Case-Based Rheumatology

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Disclosure

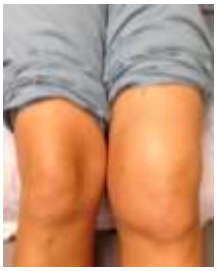
- Speaking fees:
  - Novartis
- Clinical Investigator:
  - EMD Serono, Inc
  - Amgen
  - Roche/Genentech

Learning Objectives:

- Crystalline arthropathy
- GCA/PMR
- Infectious arthritis
- Spondyloarthritis
- Connective tissue disorders

Case #1

- A 74 year old woman presents with 2 days of spontaneous L knee swelling and moderate pain with weight bearing. Symptoms are worsening, though improved with OTC ibuprofen. She reports mild intermittent low grade fevers and occasional chills. No prior episodes. She had an uncomplicated breast mass biopsy by fine needle aspiration one week prior.
- PMH:
  - Psoriasis
  - Diabetes mellitus with CKD
- SH:
  - 1 ppd tobacco x 20 yrs
  - Moderate alcohol x yrs



- T: 100.2, rr: 16, hr: 98, bp: 110/70
- Gen: mild distress with L knee exam
- Msk: mod pain elicited with passive ROM testing in all fields; mild erythema and tenderness with moderate effusion in suprapatellar bursa
- WBC: 14K
- CRP: 79.6
- ESR: 64

Question 1

- What is the best next approach for work up/treatment for this patient:
  - AP films of bilateral knees
  - ✓ Arthrocentesis of L knee
  - Intra-articular corticosteroid
  - Colchicine
  - Cefazolin

Septic Arthritis: need to know

- Risks:
  - Elderly (>80 yo)
  - Recent surgery/mode of entry
  - Arthroplasty
  - DM, RA, HIV
- If doubt: fluid aspiration; analysis
  - Cell count, differential
  - Cultures
  - Crystals
- Sensitivity of signs/symptoms:
  - Joint pain 85%
  - Synovitis 78%
  - Fevers 57%
  - Sweats 27%
  - Rigors 19%
- Specificity :
  - WBC >100K/microlitre
  - Inflammatory arthritis 50-100K
  - PMN >90%

Margaretten, ME. Does this adult patient have septic arthritis? JAMA 2007 Apr 4;297(13):1478-88.

Synovial Fluid Analysis

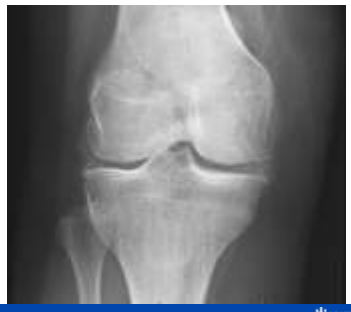
	Noninflammatory Type I	Inflammatory Type II	Septic Type III	Hemorrhagic Type IV
Appearance	Amber-yellow	Yellow	Purulent	Bloody
Clarity	Clear	Cloudy	Opaque	Opaque
Viscosity	High (+ String sign)	Decreased (- string)	Decreased (- string)	Variable
Cell Count (%PMN)	200-2000 (< 25% PMN)	2000-75,000 (>50% PMN)	> 60,000 (>80% PMN)	RBC >> wbc
Examples	OA Trauma Osteonecrosis SLE	RA, Reactive SLE, gout Tbc, fungal	Bacterial, Gout	Trauma, Fx, Ligament tear Charcot Jt. PVS

Used with permission

This patient….

- WBC: 75K
  - PMN: 70%
- Culture negative
- Crystals: none seen

- Plain films were obtained next…….

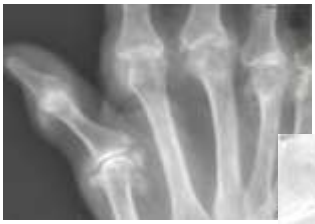


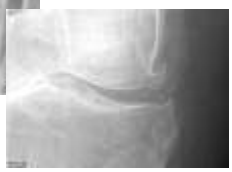
Question 2

- What is the most likely cause of her swelling?
  - Psoriatic arthritis
  - Gout
  - Osteoarthritis
  - ✓ Calcium pyrophosphate deposition
  - Polymyalgia rheumatica

Calcium Pyrophosphate Deposition Disease (CPPD) – formerly pseudogout

- Key Points:
  - Crystals are metabolic product of aging
  - Knees, wrists, shoulders, metacarpophalangeals (MCP)
  - Episodes last days to weeks or chronic
  - 'pseudogout', 'pseudo-RA', 'pseudo-OA'
- Epidemiology
  - ~3% in >60 yo; ~50% in >90 yo
  - Risk factors: hypothyroid, DMII, hemochromatosis, hyperPTH
- Radiographic features:





chondrocalcinosis

Crystals: microscopy

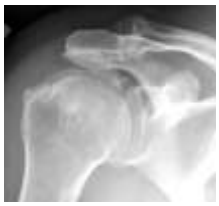
CPPD: weakly positively birefringent, rhomboidal or irregular under compensated polarized light

MSU: strongly negatively birefringent, intracellular needle shaped

ACR Slide Collection

Need to know: CPPD

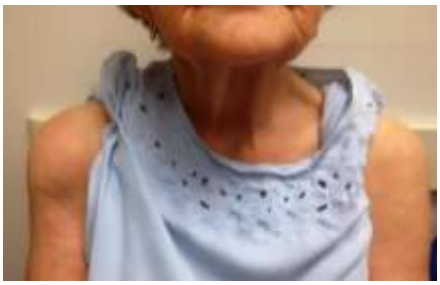
- CPPD: common cause of acute inflammatory arthritis
- Variable presentations; prevalence and RF's
- Recognize chondrocalcinosis on xrays
- Treatments:
  - Acutely:
    - Ice, arthrocentesis and steroid injection
    - NSAIDs or colchicine
  - Long term:
    - Low dose colchicine
    - Methotrexate/Hydroxychloroquine



Zhang, et al. EULAR recommendations for calcium pyrophosphate deposition. Part II: Management. Ann Rheum Dis 2011: 571-575

Case #2

- 84 yo woman presents with one month of gradually worsening shoulder pain, stiffness and aching – R>L. Hard to raise arms overhead. Moderate aching in hands as well. Spontaneous and minimal effects with OTC motrin, though slightly better with rest. Hips and legs feel well.
- SH: regular tob use x yrs; no etoh
- FH: sister with "RA"
- Exam:
  - Limited abduction in shoulders – R>L
  - Swelling in R shoulder
  - Moderate osteoarthritic carpalmetacarpal and distal interphalangeals with trace swelling in several proximal interphalangeals



Component	Latest Ref Rng & Units	1/10/2019
CREAT	<=1.10 mg/dL	0.61
GFR	mL/min/BSA	117
RACE		Non Black
ALT	<=54 U/L	17
ALKP	<=125 U/L	46
TBILI	<=1.0 mg/dL	0.3
VITAMIN D, 25-HYDROXY, D3	ng/mL	31
VITAMIN D, 25-HYDROXY, D2	ng/mL	<4
VIT D, 25-OH	30 - 100 ng/mL	31
ESR	0 - 20 mm/Hr	20
RF	<=14 IU/mL	10
CCP IGG	<=4.9 U/mL	274.9 (H)
CRP	<=7.4 mg/L	12.2 (H)

Question 3:

- What is the most likely diagnosis?
  - Polymyalgia rheumatica
  - Gout
  - CPPD
  - Rotator cuff syndrome
  - ✓ Rheumatoid arthritis

2010 ACR/EULAR Classification Criteria for RA

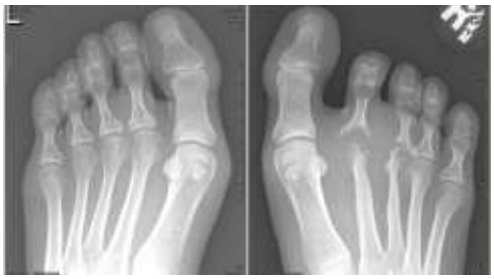
JOINT DISTRIBUTION (0-5)	
1 large joint	0
2-10 large joints	1
1-3 small joints (large joints not counted)	2
4-10 small joints (large joints not counted)	3
>10 joints (at least one small joint)	5
SEROLOGY (0-3)	
Negative RF AND negative ACPA	0
Low positive RF OR low positive ACPA	2
High positive RF OR high positive ACPA	3
SYMPTOM DURATION (0-1)	
<6 weeks	0
≥6 weeks	1
ACUTE PHASE REACTANTS (0-1)	
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1

≥6 = definite RA, assuming other conditions are ruled out

What if the score is <6?

Patient might fulfill the criteria…

→ **Prospectively** over time especially if the serologies are present



RA diagnosis – need to know

- Chronic systemic inflammatory arthritis
- Newer criteria emphasize auto antibodies and acute phases
  - Anti-cyclic citrullinated peptide antibodies (CCP)
  - Rheumatoid factor (RF)
  - CRP/ESR
- Less emphasis on symmetry and radiographic changes for classification

Aletaha et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology / European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2010;69:1580-1588.

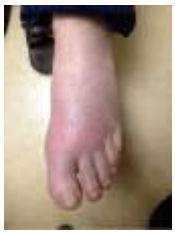
Case #3

- CC: finger pain, swelling
- HPI: 84 yo female with known OA complains of chronic aching and swelling of DIPs – gradually over past year; episodes of warmth and tenderness that comes and goes, but no pain in feet, knees or swelling elsewhere.
- PMH: hypertension, DMII, no psoriasis, crohns
- Meds:
  - hydrochlorothiazide 25 mg daily
  - metformin 500 mg bid
- Exam:
  - Moderate heberden and bouchard nodes, moderate mal-alignment, but with no MCP synovitis
  - soft tissue swelling in DIPs of L hand


Question #4: What is the best explanation for these symptoms?

1. Erosive osteoarthritis
2. ✓ Elderly onset gout
3. Calcium pyrophosphate deposition disease
4. Rheumatoid arthritis
5. Multicentric reticulohistiocytosis

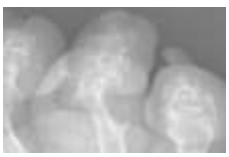
Gout:



- Common in men >40 yrs but rising in women
  - ↑prevalence (~4%)
    - chronic disease, aging, ↓GFR
    - ↑obesity
    - medications
- Uric acid often deceptively low/normal during attacks (our pt: 11.3 mg/dL), adjusting treatments can precipitate attacks
- Phases:
  - acute
  - chronic tophaceous →
  - intercritical period

Elderly Onset Gout (EOG)

- subacute/chronic polyarticular hand involvement
- localization of tophi on heberden nodes
- increased female:male ratio
- association with drugs → decrease renal urate excretion (diuretics and low-dose aspirin)



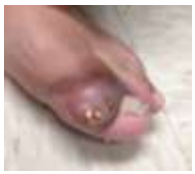
De Leonardis, Elderly-onset gout: a review. Rheum Int. 2007

Treatment Principles

- Terminate the acute attack
  - High dose NSAIDs
  - Corticosteroids (PO or intra-articular with arthrocentesis)
  - Colchicine, if early
    - FDA indication 2009
      - 1.2 mg then 0.6 an hour later then qd-tid
- Treat hyper-uricemia to limit progression
  - Lower serum uric acid
    - Xanthine oxidase inhibitors
      - Allopurinol
      - Febuxostat (2009)
    - Pegloticase (2011)

Gout: Need to know…

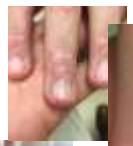
- Gout prevalence is on the rise (acute, chronic, EOG)
- Risk factors are traditional (diet) - and more recently recognized
- Serum uric acid is not always elevated during attacks
- Newer approaches to treatment:
  - Colchicine dosing
  - Start allopurinol in low dose; titrate gradually
  - Febuxostat if allopurinol intolerant, ckd
  - Pegloticase for severe tophaceous gout

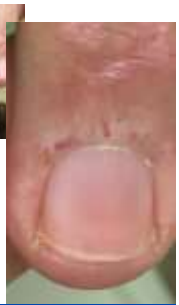


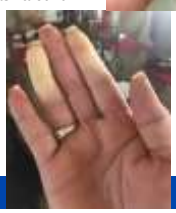
Khanna et al. 2012 American College of Rheumatology Guidelines for Management of Gout. Part 1: Systematic Nonpharmacologic and Pharmacologic Therapeutic Approaches to Hyperuricemia. Arthritis Care & Research, 2012

Case #4

- HPI: 32 year old woman presents with 2 months of fatigue, mild dyspnea and finger color changes that are worse in cold temperatures. She reports mild aching and swelling in fingers and a red rash around fingernails.
- SH: 1 ppd tobacco
- Exam:
  - Full, puffy fingers
  - Pallor
  - Periungual erythema

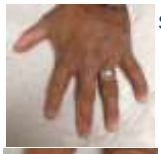




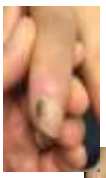


Question 5

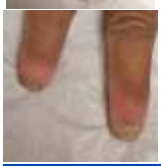
- The patient later develops skin tightness and esophageal dysmotility and dyspnea. What autoantibody is most likely to be present on lab testing?
  - Anti-synthetase
  - Anti-HMG coA reductase
  - ✓ Anti-RNA polymerase III
  - Anti-Smith
  - SSA



Scleroderma: clinical features



- Early
  - Fatigue/Fevers
  - Raynaud's
  - Lymphadenopathy
  - Swollen fingers



- Vasculopathy
  - Dilated nailfold capillary loops
  - Digital pits/ulcers
- Fibrosis
  - sclerodactyly
- Cardiopulmonary

Van Roon, AM, Abnormal Nailfold Capillaroscopy Is Common in Patients with Connective Tissue Disease and Associated with Abnormal Pulmonary Function Tests. J Rheumatol. 2018 Dec 15

2013 ACR / EULAR Criteria For The Classification Of Systemic Sclerosis (Scleroderma)*

Item	Sub-item(s)	Weight/score †
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints (sufficient criterion)		9
Skin thickening of the fingers (only count the highest score)	Sclerodactyly	2
	Fingertip lesions (digital pitting scar or loss of substance of the pulp of the finger)	2
Telangiectasia		2
Abnormal nailfold capillaries		2
Pulmonary arterial hypertension and/or interstitial lung disease (maximum score is 2)	Pulmonary arterial hypertension	2
	Interstitial lung disease	2
Raynaud's phenomenon		3
Scleroderma related antibodies (anti-centromere, anti-topoisomerase I (anti-Scl-70), anti-RNA polymerase III) (maximum score is 3)	Anticentromere	3
	Anti-topoisomerase I	
	Anti-RNA polymerase III	

* The criteria are not applicable to patients with skin thickening limited to the fingers or to patients who have a scleroderma-like disorder that better explains their manifestations (e.g., morphea/generalized morphea, eosinophilic fasciitis, scleredema, scleromyxedema, porphyria, lichen sclerosus, graft-versus-host disease, diabetic sclerodactyly).

† The total score is determined by adding the highest weight/score in each category. Patients with a total score of ≥ 9 are classified as having definite scleroderma.

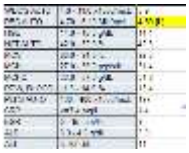
Scleroderma: need to know

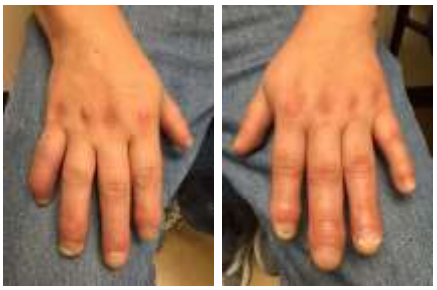
- Heterogeneous autoimmune inflammatory disease
  - Vasculopathy
  - Fibrosis
  - Cardiopulmonary
- Scl-70, Centromere, RNA polymerase III antibodies
- Limited treatment options
  - Calcium channel blockers
  - Mycophenolate mofetil
  - Methotrexate
  - Cyclophosphamide
  - Nintedanib
  - Tocilizumab

Gabrielli, A. Scleroderma. N Engl J Med 2009; 360:1989-2003
Khanna, D. Efficacy and Safety of Tocilizumab for the Treatment of Systemic Sclerosis: Results from a Phase 3 Randomized Controlled Trial. Abstract 898, ACR 2018

Case 5

- HPI: 32 year man presents with one month of gradually worsening stiffness and aching in fingers that improves with use and OTC ibuprofen. Moderate morning stiffness in low back x 1 hour. Significant limitation in daily function.
- SH: moderate etoh; no drugs/tobacco
- FH: mother with psoriasis
- Labs:
- Exam…….

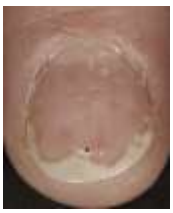




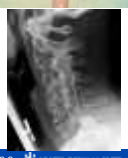
Question 6

- According to 2018 ACR/NPF guidelines, what is recommended as treatment for this degree of inflammation?
  - Leflunomide
  - Apremilast
  - Secukinumab
  - ✓ Golimumab
  - Methotrexate

Psoriatic Arthritis Domains



- Peripheral arthritis
- Dactylitis/Enthesitis
- Axial disease
- Skin domain
  - Nail disease
- Arthritis mutilans



Taylor, W. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthitis Rheum. 2006 Aug;54(8):2665-73.

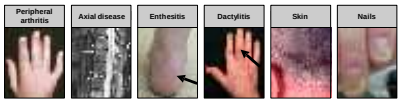
2018 ACR/NPF Psoriatic Arthritis Treatments

Non-pharmacologic therapies	• physical therapy, occupational therapy, smoking cessation, weight loss, massage therapy, exercise
Symptomatic treatments	• nonsteroidal anti-inflammatory drugs, glucocorticoids, local glucocorticoid injections
DMARD	• methotrexate, sulfasalazine, cyclosporine, leflunomide, apremilast
TNFi	• etanercept, infliximab, adalimumab, golimumab, certolizumab pegol
IL12/23i	• ustekinumab
IL17i	• secukinumab, ixekizumab, brodalumab
CTLA4-Ig	• abatacept
JAKi inhibitor	• tofacitinib

Singh JA, et al. 2018 ACR/NPF Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019; 71 (1) 5-32. Epub 2018 Nov 30

Case 5: Psoriatic arthritis key points

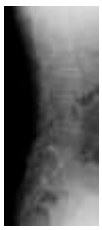
- Another multi-domain condition
- Recognition and refer
- Newer therapies depending on domains
  - Traditional dmards (skin and mild disease)
  - Biologics (TNF's in severe disease first line)

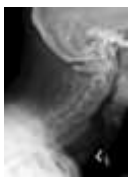


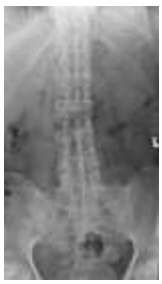
Singh JA, et al. 2018 ACR/NPF Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019; 71 (1) 5-32. Epub 2018 Nov 30
Coates LC, et al. Arthritis Rheumatol. 2016;68:1060-1071

Axial SpA (Ankylosing Spondylitis): Key Points

- Inflammatory back/sacroiliac pain; young men
- Genetic basis of disease
- Biologics and complications







Case 7

- 85 yo male with 3 months of bilateral hip and shoulder joint pain, weakness, gradually worsening. Worse with shoulder abduction; hip extension. Most severe in mornings with stiffness for 90 minutes. No swollen joints. Moderate loss of appetite and 20 lbs weight loss. OTC ibuprofen helps minimally.
- ROS: mild intermittent diffuse headaches; no vision changes or skull tenderness, no bowel changes
- PMH: gout, htn, ckd
- Labs:……..

Question 7

- What is the most likely diagnosis:
  - ✓ Polymyalgia rheumatica
  - CPPD
  - Osteoarthritis
  - Paget's
  - Fibromyalgia

Polymyalgia Rheumatica

Clinical Features

- Elderly (average age 70), F>M, northern european
- Pelvic, shoulder girdle aching; morning stiffness >45 mins
- Anemia; acute phase reactants
- Rapid response to low doses of corticosteroids (10-15 mg qd)

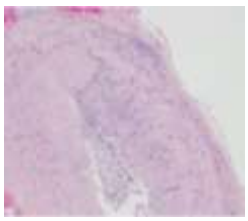
Differential Diagnosis

- Occult infection, malignancy
- Hypothyroidism
- CPPD

Dasgupta, B. Provisional Classification Criteria for Polymyalgia Rheumatica: A EULAR/ACR Collaborative Initiative. Ann Rheum Dis 2012; 71:484-492

PMR – need to know

- Common cause of shoulder and pelvic girdle stiffness, tenderness in elderly
- High acute phases; anemia
- Robust response to low dose prednisone
  - 10-15 mg daily
- Relationship with GCA
  - Corticosteroids doses



In Summary: High Yield Points

- Septic arthritis has key history, risk factors and joint fluid analysis results and can mimic other forms of arthritis
- Radiographic findings and joint distribution are important clues in the under-recognized CPPD patterns of crystal induced arthritis
- Anti-CCP is a specific auto-antibody in RA
- Gout is on the rise and can present in atypical fashion (elderly onset, DIP, low SUA at time of attack)
- Scleroderma is a heterogeneous autoimmune condition with new classification criteria
- Psoriatic arthritis has many domains of disease – dactylitis, spondylitis, skin; and is in the family of spondyloarthritis (prototypical: AS)
- PMR is a common cause of inflammatory limb girdle stiffness and tenderness that is associated with GCA

MAYO CLINIC

Thank you!

Questions?

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