INSTRUCTIONS

The following article, “Fibromyalgia Syndrome: Diagnosis and Management,” is a continuing medical education (CME) article. To earn credit, read the article and complete the CME evaluation form on page 68.

OBJECTIVES

After participating in the CME activity, primary care physicians should be able to:
1. Describe clinical features of fibromyalgia syndrome (FMS)
2. Understand the technique of tender point examination
3. Evaluate a patient with widespread pain and make a diagnosis of FMS based on the syndrome’s characteristics
4. Recognize that concomitant conditions are often present and should be appropriately treated
5. Employ both the pharmacologic and nonpharmacologic interventions used in the management of FMS

Fibromyalgia syndrome (FMS) is a common chronic musculoskeletal pain disorder. Approximately 90% of patients with FMS are women [1–3]. American College of Rheumatology (ACR) criteria for the diagnosis of FMS are widespread pain (pain in the left and right side of the body, above and below the waist, and in the axial skeleton) for at least 3 months and tenderness of at least 11 of 18 tender points on palpation (Figure) [1]. Alldynia (pain on usually nonpainful stimulus such as touch or massage) also presents in many patients. Besides pain, other characteristic symptoms of FMS include fatigue, sleep difficulties, morning fatigue, paresthesias, and subjective swelling of the extremities. Associated features are migraine and tension-type headaches, irritable bowel syndrome (IBS), restless legs syndrome (RLS), female urethral syndrome (irritable bladder syndrome), primary dysmenorrhea, sicca symptoms, anxiety, and depression (Table 1) [1–4]. Some patients also report cognitive dysfunction such as word groping and difficulties with short-term memory and concentration [5,6]. Associated features are particularly helpful if a patient has 8 to 10 tender points but are not essential for diagnosis of FMS by ACR criteria.

Most patients with FMS have symptoms for 5 to 7 years before a diagnosis is made [1,7]. Delay in diagnosis of FMS often proves costly and frustrating to the patient and may lead to inappropriate therapy [8]. Patients commonly have high hospitalization rates prior to diagnosis of fibromyalgia, both for musculoskeletal and nonmusculoskeletal hospitalizations, but these rates drop following diagnosis [9]. Thus, early diagnosis of FMS may prevent costly diagnostic tests and unnecessary treatment and may improve patients’ quality of life.

CASE STUDY
Initial Presentation

A 60-year-old retired teacher visits her primary care physician for evaluation of severe fatigue and pain in her neck, hands, shoulders, pelvic girdle area, and legs that have persisted for more than 1 year.

History

The patient explains that she has had mild pain and stiffness in her extremities for almost 5 years, but over the past year the pain has become severe, widespread, and persistent. She says, “Now I have pins and needles from head to toe. It hurts badly all over, all the time.” The pain is aggravated by work, stress, cold weather, and humidity and somewhat alleviated by local heat and rest. She says that she cannot hug her grandchildren because pressure or even light touch causes much pain. In addition, the patient reports always feeling tired, and that simple daily activities, such as shopping or cooking, exhaust her. She reports difficulty falling asleep, saying “No matter how long I sleep, I wake up very tired in the morning. There are some days that I don’t want to get out of bed.” She adds that her hands and feet feel swollen and numb and that she has 3 hours of stiffness in her joints on waking.

- What are the possible causes of this patient’s symptoms?
A variety of disorders may cause diffuse musculoskeletal pain and fatigue; therefore, a systematic approach to the differential diagnosis is essential. Of the entities listed in Table 2, the ones more likely to cause musculoskeletal pain and fatigue in a woman 60 years of age are fibromyalgia, polymyalgia rheumatica, vasculitis, and inflammatory arthritides. In addition, hypothyroidism, which causes stiffness and cramping pain, should be considered, particularly because of the patient’s severe fatigue. However, FMS is a likely diagnosis at this point because several characteristic features of FMS are present, including widespread pain, severe fatigue, allodynia (patient cannot hug her grandchildren), and poor sleep.

To narrow the differential diagnosis, the physician should take a complete history, including any constitutional symptoms (eg, fever, weight loss), and perform a careful physical examination. Examination of the hands will help to determine the presence of inflammatory arthritides. Because fibromyalgia is a likely diagnosis at this point because several characteristic features of FMS are present, including widespread pain, severe fatigue, and allodynia (patient cannot hug her grandchildren), and poor sleep.

Further History

On further questioning, the patient denies fever, increased perspiration, and change of appetite or weight. She has not noted skin thickening or rash, Raynaud’s phenomenon, dry eyes or mouth, vision problems, hair loss, or respiratory difficulties. She notes dry skin and intolerance to cold weather. The patient describes a 2-year history of constipation and abdominal pain worsened by bowel motion, but no nausea, vomiting, dysphagia, or heartburn. In the past year she has had problems with finding the right words while speaking, concentration, short-term memory, and performing simple mental tasks. She denies significant anxiety or depression but feels “frustrated” by her disabling symptoms and reports some stress from her pain and a demanding husband.

There is no history of allergies. Past medical history includes periodic migraine headache that first occurred at age 26 years and “quit” at 40 years. She now experiences tension-type headaches, which she describes as diffuse in the scalp and the neck and without features of migraine. She was taking naproxen 220 mg as needed for headaches, and notes that she had stomach pain if she took more than 1. The frequency of the headaches has increased in the past year. A gastric ulcer was diagnosed 9 years ago. Six months ago, she had persistent chest pain on the left side. At that time, physical examination and laboratory investigation revealed no intrathoracic pathology. She still occasionally has chest pain, irrespective of rest or exercise. She denies cough, palpitations, and shortness of breath. Recent gynecologic and breast examinations,
mammography, and bone mineral density measurement were all within normal limits.

Family history is remarkable for her mother, who had osteoporosis and frequently complained of constipation. For the past 4 years, the patient has been taking acetaminophen 500 mg as needed (usually 2 to 3 tablets daily), calcium carbonate 500 mg/day, and vitamin D 400 IU/day. She does not smoke and has 1 alcoholic drink per month.

**Physical Examination**

The patients appears healthy on examination. She is not obese and is mentally alert with normal speech. Vital signs include temperature of 36.5°C, regular pulse of 67 bpm, and blood pressure of 120/80 mm Hg. Her skin is dry and her body and scalp hair is rather sparse. Head, ear, eyes, neck, and thyroid examination are unremarkable; mouth is moist. Temporal arteries are not tender but mild periorbital puffiness is noted. There is no lymphadenopathy, skin rashes, or skin thickening. Examination of the lungs and heart is unremarkable. Distal artery pulses are palpable, and there is no discoloration of the skin or edema in the extremities. Abdominal examination reveals tenderness in both iliac fossa; no masses are felt, and no bruit is heard. Muscle tone and strength are normal, and there is no muscle atrophy. Light touch, pinprick, joint position, and vibration sensations are normal in the extremities, as are cranial nerves and reflexes. Cerebellar signs are absent. Musculoskeletal examination reveals normal range of motion of the joints, except for mild pain and some restriction of neck extension, flexion, and rotations. Joints are not swollen or warm, but the fingers and hand joints are diffusely tender. There is no joint deformity. Seventeen of 18 tender point sites are tender, with the patient reporting mild to severe pain on palpation. Palpation of the chest wall shows rather diffuse tenderness. The lumbar region is also tender.

**Diagnosis**

The physician makes a diagnosis of FMS based on the presence of widespread pain and more than 11 tender points. The presence of associated features of FMS, including fatigue, poor sleep, IBS, cognitive difficulties, subjective swelling of the hands, and headaches, support this diagnosis.

- How common is FMS?
- What causes FMS?

**Epidemiology**

An estimated 7 million people in the United States have FMS by ACR criteria [10,11], but the number with a clinical diagnosis of FMS is likely higher. FMS patients constitute 2.1% to 5.7% of the outpatient internal medicine or family practice practice...
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**Table 3. Common Factors That Aggravate Fibromyalgia Symptoms**

<table>
<thead>
<tr>
<th>Common Factors</th>
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<tbody>
<tr>
<td>Sleep difficulties</td>
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<tr>
<td>Physical deconditioning, muscle overload, poor posture</td>
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<tr>
<td>Psychological factors: stress, anxiety, depression, poor coping skills</td>
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<td>Environmental factors: hot/cold temperature, humidity, noise</td>
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<td>Occupational factors: repetitive trauma, ergonomic factors</td>
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<tr>
<td>Physical overuse/unaccustomed exercise</td>
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<tr>
<td>Coexisting/associated conditions: arthritis, neuritis, restless legs syndrome, hypothyroidism, headaches, irritable bowel syndrome, irritable bladder syndrome</td>
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... clinic population and 10% to 20% of outpatient rheumatology visits [12]. It is the second most common diagnosis in rheumatology clinics [13]. The population prevalence of FMS is 2% to 3%. However, FMS is much more common among women (population prevalence of 3.4% to 4.9% in women versus 0.5% to 1.6% in men) [10,14], and although it is seen in all age groups [15], its population prevalence increases with age, reaching greater than 7% in women aged 60 to 79 years [10]. The clinical features of juvenile fibromyalgia are similar to those in adult FMS [15]. However, men have less fatigue, morning fatigue, and IBS and fewer tender points than women [16].

**Etiology**

The etiology and pathophysiologic mechanisms of FMS are not fully understood but are considered to be multifactorial. Dysfunction of the neuroendocrine system that leads to an aberrant central pain mechanism with central sensitization is currently thought to be the most important mechanism [17–19]. Several forms of neuroendocrine dysfunction have been described, including low serum serotonin, increased substance P in the cerebrospinal fluid, decreased insulin-like growth factor-1, and an abnormal hypothalamic-pituitary-adrenal axis [17,18,20–22]. Poor sleep, physical deconditioning, emotional distress (including anxiety and depression), trauma, and environmental and workplace factors contribute to FMS symptoms in varying degrees in different patients [17,18,23–25] (Table 3). Genetic predisposition seems likely [26]. Psychological factors, including coping skills, are important determinants of pain in a subgroup of patients [27]. Anxiety, depression, and mental stress are present in 30% to 40% of patients who have FMS [1,27], but in most cases they seem to be secondary to chronic pain [27].

IBS, headaches, RLS, chronic fatigue syndrome (CFS), and temporomandibular pain syndrome are more common in FMS patients than in healthy and chronic pain controls, and these conditions cluster in the same group of patients [1–4,10,27–31]. In addition, these conditions share many clinical features (eg, female preponderance, pain without tissue damage, fatigue, and poor sleep) and respond to a similar group of medications [29,32–39]. Based on these observations and evidence for central sensitization in these overlapping syndromes, Yunus suggested that central sensitization is a common physiologic glue that binds this group of conditions and called them “central sensitivity syndromes” [18,40].

- What possible diagnoses warrant further evaluation in this patient?

**Other Causes of Musculoskeletal Pain and Fatigue**

This patient has FMS by history and physical examination. Although FMS is not a diagnosis of exclusion [1,18], conditions frequently coexist with FMS, and laboratory tests and radiography should be performed if clinically indicated to evaluate for conditions in the differential that might contribute to this patient’s symptoms but cannot be reasonably excluded by history and physical examination.

**Other Rheumatic Conditions**

Polymyalgia rheumatica with or without temporal arteritis most often affects patients aged 60 years and older, but lack of constitutional symptoms and temporal artery tenderness argues against them. Also, stiffness in the shoulder and pelvic girdles, rather than pain, is a prominent symptom of polymyalgia rheumatica. A normal erythrocyte sedimentation rate (ESR) would exclude this entity. In the absence of constitutional symptoms, vasculitis or a connective-tissue disease are unlikely. The patient has no signs of joint inflammation (eg, objective swelling, warmth, and erythema) or evidence of systemic inflammatory diseases (eg, fever, weight loss, skin rashes, skin thickening or vasculitic lesions, oral ulcers, dry eyes and mouth, dysphagia, subcutaneous nodules, signs of cardiac or pulmonary involvement, pleural and pericardial effusions, lymphadenopathy, hepatosplenomegaly, and neurologic findings), further excluding systemic rheumatic diseases. The patient does have diffuse tenderness in her fingers and hand joints on palpation, but this is common in FMS, a disorder of global hyperalgesia. Scleroderma is quite unlikely in the absence of hand changes or Raynaud’s phenomenon. Myopathy, including polymyositis, is unlikely in the absence of muscle weakness, particularly proximal weakness, although muscle pain is not usual in these disorders.

Spinal osteoarthritis primarily affects the lumbar and cervical regions, and the patient has neck and back pain and limitation of range of motion of the cervical spine. A
concomitant presence of FMS and osteoarthritis at age 60 years is not uncommon, so it is reasonable to order radiographs of the patient’s neck and spine.

**Chronic Fatigue Syndrome**

CFS is characterized by chronic debilitating fatigue, is worsened by even mild activities, and lasts more than 6 months. Other features include fever, pharyngitis, myalgias, adenopathy, arthralgias, sleep difficulties, cognitive dysfunction (as in FMS), and disorders of mood. Cognitive problems are much more frequent in CFS than in FMS. Fever and pharyngitis are often subjective. In the majority of patients, the illness starts suddenly with an acute “flu-like” illness [41,42]. FMS and CFS have similar clinical and demographic features, and they also overlap with other similar syndromes (eg, IBS and headaches) [43,44].

**Metabolic Disorders**

Dry skin, fatigue, cold intolerance, paresthesia, and periorbital puffiness are valuable clues of hypothyroidism. Her bowel symptoms suggest IBS, although constipation may be caused by hypothyroidism in this patient. Primary hypothyroidism is common and generally occurs after age 40 years. The musculoskeletal symptoms of hypothyroidism are stiffness and muscle cramping rather than generalized muscle and joint pain. Thyroid function tests should confirm whether hypothyroidism is present.

Patients with osteomalacia and hyperparathyroidism may have bone pain, proximal muscle weakness, severe pruritus, polyuria, anorexia, nausea, impaired cognitive function, depression, and hypertension. However, widespread muscular pain or muscular tender points are not the characteristic features of these diseases; tenderness is usually limited to bone. Osteomalacia occurs among those with inadequate dietary intake of vitamin D, malabsorption, and renal disease. Measurement of serum calcium, phosphate, bone-specific alkaline phosphatase, and parathyroid hormone levels is necessary to assess for metabolic bone diseases; however, these diseases are quite unlikely in this patient.

**Infection/Malignancy**

In patients with chronic infections and malignancy, constitutional symptoms are accompanied by signs and symptoms specific for the organs involved.

**Somatization Disorder**

Patients with somatization disorders present with subjective complaints affecting multiple organ and body systems that cannot be explained by a medical condition or known pathophysiologic mechanism. Since FMS is a well-characterized condition with a well-established pathophysiology [17–21], psychogenic pain should not be diagnosed in this patient. Also, symptoms in somatization disorder begin before the age of 30 years.

- **Is further evaluation of the patient's chest pain warranted?**

Organic causes of chest pain include ischemic heart disease, pericardial disease, pulmonary diseases, aortic aneurysm, and upper gastrointestinal diseases. The musculoskeletal structures of the thoracic wall are a relatively common source of chest pain that is often mistaken for angina pectoris or pleural pain. FMS is the most common cause of chest pain in patients who have no intrathoracic pathology [45–48]. The history of pain (ie, location, duration, radiation of pain, and factors that cause, aggravate, or alleviate pain) and symptoms such as shortness of breath, hemoptyis, cough, and palpitation are very useful in distinguishing between intrathoracic and chest wall causes of chest pain. In FMS, the pain is constant but may be aggravated by activities that involve use of chest wall muscles. Chest wall tenderness on palpation often reproduces pain. This patient did not have a typical history of cardiac pain (ie, heavy or squeezing central chest pain lasting 3 to 10 minutes with radiation to the arm, neck or jaw, and brought on by exertion and relieved by rest). Additionally, she lacked other symptoms and signs of intrathoracic pathology. On the other hand, the diffuse tenderness of the chest wall by palpation, along with other features of FMS, would suggest that her chest pain is due to fibromyalgia. However, because diseases may coexist, in a patient with a suggestive history and physical examination, intrathoracic disease should be ruled out even if the patient has FMS.

**Laboratory Evaluation**

The physician orders routine laboratory tests, including complete blood count, ESR, C-reactive protein, serum electrolytes, liver enzymes, blood glucose, renal function tests, thyroid function tests, and urinalysis. Anteroposterior, lateral, and oblique radiographs of cervical and lumbar spine are also requested to evaluate the patient’s neck and back pain and limitation of range of motion of the cervical spine. Antinuclear antibodies, serum complement, and rheumatoid factor tests are not done since the patient does not have symptoms or signs of systemic rheumatic disease.

The results of the laboratory tests are within normal limits except for an elevated ESR at 36 mm/hr and
abnormal thyroid function test results: total thyroxine (T4) = 3 µg/dL (normal, 4–11 µg/dL); free T4 index = 66 (normal, 96–396); thyroid-stimulating hormone (TSH) = 38 µIU/mL (normal, 0.4–4.8 µIU/mL). Urinalysis is unremarkable.

Cervical and lumbar spine radiographs reveal mild to moderate intervertebral disk-space narrowing, sclerosis of vertebral end plates, and osteophytosis.

• What is the significance of these findings?

The elevated TSH level confirms the diagnosis of primary hypothyroidism, and the radiographic findings confirm the diagnosis of mild to moderate osteoarthritis of the cervical and lumbar spine. At 36 mm/hr, the patient’s ESR is elevated, but only mildly so given her age. ESR increases with age and is higher in women. A general rule for calculating the age- and sex-adjusted upper limit of normal ESR for women is age plus 10 divided by 2 [49]. Thus, polymyalgia rheumatica is ruled out in this patient.

As mentioned, co-occurrence of other conditions with FMS is not unusual. FMS may be classified as concomitant when another condition is present and contributes to pain or fatigue of FMS. The clinical characteristics, diagnosis, and management of concomitant FMS are not different from primary fibromyalgia, but concomitant conditions should be treated appropriately since they may add to the patient’s symptoms.

• What is the approach to management of FMS?

Overview of FMS Management
The goals of FMS management are to alleviate pain and other symptoms, to eliminate or modify possible aggravating factors, to improve sleep quality, to achieve physical fitness, to enhance patient’s coping skills, and to improve quality of life [50]. Management of FMS is usually challenging, since many different factors interact to cause symptoms and their relative importance varies from patient to patient. Therefore, the approach to treatment should be individualized according to a patient’s symptoms and severity of FMS. Both nonpharmacologic and pharmacologic interventions are used to treat FMS patients (Table 4); however, nonpharmacologic approaches should be emphasized before any drug is prescribed. A combination of pharmacologic and nonpharmacologic interventions was found to be more efficacious in improving self-reported symptoms of FMS than pharmacologic treatment alone [51]. Interdisciplinary group treatments are also reported to be beneficial [52,53].

Nonpharmacologic Therapy
Following diagnosis of FMS, patient education is important and should be continued in all subsequent visits. The physician should inform the patient about currently known physiologic mechanisms of FMS, including aggravating factors. The patient should be reassured that although FMS can be chronic, it is not a malignant condition and does not cause tissue damage. However, the physician should avoid characterizing FMS as a “benign condition” because patients who have severe and disabling pain often resent it. A positive and empathetic attitude on the part of the physician is essential.

Coexisting or associated conditions may aggravate FMS symptoms by producing an extra burden of stress, pain, or fatigue, by disturbing sleep, and by limiting aerobic activity (Table 3). Because the presence and significance of coexisting conditions differ from patient to patient, the physician should inquire about each of them, discuss them with the patient, and try to eliminate or treat them satisfactorily.

Restoring sleep hygiene, gradually increasing physical
fitness, and eliminating any psychological distress are key points of successful management. Poor sleep can be helped by sleeping in a quiet and uncluttered room, keeping regular sleep hours, avoiding alcohol and caffeine in the evening, exercising regularly (but at least 3 to 4 hours before bedtime), and avoiding psychological distress. Psychological stresses can be decreased by relaxation techniques, pacing daily activities, and cognitive approaches. Physical fitness exercises improve physical conditioning; provide resistance to micro-trauma; enhance strength, endurance, and flexibility; increase sense of control; and have relaxation and pain modulation effects [54,55]. Stretching exercises provide short-term help, but aerobic exercises are the most beneficial. The key is to start exercise at a low level, to increase exercise time gradually, and to exercise regularly. Patient compliance in physical exercise is generally poor. We insist that our patients keep a weekly diary or graph that includes highest sustained pulse rate achieved during exercise and average time spent exercising in a week and ask them to bring the diary or the graph during their next visit. Graphs are better than diaries since they can be read more quickly.

Cognitive behavioral therapy (usually undertaken by a psychologist) includes relaxation training, reducing negative pain behavior, coping skills training, and fostering a positive, “I can do” attitude [56,57]. This modality should be used in patients with poor coping skills.

Pharmacologic Therapy
Pharmacologic treatment options for FMS include simple analgesics and antidepressants. Because patients often have a negative perception about “antidepressants,” particularly patients who are not depressed, we refer to antidepressants as “serotonin boosters to help pain and sleep.” Amitriptyline, cyclobenzaprine, and fluoxetine/amitriptyline combination have been shown to alleviate pain, improve poor sleep, and reduce fatigue. These antidepressants have been shown to consistently improve patient-assessed global severity, although they do not always decrease the number of tender points. Amitriptyline is the most widely prescribed tricyclic antidepressant in FMS [58]; it has been shown to be effective in double-blind, placebo controlled studies [59–62]. The usual dose is 10 to 50 mg/day. Cyclobenzaprine, a tricyclic antidepressant that is marketed as a muscle relaxant, has short-term efficacy in FMS [63,64]. The combination of fluoxetine with amitriptyline has been shown to be effective [64], and 1 study showed the combination to be more effective than either drug alone [65].

Tramadol is a centrally acting analgesic with both µ opioid-receptor binding and norepinephrine and serotonin reuptake inhibition; it has been found to decrease pain in a controlled study [66]. The usual dose is 100 to 400 mg/day. Although a beneficial effect of acetaminophen in FMS has not been reported by blinded and controlled studies, some patients find this relatively safe drug helpful. Many patients also report benefit from NSAIDs, but data do not support the efficacy of an NSAID alone in FMS. NSAIDs may be prescribed for a concomitant disease such as osteoarthritis with the usual precautions regarding side effects. Acetaminophen 500 mg with codeine 30 mg 3 to 4 times per day may be prescribed during a flare or in difficult patients with severe symptoms who do not respond to other interventions [67]. Injection of lidocaine into tender points is a valuable adjunctive therapy in patients with a limited number of painful sites that are especially bothersome [68]. Patients who receive injections should apply ice at injected sites for 20 minutes each hour for 4 to 6 hours and rest the injected areas for 48 hours to avoid post-injection flare of pain.

Amitriptyline, cyclobenzaprine, fluoxetine/amitriptyline combination, citalopram, and tramadol have been found to be efficacious in FMS by double-blind controlled studies [50]. A stepwise approach to pharmacologic treatment may be employed. Mildly symptomatic patients may be treated with simple analgesics and low-dose tricyclic antidepressants; moderately affected patients may be prescribed the maximum tolerated dose of tricyclic antidepressants or a combination of tricyclic antidepressants and selective serotonin reuptake inhibitors. Low-dose central analgesics (ie, tramadol) may be prescribed if the patient does not have a history of alcoholism or other drug addictions. In severe cases, other medications in the same classes as those above and tender point injection with a local anesthetic agent may be useful.

Management of the Patient
The patient is prescribed levothyroxine 25 µg/day for her hypothyroidism. Evaluation of the progress of treatment of primary hypothyroidism consists of measurement of serum total T<sub>4</sub> and TSH as well as clinical status, bearing in mind that in a FMS patient, fatigue is unlikely to improve satisfactorily, even when TSH is normal. For her cervical osteoarthritis, the patient is advised to avoid activities that are particularly stressful to the neck, to apply moist heat for relaxation of tight neck muscles as needed, and to perform active range-of-motion exercises.

The physician discusses the nature of FMS with the patient and gives her an information booklet on the condition. Factors that aggravate her symptoms—sleep difficulties, cold weather, emotional stress—are discussed. To restore sleep hygiene, she is advised to avoid heavy meals, caffeine, or alcohol before bedtime and to eliminate disturbing factors such as noise and light from her sleep environment. She is asked to sleep/wake on a regular schedule and to sleep at least 7 to 8 hours each
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night. The patient is advised to walk for exercise or swim in a warm pool for 5 minutes per day and to gradually increase the time to 30 minutes per day (ie, in 2- to 3-minutes increments every week). Walking on a treadmill or riding an exercise bicycle are recommended in case of low outdoor temperature. The goal of physical exercise is to achieve cardiovascular fitness with an appropriately elevated pulse rate during exercise. Additionally, she is taught stretching exercises for her aching muscles. The importance and benefits of exercise (eg, pain relief, relaxation, and better sleep) are emphasized. She is also referred for physical therapy, including stretching, local heat, massage, and ultrasound.

The physician prescribes amitriptyline 10 mg at bedtime, to be increased to 20 mg after a week if tolerated. He explains that the amitriptyline is prescribed to improve the patient’s sleep and pain, and not as an antidepressant. He also tells the patient that it might take 3 to 4 weeks for the amitriptyline to work and informs her about its possible side effects. The physician increases the acetaminophen dose to 3 to 4 g/day. The patient is scheduled for an office visit in 4 weeks.

Follow-up

At 4 weeks after diagnosis, the patient’s TSH level is 12 µIU/L, and there is some improvement in her fatigue. The physician increases the dose of levothyroxine to 50 µg/day. At 8 weeks, the patient’s pain has improved somewhat but the fatigue remains the same; her TSH level is 10 µIU/L. The physician increases the dose of levothyroxine to 75 µg/day. Her sleep and headaches have improved, but she still has pain in her neck, hands, shoulders, legs, and particularly in her arms and thighs as well as stiffness and morning fatigue. She reports that physical therapy has helped to some extent.

12 Weeks

At 12 weeks, the patient is regularly taking amitriptyline 20 mg/day at bedtime and does not complain of any side effects except for dry mouth. She is doing stretching exercises as regularly as possible but generally experiences post-exercise pain after 20 minutes of brisk walking. She is taking 6 tablets of acetaminophen (500 mg each tablet) per day. The physician prescribes the cyclooxygenase-2 (COX-2) inhibitor rofecoxib at a dose of 12.5 mg/day because the osteoarthritis of her cervical spine could be contributing to her neck pain and acetaminophen has not been helpful. A COX-2 inhibitor is selected because the patient had previous gastrointestinal intolerance with naproxen, has a history of gastric ulcer, and has mildly increased risk of peptic ulcer disease at age 60 years. The physician schedules TSH measurement in 4 weeks and asks the patient to return for an office visit in 6 weeks. The patient comments that she is feeling rather discouraged.

18 Weeks

The patient still complains of significant pain and fatigue, although both have improved. Physical examination reveals that her skin dryness and periorbital puffiness are much improved. There is some restriction of the neck range of motion with pain, as before. Sixteen of 18 tender points are painful on palpation. Because the patient’s TSH level 2 weeks earlier was 9 µIU/L, the dose of levothyroxine is increased to 100 µg/day.

To reassure the patient, the physician discusses her symptoms and aggravating factors and the chronic nature of FMS again. The physician encourages her to take an active role in the management of her symptoms and to have an optimistic attitude. He advises the patient to modify the exercise program according to her pain, but to continue exercising regularly with gradual increases in the exercising time and to continue the physical therapy program. He also asks the patient to apply moist heat on the most painful sites. The physician increases the amitriptyline to 40 mg/day (since dry mouth is still mild) and the levothyroxine to 125 µg/day after 1 week. The next office visit is scheduled for 2 months.

27 Weeks

Two months later, the patient’s TSH level is 4.3 µIU/L (normal), but her fatigue and pain are only mildly improved compared to the previous visit. The neck pain, however, is significantly improved. The patient reports that she was better for 2 months, but then her pain and fatigue gradually worsened. She has difficulty falling asleep again and has frequent awakenings. She says that she cannot tolerate exercise anymore. She notes increased stress with interpersonal relationships, both in family and in social environments, because the severe pain and fatigue interfere with daily functioning. She says that she is “beginning” to feel depressed. Physical examination shows that her skin dryness and periorbital edema have nearly disappeared. The tender points on palpation seem worse, and on questioning, the patient says that 4 areas are particularly painful. Fluoxetine 20 mg in the morning is added, and the 4 most symptomatic tender points areas are injected with 0.5 mL of 1% lidocaine. The physician asks her to continue heat therapy at home and to return in 10 weeks.

37 Weeks and 44 Weeks

The patient’s pain and fatigue have improved, but the fatigue remains troublesome. Her TSH level is 4.2 µIU/L. She reports that the tender point injections have helped significantly and overall she feels better. She is asked to return in 3 months.

At 44 weeks, the patient says that she has “slipped back” and now has much pain and fatigue and is unable to carry
out daily activities. She hurts all over but does not feel more depressed, however. On physical examination, all tender points are markedly tender. Range of motion of the neck and low back are mildly restricted and somewhat painful. The physician injects the most symptomatic tender point areas again. Given her continued symptoms, she is referred to a psychologist with expertise in cognitive behavioral therapy and coping skills. Despite pain, regular physical exercise is encouraged. Neither the dose of fluoxetine or amitriptyline are increased, because fluoxetine may increase amitriptyline levels and cause side effects. The patient is asked to return in 10 weeks. The patient's TSH level is normal, so further increasing the levothyroxine is not likely to be helpful.

54 Weeks and Beyond

The patient has continued cognitive behavioral therapy and previous medications, and she is exercising regularly. Her symptoms remain moderately severe, but she is able to perform daily activities better than before. Tender point injections are repeated every 3 to 4 months, as necessary. Because the patient has no personal or family history of seizure, she is permitted to take tramadol 50 to 150 mg (1 to 3 tablets) per day on an as needed basis. She is not to exceed 3 tablets (150 mg) in 24 hours because she is taking amitriptyline and fluoxetine.

• What factors should be considered over the long term in patients with FMS?

FMS Over the Long Term

As this case demonstrates, FMS is a chronic condition characterized by remissions and exacerbations of symptoms. Patients with an acute flare-up, often triggered by physical or emotional distress, may be managed by reassurance, physical therapy, relative rest, injection of tender points, and increasing the dosage of medications up to maximum tolerated dose. In patients who do not respond sufficiently to the optimal dose of first-choice drugs (eg, amitriptyline and cyclobenzaprine), it is reasonable to prescribe another drug (eg, doxepin, imipramine, desipramine, tramadol, trazodone, nefazodone, paroxetine, citalopram, or sertraline). Benzodiazepines such as alprazolam 0.25 to 0.5 mg [69], lorazepam, or buspirone may be useful in some patients, particularly those who have significant anxiety. However, long-term use of benzodiazepines should be avoided whenever possible because of potential dependence and withdrawal seizures associated with them. Hypnotics such as zolpidem [70] may be prescribed in patients whose sleep difficulties have not been adequately improved by sleep hygiene and tricyclic agents, although these agents do not help pain [50,70]. Hypnotics should be taken at bedtime or after supper if there is morning grogginess. Patients whose compliance is low may be referred to a supervised group exercise program. Significant psychologic distress can be helped by emotional support combined with higher doses of antidepressants than pain management dose; however, psychiatric referral should be made when these attempts are not adequate for improvement. The patient was doing moderately well as of the last visit, but exacerbations would not be uncommon in the future. Follow-up studies of more than 11 years have shown that FMS symptoms remain essentially unchanged over this time period [71].

Systemic diseases and other musculoskeletal or non-musculoskeletal conditions may develop during the course of FMS. Any new symptom that is not compatible with a diagnosis of FMS or a change in the nature of symptoms should be evaluated carefully, since it may be the clue of a new, coexistent disease. Failure to recognize and treat concomitant conditions may augment patient’s symptoms and result in unsuccessful management of FMS. A diagnosis of associated RLS and periodic limb movement disorder (PLMD) should not be missed, because both are likely to disturb sleep and can be treated with specific therapy such as benzodiazepines (clonazepam 0.5–1.5 mg/day), dopaminergic drugs (L-dopa or carbidopa/levodopa combination), anticonvulsants (gabapentin or carbamazepine), and opioids (codeine, propoxyphene, and hydrocodone) [72–76]. The addictive property of many of these drugs should be kept in mind. Clonazepam 0.5 mg at bed time is usually prescribed first, followed by dopaminergic drugs. It has been reported that PLMD symptoms may be worsened by tricyclic agents that block noradrenaline uptake [77] and by selective serotonin reuptake inhibitors [78]. In addition, RLS may be induced or exacerbated by mianserin, a tetracyclic antidepressant [79], and by paroxetine [80] and sertraline [81]. However, these observations are mostly based on case reports, and further studies are needed to confirm them.

• What is the impact of FMS in terms of quality of life and cost?

Quality of Life

As this case also demonstrates, FMS can cause a high level of functional disability and have a significant negative impact on quality of life (QOL). The severity of self-assessed disability in FMS is similar to that of rheumatoid arthritis and osteoarthritis [82–85]. Pain, fatigue, and weakness are most often reported to affect working capacity [86]. Although most
patients are able to remain employed and work most or all days, they often require job modifications, changes in ergonomics, and a reduction in work hours [85,87,88]. FMS patients have reported poorer QOL compared to women with rheumatoid arthritis, osteoarthritis, permanent ostomies, chronic obstructive pulmonary disease, insulin-dependent diabetes, and healthy controls [83,89]. In addition, patients with FMS have been reported to have similar impairments of QOL as patients with systemic inflammatory arthritis [90,91]. Moreover, impaired QOL in patients with FMS may adversely affect their families [92].

**Costs**

The average yearly cost per patient associated with FMS has been estimated at approximately $1000 in 1991 [93] and $2274 in 1996 [94]. Patients average almost 10 visits to outpatient clinics for traditional medical treatment and 2 visits for nontraditional therapy each year. Additionally, FMS is an increasingly important reason for disability claims and payments [95,96]. In a 6-center study of disability status among 1604 patients with FMS in the United States, 26.5% reported receiving at least 1 form of disability payment [94]. In Canada, McCain reported that private insurers pay more than $200 million annually in long-term disability claims for FMS [97]. In Norway, the most common reason for long-term disability payments in 1988 was FMS [98].

**SUMMARY**

FMS is a common, painful, disabling condition. The diagnosis of FMS with widespread musculoskeletal pain and 11 or more tender points among 18 specified sites by ACR criteria is not difficult. However, physicians should be familiar with the symptoms, associated disorders and, importantly, the technique of tender point examination. Those not trained in proper technique of this examination tend to undercount the number of tender points. However, some patients may not have an adequate number of tender points even in expert hands but should be treated for FMS if other symptoms are present.

Education, reassurance, psychological support, and reminders to exercise regularly are important in all follow-up visits. Tender point injection is a valuable adjunctive therapy in any step of treatment. Physical therapy may help to reduce pain. A combination of pharmacologic and nonpharmacologic interventions provides better results than either approach alone. Various other nonpharmacologic modalities such as electroacupuncture or electromyogram biofeedback may be tried when a patient is not doing well.

**References**


89. Kaplan RM, Schmidt SM, Cronan TA. Quality of well being

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EVALUATION FORM: Fibromyalgia Syndrome: Diagnosis and Management

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Part 1. Please respond to each statement. Strongly Agree Strongly Disagree

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Additional comments: ______________________________________________________________________________________
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Part 2. Please complete the following sentence.
As a result of reading this case study, I . . .
❑ see no need to change my practice.
❑ will seek more information before modifying my practice.
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