UPMC Rehab Grand Rounds

Physical Medicine and Rehabilitation Approach to Fibromyalgia

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Clinical Vignette History

PC is a 51-year-old female who was seen in the office for total body pain. The symptoms began with tightness and pain in the neck associated with headaches. She denied any trauma or injury. She dates the onset of symptoms to her twenties after she stayed up late during final exams. The symptoms would reappear during stressful times and she had not been able to seek treatment for her symptoms until recently. Over the last year, she had been taking care of her ailing mother who is suffering from end-stage Alzheimer's disease. PC has not been sleeping well during the night. In addition to her neck pain and headaches, she reports occasional hip pain and electrical sensations down her legs. Her hands and finger joints are achy and stiff in the morning and she is tired all the time.

Her PCP screened for rheumatological and endocrine diseases yet all results were normal including x-rays of her neck, back, and hands. She was prescribed antidepressant medications to help cope with her mother's illness, yet she did not fill her prescription because she felt her emotional state was not beyond the expected sadness of caring for her dying mother. She also was concerned about the electrical sensations down her legs. The patient sought a second opinion at the UPMC Physical Medicine and Rehabilitation clinic. On examination, PC appeared mildly overweight and was tearful when she spoke about her mother. Her cervical and lumbar range of motion were full although her movements were stiff. Multiple tender points were noted during her examination. She had full range of motion in her extremities and there was no joint swelling or warmth noted. She was hypersensitive to touch in her arms and legs in a non-dermatomal distribution. Motor testing and reflexes were intact. PC is hopeful that, at the conclusion of this visit, her symptoms can be significantly improved.

Incidence:

It is estimated that fibromyalgia syndrome affects 2% to 4% of the general population in the United States.[1] Fibromyalgia increases with age and is three times more prevalent in women as compared to men. It tends to develop in early to mid adulthood and patients with fibromyalgia typically incur high medical costs and have a high rate of disability.[2] Increased health care costs are due to the high occurrence of insurance claims for prescription medications, as well as frequent visits to general practitioners because of comorbidities associated with the disease (i.e. pain, sleep disturbance, and depressed mood).[3]

Diagnosis:

Fibromyalgia was first coined by Gowers in 1904 when he used the term "fibrositis" to describe inflammation of subcutaneous tissue or fibrous tissue.[4] This term was expanded by Hench who described fibromyalgia as simply "pain and no physiologic explanation," and the diagnosis was made by ruling out all other possible explanations.[5] In 1979, Smythe developed the criteria for diagnosing fibromyalgia that included tenderness in 12 of 14 tender points using 4 kg of manual pressure, along with diffuse pain for three months' duration, disturbed sleep, trapezius skin roll tenderness, and normal laboratory findings.[6] These criteria were used to define what we now term "fibromyalgia syndrome." In 1990, the American College of Rheumatology defined fibromyalgia as having diffuse or widespread pain for greater than three months' duration with tenderness in 11 of 18 "tender points" on the body.[7] Widespread pain is defined as pain in the axial skeleton, including cervical, thoracic or low back pain, as well as pain in all four body quadrants. The criteria of widespread pain along with 11 of 18 tender points have a sensitivity and specificity near 85%.[8] The presence of a second clinical diagnosis does not exclude the diagnosis of fibromyalgia and therefore it is not a diagnosis of exclusion.[8]

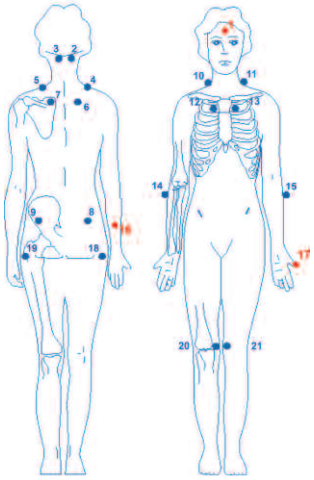

Figure 1: This diagram shows the "tender points" (blue) that are characteristic of fibromyalgia. The criteria of fibromyalgia require tenderness in 11 of the 18 total possible tender points. The control points are shown in red and are not tender to palpitation compared to other points.

The illustration is used with permission from Dr. Terrence Starz.

Adapted from The Manual Tender Point Survey, D. Sinclair, T. Starz, D. Turk; FMOnline, October, 2005, National Fibromyalgia Association website: www.fmaware.org/site/News2?page=NewsArticle&id=6263

Clinical Presentation

Common symptoms of fibromyalgia include allodynia (pain from a stimulus that normally should not cause pain), hyperalgesia (an exaggerated pain response from a painful stimulus), and temporal summation (increasing pain from repetitive pressure).[8] Other associated symptoms include disturbance of sleep, fatigue, decreased cognitive function with short-term memory loss, decreased alertness, and problems with multi-tasking.[8] Some comorbid conditions associated with fibromyalgia are depression, anxiety, chronic fatigue, inflammatory bowel syndrome, restless leg syndrome, migraine headaches, temporomandibular dysfunction, and female urethral syndrome.[8]

There is great controversy within the medical community about whether fibromyalgia is a true disease. Hadler argued that fibromyalgia should not be labeled as a "real disease" because it "lacks biomedical evidence" for its etiology.[9] Others such as Wolfe believe that labeling fibromyalgia as a disease produces "medicalization" of the symptoms defined as a condition where non-pathologic symptoms are treated as medical problems and this promotes patient victimization with psychosomatic symptoms.[2] The lack of widespread acceptance of this disorder is thought to place a significant social burden on fibromyalgia patients and the medical community.[9] However, advancements in the research of chronic pain mechanisms have enlightened clinicians and researchers to consider fibromyalgia as a true disorder.

Physical Exam

One of the criteria for diagnosing fibromyalgia is the presence of tender points as shown in Figure 1. A detailed exam should be conducted to rule out other possible etiologies, including rheumatologic, neurological, endocrine, and infectious causes.

Differential Diagnosis

The differential diagnosis is large and is summarized in Table 1. Chronic fatigue syndrome and myofascial pain syndrome can mimic the presentation of fibromyalgia. Chronic fatigue syndrome (CFS) is defined as clinically unexplained and persistent or relapsing fatigue for at least six months.[7] The fatigue in CFS is not a result of exertion and is not relieved by rest. CFS symptoms should include at least four of the following: unusual post-exertional malaise, unrefreshing sleep, impaired memory/cognition, headache, muscle pain, joint pain, sore throat or tender lymph nodes.[10] Epstein-Barr viral titers may be elevated in this condition.

Myofascial pain syndrome is characterized by the presence of "trigger points" located within a block of skeletal muscle that are hypersensitive and hyperirritable. It has been shown that these trigger points have abnormal spontaneous electrical activity when tested with EMG. This represents a dysfunctional muscle spindle which releases excessive amounts of acetylcholine at the motor endplate causing sustained contraction and increases the metabolic demands of the muscle. One important characteristic found in trigger points of myofascial pain syndrome is local twitch response which is a quick contraction of muscle fibers. This response is produced when one grabs a taut band of muscle believed to be a localized trigger point in a perpendicular direction to the muscle fibers. Studies show that eliciting one of these responses during dry needling produces a therapeutic benefit.[11] The difference between the trigger points in myofascial pain syndrome and the tender points of fibromyalgia is that trigger points may lead to referred pain, whereas tender points are just localized to one area.[12] Because fibromyalgia and myofascial pain syndrome both involve the soft tissues, trigger points also can be found in fibromyalgia. These disorders are summarized in Table 2.

TABLE 1: Differential Diagnoses of Fibromyalgia

- **Chronic Fatigue Syndrome, Myofacial Pain Syndrome**
- **EBV**
- **Hepatitis C**
- **HIV**
- **Hyperthyroidism, Cushing's Syndrome**
- **Hypothyroidism**
- **Lyme Disease**
- **Polymyalgia rheumatica**
- **Rheumatoid arthritis**
- **Sjogen's syndrome**
- **Systemic lupus erythematosus**

TABLE 2: Symptom Criteria for Diagnosis

Fibromyalgia

- Diffuse or widespread pain (>3 months)
- At least 11 of 18 "tender points" per ACR guidelines

Chronic Fatigue Syndrome

- Clinically unexplained, persistent or relapsing fatigue (>6 months)
- At least four of the following symptoms: post-exertional malaise, unrefreshing sleep, impaired cognition, headache, muscle pain, joint pain, sore throat, tender lymph nodes

Myofascial Pain Syndrome

- Palpation of "trigger points" that produce diffuse pain and/or referred pain that is away from the affected area

Pathophysiology

Biomarkers of Fibromyalgia

There are several biomarkers that have been linked to fibromyalgia. Cytokines, neuropeptides, HPA/stress response hormones, and the intrinsic analgesic system involving endorphins have all been studied in the quest to determine the pathophysiology of fibromyalgia. It has been hypothesized that pro-inflammatory cytokines (i.e. IL-1, IL-6, IL-8, and TNF-alpha) worsen symptoms of fibromyalgia in response to stress. Although fibromyalgia is not an inflammatory disorder, several studies have shown that many symptoms (i.e. hyperalgesia, fatigue, sleep disturbance, fever, pain, stress response, anxiety, myalgia, cognitive dysfunction) are influenced by pro-inflammatory cytokines.[13] Low levels of serum prolyl endopeptidase (PEP) have been correlated with severity of pressure hyperalgesia in fibromyalgia. Pro-inflammatory cytokines also have been shown to increase secretion during sickness or infection with associated characteristic behavior changes such as decreased motivation to eat, listlessness, fatigue, malaise, loss of interest in social activities, and sleep disturbance.[13] These biomarkers have not been shown to specifically correlate with fibromyalgia, but seem to be involved in many chronic pain disorders such as fibromyalgia, complex regional pain syndrome, and myofascial pain syndrome.[14]

Etiological Mechanisms: Central Sensitization and Dysfunctional Pain Inhibition

Paiva et al. described central sensitization as the main pain pathway thought to be involved in fibromyalgia.[15] The ascending pathways, including the dorsal horn neurons and brain, are believed to be the main sites of modulation and amplification of pain in fibromyalgia as compared to peripheral sensitization of nociceptors involved in inflammatory pain pathways.[15] There may be an increase in substance P in the CSF in fibromyalgia patients that leads to an increased number of pain neurotransmitters in the spinal cord. Substance P is thought to cause spatial pain spreading from activation of interneurons, thus lowering the excitatory synaptic threshold.[15] However, substance P is not specific for fibromyalgia thus it is likely only a biomarker for chronic pain.[14]

There also has been evidence that fibromyalgia patients have decreased thalamic blood flow on PET scans when compared to normal controls, and some studies show increased areas of brain activation on functional brain MRI when compared to normal controls.[16, 17] This further supports the hypothesis of a central nervous system mechanism that occurs when patients are suffering from fibromyalgia.

Treatment:

Pharmacologic treatment is typically directed to three main categories: antidepressants, anticonvulsants, and analgesics. Antidepressants include tricyclics, antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin and norepinephrine reuptake inhibitors (SNRIs). These medications are primary amines that act to inhibit the re-uptake of serotonin and norepinephrine and have been shown to improve sleep quality with some improvement in tender points, stiffness, and fatigue.[8] SNRIs are first-line agents and are preferred over TCAs due to the side-effect profile of TCAs, which includes dry mouth, weight gain, urinary retention, and more serious cardiac arrhythmias. Recent studies show that duloxetine at 60 mg daily or at 60 mg BID improved pain control in fibromyalgia patients regardless of whether the patient had depression. A recent multicenter, double-blind placebo-controlled study showed that another SNRI, milnacipran, at doses of 100 mg to 200 mg a day significantly improved symptoms of pain and overall physical function in patients with fibromyalgia. The main adverse effects of milnacipran reported were nausea, constipation, and dry mouth.[1]

SSRIs such as paroxetine and fluoxetine are effective in fibromyalgia. However, citalopram did not prove to be effective. Thus there are mixed results using SSRIs in treatment for fibromyalgia.

Anticonvulsants such as pregabalin have shown promising results to help improve symptoms associated with fibromyalgia. Pregabalin is a GABA analog with anesthetic, anticonvulsant, and anxiolytic properties. It does not work on GABA receptors, but rather on the alpha-2-delta subunit of the presynaptic calcium channels, preventing the release of excitatory neurotransmitters, including glutamate, norepinephrine, and substance P.

Several studies have shown an improvement in pain compared to placebo with doses ranging from 300 mg to 600 mg a day.[18] Common side effects include dizziness, sleepiness, weight gain, and peripheral edema.[19] A new drug, sodium oxybate (a gamma-aminobutyric currently FDA-approved for treatment of cataplexy in people with narcolepsy) was recently tested in a multi-center randomized controlled trial and showed significant improvement in pain, fatigue, and restorative sleep. These findings were found when given doses of 4.5 gm/night to 6 gm/night with side effects including nausea, vomiting, dizziness, and somnolence.[18]

Tramadol is a centrally acting analgesic with weak mu-opioid activity and serotonin and norepinephrine reuptake inhibition. Tramadol, in combination with acetaminophen, improved overall pain scores, yet this medication should be avoided when using other serotonin-acting medications to avoid serotonin syndrome. NSAIDS have been used for treatment of fibromyalgia with minimal side effects.[8]

Non-pharmacological treatments of fibromyalgia include exercise, stress management techniques, and acupuncture. Once-daily supervised aerobic exercises have been shown to improve tender points and overall global well being.[8] Schneider et al. showed in a meta-analysis that light aerobic exercise improved symptoms of fibromyalgia.[20] Cognitive behavioral therapy (CBT) is a goal-oriented psychotherapy that focuses on self management and relaxation skills that can be useful in this condition.[8]

Acupuncture and complementary medicine are becoming more popular to treat fibromyalgia symptoms.[21] Acupuncture is thought to have existed since the Xia Dynasty (2000-1500 B.C.) and was

TABLE 3: Treatments for Fibromyalgia

Pharmacological	Non-pharmacological
Antidepressants: Tricyclics SSRIs SSNRIs	Light aerobic exercises Yoga Tai chi
Anticonvulsants: Pregabalin	Stress management Behavior modification
Analgesics: Tramadol Sodium oxybate	Acupuncture

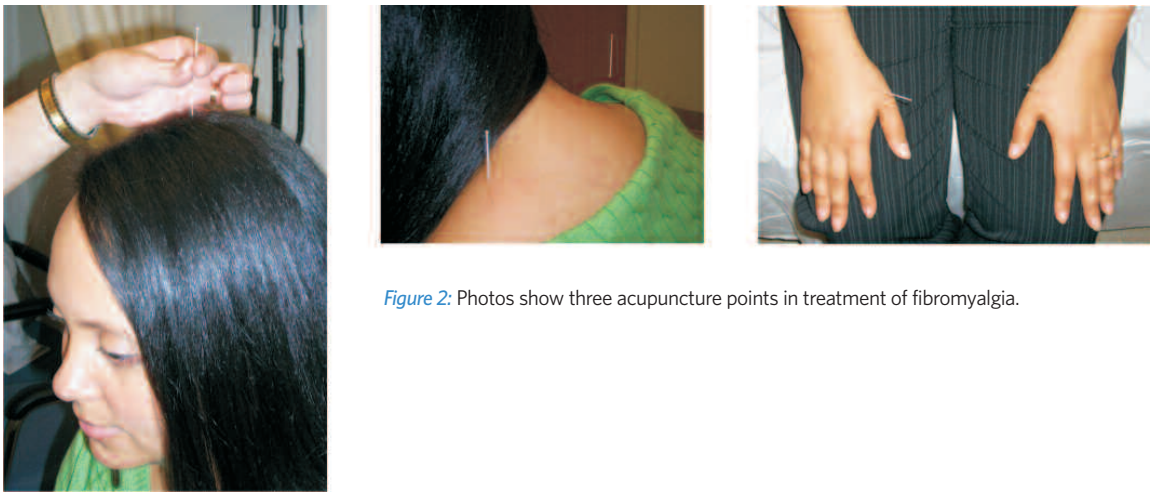

Figure 2: Photos show three acupuncture points in treatment of fibromyalgia.

eventually introduced to the United States in the 18th century by Sir William Osler who recommended acupuncture for the treatment of lumbago. It is believed that Qi is a life force that circulates throughout the body. Pain is thought to arise from blockage of Qi flow or an imbalance of the Yin and Yang portions of the body. Needling is thought to release endogenous endorphins to provide pain relief and, when passed through deep fascia, is thought to create sensory signals via mechanotransduction.[22]

There is a paucity of research studies validating acupuncture for fibromyalgia. In 2005, Harris et al. conducted a randomized control trial to determine if needling a specific location corresponding to a particular acupuncture meridian had an effect on pain fatigue and/or physical function.[23] The results showed that needling made little difference in outcomes.

In the NIH Consensus Statement on Acupuncture published in 1997, expert review of the literature showed improved outcomes when using acupuncture for postoperative pain, chemotherapy-induced and pregnancy-related nausea, and relief of dental pain.[10] However, while there were single studies that showed decreased pain in fibromyalgia, there were others that dispute the role of acupuncture in this condition.

Many of the studies had small cohorts and diverse acupuncture treatments. Acupuncture is often added to other physiatric treatment options due to the unpredictable success rates of available Western approaches and the frequent intolerance of patients to medications. Due to its holistic philosophy, acupuncture can address the multidimensional symptoms of fibromyalgia. See Table 3 and Figure 2.

Clinical Vignette Outcome

To help regulate sleep, trazadone was prescribed titrating up to 100 mg daily, but this did not help. PC was switched to nortriptylline 100 mg at night with improvement of insomnia and headaches. She also took over-the-counter ibuprofen 400 mg as needed for myalgias. She was prescribed pool therapy for long-term, low-impact aerobic conditioning in a warm environment and concomitant acupuncture totaling 10 treatments that were administered to her neck and shoulders. She was seen by a massage therapist once a month and began to do home yoga exercises. All of the above interventions enabled her to be more active and less stiff in the mornings. Her mother has since passed away and PC has returned to work after taking time off caring for her mother. Recently, someone recommended that she should join an online fibromyalgia support group.

Overall, fibromyalgia is a chronic and controversial diagnosis that is treated with a number of modalities. Successes have been observed using both Western and/or alternative medicine techniques.

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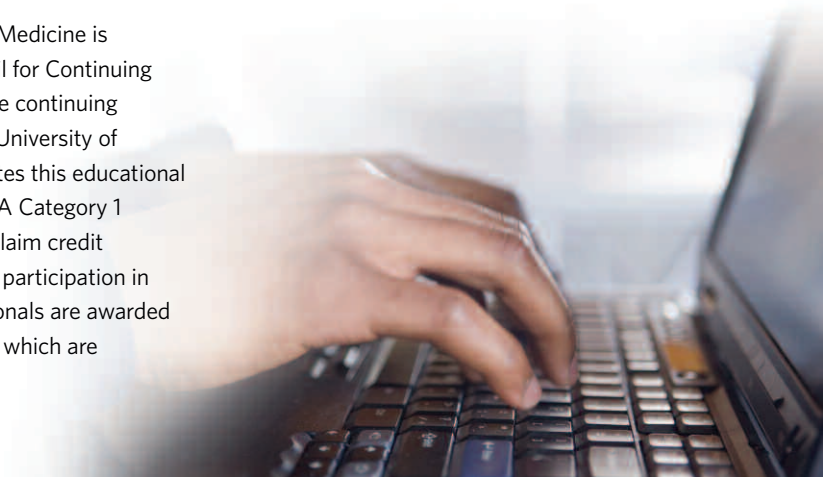

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