Missed, Misdiagnosed & Mistreated: De-Mystifying Three Common Rheumatic Diseases

Cong-Qiu Chu, MD, PhD
Assistant Professor of Medicine
Oregon Health & Science University and
Portland VA Medical Center
Portland, OR
Disclosure

- Bristol-Myers Squibb – Speakers Bureau
- Covidien - Consultant
Commonly Missed......

- Backache is a very common problem in family practice

- History and physical examination is Still more important than investigations in a ‘simple’ case of backache...........
Case #1

• The first patient is a 27 year old man with low back pain interfering with his job in construction

What do you ask?

“Tell me about your back pain”
Case #1 (continued)

- Onset 9 years ago, insidious onset
- Waxing/waning
- No precipitating cause, no H/O trauma
- Quite stiff in mornings lasting 2-3 h
- Loosens up at work and pain reduced with exercise
- Sometimes awakens at night with back pain and stiffness – has to get out of bed and walk around to get comfort
Case #1: Question

- What type of back pain does this 27 year old man have?
- How would you describe it?
How to Differentiate between

‘Mechanical’ vs ‘Inflammatory’
back pain
Low Back Pain

94%

**Mechanical**

- AM stiffness
- Usually minor
- Maximum pain/stiffness
- Late in day
- Exercise/activity
- Worsens symptoms
- **Duration** Acute or chronic
- **Age at onset** 20-65 years
- **Radiographs**
- Osteophytes
- Disc space narrowing
- Vertebral malalignment

1%

**Pathological**

(Tumor/Infection/Fracture)

- Onset > 60 years
- Progressive over weeks
- Night/rest pain
- Systemic symptoms
- H/O Malignancy
- Infection
- Osteoporosis risk factors
- Trauma

5%

**Inflammatory**

- AM stiffness
- Usually prolonged
- Maximum pain/stiffness
- After midnight, early AM
- Exercise/activity
- Improves symptoms
- **Duration** Chronic
- **Age at onset** <40 years
- **Radiographs**
- Sacroiliitis
- Syndesmophytes
- Spinal ankylosis
# Inflammatory vs. Mechanical Back Pain

<table>
<thead>
<tr>
<th>Features</th>
<th>Inflammatory Back Pain</th>
<th>Mechanical Back Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning stiffness</td>
<td>Prolonged, ≥1 hour</td>
<td>Usually less than 30 min</td>
</tr>
<tr>
<td>Max. pain/stiffness</td>
<td>After midnight &amp; early morning</td>
<td>Late in day</td>
</tr>
<tr>
<td>Exercise/activity</td>
<td>Improves symptoms</td>
<td>Worsens symptoms</td>
</tr>
<tr>
<td>Duration</td>
<td>Chronic</td>
<td>Acute or chronic</td>
</tr>
<tr>
<td>Age at onset</td>
<td>12-40 yrs</td>
<td>20-65 yrs.</td>
</tr>
<tr>
<td>Radiographs</td>
<td>Sacroiliitis, Syndesmophytes, Spinal ankylosis</td>
<td>Osteophytes, Disc space narrowing, Vertebral mal-alignment</td>
</tr>
</tbody>
</table>
Case #1: Question

How would you describe the back pain in this 27 year old man?

A. Mechanical back pain
B. Inflammatory back pain
C. Back pain due to degenerative disc disease
D. Sciatica
E. Spondylolysthesis
Case #1: Answer

• **Correct Answer: B. Inflammatory Back Pain**

• This is **not** ‘mechanical low back pain’ - started without a precipitating cause; waxing and waning; worse at rest

• **He has ‘inflammatory’ back pain** - significant morning stiffness, worse pain being at night and improvement in pain by activity

• **Degenerative disc disease, spondylolysis, and sciatica** are examples of mechanical back pain which worsen with activity and are usually improved with rest
Inflammatory Backache: Think of Spondyloarthropathies

SpA are a group of rheumatic disorders that share several common factors:

1. Inflammatory back pain
2. Associated with HLA-B27

SpA Prevalence ~ 1-2%
Case #1 (continued)

- ROS: positive for alternating buttock pain but negative for bowel, bladder symptoms, eye pain or redness, peripheral joint arthritis
- Back pain responds very well to NSAIDs
- O/E: Normal skin & eyes, normal musculoskeletal examination except forward flexion of lumbar spine (Schober’s test) marginally limited to 4 cm (normal: ≥ 5cm)
- HLA B-27 positive, X-ray of the lumbar spine shows erosion and sclerosis of the left sacroiliac joint suggestive of sacroiliitis
Case #1: Question

With the information available to you, can you say that this patient has Ankylosing Spondylitis?
Clinical criteria:

- Low back pain and stiffness for more than 3 months that improves with exercise, but is 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

Radiological criterion:

- Sacroiliitis grade $\geq 2$ bilaterally or grade 3-4 unilaterally

**Definite AS:**

If the radiological criterion is associated with at least 1 clinical criterion

Ankylosing Spondylitis

- A chronic, systemic, inflammatory disorder involving the SI joints, spine & often hips
- Axial joints are always involved, peripheral joints are frequently affected
- Characterized by inflammatory back pain, loss of spinal mobility
- In severe cases, extensive fusion (ankylosis) of spinal vertebrae can increase the risk of spinal deformity, fracture, & disability
Clinical ‘Pearl’ #1

• Backache is a very common complaint

• **Inflammatory back pain** - Simple questions for important clues:
  – “does exercise improve or worsen your back pain” or
  – “do you wake up in the middle of the night because of stiffness in the back and walk around the room to get relief”
Commonly Misdiagnosed……

• ANA *should NOT be ordered* just because someone complains of aches and pains

• History and physical examination is STILL more important than investigations in a ‘simple’ case of aches and pains……….
Case #2

- The second patient, 44 y/o woman, 3 months of “worsening arthritis & fatigue”
- On enquiry: pain in shoulders, back, hips, hands and overwhelming fatigue
- She has not been sleeping well due to stress and depression and feels stiff “all day”
- O/E
  - Depressed mood; afebrile
  - No skin rash; no mucosal lesions
  - Lungs, Cardiovascular, Abdominal exam WNL
  - Tender everywhere: neck, shoulders, back, no joint swelling
Case #2 (Continued)

- Labs
  - CBC normal, ESR 11
  - “Arthritis Panel”: ANA + 1:40, RF: negative, Uric acid 5 mg/dl, HLA B27 negative
  - UA – no protein, cells, casts

Patient has lupus?
Case #2: Question

- What does this 44 year old lady have?
- Did the “Arthritis Panel” results help you?
How test results can be misleading

‘Low titer positive ANA’ does not diagnose anything
ANA (Antinuclear Antibody)

Hep -2 cell

ANA

2nd antibody (anti-human IgG)

Fluorescein
ANA Patterns
What % of normal people have + ANA tests?

What % of normal people make ANAs?
ANA

% of Patients

ANA Titer

Screening Dilution

Normal
Normal (Elderly)
• What % of normal people have + ANA tests?
  – Young: 2-5%
  – Old: 10-20%

• What non-rheumatic diseases are associated with + ANAs?
  - SBE
  - Hepatitis B
  - Hepatitis C
  - Viral infections
  - Malignancy
  - Lymphoma
  - Leukemia
  - Thyroiditis
  - Alcoholic hepatitis
  - Autoimmune hepatitis
  - Multiple sclerosis

→ 70%
ANA in Rheumatic Diseases

- What rheumatic diseases are associated with + ANAs?
ANA

• What % of normal people have + ANA tests?
  – Young: 2-5%
  – Old: 10-20%

• What non-rheumatic diseases are associated with + ANAs?
  – Multiple infectious/inflammatory/neoplastic - up to 70%

• What rheumatic diseases are associated with + ANAs?
  – SLE 99%
  – Other rheumatic diseases 10-90+%
Followup of + ANA

- Anti-dsDNA
  - SLE
  - renal SLE

- Anti-ENA
  - anti-Sm
  - anti-RNP
  - anti-Ro (SSA)
  - anti-La (SSB)
  - anti-centromere
ANA

- Indication: ONLY IF clinical syndrome suggesting SLE
- Interpretation
  - negative ANA excludes SLE
  - + ANA does NOT diagnose SLE
  - +/- ANAs of ? utility in other rheumatic diseases
  - + ANAs found in some non-rheumatic diseases
  - consider following up clinically significant + ANA with anti-dsDNA, anti-ENA (Sm, RNP, etc)
In Rheumatologist Office: reaffirmed complaints of

Generalized aches and pains, severe fatigue, poor sleep at night but feeling drowsy throughout the day, tingling and numbness in all four limbs, abdominal pain with alternating constipation and diarrhea, headaches, increased frequency of urination, restless legs, dizziness, palpitations, chest pain, shortness of breath, “swelling” of hands and feet, rashes all over, fingers becoming white in cold weather, dryness of mouth, forgetfulness, cognitive dysfunction and loss of libido
What is the Diagnosis?

• On examination: Overweight and depressed with multiple tender points, otherwise WNL

• Apart from the ANA positive at 1:40, all other investigations are normal
Fibromyalgia

- A very common syndrome of generalized aches & pains
- Multiple other complaints lead to poor quality of life
- Does not respond to steroids
- Treatment involves:
  - Aerobic conditioning
  - Improving sleep quality
  - Treating assoc. depression & anxiety
  - Patience/compassion!
Clinical Pearl #2

- SLE is a clinical diagnosis that is suspected by history and physical exam
- “Generalized aches and pains & Fatigue” without true swollen joints or photosensitive skin rash, and with normal CBC, ESR, urinalysis is UNLIKELY to be lupus and therefore ANA should NOT be ordered
- A positive ANA DOES NOT equal SLE
- A negative ANA essentially excludes SLE
And Finally, Commonly Mistreated……

- Gout is the MOST COMMON inflammatory arthritis affecting nearly 3% of the population

- It is important to learn how to use Colchicine and Allopurinol correctly……
Case #3

- Third patient, 64 year old man, known to have gout for the last 10 years
- He also has HTN & mild renal insufficiency (Cr 1.4)
- He is irregular in the clinic and does not take his medication (Allopurinol & HCTZ) regularly
- Seen last week for an acute attack of gout in his right 1st MTP joint
- Serum Uric Acid was 11 mg/dl (normal <7mg/dl) and hence you prescribed Indomethacin three times a day & Allopurinol 300 mg/day
- He is back today with no relief and worsening pain in the right foot that looks worse than last week
Case #3 (continued)

• O/E:
  – Patient hobbles to the examination table, using a cane in one hand and leaning on his wife’s shoulder
  – Painful and swollen R great toe with redness spreading on the dorsum of the right foot
Case #3: Question

- What went wrong?
- Why did he not respond to the Indomethacin and Allopurinol combination?
During an acute attack of Gout,

Do not start, stop or change the dose of allopurinol
Principles of Successful Gout Treatment: 1

• Treat the acute attack of gout effectively
  – All NSAIDs are created equally and Indomethacin *DOES NOT* have any magical properties
  – Colchicine 1.2 mg stat & one pill 90 minutes later is enough
  – *BEWARE* of using NSAIDs or Colchicine in patients with renal insufficiency
  – Corticosteroid (Intraarticular or oral) is a valid choice
  – DO NOT start, stop, change the dose of allopurinol
Principles of Successful Gout Treatment: 2

- Wait for the acute attack of gout to settle for **two weeks** and then
  - Start uric acid lowering therapy such as Allopurinol 100 mg once a day along with concomitant anti-inflammatory prophylaxis (low-dose Colchicine or NSAID) to prevent “mobilization flares”
  - 2 weeks later, if the uric acid is not <6 mg/dl, increase the dose of Allopurinol to 200 mg/day and repeat this procedure every two weeks
  - Continue concomitant anti-inflammatory prophylaxis for 6 months
Principles of Successful Gout Treatment: 3

• Therapeutic goal of Gout treatment is to maintain the Serum Urate levels below 6 mg/dl
  – Check serum urate levels two weeks after changing the dose of Allopurinol
  – If the target level is not reached, change the dose and recheck serum urate
  – Maintain anti-inflammatory prophylaxis (low dose Colchicine or NSAID) for 6 months
Clinical Pearl #3

- Acute attack of Gout needs treatment with NSAIDs (not necessarily Indomethacin) or Colchicine (1.2 mg stat and 0.6 mg 90 minutes later) or Steroid

- DO NOT start, stop, change Allopurinol during acute attack

- Two weeks after the acute attack, start uric acid lowering therapy along with prophylactic anti-inflammatory drugs
MSU Crystals, Inflammasome, IL-1 & Gout
Newer Agents for Gout

- **Anakinra (Kineret)** – Recombinant IL-1 receptor antagonist (IL-1RA) : highly effective for acute gout attack. Used in those with co-morbidities, contraindicated for NSAIDs, steroid, colchicine

- **Feboxustat** – non-purine xanthine oxidase inhibitor : allopurinol intolerance

- **Uricase – Pegloticase** (Krystexxa)
OHSU Early Arthritis Clinic

- Increase rate of drug free remission if treating even earlier?

- Guidelines for referral to OHSU Early Arthritis Clinic:
  - Any patient with new symptoms of inflammatory arthritis:
    - Clinical evidence of inflammatory arthritis.
    - Disease duration 0 - 12 months from symptom onset.
    - At least 1 swollen joint or New onset of symptoms of inflammatory back pain.
OHSU Early Arthritis Clinic

- Patients will be seen within two weeks after referral
- Phone: 503 494 8637
- FAX: 503 494 1133
- chuc@ohsu.edu