Overview: Clinical Aspects of Spondyloarthritis including Psoriatic Arthritis

Joseph F. Merola, MD, MMSc
Assistant Professor, Harvard Medical School
Director, Clinical Unit for Research Innovation and Trials
Director, Center for Skin and Related Musculoskeletal Diseases
Department of Dermatology and Department of Medicine, Division of Rheumatology
Brigham and Women’s Hospital

Overview

• Axial vs. Peripheral SpA

• Prevalence

• Clinical Overview and Classification of AxSpA
  – nr-AxSpA consideration, disease progression over time
  – Focus on subsets = AS

• Clinical Overview and Classification of Peripheral SpA
  – Focus on subsets = PsA

Disclosures

• Consultant for Biogen IDEC, Abbvie, Eli Lilly, Novartis, Pfizer, Janssen, UCB, Sanummed, Science 37, Celgene, Sanofi-Genzyme / Regeneron and GSK.

• Investigator for Biogen IDEC, Pfizer, Sanofi Genzyme / Regeneron, Incyte, Novartis.

• Licensed outcome measure to Abbvie and Lilly

• Medical Board: National Psoriasis Foundation

• Steering Committee: GRAPPA

• Board of Directors: IDEOM (International Dermatology Outcome Measures), PPACMAN (Psoriasis and Psoriatic Arthritis Multicenter Advancement Network)

• Expert Panel: ACR PsA Guidelines

Slideset adapted from SPARTAN-GRAPPA Overview Set

PREVALENCE AND EPIDEMIOLOGY

Inflammatory Back Pain

Chronic back pain (3 months):
• Onset of back discomfort before the age of 40 years
• Insidious onset
• Improvement with exercise
• No improvement with rest
• Pain at night (with improvement upon arising)

4/5 = sensitivity and specificity of 80 and 74 percent for an inflammatory cause of the chronic back pain

• However, the prevalence of axSpA in the general population is low compared with that of other causes of back pain

• About 30 percent of individuals with other causes of low back pain complain of symptoms similar to those of IBP

• A considerable number of patients with axSpA will not have back pain which fulfills these IBP criteria; in one study only 5-6% of SpA patients had inflammatory back pain symptoms

Thus, the presence or absence of IBP alone is insufficient to determine the diagnosis, and this characteristic should be used together with other features of SpA in the diagnostic assessment
Prevalence Estimates

- In the US:
  - RA = 1.3 Million
  - SpA = 1.7-2.7 Million
  - (PsA + SpA + AS)

Challenges in the Epidemiology of Spondyloarthritis

- Disease heterogeneity

- Varied Criteria
  - ESSG
  - Amor
  - Axial SpA (ASAS)

- Transient nature of arthritis/enthesitis in those with peripheral involvement

- Lack of feasibility of diagnostic measures in large populations
  - MRI
  - Pelvic radiographs

- Lack of diagnostic biomarkers

Demographics

- Male/Female 2:1 – 3:1; other studies NO sex difference

- White or Hispanic > Asian > African American

- HLA B27 present in 85-90%

- Family history in 20%

- B27 positive with younger onset, higher risk of iritis

Observed Differences between Men and Women with Axial SpA

- Women tend to have a delayed diagnosis

- Evidence for increased symptom severity scores in women as compared to men

- Women generally demonstrate less radiographic damage and slower progression of damage in the axial skeleton compared to men, even with comparable (or higher) symptom severity scores

- Women have lower inflammatory markers despite comparable (or higher) symptom severity scores

- Differences between men and women have also been observed in regards to treatment response, with poorer response to treatment noted in women

- Women with AxSpA may also have concomitant "fibromyalgia" (aka central pain) partially accounting for increased symptom severity

---


Roussou E, Sultana S. Clin Rheumatol 2011; 30: 121-127;
Overview: Clinical Aspects of Spondyloarthritis including Psoriatic Arthritis

AXIAL SPONDYLOARTHRITIS

Distinguishing AS from nr-axSpA

- Inflammatory back pain occurs in 6% of the US population, but only a small percentage develop nr-axSpA
- Up to 12% of patients with nr-axSpA will develop AS within 2 years
- Up to 20% within 5 years

Radiographic Progression in the Spine

- Progression of nr-axSpA to AS occurs at a rate of ~12% over 2 years
- Progression is strongly dependent on the presence of the following risk factors:
  - Syndesmophytes at baseline
  - Elevated CRP &/or ESR
  - Smoking
  - Hip joint arthritis is strongly associated with worse spinal involvement
- Radiographic progression in the spine has a strong impact on spinal mobility and functional status

CLASSIFICATION CRITERIA FOR AS: 1984 MODIFIED NEW YORK CRITERIA

A: Diagnosis

Clinical criteria:

- Low back pain and stiffness for >3 months, which improve with exercise but are not relieved by rest
- Limitation of motion of the lumbar spine in both the sagittal and frontal planes
- Limitation of chest expansion relative to normal values correlated for age and sex

Radiologic criterion:

- Sacroilitis (grade 2 bilaterally or grade 3–4 unilaterally)

B: Grading

Definite AS = radiological criterion present + ≥1 clinical criterion
Probable AS = ≥3 clinical criteria present or radiologic criterion present without any signs or symptoms satisfying the clinical criteria
**Problems with the modified New York Criteria for AS**

- Delay in development of radiographic changes (5-10 years)
- Accuracy of readings
- Inter-reader agreement poor Grade 1, 2
- Clinical criteria emphasize chronicity
- MRI more sensitive to inflammation

**Criteria for SpA**

<table>
<thead>
<tr>
<th>Amor</th>
<th>ESSG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria</td>
<td>Points</td>
</tr>
<tr>
<td>Back pain</td>
<td>3</td>
</tr>
<tr>
<td>Morning stiffness</td>
<td>2</td>
</tr>
<tr>
<td>Anterior uveitis</td>
<td>2</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral arthritis</td>
<td>1</td>
</tr>
<tr>
<td>X-ray Evidence of Sacroiliitis</td>
<td></td>
</tr>
</tbody>
</table>

Grade 3

Imaging for nr-axSpA if X-ray is non-Diagnostic

- Semicoronal (coronal oblique) MRI of SI joints:
  - T1-weighted
  - Short t inversion recovery (STIR) or T2-weighted with fat suppression

- Classification of active sacroiliitis by OMERACT
  - Active inflammatory lesions of the SI joints
  - Positive MRI: 2 BME* lesions on same slice or 1 lesion in the same quadrant on at least 2 consecutive slices

NOTE:
- the presence of BME on MRI, even of high intensity, was observed in up to 23 percent of patients with mechanical back pain and 7 percent of healthy volunteers


Spinal MRI

- A 2012 consensus of opinion on what spinal lesions on MRI are typical of spondylitis by the ASAS/OutcomeMeasures in Rheumatology (OMERACT) MRI working group:
  - A positive spinal MRI for inflammation can be defined as:
    - the presence of anterior or posterior spondylitis in at least three sites
    - (a single vertebral lesions is relatively nonspecific)
    - the presence on MRI of the spine of either at least five inflammatory lesions or at least five fatty lesions resulted in specificity of at least 95 percent
The Association of Ankylosing Spondylitis and HLA-B27 Prevalence

<table>
<thead>
<tr>
<th>Group</th>
<th>Prevalence of AS %</th>
<th>Frequency of HLA-B27%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haida Amerinds1</td>
<td>6.1</td>
<td>50</td>
</tr>
<tr>
<td>Norway2</td>
<td>1.2-1.4</td>
<td>14</td>
</tr>
<tr>
<td>Germany3</td>
<td>0.55</td>
<td>9.0</td>
</tr>
<tr>
<td>United States4</td>
<td>0.52</td>
<td>6.1</td>
</tr>
<tr>
<td>Netherlands5</td>
<td>0.1</td>
<td>8.0</td>
</tr>
<tr>
<td>China6</td>
<td>0.1-0.5</td>
<td>3.6-5.7</td>
</tr>
</tbody>
</table>

HLA-B27 positive vs. HLA-B27 negative disease

HLA-B27 (+) patients with AS show:
- Younger age of onset
- Earlier age at diagnosis
- Greater familial occurrence
- More often acute anterior uveitis
- Less often associated Ps and IBD

Genetic associations are similar, but association with ERAP1 is present only in HLA-B27 positive cases

Clinical Utility of the Clinical Parameters of SpA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory back pain (updated information)</td>
<td>80%</td>
<td>72%</td>
<td>2.9</td>
</tr>
<tr>
<td>Enthesitis (heel pain)</td>
<td>37%</td>
<td>89%</td>
<td>3.4</td>
</tr>
<tr>
<td>Peripheral arthritis</td>
<td>40</td>
<td>90</td>
<td>4.0</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>18</td>
<td>96</td>
<td>4.5</td>
</tr>
<tr>
<td>Acute anterior uveitis</td>
<td>22</td>
<td>97</td>
<td>7.3</td>
</tr>
<tr>
<td>Positive family History for AS, AAU, IBD, ReA</td>
<td>32</td>
<td>95</td>
<td>6.4</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>10</td>
<td>96</td>
<td>2.5</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>4</td>
<td>99</td>
<td>4.0</td>
</tr>
<tr>
<td>Good response to NSAIDs</td>
<td>77</td>
<td>85</td>
<td>5.1</td>
</tr>
<tr>
<td>Erode phase reactants</td>
<td>50</td>
<td>80</td>
<td>2.5</td>
</tr>
<tr>
<td>HLA-B27 (updated information)</td>
<td>Variable</td>
<td>Variable</td>
<td></td>
</tr>
<tr>
<td>MRI (STIR) sacroiliitis (updated information)</td>
<td>Variable</td>
<td>Variable</td>
<td></td>
</tr>
</tbody>
</table>

Remains a clinical diagnosis...

ASSESS WHO IS AT RISK FOR PROGRESSION

Factors observed during the first 2 years of disease:
- AS patients with:
  - Hip arthritis (6 points)
  - Dactylitis (3 points)
  - Poor efficacy of NSAIDs (3 points)
  - Ulcerative Colitis and/or Crohn's disease (2 points)
  - Intestinal deterioration (2 points)
  - Ankylosing spondylitis (3 points)
  - Positive family history of AS patients age (1 point)

A score of 7 indicates risk of severe outcome (sensitivity 50%, specificity 97.5%)

Of the 328 patients with SpA enrolled in the study, 131 patients had a disease duration of ≥10 years.

Overview: Clinical Aspects of Spondyloarthritis including Psoriatic Arthritis

ANKYLOSING SPONDYLITIS
**AS: Clinical and Radiographic Characteristics**

- Chronic inflammatory disease
- Sites affected
  - Axial skeleton
  - Peripheral joints
  - Extra-articular organs
- Clinical signs/symptoms
  - Chronic inflammatory back pain
  - Impaired spinal mobility
  - Chest expansion
  - Enthesitis
  - Uveitis, IBD, psoriasis
- Radiographic hallmark: sacroiliitis

**AS Clinical Characteristics:**

- **Bamboo Spine**
- **Eyes**
  - Acute Anterior Uveitis (25–45%)  
- **Skin**
  - Psoriasis & Nail Changes (5–16%)
- **Gut**
  - IBD (5–8%), Microscopic lesion (22–69%)
- **Lungs**
  - Apical Fibrocystic Disease & Pleural Thickening (1–1.3%)
- **Heart**
  - Aortitis, aortic Insufficiency, Heart Block (2–3%)  
- **Kidneys**
  - IgA Nephropathy, Secondary Amyloidosis (0.3–1.2%)  
- **Cauda Equina Syndrome**  
- **Spinal Fracture**  
  - (Osteopenia/Osteoporosis 19–62%)
- **Possible causes:**
  - Cardiovascular disease
  - Pulmonary diseases, smoking
  - Spinal fractures
  - Violence; alcohol related injury
  - Gastrointestinal bleeding
  - Miscellaneous: e.g., associated diseases, radiation related, amyloidosis, etc.

**Mortality in AS: 1.5 to 4 Fold Increase**

- By 20 yrs after diagnosis 67% had survived vs 89% expected (P=0.001).
- The graph line is smoothed

**DDx: AxSpA**

- Acute or Chronic Mechanical Back Pain
- Fibromyalgia
- Diffuse idiopathic skeletal hyperostosis
- Vertebral compression fracture
- SI joint infection
- Osteitis condensans Ilii
- Erosive osteochondrosis and Schmorl’s Nodes
- FMF
Psoriatic Arthritis

- 3.2% of Americans with psoriasis: 10%–30% develop PsA\(^1\)
- Age of onset for PsA is typically 30–50 years
- Male: Female Ratio is 1:1

PsA Presentation

- Skin disease typically precedes joint disease by up to 10 years
- 70-85% presents with skin before joint involvement
  - 10-15% present with joint disease first, skin later
- Nail findings associated with DIP joint disease and enthesitis (predictive of distal enthesitis on U/S)
- Can deform joints in 40-60%

PsA Clinical Features (cont.)

- Axial Spondylitis (~20%)
- Dactylitis (~40-50%)
- Enthesitis (~40-50%)
- Patients may exhibit any combination of manifestations
  - Vary over time
  - Overlap
PsA Differential Diagnosis

- **Osteoarthritis**
  - Brief morning stiffness (“gelling”)
  - Bony DIP and PIP growth without inflammation
  - Slowly progressive

- **Rheumatoid arthritis**
  - Symmetrical arthritis
  - Doesn’t involve DIPs in general
  - Rheumatoid factor, anti-CCP antibodies
  - Radiographic differences

- **Crystal Arthropathy (Gout and Calcium Pyrophosphate Disease)**
  - Acute onset (although may be chronic)
  - Increased risk among patients with PsO/PsA

- **Fibromyalgia**
  - May have morning stiffness; no joint swelling
  - More soft tissue pain; pain is more widespread (all 4 limbs)

- **Lyme arthritis**
  
  *Merola JF, Wu S, Choi HK, Qureshi AA. Psoriasis, psoriatic arthritis, and risk of gout in U.S. men and women. Results of the Rochester Epidemiology Project.*

---

**Table 3: Clinical Features of Various Forms of Sporadic Arthritis.**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Psoriatic Arthritis</th>
<th>Reactive Arthritis</th>
<th>IBD-Associated Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset (yr)</td>
<td>36</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Male:female ratio</td>
<td>1.3</td>
<td>5.1</td>
<td>3.3</td>
</tr>
<tr>
<td>Peripheral joints affected (% of cases)</td>
<td>96</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>Axial joints affected (% of cases)</td>
<td>50</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>Common</td>
<td>Absent</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>Common</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Psoriasis (% of cases)</td>
<td>100</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Nail lesions</td>
<td>87% of cases</td>
<td>Uncommon</td>
<td>Uncommon</td>
</tr>
<tr>
<td>HLA-B27 (% of cases)</td>
<td>40–50</td>
<td>90</td>
<td>70</td>
</tr>
</tbody>
</table>

* IBD denotes inflammatory bowel disease.
Testing

- ESR, CRP
  - Approx 40% elevated in PsA
  - Elevation correlates with disease severity / erosion / progression

- RF (rheumatoid factor) / anti-CCP (anti-cyclic citrullinated peptide)

- Imaging considerations
  - Radiographs
    - Hand/foot x-rays (diagnostic / baseline)
    - SI-joint films (modified Ferguson view)
  - Additional (as appropriate)
    - MSK Ultrasound with Doppler
    - MRI

- Vaccinations, TB testing, baseline basic labs etc

PsA: Radiographic Features

- Juxta-articular periostitis & ankylosis
- Joint osteolysis (pencil-in-cup)

Other Radiological Features of PsA

- Juxtaarticular periostitis & ankylosis
- Joint osteolysis (pencil-in-cup)
- Other radiological features include:
  - Periostitis
  - Tuft resorption

Axial Psoriatic Arthritis

PsA: Axial Involvement

**CASPAR Criteria For the Classification of PsA**

PsA is diagnosed when ≥3 points below are assigned in the presence of inflammatory articular disease (joint, spine, or enthesae).

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current psoriasis, or personal or family history of psoriasis</td>
<td>Psoriatic skin or scalp disease confirmed by dermatologist or rheumatologist; history of psoriasis from patient, family physician, dermatologist, rheumatologist, or other qualified practitioner; patient-reported history of psoriasis in first- or second-degree relative</td>
<td>2</td>
</tr>
<tr>
<td>Psoriatic nail dystrophy on current physical exam</td>
<td>Includes onycholysis, pitting, and hyperkeratosis</td>
<td>1</td>
</tr>
<tr>
<td>Negative for rheumatoid factor (RF)</td>
<td>Enzyme-linked immunosorbent assay or nephelometry preferred (no latex) using local laboratory reference range.</td>
<td>1</td>
</tr>
<tr>
<td>Current dactylitis or history of dactylitis documented by a rheumatologist</td>
<td>Swelling of entire digit</td>
<td>1</td>
</tr>
<tr>
<td>Radiographic evidence of juxtaarticular new bone formation</td>
<td>X-defined ossification near joint margins excluding osteophyte formation, on plain x-rays of hand or foot</td>
<td>1</td>
</tr>
</tbody>
</table>

*CASPAR=Classification Criteria for Psoriatic Arthritis


Nail plate crumbling

Distal onycholysis

Splinter hemorrhages
Psoriasis Phenotypes

- plaque
- Nail
- Scalp
- Inverse / Intertriginous
- genital
- guttate
- palmo-plantar
- pustular

Increased PsA Risk

Negative Effects of Psoriasis by Age

<table>
<thead>
<tr>
<th>Activities of Daily Living</th>
<th>Respondents by Age Group (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18-34 Yr (n=1916)</td>
</tr>
<tr>
<td>Sleeping</td>
<td>20</td>
</tr>
<tr>
<td>Sexual activity</td>
<td>27</td>
</tr>
<tr>
<td>Using hands</td>
<td>8</td>
</tr>
<tr>
<td>Walking</td>
<td>7</td>
</tr>
<tr>
<td>Performing job duties</td>
<td>10</td>
</tr>
<tr>
<td>Psychosocial Activities Affected</td>
<td>Contemplating suicide</td>
</tr>
</tbody>
</table>

Co-morbidities / Co-Prevalent Disease in Psoriatic Disease

- Psoriatic arthritis
- Inflammatory bowel disease
- Uveitis
- Renal disease
- Hepatosteatosis
- COPD
- Sleep apnea
- Depression
- Alcoholism
- Smoking
- Diabetes
- Dyslipidemia
- Obesity
- Peripheral vascular disease
- Myocardial infarction
- Stroke
- Cardiovascular death
- Gout

Spondyloarthritis and PsA Summary

- Inflammatory arthritis involving the axial skeleton, peripheral joints and entheses
- Common clinical features
  - But key differences
- Common extra-articular features
  - With varying frequencies
- Common co-morbidities

**Lin J, Merola JF, Li T, Han I, Qureshi AA. The association between inverse psoriasis and risk of psoriatic arthritis. Submitted


Thank You

- Dr. Joerg Ermann