—Intracranial hemorrhage (Figs 25, 26) occurs in up to 42% of SLE patients with uremia, thrombocytopenia, and hypertension (40,44,45). In younger patients, intracranial hemorrhage in the absence of trauma or

coagulopathy is quite uncommon and should suggest the possibility of SLE involving the CNS.

The prevalence of subarachnoid hemorrhage due to rupture of intracranial aneurysms is higher in SLE patients than in the general population, a phenomenon that is thought to be due to focal transmural lupus angiitis causing rupture (50). In contrast to the pathogenesis of small vessel disease, fibrinoid necrosis predominates over endothelial proliferation in large vessel disease. Thus, rather than occlusion of the vessel, there is focal weakness in the vessel wall, and the wall mechanics of the vessel are affected (50,51).

Other factors that may contribute to the development and rupture of these aneurysms in patients with SLE include hypertension, accelerated atherosclerosis, vasculitis, and concurrent organ dysfunction as in chronic renal failure, all of which are related to vascular hemodynamics. Therefore, SLE patients have two concurrent problems related to the cerebral vasculature: *(a)* abnormal wall mechanics due to inflammatory connective tissue breakdown, and *(b)* abnormal vascular hemodynamics.

Cerebral Abscess.—Cerebral abscess (Fig 27) is uncommon in the absence of intravenous drug abuse, acquired immunodeficiency syndrome, or diabetes. SLE patients with Libman-Sacks endocarditis have mitral and aortic valve abnormalities that can lead to septic cerebral embolism. At contrast-enhanced CT, a cerebral abscess manifests as a low-attenuation mass with an enhancing peripheral rim. Similar findings are seen at gadolinium-enhanced MR imaging, which may depict the abscess with variable signal intensity surrounded by an enhancing rim. Typically, abscesses occur in the frontal and temporal lobes at the junction of the gray and white matter, and surrounding edema may be absent when the patient is being treated with corticosteroids. Patients receiving corticosteroid therapy are also more prone to opportunistic organisms such as *Nocardia* and *Candida* species. Analysis of the cerebrospinal fluid may be helpful when imaging findings are unusual or are discordant with the clinical picture.

Finally, neuropsychiatric disturbances, which constitute one of the 11 criteria used to make the diagnosis of SLE, can be a manifestation of underlying organic brain disease. When a patient with SLE presents with a neurologic disturbance, it is important to identify reversible causes. Therefore, it becomes crucial to image these patients promptly, initially with unenhanced CT to exclude hemorrhagic complications, then with gadolinium-enhanced MR imaging to evaluate for stroke or abscess.

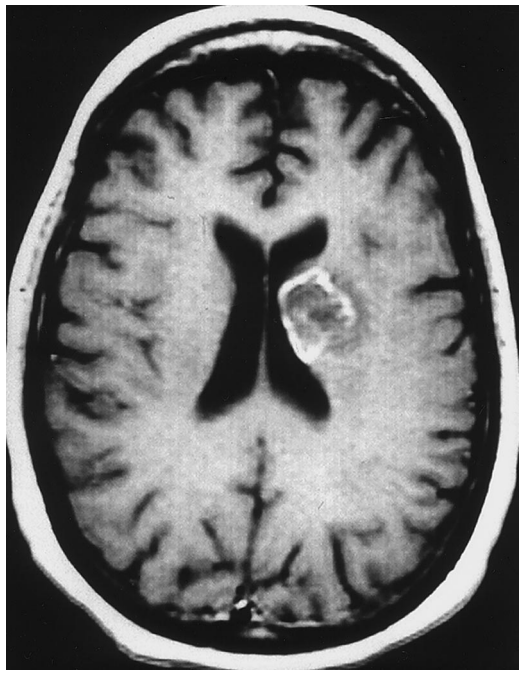


Figure 27. *Candida* cerebral abscess in a 39-year-old woman with SLE and mitral valve endocarditis who was undergoing immunosuppressive therapy. Gadolinium-enhanced T1-weighted MR image shows a right periventricular mass with peripheral rim enhancement surrounding a low-signal-intensity area of central necrosis.

Conclusions

The treatment of patients with SLE is a formidable task due to multisystem involvement, a wide spectrum of disease manifestations, and significant complications that may arise from therapy. SLE has far-reaching implications for long-term morbidity and quality of life with regard to osteonecrosis and joint replacement, renal disease and organ transplantation, and peripheral cardiac and cerebral vascular disease as well as the long-term sequelae that result from related complications.

SLE is not well described in the radiology literature, even though it is encountered in every radiology subspecialty because of its multisystem involvement and the wide age range of affected

patients. It is important for radiologists to understand the pathophysiologic features of SLE and its complications as well as possible complications of therapy so that they can actively participate in the treatment of affected patients.

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