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Vasculitis affecting the kidney

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Vasculitis refers to vessel wall leukocyte infiltration, often with necrosis, and can involve any of one or more vessels in the body. The kidney is commonly affected by vasculitis. Vasculitis is best classified based on the size of the involved vessels into large, medium, and small vessel disease. Small vessel vasculitis (SVV) that includes glomerulonephritis is by far the most frequent vasculitic lesion in the kidney, and the defining renal lesion is a necrotizing crescentic glomerulonephritis. Medium vessel vasculitis occasionally involves the kidney as necrotizing arteritis, and large vessel vasculitis only rarely affects the kidney, and most often secondarily by ischemia from proximal arterial narrowing. In this review, we describe the clinical and pathologic features of the various vasculitides that affect the kidney, with emphasis on SVV, particularly the type that is associated with anti-neutrophilic cytoplasmic antibodies (ANCA). We will also discuss the relevance of ANCA and describe evidence supporting the pathogenic role of these antibodies. It is important to remember that a histopathologic vasculitic lesion can be shared by several vasculitides, so that clinical data are most often required for disease classification.

The vasculitides are a heterogeneous group of disorders defined by vessel wall inflammation and necrosis. A vessel involved in an inflammatory process beginning elsewhere, such as from an adjacent abscess or leukocyte diapedesis in postcapillary venules, is not classified as vasculitis. Vasculitis can be idiopathic (primary) or secondary to rheumatologic diseases, concurrent with infections, or caused by drugs. Direct invasion of endothelial cells by microorganisms produces a picture resembling vasculitis (infectious vasculitis), but is generally not considered a vasculitic lesion.

The manifestations of disease are protean because the vasculitides can engage one or more vessels anywhere in the body from the aorta to the various capillaries and venules, and even veins. Clinical disease is a consequence of systemic inflammation, local inflammation, vascular narrowing, occlusion, or rupture, and usually manifests in the skin, connective tissue, kidney, gastrointestinal tract, lung, or peripheral nerves. Renal involvement is common and may be the first expression of a systemic vasculitis. The nonspecific clinical features and the low incidence of disease make the diagnosis difficult in the absence of a biopsy, particularly in the case of small vessel vasculitis (SVV).[1] Careful correlation with all available clinical and other laboratory data is usually required to make a definite diagnosis.

A first attempt at classification of the vasculitides was made in 1952 and included hypersensitivity angiitis, allergic granulomatous angiitis, rheumatic arthritis, periarteritis nodosa, and temporal arteritis.[2] Many classification systems have since been proposed, and none is universally accepted.[3,4] The major two in use are the American College of Rheumatology classification from 1990, based largely on clinical criteria,[5] and the subsequent Chapel Hill Nomenclature system from 1994, which provides definitions for the various vasculitides using pathologic features.[6] According to the Chapel Hill classification system, which is probably the most accepted and the one we will follow, vasculitis is

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Table 1 Classification of primary vasculitis*

Large vessel vasculitis
Giant cell (temporal) arteritis
Takayasu's arteritis
Medium vessel vasculitis
Polyarteritis nodosa
Kawasaki disease
Small vessel vasculitis
ANCA-associated
- Wegener's granulomatosis
- Microscopic polyangiitis
- Churg-Strauss syndrome
- Renal limited vasculitis

Henoch-Schonlein purpura
Essential cryoglobulinemic vasculitis
Cutaneous leukocytoclastic angiitis

*Chapel Hill classification (developed at the Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitis).[7]

classified based on size of involved vessels into large vessel vasculitis (LVV), medium vessel vasculitis (MVV), and SVV (Table 1). LVV primarily involves the aorta and its branches; MVV primarily involves arteries other than the aorta; and SVV primarily involves arterioles and capillaries (Figure 1). The most important distinction lies in the recognition of involvement of arterioles or capillaries, which precludes a diagnosis of vasculitis other than that of the small vessels. Hence, in the context of primary vasculitis, glomerulonephritis is exclusive to the small vessel vasculitides, and the presence or absence of glomerulonephritis is helpful in evaluating vasculitis affecting the kidney (Table 2).

Small vessel vasculitis

The small vessel vasculitides that affect the kidney include (1) anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (ANCA-SVV), which includes Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome, and renal limited vasculitis (sometimes referred to as idiopathic necrotizing crescentic glomerulonephritis); and (2) immune complex-mediated vasculitis, which includes

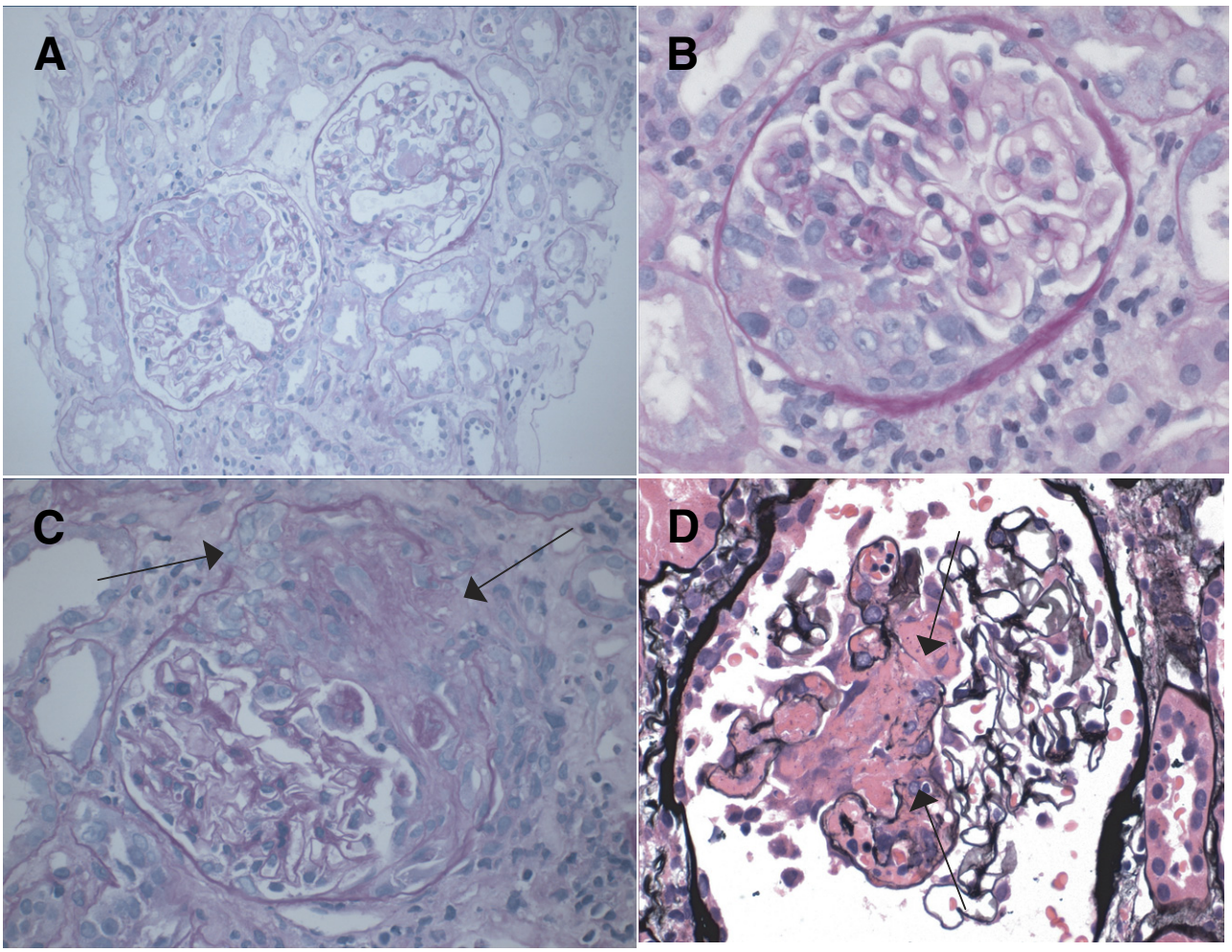

Figure 1 (A, B) Necrotizing crescentic lesions in ANCA-SVV are typically segmental, and the remainder of the tuft appears normal without an increase in cellularity (A: PAS, ×200; B: PAS, ×400). (C) Large crescents are often associated with breaks (arrows) in Bowman's capsule; the remainder of the glomerular tuft may still appear normal (PAS, ×200). (D) Glomerular basement membrane breaks (arrows) are a common finding and pathogenetically linked to crescent formation in cases of ANCA-SVV (PASML, ×400).