

Rheumatology Pearls for the Primary Care Physician

Kristine Uramoto, MD

Objectives

- Learn what information a rheumatologist would want when referring a patient.
- Learn when to consider referring a patient.
- Learn the difference between diagnostic antibodies/tests and antibodies/tests that reflect disease
- Learn how to treat challenging rheumatology cases

History

- Onset – acute, subacute
- Joint involvement – monoarticular vs. polyarticular, which joints involved
- Inflammatory vs. non inflammatory – morning stiffness, synovitis
- Aggravating/alleviating factors
- Family History
- Associated symptoms

Rheumatologic Review of Systems

- Unexplained fever
- Dry eyes, dry mouth
- Oral or nasal ulcers
- Photosensitive rash
- Malar rash
- Pleurisy – pleuritic chest pain
- Joint pain/swelling
- Raynaud's phenomenon
- Seizures
- Diagnosed kidney disease

Physical Exam

- Joint examination – swollen, tender joints
- Pattern of joint involvement
 - e.g., wrist, MCP joint synovitis – RA
 - DIP joint involvement (OA if non-inflammatory, PsA if inflammatory)
- Extra-articular manifestations – e.g., psoriasis
- Hot, swollen joint - aspiration

Laboratory Testing

- CBC
- Comprehensive metabolic profile
- Urinalysis
- TSH
- Sedimentation rate/CRP
- ANA
- Rheumatoid factor/anti-CCP

Rheumatologic Labs

- If ANA significantly positive or if patient has symptoms (Rheum ROS), consider referral to rheumatologist. Significant positive ANA – 1:160 titer.
- If ANA positive, can consider ordering the following: anti-Ro, La, RNP/Smith, dsDNA, c3, c4.
- Depending upon other symptoms, can consider ordering CK/aldolase, anti-Jo-1, anti-Scl 70.

Rheumatoid Factor

- Rheumatoid arthritis
- Sjogren’s syndrome
- MCTD
- SLE
- Cryoglobulinemia
- Polymyositis/Dermatomyositis

Rheumatoid Factor

- Indolent or chronic infections such as SBE (subacute bacterial endocarditis) and Hepatitis B and C
- Inflammatory or fibrosing pulmonary disease
- Primary biliary cholangitis
- Malignancies
- Patients with no disease

Diseases associated with a positive ANA

| Disease | Percent with positive ANA |
|---|---------------------------|
| Systemic autoimmune diseases | |
| SLE | 95 percent |
| MCTD | 95 to 100 percent |
| Rheumatoid arthritis | 85 percent |
| Sjogren’s syndrome | 80 percent |
| Wegener’s granulomatous disease | 70 percent |
| Drug-induced SLE | 60 to 93 percent |
| Raynaud’s phenomenon | 40 percent |
| Polymyositis/dermatomyositis | 30 percent |
| Systemic sclerosis/scleroderma | 15 to 40 percent |
| Organ specific autoimmune diseases | |
| Hepatitis B | 30 percent |
| Celiac disease | 10 percent |
| Autoimmune hepatitis | 10 percent |
| Primary biliary cirrhosis | 50 to 70 percent |
| Infectious diseases* | |
| Tuberculosis | |
| EBV | |
| Histoplasmosis | |
| CMV | |
| Parvovirus B19 | |
| Bacterial | |
| SBE | |
| Brucella | |
| Malignancies* | |
| Lymphoproliferative diseases | |
| Paraneoplastic syndromes | |
| Miscellaneous diseases* | |
| Inflammatory bowel disease | |
| Idiopathic pulmonary fibrosis | |

ANA, antinuclear antibodies; SLE, systemic lupus erythematosus; EBV, Epstein-Barr virus; CMV, hepatitis C virus; SBE, subacute bacterial endocarditis.
 *Although positive tests of ANA are reported in these diseases more often than in healthy controls, precise estimates vary.
 Courtesy of Donald B. Roth, MD. UpToDate

Labs to follow patients

- If the diagnosis is already established or if the patient already had a positive result, do not order repeat ANA or RF.
- ANA and RF are not activity markers, but used for diagnosis.
- For SLE, activity markers include CBC, Chemistry panel, UA, ESR, complements (c3, c4, CH50), anti-dsDNA.
- For RA, activity markers include ESR and CRP.

Case 1: Don’t miss this diagnosis

Patient is a healthy 20-year-old female who developed fatigue and pain in the lower back and neck 6 years ago. She was being treated by pain management with NSAIDs, Topamax, etc. with partial benefit. No swollen joints. Morning stiffness 3 hours.

Case #1 (continued)

- Rheum ROS: photosensitivity, Raynaud's phenomenon. Diagnosed with irritable bowel syndrome.
- Physical exam: unremarkable. No synovitis.
- Labs: CBC, Chem panel, ESR, UA unremarkable.
- Rheum labs: ANA and RF borderline positive. CCP negative. HLA B27 negative. Later found to have positive anti-cardiolipin IgG.

Case #1 (continued)

- Xrays: Sacroiliac joints showed joint space narrowing and subchondral sclerosis.
- Xrays of hands and feet negative.
- MRI scan of SI joints: erosion, left sacroiliac joint.

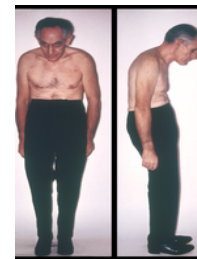


Case #1 (continued)

- Diagnosis: Ankylosing spondylitis.
- Possible overlapping SLE.
- Treatment: allergic to sulfasalazine. Considering other DMARD option – hydroxychloroquine, methotrexate, biologics.

Seronegative Spondyloarthropathies

- Don't forget to ask the inflammatory questions in the HPI (prolonged morning stiffness)
- Consider this diagnosis in young men and women (women get this disease, too!)
- All rheumatologic labs may be negative – consider referral if patient continues to have inflammatory symptoms despite trials of NSAIDs

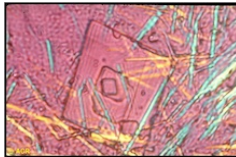


Case #2

- Patient is a 37-year-old male who presented with a year of on and off pain in the big toe and foot (attacks about once a month). At the time of his consult, he had pain in the right foot for a month. No precipitating dietary changes or other factors. He was initially treated with indomethacin 50 mg bid, which did not work, then treated with prednisone 50 mg daily for 7 days, which helped. He was started on allopurinol 300 mg 2 weeks prior to presentation. Colchicine did not work in the past.

Case #2 (continued)

- Family history negative for gout.
- ROS: no kidney stones.
- Physical Exam: no tophi, mild synovitis of the right first MTP joint.
- Labs: Uric acid 5/2018 - 9.3, 5/2019 -10.5.



Case #2 (continued)

- Diagnosis: Gout, not controlled.
- Consider arthrocentesis if appropriate joint inflamed. Check synovial fluid for cell count, crystals, GS, C & S.
- What could have been done better?

Case #2 (continued)

- Do not start allopurinol during an acute attack.
 - This can prolong the attack (as in this case).
 - Wait until the acute attack has resolved before starting allopurinol.
 - Start allopurinol gradually to decrease large shifts in the uric acid level – e.g. allopurinol 100 mg daily for 2 weeks, 200 mg daily for 2 weeks, then 300 mg daily.
 - You may use prophylactic colchicine.

Case #2 (continued)

- Indications for starting urate-lowering medication:
 - Frequent attacks (3 or more per year)
 - Tophi
 - Gouty erosions on Xrays
 - Gout with renal insufficiency
 - Recurrent uric acid kidney stones
 - High uric acid level (definitely treat double digit uric acid!)



Case #2 (continued)

- Goal uric acid – less than 6 (or even 5).
- Consider screening for HLA B*5801 gene in Han Chinese, Thai or Korean patients. Patient with this gene, may have severe cutaneous adverse reactions.

Case #2 (continued)

- Which urate-lowering medication to use?
- Choices: allopurinol, febuxostat, probenecid, pegloticase.
- My preference – allopurinol, unless patient has moderate to severe renal insufficiency or contraindication (allergy).
- Febuxostat useful in patients with renal insufficiency, but has black box warning regarding increased risk of cardiovascular events compared to allopurinol.
- Probenecid – can be used in patients without history of uric acid kidney stones and with normal renal function.
- Pegloticase – used in tophaceous gout, risk of infusion reactions.

Case #3 (Interesting case)

- Patient is a 74-year-old Caucasian male with a history of metastatic prostate cancer. He was treated by his oncologist with Tecentriq (atezolizumab), which is an immune checkpoint inhibitor. After the third treatment with he developed muscle pain, then joint pain and swelling of the hands, shoulder girdle and hip girdle. He has prolonged morning stiffness and can barely get out of bed. He tried Celebrex, which did not help. He was then started on prednisone 20 mg daily, which helped partially.

Case #3 (continued)

- Past History significant for psoriasis.
- Family History: father – psoriasis, sister – Crohn's disease.
- ROS noncontributory.
- Physical Exam: synovitis of wrists and MCP joints.
- Labs: ESR 54, CRP 49.2, ANA and RF negative.

Case #3 (continued)

- Rheumatologic manifestations of check point inhibitors can include
 - Inflammatory arthritides – can look like rheumatoid arthritis, reactive arthritis, psoriatic arthritis
 - Sicca symptoms as in Sjogren's syndrome
 - Polymyalgia rheumatica/Giant cell arteritis
 - Inflammatory myopathy
 - Other rare manifestations – eosinophilic fasciitis, scleroderma, digital ischemia, vasculitis.

Case #3 (continued)

- Back to our patient – on prednisone 20 mg daily, his ESR was 37 and CRP 10.
- Prednisone dose increased to 25 mg daily and his symptoms improved.
- Started methotrexate and patient now able to taper prednisone.