Rheumatology Cases for the Internist

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Objectives

- To present and discuss three cases that represent the most common reasons for referral to my academic rheumatology practice at both the University of Maryland and Baltimore VA Medical Center.
Case 1: History

- 45-year-old woman who presents for evaluation of polyarticular joint pain of several years duration.
- She admits to AM stiffness lasting ~1 hour, gel phenomenon, but denies joint swelling or redness.
- Review of systems is positive for difficulty falling asleep, difficulty staying asleep, snoring, fatigue and diffuse myalgias; pertinent negatives include lack of fever or weight loss.
Case 1: History

- There is no h/o sicca symptoms, rash, mucosal ulcers, Raynaud phenomenon or Lyme disease.
- Family history is non-contributory.
- Social history is positive for modest alcohol consumption (average 4 drinks per week), former smoker, no illegal drug use. She lives in Baltimore City and currently works as an administrative assistant.
Case 1: Physical Examination

- Normal vital signs
- No evidence of active or chronic synovitis, joint effusions or deformity.
- Normal muscle strength.
- Tender at 14/18 “tender points.”
- Remainder of examination, including neurologic exam, is within normal limits.
The 18 "tender points" important for the diagnosis of fibromyalgia. Note the bilateral symmetry of the labeled regions. Tenderness on palpation of at least 11 of these sites in a patient with at least a three-month history of diffuse musculoskeletal pain is recommended as a diagnostic standard for fibromyalgia.

## Differential diagnosis of fibromyalgia

<table>
<thead>
<tr>
<th>Disease</th>
<th>Features not present in fibromyalgia</th>
<th>Pitfalls in diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>Joint swelling, elevated ESR and CRP</td>
<td>“False positive” rheumatoid factor in FM occasionally</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Rash and renal, cardiac, pulmonary, and neurologic features</td>
<td>“False positive” antinuclear antibody in some with FM and many symptoms</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
<td>Severe stiffness in the morning and when sedentary, elevated ESR and CRP, usual onset &gt;60 years, rapid response to glucocorticoids</td>
<td>Like FM, often no abnormal physical findings in polymyalgia rheumatica</td>
</tr>
<tr>
<td>Polymyositis</td>
<td>Muscle weakness, elevated muscle enzymes, abnormal EMG/NCV</td>
<td>FM patients often feel weak (but have normal strength)</td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>Restricted spinal motion, elevated ESR or CRP</td>
<td>May be no peripheral joint abnormality in spondyloarthritis</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>Characteristic rash, joint swelling, serologic tests confirmatory</td>
<td>&quot;Post-Lyme&quot; FM symptoms; false positive serologic tests, early flu-like symptoms</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Abnormal thyroid function tests, pain not prominent</td>
<td>Hypothyroidism may present with a myopathy/mild myalgia</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Sensory or motor deficits, abnormal EMG/NCV</td>
<td>Subtle neurologic disorders, small fiber neuropathy in some with FM</td>
</tr>
</tbody>
</table>

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; FM: fibromyalgia; EMG: electromyogram; NCV: nerve conduction velocity.
Hints for early and cost-effective diagnosis of fibromyalgia

Chronic widespread musculoskeletal pain for ≥three months
Absence of other systemic condition accounting for pain
Excess tenderness in soft-tissues

Characteristic symptoms:
- "I hurt all over"
- "It feels like I always have the flu"
- Fatigue, sleep and mood disturbances
- IBS, irritable bladder, multiple other somatic complaints

Exclusion of structural or systemic disease
- Not a "fishing" expedition
- Avoid "screening" rheumatology tests
- Most efficient with early subspecialty referral

IBS: irritable bowel syndrome.

Courtesy of Don L Goldenberg, MD.
**Recommended diagnostic workup for fibromyalgia**

1. **History of chronic, widespread pain for ≥3 months**
2. **Rule out other conditions that may present with chronic widespread pain**
   - General physical exam, neurologic exam, CBC, and ESR and/or CRP (additional selected testing based upon clinical features, such as TSH or CK in patients suspected clinically of thyroid or inflammatory muscle disease, respectively; avoid screening serologic testing)
   - Sleep and mood evaluation
3. **Confirm presence of tender points (? need 11 of 18)**
4. **Confirm diagnosis of fibromyalgia**

Establishing the diagnosis is an essential component of FM management. Diagnostic criteria for FM include the ACR and the Canadian Consensus Guidelines. A complete history, physical exam, and laboratory testing should be done to exclude diseases that may mimic or complicate FM. Each patient should be assessed for a ≥three-month history of chronic widespread pain; patient self-report should be used as an index of pain. The presence of tender points should be confirmed. However, tenderness is subjective and depends upon the examiner’s strength of palpation.

CBC: complete blood count; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; TSH: thyroid-stimulating hormone; CK: creatine kinase; FM: fibromyalgia; ACR: American College of Rheumatology.

Fibromyalgia: Treatment

• Non-pharmacologic modalities
  – Patient education, good sleep hygiene, cognitive behavioural therapy and aerobic exercise program; consider acupuncture, tai chi and/or yoga

• Pharmacologic modalities
  – Amitriptyline or cyclobenzaprine followed by duloxetine or milnaciprin, pregabalin or a combination of the above
  – Avoid opioid analgesics!
2017 EULAR Management Recommendations.

History and physical examination

Diagnosis of fibromyalgia

Patient education and information sheet

Physical therapy with individualised graded physical exercise (can be combined with other recommended non-pharmacological therapies such as hydrotherapy, acupuncture)

Reassessment of patient to tailor individualised treatment

Additional individualised treatment

Pain-related depression, anxiety, catastrophizing, overly passive or active coping

Psychological therapies

• Mainly cognitive behavioural therapy
• For more severe depression / anxiety consider psycho-pharmacological treatment

Severe pain
• Duloxetine
• Pregabalin
• Tramadol (or in combination with paracetamol)

Severe sleep problems
• Low-dose amitriptyline
• Cyclobenzaprine or
• Pregabalin at night

Severe pain / sleep disturbance

Pharmacotherapy

Severe disability / sick-leave

Multimodal rehabilitation programs
Case 1: Questions
Case 2: History

• 45-year-old woman who presents for evaluation of polyarticular joint pain of several months duration.

• She admits to AM stiffness lasting ~1 hour, gel phenomenon and joint swelling with difficulty performing her usual daily activities.

• Review of systems is positive for fatigue, depressed mood, low grade fever, anorexia and weight loss.
Case 2: History

- Positive for h/o sicca symptoms; however, she denies rash, mucosal ulcers, chest pain, muscle weakness or Raynaud phenomenon.
- Family history is positive for RA in her mother.
- Social history is positive for modest alcohol consumption (average 4 drinks per week), current smoking, but no illegal drug use. She lives in Baltimore County and currently works as an administrative assistant.
Case 2: Physical Examination

• Normal vital signs
• Combination of both active and chronic synovitis involving all PIP and MCP joints of both hands and both wrists as well as tenderness across MTP joints of the feet bilaterally.
• Normal proximal muscle strength; however, grip strength is reduced bilaterally.
• No subcutaneous nodules or skin rash
• Remainder of examination, including neurologic exam, is within normal limits.
Synovial thickening of the metacarpophalangeal joint

Bilateral swelling of the MCP joints is evident in this patient with rheumatoid arthritis. Note also the mild swan neck deformities present in several fingers, particularly the left middle and fifth fingers.

MCP: metacarpophalangeal.

Courtesy of Patrick J Venables, MD.
<table>
<thead>
<tr>
<th>Feature</th>
<th>Rheumatoid arthritis</th>
<th>Osteoarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary joints affected</td>
<td>Metacarpophalangeal</td>
<td>Distal interphalangeal</td>
</tr>
<tr>
<td></td>
<td>Proximal interphalangeal</td>
<td>Carpometacarpal</td>
</tr>
<tr>
<td>Heberden's nodes</td>
<td>Absent</td>
<td>Frequently present</td>
</tr>
<tr>
<td>Joint characteristics</td>
<td>Soft, warm, and tender</td>
<td>Hard and bony</td>
</tr>
<tr>
<td>Stiffness</td>
<td>Worse after resting (e.g., morning stiffness)</td>
<td>If present, worse after effort, may be described as evening stiffness</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td>Positive rheumatoid factor</td>
<td>Rheumatoid factor-negative</td>
</tr>
<tr>
<td></td>
<td>Positive anti-CCP antibody</td>
<td>Anti-CCP antibody-negative</td>
</tr>
<tr>
<td></td>
<td>Elevated ESR and CRP</td>
<td>Normal ESR and CRP</td>
</tr>
</tbody>
</table>

CCP: cyclic citrullinated peptide; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.
Case 2: Laboratory Evaluation

• CBC with differential
• Chemistry profile
• Acute phase reactants
• Serology
  – Rheumatoid factor
  – Anti-citrullinated peptide antibodies (ACPA)
Case 2: Imaging Evaluation

• Definite
  – Plain radiographs of affected joints

• Possible
  – Color Doppler ultrasound
  – Magnetic resonance imaging
2010 ACR-EULAR classification criteria for rheumatoid arthritis

Target population: Patients who have at least 1 joint with definite clinical synovitis (swelling) with the synovitis not better explained by another disease.

Classification criteria for RA (score-based algorithm: add score of categories A-D; a score of ≥6/10 is needed for classification of a patient as having definite RA).

The metacarpophalangeal joints, proximal interphalangeal joints, the interphalangeal joint of the thumb, second through fifth metatarsophalangeal joint and wrist as small joints, and shoulders, elbows, hip joints, knees, and ankles as large joints.

A. Joint involvement

<table>
<thead>
<tr>
<th>Number of Large Joints</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2-10</td>
<td>1</td>
</tr>
<tr>
<td>1-3</td>
<td>2</td>
</tr>
<tr>
<td>4-10</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10</td>
<td>5</td>
</tr>
</tbody>
</table>

B. Serology (at least 1 test result is needed for classification)

<table>
<thead>
<tr>
<th>Serology Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative RF and negative ACPA</td>
<td>0</td>
</tr>
<tr>
<td>Low-positive RF or low-positive ACPA</td>
<td>2</td>
</tr>
<tr>
<td>High-positive RF or high-positive ACPA</td>
<td>3</td>
</tr>
</tbody>
</table>

C. Acute-phase reactants (at least 1 test result is needed for classification)

<table>
<thead>
<tr>
<th>Acute-phase Reactants</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal CRP and normal ESR</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal CRP or abnormal ESR</td>
<td>1</td>
</tr>
</tbody>
</table>

D. Duration of symptoms

<table>
<thead>
<tr>
<th>Duration</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥6 weeks</td>
<td>1</td>
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</table>
RA: Approach to Management

• Refer to rheumatologist!
• All patients with active RA should receive a disease-modifying antirheumatic drug (DMARD)
• All patients should receive non-pharmacologic modalities including patient education, OT/PT
• NSAIDs and glucocorticoids are adjunctive agents for control of symptoms
Case 2: Questions
Case 3: History

- 45-year-old man who presents for evaluation of polyarticular joint pain and swelling involving the left foot/ankle, right knee and wrist of several weeks duration.
- He has a h/o recurrent episodic monoarthritis previously involving the big toe bilaterally, left ankle and right elbow. These were previously treated with OTC NSAIDs; he has never had a joint aspirate or been treated with colchicine or urate lowering therapy.
- Review of systems is positive for low grade fever and anorexia.
Case 3: History

- Positive for h/o hypertension treated with HCTZ and lisinopril, and hyperlipidemia treated with simvastatin.
- Family history is positive for kidney stone and gout in his father.
- Social history is positive for moderate alcohol consumption (average 10 drinks per week), current smoking, but no illegal drug use. He lives in Baltimore County and formerly worked at Bethlehem Steel.
Case 3: Physical Examination

- Normal vital signs
- Combination of active synovitis involving left foot and ankle, right knee and right wrist with warmth, tenderness and soft-tissue swelling; right knee effusion present with positive bulge sign.
- Subcutaneous nodule in right olecranon bursa.
- Remainder of examination is within normal limits.
### Risk factors for hyperuricemia and gout (may not be causal)

<table>
<thead>
<tr>
<th>Nonmodifiable risk factors</th>
<th>Modifiable risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Obesity</td>
</tr>
<tr>
<td>Gender</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Genetic variants</td>
<td>Cardiovascular disease</td>
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<tr>
<td></td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>Chronic kidney disease</td>
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<tr>
<td></td>
<td>Dietary factors</td>
</tr>
<tr>
<td></td>
<td>Alcohol</td>
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<tr>
<td></td>
<td>Medications altering urate balance</td>
</tr>
</tbody>
</table>
Diagnosis of gout flare*

Can aspiration and synovial fluid analysis of the affected joint or bursa be readily performed?

- Yes
- No

Are negatively birefringent needle-shaped crystals (characteristic of monosodium urate) seen in the synovial fluid sample by compensating polarized light microscopy?

- Yes
- No

Has an alternative diagnosis been identified (e.g., acute CPP crystal arthritis, infection)?

- Yes
- No

Is gout still suspected based upon clinical and synovial fluid findings (e.g., inflammatory fluid without neutrophils)?

- Yes
- No

Further evaluation for gout is not required, and alternative diagnoses should be considered and treated.

Apply "clinical diagnostic rule" with scoring for each element present:
- Male sex (2 points)
- Previous patient reported arthritis attack (2 points)
- Onset within one day (0.5 points)
- Joint tenderness (1 point)
- First metatarsophalangeal joint involvement (2.5 points)
- Hypertension or at least one cardiovascular disease (1.5 points)
- Serum urate level greater than 5.88 mg/dL (1.5 points)

Score 0-4: Probability of gout is low
- Consider alternative diagnosis

Score >4 and <8: Probability of gout is intermediate
- Probability of gout is high

Score 8:
- Probability of gout is high
- Consider alternative diagnosis

CPP: calcium pyrophosphate.

* Refer to the UpToDate topic on the clinical manifestations and diagnosis of acute gout, which should be used together with this algorithm, for further information. Use of imaging for diagnosis requires particular expertise in the relevant imaging techniques and their interpretation, as well as ready availability of the technology.

† Synovial fluid analysis should include white cell count and differential, Gram stain and culture, and crystal search under compensating polarized light microscopy.

∆ Refer to UpToDate topic review on septic arthritis or septic bursitis, depending upon the affected region. Consultation with an expert on arthrocentesis (e.g., a rheumatologist or orthopedist) or an interventional radiologist is required to obtain synovial fluid for analysis if there is clinical suspicion of septic arthritis.

The sensitivity of the joint fluid analysis can be improved by examination of the sediment in a centrifuged specimen. Additional approaches to consider in the event of a negative (no urate crystals seen) study during the acute attack include aspiration of a concurrently inflamed joint or aspiration of an uninfamed but previously involved joint or of a tophus if either is present, although aspiration of an uninfamed joint or tophus is less helpful in excluding an accompanying cause for the acute event.

© Coexisting infection should be excluded based upon the synovial fluid analysis, including Gram stain and culture.

The evaluation and management of patients in this group is complex. Refer to the UpToDate topic on the clinical manifestations and diagnosis of gout for additional discussion.
Correct Nomenclature

• Gout is a chronic inflammatory arthritis that results from monosodium urate (MSU) crystal deposition in tissues or joints resulting from supersaturation of uric acid in extracellular fluids

• Gout is a disorder of uric acid metabolism

• Hyperuricemia is defined as serum uric acid >2 SD above the mean (> 7.0 mg/dL for men, > 6.0 mg/dL for women)

• Hyperuricemia is a necessary but not sufficient precursor to gout
Gout: Stages

- Asymptomatic hyperuricemia
- Acute episodic monoarthritis
- Intercritical gout
- Chronic polyarthritis, often with tophaceous deposits
Case 3: Evaluation

• Laboratory tests
  – CBC with differential
  – Chemistry profile, including serum uric acid
  – Acute phase reactants

• Imaging
  – Plain radiography
  – Ultrasonography (double contour sign)
  – Dual-energy CT
Gout: Treatment of Arthritis

• Treat acute/chronic arthritis
  – Colchicine
  – NSAIDs
  – Glucocorticoids
  – IL-1 inhibition
Gout: Prevention of Recurrent Attacks

• Oral colchicine
• Urate lowering therapy
  – Xanthine oxidase inhibition
    • Allopurinol
    • Febuxostat
  – Uricosuric agents
    • Probenecid
    • Lesinurad (Zurampic™) specific URAT1 inhibitor
Case 3: Questions
Choosing Wisely: Rheumatology

• Don’t test ANA sub-serologies unless the ANA is positive in a clinically significant titer
• Don’t test for Lyme disease without an exposure history and appropriate exam findings
• Don’t perform MRI of the peripheral joints to monitor inflammatory arthritis
• Don’t prescribe biologic DMARDs for RA before a trial of MTX or other conventional DMARD
Rheumatology Referral Guidelines

• Evaluation of patients with unclear diagnoses
• Evaluation and management of patients with
  – Inflammatory arthritis
  – Systemic autoimmune rheumatic diseases
    • Connective tissue diseases and vasculitides
• Diagnostic or treatment plan for rheumatic manifestations of other primary diseases

Approved by ACR Board of Director, August 2015 (modified by MCH)
Thank you for your kind attention.