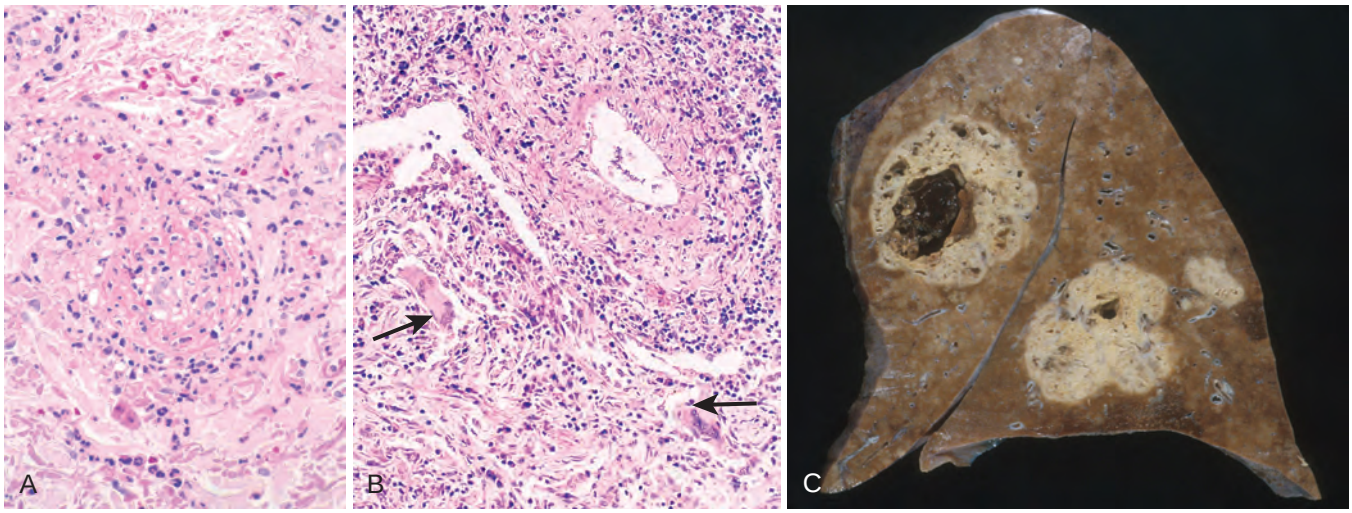

Figure 11-27 Small vessel vasculitis. **A,** Leukocytoclastic vasculitis (microscopic polyangiitis) with fragmentation of neutrophils in and around blood vessel walls. **B** and **C**, Granulomatosis with polyangiitis. **B,** Vasculitis of a small artery with adjacent granulomatous inflammation including epithelioid cells and giant cells *(arrows)*. **C,** Gross photo from the lung of a patient with fatal granulomatosis with polyangiitis, demonstrating large nodular centrally cavitating lesions. (**A,** Courtesy Scott Granter, MD, Brigham and Women's Hospital, Boston, Mass.; **C,** Courtesy Sidney Murphree, MD, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas.)

Clinical Features. Depending on the vascular bed involved, major clinical features include hemoptysis, hematuria and proteinuria, bowel pain or bleeding, muscle pain or weakness, and palpable cutaneous purpura. Except in those in whom widespread renal or brain involvement develop, immunosuppression induces remission and markedly improves long-term survival.

Churg-Strauss Syndrome

Churg-Strauss syndrome is a small-vessel necrotizing vasculitis classically associated with asthma, allergic rhinitis, lung infiltrates, peripheral hypereosinophilia, and extravascular necrotizing granulomata. Also called allergic granulomatosis and angiitis, it is a relatively rare disease (roughly one in a million people). Vascular lesions can be histologically similar to polyarteritis nodosa or microscopic polyangiitis, but are also characteristically accompanied by granulomas and eosinophils. ANCAs (mostly MPO-ANCAs) are present in less than half the cases, and suggest that there are distinct subsets of patients with the syndrome. Nevertheless, when present, the ANCAs are likely involved in the pathogenesis of the vascular lesions.

Churg- Strauss syndrome is a multisystem diseases with cutaneous involvement (palpable purpura), gastrointestinal tract bleeding, and renal disease (primarily as focal and segmental glomerulosclerosis). Myocardial involvement may give rise to cardiomyopathy; the heart is involved in 60% of patients and accounts for almost half of the deaths in the syndrome. Involvement of the heart is associated with the presence of eosinophilic infiltrates. The syndrome may be a consequence of hyperresponsiveness to an allergic stimulus; in patients with asthma, leukotriene receptor antagonists have been reported to be a trigger.

Behçet Disease

Behçet disease is a small- to medium-vessel neutrophilic vasculitis that classically presents as a clinical triad of recurrent oral aphthous ulcers, genital ulcers, and uveitis. There can also be gastrointestinal and pulmonary manifestations, with disease mortality related to severe neurologic involvement or rupture of vascular aneurysms. There is an association with certain HLA haplotypes (HLA-B51, in particular) and a cross-reactive immune response to certain microorganisms is implicated. T_H17 cells (Chapter 6) play a significant role by contributing to the recruitment of neutrophils, which are seen infiltrating vessels walls. However, the findings are nonspecific and the diagnosis requires an appropriate clinical story. Immunosuppression with steroids or TNF-antagonist therapies are generally effective.

Granulomatosis with Polyangiitis

Previously called Wegener granulomatosis, granulomatosis with polyangiitis is a necrotizing vasculitis characterized by a triad of:

- *Necrotizing granulomas* of the upper respiratory tract (ear, nose, sinuses, throat) or the lower respiratory tract (lung) or both.
- *Necrotizing or granulomatous vasculitis* affecting small- to medium-sized vessels (e.g., capillaries, venules, arterioles, and arteries), most prominent in the lungs and upper airways but involving other sites as well.
- *Focal necrotizing, often crescentic, glomerulonephritis.*

"Limited" forms of this disease may be restricted to the respiratory tract. Conversely, a widespread form of the disease can affect eyes, skin, and other organs, notably the heart; clinically, this resembles PAN except that there is also respiratory involvement.

Pathogenesis. Granulomatosis with polyangiitis likely represents a form of T-cell–mediated hypersensitivity response to normally "innocuous" inhaled microbial or other environmental agents; such a pathogenesis is supported by the presence of granulomas and a dramatic response to immunosuppressive therapy. PR3-ANCAs are also present in up to 95% of cases; they are a useful marker of disease activity and may participate in disease