

Overview and Classification of Systemic Vasculitides

TERMINOLOGY

Synonyms

- Primary systemic vasculitides

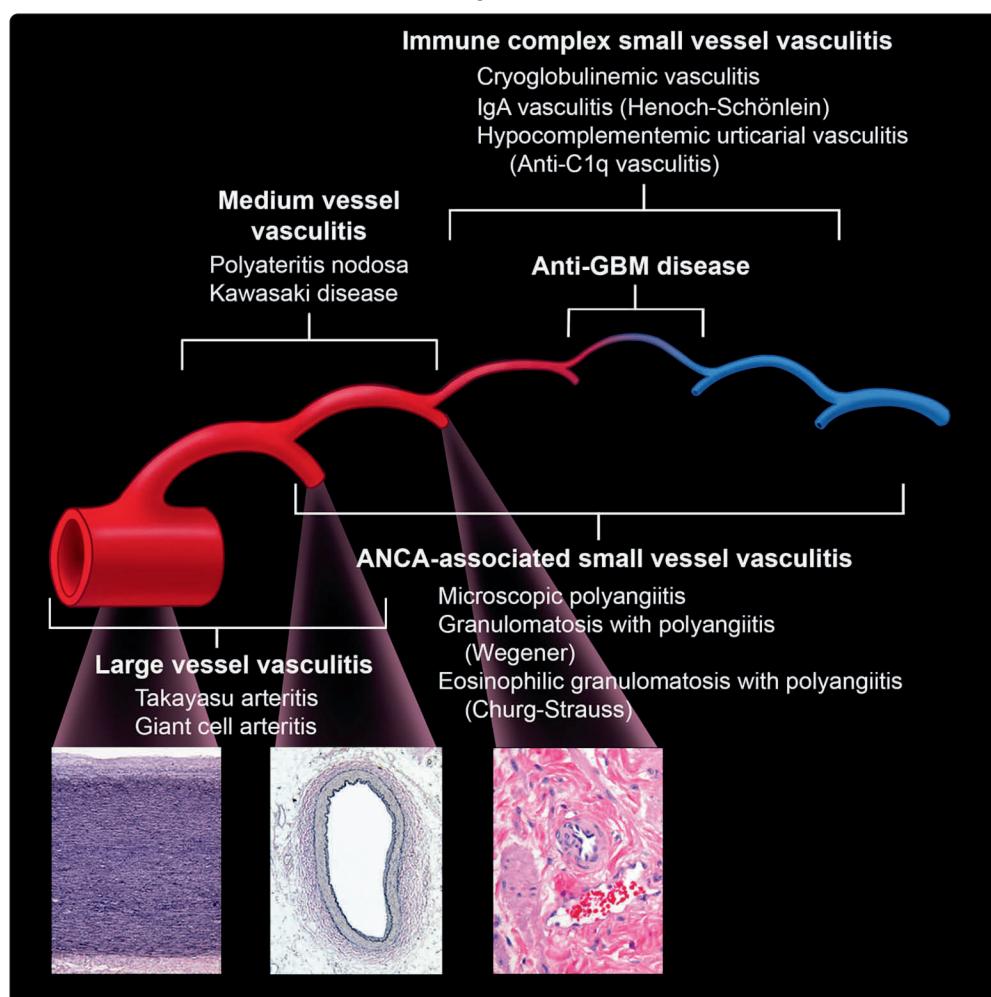
Definitions

- Pathological
 - Vasculitis defined as inflammation of blood vessels with demonstrable structural injury, such as disruption of elastic lamina ± fibrinoid necrosis
 - Occlusive changes due to inflammatory infiltrate or thrombosis often evident
- Clinical
 - Clinical definition not possible due to organ-specific or multisystemic disease
 - Rapid or prolonged evolution of clinical features over time may impede or delay definitive diagnosis
 - Thorough correlation with pathophysiologic mechanisms, serology, and imaging studies essential

History

- Vasculitis 1st described by Kussmaul and Maier in 1866
 - Termed "periarteritis nodosa"
- Giant cell arteritis described by Hutchinson (1890)
- Multiple vessel involvement and transmural arterial inflammation led to term "polyarteritis nodosa" by Ferrari (1903) and Dickson (1908)
- Takayasu arteritis described by Takayasu (1909)
- Granulomatosis with polyangiitis (Wegener) described by Klinger (1931) and Wegener (1934)
- Eosinophilic granulomatosis with Polyangiitis described by Churg and Strauss (1951), as allergic type
- Introduction of term "necrotizing angiitis" and attempt to classify vasculitis by Zeek in 1952
- Vasculitis and mucocutaneous lymph node syndrome described by Kawasaki in 1966
- "Microscopic polyangiitis" introduced in 1994 by Jennette and colleagues

CHCC Schematic of Systemic Vasculitides 2012



This schematic shows the predominant range of vascular involvement by different vasculitides, as described in the Chapel Hill Consensus Conference (CHCC) on Nomenclature of Systemic Vasculitis (2012). Those that affect capillaries are most likely to cause glomerulonephritis (modified from Jennette JC et al, CHCC 2012).

Overview and Classification of Systemic Vasculitides

Classification Considerations

- Vasculitides may be primary or secondary to systemic disease
- Vasculitides can localize to 1 organ or affect multiple organ systems
- Consensus classifications and criteria based on demographics, clinical characteristics, and pathology
- Progress toward classification based on etiology and pathogenesis

CHAPEL HILL CONSENSUS CONFERENCE NOMENCLATURE OF SYSTEMIC VASCULITIDES (1994 AND REVISED 2012)

General

- Developed definitions and standardized diagnostic terminology
- Categorization based on etiology, pathogenesis, pathology, and clinical characteristics
- Classification based on size of arterial vessel involved and type of inflammatory reaction
- Introduction of new terms in small vessel vasculitis to replace those with eponyms
- Division of small vessel vasculitis into ANCA-associated vasculitis (AAV) and immune complex (SVV)
- Emphasize role of ANCA (MPO-ANCA, PR3-ANCA) in pauci-immune small vessel vasculitis and crescentic glomerulonephritis
- Pathological correlation with clinical and laboratory features may identify specific therapeutic groups
- Pulmonary renal syndromes of pauci-immune small vessel vasculitides may have similarities and be distinguished by ANCA serology
- Inclusion of variable vessel vasculitis (2012)
- Inclusion of secondary form of vasculitis (2012)
- Disease in single organ may progress to systemic vasculitis

Large Vessel Vasculitis (LVV)

- Giant cell (temporal) arteritis (GCA)
 - Granulomatous arteritis of aorta and its major branches
 - Common in extracranial branches of carotid artery
 - Usually occurs in patients > 50 years
 - Often associated with polymyalgia rheumatica
- Takayasu arteritis (TAK)
 - Granulomatous inflammation of aorta and its major branches usually in patients < 50 years

Medium-Sized Vessel Vasculitis (MVV)

- Polyarteritis nodosa (PAN)
 - Necrotizing inflammation of medium-sized or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules
- Kawasaki disease (KD)
 - Arteritis involving large, medium-sized and small arteries
 - Associated with mucocutaneous lymph node syndrome
 - Coronary arteries often involved
 - Aorta and veins may be involved
 - Usually occurs in children

Small Vessel Vasculitis Including Capillaries, Venules, Arterioles, and Arteries (SVV)

- Antineutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV)
 - Granulomatosis with polyangiitis (Wegener) (GPA)
 - Granulomatosis inflammation involving respiratory tract and necrotizing vasculitis affecting small to medium-sized vessels
 - Necrotizing glomerulonephritis is common
 - Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss)
 - Eosinophil-rich and granulomatous inflammation involving respiratory tract and necrotizing vasculitis affecting small to medium-sized vessels; associated with asthma and eosinophilia
 - Crescentic glomerulonephritis when ANCA present
 - Microscopic polyangiitis (microscopic polyarteritis)
 - Necrotizing vasculitis with few or no immune deposits, affecting small and medium-sized vessels
 - Necrotizing glomerulonephritis very common
 - Pulmonary capillaritis often occurs
- Immune complex vasculitis
 - Vasculitis with moderate to marked vessel wall deposits of immunoglobulins &/or complement components
 - Predominantly affects small vessels: Capillaries, arterioles, venules, small arteries
 - Glomerulonephritis frequent
- Antiglomerular basement membrane (anti-GBM) disease
 - Vasculitis affecting glomerular capillaries, pulmonary capillaries, or both
 - GBM deposition of anti-GBM autoantibodies
 - Lung involvement causes pulmonary hemorrhage
- IgA vasculitis (Henoch-Schönlein) (IgAV)
 - Vasculitis with IgA-dominant immune deposits, affecting small vessels
 - Typically involves skin, gut, and glomeruli, and associated with arthralgias or arthritis
- Cryoglobulinemic Vasculitis
 - Small vessel vasculitis with cryoglobulin immune deposits
 - Associated with serum cryoglobulins
 - Skin, glomeruli and peripheral nerves often involved
- Hypocomplementemic urticarial vasculitis (HUV) (anti-C1q vasculitis)
 - Vasculitis with urticaria and hypocomplementemia
 - Affects small vessels
 - Associated with anti-C1q antibodies
 - Glomerulonephritis, arthritis, obstructive pulmonary disease, ocular inflammation common

Variable Vessel Vasculitis (VVV) Affecting Any Size Vessel

- Behçet disease (BD)
 - Vasculitis can affect arteries or veins
 - Recurrent oral &/or genital aphthous ulcers
 - Inflammatory lesions in cutaneous, ocular, articular, gastrointestinal, &/or central nervous system
 - SVV, thromboangiitis, thrombosis, arterial aneurysms
- Cogan syndrome (CS)
 - Ocular inflammatory lesions
 - Inner ear disease

Overview and Classification of Systemic Vasculitides

- Arteritis of all sizes, aortitis/aneurysms, aortic and mitral valvulitis

Single Organ Vasculitis (SOV)

- Vasculitis of arteries or veins of any size in single organ
- Skin, central nervous system, isolated aortitis
- Unifocal or multifocal
- May progress to septic vasculitis

Vasculitis Associated With Systemic Disease

- Rheumatoid vasculitis
- Lupus vasculitis
- Sarcoid vasculitis

Vasculitis Associated With Probable Etiology

- Drug induced vasculitis e.g., hydralazine
- Infection related vasculitis
- Hepatitis C virus-associated cryoglobulinemic vasculitis
- Hepatitis B virus-associated vasculitis
- Syphilis-associated aortitis
- Drug-associated immune-complex vasculitis
- Drug-associated ANCA-associated vasculitis
- Cancer-associated vasculitis

OTHER CLASSIFICATION SYSTEMS

American College of Rheumatology (1990) (ACR)

- Criteria for diagnosis of vasculitides
 - Clinical criteria developed to standardize cohorts of patients in almost all primary systemic vasculitides
 - ≥ 3 criteria associated with high degree of sensitivity and specificity for diagnosis in appropriate context
 - Application of criteria for individual patients may not be entirely helpful
 - ANCA not used in this classification process

EULAR/PRES Classification of Pediatric Vasculitis (European League Against Rheumatism/Pediatric Rheumatology European Society)

- Predominantly large vessel
 - Takayasu arteritis
- Predominantly medium vessel
 - Childhood polyarteritis nodosa
 - Cutaneous polyarteritis
 - Kawasaki disease
- Predominantly small vessel
 - Granulomatous
 - Granulomatosis with polyangiitis (Wegener)
 - Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
 - Nongranulomatous
 - Microscopic polyangiitis
 - Henoch-Schönlein purpura
 - Isolated cutaneous leukocytoclastic vasculitis
 - Hypocomplementemic urticarial vasculitis
- Other
 - Behçet disease
 - Vasculitis secondary to infection, malignancy, drugs
 - Isolated vasculitis of central nervous system
 - Cogan syndrome
 - Unclassified

EPIDEMIOLOGY

Incidence

- Depends on specific types of vasculitis and associated primary or secondary systemic diseases

Ethnicity and Distribution

- Takayasu arteritis and Kawasaki disease most common in Asia and Far East countries
- Granulomatosis with polyangiitis and eosinophilic granulomatosis and polyangiitis have predilection for North America and Northern Europe, mainly in Caucasians
- Higher incidence of microscopic polyangiitis in Asia

Age Range

- Adults: Age range depends on type of disease
- Children at or below 18 years old
 - Annual incidence: 53.3/100,000
- Geographical variations of diseases may reflect environmental and ethnic influences

ETIOLOGY/PATHOGENESIS

Etiology

- Immune complexes
 - Mixed cryoglobulinemia
 - Lupus erythematosus
 - Henoch-Schönlein purpura (IgA Vasculitis)
- Autoantibodies
 - ANCA
 - Microscopic polyangiitis
 - Granulomatosis with polyangiitis (Wegener)
 - Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
 - Possibly other forms of vasculitides
- Idiopathic
 - Takayasu arteritis
 - Kawasaki disease
 - Giant cell arteritis
- Other factors
 - Infections
 - Bacteria, viruses, fungi, rickettsia, parasites
 - Drug reaction

CLINICAL IMPLICATIONS

Clinical Presentation

- General constitutional symptoms are common with all forms of vasculitis in initial or acute stage
- Specific signs and symptoms depend on several factors
 - Single or multiple organ system involvement
 - Size and type of vessel involved
 - Pathogenetic mechanisms
 - Pathological findings
 - Severity of disease
- Specific presenting symptoms of complications of vasculitis
 - Vascular stenosis, occlusion, aneurysm, hemorrhage
- Symptoms can be acute, subacute, or chronic
- Clinical features of vasculitis can mimic vasculitis-like diseases, vasculopathies, and, rarely, nonvascular diseases
- Renal findings in vasculitis

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- Hematuria, subnephrotic proteinuria
- Rapidly progressive renal failure
- Chronic renal failure
- Benign or malignant hypertension

Laboratory Findings

- Acute phase response associated with active vasculitis
- Complete blood counts
 - Varied granulocytosis or lymphocytosis
 - Thrombocytosis
 - Anemia
- Specific organ function tests
 - Kidney, lung, heart, liver, pancreas, endocrine
- Serologic tests
 - Various types of infections
 - Autoantibodies
 - Antineutrophil cytoplasmic antibodies
 - Antinuclear antibodies
 - Rheumatoid factor
 - Antiglomerular basement membrane
 - Other less frequent but specific antibodies
 - Complement levels
 - C3, C4, C1q
 - Urinalysis
 - Hematuria, proteinuria, casts, cells

Imaging Findings

- Most useful in large and medium-sized vessel vasculitides
- Each diagnostic category has several vascular patterns
- Variety of imaging modalities may be used
 - Plain x-ray
 - Angiography
 - Computed tomogram
 - Magnetic resonance
 - Doppler studies
 - Tc-99m DMSA scanning

Prognosis

- Vasculitides range from self-limiting to relapsing disease
- Significant diagnostic delays occur due to frequent clinical overlap and nonspecific findings leading to worse prognosis
- Varied morbidity and mortality
 - Specific organ involvement
 - Severity of vasculitis
 - Complications
- Sequelae of vasculitis contribute to further organ damage
- Infectious complications due to immunosuppression

Treatment

- Ideally, therapeutic approaches should be based on etiology &/or pathophysiology of the vasculitides
 - Corticosteroid therapy alone useful for giant cell arteritis and eosinophilic granulomatosis with polyangiitis without renal involvement
- Clinical heterogeneity and varied immune-mediated pathogenetic mechanisms prompt empirical initial therapy
- Number of treatment protocols used for primary and secondary vasculitides
 - Cyclophosphamide and steroids in small vessel vasculitides
 - Plasmapheresis and anti-CD20 antibody in severe disease

- Oral steroids, methotrexate, and azathioprine employed for maintenance of remission
- New biological agents being tested

MACROSCOPIC

General Features

- Large and medium-sized vessel vasculitides display distinctive gross characteristics from specimens obtained following excision during surgery or autopsy specimen
- Renal vasculitides of all sizes may result in segmental/total infarction and parenchymal atrophy in renal artery stenosis
- Cortical petechial hemorrhages in small vessel vasculitides

MICROSCOPIC

General Features

- Types of vascular inflammation in vasculitis can be
 - Neutrophil, eosinophil, or lymphocyte rich
 - Granulomatous
 - Necrotizing
 - Can be focal, segmental, or circumferential in distribution
- Other findings
 - Endothelial injury and necrosis
 - Disruption of internal &/or external elastic lamina
 - Focal medial laminar lysis of elastic fibers
 - Medial and adventitial inflammation
 - Intravascular thrombosis
 - Tissue infarction
 - Fibromyointimal thickening of healed lesions
- Organ-specific changes
 - Kidneys showing crescentic glomerulonephritis and medullary angiitis
 - Alveolar capillaritis and lung hemorrhage
 - Leukocytoclastic vasculitis in skin
 - Myocardial inflammation and valvulitis

CONDITIONS THAT MIMIC VASCULITIS

Large Arteries

- Fibromuscular dysplasia
- Extensive atherosclerosis
- Other forms of aortitis

Medium-Sized Arteries

- Embolic phenomena

Small Vessel Disease

- Atheroemboli
- Bacterial endocarditis
- Thrombotic microangiopathy
 - Antiphospholipid antibody syndrome
- Atrial myxoma
- Amyloid angiopathy

SELECTED REFERENCES

1. Flores-Suárez LF et al: Critical appraisal of classification criteria for vasculitides. *Curr Rheumatol Rep.* 16(6):422, 2014
2. Jennette JC: Overview of the 2012 revised International Chapel Hill Consensus Conference nomenclature of vasculitides. *Clin Exp Nephrol.* 17(5):603-6, 2013

Overview and Classification of Systemic Vasculitides

Differential Diagnosis

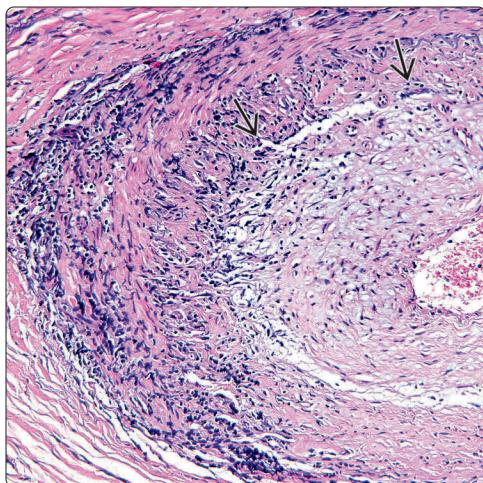
Type	Clinical Features	Serology	Pathologic Features	Glomerular Lesion
Large Vessel Vasculitis (Large, Aorta and Major Branches)				
Giant cell arteritis: Usually > 50 years, M:F 1:2-6	Polymyalgia rheumatica (50%), mostly head and neck symptoms	ANCA(-)	Commonly temporal arteritis, mononuclear infiltration with multinucleated giant cells	Ischemic changes; amyloidosis
Takayasu arteritis: Usually 30-50 years, M:F = 1:8	Initial nonspecific symptoms, later ischemic effects of tissues	ANCA(-)	Granulomatous panarteritis with multinucleated giant cells	Ischemic changes; mesangial or focal proliferative GN
Medium-Sized Vessel Vasculitis (Medium-Sized Arteries)				
Polyarteritis nodosa: Peak 40-60 years, M:F = 2:1	Multisystem, hypertension, organ ischemic symptoms	Rarely MPO+; Hepatitis B virus (+)	Fibrinoid necrotizing arteritis, transmural, healed lesions, stenosis, aneurysms	Ischemic changes; rare pauci-immune crescentic GN
Kawasaki disease: < 3 years in most cases; M:F = 5:1	Mucocutaneous lymph node syndrome; coronary artery vasculitis	Systemic atypical cytoplasmic ANCA(+)	Depending on stage: Acute neutrophilic arteritis, aneurysm formation, chronic inflammation, and scarring	Rare mesangial proliferative GN; patchy interstitial inflammation
Small Vessel Vasculitis (Small Arteries, Arterioles, Venules, Capillaries)				
Microscopic polyangiitis: Any age, peak: 50 years; M = F	Multisystemic, kidney (90-100%), nephritic syndrome, rapidly progressive renal failure, no asthma	MPO ANCA (+) 60%, PR3 ANCA (+) 15%	Fibrinoid necrotizing vasculitis	Pauci-immune crescentic GN
Granulomatosis with polyangiitis: Any age, peak: 30-50 years, M > F	Multisystemic, upper airway, lung and kidneys (90%), rapidly progressive renal failure, no asthma	PR3 ANCA (+) > 75%, MPO ANCA (+) < 25%	Necrotizing, vascular or extravascular granulomatous inflammation	Pauci-immune crescentic GN, acute, subacute, and chronic
IgA vasculitis: 90% before 10 years; M > F; adult/secondary	Multisystemic, kidney, lung, gastrointestinal tract	↑ serum IgA, normal complement, ANCA(-)	Leukocytoclastic vasculitis, dominant IgA and C3 deposits	Mesangial or endocapillary proliferation ± crescents and IgA deposits
Eosinophilic granulomatosis with polyangiitis: Peak: 40-60 years; M = F	Multisystemic, asthma, eosinophilia, renal manifestations in < 30% of cases	ANCA(+) (40-70%), mostly anti-MPO	Eosinophil-rich fibrinoid necrotizing vasculitis and granulomatous inflammation	Commonly mesangial, occasional pauci-immune, proliferation, focal GN with crescents
Cryoglobulinemic vasculitis: Adults	Multisystemic, skin and kidney frequently involved	Elevated monoclonal IgM κ RF, 90% HCV(+)	Leukocytoclastic vasculitis with cryoprecipitates, IgM κ, IgG, and C3 deposits	Membranoproliferative GN ± crescents and cryo deposits
Systemic lupus erythematosus: Any age, M:F = 1:9	Multisystemic, skin and kidney (90%)	ANA(+), dsDNA(+), sometimes ANCA(+)	Necrotizing vasculitis	Immune complex GN ± crescents; rarely, pauci-immune crescentic GN

Vascular Diseases Mimicking Vasculitis

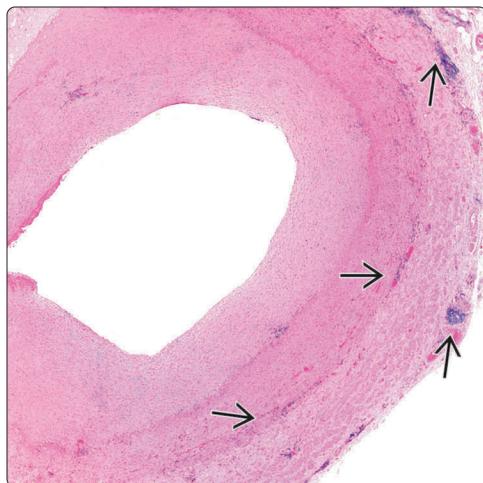
Disease	Location	Pathology	Inflammation	Pathogenesis
Antiphospholipid antibody syndrome	All calibers of arteries and veins, capillaries	Fibrin or organizing vascular thrombi, focal recanalization	Rare or none	Antiphospholipid antibodies or lupus anticoagulant
Thrombotic microangiopathy	Small arteries, arterioles, capillaries	Endothelial swelling, mucoid change, fibrin, thrombi; intact elastic lamina	Minimal mononuclear	Abnormalities of ADAMTS13; immune complexes; drug induced
Atheroembolism	All calibers of arteries up to capillaries	Luminal occlusion by crystalline cholesterol clefts ± thrombosis	Giant cell reaction in older lesions	Emolic phenomenon from atherosomas of larger arteries
Amyloid angiopathy	Medium and small arteries, arterioles, and capillaries	Congo red positive, amorphous, acellular, vascular amyloid	None	AL amyloid; rarely other forms of amyloid
Atrial myxoma (intracardiac tumor)	Small arteries, arterioles, and capillaries	Luminal occlusion by fragments of myxoma	None	Emboli from cardiac tumor
Bacterial endocarditis	Small arteries, arterioles, and capillaries	Local ischemic changes, focal glomerulonephritis	Sometimes	Emboli from valvular vegetations, bland or septic

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Giant Cell (Temporal) Arteritis

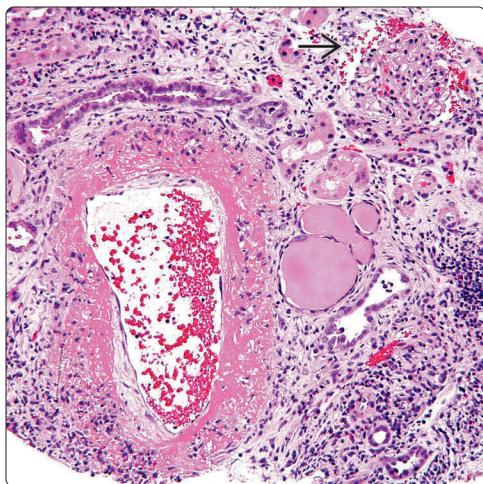


Takayasu Arteritis

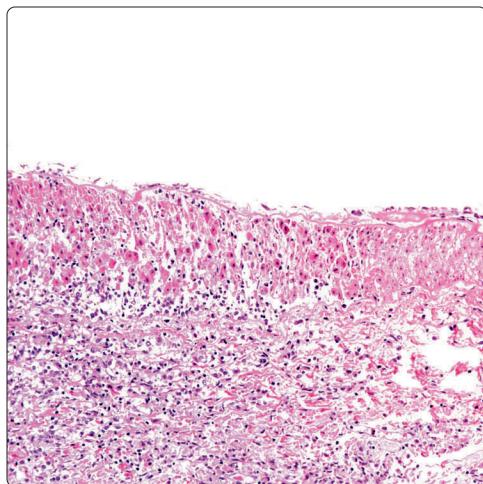


(Left) Segment of temporal artery with giant cell arteritis shows transmural arteritis with inflammatory cell infiltration in the adventitia and the media with marked fibromyointimal thickening. Rare multinucleated giant cells are noted □. (Right) Cross section of a thickened large artery from a young female with Takayasu arteritis shows myointimal proliferation with inflammation and focal medial and adventitial inflammation □ (Courtesy J.C. Jennette, MD.)

Polyarteritis Nodosa

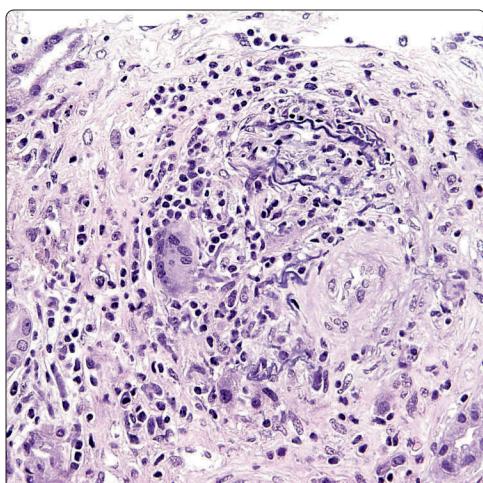


Kawasaki Disease, Coronary Artery

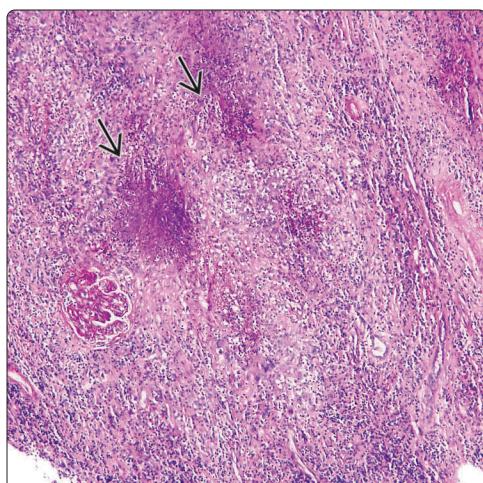


(Left) A renal artery larger than interlobular type with polyarteritis nodosa shows circumferential, transmural fibrinoid necrosis accompanied by primarily neutrophilic infiltrate. An uninvolved glomerulus is seen □. (Right) Microscopic section of a coronary artery from a patient with Kawasaki disease shows medial and intimal mixed inflammatory cell infiltrate without significant fibrinoid necrosis. (Courtesy J.C. Jennette, MD.)

Granulomatous Arteritis



Necrotizing Interstitial Granulomatous Inflammation in GPA

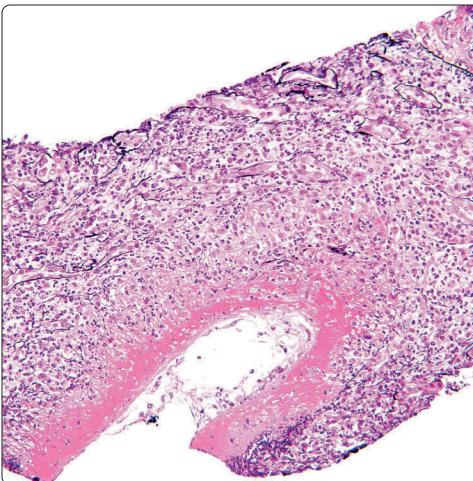


(Left) Case of GPA with organizing granulomatous arteritis showing disruption and fragmentation of the elastic lamina by GMS stain. (Right) PAS-stained kidney section with granulomatosis with polyangiitis (Wegener) shows typical irregular necrotizing granulomatous inflammation with a neutrophilic center □. An adjacent glomerulus with ischemic change is noted. (Courtesy W. Travis, MD.)

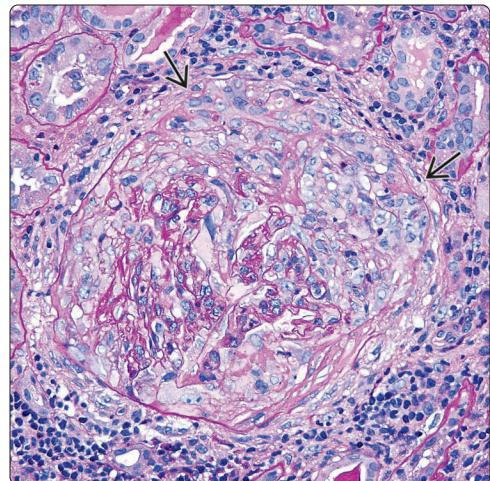
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(Left) A specimen from a patient with high-titer MPO-ANCA shows full-thickness necrotizing vasculitis of a small intrarenal artery surrounded by active neutrophilic and lymphocytic infiltrate with loss of elastic lamina, consistent with microscopic polyangiitis. There is interstitial inflammation and tubulitis. **(Right)** Glomerulus from a patient with PR3-ANCA(+) shows a large, almost circumferential cellular crescent. Part of the Bowman capsule is disrupted by periglomerular inflammatory infiltrate ↗.

Necrotizing Vasculitis in Intrarenal Artery of MPA

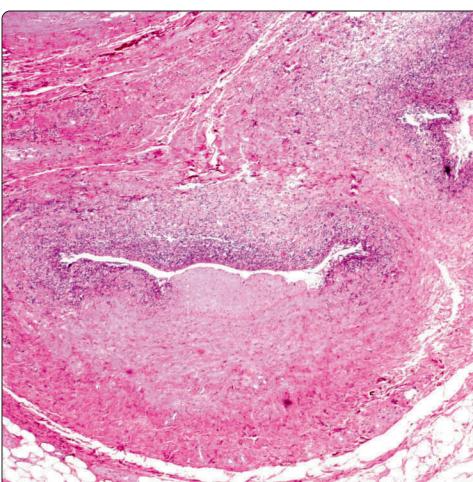


Glomerulus With Circumferential Cellular Crescent

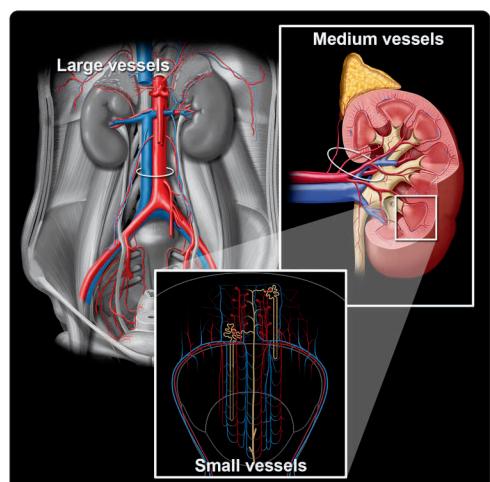


(Left) Subcutaneous, medium-sized artery from a patient with eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss) shows segmental transmural inflammation with many eosinophils. **(Right)** Detailed diagram of the arterial vessels involved by large, medium, and small vessel vasculitides as proposed by The Chapel Hill Consensus Conference 2012.

EGPA (Churg-Strauss) in a Subcutaneous Artery

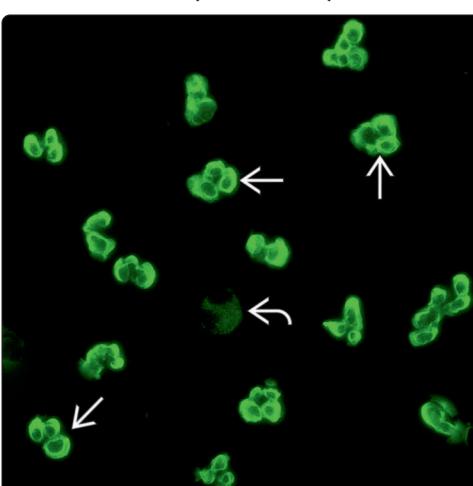


Diagrams Representing Large, Medium and Small Vessels Associated With Kidney

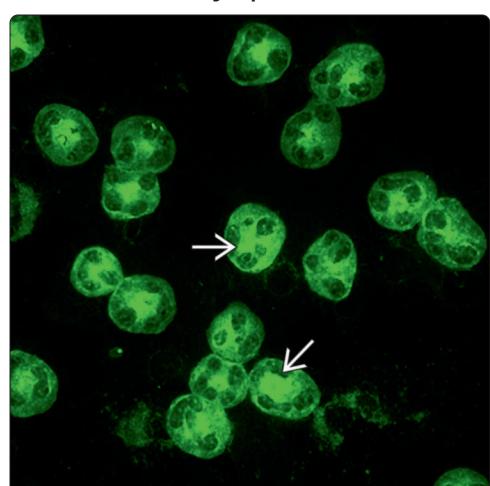


(Left) p-ANCA (perinuclear) pattern ↗ due to MPO IgG antibodies is demonstrated by indirect IF with a patient's serum incubated on alcohol-fixed normal neutrophils. The cytoplasm is not visible. A negative eosinophil is also present ↗. (Courtesy A.B. Collins, BS.) **(Right)** The c-ANCA (cytoplasmic) pattern ↗ due to PR3 antibodies is demonstrated by indirect IF with a patient's serum incubated on an alcohol-fixed smear of normal neutrophils. (Courtesy A.B. Collins, BS.)

MPO-ANCA (Perinuclear) Pattern

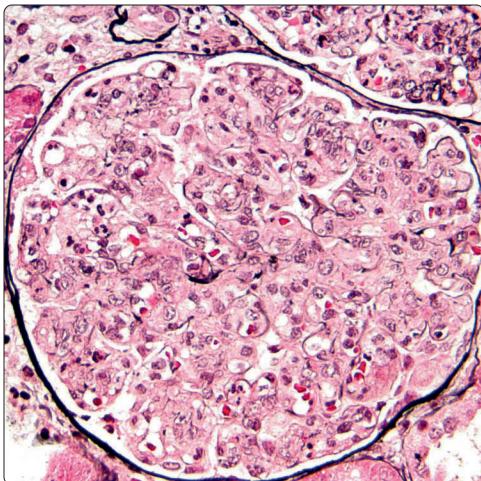


PR3-ANCA Cytoplasmic Pattern

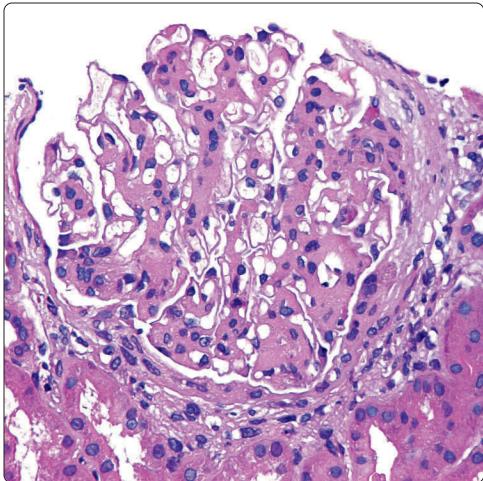


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Global Proliferative Glomerulonephritis in HUVS

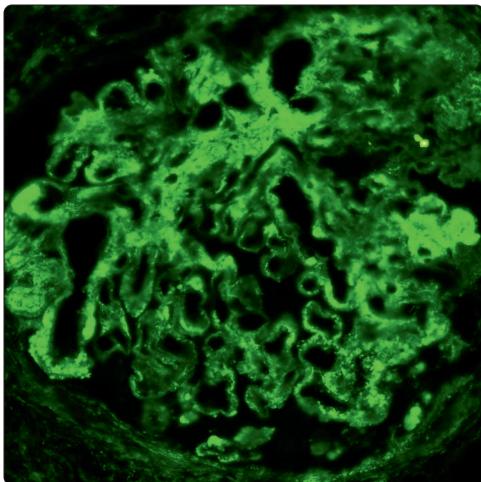


Global Mesangial Proliferative GN in HUVS

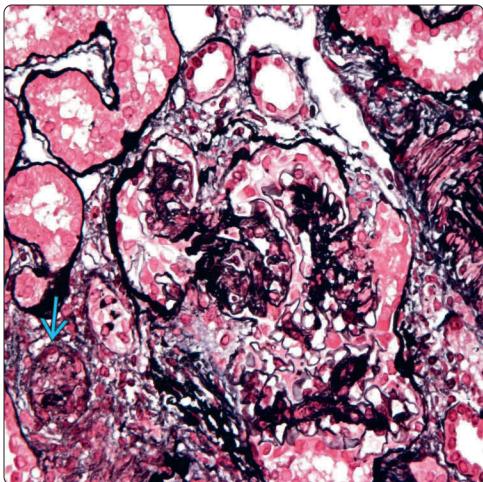


(Left) Glomerular capillaries are filled with leukocytes, including neutrophils and mononuclear cells. The glomerular basement membrane appears normal, without duplication. The mesangium is hypercellular. (Courtesy S. Florquin, MD.) (Right) A case of HUVS showing diffuse mesangial proliferation and segmental capsular adhesion containing increased mesangial immune complex deposits. The peripheral capillary walls appear mostly uninvolved. (Courtesy D. Ferluga, MD.)

Global Capillary Wall IgG Deposits

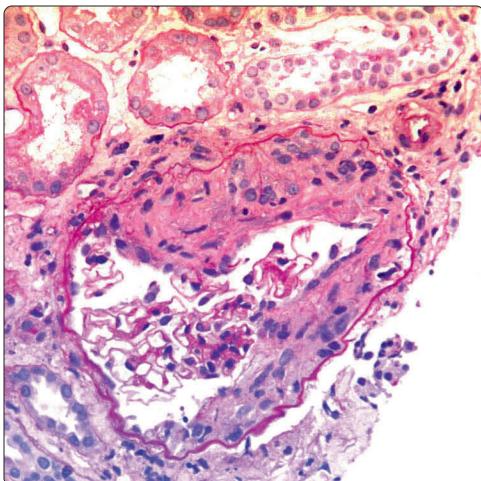


Mesangial GN With Necrotizing Small Vessel Vasculitis

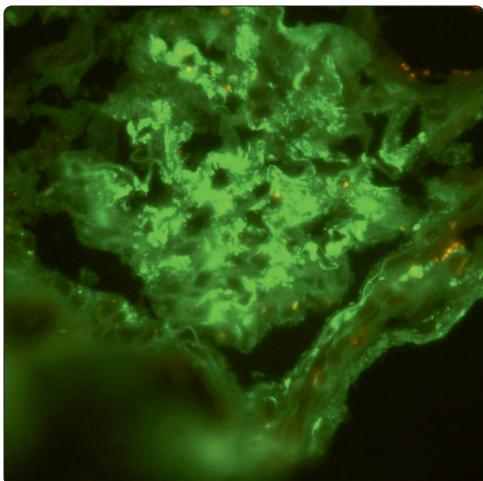


(Left) A case of hypocomplementemic urticarial vasculitis with glomerulonephritis showing granular 3+ IgG deposits within the glomerular capillary walls and mesangial areas in global distribution along with C1q deposits in the same areas. (Courtesy A. Vizjak, PhD.) (Right) This case of HUVS shows a focus of small vessel vasculitis with thrombosis □ and mesangial proliferative glomerulonephritis with capsular adhesion. (Courtesy D. Ferluga, MD.)

Immune Complex Glomerulonephritis With Crescent



Global Mesangial and Capillary Wall Immune Deposits

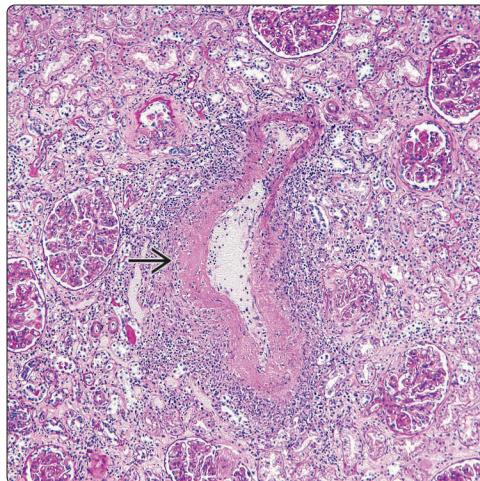


(Left) A case of Behcet disease presented with nephritic syndrome and immune complex glomerulonephritis with crescents. This image shows a fibrocellular crescent. (Courtesy B. Fyfe, MD.) (Right) Image from the same case shows mild proliferative and crescentic glomerulonephritis with deposits composed of polyclonal IgG, IgM and C3. (Courtesy B. Fyfe, MD.)

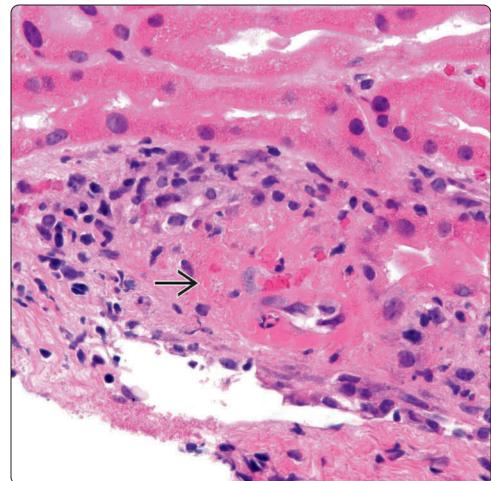
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(Left) Florid arteritis in an SLE patient is manifested by an interlobular artery with transmural fibrinoid necrosis → and inflammatory infiltrate of neutrophils and lymphocytes. (Courtesy B. Fyfe, MD.) **(Right)** SVV in mixed cryoglobulinemia with eosinophilic material resembles fibrin → composed of precipitated immune complexes of monoclonal IgM rheumatoid factor and IgG. In contrast to fibrin, these deposits are rounded, PAS(+), and stain for IgM and IgG.

Necrotizing Lupus Vasculitis Resembling MPA

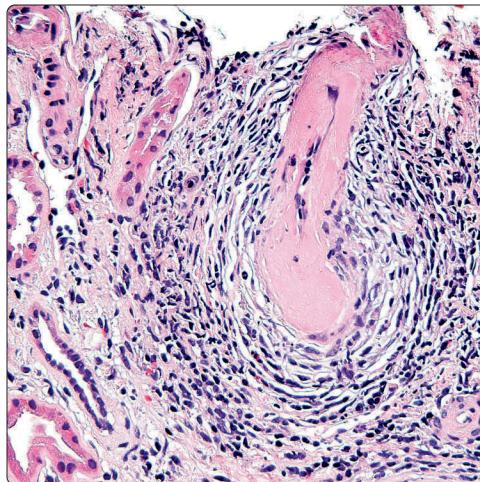


Cryoglobulinemic Vasculitis

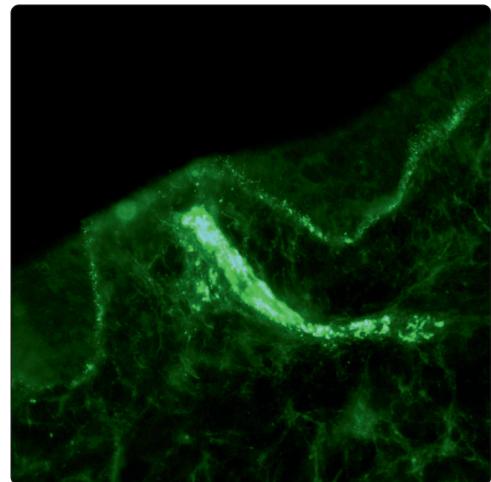


(Left) Cryoglobulin-associated small vessel vasculitis typically has amorphous pale eosinophilic vascular cryoglobulin deposits. Here, they narrow the lumen in a kidney biopsy from a patient with HCV and cryoglobulinemic glomerulonephritis. **(Right)** Immunofluorescence microscopy of skin shows positive cryoglobulin deposits that stain for IgM within the dermal vessels. These deposits also stain for IgG and C3. The IgM is a monoclonal (kappa) rheumatoid factor.

Cryoglobulinemic Vasculitis in HCV Patient

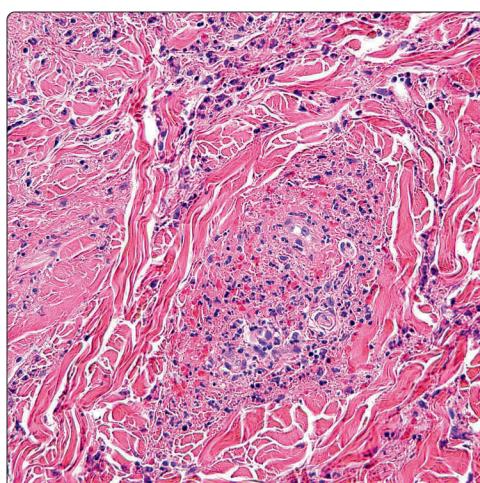


IF of Skin With IgM Cryoglobulin Deposits

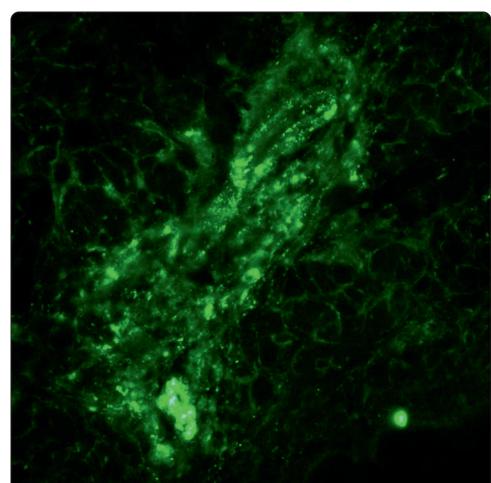


(Left) Skin biopsy shows leukocytoclastic vasculitis and extravasation of red blood cells in a patient with Henoch-Schönlein purpura (HSP). **(Right)** Immunofluorescence of skin biopsy from a patient with Henoch-Schönlein purpura shows dominant granular staining for IgA in the vascular and perivascular areas enabling the diagnosis of HSP to be made.

Skin Biopsy With IgA Leukocytoclastic Vasculitis

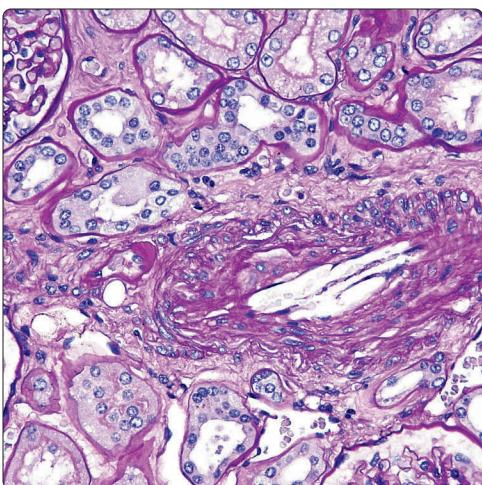


Skin Biopsy With IgA Vasculitis

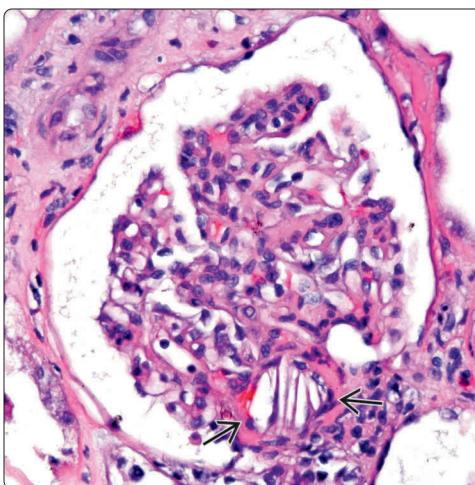


Overview and Classification of Systemic Vasculitides

Intrarenal Arterial Atheroemboli

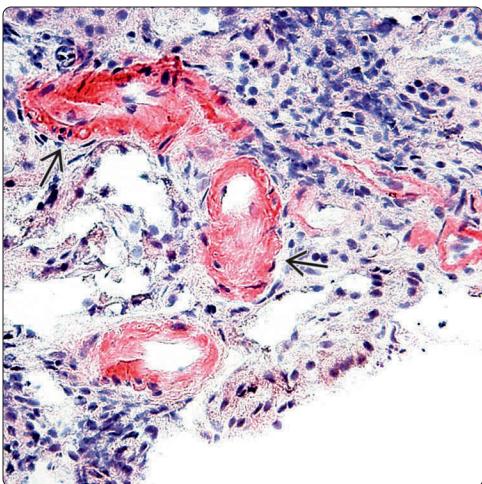


Glomerular Hilar Arteriole With Atheroemboli

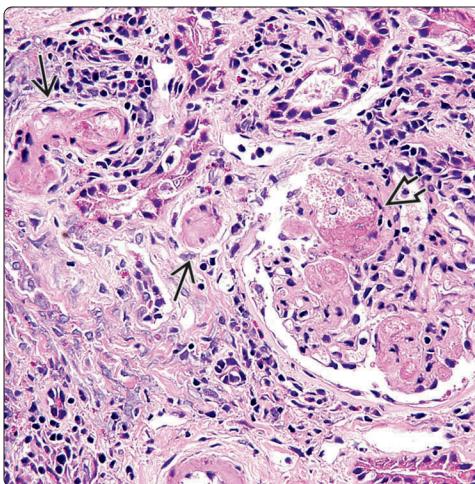


(Left) A biopsy from an elderly patient presenting with acute renal failure, skin rash, and early gangrenous changes of digits in the foot shows atheroemboli within an interlobular artery characterized by needle-shaped spaces signifying cholesterol crystals washed off during processing of the tissue. (Right) A glomerulus shows needle-shaped atheroemboli □ within the hilar arteriole that led to mild to moderate ischemic collapse of the capillary tuft. (Courtesy L. Barisoni, MD.)

Renal Arteriolar and Capillary Amyloid Deposits

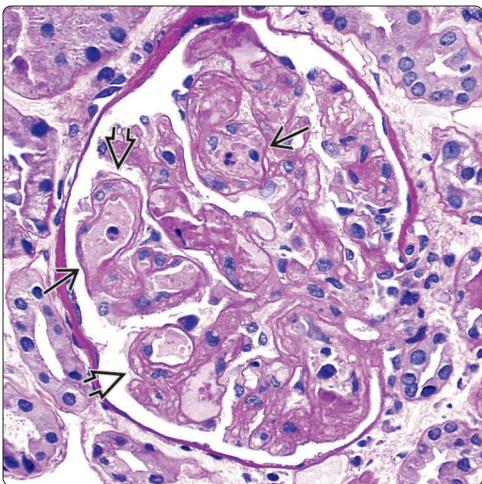


Phospholipid Antibody Syndrome With Microvascular Thrombi

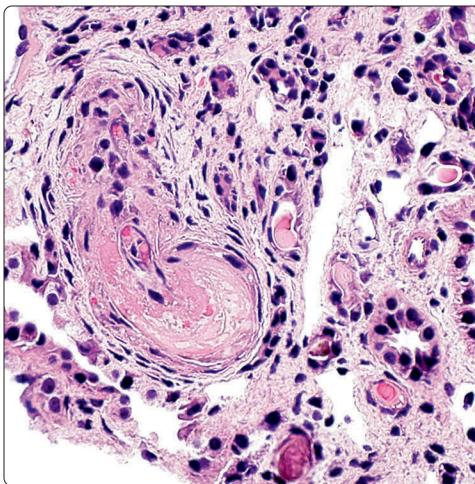


(Left) Amyloid angiopathy is shown. Kidney biopsy from an older patient presenting with heart and liver disease and progressive renal failure with minimal proteinuria shows exclusively vascular and microvascular □ amyloid deposits by Congo red. (Right) A kidney biopsy from a patient with antiphospholipid antibody syndrome having livedo reticularis, stroke, and acute renal failure shows noninflammatory microvascular thrombi within the arterioles □ and glomerulus □.

Thrombotic Microangiopathy in a Glomerulus



Renal Arteriole With Thrombotic Microangiopathy



(Left) Glomerulus in a patient with thrombotic thrombocytopenic purpura shows focal intracapillary microthrombi □ and thickening of the peripheral capillary wall with segmental double contours □. (Right) Renal biopsy from a patient with thrombotic thrombocytopenic purpura shows noninflammatory endothelial injury of an arteriole with detachment, subendothelial widening, and accumulation of a fibrin thrombus. Focal trapped fragmented RBCs are noted.