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Fibromyalgia - case report

Iwona Filipczak-Bryniarska[1], Jarosław Woroń[2], Justyna Kleja[1], Krzysztof Bryniarski[3], Jerzy Wordliczek[1]

[1] Departament of Chronic Pain Treatment and Palliative Care of the Jagiellonian University Medical College, Kraków, Poland
[2] Chair of Pharmacology Department of Clinical Pharmacology of the Jagiellonian University Medical College, Kraków, Poland
[3] Department of Immunology of the Jagiellonian University Medical College, Kraków, Poland

Summary

Fibromyalgia is a chronic syndrome that causes widespread musculoskeletal pain and stiffness throughout the connective tissues that support and move the bones and joints. Pain and localized tender points occur in the muscles, particularly those that support the neck, spine, shoulders, and hips. Moreover the disorder includes fatigue, depression, sleep disturbances and constipation. A combination of treatments including medications, patient education, physical therapy, and counseling are usually recommended. *Anestezjologia i Ratownictwo 2011; 5: 45-51.*

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Introduction

Fibromyalgia syndrome (FM) is a chronic pain syndrome, characterized by generalized pain, tender points, disturbed sleep, and pronounced fatigue. Pain in FM is consistently felt in the musculature and is related to sensitization of central nervous system (CNS) pain pathways [1].

The pathogenesis of FM is unknown, however abnormal concentration of neuropeptides of CNS and alterations of the hypothalamic-pituitary-adrenal axis have been described [2]. There are findings indicating a gene in the serotoninergic, dopaminergic, and catecholaminergic systems in the etiology of FM. These polymorphisms all affect the metabolism or transport of monoamines, so they might lead to disturbed sensory processing and an altered stress response [3].

There is a large body of evidence for generalized lowering of pressure pain thresholds in FM patients. Importantly, this mechanical allodynia in patients with FM is not limited to tender points but appears to be widespread. In addition, almost all studies of patients with FM have shown abnormalities of pain sensitivity while using different methods of neurosensory testing [4].

By definition, FM encompasses the extreme end of chronic widespread pain in the general population and is a chronic illness that disproportionately affects women (9:1). Like many other syndromes, FM has no single specific feature but represents a symptom complex of self-reported or elicited findings. In 1990, the American College of Rheumatology (ACR) published diagnostic criteria for FM that include chronic widespread pain (>3 months) and mechanical allodynia in at least 11 of 18 tender points. Most tender point sites are located at tendon insertion areas and have shown few detectable tissue abnormalities (Figure 1). Apart from musculoskeletal pain and mechanical tenderness, most FM patients also complain of insomnia, fatigue, and distress. The familial coaggregation and frequent

comorbidity of FM with major mood disorders also suggests a role for neuroendocrine and stress-response abnormalities [4-7].

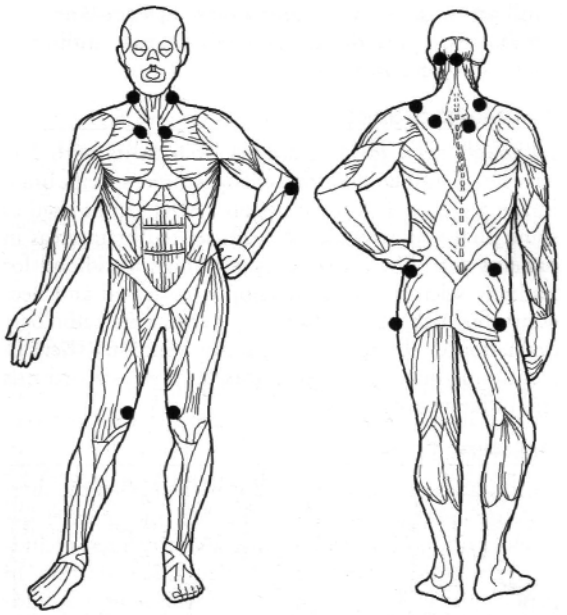

Figure 1. Locations of tender points

- Occiput, at insertions of the suboccipital muscle
- Lower neck (posterior, at the transverse processes of C5-C7
- Trapezius (anterior), at midpoint of the upper border
- Supraspinatus (anterior), above the scapular spine near the medial border
- Anterior chest, second costochondral junction
- Lateral epicondyle, 2 cm distal to epicondyles
- Gluteal, upper outer quadrants of buttocks
- Greater trochanter, posterior to the trochanteric prominence
- Knees, at medial fat pad proximal to the joint line

Adapted from Current Diagnosis &Treatment Pain Jaime H. Von Roenn et al.

Case

A 57-year old woman was admitted (May 2009) to the Department of Chronic Pain Treatment, Palliative Care of the Jagiellonian University Medical College for diagnostic purpose. The patient suffered from chronic widespread musculoskeletal pain which was reported in all four quadrants of the body as well as the lower back with the presence of multiple myofascial tender points. It had been present for four years and in particular for at least 10 months. The pain was described as constant and dull, typically coming from the muscles and sometimes it was intense burning. It was quite often worse in the morning, and muscle groups that are used repetitively may have hurt more. The pain increased with physical activity, cold or damp weather, anxiety, and stress. She often woke up tired, even though she seemed to get plenty of sleep. Apart from that she complained of chronic fatigue, morning stiffness, sleep problems, headaches, constipation, numbness in hands and feet, depression, and anxiety. The quality of life and different levels of psychosocial functions deteriorated because of the symptoms. Since 1990 she had been treated for Parkinson's disease, at first with L-Dopa, then when drugs failed to control the symptoms of this disease the brain surgery (right and left thalamotomy). At present she is treated with L-Dopa. In 2006 she was diagnosed in the direction of rheumatoid arthritis and borreliosis (Lyme disease). Finally these diagnoses were excluded. During her stay at the clinic, Mrs. S. willingly cooperated with the medical personnel. She was outwardly open, pleasant and seemingly at ease. Psychological assessment revealed a myriad of emotional difficulties which had troubled her for the past 4 years. In her view the most difficult was the feeling of helplessness. Her illness particularly affected her image of herself as a physically strong individual (she was an active sportswoman in her youth). She felt her active life had been prematurely curtailed and that she was now dependant on others. Her childrens' involvement simultaneously caused feelings of gratitude and guilt that she could not repay them. The patient had trouble in finding words to describe her experiences. She believed that people outside of her family might think her illness to be imaginary and her to be emotionally unstable. This increased her feeling of psychological isolation. She would cry when talking about the most recent years of her life. Physical suffering, fear stemming from an as yet undiagnosed illness, dependency, tiredness and the belief that her active life was at an end resulted in increasing depression. Her tolerance for stress decreased and she lost control over her feelings of anger. Her dominant feelings were those of emptiness, hopelessness, extreme sadness, resignation and grief, which resulted in an exacerbation of her pain symptoms.

At the time of admission the examination sho-

wed: characteristic gait by short steps, with feet barely leaving the ground, producing an audible shuffling noise, slowness, increased muscle tone with typical "cogwheel" rigidity when the limb was passively moved, resting tremor in the upper right limb, micrographia (small, cramped handwriting), deliberation symptoms, symmetrical pairs of tender points (back of the head, between the shoulder blades, top of the shoulders, front sides of the neck, upper chest, upper hips, sides of the hips, inner knees). The syndrome was diagnosed on the basis of two diagnostic criteria of fibromyalgia (widespread pain lasting at least three months and 16 positive tender points). In our department she was treated with tramadol, mirtazapine, tender point injections with lidocaine solution and multidisciplinary rehabilitation.

Discussion

Scientists estimate that fibromyalgia affects 4% of population. For unknown reasons, between 80 and 90 percent of those diagnosed with fibromyalgia are women; however, men and children also can be affected. Most people are diagnosed during middle age, although the symptoms often become present earlier in life. Frequency of FM occurs along with age (8% of women above 70 years old). FM is a clinical syndrome that encompasses patients at the extremes of chronic musculoskeletal pain in the general population [8].

A review of 10 studies from different western countries reported a prevalence of FM according to the ACR criteria in the general adult population of between 0.7% and 3.3%, 20 with a prevalence in women between 1.0% and 4.9%, and in men between zero and 1.6%. It has been suggested that the male-female ratio reported in the literature may be biased, because most of the data comes from tertiary care centers. In the United States, about 5 million people are thought to be affected [9]. Although the 1990 ACR diagnostic criteria for FM have shown 85% specificity for this illness, they do not mean that FM exists only in persons fulfilling these definitions. Similar to systemic lupus or rheumatoid arthritis criteria, FM criteria were narrowly defined for study purposes. For clinical use, FM should be considered in all patients who have widespread pain and tenderness but who do not have structural or inflammatory tissue abnormalities. However like many chronic pain syndromes, FM becomes clinically relevant frequently after affective distress has occurred or a significant dysfunction. At this crucial point, FM sufferers often become patients and seek medical care. However, epidemiologic research has clearly shown that secondary gain or malingering do not seem to play a major role for FM patients seeking health care. Most important for the diagnosis of FM is widespread chronic musculoskeletal pain of unknown origin that has led to functional impairment or distress. Pain has to be reported in all four quadrants of the body as well as the lower back. However, the pain does not have to be in all body quadrants at the same time. Pain is considered to be chronic when it has been present for at least 3 months. This syndrome is frequently associated with several other comorbid conditions, such as migraine, chronic fatigue syndrome, depression, irritable bowel syndrome, restless leg syndrome and temporomandibular joint dysfunction. There are no specific laboratory abnormalities detectable in patients with FM [7,10-13].

Fibromyalgia can be difficult to treat. A combination of treatments including medications, patient education, physical therapy, and counselling are usually recommended. Treatment of patients with chronic widespread pain needs to be individually tailored. This includes the assessment of biopsychosocial abnormalities, which are readily detectable in most patients with FM. Importantly, the identification of pain generators is essential for an effective treatment plan. Recently, a large number of drugs and interventions have been tested in controlled trials for their efficacy in FMS, and meta-analyses have been written on most of these interventions.

We presented drugs recommended by Food and Drug Administration (FDA) & other therapeutic possibilities.

In 2007, the FDA approved Pregabalin as the first drug for the treatment of fibromyalgia. Pregabalin is a medication developed to treat neuropathic pain in dose 450 mg/d. A meta-analysis of the trials with pregabalin and gabapentine also showed effects on reduction of pain, improved sleep, and quality of life [14].

In June 2008, a second drug, duloxetine which was previously approved for treating depression, was FDA approved for treating fibromyalgia as well, dose 30-60 mg/d.

In 2009 the FDA approved milnacipran for the treatment of fibromyalgia. Comparing the drugs licensed by the U.S. FDA for FM-duloxetine, milnacipran, and pregabalin - we found that the three drugs were

superior to placebo, except for duloxetine for fatigue, milnacipran for sleep disturbance, and pregabalin for depressed mood [15]. Adjusted indirect comparisons indicated no significant differences for 30% pain relief and dropout rates due to adverse events for the three drugs. Side effect profiles differed, as we had expected [13].

Studies show that antidepressants in low doses can decrease depression, relax craniofacial and skeletal muscles, improve sleep quality, and release pain-killing endorphins. Most patients with FM respond to low-dose tricyclic antidepressants, such as amitriptyline as well as cardiovascular exercise, cognitive-behavioral therapy, patient education, or a combination of these therapies.

Some examples of tricyclic medications used to treat fibromyalgia include amitriptyline hydrochloride, nortriptyline. Amitriptyline has been proven useful for the treatment of fibromyalgia. Tricyclic antidepressants (TCA) are effective for pain, mood, function, and quality of sleep. Sometimes we use another group of antidepressants. Doxepin and mirtazapine are an example. If the patient has not taken a TCA before, the following drugs and dosages can typically be used: amitriptyline 10 mg at bedtime; nortriptyline 10 mg at bedtime, doxepin 10 mg at bedtime, mirtazapine 15 mg at bedtime. Some patients find TCA unacceptable owing to anticholinergic side effects, such as tachycardia, dry mouth, and constipation. Most TCA cause some weight gain, but in certain patients this may amount to 20% of their initial body weight and is thus unacceptable. Several trials have demonstrated effectiveness of amitriptyline (10 to 50 mg) in trials lasting 6 to 12 weeks [11]. Some fibromyalgia patients are intolerant of TCA. If a tricyclic antidepressant fails to bring relief, doctors sometimes prescribe a selective serotonin reuptake inhibitor (SSRI). By promoting the release of serotonin, these drugs may reduce fatigue and some other symptoms associated with fibromyalgia. The group of SSRIs includes fluoxetine, paroxetine. Never do SSRIs such as citalopram or escitalopram seem to work for pain as well as the older SSRIs. SSRIs may be prescribed along with a tricyclic antidepressant. Studies have shown that a combination therapy of the tricyclic amitriptyline and the SSRI fluoxetine resulted in greater improvements in the study participants' fibromyalgia symptoms than either drug alone. Less strong evidence is available for the effectiveness of selective serotonin reuptake inhibitors, such as nuoxetine, in managing FM pain. Serotonin and norepinephrine reuptake inhibitors, such as venlafaxine (150 to 300 mg/d) as well as mentioned above duloxetine (60 mg/d), demonstrated improvement of pain, sleep, and function in FM patients. Selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and anticonvulsants have been found to be moderately effective. Some antidepressants raise levels of both serotonin and norepinephrine and are therefore called mixed reuptake inhibitors. Examples of these medications include venlafaxine (150 to 300 mg/d), duloxetine and milnacipran. In general, these drugs work better for pain than SSRIs, probably because they also raise norepinephrine, which may play an even greater role in pain transmission than serotonin [15,16]. Unless the patient has a concomitant major depressive illness, scientists advocate selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine because they may exacerbate insomnia and cause agitation. Benzodiazepines can sometimes help people with fibromyalgia by relaxing tense, painful muscles and stabilizing the erratic brain waves. Tramadol has been effective in patients with FM. There is, however, no evidence that nonsteroidal anti-inflammatory drugs (NSAIDs) improve FM pain, although they may be useful when combined with tricyclic antidepressants. There is no good evidence to recommend opioids for FM pain. However, opioid analgesics should be considered after all other medicinal and nonmedicinal therapies have failed [11].

Thus, which drug to start with is an individual choice, depending on the patient's symptoms, comorbidities, and preferences. There is weaker evidence for the effect of some other drugs, such as tramadol, and for some drugs there is good evidence that they are not effective (Table 1) [7].

Some doctors have reported success using tender point injections. Patients that have been injected at the tender points with lidocaine solution have experienced pain relief. Tender point injections can help when used with other relief methods [17].

Nonpharmacological treatment contains:

1. Physical therapy - cardiovascular aerobic exercise is one of the most effective treatments for FM. Pool exercise is usually well tolerated and especially helpful. In addition, aerobic exercise including cycling, dance, and walking in-doors significantly improves FM pain and function. The combination of aerobic exercise with education can significantly improve physical function,

Table 1. Drug with positive effects on FM in randomized controlled trials

Drug with positive effects on FM in randomized controlled trials			
Drug	Strength of Evidence*	Recommended Dose Range	
Amitriptyline	1a	10–50 mg	Large body of evidence, frequent side effects
Duloxetine	1a	30-60 mg	FDA approved, long-term efficacy shown
Milnacipran	1a	25-200 mg	FDA approved
Pregabalin	1a	150-450 mg	FDA approved, long-term efficacy shown
Gabapentin	1b	1200-2400 mg	One large RCT
Cyclobenzaprine	2a	10-40 mg	An antidepressant and muscle relaxant. Not widely available outside the United States. RCTs included in this meta-analysis were short-term and of low quality.
Fluoxetine	2a	2-60 mg	Three small RCTs
Paroxetine	2b	20 mg	One large RCT
Tramadol	2b	50-300 mg	Two RCTs of tramadol 150 mg/acetaminophen (paracetamol) 1300 mg

* Oxford classification of levels of evidence: 1a: systematic review (with homogeneity) of randomized controlled trials (RCTs); 1b: individual RCT; 2a: systematic review of cohort study or low-quality RCT; 2b: Individual cohort study or low-quality RCT.

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global well-being, fatigue, and sleep**.** Improved fitness through exercise is recommended. The best way to begin a fitness program is to start with short sessions of just a few minutes of gentle, low-impact exercises such as walking and swimming. The length of each session can be increased slowly, as tolerated. Attempts at keeping to an exercise program often fail because they are begun too aggressively, with sessions that are too long or too intense. Starting out slowly and gently can help ease the patient into an effective program he or she can stick with.

A review of 46 exercise treatment studies in FM reported that the strongest evidence was in support of aerobic exercise. Busch and coworkers systematically reviewed 34 studies. Meta-analysis of six studies provided moderate-quality evidence that aerobic-only exercise training at intensity levels recommended by the American College of Sports Medicine has positive effects on global well-being, on physical function, and possibly on pain. A recent study showed that self-selected physical activity reduces FM symptoms in minimally active adults. Interestingly, certain biomarkers including proinflammatory cytokines and cortisol were decreased after exercise, specifically after an aquatic program in warm water over a period of 4 months, 41 suggesting that exercise may work by its anti-inflammatory effects and by better regulation of the cytokine-HPA axis feedback. A meta-analysis found moderate evidence that hydrotherapy has short-term beneficial effects on pain and health-related quality of life in FM patients [7].

2. Cognitive - behavioral therapy: There is strong evidence that psychological and behavioral therapy, especially cognitive-behavioral therapy, is effective in managing FM pain.

3. Other treatments: There is some evidence to support the use of acupuncture in patients with FM because it can decrease pain ratings and medication use.

Patients with chronic pain often develop secondary psychological disturbances, such as depression, anger, fear, withdrawal, and anxiety. Sometimes these secondary reactions become the major problem.

Any comorbid illnesses, such as mood disturbances or primary sleep disturbances, need to be identified and treated. It is important to refer patients with high levels of depression or anxiety to a psychologist or psychiatrist [18].

A multidisciplinary approach combining each of these modalities may be most beneficial.

Patients with FM not responding to these steps should be referred to a rheumatologist, physiatrist, psychiatrist, or pain management specialist.

Eating a well-balanced diet and avoiding caffeine

may help with sleeping problems, and may help reduce the severity of the symptoms. Lifestyle measures taken to improve the quality of sleep can be effective for fibromyalgia. Some reports indicate that fish oil, magnesium/malic acid combinations, or vitamins may be effective. Prognosis: FM can be mild or disabling but often has substantial emotional and social consequences. About 50% of all patients have difficulty with or are unable to perform routine daily activities. Estimates of patients who have had to stop work or change jobs range from 30% to 40%. Patients with FM suffer job losses and social abandonment more often than people with other conditions that cause pain and fatigue.

Our patient was treated with tramadol, mirtazapine, tender point injections with lidocaine solution and multidisciplinary rehabilitation and we finally obtained improvement. We didn't use pregabaline as the first drug in the treatment because the cost of the treatment after hospitalization was too high for our patients. Because of dominant depression with sleep disturbances, Parkinson's disease as well as the danger of side effects, we used mirtazapine. In our opinion using tramadol and mirtazapine was the best therapeutic option for our patient. As a result, we obtained satisfactory pain control, improvement of mood, physical activity, function and quality of sleep.

This article presents a patient with typical symptoms of fibromyalgia which appeared four years ago independently from the symptoms of Parkinson's disease. The patient meets two diagnostic criteria of fibromyalgia (widespread pain lasting at least three months and 16 positive tender points).

From the patients medical history & documentation it appeared that after the brain surgery in 2001 the patient needed L-Dopa. At present she is treated with L-Dopa in the same dose which she received after the surgery. In my opinion as a neurologist the neurological state hasn't changed since 2001 after the operation (the comparison of valid neurological examination with neurological state in 2001). Typical clinical interview, presence of tender points, the increase of pain in connection with physical activity, cold or damp weather, anxiety, stress and additional signs like chronic fatigue, morning stiffness, sleep problems, headaches, constipation, numbness in hands and feet, depression, and anxiety point out that it's a different syndrome independent from Parkinson's disease.

In our opinion this case is a typical educative case because it points out that the fibromyalgia is a medical and social problem not often diagnosed. Our patient had had clinical symptoms for four years (when she came to our department in May 2009) and had been diagnosed since 2006 in a few specialised clinics in the direction of different illnesses, among others (rheumatoid arthritis and borreliosis-Lyme disease). Finally these diagnoses were excluded. In the process of diagnosis organic changes & abnormalities in structure of bones, muscles, joints weren't noted. In the end the patient wasn't diagnosed. In our ward there was a suspicion of fibromyalgia which was confirmed by the rheumatologist.

Adres do korespondencji:
Iwona Filipczak-Bryniarska
Klinika Leczenia Bólu, Opieki Paliatywnej
i Farmakologii Klinicznej
Katedra Gerontologii i Geriatrii, UJ CM
ul. Śniadeckich 10, 31-531 Kraków
Tel.: (+48 12) 424-77-94
E-mail: inusia_bryniarska@yahoo.pl

References

1. Staud R. New evidence for central sensitization in patients with fibromyalgia. Curr Rheumatoi Rep 2004;6:259.
2. Neeck G. Neuroendocrine and hormonal perturbations and relations to the serotonergic system in fibromyalgia patients. Scand Rheumatol Suppl 2000;113:8-12.
3. Buskila D. Developments in the scientific and clinical understanding of fibromyalgia. Arthritis Res Ther 2009;11:242.
4. Neeck G. Pathogenic mechanisms of fibromyalgia. Ageing Res Rev 2002;1:243-55.
5. Burckhardt CS, Goldenberg D, Crofford L, Gerwin R, Gowans S, Jackson K, et al. Guideline for the Management of Fibromyalgia Syndrome Pain in Adults and Children, APS Clinical Practice, Guideline Series No 4. Glenview, IL: American Pain Society; 2005.
6. Sherman JJ, Turk DC, Okifuji A. Prevalence and impact of posttraumatic stress disorder-like symptoms on patients with fibromyalgia syndrome. Clin J Pain 2000;16:127-34.
7. Staud R. Fibromyalgia from Jaime H. Von Roenn, Judith A. Paice, Michael E. Preodor Current Diagnosis&Treatment Pain. New York: Medical Publishing Division; 2006.
8. Arnold LM, Hudson JI, Hess EV, Ware AE, Fritz DA, Auchenbach MB, et al. Family study of fibromyalgia. Arthritis Rheum. 2004;50: 944-52.
9. Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum 2008;58:2-35.
10. Buskila D, Lily Neumann. The development of widespread pain after injuries. J Musculoskelet Pain. 2002;10:261-7.
11. Edgar L, Ross MD. Pain Management: Hot Topics Fibromyalgia. Hanley&Belfus, INC 2004.
12. Staud R, Domingo M. Evidence for abnormal pain processing in fibromyalgia syndrome. Pain Med 2001;2:208-15.
13. Staud R. Evidence of involvement of central neural mechanisms in generating fibromyalgia pain. Curr Rheumatol Rep 2002;4:299-305.
14. Häuser W, Bernardy K, Üçeyler N, Sommer C. Treatment of fibromyalgia syndrome with gabapentin and pregabalin: a meta-analysis of randomized controlled trials. Pain 2009;145:69-81.
15. Häuser W, Petzke F, Sommer C. Systematic review with metaanalysis: comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome J Pain 2010; Epub Apr 23.
16. Sommer C. Pain Clinical Updates Vol. XVIII Issue 4 June 2010.
17. Maquet D, Croisier JL, Demoulin C, Crielaard JM. Pressure pain thresholds of tender point sites in patients with fibromyalgia and in healthy Controls. Eur J Pain. 2004;8:111-7.
18. Bradley LA. Psychiatric comorbidity in fibromyalgia. Curr Pain Headache Rep 2005;9:79-86.