Rheumatology Pearls for the Internist

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I have no conflicts of interest to disclose...
Other than my biases as a rheumatologist
Case 1
lab testing in someone with arthralgias

45 yo healthy woman presents with 3 weeks of pain and stiffness across her hands and wrists, started to involve feet bilat past week, sees some visible swelling across MCPs bilat. Much worse in AM. Not involving other joints. No rashes. No muscle pains, no back pain, no recent other illnesses, but some fatigue over this past month. Sleep not as good past month, seemingly due to joint pains overnight causing frequent awakening when rolls over. Been taking OTC ibuprofen 200 mg tabs, 2-3 tabs at a time over past 2 weeks, and “helps 50%”

NKDA, no regular Rx, no signif PMHx, Fam Hx neg for Rheum conditions

PE: nl vitals, afebrile, exam unremarkable except for moderate synovial thickening across bilat MCPs and bilat wrists, other joints achy with extremes of ROM
Case 1 question

In this patient with a clinical presentation suggesting a new onset inflammatory arthritis, the best initial series of lab tests to order in addition to a CBC & Comprehensive metabolic panel would be:

a. a convenient "arthritis panel" which includes ESR/CRP, uric acid, Rheumatoid Factor, ANA, and HLA-B27
b. "tick panel" of antibodies against Lyme disease, Babesiosis, & Ehrlichiosis

c. comprehensive viral panel including parvovirus, hepatitis B, HIV
d. ESR/CRP, Rheumatoid Factor, anti-CCP (cyclic citrullinated peptide)
1. Why is D correct? ESR/CRP, Rheumatoid Factor, anti-CCP (cyclic citrullinated peptide)

• Without any other symptoms of other rheumatologic types of inflammatory arthritis at this time, the most likely diagnosis is rheumatoid arthritis. If she has significantly + RF and or CCP antibodies, then the diagnosis is almost certain.

• An elevated ESR/CRP supports that an inflammatory condition is present and gives a marker that can be followed going forward, especially helpful in future if/when needing to distinguish if new symptoms may or may not be inflammatory in nature.

• CBC/CMP help screen for other occult etiologies but also need to ensure their normality if/when considering medical therapies.
1. Why is A wrong?
a convenient "arthritis panel" which includes
ESR/CRP, uric acid, Rheumatoid Factor,
ANA, and HLA-B27

• Clinically not suggestive of gout
• Clinically not suggestive of lupus
• Clinically not suggestive of spondylarthropathy
• Pre-test probability is important to consider in test ordering
1. Why is B wrong?
"tick panel" of antibodies against Lyme disease, Babesiosis, & Ehrlichiosis

- Presentation has symmetrical small joint inflammatory arthritis with no fever, history of tick bite, or rash –so does not suggest any of these
- In setting of likely auto-immune inflammatory process, possibility of false positive tests on these “panels” is even greater with non-specific hypergammaglobulinemia, and that can lead to further cascades of unnecessary testing
1. Why is C wrong?
comprehensive viral panel including parvovirus, hepatitis B, HIV

• No known recent exposure to parvovirus
• Let’s at least see results of CBC & CMP before considering Hep B and HIV, but acute viral illness with them could give such a presentation, but far less likely than RA
• If not recently done, they likely will need to be done before any RA immunosuppressive medical therapy is started
• Not needed in initial series of lab tests
Pearls for case 1

- Convenient “panels” of tests do not take into account the important concept of pre-test probability and lead to a large number of positive tests of uncertain significance and can lead to a path of further unnecessary testing
- Indiscriminate test ordering must be brought under control if we are to be good stewards of healthcare delivery
- It is GOOD practice to order tests in logical stepwise process
Don’t test ANA sub-serologies without a positive ANA and clinical suspicion of immune-mediated disease.

Tests for anti-nuclear antibody (ANA) sub-serologies (including antibodies to double-stranded DNA, Smith, RNP, SSA, SSB, Scl-70, centromere) are usually negative if the ANA is negative. Exceptions include anti-Jo1, which can be positive in some forms of myositis, or occasionally, anti-SSA, in the setting of lupus or Sjögren’s syndrome. Broad testing of autoantibodies should be avoided; instead the choice of autoantibodies should be guided by the specific disease under consideration.
ACR Evidence-Based Guidelines for the Use of Immunologic Tests: ANA Testing

Arthr Care Res 2002

1. When there is a strong clinical suspicion that a patient has SLE, the ANA is the best diagnostic laboratory test to obtain. Because the ANA is present in many healthy persons and patients with a multitude of other diseases, it should not be used as a test to rule out rheumatic disease. If the ANA is positive, antibody tests to other specific antigens might be considered depending on the clinical setting. Tests for antibodies to dsDNA or extractable nuclear antigens should not be requested before a positive result on the ANA is obtained.

2. Patients suspected of having systemic sclerosis should have an ANA test performed because a negative result would prompt consideration of other fibrosing illnesses, such as eosinophilic fasciitis or linear scleroderma.
3. Current evidence suggests that the ANA is not useful for diagnosis of PM or DM, and that other connective tissue diseases (SLE or overlap syndrome) must also be considered.

4. ANA testing is not useful for diagnosing Sjogren’s syndrome. In patients with Sjogren’s syndrome possibly related to SLE, an ANA can help clarify whether an underlying connective tissue disease exists.

5. Although positive ANA testing is not uncommon in patients with RA, the presence of the ANA has no diagnostic significance in RA, and ANA testing is not useful in patients suspected of having RA.
Other ACR recommendations

*A practice that has been advocated for sera found to be positive on ANA testing is for the automatic subsequent testing of panels of other autoantibodies. This “reflex testing” or “cascade testing” cannot be recommended.

*Fluorescent ANA on HEp-2 cell preparations is standard methodology. Before clinicians depend on the results of ANA testing performed with ELISA technology, more widespread testing should be performed.

*ANA tests should no longer be performed on substrates other than HEp-2 cells.
So how expensive are these tests?

- [https://requestatest.com/](https://requestatest.com/)
  - “Arthritis Basic Panel” (CMP, ESR, CRP, Uric Acid): $109 LC, $99 QD
  - “Arthritis Comp Panel” (above & RF, ANA): $199 LC, $179 QD
  - “Rheum Arth Panel” (RF, CCP): $109 at both
  - CCP: $79 LC, $84 QD
  - ANA: $55 at both
  - RF: $39 LC, $49 QD
  - ESR: $29 at both
  - Sjogren antibodies (Ro & La): $119 LC, $99 QD
Case 2
approach to non-specific MSK sx & fatigue

35 yo woman presents with fatigue and achiness over the past year. She has not noted any joint swelling and says the achiness seems more in different muscle areas around shoulders, posterior neck, around hips, inner knees. She has not been otherwise ill, no fevers, weight loss, rashes. While she feels she was never a “great sleeper”, she notes it has been particularly restless over the past year, with lots of disruption, tossing & turning, waking up still tired. She is a busy attorney & used to exercise regularly but with work being particularly stressful over the past 18 mos that had fallen off, and now she physically doesn’t feel up to exercise anyway. She is wondering whether work stress is making her anxious and if that explains any of this. NKDA, No meds, neg PMH. Exam normal except subjective tenderness with palpation over multiple fibromyalgia “tender points”. No labs in past 5 years, so you order CBC, CMP, TSH, ESR, & 25-OH Vitamin D level. All are normal.
Case 2 question

2. In this patient with a clinical presentation suggesting fibromyalgia, the best initial management plans would be:
   
a. start duloxetine at 60 mg per day and follow-up visit in 3 months

b. refer to psychologist for "cognitive behavioral therapy" (CBT) for sleep difficulties and follow-up visit in 4 months

c. start cyclobenzaprine 10 mg each evening and follow-up visit in 1 month

d. start lorazepam 0.5 mg each evening and follow-up visit in 1 month
2. why is C correct?
start cyclobenzaprine 10 mg each evening and follow-up visit in 1 month

• Cyclobenzaprine as sedating muscle relaxer has been shown to be frequently effective in improving sleep patterns and subjective symptoms of fibromyalgia

• Close follow-up visit is helpful to monitor progress in person, continue to validate the condition (which some patients are skeptical of, once diagnosis given)

• Tolerance of Rx and dosing needed can take fine tuning, best done in person
2. why is A wrong?

start duloxetine at 60 mg per day and follow-up visit in 3 months

• While duloxetine is FDA-approved for fibromyalgia, greater side-effect profile than cyclobenzaprine (or my 2<sup>nd</sup> choice tizanidine) and is not as immediately impactful on sleep patterns

• more costly

• discontinuation after period of time can require tricky gradual wean
2. why is B wrong?
refer to psychologist for "cognitive behavioral therapy" (CBT) for sleep difficulties and follow-up visit in 4 months

- Clinical presentation at this time suggestive of fibromyalgia and not a primary sleep disorder
- Depending on progress with treatments, CBT might be appropriate in future but not at this time
2. why is D wrong?
start lorazepam 0.5 mg each evening and follow-up visit in 1 month

- At this point the primary problem does not seem to be anxiety but rather fibromyalgia, and it is likely that improving her sleep pattern and musculoskeletal symptoms will improve the clinical situation without resorting to benzodiazepines
Pearls for case 2

• Take a good sleep history in patients with non-specific musculoskeletal symptoms and fatigue

• If clinical presentation does not suggest an inflammatory process, do consider some basic routine labs if not recently done (CBC & CMP) as well as TSH & 25-OH Vitamin D

• Sedating muscle relaxers cyclobenzaprine (or if too sedating then try tizanidine) can be remarkably helpful---and simple!
Case 3  
gout management

64 yo WM seen by you as his PCP 1 week after he was seen in ED for severe acute pain and swelling of left base great toe starting 2 days previously. He had taken OTC naproxen 220 mg twice in previous day with minimal improvement. He was told that x-ray showed soft tissue swelling but no bone/joint changes.

History of HTN on lisinopril and HCTZ, type 2 DM on metformin, mild knee DJD and takes occasional aleve 2-3 times per week as needed. NKDA.

Labs in ED with normal CBC and chem panel, uric acid 8.0.

ED physician gave him diagnosis of gout (podagra), and gave Rx for Methylprednisolone dosepak to take for typical 6 day course, and also gave him indomethacin 50 mg to take BID prn if the Methylprednisolone was not making him a lot better after 24-48 hours.

In office today, he reports that he finished Methylprednisolone yesterday, and the foot is now 90% better.
3. In this patient with recent acute gout, the best next management plan right now would be:

a. start allopurinol 100 mg per day
b. give a 2nd course of a methylprednisolone dosepak
c. start colchicine 0.6 mg BID for 1 week then decrease to QD
d. give longer course of tapering oral steroids as prednisone, 30 mg QD for 5 days then taper by 10 mg every 5 days (20 mg x 5 d, 10 mg x 5 d, then stop)
3. why is C correct?
start colchicine 0.6 mg BID for 1 week
then decrease to QD

• Risk of recurrent gout is high in several weeks after an episode and short courses of treatment might stop too abruptly
• Colchicine at low dose is generally well tolerated and has better adverse effect profile than steroids (in pt with DM) or NSAIDs
3. why is A wrong?
start allopurinol 100 mg per day

- Do not start urate-lowering therapy 1 week after an initial gout episode
- The ED uric acid level drawn in setting of acute gout may not accurately reflect the patient’s baseline uric acid level due to acute serum level decrease during episode
- There might be other interventions to make that could lower an elevated uric acid level: stop HCTZ, EtOH intake?
- Starting urate-lowering therapy as new daily Rx is a long-term therapeutic decision that should not be made prematurely
3. why is B wrong?
give a 2nd course of a Methylprednisolone dosepak

• He is 90% better, and he likely does not need this high dose of steroid to resolve this, but then he is again off any treatment with no prophylaxis for recurrence
• With underlying DM, steroids less preferable than other agents
3. Why is D wrong?

give longer course of tapering oral steroids as prednisone, 30 mg QD for 5 days then taper by 10 mg every 5 days (20 mg x 5 d, 10 mg x 5 d, then stop)

- He is already 90% better and likely does not need 2 weeks of steroids with more gradual taper when other options (colchicine) are available, especially given his DM
Pearls for case 3

- Colchicine is an excellent option for acute gout and to then maintain for at least several weeks before seeing 1 month later to check uric acid level and engage in more informed decision-making.
- Steroids and NSAIDs can be equally effective but have adverse effect profiles that might make less preferable for certain patients.
- Indomethacin is no better than other NSAIDs and has greater adverse effect profile (especially CNS) and should not be used.
- Urate-lowering therapy should not be started during gout episodes because it causes “mobilization” of urate and that is stimulatory to already sensitized inflammatory cells—“Gasoline on the fire”
Thanks for your attention!

Other Questions?

Medicine is a science of uncertainty and an art of probability.

- Sir William Osler

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