The General Practice Guide to Autoimmune Diseases

Edited by Y. Shoenfeld and P. L. Meroni

EASi™
European Autoimmunity
Standardisation Initiative


ThermoFisher
SCIENTIFIC

The General Practice Guide to Autoimmune Diseases

Edited by Y. Shoenfeld and P. L. Meroni

Pabst Science Publishers
Lengerich, Berlin, Bremen, Miami,
Riga, Viernheim, Wien, Zagreb

Bibliographic information published by Deutsche Nationalbibliothek
The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data is available in the Internet at <http://dnb.ddb.de>.

http://www.pabst-publishers.de

Printing: MercedesDruck, Berlin
Typesetting: Hilmar Schlegel, Berlin
Cover: Agentur für zeitgemäße Kommunikation Kaner Thompson
www.kanerthompson.de

ISBN 978-3-89967-770-6

Fibromyalgia syndrome

Yoav Arnson, Howard Amital

1 Introduction

Fibromyalgia (FM) is a common cause of chronic, diffuse, musculoskeletal pain. It is a disease that affects muscles and soft tissue such as tendons and ligaments. This condition is not associated with genuine tissue inflammation and the aetiology of the disorder remains poorly understood.

The estimated prevalence of FM in the general community ranges between 2 % to 5 % of the population; women are affected almost 10 times more than men. The prevalence increases with age, reaching over 7 % in women aged 60 to 79 years. As mentioned above, the cardinal manifestation of FM is diffuse musculoskeletal pain. Although the pain may initially be localized, often in the neck and shoulders, it eventually involves many muscle groups of upper and lower extremities. Patients typically complain of diffuse pain over the neck, middle, and lower back, chest wall and upper and lower limbs. The pain is chronic and persistent, although it usually varies in intensity. Patients often have difficulty distinguishing joint from muscle pain and also report a burning sensation with swelling, however, the joints do not appear swollen or inflamed on examination. Pain is often aggravated by exertion, stress, lack of sleep, weather changes and shifts of mood. Sensations of numbness, tingling, burning, or a crawling perception are often described.

Patients also may have a variety of poorly understood pain symptoms, including abdominal and chest wall pain and symptoms suggestive of irritable bowel syndrome, pelvic pain and bladder symptoms of frequency and urgency suggestive of the female urethral syndrome or of interstitial cystitis [1].

2 Signs and symptoms

Fatigue is present in more than 90 percent of cases and is occasionally the chief complaint. Most patients report light sleep and feeling un-refreshed in the morning, while others report symptoms suggestive of pathologic sleep disturbances such as sleep apnoea or nocturnal myoclonus. Light-headedness, dizziness, and feeling faint are common symptoms. Headaches (either muscular or migraine-type)

are present in a majority of patients. Psychological features presented including mood disturbances, especially depression, anxiety, post-traumatic stress disorder and heightened somatic concern, and cognitive dysfunction especially short term memory loss [2].

Additional symptoms and clinical manifestations may include complaints of ocular dryness, multiple chemical sensitivity and "allergic" symptoms, palpitations, dyspnoea, vulvodynia, dysmenorrhoea, non-dermatomal paresthesias, weight fluctuations, night sweats, dysphagia, dysgeusia, glosodynia, and weakness. FM is often accompanied by other co-morbidities. As many as 80 % of patients with FM also fulfil criteria for chronic fatigue syndrome, up to 80 % have headaches, 75 % have temporomandibular disorders, and up to 60 % may have irritable bowel syndrome.

3 Diagnostic criteria

FM diagnosis is problematic because of the difficulty classifying somatic syndromes that lack objective physical or laboratory features or well-characterised pathologic findings. Diagnosing fibromyalgia is based on the combination of patient history, physical examination and exclusion of other causes for symptoms attributed to FM. The clinical diagnosis of FM is based largely upon the patient's history of chronic, generalized pain and associated features. The features include fatigue, sleep disturbances, headache, cognitive difficulties and mood disturbances (Table 1).

FM is currently diagnosed using the American College of Rheumatology (ACR) classification criteria from 1990 (Table 2) [3]. The diagnostic criteria are based on the occurrence of widespread musculoskeletal pain and excess tenderness in of least 11 of 18 predefined anatomic sites (Fig. 1). The existence of both criteria confers an 80 percent sensitivity and specificity differentiating patients with FM from patients with other chronic pain disorders. These ACR classification criteria, performed well in specialty clinics, are very useful in providing some patient homogeneity for clinical trials. However, they have not been widely embraced in primary care and their absence certainly does not exclude the possibility of FM since daily fluctuations might occur.

In recent years the case definition of FM has changed somewhat with increasing recognition of the importance of cognitive problems and somatic symptoms, factors that were not integrated in the 1990 ACR classification criteria. In 2010 Wolfe et al suggested a new set of criteria designed at diagnosing FM [4]. Their criteria are based on two variables: the widespread pain index (WPI) (the number of 19 defined body regions) and the fibromyalgia symptom severity scale (SS) (fatigue, waking unrefreshed, cognitive symptoms) plus the extent (severity) of somatic symptoms in general (Table 3). In their model the WPI strongly correlates with the ACR tender point count, and the SS scale correlates with the other disease

Table 1. Clinical features associated with the FM syndrome.

Cardinal signs:
Generalized pain
Tender points sensitive to pressure
Characteristic manifestations (more than 75 % of the patients):
Fatigue
Non restorative sleep
Sleeping Disorders
Stiffness (especially in the morning)
Common Manifestation (More than 25 % of the patients):
Irritable colon
Raynaud's Phenomenon
Headache
Sensation of swelling
Parasthesia
Functional impotence
Psychiatric co-morbidities (e. g. anxiety, depression)
Symptomatic sensitivity (e. g. cold or stress)

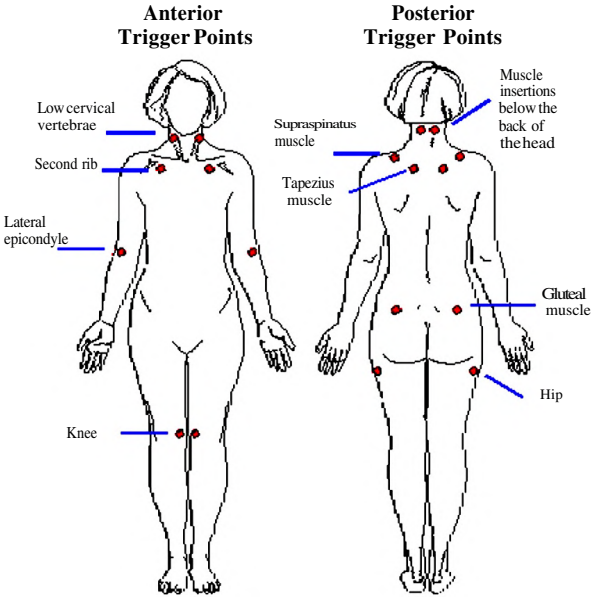

Figure 1. Illustration demonstrating the anatomical location of the tender points assessed in Fibromyalgia.

Table 2. The American College of Rheumatology 1990 Criteria for the Diagnosis of Fibromyalgia.

History of widespread pain, with all of the following present: pain in the left side of the body, pain in the right, pain above the waist and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present.
Pain in 11 of 18 tender point sites on digital palpation: **Occiput:** Bilateral, at the sub occipital muscle insertions **Low cervical:** Bilateral at the anterior aspects of the intertransverse spaces at C5-C7 **Trapezius:** Bilateral at the midpoint of the upper border **Supraspinatus:** Bilateral, at origins above the scapula spine near the medial border **Second rib:** Bilateral at the second costochondral junctions just lateral to the junctions on upper surfaces **Lateral epicondyle:** Bilateral, 2 cm distal to the epicondyles **Gluteal:** Bilateral, in upper outer quadrant of buttocks in anterior fold of muscle **Greater trochanter:** Bilateral, posterior to the trochanteric prominence **Knee:** Bilateral, at the medial fat pad proximal to the joint line.
Digital palpation should be performed with an approximate force of 4 kg. For a tender point to be considered "positive" the subject must state that the palpation was "painful". "Tender" is not to be considered painful. For classification purposes, patients will be said to have FM if both criteria are satisfied. Widespread pain must have been present for at least 3 months. The presence of a second clinical disorder does not exclude the diagnosis of FM.

components. In their paper, FM diagnosis was considered with a composite value of WPI $\geq$ 7 and SS $\geq$ 5 or WPI = 3–6 and SS $\geq$ 9. SS scale can be used alone as a measure of FM disease severity. The new set of diagnostic criteria correctly classifies 88.1 % of cases classified by the ACR classification criteria, and *does not require a physical or tender point examination*.

One of the greater drawbacks of both diagnosing systems mentioned here is that disease diagnosis is based on symptom severity. The loss of tender points or painful regions due to any cause, including successful treatment can result in failure to meet diagnostic criteria, unlike other rheumatic diseases like systemic lupus erythematous or rheumatoid arthritis.

4 Clinical and laboratory

There are no specific laboratory tests for diagnosing FM. No biomarkers or serologic tests are specific or of diagnostic value in FM. The pathophysiology of FM is considered to be related to aberrant central pain mechanisms. Various central nervous system processes in the brain and spinal cord manifest abnormalities in

Table 3. Suggested 2010 Fibromyalgia diagnostic 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.
WPI: The number of areas in which the patient has had pain over the last week. Score will be between 0 and 19: left shoulder girdle, right shoulder girdle, left hip, right hip, left jaw, right jaw, upper back, lower back, left upper arm, left lower arm, left upper leg, left lower leg, right upper arm, right lower arm, right upper leg, right lower leg, chest, neck, abdomen
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. SS scale score: 1. Fatigue 2. Waking unrefreshed 3. Cognitive symptoms For the each of the 3 symptoms above, indicate the level of severity over the past week using the following scale: 1. No problem 2. Slight or mild problems, generally mild or intermittent 3. Moderate, considerable problems, often present and/or at a moderate level 4. Severe: pervasive, continuous, life-disturbing problems
Considering somatic symptoms in general, indicate whether the patient has: 1. No symptoms 2. Few symptoms 3. A moderate number of symptoms 4. A great deal of symptoms 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, diarrhoea, 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.

patients with FM. Fluctuations of various neurotransmitter concentrations were reported in FM, especially of serotonin and substance P. However, it is far from being clear whether these changes are causative or consequential. The hypothalamic-pituitary-adrenal axis, which is responsible for stress response exhibits mostly diminished response to TRH.

5 Management

Given the unclear aetiology of fibromyalgia, and the heterogeneous presentations of the disease, it has become clear that no single therapy is broadly efficacious. Many patients with FM benefit from a multidisciplinary approach in clinical practice. The complex nature of FM suggests that multimodal, individualised treatment programmes that combine pharmacologic and non-pharmacologic therapies may be necessary to achieve optimal outcomes in patients with this syndrome [5].

Pharmacotherapy

A wide range of agents have been employed in the treatment of patients with FM. However, only a small number of these medications have demonstrated effectiveness in controlled clinical trials. Antidepressants, primarily tricyclics, are effective, but they have a relatively narrow therapeutic index, and their use may be limited by poor tolerability. SSRIs have better tolerability than tricyclics, but do not appear to be as effective in relieving the wide range of FM-associated symptoms. Medications that inhibit re-uptake of both norepinephrine and serotonin (SNRI) show promise in treating both pain of FM and associated symptoms of sleep disturbance and fatigue as well as coexistent affective aspects, with fewer side effects than traditional tricyclics. The new antiepileptic pregabalin has been shown to be effective in reducing many of the symptoms associated with FM and is well tolerated. Recently this drug was granted FDA approval for the indication of FM. Few studies support the use of the mixed opiate tramadol for pain management in FM.

Although commonly prescribed, there is little objective evidence to assess the efficacy of nonsteroidal anti-inflammatory drugs (NSAIDs). In one double-blind, placebo controlled trial, ibuprofen was no better than placebo and in another, naproxen led to minor but insignificant symptom improvement. One trial of oral corticosteroid use found no efficacy.

Non-pharmacologic Treatment

A variety of non-pharmacologic treatments have been demonstrated to have at least modest efficacy in patients with FM. A 2004 systematic review found strong evidence for effectiveness of cardiovascular exercise, cognitive behavioural therapy (CBT), patient education, and multidisciplinary interventions that combined

elements of aerobic exercise, CBT and patient education. The same review found moderate evidence for efficacy of strength training, hypnotherapy, biofeedback, and mineral springs or salt baths (balneotherapy). Weak evidence exists for manipulative and manual therapies (chiropractic, massage) and physical modalities including electrotherapy and therapeutic ultrasound. While moderate evidence was also found for acupuncture. Since then, other forms of physical activity, such as tai chi, have been found to be useful treatments in the management of FM.

Multidisciplinary Treatment

There is strong evidence that a multidisciplinary approach is effective in treating FM. Five studies of multidisciplinary treatment that combined education, CBT, or both with exercise found beneficial effects on patient self-efficacy and overall FM.

The current guidelines for treating fibromyalgia are that the FM diagnosis must first be confirmed and the condition explained to the patient and family. Any comorbid illness, such as mood disturbances or primary sleep disturbances, should be identified and treated. Medications to consider initially are low doses of tricyclic antidepressants or cyclobenzaprine. Some SSRIs, SNRIs, or anticonvulsants may become first-line FMS medications as more trials are reported.

All patients with FM should begin a cardiovascular exercise program. Most patients will benefit from CBT or stress reduction with relaxation training. A multidisciplinary approach combining each of these modalities may be the most beneficial. Patients with FM who do not respond well to these steps should be referred to a rheumatologist, physical therapy specialist, psychiatrist, or pain management specialist.

6 Follow up

There is no single parameter or set of variables that are sufficient for following up on in order to assess disease activity or severity. The complex nature of FM requires assessing and following many variables that are all part of the disease pathology.

Measurement of global sense of well-being, quality of life, and functional capacity in multiple dimensions (physical, vocational, social, emotional) is a key area of assessment and is considered essential by regulatory agencies when contemplating approval of medications for chronic pain states. The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) is a generic instrument with 8 subscales. Assessment with the SF-36 has shown that patients with FM have reduced physical functioning, physical role functioning, general health, vitality, and social functioning but increased body pain versus healthy subjects.

The *FM Impact Questionnaire* (FIQ) is a simple instrument specifically designed to reflect changes in the FM patient's general status over time. It includes 10

questions and assessing the disease severity, the clinical course and the response to treatment are pain, fatigue, sleep quality, quality of life and psychiatric assessment.

7 Requirements for family practitioners

As most patients with symptoms suggestive of FM are first seen by primary-care physicians, it is imperative that these physicians should be acquainted with the FM construct; and especially with the diagnosis and basic approach to these patients. The significant burden this disorder has on medical services and expenses warrants a proper understanding and management by all medical professionals.

References

[1] Wolfe F, Ross K, Anderson J, et al. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995; 38: 19–28.
[2] Buskila D. Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome. Curr Opin Rheumatol 1999; 11: 119–26.
[3] Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990; 33: 160–72.
[4] Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res (Hoboken) 2010; 62: 600–10.
[5] Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. JAMA 2004; 292: 2388–95.