Disclosures

• Speakers Bureau
  — Pfizer
  — Eli Lilly
  — Forest

Fibromyalgia: Diagnosis and Management

Peng Thim Fan, MD
Clinical Professor of Medicine
Division of Rheumatology
David Geffen School of Medicine at UCLA

The Evolution of the Fibromyalgia Concept

• Muscular Rheumatism: c.1700
• Valliex (1841) tender points
• Fibrositis (Gowers): 1904
• Fibromyalgia (Yunus): 1981
• ACR Classification Criteria: 1990
• ACR Diagnostic Criteria (Preliminary): 2010

Case Presentation

• Ms. JD is a 51 year-old female who complains of severe pain and swelling of her hands and generalized stiffness lasting over an hour in the morning. Her joints do not move well and she cannot grip objects without pain.

Q: what would lead you to suspect a diagnosis of FM (fibromyalgia) rather than early rheumatoid arthritis (ERA) or another inflammatory arthritis?

Differential Diagnosis

• Is age 51 too old for either FM or ERA?
  — No for both. FM commonly occurs in individuals aged 25 to 60; highest incidence age 50. Durations of symptoms at diagnosis about 5 years.
  — Early RA trials (disease within 6 months) mean age 50.

• Does morning stiffness of over an hour distinguish inflammatory arthritis from FM?
  — No. Severe morning stiffness that may last hours is a hallmark of both FM and ERA.

The Prevalence of Fibromyalgia

• General medicine clinics: 5-10%
• Rheumatology practice: 15%

• General population: 2%
  — Incidence estimated at 3.6 million

• Women: 3%  Men: 0.5%
  — At least 6x more prevalent in women in a clinic setting

• Wolfe (1995): prevalence increases with age, most common in women >50
Fibromyalgia more prevalent than rheumatoid arthritis

### Differential Diagnosis

- **What symptoms would lead us towards FM?**
  - **Pain**
    - Symptoms start insidiously but then maintain consistent severity for at least 3 months
    - Widespread symmetrical pain: axial and truncal, jaw, shoulder and hip girdles, upper and lower arms and legs
  - **The other major symptoms:**
    - Fatigue (I feel like I always have the flu)
    - Waking unrefreshed (no matter how much sleep I have had I feel exhausted as if I have not slept at all)
    - Cognitive symptoms (I cannot focus my thoughts, I have trouble remembering, I cannot do simple math)

### Differential Diagnosis

- **What other symptoms would lead us towards FM?**
  - **General Somatic symptoms:**
    - Irritable bowel syndrome: abdominal pain and cramping, food intolerance, constipation, diarrhea, nausea, heartburn, vomiting
    - Neurologic: headaches, muscle cramps and weakness, numbness and tingling, loss or change of taste, ringing in the ears, dizziness, seizures
    - Irritable bladder symptoms: frequent urination, painful urination, bladder spasms
  -  
  - Depression, insomnia, many allergies, chemical sensitivity, nervousness
  - Raynaud's Phenomenon, cold and heat intolerance, sun sensitivity, dry skin, dry eyes and throat
  - Hives/welts, easy bruising, hair falling out
  - Loss or change of taste, loss of appetite

### Differential Diagnosis

- Past medical history is variable
  - Many have symptoms dating back to childhood; others claim an abrupt change, previously healthy and productive
  - Many claim symptoms started after physical trauma, infection, social stressors (e.g. divorce)
- Family history often positive
- Many drug allergies but mostly intolerance rather than rashes, hives, difficulty breathing or wheezing

### Physical examination

- General examination is normal.
- Musculoskeletal examination is normal.
  - Joints are NOT swollen, range of motion is normal.
  - Strength is limited by pain; no muscle atrophy or fasciculation; reflexes are normal; sensation is intact
  - Widespread tender points are seen in the majority of patients but a formal tender point examination to diagnose FM is no longer used for diagnosis
  - Should we accept a diagnosis of FM in the absence of ANY tender points?
RA Symmetrical synovitis

Fibromyalgia tender points

Fibromyalgia tender points

ACR Fibromyalgia Criteria

From History: widespread pain of 3 months duration

From Examination: tender points defined by digital palpation with a force of 4 kg pain experienced in at least 11 of 18 tender point sites


Map of 18 Possible Tender-Points in Fibromyalgia

The Tender Point: Key to Fibromyalgia Diagnosis

- Excessively tender, discrete area of soft tissue
- Palpated with thumb or first two fingers
- Palpation pressure: ~ 4 kg/cm, enough to whiten nail

Tender-Point Palpation: I. Head
- Insertion of suboccipital muscle

Tender-Point Palpation: IV. Neck and Chest
- Lower sternocleid
- Second costochondral junction

Tender-Point Palpation: II. Upper Back
- Mid upper trapezius
- Origin of supraspinatus

Tender-Point Palpation: V. Arms
- Lateral epicondyle

Tender-Point Palpation: III. Lower Back
- Upper outer buttock quadrant

Tender-Point Palpation: VI. Legs
- Prominence of greater trochanter
- Medial fat pad of the knee
### ACR Preliminary Diagnostic Criteria for Fibromyalgia

**3 components:**

1. **Widespread pain index (WPI) > 7**
   
   and Symptom severity (SS) scale score ≥ 5
   
   or WPI 3-6 and SS scale score ≥ 9

2. **Symptoms have been present at this level for at least 3 months**

3. **The patient does not have a disorder that would otherwise explain the pain.**


**WPI: count the number of areas in which the patient had pain in the last week. Score is 0 to 19**

- Jaw L or R (2)
- Neck (1)
- Back Upper or Lower (2)
- Shoulder girdle L or R (2)
- Chest (1)
- Abdomen (1)
- Upper Arm L or R (2)
- Lower Arm L or R (2)
- Hip (buttock, trochanter) (2)
- Upper Leg L or R (2)
- Lower Leg L or R (2)

**SS scale score: 0 = no problem**

- 1 = mild or slight or intermittent, few
- 2 = moderate, frequent, moderate number
- 3 = severe, continuous, great number

1. **Fatigue**
2. **Waking unrefreshed**
3. **Cognitive symptoms**
4. **General somatic symptoms**

Total score for SS scale is between 0 and 12


### Differential Diagnosis

- What laboratory studies should we perform?

- All laboratory studies are normal in FM. Tests are performed to screen for other systemic illnesses:
  - CBC, comprehensive metabolic panel, ESR, CRP, CK, TSH
  - Do NOT perform RF or ANA as screening studies
  - Serum 25 (OH) D probably not helpful unless very low
  - Vitamin D (< 9 ng/ml) mimics FM

### Proposed Pathogenesis of Fibromyalgia

- Emotional trauma
- Physical trauma
- Chiari malformation, syringomyelia, spinal stenosis
- Genetic predisposition
- Low serotonin production and levels
- High CSF nerve growth factor levels
- High CSF Substance P levels
- Dysfunctional sleep
- Neuroendocrine dysfunction
- Low production of growth hormone and insulin-like growth factor-1


**ANA:** speckled pattern

15-23% of FMS and CFS patients have a positive ANA
Proposed Pathogenesis of Fibromyalgia

• Fan: The sensitive to everything syndrome

Fibromyalgia as a problem of Central Sensitization

Persistent activation of C-fiber sensory nerves
Sensitized neurons in the dorsal horn of the spinal cord
Exaggerated neuronal response to normal input
Physical manifestations include
  • Increased receptive field
  • Hyperalgesia
  • Allodynia

Pathophysiology of Pain

Transmission of pain sensation

◆ A fibers: large myelinated
  - α  motor
  - β  touch
  - γ  position
  - δ  pain and temperature
◆ B fibers: myelinated – autonomic
◆ C fibers: small, unmyelinated
  - Pain and temperature

Mechanisms of Pain

Central Sensitization

Mechanisms of Pain

Expansion of Receptive Field

Mechanisms of Pain

Hyperalgesia

Pathophysiology of Pain
Transmission of pain sensation

- A fibers: large myelinated
  - α motor → pain
  - β touch → pain
  - γ position
  - δ pain and temperature
- B fibers: myelinated – autonomic
- C fibers: small, unmyelinated
  - Pain and temperature

Mechanisms of Pain

Allodynia

Mechanisms of Pain

Neuropathic
Neuronal plasticity in FM

- Neural plasticity: the capacity of neurons to change their function, chemical profile, or structure
- Primary sensory and dorsal horn neurons undergo activation, modulation and modification.
- Gain is increased and results in hypersensitivity

Woof CJ, Salter MW: Science 2000;288:1765-68

Pneumatic pain stimulator for fMRI studies

Pathophysiology of Fibromyalgia: The Role of Central Sensitization

1. First, impulses from afferents depolarize dorsal horn neurons
2. Then, extracellular Ca²⁺ and nitric oxide diffuse into neurons and cause exaggerated release of substance P and glutamate; this results in neuronal hyperexcitability
3. Finally, a pain signal is sent to the brain from the dorsal horn

Descending pathway modulates pain
Acts through norepinephrine and serotonin

Despite extensive research, the pathogenesis of pain in FM is not clearly understood. However, central sensitization has emerged as a leading theory of disease mechanism.

Staud.

Syndromes That Overlap with Fibromyalgia

The neurologist sees chronic headache, the gastroenterologist sees IBS, the otolaryngologist sees TMJ syndrome, the cardiologist sees costochondritis, the rheumatologist sees fibromyalgia, and the gynecologist sees PMS.

Clinical Features of Fibromyalgia

<table>
<thead>
<tr>
<th>Criterion</th>
<th>% positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Widespread Pain</td>
<td>97.6</td>
</tr>
<tr>
<td>Tenderness 11 of 18 tender points</td>
<td>90.1</td>
</tr>
<tr>
<td>Fatigue</td>
<td>81.4</td>
</tr>
<tr>
<td>Morning stiffness &gt; 15 minutes</td>
<td>77.0</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>74.6</td>
</tr>
<tr>
<td>Paraesthesia</td>
<td>62.8</td>
</tr>
<tr>
<td>Headache</td>
<td>52.9</td>
</tr>
<tr>
<td>Anxiety</td>
<td>47.8</td>
</tr>
<tr>
<td>Dysmenorrhea</td>
<td>45.6</td>
</tr>
<tr>
<td>Sclera symptoms</td>
<td>35.8</td>
</tr>
<tr>
<td>Prior depression</td>
<td>31.5</td>
</tr>
<tr>
<td>Irritable Bowel syndrome</td>
<td>29.6</td>
</tr>
<tr>
<td>Urinary urgency</td>
<td>26.3</td>
</tr>
<tr>
<td>Raynaud's phenomenon</td>
<td>15.7</td>
</tr>
</tbody>
</table>
Clinical Features of Chronic Fatigue Syndrome

<table>
<thead>
<tr>
<th>Criterion</th>
<th>% positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>100</td>
</tr>
<tr>
<td>Low grade fever</td>
<td>96</td>
</tr>
<tr>
<td>Allergy</td>
<td>65</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>57</td>
</tr>
<tr>
<td>Adenopathy</td>
<td>48</td>
</tr>
<tr>
<td>Migraine</td>
<td>39</td>
</tr>
<tr>
<td>Headache</td>
<td>35</td>
</tr>
<tr>
<td>Psychoneurosis</td>
<td>35</td>
</tr>
<tr>
<td>Mild myalgia</td>
<td>30</td>
</tr>
<tr>
<td>Weight loss &gt;5kg</td>
<td>22</td>
</tr>
<tr>
<td>Gastrointestinal complaints</td>
<td>22</td>
</tr>
<tr>
<td>Tachyarrhythmia</td>
<td>17</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>13</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>9</td>
</tr>
</tbody>
</table>

The Fibromyalgia Complex: Central Sensitivity Syndromes

- Chronic Fatigue Syndrome
- Fibromyalgia
- Irritable bowel syndrome
- Temporomandibular joint disorder
- Migraine and tension headaches
- Multiple allergies syndrome
- Multiple chemical sensitivities
- Idiopathic low back pain
- Irritable bladder syndrome
- Restless leg syndrome
- Primary dysmenorrhea
- Interstitial cystitis/chronic prostatitis/painful bladder syndrome
- Myofascial pain syndrome
- Regional soft tissue pain syndrome

Silicone implant induced "Atypical connective tissue disease"

Tom Wesselman: The Great American Nude

Silicone implant induced "Atypical connective tissue disease"

Treatment of Fibromyalgia

- Relieve pain
- Education
- Improve sleep
- Exercise
- Improve sense of well-being and overall function

Treatment of Fibromyalgia / CFS

- Education: cognitive behavioral therapy.

A psychological treatment to modify thoughts and beliefs about FM and modify behavior by teaching coping skills and more effective use of rest, sleep and activity

Treatment of Fibromyalgia

- Education:
  - Fibromyalgia is a well-recognized disorder
  - Stop further diagnostic studies
  - Reassure benign nature of complaints
  - Amelioration of symptoms is possible although there is no cure
Components of the cognitive behavior therapy approach

- Education
- Meditation
- Cognitive restructuring
- Distraction
- Pacing
- Laughter

Treatment of Fibromyalgia

- Exercise: needs to be sustained
  - Aerobic exercise, mineral baths, spa therapy proven effective
  - Emphasize that exercises improves energy and well-being but does NOT reduce pain

Pain, stress and fatigue

Fatigue ↓
Inactivity ↓
Deconditioning ↓ →
Susceptibility to DOMS ↓
Muscle Pain → Inactivity

Nonpharmacologic Treatment

Aquatic Exercise Twinges-in-the-Hinges Aquatics
Program Fibromyalgia Self-Help Course Stretching Low impact aerobics

Pharmacologic treatment of Fibromyalgia

- Improve sleep:
  - Pediatric doxepin 10mg/ml, start with 6 drops at bedtime = 3mg
  - Alternative is low-dose amitriptyline 10mg nightly with slow increase to 50mg
  - Cyclobenzaprine 5 – 10mg nightly
### Pharmacologic Treatment of Fibromyalgia

#### Depression:
- 30% have major depression at time of diagnosis
- Lifetime prevalence of depression is 74% and anxiety disorder 60%
- SSRIs are not effective in reducing pain by themselves
- Teach simple relaxation techniques
- Formal stress-reduction program
- Sleep hygiene
- Correct sleep disorder

#### General rules:
- Start with a low dose and build up slowly
- Build upon a tricyclic at bedtime to improve sleep
- For patients with prominent sleep problems add pregabalin (alternative gabapentin) to tricyclic
- For patients with poor energy and exhaustion add duloxetine or milnacipran to tricyclic

#### Anticonvulsants: pregabalin and gabapentin
- Pregabalin: start with 25mg at bedtime
- Warn patient about dizziness and somnolence
- Gradually build the dose up to 150mg to 225mg twice a day (300 - 450mg daily)
- Aim for 50% pain reduction; also improved sleep, fatigue and quality of life
- Weight gain of over 7% seen in 8 – 10%
- Alternative is gabapentin
- Start at 100mg nightly, build up to 1200 to 2400mg

#### SNRIs: duloxetine, milnacipran and venlafaxine
- Duloxetine: start with 20-30mg in the morning
- Gradual increase to 60mg once a day
- Improves pain within 1 week and also mental fatigue
- Side effects are nausea, headache and dry mouth
- Milnacipran: start with 12.5mg in the evening
- Gradual increase with twice a day dosing to 100mg daily; rarely beneficial at 200mg daily
- Improves pain, global status and physical function
- Side effects nausea, headache, constipation
- SNRIs may cause rapid heart rate
- Venlafaxine: final mean dose of 167mg daily was effective in one study

#### Others
- Fluoxetine 20mg in the morning combined with amitriptyline 25mg at bedtime
- Acetaminophen-tramadol combination up to four times a day
- Dopamine receptor agonists: ropinirole, pramipexole*
- GHB (gamma-hydroxybutyrate) sodium oxybate
- Nabilone – synthetic cannabinoid
- NSAIDs and prednisone do not work better than placebo
Treatment of Fibromyalgia

- Multicomponent therapy
  - Education, physical therapy, psychological component, pharmacotherapy
- Meta-analysis:
  - reduced pain, fatigue, depressive symptoms and limitations on QOL scales
  - improved self-efficacy pain and physical fitness
  - * no sustained benefit at 4-15 months

Hauser W, Arthritis Care Res 2009; 61:216

Dubious treatments:
- growth hormone
- pressors: fludrocortisone
- Alternative Medicine: NADH, SAM-e, malic acid, acupuncture
  - Botulinum toxin, nerve blocks, trigger point injections, rhizotomies, facet blocks, etc

Acupuncture for Fibromyalgia


References

5. Milnacipran: Mease, J Rheumatol 2009; 36:398
“We are all strong enough to bear the misfortunes of others.”
- de la Rochefoucauld

THE END

Van Gogh:
“Old Man in Sorrow”