Vasculitides

Anna Chacon, MD

Diagnosis	Epidemiology	Pathogenesis	Clinical Features	Diagnostic Approach	Pathology	Therapy	Complications/ Associations
SMALL VESSEL VASCULITIS							
Cutaneous small vessel vasculitis [(CSVV), cutaneous leukocytoclastic vasculitis (LCV)/angiitis, hypersensitivity angiitis, allergic vasculitis, cutaneous necrotizing venulitis]							
Henoch-Schönlein purpura (anaphylactoid purpura, purpura rheumatica, CSVV secondary to circulating IgA immune complexes)	Most common in children < 10 yrs; associated w/ preceding respiratory infection- 75% by GAS. May be seen in adults. Slight male predominance.	IgA-dominant immune deposits in small blood vessel walls. Dx supported by IgA predominance in the correct clinical setting.	1 - Intermittent palpable purpura on extensor extremities & buttocks 2 – arthralgias, arthritis 3 - abdominal pain/ melena; bowel angina/ischemia 4 – renal involvement (hematuria & RBC casts).	Palpable purpura (required) w/ at least 1 of the following: arthritis/ arthralgia, diffuse abdominal pain, renal involvement, bx w/IgA deposition.	Necrotizing vasculitis. Immunoreactants deposited in skin are IgA. DIF: perivascular IgA, C3 & fibrin deposits.	Self-limited, supportive. Dapsone & colchicine may decrease duration of skin lesions. Systemic steroids: Rx for arthritis & abdominal pain. Nephrology referral w/ renal involvement.	Renal vasculitis often mild but can be chronic. May be associated w/underlying malignancy in adults.
Acute hemorrhagic edema of infancy (Finkelstein's dz, Seidlmayer syndrome, purpura en cocarde avec edema, postinfectious cockade purpura)	Seen primarily in children 4-24 months of age. Child is well appearing.	Unknown. 75%: associated w/infxn, drug exposure, or immunization. Thought to involve immune complex deposition responding to antigenic trigger.	Benign clinical course. Annular, circular, or targetoid purpuric plaques on face & extremities. Tender, non-pitting edema of acral sites.	Routine labs: nonspecific. Dx based on clinicopathologic correlation. Characteristic: age onset < 2 yrs., disease confined to skin, brief duration.	LCV involving capillaries & postcapillary venules of upper & mid-dermis. DIF: IgA deposits in vascular pattern in 1/3 – 1/4 of cases.	Spontaneous resolution within 1-3 weeks. Antihistamines for symptomatic relief.	Extracutaneous involvement rare. Two-thirds of pts have infectious prodrome.
Urticarial vasculitis (chronic urticaria as a manifestation of venulitis, urticaria & arthralgia w/ necrotizing angiitis)	Uncommon. Peak incidence: 5th decade. 60-80% female. Hypocomplementemic form: almost exclusively in women.	Complement activation triggers mast cell release of inflammatory mediators. Idiopathic or associated with SLE, Sj□gren's, cryoglobulinemia, or Wegener's granulomatosis.	Painful/burning urticarial lesions lasting >24 hrs; resolve leaving behind hemosiderin, causing red-brown maculae/ postinflammatory hyperpigmentation.	Lab: ESR, CRP, SPEP, ANA, autoantibodies (anti-SS-A/Ro, anti-SS-B/La), complement levels (CH50, C3, C4). Further evaluation can include: CXR, PFTs, RFTs.	Typically hive w/edema but also w/LCV. A perivascular lymphocytic infiltrate is not enough for dx.	Difficult. Try: antihistamines, dapsone, NSAIDS, antimalarials. Unresponsive/ systemic: steroids & perhaps additional immunosuppressants.	Many pts have hives persisting >24 hrs, but few have urticarial vasculitis w/signs & sxs. Systemic: arthritis, nephritis, abdominal distress. Lung involvement can be fatal.
Erythema elevatum diutinum (extracellular cholesterosis)	Uncommon, rare. Can develop at any age. No racial/gender predilection.	Suspicion that streptococci are trigger for chronic immune complex reaction. Occurs in HIV/AIDS, unclear if result of other factors vs. immunosuppression.	Symmetrical, slowly developing red-brown papules & nodules favoring backs of hands, over digital joints, knees, & elbows. Rarely more widespread. Usually asymptomatic.	Skin biopsy. Serum protein electrophoresis (SPEP).	LCV w/thickening of vessel walls; later – fibrosis, granulomatous inflammation, occasional cholesterol deposits.	Limited: intralesional or high-potency topical steroids. Widespread/ resistant: dapsone. Nicotinamide & tetracycline may help.	Association with IgA monoclonal gammopathy or even multiple myeloma. Earlier onset more often in HIV setting.
Secondary causes of CSSV: Drugs; infections; malignancies, most often hematologic							
SMALL & MEDIUM-SIZED VESSEL VASCULITIS ("MIXED")							
Cryoglobulinemia [types I, II, III; types II & III: "mixed"); "Types 2 & 3, LCV"	Frequency varies w/geography, may reflect prevalence differences in HCV. Higher prevalence in Southern Europe.	Circulating Ig complexes that precipitate when incubated at <4° C. Compositions: I – monoclonal IgG or IgM; II – monoclonal IgM + polyclonal IgG; III – polyclonal IgG.	Type I: thrombosis, livedo, Raynaud syndrome, ulcers. Types II-III: chronic immune complex vasculitis, skin & kidneys.	Blood must be transported to lab at 37°C then cooled to < 4° C; cryocrit is then determined & protein selectively analyzed. Reactive hypocomplementemia.	Papular lesions show LCV, while necrotic or ulcerated lesions may demonstrate medium-sized vessel vasculitis. DIF: granular deposits w/IgM & C3 in vascular pattern in papillary dermis.	Avoid cold. Treat underlying disease. If HCV involvement: interferon + ribavirin. Progressive: MTX or cyclophosphamide + systemic steroids, +/- plasma exchange.	Peripheral neuropathy & glomerulonephritis can develop. Types II-III: most commonly in the setting of HCV infection, 80%.
ANCA-Associated Vasculitides							
Microscopic polyangiitis (microscopic polyarteritis, microscopic polyarteritis nodosa)	Estimated incidence 3-24/million. Men > women. Mean age of onset = 57 years, peak 65-75 yrs.	Unknown. May be associated w/infectious endocarditis. Medications/ malignancy may be a trigger. ANCA is thought to play a role.	Palpable purpura, erythematous macules & patches, splinter hemorrhages & ulcers. Constitutional sxs, crescentic necrotizing glomerulonephritis & alveolar hemorrhage.	Presence of P-ANCA. Additional testing: CXR, EMG/nerve conduction studies, lung/nerve/kidney bx.	Segmental necrotizing vasculitis of smallest blood vessels & less often of small/ medium-sized arteries. Absence of granuloma formation.	2 phases: 1) Remission – initially steroids, cyclophosphamide or rituximab for significant organ involvement. 2) Maintenance: MTX, azathioprine, MMF, IVIg. Plasma exchange may be beneficial.	More severe renal vasculitis favors older pts. ANCA persistence despite remission – increased risk of relapse.
Wegener's granulomatosis (granulomatosis with polyangiitis)	Incidence = 0.3/100,000 annually; USA: prevalence 1/25,000. Most often in Caucasians. Slight female predominance.	Unknown. Infections, including S. aureus, are suspected triggers.	Stages - 1st: general signs & sxs – fever, malaise, upper airway problems. 2nd: lower airway: cough, dyspnea, hemoptysis, pleurisy. 3rd stage: generalized involvement incl. skin. Skin: polymorphic picture including LCV, urticarial vasculitis, necrotizing pyodermas, panniculitis. Oral ulcers, recurrent epistaxis, nasal septal perforation	Tissue dx: usually airway/renal bx, sometimes skin helps. Investigate: upper airways, kidneys, lungs. C-ANCA positive in 50% during early phase, >90% when generalized.	Triad: necrotizing LCV, necrosis, granuloma formation. Granulomas can be in vessel walls or adjacent; palisading, or rich in giant cells. Irregular necrosis – "geographic."	Fauci regimen: prednisone & cyclophosphamide. Unresponsive: agents can be increased. If + response, taper steroid. Other immunosuppressants under investigation: Cyclophosphamide induction followed by MTX. Recurrence/ localized: co-trimoxazole.	Frequency of organ involvement: lungs 95%, upper airway 90%, kidneys 85%, joints 70%, eyes 60%, ears 60%, skin 45%, nerves 20%, heart 10%.

Anna Chacon, MD, is a preliminary resident at Orlando Regional Medical Center. She will be a dermatology resident at the University of Maryland Medical Center beginning July 2014.

Vasculitides (cont.)

Anna Chacon, MD

	Diagnosis	Epidemiology	Pathogenesis	Clinical Features	Diagnostic Approach	Pathology	Therapy	Complications/ Associations
	SMALL & MEDIUM-SIZED VESSEL VASCULITIS ("MIXED")							
ANCA-Associated Vasculitides	Churg-Strauss syndrome (allergic granulomatosis & angiitis, granulomatous vasculitis of Churg-Strauss)	Extremely rare. 0.3/100,000 yearly, perhaps associated w/atopy.	Unknown. Speculation: role of leukotriene antagonists, vaccines, rapid D/C of corticosteroids, desensitization may trigger disorder.	Asthma > 80%, often presenting symptom. Later: pulmonary infiltrates, vasculitis. Transient pulmonary eosinophilic infiltrates occur. Granulomatous inflamxn of myocardium = leading cause of death Skin: involved in 70% - purpura, nodules, urticarial vasculitis.	Tissue dx: skin or lung. Investigate lungs & other organs based on signs & sxs. Labs: elevated ESR, hypereosinophilia, elevated IgE, cryglobulins, immune complexes. Both cANCA & pANCA can be positive, about 20% for each.	Striking palisading granulomas w/ marked necrosis, both associated w/vessels & at a distance. Marked eosinophilia, nuclear dust, giant cells.	Very steroid responsive – i.e. prednisolone. Reserve immunosuppressants for tx failures or life-threatening dz. Both IFN-a & IVIg have shown promise.	Multi-organ involvement: mononeuritis multiplex 60%, kidneys 50%, heart 40%, GI tract 40%. Localized granulomas: sometimes limited to skin, mostly associated w/RA, also infections, lymphoma, idiopathic.
	Secondary causes: Infections, Inflammatory disease (e.g., AI-CTD)							
	MEDIUM-SIZED VESSEL VASCULITIS							
	Polyarteritis nodosa [(PAN), panarteritis nodosa, Kussmaul-Maier dz)	Rare. Incidence = 0.5/100,000 yearly. Mostly affects middle-aged men. Associations: HBV, HIV/AIDS; strep	Involvement in segments. Favors areas where branching occurs. Small aneurysms frequently develop.	Fevers, wt loss, arthralgias. Skin: frequent involvement; livedo racemosa, digital gangrene, SQ nodules, ulcers, LCV. Cutaneous PAN: limited to skin; benign, chronic course; nodules & punched-out ulcers usually on legs.	Histologic confirmation: usually skin or muscle bx. Imaging: angiography can reveal microaneurysms in GI or renal aa. Labs: few changes, high ESR, anemia, thrombocytosis, microscopic hematuria. Check HBsAg. ANCA+ <5%.	Segmental involvement makes it hard to find lesions. Initial inflammatory infiltrate is neutrophilic, later replaced by mononuclear cells w/intimal proliferation, finally granulomas & fibrosis.	Systemic steroids; can start w/pulse therapy. Unresponsive or major organ involvement: add cyclophosphamide or other immunosuppressants. If HBsAg+: start w/ prednisone & plasma exchanges, followed by IFN & lamivudine – hepatology consult.	Thrombosis leads to infarcts & vessel-wall obliteration. GI tract: "intestinal angina," ischemic bowel perforation, mesenteric a. thrombosis or rupture. Peripheral neuropathy. Kidney: 10%. Heart: MI or CHF. CNS: stroke risk, HTN changes.

REFERENCES

1. Sterry W, Paus R, Burgdorf W: Purpura and Vasculitis. In: *Dermatology*. edn. New York, NY.: Thieme.; 2006: 245-261.
2. Wolff K, RA Johnson.: The Skin Signs in Immune, Autoimmune, and Rheumatic Disorders. In: *Color Atlas & Synopsis of Clinical Dermatology*. edn. United States of America: McGraw Hill; 2009: 397-410.
3. Shinkai K, Fox L: Cutaneous Vasculitis. In: *Dermatology. Volume 1.* , edn. Edited by Bolognia JL, Jorizzo JL, Schaffer JV: Elsevier.; 2012: 385-409.

Double dose of Boards' Fodder!

In addition to this issue's Boards' Fodder, Vasculitides, don't forget to download the new Board's Fodder online exclusive from **www.aad.org/DIR**, *where a new chart is published each quarter. The Summer 2014 online Boards' Fodder is phototherapy by Rebecca Bialas, MD.*

To view, download, or print every Boards' Fodder ever published, both in print and online, check out the complete archives at **www.aad.org/BFarchives**.