Spondyloarthropathy

แพทย์หญิงนันทนา กสิตานนท์
คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่
Spondyloarthritis: SpA

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OSTEOARTHRITIS
neck
LS spine
hip
knee
foot: 1st MTP
hand: 1st CMC
DIP
PIP

ANKYLOSING SPONDYLITIS
spine (entire)
SI joints
hip
shoulder

RHEUMATOID ARTHRITIS
proximal joints of digits
symmetric

REITER'S SYNDROME
lower extremity: foot
knee
ankle
hip

PSORIATIC ARTHRITIS
hands and feet (distal)
LS spine
SI joints
asymmetric
Spondyloarthritis: SpA

- Ankylosing Spondylitis (AS)
- Reactive Arthritis (ReA)
- Arthritis Associated with Psoriasis (PsA)
- Arthritis Associated with Inflammatory Bowel Disease (IBD)
- Undifferentiated Spondylitis (USpA)
- Juvenile Onset AS (JoAS)
SpA Common Features

- Enthesopathy is hallmark
- Inflammatory arthritis of the spine (inflammatory back pain)
- Peripheral arthritis
- Radiological evidence of sacroiliitis
- Familial aggregation and genetic predisposition
- Absence of rheumatoid factor
Enthesopathy

- The "enthesis" is the anatomic location where tendon, ligament, or joint capsule fibers insert into the bone.
- Subchondral bone inflammation and resorption
- Periosteal new bone formation
Enthesopathy

• Clinical manifestations: Achilles tendonitis, plantar fascitis, dactylitis.
Calcaneal enthesitis
Dactylitis

- A combination of enthesitis of the tendons and ligaments and synovitis involving a whole digit.
SpA Common Features

- Enthesopathy is hallmark
- Inflammatory arthritis of the spine (inflammatory back pain)
- Peripheral arthritis
- Radiological evidence of sacroiliitis
- Familial aggregation and genetic predisposition
- Absence of rheumatoid factor
What is the DDx of low back pain?
**TABLE 1. DIFFERENTIAL DIAGNOSIS OF LOW BACK PAIN.**

<table>
<thead>
<tr>
<th>MECHANICAL LOW BACK OR LEG PAIN (97%)†</th>
<th>NONMECHANICAL SPINAL CONDITIONS (ABOUT 1%)‡</th>
<th>VISCERAL DISEASE (2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar strain, sprain (70%)§</td>
<td>Neoplasia (0.7%)</td>
<td>Disease of pelvic organs</td>
</tr>
<tr>
<td>Degenerative processes of disks and facets, usually age-related (10%)</td>
<td>Multiple myeloma</td>
<td>Prostatitis</td>
</tr>
<tr>
<td><strong>Herniated disk (4%)</strong></td>
<td>Metastatic carcinoma</td>
<td>Endometriosis</td>
</tr>
<tr>
<td><strong>Spinal stenosis (3%)</strong></td>
<td>Lymphoma and leukemia</td>
<td>Chronic pelvic inflammatory disease</td>
</tr>
<tr>
<td>Osteoporotic compression fracture (4%)</td>
<td>Spinal cord tumors</td>
<td>Renal disease</td>
</tr>
<tr>
<td>Spondylolisthesis (2%)</td>
<td>Retroperitoneal tumors</td>
<td>Nephrolithiasis</td>
</tr>
<tr>
<td>Traumatic fracture (&lt;1%)</td>
<td>Primary vertebral tumors</td>
<td>Pyelonephritis</td>
</tr>
<tr>
<td>Congenital disease (&lt;1%)</td>
<td>Infection (0.01%)</td>
<td>Perinephric abscess</td>
</tr>
<tr>
<td>Severe kyphosis</td>
<td>Osteomyelitis</td>
<td>Aortic aneurysm</td>
</tr>
<tr>
<td>Severe scoliosis</td>
<td>Septic diskitis</td>
<td>Gastrointestinal disease</td>
</tr>
<tr>
<td>Transitional vertebrae</td>
<td>Paraspinal abscess</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Spondylolysis†</td>
<td>Epidural abscess</td>
<td>Cholecystitis</td>
</tr>
<tr>
<td>Internal disk disruption or diskogenic low back pain</td>
<td>Inflammatory arthritis (often associated with HLA-B27) (0.3%)</td>
<td>Penetrating ulcer</td>
</tr>
<tr>
<td>Presumed instability**</td>
<td>Ankylosing spondylitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psoriatic spondylitis</td>
<td></td>
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<tr>
<td></td>
<td>Reiter’s syndrome</td>
<td></td>
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<tr>
<td></td>
<td>Inflammatory bowel disease</td>
<td></td>
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<tr>
<td></td>
<td>Schmor-Ruppin’s disease (osteochondrosis)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paget’s disease of bone</td>
<td></td>
</tr>
</tbody>
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* Deyo RA, NEJM 2001
Mechanical LBP
- 97% of low back pain
- last < 8 wks
Historic clues to R/O mechanical pain (R/I inflammatory back pain)

- Age of onset < 40 years
- Insidious onset
- Back pain last > 12 wks
- Back pain implies inflammatory disease
- Bilateral buttocks pain
- The Occiput to wall/ Schoeber test identifies decreased expansion of the cervical/ lumbar vertebrae on flexion
- Tenderness over the buttocks suggests sacroiliitis
Proposed new criteria for inflammatory back pain in young to middle-aged adults (<50 years old) with chronic back pain, and application as classification and diagnostic criteria*

Individual parameters of the inflammatory back pain criteria
1. Morning stiffness of >30 minutes’ duration
2. Improvement in back pain with exercise but not with rest
3. Awakening because of back pain during the second half of the night only
4. Alternating buttock pain

Application as classification criteria
The criteria are fulfilled if at least 2 of the 4 parameters are present†
- Sensitivity 70.3%
- Specificity 81.2%
- Positive LR 3.7
• Imagining of Inflammatory disease of the spine
  – Shiny corners (Romanus lesion)
  – Squaring of the vertebral bodies
  – Gradual ossification of the outer layers of the annulus fibrosis: syndesmophytes
  – Bamboo spine
Intervertebral disc
Ankylosing spondylitis: lumbar vertebrae, Shiny corners (Romanus lesion)
Ankylosing spondylitis: thoracic and lumbar vertebrae "squaring," osteopenia, and ossification
Ankylosing spondylitis: lumbar vertebrae, syndesmobamboo spine
OSTEOARTHRITIS
- neck
- LS spine
- hip
- knee
- foot: 1st MTP
- hand: 1st CMC
- DIP
- PIP

ANKYLOSING SPONDYLITIS
- spine (entire)
- SI joints
- hip
- shoulder

RHEUMATOID ARTHRITIS
- proximal joints of digits
- symmetric

REITER'S SYNDROME
- lower extremity: foot
- knee
- ankle
- hip

PSORIATIC ARTHRITIS
- hands and feet (distal)
- LS spine
- SI joints
- asymmetric
Radiologic evidence of Sacroiliitis

- Sacroiliitis

<table>
<thead>
<tr>
<th>Grade</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Suspected narrowing of joint</td>
</tr>
<tr>
<td>2</td>
<td>Sclerosis and minimal erosions of joint surface</td>
</tr>
<tr>
<td>3</td>
<td>Pseudo-widening</td>
</tr>
<tr>
<td>4</td>
<td>Bony fusion across the joint</td>
</tr>
</tbody>
</table>

Film pelvis: Ferguson views (30 degree cephalad)

MRI: demonstrate inflammation and edema in early sacroiliitis
Ankylosing spondylitis: early sacroiliitis
Ankylosing spondylitis: Pseudo-widening
Ankylosing spondylitis: advanced sacroiliitis
SpA Subtypes

- Ankylosing Spondylitis (AS)
- Reactive Arthritis (ReA)
- Arthritis Associated with Psoriasis (PsA)
- Arthritis Associated with Inflammatory Bowel Disease (IBD)
- Undifferentiated Spondylitis (USpA)
- Juvenile Onset AS (JoAS)
### Ankylosing spondylitis (AS)

<table>
<thead>
<tr>
<th>Prevalence:</th>
<th>Asian</th>
<th>0.1 – 0.5 (HLA B27: 2 - 6%)</th>
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<tbody>
<tr>
<td></td>
<td>Caucasian</td>
<td>0.5 – 6.2 (HLA B27: 8 - 50%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td>Male to Female ratio 10:1 (Thai)</td>
</tr>
<tr>
<td>Age of onset</td>
<td></td>
<td>10 – 30 years</td>
</tr>
<tr>
<td>HLA B27 positive</td>
<td></td>
<td>90%</td>
</tr>
<tr>
<td>Usual presenting symptom</td>
<td></td>
<td>Inflammatory back pain (50 – 80%)</td>
</tr>
</tbody>
</table>
• Axial joints
  • Low back pain: gel phenomenon improve with exercise
  • Ascending pain: L → T → C
  • Buttock pain
Ankylosing spondylitis: progression of deformities
• Articular manifestation: (continue)
  – Peripheral joints
    • Large joints: hip, shoulder, knee, ankle
    • Insidious onset
  – Enthesitis/ Tendinitis
    • Achilles tendon
    • Calcaneus, lateral epicodyle, ischial tuberosity, trochanter, tibial tuberosity, pubic symphysis
Test for sarcoiliitis

• Compression test
• Faber \((\text{Flexion, Abduction, External Rotation})\) test
• Gaenslen’s test
Sacroiliac joint
Erector spinae

Posterior median furrow

Skin dimple indicating posterior superior iliac spine
Testing for sacroiliac tenderness  The patient can be examined for sacroiliac joint tenderness due to active sacroiliitis by applying direct pressure over each sacroiliac joint. Courtesy of Craig W Wiesenhutter, MD.
Spinal mobility measurement

- Occiput-to-wall test
- Schober’s test
- Chest expansion test
Cervical flexion deformity in AS The severity of cervical flexion deformity in ankylosing spondylitis can be assessed by measuring the occiput to wall distance (Flesche test). With the patient standing erect, the heels and the buttocks are placed against a wall. The patient is then instructed to extend his or her neck maximally in an attempt to touch the wall with the occiput. The distance between the occiput and the wall is a measure of the degree of flexion deformity of the cervical spine. Courtesy of Craig W Wiesenhutter, MD.
Testing for low back flexion  Schober test to measure the forward flexion of the lumbar spine in a patient with suspected or proven ankylosing spondylitis. With the patient standing erect, make a mark over the spinous process of the 5th lumbar vertebra or on the imaginary line joining the posterior superior iliac spine. Make another mark 10 cm above it in the midline. When the patient bends maximally forward, the distance between the two points normally exceeds 15 cm. Courtesy of Craig W Wiesenhutter, MD.
Chest expansion

• measure at the level of the 4\textsuperscript{th} intercostal space or just below the breast in females
• exert a maximal forced expiration followed by a maximal inspiration
• expansion > 5 cm in normal
• expansion < 2.5 is abnormal
Extraarticular manifestation

- Constitutional symptoms
- Ocular manifestation: anterior uveitis
- Cardiovascular manifestation: ascending aortitis
- Pulmonary manifestation: upper lobe fibrosis
- Gastrointestinal manifestation: diarrhea
- Neurologic manifestation: nerve root
- Renal manifestation: IgA nephropathy
- Bone lesion: osteoporosis
Modified New York criteria for diagnosis of ankylosing spondylitis

• Definite ankylosing spondylitis If: radiological criterion plus $\geq 1$ clinical criteria

1. Clinical criteria:
   – Limited lumbar motion
   – Low back pain and stiffness for 3 months improved with exercise not relieved by rest
   – Limited chest expansion

2. Radiological criterion:
   – Bilateral, grade 2 to 4, sacroiliitis on X-ray
   – Unilateral, grade 3 to 4, sacroiliitis on X-ray

van der Linden, Arthritis Rheum 1984;27:361
Ankylosing spondylitis/ Axial SpA
Why Early Diagnosis?

• New effective treatments are available to alleviate symptoms

• Potential to prevent damage (structure) or modify disease (function, QOL)

• To study the natural history, outcomes, prognostic factors
Diagnosis: The Future for Individual Patients

• Based on IBP questions and other clinical or lab features and

• Imaging
  – Radiographs
  or
  – MRI
  or
  – Ultrasound
Reactive Arthritis (ReA)

• Aseptic arthritis
  – Predominantly of lower limbs, asymmetric oligoarthritis
  – Axial involvement: 50%

• Antecedent infectious event within 4 weeks:
  – Urethritis
  – Enteritis
  – Cervicitis/ vaginitis

(Chlamydia, Salmonella, Shigella, Yerdinia, Campylobacter)
• Extra-articular manifestations
  – General symptoms
  – enthesitis
  – Ocular manifestation: conjunctivitis, uveitis
  – Mucocutaneous involvement: balanitis circinata, keratodermia blenorrhagica

Etc.
Reactive arthritis: keratoderma blennorrhagica, foot
Reactive arthritis: balanitis circinata
Reactive arthritis (ReA)

- Eye inflammation
- Lower back pain
- Diarrhoea
- Scaly skin patches on genitalia
- Swelling in knee, heel or ball of foot
- Flaky skin patches on sole
- ‘Sausage’ toes

You may have only some of these symptoms.
Psoriatic Arthritis (PsA)

- The prevalence of PsA
  - in general population of the US ~ 0.1-0.25%
  - in “psoriasis” pts ~ 6-42%
- 84% of pts with PsA had cutaneous manifestations for an average of 12 years before the onset of PsA.
- Peak age onset: 30 – 50 years
- PsA affects men and women equally.
Psoriatic Arthritis (PsA)

- Psoriasis
  - Thickened, scaly, erythematous lesions
  - Frequently involves exterior surface of elbows and knees
  - May also hide in the scalp, navel, and anal crease
Psoriasis
Nail disease
(psoriatic onychodystrophy)

Nail changes include:

– pitting,
– onycholysis,
– subungual hyperkeratosi,
– oil-drop sign
– Nail plate dystrophy
Pitting  
Onycholysis  
Subungal Hyperkeratosis
Oil drop sign

Nail plate dystrophy
• Articular presentation
  – Oligoarthritis
  – Distal interphalangeal joint
  – Arthritis mutilans
  – Symmetric polyarthritis
  – Spinal involvement: 20 – 40%
Chronic PolyArthritis

Inflammation

Axial

AS
Reiter’s
PsA
Enteropathic

No axial

Symmetric

RA
PsA
CTD
Crystal induce

Asymmetric

Crystal induce

PsA

CTD

Vasculitis:

TB
Behcet’s disease, PAN

Fungus
Relapsing polychondritis

SpA: AS, ReA, PsA
Sarcoidosis

CTD
Amyloidosis

Non-inflammation

Osteoarthritis
Metabolic

Primary
Secondary
Arthritis of the DIP joints
Psoriatic arthritis: "sausage digits and rash"
Destructive (mutilans) arthritis
Symmetric polyarthritis

PsA

RA
Resorption of the distal phalanges: "pencil-in-cup" lysis of the distal end of a phalanx with remodeling of the proximal end of the more distal phalanx.
Arthritis Associated with Inflammatory Bowel Disease (IBD)

Ulcerative colitis and Cronh’s disease

- Articular manifestations
  - Peripheral joints: 10 – 22 % of IBD
    - Predominantly of lower limbs, large joints, asymmetric oligoarthritis
    - Symmetric polyarthritis, small joints, fingers and toes
      (Cronh 20: 40: 40)
  - Axial joints: 5 – 12 % of IBD
    - Asymptomatic sacroiliitis: 4 – 25%
• Extra-articular manifestations
  – General symptoms
  – enthesitis
  – Ocular manifestation: uveitis
  – Mucocutaneous involvement:
    • pyoderma gangrenosum
    • erythema nodosum
    • clubbing of fingers
Undifferentiated Spondylitis (USpA)

- Met SpA symptoms, but not fulfill classification criterion of specific disease
  - Early disease
  - Abortive form
  - Overlap syndrome
  - Other entities
Which diagnostic tests are recommended to help make the diagnosis of inflammatory back pain?

- To identify systemic inflammatory disease
  - CBC
  - Alb/Glob
  - ESR
- Plain sacroiliac radiographs
- HLA-B27 testing
  - Only patient has a clinical suggestive of inflammatory back disease and negative sacroiliac radiographs
- Bone scan
- MRI
  - To identify sacroiliitis in patients with negative plain sacroiliac radiographs
Rx in SpA

Education

Joints

Enthesitis

Dactylitis

Axial

PT

NSAIDs

Local injection

SSZ, MTX, AZA, CsA, Lef, gold

Rehabilitation

Anti-TNF Rx/ Biologic
Biological treatment:
Tumor necrosis factor (TNF) inhibitor

<table>
<thead>
<tr>
<th></th>
<th>Etanercept</th>
<th>Infliximab</th>
<th>Adalimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>2 soluble human TNF receptors (p75) conjugated</td>
<td>Human-mouse chimeric anti-TNF</td>
<td>Human anti-TNF antibody</td>
</tr>
<tr>
<td></td>
<td>to human IgG1 antibody</td>
<td>IgG1κ antibody</td>
<td></td>
</tr>
<tr>
<td><strong>Target of binding</strong></td>
<td>Soluble and cell-bound TNF, lymphotoxin-α</td>
<td>Soluble and cell-bound TNF</td>
<td>Soluble TNF; probably cell-bound TNF as well</td>
</tr>
<tr>
<td><strong>Route of administration</strong></td>
<td>Subcutaneous (SC)</td>
<td>Intravenous (IV))</td>
<td>SC/IV</td>
</tr>
<tr>
<td><strong>Dose/Frequency of administration</strong></td>
<td>25 mg twice weekly</td>
<td>3-10 mg/kg every 4 to 8 weeks in combination with MTX</td>
<td>40 mg every 2 weeks</td>
</tr>
<tr>
<td><strong>Serum half-life</strong></td>
<td>102±30 hr</td>
<td>8-9.5 days</td>
<td>10 days</td>
</tr>
</tbody>
</table>

Improved:
- Spinal Pain
- Peripheral jts
- Function
- Enthesitis
- Uveitis
Principle for AS management

1. no cure
2. early diagnosis very important
3. education of patient to increase compliance
4. appropriate use of antirheumatic drugs, primarily NSAIDs
5. continuity of care
6. daily exercise very important (swimming), physiotherapy
7. sleep on firm mattress
8. appropriate sport and recreation
9. supportive measure and counseling
10. avoid smoking
11. avoid trauma (osteoporosis of the spine)
12. patient support group
13. family counseling
Therapeutic approach in ReA

- Majority of case is self limiting
- Eradicate acute bacterial infection with ABO
- Most trial: ABO effective in Chlamydia reactive arthritis
- ABO has no place in treatment of enteric reactive arthritis
- Use NSAIDs to relieve pain and inflammation
- Intraarticular steroid injection
- add DMARDs if disease still active and progressive
  - Sulfasalazine
Treatment Modalities Used for Different Features of PsA


Managing arthritis complicating IBD

Pharmacological

**NSAIDS**
- pain control, ↑ gut permeability and may exacerbate gut inflammation

**DMARDS**
- Sulfasalazine is of proven value in long-term management
- Other: Azathioprine, glucocorticoid, MTX

**Biologic:**
- Infliximab (not with etanercept) → 60% remission in Crohn’s disease