Clinical Pearls : Rheumatology

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Disclosures

• None
Learning Objectives

• correctly manage mono-articular arthritis
• identify when to suspect a diagnosis of systemic lupus erythematosus (SLE)
• select appropriate testing to confirm a suspected diagnosis of SLE
• recognize when a patient has more than polymyalgia rheumatica (PMR)
• anticipate complications of treatment of PMR and giant cell arteritis (GCA)
Learning Objectives

• correctly manage mono-articular arthritis
• identify when to suspect a diagnosis of lupus
• select appropriate testing to confirm a suspected diagnosis of lupus
• recognize when a patient has more than polymyalgia rheumatica (PMR)
• anticipate complications of treatment of GCA
Case 1

50yo man just returned from Sturgis c/o left knee pain and swelling

- History of 10 years of episodic first MTP swelling that tends to occur during periods of heavy alcohol use and peels afterwards
- PMH: Diabetes, Hep C
- PE: T 38.0, other VS normal. Centrally obese. Left knee warm, with large effusion and no other swollen joints.
- LABS (3 months ago) a1c 10, creatinine 1.0

MTP = metatarsal phalangeal joint
Case 1:

Next Step?

1. Naproxen 500 BID  20%
2. Prednisone 40 mg followed by taper  20%
3. Left knee intra-articular steroid injection  40%
4. Knee aspiration  20%
Why aspirate?

- Rule out septic arthritis
- Gout and septic arthritis can co-exist\(^1\)
- Evaluation of aspirated fluid
  - CBC with differential
  - Gram stain and culture
  - Crystal evaluation

\(^1\)Doherty Rheumatology 2009
Challenges in aspiration

• “dry tap” – no fluid obtained
  – Thick synovial fluid – use a large bore needle
  – In the knee, medial plica or fat pad can block the needle – take a lateral approach
  – Smaller joints are unlikely to yield much fluid – if you have capacity to use polarizing scope, make a slide

• Ensure you have tubes for all studies – double check with lab if unsure

• Send for analysis in timely fashion
Aspirate monoarticular arthritis
Learning Objectives

• correctly manage mono-articular arthritis
• **identify when to suspect a diagnosis of lupus**
• select appropriate testing to confirm a suspected diagnosis of lupus
• recognize when a patient has more than polymyalgia rheumatica (PMR)
• manage complications of treatment of GCA
Patient A

- 27 year old black woman with complaints of fatigue, full body pain, trouble concentrating, sleep disturbance
- Denies photosensitivity, rashes, oral ulcers, Raynaud’s
- PE : normal

Patient B

- 27 year old black woman with complaints of fatigue, joint stiffness, oral ulcers, Raynaud’s, pleuritic chest pain
- PE : VS normal, ulcerations noted on soft palate, synovitis across 2-5th PIPs bilaterally
Which patient warrents checking an anti-nuclear antibody (ANA)?

1. Patient A

2. Patient B
Why is the ANA not a screening test?

• Present in healthy individuals
  – Especially healthy relatives of patients with SLE
  – Elderly patients

• Present in many other diseases

  • Mixed connective tissue disease (MCTD)
  • Systemic sclerosis
  • Rheumatoid arthritis
  • Primary Sjogren’s syndrome
  • Anti-phospholipid antibody syndrome

  • Autoimmune thyroid disease
  • Autoimmune liver disease
  • Primary pulmonary hypertension
  • Multiple sclerosis

  • Malignancy (lymphoma)
  • Chronic infection
ANA should be ordered in the setting of suspicion of autoimmune disease
When to suspect SLE

- Epidemiology
- Personal history of autoimmune disease
- Family history of autoimmune disease

- Clinical & historical features
  - Fatigue, weight loss
  - Ulcers
  - Joint symptoms
  - Rash
  - Photosensitivity
  - Hair loss
  - Raynaud’s
  - Dyspnea or pleuritic chest pain
  - Gynecologic history – recurrent or late miscarriage
  - History of DVT/PE
When to suspect SLE

- Physical exam
  - Ulcers (nasal or oral)
  - Hair loss
  - Rashes
  - Livedo
  - Raynaud’s, digital ulcerations
  - Synovitis
When to suspect SLE

• Findings on basic labs that may be supportive
  – Elevated creatinine
  – Leukopenia or other unexplained cytopenias
  – Abnormal urinalysis
SLE classification criteria

- American College of Rheumatology (ACR) 1997 criteria
- Requires 4 of 11
- Does not distinguish between clinical and immunologic criteria
SLE classification criteria

- American College of Rheumatology (ACR) 1997 criteria
  - Requires 4 of 11
  - Does not distinguish between clinical and immunologic criteria

  - 4 of 17 criteria
  - at least one clinical criterion and one immunologic criterion
  - Alternatively, biopsy-proven lupus nephritis

Hochberg Arthritis Rheum 1997
Petri Arthritis Rheum 2012
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Confirmation in a high probability clinical scenario and positive ANA

- CBC with differential
- Comprehensive metabolic panel, if not done
- Urinalysis with microscopy
  - Quantify proteinuria
  - If active urine sediment (cells, casts) should have renal evaluation
- Anti-SSA/SSB
- Anti-smith
- Anti-RNP
- Anti-double stranded DNA
- Complements
  - C3, C4, CH50
- Antiphospholipid antibodies
  - Anti-cardiolipin
  - Anti-beta2 glycoprotein\(^1\)
  - Lupus anti-coagulant\(^2\)

\(^1\)not to be confused with beta2 microglobulin
\(^2\)not reliable if patient anti-coagulated
Choosing Wisely

American College of Rheumatology

Five Things Physicians and Patients Should Question

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.

Employ a step-wise approach to antibody testing
Confirmation in a high probability clinical scenario and positive ANA

- Consider skin biopsy
- If concern for alternative causes of mucosal ulceration, consider swab for viral PCR
- If concern for pericarditis, electrocardiogram, echocardiogram
- Consider chest x-ray to evaluate for pleural effusion
- If joint symptoms, x-ray of involved joints
- If seizure or psychosis, will need lumbar puncture and CNS imaging – this is a high risk patient who should be admitted
Brief notes on management

• High risk manifestations
  – CNS involvement
  – Hemolytic anemia
  – Severe thrombocytopenia
  – Lupus nephritis
  – Serositis
  – Severe anti-phospholipid antibody manifestations e.g. CAPS

• Consider transfer to higher level of care when stable
Brief notes on management

• Milder cases
• Absence of severe manifestations and has undergone appropriate workup
• Still would benefit from rheumatology referral

• Hydroxychloroquine ≤ 6.5 mg/kg (and not above 400 mg) daily
• Baseline eye exam
• Sun protection
• Avoid meds that induce photosensitivity
• Smoking cessation
• Vaccination
• Contraception
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Case 3

- 70 year old woman with 3 months of severe shoulder and hip pain, morning stiffness, increasingly unable to manage ADLs that require reaching above her head and trouble standing out of a chair
- She denies vision changes, headache, jaw claudication
Case 3

• PE: VS normal, breakaway weakness with shoulder abduction, unable to rise from seated position; no bruits are noted

• LABS: sedimentation rate (ESR) 25 mm/hour, C-reactive protein (CRP) 60 mg/L

• Other labs are unremarkable
Case 3:

Can you have a normal ESR in PMR?

1. Yes  

2. No
A quick comment on labs

• Elevated ESR
  – Can be < 30 or normal in 10%

• C-reactive protein (CRP) more sensitive

• Normal ESR in folks > age 50
  – men: age / 2
  – Women: [age + 10] / 2

Kermani et al Lancet 2012
West Rheumatology Secrets 2015
ESR
Changes more slowly
May be normal
Can be affected by other processes

CRP
Changes quickly
Very sensitive
Check a CRP with the ESR if concerned about PMR
PMR: labs

- Normocytic anemia, increased platelets
- Alkaline phosphatase elevated in up to 33%
- Negative RF and ANA
- Lab evaluation includes: ESR, CRP, CBC, comprehensive metabolic panel, TSH, CK, SPEP, UA
- Goal of evaluation is to help exclude mimicking conditions

Kermani et al Lancet 2012
Case 3

• Started on 20 mg prednisone
• After 1 month, her inflammatory markers remain high and you have been unable to taper her steroids
Case 3 continued:

What Now?

1. Look for alternative diagnosis
2. Re-evaluate possibility of GCA
3. Refer to rheumatology
4. All of the above
Consider rheumatology referral

• Refractory to glucocorticoid therapy
• Relapses or prolonged therapy
• Atypical presentation
  – Young e.g. < 60
  – Peripheral arthritis
  – Low inflammatory markers

Dejaco Arthritis Rheum 2015
Reconsider the diagnosis if unable to taper prednisone in PMR
Case 3

- She also now has right sided headache, and a few days of stuttering right sided “darkness” and now monocular vision loss
- PE: no bruits, symmetric upper extremity blood pressures
Case 3 continued:

Immediate Next Step? In addition to urgent ophthalmology evaluation

1. Methylprednisolone 1 mg gram IV

2. Prednisone 60 mg PO

3. Call ENT for a stat temporal artery biopsy

20
Do steroids change the biopsy?

- Ideally biopsy in one week
- Pathology is not affected by < 2 weeks of high dose prednisone
- Prospective study actually looked at people at 1 week, 2-3 weeks, and > 4 weeks; still had positive biopsies at 4 weeks
- Histology becomes less typical

Borchers Autoimmunity Review 2012
GCA : treatment

- *Do not delay treatment with steroids to wait for biopsy*
- Visual symptoms? Call ophtho
- Prednisone 1 mg/kg up to 60 mg
- OR If there is acute visual loss within 24 hours admit for pulse steroids
  - methyprednisolone 1 gram x 3 days
- Call ENT (or appropriate specialist) for temporal artery biopsy
- Call rheumatology
If concern for impending visual loss in GCA, do not delay steroid treatment to wait for a biopsy
Case 3 continued:

In addition to higher dose of prednisone-

1. Start calcium, vitamin D and bisphosphonate

2. Check a hemoglobin a1c and consider a PPI

3. Start aspirin

4. Get a baseline chest x-ray

5. All of the above
• **Average duration of steroid treatment is 2-3 years**

• Estimated that ~ 50% of patients with PMR/GCA have steroid related complication

Nesher Rambam Maimonides Med J 2016
Nesher J Rheum 1994
ACR Recommendations for the Prevention and Treatment of GC-Induced Osteoporosis

Bisphosphonate therapy is recommended even for low risk patients > age 50 starting steroid therapy anticipated > 3 months

Grossman et al. Arthritis Care Res 2010
Why aspirin?

• Risk of death in giant cell arteritis typically from vascular complications
• Retrospective data to support anti-platelet therapy to decrease visual loss and cerebral ischemic events\(^1,^2\)
• Aspirin + steroids = \(\uparrow\) risk GI bleed\(^3\)
• Control other vascular risk factors
  – Control blood pressure
  – Quit smoking

\(^1\text{Nesher Arthritis Rheum 2004}\)
\(^2\text{Lee Arthritis Rheum 2006}\)
\(^3\text{Lanza Am J Gastro 2009}\)
Long term complications

• Thoracic aortic aneurysms can appear in delayed fashion after diagnosis
• Patients should get an annual chest x-ray
Anticipate and manage the complications from disease and long term corticosteroid therapy in PMR/GCA
Summary

- Aspirate monoarticular arthritis
- ANA should be ordered in the setting of suspicion of autoimmune disease
- Employ a step-wise approach to antibody testing
Summary

- Reconsider the diagnosis if unable to taper prednisone in PMR
- If concern for impending visual loss in GCA, do not delay steroid treatment to wait for a biopsy
- Anticipate and manage the complications from disease and long term corticosteroid therapy in PMR/GCA
Thank you

Questions?

Contact
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References