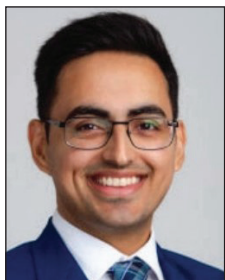


boards fodder



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Vasculopathy

By Taha Rasul, MD, Benjamin Cooper, DO, and Karan Rajalingam, MD

Vasculopathy refers to vascular compromise due to thrombosis, embolization, calcification, or other occlusive injury, usually without primary inflammatory destruction of the vessel wall. Clinically, it often presents with retiform purpura, livedo racemosa, painful ulcers, or cutaneous necrosis. Distinguishing vasculopathy from vasculitis is critical because the workup, systemic associations, and treatment priorities differ substantially. Palpable purpura generally favors vasculitis; retiform purpura generally favors vasculopathy.

Thrombotic and coagulation-related

Diagnosis	Pathogenesis	Clinical clues	Histopathology	Workup	Treatment	Board pearl
Warfarin skin necrosis	Protein C depletion causing transient hypercoagulable state early in therapy	Painful purpuric plaques progressing to necrosis on fatty areas (breasts, thighs, abdomen)	Dermal vessel thrombosis without significant inflammation	Medication history; protein C levels (decreased)	Stop warfarin, administer vitamin K (phytonadione) IV to reverse anticoagulation. Therapeutic anticoagulation with unfractionated heparin (UFH) or LMWH	While warfarin is an anticoagulant, there is a paradoxical increase in coagulability due to early decrease of anticoagulant proteins, protein C and S; necrosis 3–8 days after starting warfarin
Heparin-induced skin necrosis	Heparin-induced thrombocytopenia (HIT) causing platelet activation and thrombosis due to autoantibodies to platelet factor 4 complexes	Painful necrotic plaques at injection sites	Dermal vessel thrombosis without significant inflammation	HIT antibody testing, platelet count	Stop heparin; start non-heparin anticoagulant (argatroban, fondaparinux)	Necrosis at heparin injection sites + thrombocytopenia
Factor V Leiden	R506Q mutation causing activated protein C (APC) resistance and impaired anticoagulation	Cutaneous manifestations uncommon. When present: painful ulcers, purpura, or livedoid vasculopathy pattern on lower legs; often associated with other thrombotic events (DVT/PE) or pregnancy loss	Dermal vessel thrombosis without significant inflammation	Factor V Leiden genetic testing; APC resistance assay; consider full thrombophilia panel	Acute VTE: direct oral anticoagulants (rivaroxaban, apixaban) or LMWH/warfarin; duration based on provoked vs. unprovoked event; heterozygotes typically do not need long-term anticoagulation for isolated skin findings	Most common inherited thrombophilia (5% of Caucasians); skin findings rare but may be sole manifestation

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Diagnosis	Pathogenesis	Clinical clues	Histopathology	Workup	Treatment	Board pearl
Protein C or S deficiency	Inherited or acquired deficiency causing hypercoagulability	Purpura fulminans in neonates or thrombosis in adults	Dermal vessel thrombosis without significant inflammation	Protein C/S levels	Anticoagulation, protein replacement in severe cases	Neonatal purpura fulminans can be due to protein C or S deficiency
Thrombotic thrombocytopenic purpura (TTP)	ADAMTS13 deficiency causing platelet-rich microthrombi	Petechiae, purpura, neurologic symptoms, renal dysfunction, fever	Platelet thrombi in small vessels without inflammation	CBC showing thrombocytopenia and hemolytic anemia; ADAMTS13 activity	Urgent plasma exchange, steroids, rituximab	Classic pentad (<10% of cases): MAHA + thrombocytopenia + neurological changes + renal dysfunction + fever
Disseminated intravascular coagulation (DIC)	Systemic activation of coagulation causing widespread microthrombi and bleeding	Diffuse purpura, ecchymoses, acral ischemia, bleeding in critically ill patient	Fibrin thrombi in small vessels	PT/PTT, fibrinogen, D-dimer, platelets	Treat underlying cause; supportive care	Both thrombosis and bleeding in severe illness
Purpura fulminans	Microvascular thrombosis due to severe infection and DIC	Rapidly progressive purpura, necrosis, systemic toxicity	Dermal vessel thrombosis and hemorrhage	Coagulation studies, blood cultures	Treat infection urgently, supportive care	Toxic patient + rapidly progressive purpura = purpura fulminans. Highly thrombotic subtype of DIC
Antiphospholipid syndrome (APS)	Autoantibodies causing arterial and venous thrombosis	Livedo racemosa, retiform purpura, necrosis; history of thrombosis or pregnancy loss	Dermal vessel thrombosis without significant inflammation	Lupus anticoagulant, anticardiolipin, anti-β2 glycoprotein antibodies	Long-term anticoagulation	Retiform purpura + thrombosis history → screen for APS
Livedoid vasculopathy (atrophie blanche)	Thrombotic occlusion of superficial dermal vessels; often associated with hypercoagulability	Painful purpura and ulcers on ankles/lower legs; atrophie blanche (porcelain-white scars)	Hyalinized vessel walls, fibrin thrombi, endothelial proliferation; minimal inflammation	Hypercoagulable workup (APS antibodies, protein C/S deficiency, factor V Leiden), CTD workup	Antiplatelets, anticoagulation (DOAC, warfarin), pentoxifylline	Painful ankle ulcers + atrophie blanche = livedoid vasculopathy
Calciophylaxis	Vascular calcification and thrombosis of small/medium vessels; often in renal failure	Extremely painful retiform purpura and necrotic plaques; thighs, abdomen common	Medial calcification of vessels, intimal hyperplasia, thrombosis	Calcium/phosphate/PTH, renal disease evaluation	Sodium thiosulfate, wound care, pain control	Pain out of proportion + ESRD + retiform purpura = calciophylaxis
Sneddon syndrome	Non-inflammatory arteriopathy associated with APS and cerebrovascular disease	Livedo racemosa with recurrent strokes	Arteriolar occlusion without vasculitis	APS testing, neurologic imaging	Anticoagulation	Livedo racemosa + strokes = Sneddon syndrome

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Diagnosis	Pathogenesis	Clinical clues	Histopathology	Workup	Treatment	Board pearl
Degos disease (malignant atrophic papulosis)	Thrombo-obliterative vasculopathy affecting small/medium vessels	Porcelain-white atrophic papules with erythematous rim; GI and CNS involvement	Wedge-shaped dermal necrosis, vessel thrombosis	Clinical diagnosis ± biopsy	Antiplatelets, complement inhibitors in severe disease	Porcelain-white papules with telangiectatic rim

Cold-related

Diagnosis	Pathogenesis	Clinical clues	Histopathology	Workup	Treatment	Board pearl
Cryoglobulinemia type I	Monoclonal immunoglobulin (IgM, IgG, or IgA) precipitation in cold temperatures causing mechanical vascular occlusion; arises from clonal B-cell expansion (indolent to malignant)	Severe acral ischemia, cold-triggered purpura, skin ulcers/gangrene, hyperviscosity symptoms; more severe cutaneous involvement than mixed types	Dermal vessel thrombosis without significant inflammation	Cryoglobulin testing (warm handling); SPEP/SIFE; bone marrow biopsy; evaluate for Waldenström's (27%), MGCS (31%), multiple myeloma (15%), NHL (20%), CLL (7%)	Treat underlying hematologic disorder: IgM type → rituximab ± bendamustine; IgG/IgA type → bortezomib, anti-CD38 agents; plasma exchange for acute symptoms; avoid cold exposure	Palpable purpura worsened by cold → cryoglobulinemia. Mixed cryoglobulinemia types II/III cause true leukocytoclastic vasculitis. Always evaluate for underlying gammopathy or hematologic malignancy
Cryofibrinogenemia	Cold-precipitable fibrin complexes causing thrombosis	Painful ulcers, livedo racemosa, purpura on cold-exposed areas. Microlivedo (short hyperpigmented linear streaks around ulcers) is characteristic	Dermal vessel thrombosis without vasculitis	Plasma cryofibrinogen testing	Cold avoidance; stanazolol (enhances fibrinolysis); antithrombotic agents; steroids/immunosuppressants; plasmapheresis for severe cases;	Retiform purpura triggered by cold exposure. Cryofibrinogen precipitates in plasma only (not serum) vs. cryoglobulin precipitates in serum

Embotic/ischemic

Diagnosis	Pathogenesis	Clinical clues	Histopathology	Workup	Treatment	Board pearl
Embotic vasculopathy	Cholesterol or cardiac emboli occluding vessels	Retiform purpura, livedo racemosa, blue toe syndrome	Cholesterol clefts or embolic material in vessels	Cardiac evaluation, vascular imaging	Treat underlying embolic source	Sudden livedo after vascular procedures
Martorell hypertensive ischemic ulcer	Arteriolosclerosis from chronic hypertension causing ischemia	Extremely painful ulcers on posterolateral lower legs	Arteriolar narrowing and thrombosis	Evaluate hypertension, vascular disease	Blood pressure control, surgical management	Severe pain + lateral leg ulcer in hypertensive patient

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Mixed pattern

Diagnosis	Pathogenesis	Clinical clues	Histopathology	Workup	Treatment	Board pearl
Levamisole-associated vasculopathy	Immune-mediated vascular injury and thrombosis triggered by levamisole-adulterated cocaine; often associated with ANCA production and neutrophil activation	Retiform purpura and necrosis with predilection for ears, cheeks, and extremities; may have leukopenia/neutropenia and history of cocaine use	Thrombotic vasculopathy ± leukocytoclastic vasculitis; small-vessel thrombosis with fibrin deposition	Urine toxicology for cocaine, ANCA testing (often p-ANCA or dual ANCA), CBC showing leukopenia/neutropenia	Cessation of cocaine, supportive care; systemic steroids sometimes used in severe disease	Retiform purpura of the ears in a cocaine user → think levamisole vasculopathy

Abbreviations: DVT = deep vein thrombosis, PE = pulmonary embolism, VTE = venous thromboembolism, LMWH = low molecular weight heparin, MAHA = microangiopathic hemolytic anemia, DOAC = direct oral anticoagulant, CBC = complete blood count, CTD = connective tissue disease, PTH = parathyroid hormone, ESRD = end-stage renal disease, SPEP = serum protein electrophoresis, MGCS = monoclonal gammopathies of clinical significance, NHL = non-Hodgkin lymphoma, CLL = chronic lymphocytic leukemia, ANCA = antineutrophil cytoplasmic antibodies.

Cryoglobulinemia type I, warfarin skin necrosis, heparin-induced skin necrosis, DIC, antiphospholipid syndrome, Factor V Leiden mutation, and protein C or S deficiency have similar histopathologic features and rely on clinical presentation.

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