Polyarteritis Nodosa

Diagnosis/ Clinical symptoms of Systemic PAN	• EULAR/PRINTO/PRES Criteria: biopsy for histopathology/immunofluorescence (necrotizing vasculitis) OR angiography (aneurysms, stenosis, occlusions), AND ≥ 1 of: ▪ Skin: livedo reticularis, tender subcutaneous nodules, superficial/deep skin infarctions ▪ Rheum: Myalgia or muscle tenderness ▪ Cardio: HTN ▪ Neuro: Peripheral neuropathy, sensory or motor mononeuritis multiplex ▪ Renal: proteinuria, hematuria, RBC casts, GFR <50% normal for age • Labs: ANCA negative
Differential Diagnosis	• Systemic inflammatory dz (SLE, RA, systemic sclerosis) • Infection (bacterial, endocarditis, chronic viral hepatitis) • Embolic or thrombotic dz, drug-induced vasculitis
Possible Complications	• Acute: organ failure (cardiac, pulmonary, renal), thrombi, hemorrhage, infection • Chronic: HTN, ischemic cardiomyopathy, CKD, mesenteric arteritis, hearing loss, orchitis
Laboratory Studies	• Cr, CK, LFTs, von Willebrand factor antigen (marker of vessel inflammation /damage, HBV and HCV serologies, HIV, UA, ESR, CRP, BCx • Rheumatologic workup may include ANCA, ANA, C3/4, cryoglobulins
Treatment	• Mild (normal renal function, no significant/life-threatening complications): ▪ Steroids, may add Azathioprine or MTX • Moderate to severe (ex: kidney involvement, proteinuria, neuro/cardiac/GI complications): ▪ Steroids plus Cyclophosphamide, with eventual switch from Cyclophosphamide to Azathioprine or MTX ▪ TNF inhibitors useful as well, especially in cutaneous PAN and DADA2 • Pheresis considered in organ threatening disease • HTN: ACE Inhibitor

Connective Tissue Disorders

SLE	
Clinical	Rash (malar, discoid), photosensitivity, serositis, nephritis, oral/nasal ulcers, seizure, psychosis, arthritis
Lab markers	• Cytopenias (+) anti-RNP (30%) • +anti-dsDNA (40-60%, assoc w SLE activity and lupus nephritis) • +anti-Smith (30%, w/ high specificity, remains + in remission) • +anti-SS-A (Ro, 40%) • +anti-SS-B (La, 10-15%, more specific than Ro)
Polymyositis	
Clinical	Proximal muscle weakness +/- tenderness
Lab markers	• CK • Aldolase • LDH • AST and ALT (rarely nl unless "burnt out") • +anti-JO (20%, a/w ILD, mechanic hands) • +anti-mi2 (5-7%, a/w acute onset, shawl sign, good prognosis)
Dermatomyositis	
Clinical	• Proximal muscle weakness +/- tenderness • Rash (heliotrope on upper eyelids Shawl sign on back • V-sign on chest) • Gottron's papules or scaly eruption over extensor surfaces such as knuckles (pathognomonic)

Connective Tissue Disorders

Dermatomyositis

Other	• In adults ~ 25% a/w malignancy; rarely associated in children • ILD in 10%, upper esophageal involvement (dysphagia) in 25%; may cause life-threatening aspiration
Lab markers	• +anti-JO (20%, a/w ILD, mechanic hands) • +anti-mi2 (5-7%, a/w acute onset, shawl sign, good prognosis)

Sjogren's

Clinical	• Sicca sx (dry mouth/eyes) • Vasculitis	• Interstitial nephritis • Neuropathy; 5% lifetime risk of NHL
Lab markers	• (+) ANA • +anti-SS-A (Ro, 70%)	• +anti-SS-B (La, 50-70%, more specific) • +RF

Scleroderma

Clinical	• Skin tightening & thickening prox to forearms • Nail fold capillary dilatation & dropout • ILD & later stages PAH	• GI dysmotility • Renal crisis (tx w/ ACE-I)
Lab markers	• +anti-Scl 70 (30%) • +anti-centromere (15%)	

CREST

Clinical	• Calcinosis • Raynaud's phenomenon • Esophageal dysmotility	• Sclerodactyly • Telangiectasias
Lab markers	• PAH +anti-centromere (60%) • +anti-Scl 70 (15%)	

Behcet Disease

Epidemiology	• Young adults • Turkish, Middle Eastern, or Asian descent	
Clinical	• Recurrent/painful oral apthous ulcers • Genital ulcers • Eye lesions (esp uveitis)	• Skin lesions (ex: erythema nodosum, acneiform lesions) • Thromboses
Skin Testing	Pathergy (exaggerated skin ulceration w/ minor trauma – ex: needlestick)	

Mixed Connective Tissue Disease

Clinical	• Overlapping features of SLE • Polymyositis • Systemic sclerosis • Raynaud phenomenon • Swollen fingers	• Arthritis • Inflam myopathy • Pleuritic • Pulm fibrosis, etc.
Lab Markers	Anti-U1-RNP (Ribonucleoprotein) Antibodies	
Treatment	• NSAIDs • Corticosteroids	• ACE-I • Supportive measures

Connective Tissue Disorders continued on next page →

Immunologic Markers by Disease	
SLE	ANA (95%), Anti-dsDNA (60%), Anti-Smith, False-positive RPR/VDRL, Anti-Histone (drug-induced)
RA	RF (75%), ACPA, ANA (<50%), HLA-DR4
Poly/Dermatomyositis	ANA, Anti-Jo-1
Scleroderma, CREST syndrome	Anti-scl-70 (anti-topoisomerase), ANA, Anticentromere (CREST)
Mixed Connective Tissue Disease	Anti-RNP (ribonucleoprotein)
Sjogren Syndrome	Anti-Ro (anti-SSA) ANA, Anti-La (anti-SSB) ANA

Systemic Lupus Erythematosus

Definition	Multiorgan system autoimmune disorder with markedly variable presentations/course
Epidemiology	• F>M • Most often after age 8 yo • Median age of onset for juvenile SLE 12-13 yo • More common in people of Asian, African, and Hispanic race/ethnicity vs Caucasian
Other presenting symptoms	• Fever • Weight loss • Anorexia • Raynaud's • LAD • HSM • HTN
Neonatal Lupus Erythematosus (NLE):	• 1-2% of Infants born to mothers w/ anti-Ro and/or anti-La antibodies (transplacental) • Auto-Ab interfere w/ development of cardiac conduction system → permanent AV block • Flat/erythematous, annular, photosensitive rash that spontaneously resolves ~6 mo of age (as maternal Abs dissipate) • No increased risk of autoimmune diseases later in life

SLICC Criteria
(not validated in children/adolescents)

4+ criteria, including 1+ clinical and 1+ immunologic (serial or simultaneously), w/o alternative explanation OR SLE nephritis with +ANA/+dsDNA

Acute cutaneous lupus	Malar rash, bullous, TEN variant, photosensitive rash
Chronic cutaneous lupus	Discoid, hypertrophic/verrucous, panniculitis, mucosal, chilblains, erythem. timidus
Non-scarring alopecia	Diffuse thinning or hair fragility with visible broken hairs
Oral/Nasal Ulcers	Palate, buccal, tongue, or nasal
Joint Disease	Synovitis in 2+ joints (swelling/effusion) OR 2+ joint tenderness+ ≥30m AM stiffness
Serositis	Pleurisy or pericardial pain ≥1d, pleural or pericardial effusion, pleural or pericardial rub, pericarditis on TTE
Renal	≥ 500 mg protein/day or RBC casts
Neuro	Seizures, psychosis, mononeuritis multiplex, myelitis, peripheral/cranial neuropathy,
Hemolytic anemia	Autoimmune (direct Coombs+), thrombotic MAHA (TTP, HUS)

Systemic Lupus Erythematosus

SLICC Criteria continued	
Leuko/lymphopenia	Leukopenia <4000/mm^3, lymphopenia <1000/mm^3
Thrombocytopenia	<100,000/mm^3, including ITP, TTP
Immuno	ANA (+) , Anti-dsDNA (+) or >twofold reference range on ELISA
Low complement	Low C3, C4, or CH50
Direct Coombs test	Positive in absence of hemolytic anemia
Antiphospholipid	Lupus anticoagulant, RPR (false positive), anticardiolipin Ab, or beta 2-glycoprotein I

Treatment

Initial	Hydroxychloroquine (≤ max 5 mh/kg/d, need regular ophtho evals for visual field testing and color
Mild	No renal/organ involvement→hydroxychloroquine, NSAIDS - arthralgia, Dapsone - derm, MT - arthritis. Can use LD prednisone (<0.35 mg/kg/d), but if needs >3 mo consider second-line agent (ex: MMF)
Mod	Renal/organ involvement → consider MMF, azathioprine, rituximab, systemic steroids
Severe	Substantial renal/neuro disease → cyclophosphamide
Flares	Steroids + MMF, or cyclophosphamide if already on MMF/azathioprine

Inflammatory Myopathies

	Polymyositis	Dermatomyositis	Inclusion Body Myositis
Path	CD8+ T cells	CD4+ T Cells	Inflam/neurodegen
Clinical	Symmetric proximal muscle weakness (shoulders)	• Symmetric proximal muscle weakness • Gottron papules, heliotrope (periorbital) rash,"shawl+face 'rash,"mechanics hands"	Distal >> Proximal muscle weakness
Labs	Increased CK, ANA (+)		
	Anti-MI-2/MJ	Anti-Jo-1 (Anti-tRNA-synthetase)	Anti-cN1A
	Bx: Endomysial inflam	• Bx: Perimysial inflam/atrophy (myopathic) • Von Willebrand Factor Ag	• Basophilic rimmed vacuoles • Regged-red fibers
Assoc.	Autoimmune (Crohn's, Vasculitis, Sarcoidosis, MG)	• Lipodystrophy, Calcinosis, ILD, GI bleed • Juvenile DM *NOT* assoc. w/ malignancy like adults	
Treatment	Steroids (prednisone) followed by long-term immunosuppression (MTX, cyclosporine)		Not steroid responsive

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