Spondyloarthritis

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What is meant by spondyloarthropathy?

- Derived from the Greek: “ankylos” meaning “bent” and “spondylos” meaning spinal vertebrae.
  - The term initially described the progression to a bent spine but in modern vernacular anylosis is associated with fusion.

- The first documented ankylosing spondylitis case was reported in 1691, although it may have been present in ancient Egypt as there is evidence of spondyloarthropathy remains in Ramseys II.
SpA Family

- Together these conditions are often termed Seronegative Spondyloarthropathies
  - Seronegative b/c not associated with a Rheumatoid Factor

- Typic players:
  - Ankylosing Spondylitis
  - Reactive Arthritis
  - Enteropathic Arthritis
  - Psoriatic Arthritis
  - Isolated Anterior Uveitis
  - Undifferentiated Spondyloarthitis
The SpA are associated with HLA-B27 MHC I group

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent of people with the condition who are HLA-B27 positive</th>
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</thead>
<tbody>
<tr>
<td><strong>Ankylosing Spondylitis</strong></td>
<td>• Caucasians: 92%</td>
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<tr>
<td></td>
<td>• African-Americans: 50%</td>
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<tr>
<td><strong>Reactive arthritis</strong></td>
<td>60-80%</td>
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<tr>
<td><strong>enteropathic spondylitis</strong></td>
<td>60%</td>
</tr>
<tr>
<td><strong>Psoriatic arthritis</strong></td>
<td>60%</td>
</tr>
<tr>
<td><strong>Isolated acute anterior uveitis</strong></td>
<td>50%</td>
</tr>
<tr>
<td><strong>Undifferentiated spondyloarthropathy</strong></td>
<td>20-25%</td>
</tr>
<tr>
<td><strong>General population without disease</strong></td>
<td>5-15%</td>
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</table>
HLA-B27

- HLA-B27 participates in antigen presentation.
- Among individuals with HLA-B27 the protein is expressed ubiquitously but most abundant on APCs (macrophages and dendritic cells).
- The theory of molecular mimicry is that self-peptides displayed by these HLA-B27 /B2 complexes are targeted by CD8 T-cells.
- Subsequent cascades lead to the overexpression of TNF-alpha, TGF (transforming growth factor)-beta, IL-1, IL-6 and IL-10, and BMP.
HLA-B27 Associations

- HLA-B*2705 having the strongest association.
- HLA-B*2702, *2703, *2704, and *2707 are also associated with ankylosing spondylitis.
- HLA-B27–restricted CD8\(^+\) (cytotoxic) T cells may play an important role in bacterial-related spondyloarthropathies such as reactive arthritis.
  - Klebsiella, Yersinia, Chlamydia, Campylobacter and Shigella and Salmonella are HLA-B27 binding antigens owing to their association with SpA.
Animal Models

- Transgenic rats expressing human HLA-B27 and B2-microglobulin develop an illness similar to spondyloarthropathy.
- Germ free environment with HLA-B27 + rats do not develop clinical disease.
- Exposed to bacteria, the rats develop clinical manifestations of spondyloarthropathy, suggesting an important interaction between genetic and environmental factors.
Enthesitis is a hallmark.
Characterized by erosive, inflammatory lesions with recruitment of osteoclasts and infiltration of the bone marrow.
Inflammation leads to destruction and simultaneous rebuilding of both the cortex and spongiosa of the vertebral bodies.
- Destructive osteitis and repair leads to ankylosis.
Diagnosis: Classification Criteria

• Classification Criteria for AS
  o Rome (did not require sacroilitis)
  o Modified New York Criteria
  o European Spondyloarthropathy Study Group (ESSG) criteria
  o Amor criteria

• CASPAR : Classification Criteria for Psoriatic Arthritis (CASPAR)
For the purpose of research

- **Rome Criteria** 1963 in the presence of b/l sacroilitis grade 2 or higher.
  - Low back pain and stiffness for >3 months that is not relieved by rest
  - Pain and stiffness in the thoracic region
  - Limited motion in the lumbar spine
  - Limited chest expansion
  - History of uveitis

- **Modified New York Criteria**: (1968, 1984)
  - Low back pain of at least 3 months inflammatory in nature
  - Limitation of lumbar spine motion in sagittal and frontal planes
  - Decreased chest expansion relative to age
  - Bilateral sacroiliitis grade 2 or higher
  - Unilateral sacroiliitis grade 3 or higher
Diagnosis of Spondyloarthropathies (1)

Is there:

- **Inflammatory arthritis** that is asymmetric or predominantly lower extremity?
  and/or

- **Back pain** of insidious onset of \( \geq 3 \) months duration associated with **morning stiffness** and **improvement with activity**?
Spondyloarthropathies

Inflammatory back pain--characteristics

- insidious onset before age 40
- persistence for at least 3 months
- accentuation of back pain in A.M. or after prolonged rest
- back pain improves with exercise
Diagnosis of Spondyloarthropathies (1)

Is there:
- Inflammatory arthritis that is asymmetric or predominantly lower extremity?
  and/or
- Back pain of insidious onset of $\geq$ 3 months duration associated with morning stiffness and improvement with activity?

NO

Unlikely to be a spondyloarthropathy

YES

Is there evidence of psoriasis or inflammatory bowel disease?
Diagnosis of Spondyloarthropathies (2)

Is there evidence of psoriasis or inflammatory bowel disease?

NO      YES

Is There One or More of the Following:
- Radiographic evidence of sacroiliitis?
- Enthesopathy?
- Dactylitis?
- Buttock pain (unilateral or alternating)?
- Family history
- Iritis?
- Acute diarrhea or non-GC urethritis or cervicitis within 1 month of arthritis onset?
Diagnosis of Spondyloarthropathies (2)

Is there evidence of psoriasis or inflammatory bowel disease?

NO → YES

Consider:
- Enteropathic or
- Psoriatic Arthritis
Diagnosis of Spondyloarthropathies (3)

Is There One or More of the Following:
- Radiographic evidence of sacroiliitis?
- Enthesopathy?
- Dactylitis?
- Buttock pain (unilateral or alternating)?
- Family history
- Iritis?
- Acute diarrhea or non-GC urethritis or cervicitis within 1 month of arthritis onset?

NO

Unlikely to Be a Spondyloarthropathy

YES

Likely to Be a Spondyloarthropathy
Spondyloarthropathies

Probably Reactive Arthritis or Reiter’s Syndrome

Is there evidence of chlamydial infection? (ie elevated antichlamydial antibodies)

NO

Reactive Arthritis (Reiter’s Syndrome)

YES

Chlamydia-Associated Reactive Arthritis
Spondyloarthropathies
ESSG Criteria

**Primary**

- Inflammatory Back Pain

  OR

- Synovitis
  - Asymmetric
  - Predominantly in lower extremities

**Secondary**

- Plus one of following:
  - Psoriasis
  - IBD
  - Positive family history
  - Urethritis, cervicitis, or acute diarrhea within 1 month of arthritis
  - Alternating buttock pain
  - Enthesopathy
  - Sacroiliitis
Physical exam testing

- Tragus to Wall/Occiput to Wall
- Chest Expansion
- Schober Test
- Pelvic Compression
- Gaenslen’s Test
- Patricks (FABER) Test:
Occiput or Tragus to Wall
Schober Test

Place mark at the level of the posterior superior iliac spine and 10cm above this.

With knees locked measure distance in full forward flexion.

Minimum excursion is 5 cm (15cm for 2 lines).
Pelvic Compression

- With the patient lying on one side, compression of the pelvis should elicit SI joint pain.
- This can be done as sacral compression in prone position or AP compression in supine
Gaenslen’s Test

- Patient supine, one leg is extended over the side of the exam table while the patient draws the other leg toward chest.
- + test is pain at the dropped leg SIJ
FABER

- Flexion, Abduction, External Rotation downward pressure on the flexed knee
- + will elicit contralateral SI joint tenderness.
Lab Testing

- Anemia
  - secondary to chronic disease
  - blood loss: UC or Crohn’s
- ESR/CRP
- Renal function, urinanalysis,
- Serum IgA elevation
- Negative RF
- HLA B27
Other manifestations

- **Ocular:**
  - acute anterior uveitis—unilateral eye pain, photophobia, blurred vision, and increased lacrimation
- **Osteoporosis—**
  - d/t increased inflammation, syndesmophytes can lead to falsely elevated DEXA score
- **GI:** Small or large bowel inflammation
- **Cardiac:**
  - ascending aortitis, AR, conduction abnormalities, and myocardial disease
- **Pulmonary:**
  - apical fibrobullos disease
- **Neuro:** spinal fracture, cauda equina syndrome
- **Rare:** secondary amyloidosis, retroperitoneal fibrosis
Spondylo-arthropathies

Iritis (Uveitis)

Likelihood of Iritis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Ank spondylitis</td>
<td>20-30</td>
</tr>
<tr>
<td>Reiter’s</td>
<td>12-37</td>
</tr>
<tr>
<td>Psor Spondylitis</td>
<td>7-16</td>
</tr>
<tr>
<td>IBD</td>
<td>2-9</td>
</tr>
<tr>
<td>Undiff SA</td>
<td>ND</td>
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</tbody>
</table>
Radiographic Testing

- **X-ray of SI joints:**
  - Iliac erosions (postage stamp serrations)
  - Erosions become more prominent and produce "pseudowidening" of the SI joint
  - Fusion with complete obliteration of the SI joint by bone and fibrous tissue.
Sacroilitis Grading

- O = normal (a)
- 1 = possible
- 2 = minimal (b)
- 3 = moderate (c)
- 4 = fused (ankylosed) (d)
Radiographic Findings Axial Spine:

- Romanus lesions - AKA "shiny corners" involves insertion of the annulus fibrois to the corners of the vertebral bodies.
- Gradual ossification of the outer layers of the annulus fibrosis (Sharpey’s fibers) forming intervertebral bony bridges (syndesmophytes).
- Ultimately fusion of the apophyseal joints and calcification of the spinal ligament with bilateral syndesmophyte formation results in complete fusion of the vertebral column giving the appearance of a bamboo spine.
MRI

- Acute sacroiliitis, spondylitis, and spondylodiscitis
- Acute inflammation of the entheses, bone, and synovium
- Detect early inflammation and accurately visualize cartilaginous and enthesal lesions
- If X-ray negative and high index of suspicion then f/u with an MRI
Ankylosing spondylitis is the most prevalent of the SpA.

- Varies within populations:
  - 0.1% in some African and Eskimo populations
  - 0.5-1% among whites in UK and US
  - 6% in Haida Native American of N. Canada

The prevalence reflects the prevalence of HLA-B27 in these distinct populations.
Progressive spinal changes in AS
Ankylosing spondylitis

A. Aortic insufficiency, ascend. aortitis, conduction defects, etc
N. Neurologic: atlantoaxial subluxation & cauda equina syndrome
K. Kidney: secondary amyloidosis
S. Spine: cervical fracture, spinal stenosis
O. Ocular: anterior uveitis (25-30% of pts)
P. Pulmonary: upper lobe fibrosis, restrictive changes
N. Nephropathy (IgA)
D. Discitis

In addition, 30-60% of pts have asymptomatic -colitis
Atypical fibrosis on CXR
Reactive Arthritis

- Autoimmune process that develops 1-3 weeks after bacterial infection
- Associated w/ C. trachomatis, gastroenteritis-SSYC
- “can’t see, can’t pee, can’t climb a tree”
- Tx underlying infection, if continues may need analgesics, steroids or immunosuppressants
- PE-Keratoderma blennorhagica, oral or genital ulcers, conjunctivitis
Reiter’s syndrome and Reactive arthritis (ReA)

- Infectious trigger factor:
  - Enterogenic: Shigella, Campylobacter, Yersinia, Salmonella
  - Genito-urinary: Chlamydia, Gonococcal
  - Others: Ureaplasma, Clostridium difficile
Reiter’s syndrome and Reactive arthritis (ReA)

- Prevalence: 16 per 100,000
- Primarily young adults, aged 20-40 years
- M:F ratio 1:1 for enterogenic reactive arthritis
- M>F ratio for urogenital reactive arthritis
- Rare in children and uncommon in Blacks

- Arthritis
  - Mono-or oligo-arthritis (< 5 joints)
  - Sacroilitis
  - Spondylitis
  - Enthesitis

- 80% resolve within 12 months
Psoriatic Arthritis

- May be present with or without skin findings
  - Look for hidden psoriasis-behind ears, hairline, nail pitting, gluteal folds
  - May precede skin findings
- Arthritis does NOT correlate with skin findings
- May cause RA-like arthritis
- Dactylitis common
- Prevalence: 100 per 100,000 (1/20 people with Ps)
- Psoriasis precedes arthritis: 67%
- Arthritis precedes psoriasis or occurs simultaneously: 33%
- Feature of HIV infection
Psoriatic Arthritis

- 5 presentation types
- **Asymmetrical oligoarticular arthritis**
  - dactylitis
- **Symmetrical polyarthritis**
- **Distal interphalangeal arthropathy**
  - Nail involvement
- **Arthritis mutilans**
  - Telescoping motion, opera hands
- **Spondylitis with or without sacroiliitis**
Psoriatic hands
Asymmetrical arthritis
Arthritis mutilans

"telescoping' of digits"
Arthritis mutilans
osteolysis of involved joints
“Sausage digits”
CASPAR for PsA

- 3 points or greater
- Current Psoriasis (2)
- H/o Psoriasis (1)
- Family history (1)
- Dactylitis (1)
- Juxta-articular bone formation (1)
- RF neg (1)
- Nail dystrophy (1)
Enteropathic arthritis

- What bowel diseases are associated?
  - Idiopathic, inflammatory bowel disease (UC, CD)
  - Microscopic colitis and collagenous colitis
  - Whipple’s disease
  - Gluten-sensitive enteropathy (celiac disease)
  - Intestinal by-pass arthritis
IBD-related SpA

- Hx of abdominal pain, bloody diarrhea
- Have an axial form and a peripheral arthritis form
Enteropathic arthritis

- Prevalence: 5 per 100,000
- M:F ratio 1:1
- Children = adults

- Arthritis: acute onset, migratory, asymmetric, oligo-articular (< 5 joints)
- Extra-articular: uveitis, erythema nodosum, aphthous stomatitis, pyoderma gangrenosum
Erythema nodosum
Treatment

- **NSAIDs**
- **Sulfasalizine**
  - SE: rash, nausea, diarrhea, and agranulocytosis (rarely)
- **TNF-α antagonists**
  - Etanercept, infliximab, adalimumab, golimumab
  - Screen for latent TB, hepatitis B, and HIV infection prior to starting therapy
  - Approximately 80% get some relief with one of these agents, and one half get 50% improvement in a composite index (ASAS50) by 12 weeks
- **Corticosteroids** - short-term or intra-articular
Methotrexate, azathioprine, cyclophosphamide, and cyclosporine have been used in SpA. Methotrexate is of questionable benefit in ankylosing spondylitis, as various studies have shown conflicting results. Useful in PsA. Leflunomide was evaluated in a randomized, double-blind, placebo-controlled study in active ankylosing spondylitis but was not found to be effective.
Follow-Up

- F/U includes assessment of fatigue, back pain, mobility, synovitis and enthesitis
- Surgery is occasionally useful to correct spinal deformities or to repair damaged peripheral joints.
- Physical therapy, including an exercise program and postural training, is important to maintain function.
References

- Emedicine.com
- Radiographics.com
- Up-to-date. *Spondyloarthropathies*