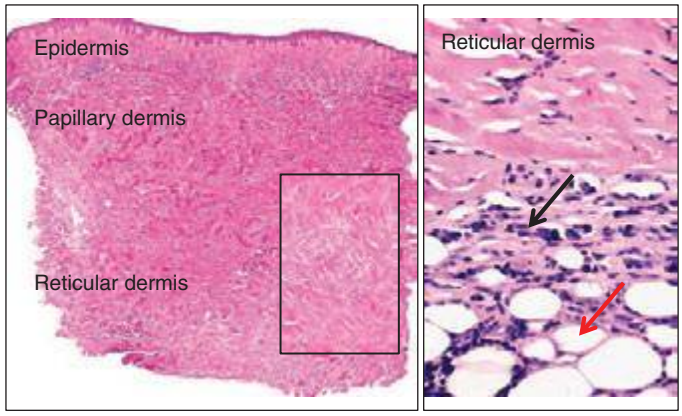
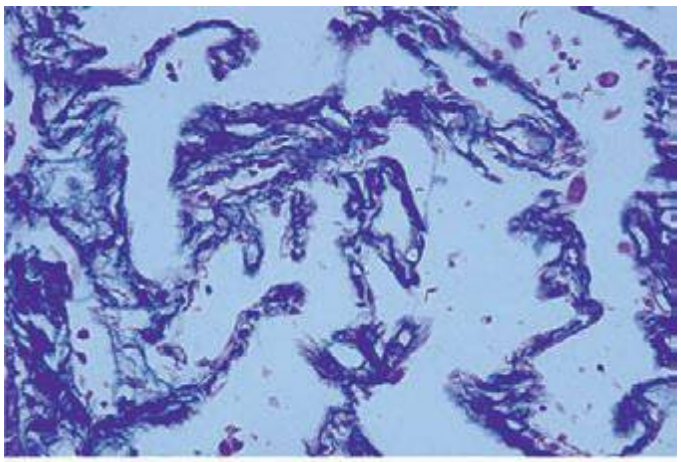


A



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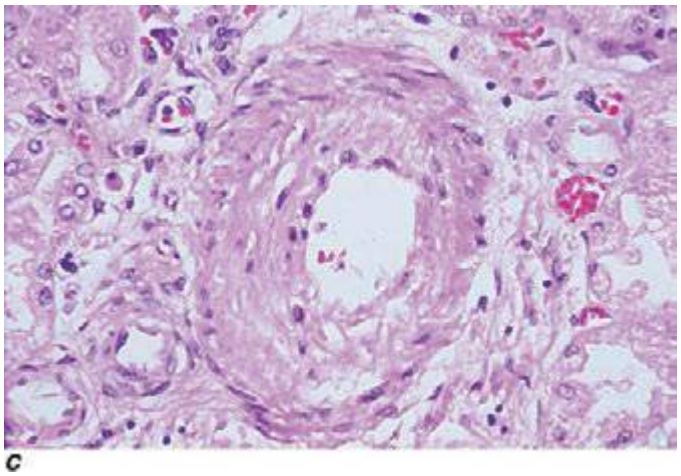

C

FIGURE 382-2 Pathologic findings in systemic sclerosis (SSc). ***A. Left panel:*** The skin is thickened due the marked expansion of the dermis. Inset, higher magnification showing thick hyalinized collagen bundles replace skin appendages. ***Right panel:*** Inflammation in the reticular dermis. Mononuclear inflammatory cells infiltrating the dermis and intradermal adipose tissue. ***B.*** Early interstitial lung disease. Diffuse fibrosis of the alveolar septae and a chronic inflammatory cell infiltrate. Trichrome stain. ***C.*** Pulmonary arterial obliterative vasculopathy. Striking intimal hyperplasia and narrowing of the lumen of a small pulmonary artery, with minimal interstitial fibrosis, in a patient with limited cutaneous SSc.

idiopathic pulmonary fibrosis (Fig. 382-2*B*). Progressive thickening of the alveolar septae results in obliteration of the airspaces and loss of pulmonary blood vessels. This process impairs gas exchange and contributes to pulmonary hypertension. Intimal thickening of the pulmonary arteries, best seen with elastin stain, underlies pulmonary hypertension (Fig. 382-2*C*) and, at autopsy, is often associated with multiple pulmonary emboli and evidence of myocardial fibrosis.

GASTROINTESTINAL TRACT

Pathologic changes can be found at any level from the mouth to the rectum. The lower esophagus shows prominent atrophy of the muscular layers and characteristic vascular lesions; striated muscle in the upper third of the esophagus is generally spared. Replacement of the normal intestinal tract architecture results in diminished peristaltic activity, with gastroesophageal reflux, dysmotility, and small-bowel obstruction. Chronic reflux is associated with esophageal inflammation, ulcerations, and stricture formation and may lead to Barrett's metaplasia.

KIDNEYS

In the kidneys, vascular lesions affecting the interlobular and arcuate arteries predominate. Chronic renal ischemia is associated with shrunken glomeruli. Acute scleroderma renal crisis is associated with a classic thrombotic microangiopathic pathology: reduplication of elastic lamina, marked intimal proliferation, and narrowing of the lumen in small renal arteries, commonly accompanied by thrombosis and hemolysis.

HEART

The heart is frequently affected, with prominent involvement of the myocardium and pericardium. The characteristic arteriolar lesions are concentric intimal hypertrophy and luminal narrowing, accompanied by contraction band necrosis reflecting ischemia-reperfusion injury and myocardial fibrosis. Fibrosis of the conduction system is common, especially at the sinoatrial node. Despite the prominent role of ischemia in SSc, the frequency of atherosclerotic coronary artery disease is comparable to the general population.

OTHER ORGANS

Synovitis may be found in early SSc; however, with disease progression, the synovium becomes fibrotic. Fibrosis of tendon sheaths and fascia produces palpable and sometimes audible tendon friction rubs. Inflammation and, in later stages, atrophy and fibrosis of the muscles are common findings. Fibrosis of the thyroid gland and of the minor salivary glands may be seen.

CLINICAL FEATURES

OVERVIEW

Virtually every organ can be clinically affected (Table 382-4). Most patients with SSc can be classified as lcSSc or dcSSc (Table 382-2). Although stratification of SSc patients into diffuse and limited cutaneous subsets is useful, disease expression is far more complex, and several distinct endophenotypes exist within each subset. For example, 10–15% of patients with lcSSc develop PAH without significant ILD. Other patients have systemic features of SSc without appreciable skin involvement (SSc sine scleroderma). Unique clinical phenotypes of SSc associate with specific autoantibodies (Table 382-3). Patients with "overlap" have typical SSc features coexisting with clinical and laboratory evidence of another autoimmune disease such as polymyositis, Sjögren's syndrome, polyarthritis, autoimmune liver disease, or SLE.

TABLE 382-4 FREQUENCY OF CLINICAL ORGAN INVOLVEMENT: LIMITED CUTANEOUS AND DIFFUSE CUTANEOUS FORMS OF SYSTEMIC SCLEROSIS (SSC)

Features	Limited Cutaneous SSc (%)	Diffuse Cutaneous SSc (%)
Skin involvement	90[a]	100
Raynaud's phenomenon	99	98
Esophageal involvement	90	80
Pulmonary fibrosis	35	65
Pulmonary arterial hypertension	15	15
Myopathy	11	23
Cardiac involvement	9	12
Scleroderma renal crisis	2	15

[a]Approximately 10% of limited cutaneous SSc patients have SSc sine scleroderma.