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Evaluating diffuse aches and pains: It's not all fibromyalgia (but often it is)

Seetha Monrad MD

Case presentation

- A patient presents with diffuse myalgias, fatigue, and weakness

Approach to evaluation

- Does this represent rheumatic symptoms of an endocrinopathy?
 - Hypo- or hyper-thyroidism
 - Hypogonadism, diabetes, acromegaly, adrenal disease, parathyroid disease
- **Could this be a toxic/drug effect?**
 - Hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins)
 - Ethanol
 - Zidovudine, clofibrate, cyclosporine
- Is this a paraneoplastic process?
- Is this a systemic inflammatory rheumatic disease?
- Is this a chronic pain syndrome?

Case 1: HPI

- A 70 year old man presents to your clinic complaining of “aches and pains”. On closer questioning, he notes
 - Gradual onset over the past 6 months
 - Morning stiffness lasting 2-3 hours
 - Symmetric pain predominantly localized in his shoulders and hips, making it difficult to get out of a chair or comb his hair
 - No other systemic symptoms

Case 1: Objective

- Elderly man in mild discomfort
- Decreased active ROM in neck, shoulders, and hip flexors; a little tenderness to palpation in those areas
- Normal strength
- Hgb 11.2 g/dL (nl 12-36)
- CK 40 IU/L (WNL)
- TSH, T4 WNL
- ESR 96 mm/hr (nl 0-20)

Polymyalgia rheumatica

- Never occurs before age 50
- Common: in older persons prevalence approaches that of rheumatoid arthritis (approximately 1 percent)
- F:M 2:1, northern latitudes, Caucasians
- HLA-DR4 association

Polymyalgia rheumatica


- Diagnosis:
 - Clinical presentation
 - Elevated inflammatory parameters (ESR) – sometimes > 100
- Differential: Some overlap with RA
- Treatment:
 - Exquisitely sensitive to “low” dose steroids (<20 mg/day)
 - Duration of treatment prolonged – 1-2 years

Relationship to giant cell arteritis

- PMR is present in about 50 percent of patients with GCA
- GCA occurs in approximately 15 percent of patients with PMR
- Significant overlap in age of presentation, ethnicity/geography, HLA associations
- Need to screen all PMR patients for GCA signs:
 - headache, scalp tenderness, visual changes, jaw claudication, prominent temporal arteries

Case 2: HPI

- A 55 year old woman presents with “aches and pains”. On closer questioning, she notes
 - Gradual onset over the past 6 months
 - Morning stiffness lasting 2-3 hours
 - Difficulty getting out of a chair, climbing stairs, combing her hair, and reaching for jars in high cupboards; not actual pain with attempting these activities
 - No difficulty holding the comb or standing on toes to get to cupboards



Drawing of a person struggling up stairs removed

Case 2: Exam & labs

- Minimal muscle tenderness; no joint swelling or tenderness
- Significant proximal muscle weakness in both upper and lower extremities
- No other neurologic abnormalities

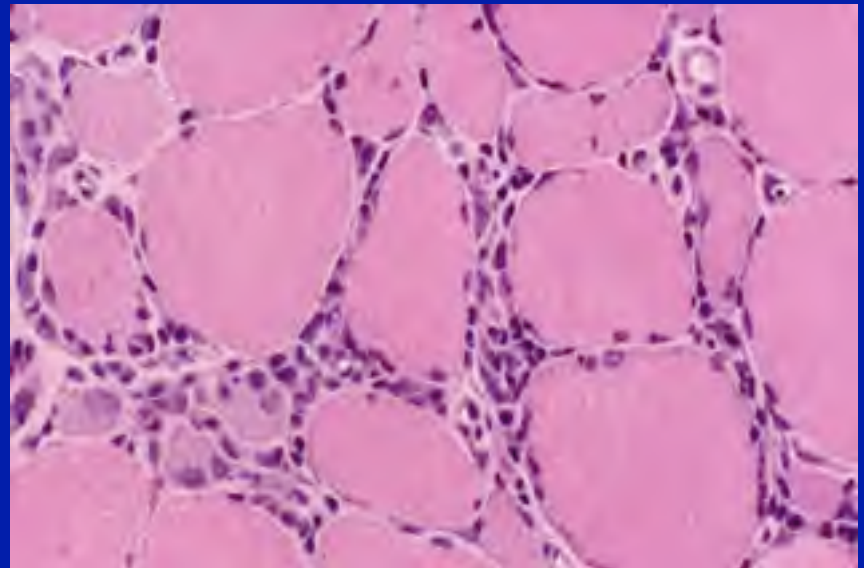
CK elevated

Important

- This could easily be a presentation of statin myopathy or hypothyroidism (and statistically these are the most likely)
- Also a presentation of an inflammatory myopathy, especially if CK highly elevated

Inflammatory myopathy

- Polymyositis, dermatomyositis (inclusion body myositis)
- Bimodal age distribution
- Female predominance; African American
- Proximal muscle weakness
- Diagnosis
 - Elevated muscle enzymes
 - EMG abnormalities
 - Muscle biopsy: inflammation



Dermatomyositis: Gottron's sign



PD-INEL Source Undetermined



PD-INEL Source Undetermined

Dermatomyositis: Heliotrope rash



PD-INEL Source Undetermined



PD-INEL Source Undetermined



Shawl sign

PC-INEL Source Undetermined

Mechanic's hands



PC-INEL Source Undetermined

Periungual erythema



PC-INEL Source Undetermined

Inflammatory myositis

- Treatment
 - Prednisone (1 mg/kg)
 - Methotrexate and/or azathioprine as steroid sparing agents
 - For rapidly progressive or refractory cases, IVIG or rituximab
- Association with malignancy (especially if older onset)

Case: History

- A 48 year old woman presents with diffuse muscle pain, weakness and significant fatigue. She reports
 - Symptoms for over 3 years that have become slightly worse in the past 6 months
 - Generalized pain and fatigue that limit her ability to work
 - Sleep disturbance

Case: Objective findings

- General physical exam:
 - Normal vital signs
 - Diffuse tenderness to palpation
 - Some tenderness around joints, but no obvious synovitis
 - Normal neurologic exam; no objective muscle weakness
- Labs: CBC, ESR, CRP, chemistry profile, TSH normal

History

- 1900s: “fibrositis”: inflammation of fibrous tissue overlying muscles
- 1970s: “fibromyalgia”
- 1990: American College of Rheumatology criteria
 - Chronic widespread pain in all four quadrants of the body and axial skeleton
 - 11/18 tender points (pain with 4 kg pressure)



Fibromyalgia

- Central pain syndrome with widespread pain and fatigue

Central pain: differs from

- Nociceptive pain
 - Neuropathic pain
- Part of a larger spectrum of central sensitivity disorders

Overlapping Systemic Syndromes

Fibromyalgia

- 2%-4% of population
- Defined by widespread pain and tenderness

Chronic Fatigue Syndrome (CFS)

- 1% of population
- Fatigue and 4 of 8 “minor criteria”

Psychiatric Disorders

- Major depression
- OCD
- Bipolar
- PTSD
- Generalized anxiety disorder
- Panic attack

Somatoform Disorders

- 4% of population
- multiple unexplained symptoms without “organic” findings

**Pain and/or
sensory
amplification**

Regional Pain Syndromes

Overlapping regional syndromes

- Tension/migraine headache
- Temporomandibular joint syndrome
- Irritable bowel syndrome
- Interstitial cystitis/ painful bladder syndrome
- Chronic pelvic pain/ vulvodynia/primary dysmenorrhea
- Idiopathic low back pain
- Cognitive difficulties
- ENT complaints (sicca, vasomotor rhinitis)
- Vestibular complaints
- Esophageal dysmotility
- Multiple chemical sensitivity, “allergic” symptoms
- Non-cardiac chest pain

Cartoon of a
thoroughly
examined elephant
removed

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.

Epidemiology

- 2-3% general population, 4% of women (using ACR criteria)
- Chronic widespread pain ~10%
- Women more likely to seek treatment ~8:1

Pathophysiology

- Genetics

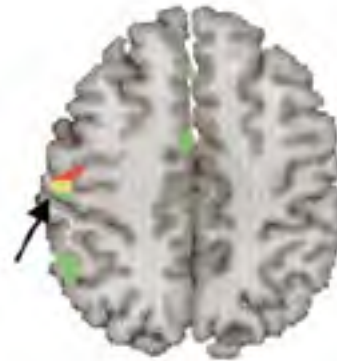
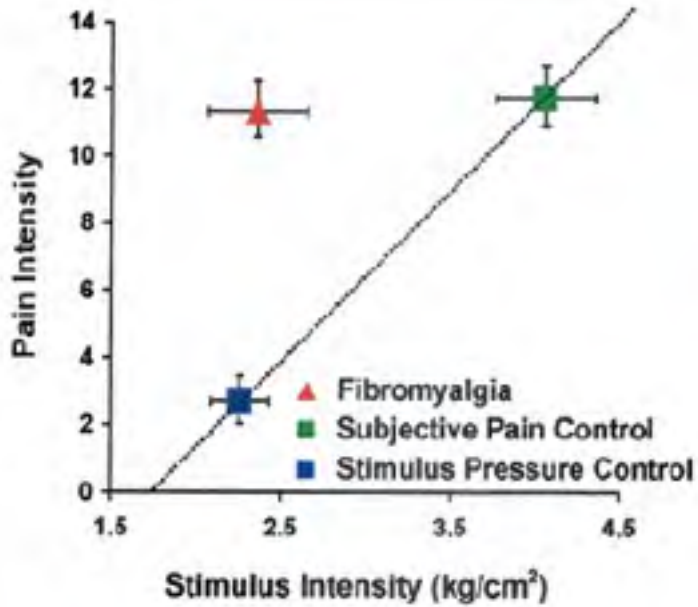
- First degree relatives have an eight-fold greater risk of developing FM
- Family members more likely to have other regional pain syndromes
- Several potentially related polymorphisms affecting metabolism/transport of monoamines

Pathophysiology

- Environmental factors: associated with FM in 5-10% of those exposed
 - Early life trauma
 - Physical trauma
 - Peripheral pain syndromes/autoimmune disorders
 - Psychological stress/distress
 - Certain infections (hepatitis C, EBV, parvovirus, Lyme disease)
 - Certain catastrophic events

Aberrant sensory and pain processing

- “Volume control” problem
- Lowered pain threshold throughout entire body
- Global problem with sensory processing:
e.g. loudness sensitivity



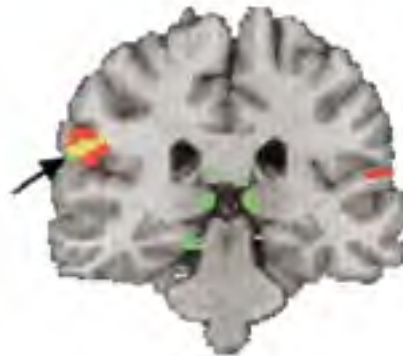
SI



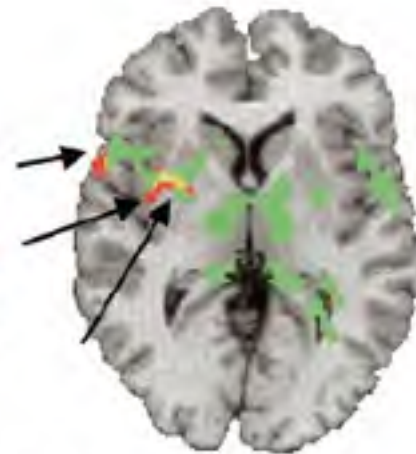
SI (decrease)



IPL



SII



STG, Insula, Putamen



Cerebellum

Other biomarkers

- Increased CSF levels of glutamate
- Normal/high levels of CSF enkephalins
- Decreased CSF levels of biogenic monoamines (products of serotonin, norepinephrine)

Diagnosis: History

- Pain
 - Current and lifetime history of widespread pain
 - Involving musculoskeletal and non-musculoskeletal areas
 - Unpredictable, worsened by stress
 - Can also have stiffness, paresthesias
- Fatigue
- Insomnia, sleep disturbance
- Memory difficulties

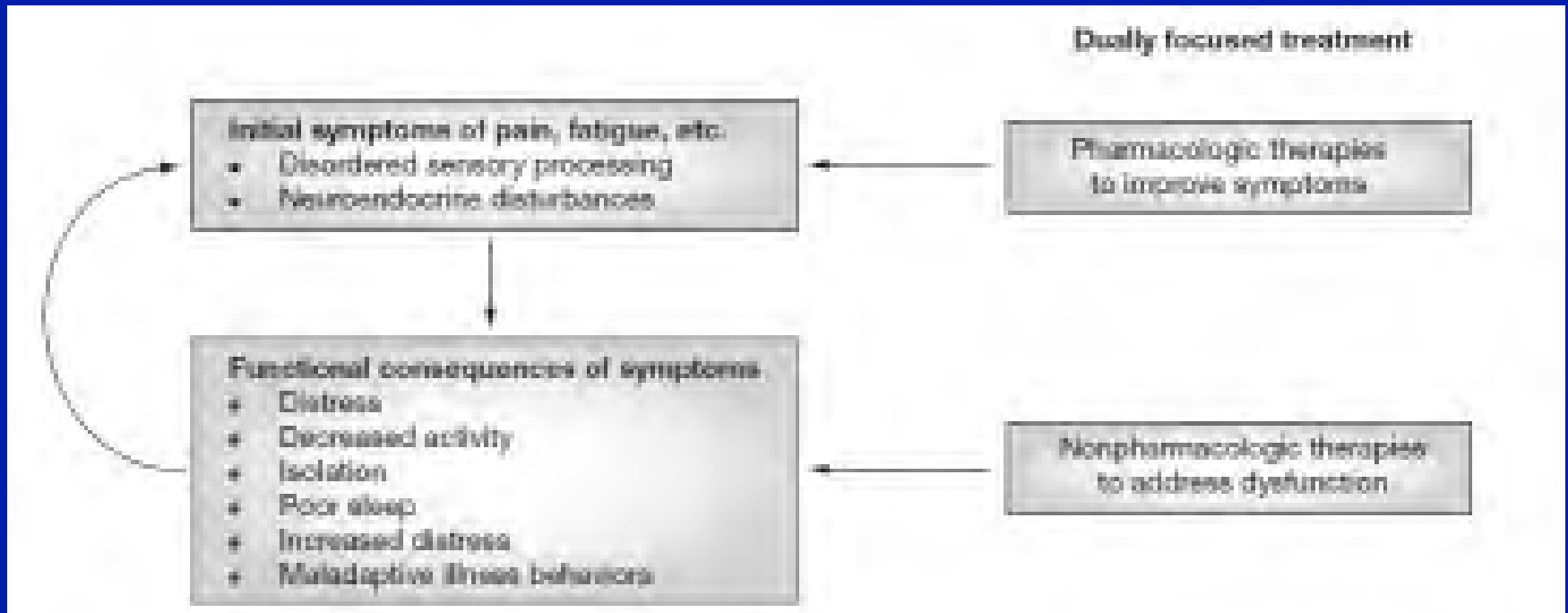
Diagnosis

- PMH: Comorbid syndromes
- FHX: other family members with pain syndromes
- PE: Diffuse tenderness

Evaluation

- If acute/subacute, may warrant further investigation, including
 - Inflammatory markers
 - CBC, chemistry profile
 - TSH, Vitamin D
 - NOT autoantibodies unless clinically indicated
- If chronic, less need for extensive work-up

Treatment: Principles



Treatment: Principles

1. Education
2. Aerobic Exercise
3. Cognitive behavioral therapy
4. Pharmacologic therapy

Treatment: Education

University of Michigan Chronic Pain and Fatigue Research Center - Windows Internet Explorer provided by UMHS

http://www.med.umich.edu/pcmfresearch/patients/index.htm

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For Patients

Advice to Patients

Lifestyle Activity & Exercise

Self-Management Skills & Techniques

Related Links

Numerous studies have supported the importance of educating patients with fibromyalgia and related conditions about the illness(es) they possess. When patients better understand why they have these symptoms and why different types of treatment work, they become more effective partners in managing their illness(es). In parallel, we educate doctors and health care providers about these illnesses and the most appropriate treatments. In the end, we strive for a partnership between health care providers and patients that makes use of drug and non-drug treatments. It is critically important for patients with this illness to understand that with the currently available drug and non-drug treatments, the overwhelming majority of patients with these illnesses can lead a normal and fulfilling life.

Get informed

Education can give patients the power to play a significant role in their own health care and well-being. Understanding what is happening inside the brain and body is crucial to understanding how to manage symptoms. Further, knowing what is happening physically will go a long way toward improving how a patient feels emotionally. To that end, this Web site can be a great resource for patients and their families.

[Learn about fibromyalgia](#), including risk factors and who is affected by it

[Learn about Chronic Multisymptom Illnesses](#), including regional and organ-specific symptoms and syndromes that often accompany fibromyalgia.

Take control of your well-being

Once you have a better idea what these illnesses are and what is going on inside your body, there are several self-management techniques you can use to manage the symptoms of your illness, as well as those of your

Local intranet 100%

Treatment: Exercise

- Aerobic
- Highly effective
- Key barriers: tolerance, compliance, adherence
- Recommendations:
 - At least twice a week (more if possible)
 - Start low, go slow
 - Treat exercise as a medication

Treatment: Cognitive Behavioral Therapy

- Teaches patients techniques to reduce symptoms, increase coping strategies, and identify/correct maladaptive behavior strategies
- Especially beneficial for improving functioning

Treatment: Pharmacologic

- Dual norepinephrine-serotonin reuptake inhibitors
 - Tricyclic antidepressants: amitriptyline, nortriptyline
 - Cyclobenzaprine
 - Venlafaxine, duloxetine, milnacipran
- Anticonvulsants
 - Pregabalin
 - Gabapentin
- Other: tramadol, selective serotonin reuptake inhibitors, sedatives

Treatment: Pharmacologic

- Not indicated in fibromyalgia
 - NSAIDs
 - Corticosteroids
 - Opioids

Summary

- Generate a broad differential for the patient presenting with diffuse aches and pains, and eliminate appropriately
- For the diagnosis of FM:
 - Education is KEY
 - Manage symptoms of pain, insomnia, comorbid depression, etc. with appropriate therapeutics
 - Emphasize the essential role of low grade exercise
 - If possible, utilize cognitive behavioral therapy to assist with improved functioning

Additional Source Information

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Slide 15: Source Undetermined; Source Undetermined

Slide 16: Source Undetermined; Source Undetermined

Slide 21: Source Undetermined

Slide 23: Clauw, *Neuroimmunomodulation*. 1997

Slide 30: Gracely, *Arthritis Rheum* 2002

Slide 35: Dadabhoy/Clauw, 2008

Slide 37: Screenshot by S. Monrad, UMHS