

Laboratory interpretation in rheumatology

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Disclosures

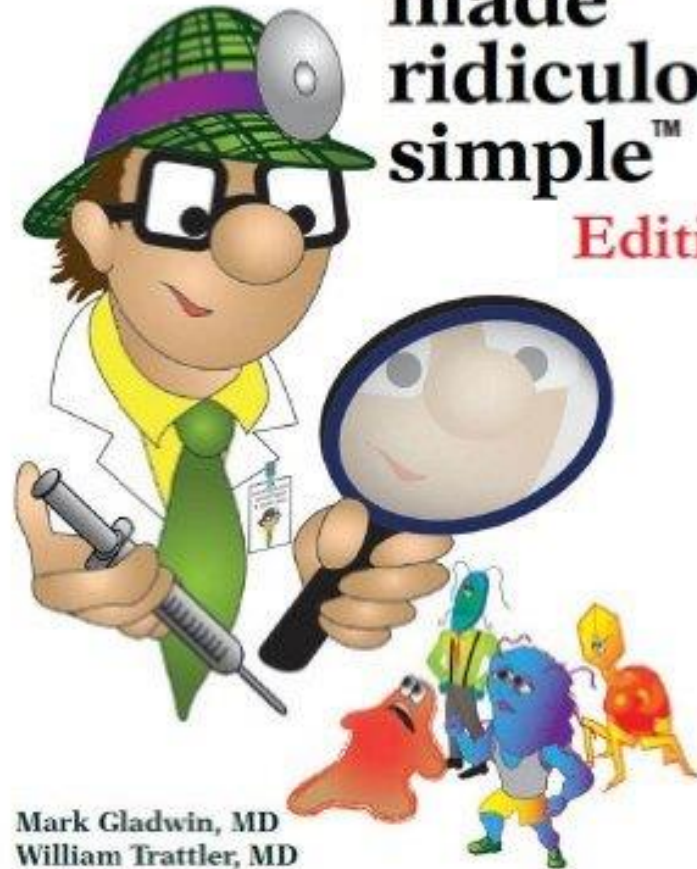
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Objectives

Rheumatology

made
ridiculously
simple™

Edition 6



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Approach

Rheumatologic disease

Inflammatory arthritis

- RA
- Spondyloarthropathy
 - Psoriatic arthritis
 - Reactive arthritis
 - IBD-associated
 - Ankylosing spondylitis
- PMR
- Crystal arthropathy
- Viral arthritis / Lyme
- Undifferentiated

Connective tissue disease

- SLE
- Sjogren's
- Scleroderma
- MCTD
- Myositis

Vasculitis

- Small vessel
- Medium vessel
- Large vessel

Case 1

- 58 yo F with no PMH p/w 6 months of pain in shoulders, hips, wrists, hands (MCPs, PIPs) and feet (MTPs). 30 minutes of morning stiffness.
- Exam – pain with ROM of b/l shoulders and hips, swelling of b/l wrists. Multiple MCPs, PIPs, MTPs tender but not swollen.
- Labs – CBC, BMP, TSH, U/A - normal

What is the most appropriate workup?

- A. ANA, DsDNA, RF, Lyme, ESR/CRP
- B. ANA, RF, CCP, ESR/CRP
- C. ANA, DsDNA, Ro/La, Smith, RNP, RF, CCP, ESR/CRP
- D. RF, CCP, uric acid, ESR/CRP
- E. RF, ESR, CRP, Lyme

Rheumatologic disease

Inflammatory arthritis

~~Connective tissue disease~~

~~Vasculitis~~

- RF
- CCP

- ANA

- ESR, CRP

ANA utility

Rheumatologic
disease

Inflammatory
arthritis

No role

Connective
tissue disease

- SLE > 95%
- Scleroderma - 90%
- MCTD > 95%
- Sjogren's – 50-70%
- Myositis – 60-80%

Vasculitis

No role

Case 1 con't

- RF – negative
- Anti-CCP – negative
- ANA – negative
- ESR – 48 (< 20mm/hr)
- CRP – 12.8 (< 8mg/L)

What is the most likely diagnosis?

- A. PMR
- B. RA
- C. Pseudogout
- D. Seronegative spondyloarthropathy
- E. Fibromyalgia

RF / CCP test characteristics

Test	Sensitivity	Specificity
RF	40-70	70
CCP	40-70	95
RF and CCP	50-80	-

Approach

Non-rheumatologic disease

Rheumatologic disease

Inflammatory arthritis

Connective tissue disease

Vasculitis

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RA Classification Criteria

Joint involvement	Score
• 1 medium-large joint	0
• 2-10 medium-large joints	1
• 1-3 small joints	2
• 4-10 small joints	3
• More than 10 joints	5
Serology	
• RF (-) and anti-CCP (-)	0
• RF (+) or anti-CCP (+)	2
• High RF (+) or anti-CCP (+)	3
Duration of symptoms	
• < 6 weeks	0
• ≥ 6 weeks	1
Acute phase reactants	
• CRP and ESR within normal	0
• elevated CRP or ESR	1

- 6 out of 10 points needed for dx
- Need 1 swollen joint

Take Home Points: Inflammatory Arthritis

- History and exam first and foremost
- Labs as supportive
- About 30% of patients with RA will have negative RF/anti-CCP antibodies
- ESR/CRP nonspecific, but can be helpful
- ANA not positive in inflammatory arthritis or vasculitis
 - But can have inflammatory arthritis as part of connective tissue diseases like SLE

Case 2

- 32 yo F is admitted with chest pain x 5 days, worse supine. ECG with diffuse STEs and PR depressions
- ROS
 - Fatigue x 6 months
 - Rash on chest after sun exposure two months ago (resolved spontaneously)
 - Several episodes of painless oral ulcers in past year
- Labs
 - CBC, BMP, U/A – wnl
 - ESR 53 (< 20mm/hr), CRP 75 (< 8mg/L)
 - ANA 1:320 speckled

What is the next diagnostic step?

- A. DsDNA, Smith
- B. DsDNA, Smith, complements, antiphospholipid antibodies
- C. DsDNA, Smith, Ro, La, RNP
- D. DsDNA, Smith, Ro, La, RNP, complements, antiphospholipid antibodies
- E. DsDNA, Smith, Ro, La, RNP, Scl70, centromere ab

Labs

- DsDNA – 1:160
- Ro – 95 (ULN 20)
- La – neg (ULN 20)
- Smith – negative
- RNP – 110 (ULN 20)
- C3 – 64 (86-184)
- C4 – 11 (16-38)
- Antiphospholipid antibodies - negative

Antibody positivity in CTD

Disease	dsDNA	Sm	Ro	La	Scl-70	Cent	Jo	RNP
SLE	50–70	30	35	15	0	0	0	30–50
				–				
Sjögren's	<5	0	55	40	0	0	0	15
Diffuse SSc	0	0	5	1	40	<5	0	30
Limited SSc	0	0	5	1	<5	70	0	30
PM-DM	0	0	0	0	10	0	25	0
MCTD	0	0	<5	<5	0	0	0	100

SLICC[†] Classification Criteria for Systemic Lupus Erythematosus

Requirements: ≥ 4 criteria (at least 1 clinical and 1 laboratory criteria)
OR biopsy-proven lupus nephritis with positive ANA or Anti-DNA

Clinical Criteria

1. Acute Cutaneous Lupus*
 2. Chronic Cutaneous Lupus*
 3. Oral or nasal ulcers *
 4. Non-scarring alopecia
 5. Arthritis *
 6. Serositis *
 7. Renal *
 8. Neurologic *
 9. Hemolytic anemia
 10. Leukopenia *
 11. Thrombocytopenia ($<100,000/\text{mm}^3$)
- } Skin
- } Things that hurt
- } Organ involvement

Immunologic Criteria

1. ANA
2. Anti-DNA
3. Anti-Sm
4. Antiphospholipid Ab *
5. Low complement (C3, C4, CH50)
6. Direct Coombs' test (do not count in the presence of hemolytic anemia)

[†]SLICC: Systemic Lupus International Collaborating Clinics

* See notes for criteria details

Approach

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Vasculitis

- SLE → DsDNA, APLAs
low complements
- Sjogren's → Ro, La
- Scleroderma → Centromere
Scl70
- MCTD → RNP
- Myositis → Jo-1, etc

Case 3

- 55 yo M p/w fatigue x 3 months, fevers x 1 month, and recent onset of rash
- CBC/CMP – normal (including Cr)
- Urinalysis – 3+ blood, 2+ protein
- ESR – 94 (< 20mm/hr)
- CRP – 125 (< 8mg/L)



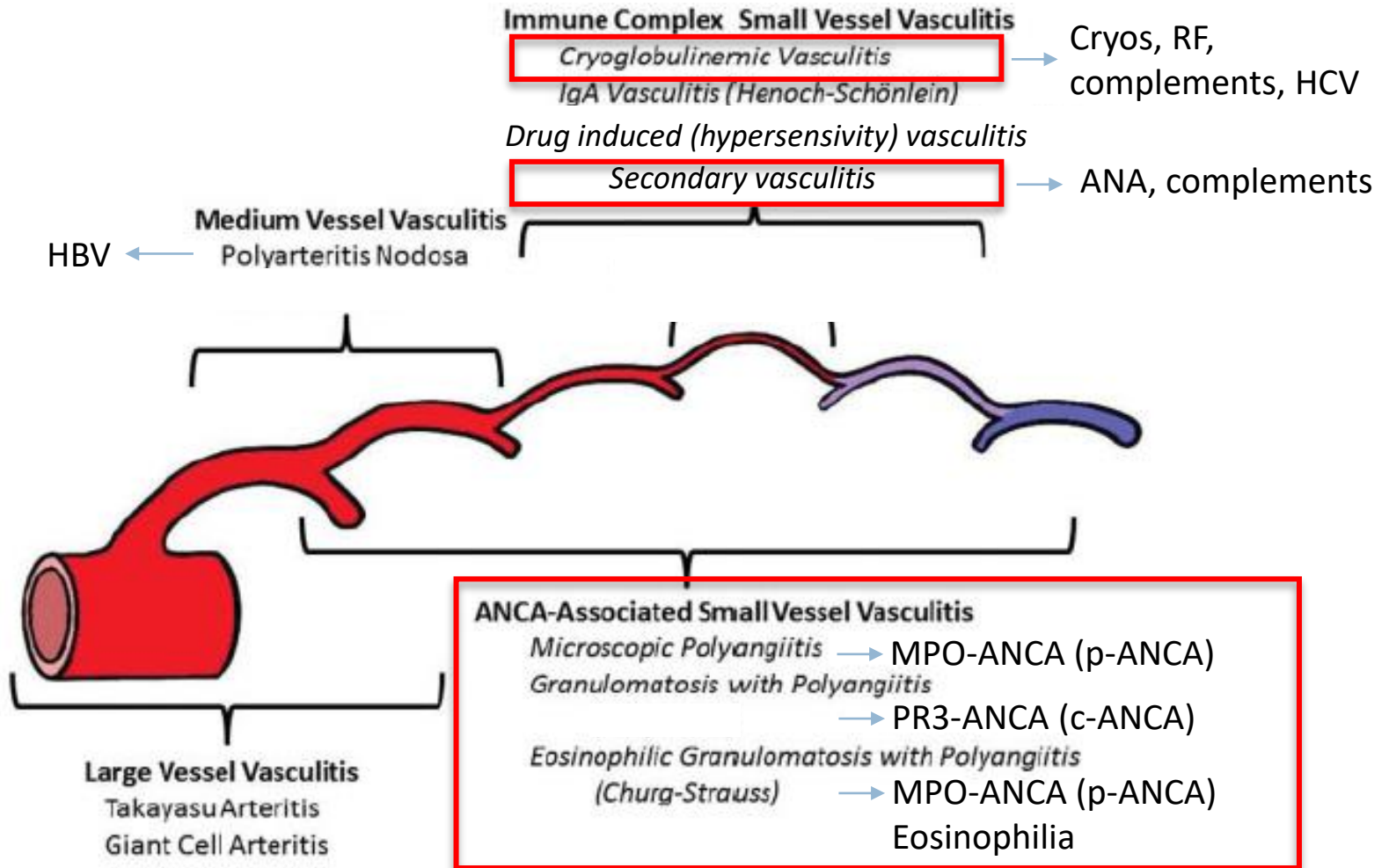
What is the most appropriate next step?

- A. Kidney biopsy
- B. ANCA, ANA, DsDNA
- C. ANCA, cryoglobulins, ANA, hepatitis serologies, complements
- D. Start prednisone and biopsy
- E. Start prednisone and ANCA, ANA, DsDNA
- F. Start prednisone and ANCA, cryoglobulins, ANA, hepatitis serologies, complements

When to consider vasculitis

- Glomerulonephritis
- Diffuse alveolar hemorrhage
- Mononeuritis multiplex
- GCA symptoms
- Prominent constitutional symptoms
- Palpable purpura
- Mesenteric ischemia

Approach to vasculitis



Differentiating small vessel vasculitis

Vasculitis	Differentiating feature
GPA	
EGPA	
MPA	
Cryo	
HSP	
"Secondary" vasculitis	

Differentiating small vessel vasculitis

Vasculitis	Differentiating feature
GPA	ANCA, Sinus/upper airway ds
EGPA	ANCA, Eosinophilia, asthma/allergic rhinitis
MPA	ANCA, no granulomas
Cryo	Cryo, HCV associated
HSP	100% skin involvement, IgA
“Secondary” vasculitis	SLE, Sjogren’s, RA

Summary

- Considering categories of disease can help simplify diagnostic workup
 - Inflammatory arthritis – RF, CCP, ANA
 - Connective tissue disease – ANA first
 - Vasculitis – ANCA, cryo, ANA, hep serologies, complement
- Beware of:
 - Disease without antibodies
 - Antibodies due to another disease
 - Antibodies without disease

Thank you