Approach to the patient with spondyloarthritis

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Disclosures

• Past 12 months:
• Honoraria from UCB for advisory boards and unbranded speaking engagement
• Investigator-initiated research grant from Pfizer
• Honoraria for unbranded speaking engagement and investigator-initiated research grant from the Spondylitis Association of America
Learning Objectives

Working through clinical case examples, we will:

1. Differentiate inflammatory arthritis from arthralgia
2. Identify exam features to assist in establishing a differential diagnosis
3. Select radiographic and laboratory tests that aid in diagnosis
4. Outline an initial treatment strategy
Example case #1:

35 year old woman presents with joint pain in the right shoulder, both knees, and back worsening over the last 2 years

Is the joint pain inflammatory or mechanical?
Review of key terminology to categorize symptoms and diagnoses

**Quality of Pain**

<table>
<thead>
<tr>
<th>Mechanical</th>
<th>Inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brief morning stiffness (&lt;1 hour)</td>
<td>Morning stiffness &gt; 1 hour</td>
</tr>
<tr>
<td>Pain worse with use; at end of day</td>
<td>Improves with “activity”</td>
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</table>

**Inflammatory Back Pain:**

Above features **PLUS**

- Age of onset <40
- Pain wakes patient early
- Alternating buttock pain
- Response to NSAIDs

**Distribution**

- Peripheral
- Axial

**Number of Joints**

- Monoarticular = 1
- Oligoarticular = 2-5
- Polyarticular = >5

**Arthritis vs Arthralgia**

- Inflammation
- Pain

Sensitivity 95% and Specificity ~50% for diagnosis of AS if 3/5 inflammatory back pain features are present

Seiper et al. *Ann Rheum Dis* 2009
Is the joint pain inflammatory or mechanical?

Address each site individually:

• Shoulder pain only when lifting arm, clearly started after playing catch with daughter

• Knees worse when climbing stairs, but notes occasional swelling in the left knee without a clear trigger

• Back pain wakes her early in the morning but gets better after about 1-2 hours as she gets going with her day, may have had off and on symptoms when younger but thought just needed to exercise more since it always improved when she is more active
Question #1: So far, we can establish that our patient has:

A. Peripheral oligoarticular arthralgia and axial arthritis

B. Peripheral and axial arthralgias

C. Inflammatory joint pain of the spine and possibly mechanical pain of the peripheral joints, although the left knee needs further assessment
So far, we can establish that our patient has:

A. Peripheral oligoarticular arthralgia and axial arthritis

B. Peripheral and axial arthralgias

C. Inflammatory joint pain of the spine and possibly mechanical pain of the peripheral joints, although the left knee needs further assessment
Supporting features of SpA, by history or exam, helps categorize the sub-type.
Physical exam findings in SpA may be subtle due to their involvement of the enthesis

The pathologic site in SpA is the *enthesis*, causing *tendinitis* or *tenosynovitis*.
But… is it enthesitis or fibromyalgia?!??!

**Enthesitis**

Additional objective findings:
Psoriasis or other SpA-features
Swelling, warmth, erythema

Qualitative Features:
Improvement with mobility
And worsen with immobility

Therapeutic trial:
Scheduled NSAIDs
Steroid injection

**Fibromyalgia**

Additional symptoms:
Sleep disturbance
Mood symptoms/associations

Qualitative Features:
Worsens with mobility or stress

Failed therapeutic trial:
Scheduled NSAIDs
Steroid injection

Not mutually exclusive
Frequent reassessment

Marchesoni et al. *Rheumatology* 2018
Additional exam maneuvers and findings that indicate SpA

- Limited Spine ROM
- Dactylitis
- Arthritis
- FABER
- Gaenslen’s
Our case…

• Full MSK exam notable for:
  • TTP of the right medial epicondyle, but no swelling or warmth
  • Right shoulder with normal ROM but positive Lift-Off test
  • Left knee with small effusion and warmth, TTP of the inferior patellar tendon insertion
  • TTP of the right SIJ and pain with FABER and Gaenslen’s maneuvers but normal spine ROM

• No skin or nail findings
• HEENT, CV, Pulm, Abd exams normal
Classification of SpA is moving away from AS, PsA, etc. and towards axial versus peripheral disease.

- Spine ± Asymmetric oligoarticular arthritis
- Symmetric, polyarticular, only peripheral, & small joints: consider RA instead
Question #2: The DDx thus far should include the following EXCEPT

A. Axial SpA
B. Peripheral SpA
C. Rotator cuff injury
D. Fibromyalgia
The DDx thus far should include the following EXCEPT

Axial SpA  A
Peripheral SpA  B
Rotator cuff injury  C
Fibromyalgia  D
Question #3: In addition to an ESR and CRP, what do you order to confirm your suspicions?

A. Radiograph of the pelvis, and if the radiograph is normal, an MRI of the pelvis
B. Radiograph of the pelvis
C. HLA-B27, radiograph of the lumbar spine and possibly future MRI of the lumbar spine
D. RF, CCP, ANA, HLA-B27, radiograph of the lumbar spine
In addition to an ESR and CRP, what do you order to confirm your suspicions?

A. Radiograph of the pelvis, and if the radiograph is normal, an MRI of the pelvis

B. Radiograph of the pelvis

C. HLA-B27, radiograph of the lumbar spine and possibly future MRI of the lumbar spine

D. RF, CCP, ANA, HLA-B27, radiograph of the lumbar spine
Inflammatory markers are unlikely to be elevated in early SpA, but can be helpful if elevated. 

A

CRP

<table>
<thead>
<tr>
<th>axSpA</th>
<th>Back Pain Controls</th>
</tr>
</thead>
</table>

B

ESR

| axSpA | Back Pain Controls |

Turina et al. RMD Open 2017
De Vries et al Arthritis Rheum 2009
The same lack of inflammatory marker elevation is also seen in those with psoriatic disease
Caveat emptor: HLA-B27 does not make or break the diagnosis!

- The prevalence of HLA-B27 within patient populations with SpA ranges 50-95%.
  - Higher in axial disease, lower in peripheral

- SpAs occur in about 2% of the general population and in just over 10% of HLA-B27 positive individuals.

- Despite a strong association of AS with HLA B27:
  - ~80% of individuals with the gene don’t get AS
  - ~20% of individuals with AS don’t have the gene

Hwang et al. Clinical Rheumatology 2021
Radiography

- Peripheral arthritis generally non-erosive
- Axial arthritis similar to AS
  - Always examine pelvic imaging first!
MRI is more sensitive for active inflammation

Semi-coronal STIR of pelvis with unilateral osteitis

Sagittal T2 of L-spine with “shiny corners”

Again, always start with pelvic imaging even if symptoms elsewhere in the spine!

Rheumatology Image Library
© American College of Rheumatology

Case courtesy of Dr Hani Al Salam, Radiopaedia.org, rID: 29896
Peripheral joint disease may be better appreciated by ultrasound

- More sensitive at identifying enthesitis compared to physical exam

- Enables differentiation from tenderness due to fibromyalgia

Dubash et al. Front Med 2020
Aydin et al. J Rheumatol 2020
Polachek et al. Ann Rheum Dis 2021
Example Case #2:

25 year old obese man presents with 6 months of hand, back, and knee pain. He doesn’t exercise regularly, his work is sedentary, and he does not identify any triggers to the pains.

• Hand pain comes and goes. Notes it was present upon waking one day. Usually only 1-2 knuckles are swollen for ~1 week at a time. Ibuprofen helps.

• Back and knee pain worse with walking.

He thinks he may have had small patches of psoriasis on his elbows, but it never was evaluated or treated. He does not have any today.

Exam is notable for BMI 35, dactyritis of the 3rd digit of the left hand, and a patch of psoriasis in the umbilicus.
Question #3: To aid in your diagnosis in this patient, you order…

A. RF, CCP, ESR, CRP, and radiographs of the bilateral hands.
B. GC/CT urine, ESR, CRP, RF, CCP
C. ESR, CRP, ultrasound of the 3rd digit of the left hand
To aid in your diagnosis in this patient, you order...

A. RF, CCP, ESR, CRP, and radiographs of the bilateral hands.

B. GC/CT urine, ESR, CRP, RF, CCP

C. ESR, CRP, ultrasound of the 3rd digit of the left hand
Question #4: All of the following features increase the risk of psoriatic arthritis in this patient EXCEPT...

A. Depression/Anxiety
B. Psoriasis on the elbows
C. Obesity
D. Smoking

Soltani-Abrabshahi et al. Arch Dermatol 2010
All of the following features increase the risk of psoriatic arthritis in this patient EXCEPT...

- Depression/Anxiety
- Psoriasis on the elbows
- Obesity
- Smoking

A
B
C
D
Question #5: What is the most appropriate first-line therapy for peripheral SpA (PsA)?

A. Scheduled NSAIDs  
B. TNF inhibitor  
C. Methotrexate  
D. Sulfasalazine

Singh et al. Arthritis Care Res 2019
What is the most appropriate first-line therapy for peripheral SpA (PsA)?

Scheduled NSAIDs

TNF inhibitor

Methotrexate

Sulfasalazine
Treatment Algorithm

GI/GU Infection preceding?

- no
  - Presence of IBD?
    - no
      - Presence of psoriasis?
        - no
          - Predominantly...
            - peripheral
              - Undifferentiated pSpA
              - NSAIDs
              - DMARD
              - TNFi
            - axial
              - AxSpA/AS*
                - NSAIDs
                - TNFi
                - IL-17i
                - IL-12/23i
                - JAKi
        - yes
          - IBD-SpA
            - peripheral
              - Oral DMARD
              - TNFi
            - axial
              - TNFi
              - Celecoxib?
  - yes
    - Reactive arthritis
      - -NSAIDs
      - -IA, PO steroid
      - -DMARD
      - -Biologic (TNFi)

- yes
  - Self-limited at ~6 weeks
  - Longer than 6 months, question Dx!

*Per guidelines: Singh et al. Arthritis Care Res 2019
            Ward MM et al. Arthritis Rheumatol 2019
Question #6: What cytokine is central to the pathophysiology of all types of SpA?

A. IL-17
B. IL-23
C. IL-12
D. IL-13
What cytokine is central to the pathophysiology of all types of SpA?

IL-17 A
IL-23 B
IL-12 C
IL-13 D
The pathophysiology of SpA indicates biologic treatment pathways are different.
All treatment regimens should include physical therapy and exercise!

Physical function
Mobility

Pain
Patients’ feelings of disease being active

Regnaux et al. Cochrane Reviews 2019
Management of a patient with spondyloarthritis goes beyond joint pain

<table>
<thead>
<tr>
<th>Condition</th>
<th>Management Advice</th>
</tr>
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<tbody>
<tr>
<td>Cardiovascular Disease</td>
<td>Check blood pressure, lipid panel. Encourage smoking cessation.</td>
</tr>
<tr>
<td>Obesity</td>
<td>Council patients on the benefits of weight loss.</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Check fasting glucose or hemoglobin A1c.</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
<td>Ask about gastrointestinal symptoms; fecal calprotectin.</td>
</tr>
<tr>
<td>Eye Disease</td>
<td>Ask about eye symptoms.</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Consider yearly or periodic skin check for patients with a history of UV light therapy</td>
</tr>
<tr>
<td>Depression and Anxiety</td>
<td>Ask about symptoms of depression and anxiety.</td>
</tr>
</tbody>
</table>

Ogdie AB et al. Current Opinion Rheumatology 2015
Ward MM et al. Arthritis & Rheumatology 2016, 2019
**Pearls**

- Patients understand “activity” differently, so keep in mind when assessing inflammatory joint pain
  - "How long does it take after waking for you to get as good as you are going to get for the day?"
- Keep in mind that podagra in a premenopausal woman may be dactylitis instead
- Inflammatory markers can be negative (often)
- X-rays can be negative, consider other imaging modalities
  - Always evaluate the pelvis for axial SpA
- TNFi are a common therapeutic to most types of SpA
THANK YOU