# 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
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- 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%**

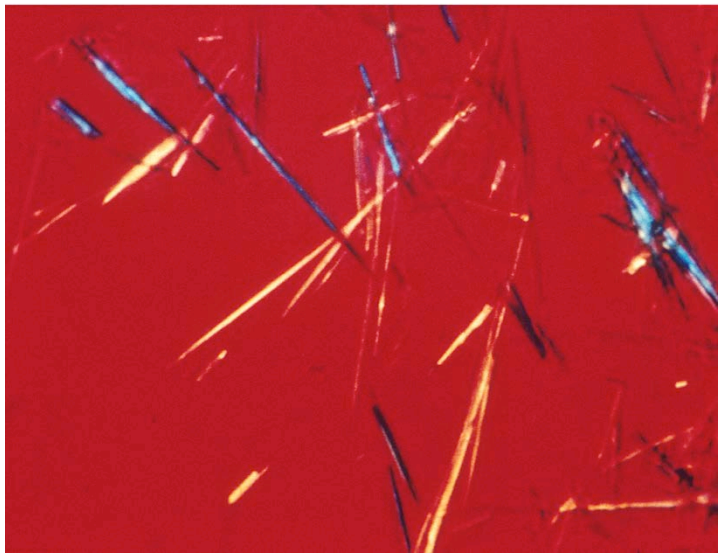
4. Knee aspiration

**20%**

0

# 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

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- **identify when to suspect a diagnosis of lupus**
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- 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 2-5$^{th}$ PIPs bilaterally

Which patient warrents checking an anti-nuclear antibody (ANA)?

1. Patient A

**50%**

2. Patient B

**50%**

20

# 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

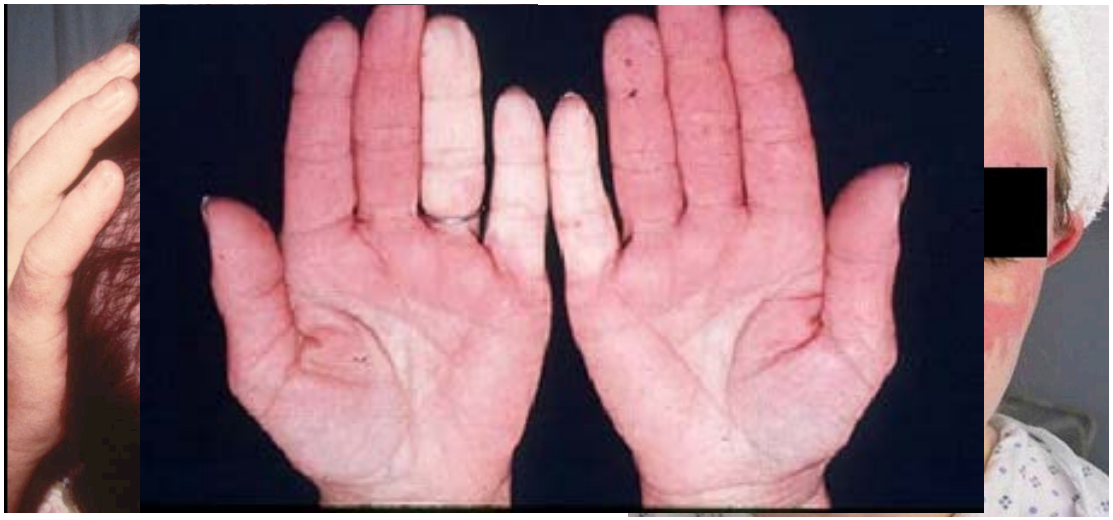
- Clinical & historical features
  - Fatigue, weight loss
  - Ulcers
  - Joint symptoms
  - rash

  - 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



http://www.med.umich.edu/scleroderma/patients/raynauds.htm

# 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

| |
|---|
| Malar rash |
| Discoid rash |
| Photosensitivity |
| Oral ulcers |
| Arthritis |
| Serositis |
| Renal disorder |
| Neurologic disorder |
| Hematologic disorder |
| Immunologic disorders |
| Antinuclear antibody |

Hochberg Arthritis Rheum 1997

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- Systemic Lupus International Collaborating Clinics (SLICC) Criteria 2012
- 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

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**Five Things Physicians and Patients Should Question**

1

## 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

**50%**

2. No

**50%**

20

# 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

# VS

# 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

**25%**

2. Re-evaluate possibility of GCA

**25%**

3. Refer to rheumatology

**25%**

4. All of the above

**25%**

20

# 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

**33%**

2. Prednisone 60 mg PO

**33%**

3. Call ENT for a stat temporal artery biopsy

**33%**

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

Ray Chaudhuri N et al. Br J Ophth 2002
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

**20%**

2. Check a hemoglobin a1c and consider a PPI

**20%**

3. Start aspirin

**20%**

4. Get a baseline chest x-ray

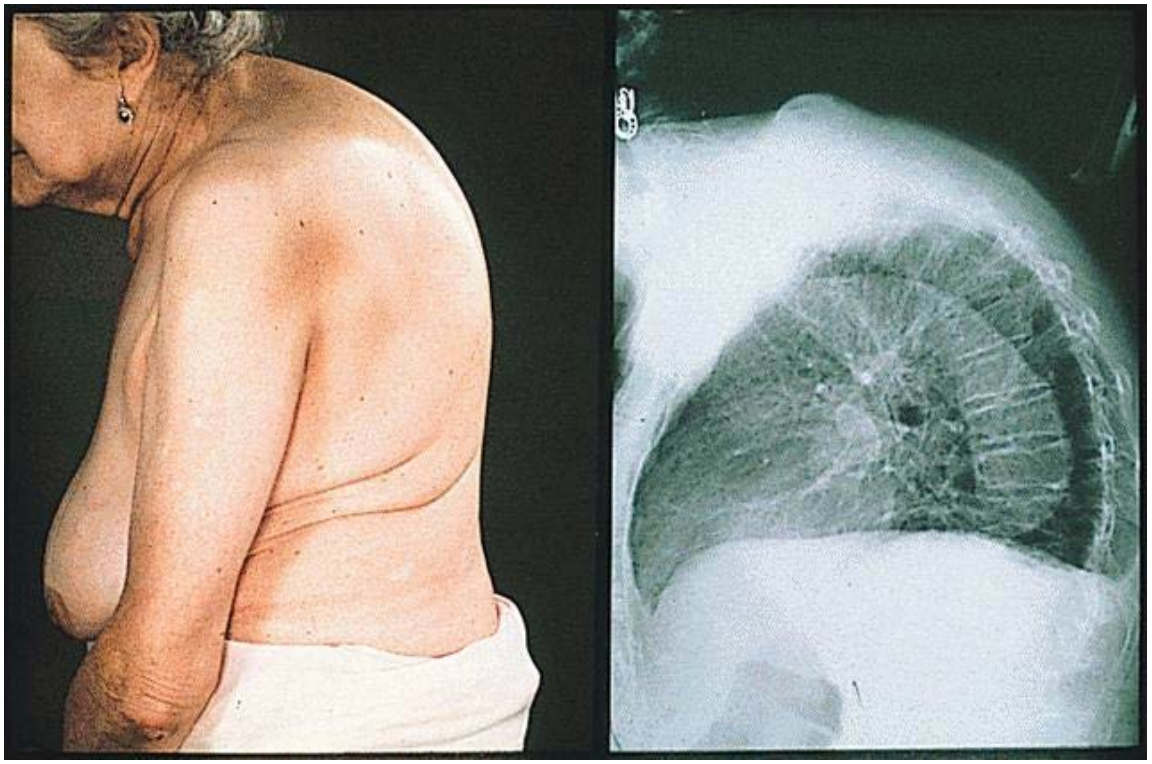
**20%**

5. All of the above

**20%**

20

- ***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 = ↑ risk GI bleed[3]
- Control other vascular risk factors
  - Control blood pressure
  - Quit smoking

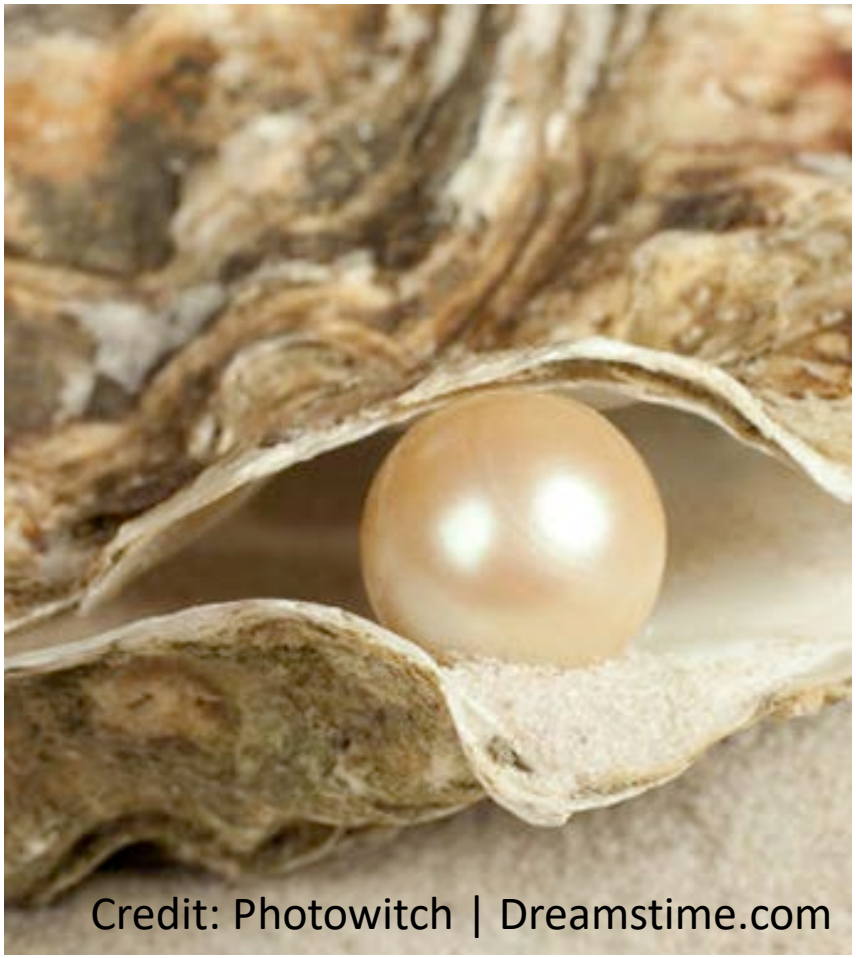
[1]Nesher Arthritis Rheum 2004
[2]Lee Arthritis Rheum 2006
[3]Lanza Am J Gastro 2009

# Long term complications

- Thoracic aortic aneurysms can appear in delayed fashion after diagnosis
- Patients should get an annual chest x-ray

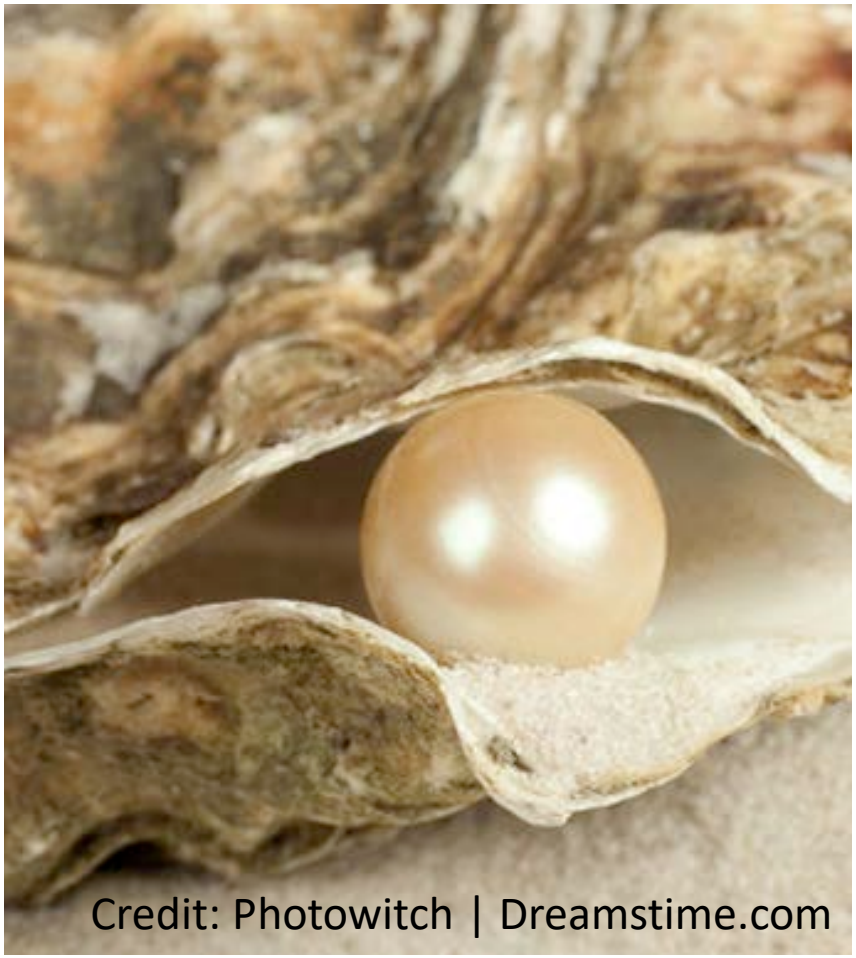
# Anticipate and manage the complications from disease and long term corticosteroid therapy in PMR/GCA

# Summary


Credit: Photowitch | Dreamstime.com

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

# Summary


Credit: Photowitch | Dreamstime.com

- **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


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