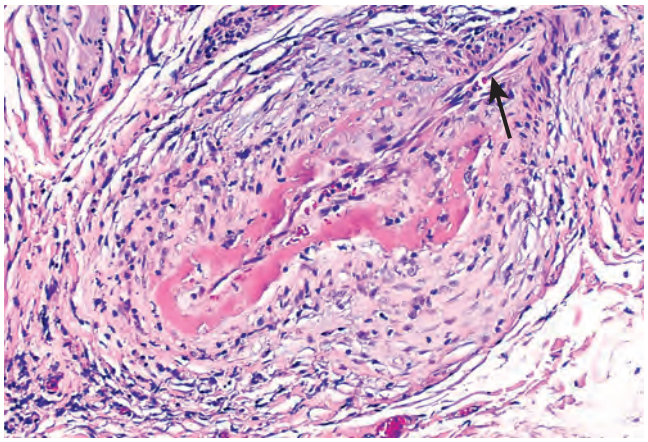

Figure 11-26 Polyarteritis nodosa. There is segmental fibrinoid necrosis and thrombotic occlusion of the lumen of this small artery. Note that part of the vessel wall at the upper right *(arrow)* is uninvolved. (Courtesy Sidney Murphree, MD, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas.)

Clinical Features. Although typically a disease of young adults, PAN can also occur in pediatric and geriatric populations. Clinical manifestations result from ischemia and infarction of affected tissues and organs. The course is frequently remitting and episodic, with long symptom-free intervals. Because the vascular involvement is widely scattered, the clinical signs and symptoms of PAN can be quite variable. A "classic" presentation can involve some combination of rapidly accelerating hypertension due to renal artery involvement; abdominal pain and bloody stools caused by vascular gastrointestinal lesions; diffuse myalgias; and peripheral neuritis, predominantly affecting motor nerves. Renal involvement is often prominent and a major cause of mortality. Untreated, PAN is typically fatal; however, immunosuppression can yield remissions or cures in 90% of cases.

Kawasaki Disease

***Kawasaki disease* is an acute febrile, usually self-limited illness of infancy and childhood (80% of patients are 4 years old or younger); it is associated with an arteritis affecting large to medium-sized, and even small vessels.** Its clinical significance stems primarily from a predilection for coronary artery involvement that can cause aneurysms that rupture or thrombose, resulting in acute myocardial infarctions. Originally described in Japan, the disease has a worldwide distribution and is the leading cause of acquired heart disease in children.

The pathogenesis of Kawasaki disease is unknown. A variety of infectious agents (mostly viral) have been implicated in triggering the disease in genetically susceptible individuals. The vascular damage is primarily mediated by activated T cells and monocytes/macrophages.

MORPHOLOGY

The vasculitis resembles that seen in polyarteritis nodosa. There is a dense transmural inflammatory infiltrate, although the fibrinoid necrosis is usually less prominent than in PAN. The acute vasculitis typically subsides spontaneously or in response to treatment, but aneurysm formation due to wall damage can supervene. As with other arteritides, healed lesions can also exhibit obstructive intimal thickening. Pathologic changes outside the cardiovascular system are rarely significant.

Clinical Features. Kawasaki disease typically presents with conjunctival and oral erythema and blistering, edema of the hands and feet, erythema of the palms and soles, a desquamative rash, and cervical lymph node enlargement (hence its other name, *mucocutaneous lymph node syndrome*). Approximately 20% of untreated patients develop cardiovascular sequelae, ranging from asymptomatic coronary arteritis, to coronary artery ectasia, to giant coronary artery aneurysms (7 to 8 mm) leading to rupture or thrombosis, myocardial infarction, and sudden death. If the disease is recognized early in its course, treatment with intravenous immunoglobulin and aspirin sharply reduce the risk of symptomatic coronary artery disease.

Microscopic Polyangiitis

Microscopic polyangiitis is a *necrotizing vasculitis that generally affects capillaries, as well as small arterioles and venules.* It is also called hypersensitivity vasculitis or leukocytoclastic vasculitis. Unlike polyarteritis nodosa, *all lesions of microscopic polyangiitis tend to be of the same age in any given patient and are distributed more widely.* The skin, mucous membranes, lungs, brain, heart, gastrointestinal tract, kidneys, and muscle can all be involved; *necrotizing glomerulonephritis* (90% of patients) and pulmonary capillaritis are particularly common. Microscopic angiitis can be a feature of a number of immune disorders, such as Henoch-Schönlein purpura, essential mixed cryoglobulinemia, and vasculitis associated with connective tissue disorders.

Pathogenesis. In some cases, antibody responses to antigens such as drugs (e.g., penicillin), microorganisms (e.g., streptococci), heterologous proteins, or tumor proteins have been implicated. These can either lead to immune complex deposition or trigger secondary immune responses (e.g., the development of ANCAs) that are pathogenic. Indeed, most cases are associated with MPO-ANCA. Recruitment and activation of neutrophils within affected vascular beds is likely responsible for the disease manifestations.

MORPHOLOGY

Microscopic polyangiitis is characterized by segmental fibrinoid necrosis of the media and focal transmural necrotizing lesions; granulomatous inflammation is absent. These lesions morphologically resemble PAN but typically spare medium-sized and larger arteries; consequently, infarcts are uncommon. In some areas (typically postcapillary venules), only infiltrating neutrophils, many undergoing apoptosis, are seen, giving rise to the term **leukocytoclastic vasculitis** (Fig. 11-27*A*). Although immunoglobulins and complement components can be demonstrated in early skin lesions, little or no immunoglobulin are found in most lesions (so-called "pauci-immune injury").