The Patient with Pain All Over

"All the Pearls in 50 Minutes"

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GOALS

• Become a better diagnostician.
• Diagnose undifferentiated connective tissue disease (UCTD) and primary Sjogren syndrome.
• Understand treatment of UCTD, polymyalgia, fibromyalgia, and polymyositis.

A 70 year old woman presents with widespread pain, stiffness and fatigue. She recently started keeping a water bottle at her bedside. Physical exam is remarkable for slight synovitis of hands & wrists, and presence of all fibromyalgia tender points. Lab data is notable for sed rate of 30 mm/hr but normal CRP at 0.7 mg/dl (nl 0 - 1.0 mg/dl), elevated C4 at 36 mg/dl. RF, CCP & ANA are negative. What is the most likely diagnosis?
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<td>Peripheral neuropathy</td>
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A. Paraneoplastic syndrome
B. Polymyalgia rheumatica
C. Rheumatoid arthritis
D. Fibromyalgia
E. Primary Sjogren syndrome
Primary Sjogren's

- Fatigue
- Pain all over
- Sicca
- Many persons with Sjogren’s fulfill criteria for fibromyalgia.


What’s in a name??

- Sjogren’s (primary) vs. undifferentiated connective tissue disease
  - Sometimes hard to distinguish initially
  - Both can be associated with widespread pain.
  - As is SLE.

What Are the Clues?

- Sicca symptoms
- Acrocyanosis
- Raynaud’s
- Family history
- Puffy hands
- Peripheral arthralgias
- Photosensitivity
- Alopecia
Sjogren's - History

- Use of eye drops?
- Can you eat crackers w/o water?
- Keep water on night table?

- Physical Exam: Nothing specific!
  - Sometimes small joint puffiness
  - Peripheral neuropathy
Sjogren's - Diagnosis

- You Can Diagnose Dry Eyes and Dry Mouth in Your Office!
- Phenol Red Thread Test
  - Zone-Quick™
- Saxon Test of Salivary Flow

Phenol Red Thread Test (Zone-Quick™)

- Alternative to the Schirmer test
- Takes 15 seconds; convenient screening test
- A test for dry eyes (not a direct test for Sjogren's!)

Saxon Test of Salivary Flow

- Takes 2 minutes
- Requires a scale that can measure to 0.1 gram (costs $100).
- Uses 4" x 4" medical gauze sponge.

Saxon Test

- Weigh the gauze in the cup
- Patient chews gauze for 2 min.
- Weigh gauze again in cup.

Saxon Test

- Most persons produce about 4g of saliva in 2 minutes.
- Abnormal if < 2.75 g in 2 minutes.
- Should D/C anticholinergic meds day before to avoid false positive.
- Anxiety may also give false positive.
Sjogren’s / UCTD - Lab

- SSA / SSB – insensitive!
- ESR often up – a little!
- ANA – speckled or negative
- CRP high normal (0.7 to 0.9 mg/dl)
- Check RNP antibody
- Check ACE level
- Check ANCA
- Check SPEP
- Check C4 (may be high or low!)

HIGH ACE LEVELS

- Sarcoidosis
- NIDDM
- Hyperthyroidism
- Renal disease
- Cirrhosis
- TB
- Gaucher
- Sjogren’s
- Histoplasmosis?
- Berrylosis
- Leprosy
- Amyloidosis
- Silicosis

Sjogren’s – Systemic Tx*

- Hydroxychloroquine
- Low-dose prednisone
- Methotrexate
- Cyclosporine
- Fibromyalgia treatments (for symptoms)

*None of these is FDA approved for systemic Sjogren’s
Polymyalgia Rheumatica

- Pain all over; sudden onset.
- Age > 50 (usually >70!)
- Weight loss
- Shoulder limitation of motion (periarthritis)
- Proximal muscle tenderness
- Sed rate > 50 mm/hr
- Anemia
- Prompt response to low dose prednisone

10-15% progress to giant cell arteritis.
Responds well to treatment.
This is a potentially serious disease that is treatable.
PMR – More Features

• Bilateral shoulder limitation of motion
• Synovitis (large > small joint)
• Bilateral carpal tunnel synd.
• Profound AM stiffness, gelling
• Strength is normal (just painful).
• Proximal muscle tenderness is different from FM tender points.

PMR – DDx
(Pain, Stiffness +/- High ESR)

• Fibromyalgia
• Polymyositis
• Rheumatoid arthritis
• Lupus
• Hypothyroidism
• Malignancy

PMR or GCA - Lab Features

• High ESR > 40 mm/hr, often 100.
  – Occasionally normal.
• Elevated CRP.
• Anemia, sometimes < 10g/dl.
• High alk phos (1/3 patients), sometimes ALT, AST.
• Low albumin.
• High globulins (polyclonal)
• CK, ANA, RF normal.
PMR – When to Biopsy?

- 15-20% of PMR patients have GCA.
- PMR + Headache = Biopsy.
- PMR + Any other symptom of temporal arteritis = biopsy.
- ESR/CRP not normalizing on low dose pred. (3-4 weeks)

PMR - Treatment

- Prednisone 15-20 mg/d
- Dramatic response (1-2 days)
- Try tapering by 2.5 mg/mo till 10 mg/d, then more slowly (by 1 mg/mo).
- Follow ESR, CRP monthly. Check BMP, CBC occasionally.
- Inform patient symptoms of GCA to report immediately.

PREDNISONE in ELDERLY

- Calcium + Vit D
- DEXA
- T/C bisphosphonate
- Eye exams: cataracts & pressure
- ↓K, ↑glucose
Amer. College of Rheum.

- Recommendations for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis 2010
- Arthritis Care & Research, Vol. 62, No. 11, November 2010, pp 1515–1526
- DOI 10.1002/acr.20295

PMR - Course

- Many patients don't follow textbook.
- Many patients require chronic steroids (2-5 mg/d).
- May progress to GCA, even 5 years later.
- Relapses occur. ESR may be normal with relapses.

WIDESPREAD NIGHT PAIN

- PMR
- Peripheral neuropathy
- Fibromyalgia
- Depression
- Malignancy (HPO)
CHRONIC INFLAMMATION

The Telltale Signs

- Anemia, normocytic or slightly microcytic
- High platelets
- Low albumin
- High globulin

Statin Myopathy

- Dose related
- Risk lowest with pravastatin, fluvastatin, rosuvastatin.


Statin Myopathy Risk Factors

- Hypothyroidism
- Renal insufficiency
- ALS
- Congenital myopathies
- SLCO1B1*5 variant
- Interacting drugs

Statin Myopathy Syndromes

- Myalgias
- CK elevation, asymptomatic
- Myositis, rhabdomyolysis
- Persistent autoimmune myopathy


WHAT IS FIBROMYALGIA?

- A syndrome of widespread pain and fatigue associated with multiple tender points and non-restorative sleep.
- More than 3 months
- Normal blood tests

MAJOR SYMPTOMS

- "Non-restorative" sleep
- Chronic fatigue
- Ache all over
- Presence of "tender points" (1990 criteria)
OTHER SYMPTOMS

- Fatigue
- Sleep Disturbance
- Headaches (migraine or tension)
- GI symptoms (IBS)
- Irritable bladder
- Panic attacks (20%)
- Vasospasm (40%)
- Dysmenorrhea
- Dry mouth
- Poor memory
- TMJ
- Subjective swelling

The Common Associates of Fibromyalgia

- Migraine headaches
- Irritable bowel
- Irritable bladder
- Panic attacks

Who gets FMS?

- Up to 2% of population.
- Most common in middle-aged women
- 8-9 females to 1 male approx.
- Patients with RA, SLE and ankylosing spondylitis often meet criteria.
- Tends to run in families.
TRIGGERS OF FLARES
The Usual Culprits

• Unaccustomed exertion
• Anxiety or emotional stress
• Inadequate or unrestful sleep
• Cold exposure, changes in weather
• Soft tissue injuries

FMS – THE ACR CRITERIA
American College of Rheumatology 1990
(There are also 2010 criteria pending)

• Widespread pain, 3 months duration
  • Above and below waist; bilateral
  • Axial pain (shoulders, back, chest)
  – 10 of 18 tender points
  • "Painful," not just "tender"
  • 4 kg force (9 lb.) needed

THE CONTROL POINTS

- Distal, dorsal third of forearm
- Midfoot, dorsal 3rd metatarsal
- Dorsal, 3rd metacarpal
- Thumbnail
- Forehead

Mimics of Fibromyalgia

- Sjogren’s, RA, SLE
- Spondyloarthropathy
- Polymyalgia rheumatica
- Myositis (statin myopathy)
- Hypothyroidism
- Depression

PREDISPOSED PERSONALITY TRAITS

- Reliable, hardworking
- Attention to detail, tries to please
- People-oriented, sensitive
- Internalizes conflict & stress
- Slightly higher anxiety level
- Difficulty learning to relax
- Occupation: elementary school teacher
Clues that Fibro May Be Due to a Connective Tissue Disease

- Acrocyanosis or True Raynaud’s
- Dry eyes and mouth
- Hand involvement
- Family history of autoimmunity
- Low C4
- Elevated C4
- Positive ANA, high ESR

A DIAGNOSTIC CHALLENGE

- More lab evaluations
- More imaging studies
- More surgery (back, neck, abdominal, gynecologic.)

THE BASIC LAB EVAL.

- CBC
- Comp. metabolic panel
- ANA
- TSH
- ESR, CRP
- CK
THE COMPLETE LAB EVAL.

- CBC
- CMP
- ANA*
- ESR, CRP
- SSA/SSB
- RNP
- CK

*If positive, then follow up with subtyping.

Pathogenesis

- Genetics
- Altered pain processing
- Sleep disturbance
- Neurohumoral perturbation
- Autonomic abnormalities
- Immunologic abnormalities

NEUROENDOCRINE ABNORMALITIES

- Reduced 24 hour free cortisol
- Heart rate fluctuations, orthostasis
- Blunted pituitary response
- Impaired growth hormone secretion
- Low IGF-1 levels
• FMS is associated with chronic low back pain (CLBP).
• 19% of pts with CLBP have FM tender points


Does Fibromyalgia Predispose to a Poorer Surgical Outcome?

A cause of prolonged post-op recovery in many studies.

TREATMENT PRINCIPLES FOR FMS

- Patient education
- Improve sleep hygiene
- Aerobic exercise
- Medications
- Possibly treat anxiety, depression
TREATMENT - 1

• Reassurance:
  – Not life threatening
  – Not crippling
  – Can be lived-with

TREATMENT - 2

• IMPROVE SLEEP HYGIENE
  – Get enough sleep.
  – Don’t take your troubles to bed.
  – Avoid caffeine, nicotine, alcohol (late in day)
TREATMENT - 3

• PHARMACOLOGIC (FDA Approved)
  – Duloxetine (Cymbalta®)
  – Milnacipran (Savella®)
  – Pregabalin (Lyrica®)

Duloxetine Clinical Trial

TREATMENT - 4

• PHARMACOLOGIC
  – Amitriptyline
  – Cyclobenzaprine
  – Gabapentin
POLYMYOSITIS

- Weakness is the key, not pain
  - Stairs, combing hair, getting out of car
- Waddling gait
- May have arthralgias, myalgias
- CK, ESR may be normal in 10%!
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- Sicca
- Synovitis
- Elevated C4, elevated ESR, high normal CRP.