Fibromyalgia: a pain amplification disorder and how we can help

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What I plan to accomplish

- Explain the condition, fibromyalgia
- Review approach to diagnosis
- Review medical treatment
- Use what we learn to treat a patient with fibromyalgia

- I welcome questions in real-time

Who are you?

What is fibromyalgia?

- A chronic pain syndrome that is probably neurological in origin
- Very common
- A frustrating condition for both the treating physician AND the patient.
- Historically has been diagnosed by rheumatologists but requires involvement and management by primary care physicians.

Start with a case

- Middle aged woman with hx of childhood abuse is treated for depression with SSRI and Cytomel. She falls from her horse and sustains a stress fracture her pelvis. She does not seek health care after the initial emergency room visit, but instead tries home treatment and toughing it out. After several months, she has wide spread pain associated with disturbed sleep, and fatigue.

Highlights

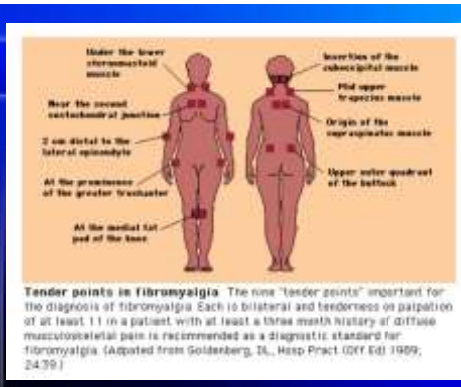
- Hx of depression
- Hx of precipitating event
- Contribution of de-conditioning
- Contribution of childhood abuse
- Associated symptoms - here fatigued, but also paresthesia, cognitive problems, IBS, headaches, etc.

Scope of the problem

•Up to 2% of women and fewer men have fibromyalgia.
•Very common referral to rheumatology by virtue of giving the condition a set a classification criteria.
•Not a diagnosis that primary practioners feel comfortable treating (but they should and can feel comfortable).
•Not just a wastebasket term but one with a specific set of classification criteria.

Criteria for diagnosis (ACR 1990)

Pain above and below the waist for >3 mon
Involving both sides of the body
Associated with fatigue, sleep disturbance, IBS, HA, cold extremities, pins and needle sensation (paresthesias), mental sluggishness or memory problems, irritable bladder, morning stiffness
>11:18 tender points painful on digital palpation of >4kg per square centimeter



Tender points in fibromyalgia The nine "tender points" important for the diagnosis of fibromyalgia. Each is bilateral and tenderness on palpation of at least 11 in a patient with at least a three month history of diffuse musculoskeletal pain is recommended as a diagnostic standard for fibromyalgia. (Adpated from Goldenberg, DL, Hosp Pract (Off Ed) 1989; 24:39.)

New (2010) criteria for FMS

- Criteria
- A patient satisfies diagnostic criteria for fibromyalgia if the following 3 conditions are met:
- 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 a similar level for at least 3 months.
- 3) The patient does not have a disorder that would otherwise explain the pain.

- Ascertainment
- 1) WPI: note the number areas in which the patient has had pain over the last week. In how many areas has the patient had
- pain? Score will be between 0 and 19.
- Shoulder girdle, upper arm, lower arm, hip (buttock/trochanter), upper leg, lower leg, jaw (each bilateral)
- neck, chest, abdomen, upper back, lower back.

2) Symptom severity (SS) scale score:

- Fatigue
- Waking unrefreshed
- Cognitive symptoms
- For the each of the 3 symptoms above, indicate the level of severity over the past week using the following scale:
- 0 no problem
- 1 slight or mild problems, generally mild or intermittent
- 2 moderate, considerable problems, often present and/or at a moderate level
- 3 severe: pervasive, continuous, life-disturbing problems
- Considering somatic symptoms in general, indicate whether the patient has:*
- 0 no symptoms
- 1 few symptoms
- 2 a moderate number of symptoms
- 3 a great deal of symptoms
- The SS scale score is the sum of the severity of the 3 symptoms (fatigue, waking unrefreshed, cognitive symptoms) plus the
- extent (severity) of somatic symptoms in general. The final score is between 0 and 12.

- * Somatic symptoms that might be considered: muscle pain, irritable bowel syndrome, fatigue/tiredness, thinking or remembering problem, muscle
- weakness, headache, pain/cramps in the abdomen, numbness/tingling, dizziness, insomnia, depression, constipation, pain in the upper abdomen,
- nausea, nervousness, chest pain, blurred vision, fever, diarrhea, dry mouth, itching, wheezing, Raynaud's phenomenon, hives/welts, ringing in ears,
- vomiting, heartburn, oral ulcers, loss of/change in taste, seizures, dry eyes, shortness of breath, loss of appetite, rash, sun sensitivity, hearing
- difficulties, easy bruising, hair loss, frequent urination, painful urination, and bladder spasms.

The continuum of FMS

- Probably on a continuum with chronic fatigue syndrome and regional pain disorder/myofascial pain syndrome.
- By the time a patient seeks care from a tertiary referral center, there is not only a pain syndrome, but maladaption to pain and lots of pain related behavior.

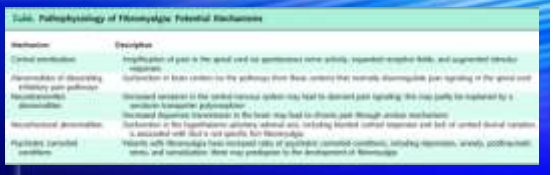
The continuum of FMS

- Range from the easily reassured to the chronic seeker of alternative diagnoses with increasing amounts of sickness behavior and psychosocial overlay.
- Some genetic predisposition - either anatomic, behavioral or neurotransmitter related.

The Cause of FMS

•NOT a chronic infection or an immune-mediated disease although background noise causes confusion.
• Likely due to disordered perception of pain by the central nervous system associated with
neuro-endocrine abnormalities and sleep disturbances.
•Unclear why this disordered perception occurs or how best to help patients manage the symptoms
•Chronic but not damaging symptoms although patients perceive them as progressive and it is disabling from the patient's point of view

•**Chronic pain is not acute pain that lasts a long time**



The concept of widespread allodynia as a synonym for FMS

- Allodynia is the perception of nonpainful stimuli as painful.
- FMS as well as IBS, irritable bladder syndrome, are now viewed as disorders of pain perception where the wiring has “gone wrong”.
- There are well studied changes in the CNS at both the spinal cord and the brain level that is associated with FMS.

Rewiring the CNS

- Muscle stimulation (?damage) is a potent activator of neurons in the dorsal horn of the spinal cord. This signal then spreads beyond the initial area of injury due to recruitment of “wide dynamic neurons”.
- The signal is transmitted to the thalamus, then the cortex.
- The cortex returns inhibitory signals to the thalamus and then to the spinal cord.

Neurotransmitters in FMS

- Glutamate, aspartate, PG,NMDA, Sub P and Nerve growth factor transmit pain in the CNS
- GABA, opioids, serotonin, taurine, acetylcholine, norepinephrine and CRH are anti-nocioceptive substances in the CNS
- Substance P is increased in FMS in the CSF; NMDA levels are increased
- Serotonin levels are reduced in brain and on platelets.

The evidence for central allodynia

- Change in the activity of certain areas of the brain by PET or functional MRI - lower levels of stimuli cause activation of the pain-processing regions of the CNS .
- Patients with FMS show lower thresholds for activation with not only pressure but also with heat and cold.

The diagnosis

- Investigate thyroid disorders, sleep disorders especially sleep apnea, Hep C, myopathies, vit D deficiency and depression. These can all present like FMS and are potentially treatable. Controversy around chronic Lyme disease.
- Look for peripheral drivers like OA, restless leg syndrome, hypermobility.
- Be aware that FMS complicates RA and SLE (well studied) and likely is associated with OA and other painful conditions like.

** FMS should not be a diagnosis of exclusion.

Treatment

- Patient education and empowerment*
- Improve sleep - pharmacologically and through behavioral changes
- Treatment of pain
- Treatment of depression
- Physical therapy
- Alternative therapies
- Exercise *
- Cognitive Behavioral therapy*

Patient education

- Patients with chronic pain have impaired coping skills
- Need to promote patient's sense on control, understanding of condition and encourage her as a source of healing power.
- Support groups
- Internet resources
- Involve families

Theory behind treatment of FMS - treatment of central pain

- Serotonin boosters
- Norepinephrine/serotonin reuptake inhibitors
- Alpha-2-delta ligands
- Dopamine agonists

- Not NSAIDs, opioids, benzodiazepines, atypical antipsychotics

Treatment of pain

- NSAIDs rarely of benefit for the FMS pain, but may help with joint or other pain.
- Tramadol (with or w/o acetominophen) works in DB, R, PC trial from Robert Bennett in Portland
- Narcotics best avoided or clearly tied to functional improvement (low levels of u-opioid receptors in FMS)
- Massage, hot and cold, acupuncture may work for some - patient in control
- Centrally acting analgesics like dextromethorphan and ketamine work on NMDA mechanism.

More pain treatments

- Duloxitine (Cymbalta)
- Milnacipram (Savella)
- Pramipexole (Mirapex)
- Pregabalin (Lyrica)
- Gabapentin (Neurontin)
- Fluoxetine (Prozac)

- The key may be to treat symptoms aggressively and completely at the initiation of pain - Newsweek, May 30, 2007

Duloxetine and milacipram

- Balanced epi and norepi reuptake inhibitor which seems to be more effective than either more selective agents like amitriptyline or nortripyline or even citralopram or fluoxetine.
- 60mg twice daily was more effective than lower doses in reducing pain and improving function
- Fairly high number of drop-outs and side effects.

- Arnold LM Arthritis and Rheuma 2004;50:2974-2984

Alpha 2 delta ligands - gabapentin or pregabalin

- Reduces release of excitatory neurotransmitters glutamine, noradrenaline, substance P
- Both gabapentin and pregabalin studied and found effective
- Only pregabalin approved for use in FMS

- Arnold Arthritis and Rheum 2007;56:1336-1344 (gabapentin)
- Crofford LJ Arthritis and Rheum 2005;52:1264-1273 (pregabalin)
- Crofford LJ Arthritis Rheum 2006;54:4118 (FREEDOM results; pregabalin)

Gabapentin

- 30% reduction in pain severity with median dose of 1800mg per day (Mean dose of 1700) with improvement in sleep, pain and FIQ.

Pregabalin

- Improvement at the 450mg per day dose with >50% reduction in pain from baseline in 30% of pts; differing from placebo or lower doses of drug (150 or 300mg)
- Other trials have shown statistical improvement at the lower levels of drug in pain, patient global impression and FIQ.
- 25% drop out rate secondary to AEs

Dopamine agonists - pramipexole

- Studied in group of FMS all-comers with good results even when used with other drugs.
- High doses required.

Improvement of sleep

- Sleep hygiene
- Tricyclics
- Cyclobenzeprine
- Benzodiazepines

What doesn't work

- Treatment with steroids
- Treatment of "Lyme disease"
- Treatment like this is lupus
- Treatment with antivirals
- Treatment to totally relieve pain
- Not involving the patient - this is like treating obesity

Treatment of depression

- Clearly accompanies chronic pain and loss of function
- History of depression more common in pt with FMS; anxiety may effect the TP count
- Large percentage of pts with FMS have a history of PTSD or abuse (but RA control are high as well).
- Duloxetin - a treatment of pain without effect on depression.

Alternative therapies and FMS

- **Certainly empower the patient**
- Diets
- Massage
- Acupuncture
- Chiropractic
- Chinese medicine
- Nutraceuticals
- Balnitherapy

Excercise

- Unclear why it works - endorphins, endocrine effects, muscle health
- Fascinating story of people who exercise regularly
- Hard prescription - must be done consistently, aerobically and indefinitely. Study after study support its benefit in terms of pain reduction and more importantly, functional status. Many types of exercise have been studied; PT is not equivalent nor is stretching alone adequate

Cognitive Behavioral therapy (we need a better name)

- Focuses on the pts maladaptive behaviors in response to chronic pain.
- Educates patients to living with pain and in spite of pain rather than on removing pain; turns to functional restoration
- Encourages patients to be in control of their destiny.
- The problem - time intensive, maybe not available locally, potentially expensive.
- But it has been shown time and again to work - some programs involve family as well.

To reiterate

- Exercise
- Cognitive Behavioral Therapy

- These two modalities work in making patients more satisfied and more functional.

Some successful strategies around work

- Work capacity assessments
- Work hardening programs
- Behavioral therapies
- Vocational changes
- Functional restoration program

So what would we do for our woman?

- Treat acute pain aggressively
- Analyze sleep
- Identify drivers - psychotherapy? Deconditioning? Vit D deficiency?
- Involve family
- Institute an exercise program as a prescription drug
- Explore what pain means to her and what pain and fatigue prevents her from accomplishing.

In summary

- Controversial conditions that affect many people, a disproportional number are women
- Much more attention in the lay and medical literature with the development of FDA approved treatment.
- Limited ability of traditional medicine to make a difference in many patients symptoms; frequent perception as disabled
- Treatment focus is on helping patients live despite the pain and with preservation of function
- Further understanding of neurobiology of chronic pain may lead to better treatment

Or as summarized by Daniel Clauw, MD

- This is primarily a neural disease and "central" factors play a critical role
- This is a polygenic disorder
- There is deficiency of NA/S activity and excess levels of excitatory neurotransmitters (G, SP)
- Therefore drugs aimed at periphery as unlikely to be extremely efficacious
- There will be subgroups of FMS
- Drugs that raise norepinephrine and serotonin will be efficacious in some; lowering excitatory neurotransmitters will help in others.

- Lack of exercise or sleep increases pain and other somatic sx, even in normals
- How FM pts think about their pain (cognition) may directly influence pain levels.
- Exercise, sleep hygiene and other behavioral interventions help for biologic reasons
- Cognitive therapies are effective in FM and have a biologic substrate

Thank you!

Bibliography

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Questions - 1

- FMS is considered what kind of a pain problem?
- Wide spread allodynia due to central sensitization and disturbances in pain modulation, reaction to pain and pain behavior

Questions - 2

- What are the two (maybe three) treatments that have been shown to work in fibromyalgia?
- Exercise, CBT and pregabalin

Questions - 3

- Pain and fatigue are exceedingly common in FMS; what are other features of the condition?
- Nonrestorative sleep, IBS, IBIS, paresthesias, stiffness, cold extremities, headaches, vulvodynia, dry eyes

Questions - 4

- What neurotransmitters are overactive in FMS? Which are deficient?
- NMDA, glutamine, substance P
- Serotonin, norepinephrine, dopamine

Questions - 5

- What are some of the drivers of FMS?
- Sleep disorders, hypothyroidism, vit D deficiency, OA, RA, SLE, myopathies, sleep apnea