Spondyloarthropathies

Inflammatory Arthritis

RHEUMATOLOGY LECTURE
Disclosures

- NONE
What is meant by spondyloarthropathy?

- Literally translated to “inflamed spine growing together”

- The first documented ankylosing spondylitis case was reported in 1691, although it may have been present in ancient Egyptians
Seronegative SpA

- Inflammatory axial spine involvement
  - Spondylitis, sacroilitis
- Asymmetric peripheral arthritis
  - DIP involvement, dactylitis ("sausage digits")
- Inflammatory eye disease
- Mucocutaneous features
- Enthesopathies:
  - Achilles tendinitis
  - Plantar fasciitis
- Tenosynovitis

- Familial aggregation
- HLA-B27 association
SpA’s include

- Ankylosing spondylitis
- Reactive arthritis
- Psoriatic arthritis/spondylitis
- Arthritis/spondylitis of inflammatory bowel dz
- Juvenile spondyloarthropathy
- Undifferentiated spondyloarthropathies
- ?Whipple dz, Bechet’s dz, Celiac Dz
Prevalence

- 2.4 million adults in the United States have seronegative SpA
  - Rheumatoid arthritis only affects 1.3 million adults, down from the previous estimate of 2.1 million

- Ankylosing spondylitis is the most prevalent of the classic spondyloarthropathies.

- Prevalence AS is 0.1-1% overall, but is higher in certain Native American populations and lower in African Americans
  - highest prevalence in northern European countries and the lowest in sub-Saharan Africa
Who’s affected?

- Male-to-female ratio of AS is 3:1
- Male-to-female ratio of PsA is 1:1
- Age of onset for AS is from late teens to 40 yo.
  - Approximately 10%-20% of all pts have onset of symptoms before 16 yo
Relationship with HLA-B27

- Strong association with HLA-B27

<table>
<thead>
<tr>
<th>Population or Disease Entity</th>
<th>HLA-B27 +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy whites</td>
<td>8%</td>
</tr>
<tr>
<td>Healthy African Americans</td>
<td>4%</td>
</tr>
<tr>
<td>Ankylosing spondylitis (whites)</td>
<td>92%</td>
</tr>
<tr>
<td>Ankylosing spondylitis (African Americans)</td>
<td>50%</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>60-80%</td>
</tr>
<tr>
<td>Psoriasis associated with spondylitis</td>
<td>60%</td>
</tr>
<tr>
<td>IBD associated with spondylitis</td>
<td>60%</td>
</tr>
<tr>
<td>Isolated acute anterior uveitis</td>
<td>50%</td>
</tr>
<tr>
<td>Undifferentiated spondyloarthropathy</td>
<td>20-25%</td>
</tr>
</tbody>
</table>
Diagnosis

- Inflammatory back pain + (enthesitis or arthritis) + radiological findings
- European Spondyloarthropathy Study Group (ESSG) criteria
- Amor criteria
- Ankylosing Spondylitis Dx
  - New York and Rome
  - CASPAR: Classification Criteria for Psoriatic Arthritis (CASPAR)
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)
New Classification Criteria

- The Assessment of SpondyloArthritis international Society (ASAS) developed a new classification criteria for Axial SpA and Peripheral SpA.
- The proposed classification criteria applies to patients in the early stages of the disease as well as those in the later stages.
- In this classification, the designation “non-radiographic axial SpA” encompasses patients who have chronic back pain and features suggestive of SpA but who do not meet the classification criteria for AS.
- The goals of are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications.
ASAS Axial SpA Classification Criteria

Table 1 – ASAS axial SpA classification criteria

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>To be applied to patients with ≥ 3 months of back pain and age &lt; 45 years at onset</td>
<td></td>
</tr>
<tr>
<td>Sacroiliitis(^a) on imaging plus ≥ 1 SpA feature(^b) OR HLA-B27 plus ≥ 2 other SpA features(^b)</td>
<td></td>
</tr>
</tbody>
</table>

ASAS, Assessment of SpondyloArthritis international Society; SpA, spondyloarthritis; IBP, inflammatory back pain; CRP, C-reactive protein.

\(^a\) Sacroiliitis on imaging defined as active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA and definite radiographic sacroiliitis according to modified New York criteria.

\(^b\) SpA features: IBP, arthritis, enthesitis (heel), uveitis, dactylitis, psoriasis, Crohn disease/collitis, good response to NSAIDs, family history of SpA, the HLA-B27 gene, elevated CRP level.
Table 3 – ASAS peripheral SpA classification criteria

<table>
<thead>
<tr>
<th>Criteria</th>
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<tbody>
<tr>
<td>To be applied to patients with only peripheral manifestations and age &lt; 45</td>
</tr>
<tr>
<td>years at onset</td>
</tr>
<tr>
<td>Arthritis or enthesitis or dactylitis plus ≥ 1 SpA feature(^a) OR ≥ 2</td>
</tr>
<tr>
<td>other SpA features(^b)</td>
</tr>
</tbody>
</table>

ASAS, Assessment of SpondyloArthritis international Society; SpA, spondyloarthritis; IBP, inflammatory back pain.

\(^a\) SpA features: arthritis, enthesitis, dactylitis, IBP at any time in the past, family history of SpA.

\(^b\) SpA features: uveitis, psoriasis, Crohn disease/ulcerative colitis, previous infection, the HLA-B27 gene, sacroiliitis on imaging.
Advantages & Uses of the new criteria

- MRI was not a part of the older criteria for classifying AS. It is now recognized as the most sensitive imaging study for active inflammation in the sacroiliac joints, with high specificity.

- Because the new criteria is more sensitive and specific than the previous criteria, diagnostic accuracy is improved and earlier diagnosis is possible with potential for Patients to be eligible for effective treatment sooner than in the past.
Diagnosis of Spondyloarthropathies (1)

Is there:

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

- **Back pain** of insidious onset of > 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  |  YES

Unlikely to be a spondyloarthropathy

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
- 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
Axial Spine

- Schober Test: expect greater than 5 cm change when pt bends forward, if <5 cm change = reduced lumbar mobility
- Spinal fusion results in irreversible impairments, but reductions in mobility also can be induced by pain or muscle spasm so may vary between visits
- With advanced disease, lead to loss of lumbar lordosis, exaggeration of thoracic kyphosis, an inability to extend the neck, and compensatory hip flexion deformities
- Costovertebral and costochondral joints commonly lead to impaired chest expansion; slight ↓ in VC & TLC
Physical examination tests to assess spinal disease in AS

- Occiput-to-wall-test
- Tragus-to-wall-test
- Chest expansion
- Schober’s test
- Sacro-iliac stress test
Schober Test
Lab Testing

- Anaemia
  - secondary to chronic disease
  - blood loss
  - ? drugs
- 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 fibrobullous disease
- Neuro: spinal fracture, cauda equina syndrome
- Rare: secondary amyloidosis, retroperitoneal fibrosis
Spondyloarthropathies

Iritis
(Uveitis)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Percent</th>
</tr>
</thead>
<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>
</tr>
</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 → complete obliteration of the SI joint by bone and fibrous tissue. The pattern of sacroiliac joint involvement is bilaterally symmetric
AS pelvis X ray
Radiographic Findings

- Romanus lesions - AKA "shiny corners", reaction to inflammation where the annulus fibrosus of the disks inserts onto the vertebral bodies
- Progressive erosions and formation of new periosteal bone → lumbar vertebral bodies become "squared off" in the lateral view.
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
AS

- Most common cause of inflammatory back pain in young adults
- Prevalence: 150 per 100,000
- Age of onset: < 40 years of age (average 26 yrs)
- M:F ratio 3:1
- Back pain (insidious onset)
- Duration longer than 3 months
- Associated with morning stiffness
- Improves with exercises
- Decreased spinal movements
- Enthesopathies
Ankylosing spondylitis

- Sacroiliitis and spondylitis
- Bamboo spine - ossification of the annulus fibrosus
  - Occurs from the lumbosacral region proximally
- Enthesitis
- Peripheral arthropathy

- Do not fit into another category
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 with 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
Balantitis
Psoriatic Arthritis

- May be present with or without skin findings
  - Look for hidden psoriasis—behind ears, hairline, nail pitting
  - 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”
Spondyloarthropathies

Enthesopathy

Erosion

New bone
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
Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis

- As per ACR / Spondylitis Association of America / Spondyloarthritis Research and Treatment Network 2015

- In Adults with active AS, NSAIDS strongly recommended

- If continued active AS despite NSAIDs, TNFi Treatment strongly recommended

- In these pts, there is no preferred TNFis

- In pts with IBD SpA- tx with TNFi monoclonal Abs over Enbrel
Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis

- For recurrent Iritis - Topical Glucocorticosteroids and Humira/Remicade

- Strongly Recommend against tx with systemic Glucocorticoids in patients with Active AS

- Physical therapy is strongly recommended in these patients

- Pts with AS and advanced hip arthritis, Total hip arthroplasty is strongly recommended

- In pts with active nonradiographic Axial SpA, despite NSAID therapy. It is conditionally recommended to treat with TNFi
Peripheral Arthritis Treatment

- Mainstay Tx in patients with Peripheral Arthritis includes NSAIDS and Synthetic DMARDs
  - MTX
  - SSZ
  - Imuran
  - Arava
- Intra-articular corticosteroids for Oligoarthritis
- Excercises
Otezla (Apremilast)

- OTEZLA is an inhibitor of phosphodiesterase 4 (PDE4)

- PDE4 inhibition results in increased intracellular cAMP levels. The specific mechanism of action in psoriatic arthritis patients and psoriasis patients is not well defined.

- OTEZLA is indicated for the treatment of adult patients with active psoriatic arthritis and patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

- Approved by FDA in 2014
The safety and effectiveness of Otezla were evaluated in three clinical trials involving 1,493 patients with active PsA.

Patients treated with Otezla showed improvement in signs and symptoms of PsA, including tender and swollen joints and physical function, compared to placebo.

Dose - Initial Dose titration to maintenance of 30mg BID, Unless Cr Clearance <30ml/min in which case dose is decreased to 30mg Daily.

Can be associated with weight loss which should be monitored during treatment.

Increased reports of Depression compared to Placebo.

Most common Side Effects during clinical Trial - Nausea/Vomiting/Diarrhea and headache.
References

- Emedicine.com
- Radiographics.com
- Up-to-date. *Spondyloarthropathies*
- American College of Rheumatology