In the name of God

S.U.M.S.

Department of Internal Medicine

Shiraz E-Medical Journal

Vol. 7, No. 4, October 2006

http://semj.sums.ac.ir/vol7/oct2006/burn.htm

Fibromyalgia

Nazarinia MA.

Assistant Professor, Section of Rheumatology, Department of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

Correspondence: Dr. Nazarinia, Department of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran, Tel. & fax. : +98(711) 626-1089, E-mail: nazariniam@sums.ac.ir

Received for Publication: April 7, 2005, Accepted for Publication: September 25, 2006.

Educationals objectives:

After reading this material physician should be able to :

- Know the definition of fibromyalgia
- Become familiar with pathogenesis of disease
- Able to diagnose fibromyalgia from other cause of body pain.
- Can treat the patient with pharmacological and nonpharmacological modalities.

Introduction:

Diffuse pain is a defining symptom of fibromyalgia. The diagnostic evaluation of an individual with diffuse pain which can be caused by a number of disorders, depends o the duration of symptoms.

Definition

Although fibromyalgia (FM) is a relatively new term, the condition is not. For centuries in medical literature, a variety of semantic terms have been applied to persons who suffer from widespread musculoskeletal pain. Fibrositis, the most recent term before FM, implied that there was an inflammatory process with the connective tissue; this term was abandoned when research showed that this condition is not due to inflammation in the tissues[1].

Diffuse pain is a defining symptom of FM. The diagnostic evaluation of an individual with diffuse pain, which can be caused by a number of disorders, depends on the duration of symptoms and the findings in the history and physical examination[2].

To fulfill the criteria for FM established by an American College of Rheumatology (ACR) committee in 1990, an individual must have both a history of chronic widespread pain involving all four quadrants of the body (and the axial skeleton) and the presence of 11 of 18 " tender points" on physical examination[3]. These criteria were never intended to be strictly applied to individual patients as diagnostic criteria, and it is widely acknowledged that many persons who have the clinical diagnosis of FM do not fulfill this definition[1].

A tender point is defined as an anatomic site where an individual complaints of pain when approximately 4 kg of pressure is applied (approximately the amount of pressure required to blanch the examiner's nail).

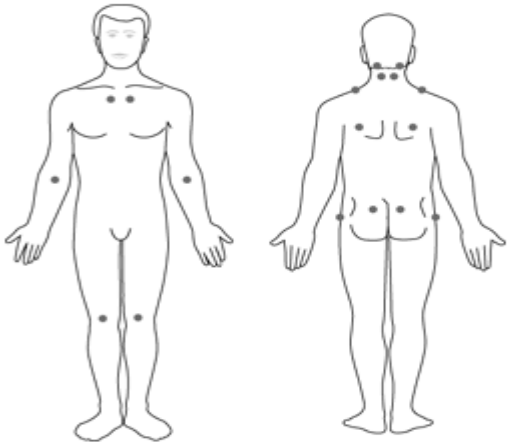

figure 1: fibromyalgia tender points

Although early studies suggested that FM patients experienced tenderness only in these discrete regions, recent data show that individuals with FM display increased sensitivity to pain throughout the body[4].

FM is a chronic musculoskeletal pain disorder characterized by widespread pain of at least three months duration and pain upon palpation at multiple sites called tender points. A majority of FM patients also complain of chronic fatigue syndrome like symptoms including fatigue and nonrestorative sleep, and a sizable minority also report dysmenorrhea, irritable bowel syndrome, tension, migraine headache, and raynaud's phenomena peoples with FM awaken form sleep with intensified muscle stiffness and aching, and prominent fatigue[5].

Patients reports of significant sleep disturbance are common in these illness. According to some theories FM are best viewed as chronic disorder of sleep-wake

cycle characterized by reduction of deep sleep (stage three and stage four slow wave). The loss of normal sleep architecture triggers a disturbance of circadian rhythm an associated neurohormones, such as cortisol and melanotin, which normally help regulate the sleep-wake cycle[5].

History of FM:

Muscular pain that limits activity, but have no observable cause has been noted in the medical literature since 1736, when Guillaume de Baillou published liver de rheumatismo describing a case that is currently accepted to be consistent with FM. The term fibrositis was officially coined in 1904 but not accepted by medical community as a condition worthy of their attention or medical treatment. In 1990 the concept of inflammation as the cause of the pain was detected as there was no support, and the name of syndrome was changed with tender points located in specific areas (table 1)[6].

Table 1. Fibromyalgia synonyms

Fibrositis
Myofascial pain syndrome
Neuromyasthenia
Neurashenia
Psychaigia
Muscular Rheumatism
Myofascitis
Myodysenuria
Chronic Rheumatism
Pressure point syndrome

Genetics:

There is some evidenceof familial aggregation for nearly all of the illnesses within this spectrum, including FM[7].

Clustering of FM has been noted which has led to a search for gentic factors in this syndrome while clustering does not confirm a genetic role in FM, and environmental factors may be the reason for such findings, it has been noted that twenty six percent of first degree relatives of people with FM also have FM. The search for a HLA association are ongoing with both positive and negative reports found in the literature[6].

Etiology

Like many illnesses, FM may occur when a person who is genetically predisposed comes in contact with certain environmental exposures that can trigger the expression of symptoms[1,2].

Environmental exposures that generally are accepted to by triggers of FM, all of which can be considered stressors, include physical trauma (especially to axial skeleton), infections (parvovirus, hepatitis C), emotional distress (acute or chronic), endocrine disorders (hypothyroidism) and immune stimulation as may occur in a variety autoimmune disorders[8].

Although studies of groups of individuals suggest there are many stressors that can trigger the development of this illness, it usually is difficult to assess with certainly the role of a single exposure in a given patients.

Pathogenesis

Most investigators in this field believe that the primary abnormality leading to the expression of symptoms in FM and related conditions is aberrant central nervous system function[1,2]. Furthermore, there is a general belief that the central components of the “stress response” are playing a major role in symptom expression, in that these systems are capable of being activated by a variety of stressors, and disturbances in this system can have

effects on sensory processing and autonomic and neuroendocrine function. The principal components of the human stress response are the corticotrophin-releasing hormone and locus caeruleus-norepinephrine / autonomic nervous systems[9].

These systems are capable of being activated by a variety of stressors; and disturbance in these system can affect sensory processing as well as autonomic and neuroendocrine function[2].

The areas of nervous system that may be playing some role in the pathogenesis of FM include sensory and processing, autonomic and neuroendocrine systems, and psychobehavioral influences[1].

Abnormalities in sensory processing:

A number of hypothesis have been generated to explain these complex biobehavioral conditions. Etiologic models range from purely biological conceptualization to sociocultural hypothesis. These models wax and wane in popularity in the scientific community, depending on the weight of current evidence for any particular models and cogency of specific theoretical formulations[5].

Some studies have demonstrated that people with FM cannot detect electrical, pressure, or thermal stimuli at lower levels than normal, but these stimuli cause pain or unpleasantness at a lower threshold (2). Some data on pharmacological treatment of FM patients may offer insight in to the mechanism involved in pain transmission. This studies suggest that spinal or supraspinal mechanisms are involved in pain maintenance in this condition and that this may be due to heterogeneous process[10].

Although nearly all of the research on sensory processing in FM has focused on the processing of pain, some data suggest a more generalized sensory processing disturbance. For example, many patients experience sensitivity to loud noises, bright lights, odors, drugs and chemicals[2].

Other investigators have attempted to identify specific neurochemical abnormalities that may be associated with abnormal pain transmission. Several groups demonstrated that patients with FM have approximately three fold higher concentrations of substance P in cerebrospinal fluid (CSF) than those of normal control subjects[1,2,11,12].

An elevated CSF level of substance P is not specific for FM this finding has also been noted in patients with osteoarthritis of hip and chronic low back pain. It is likely that these findings are related to the presence of pain, because persons with chronic fatigue syndrome do not display this findings[13].

Several other substance are known to have prominent effects on nociception that may be abnormal in FM. For example, norepinephrine has an antinocicetive function centrally, and the level of its principal metabolite, 3-methoxy-4-hydroxyuphenthylene, is low in the CSF of FM patients [14].

Finally, there is some evidence to justify a role for low central levels of serotonine in several disorders within this spectrum[14].

Hypothalamic-pituitary anis dysfunction:

Substantial data suggest that the hypothalamic-pituitary axis function abnormally in subsets of persons with FM and related disorders[15].In FM most studies have revealed low 24-hour urinary free cortisol excretion, exaggerated adenocorticotropic hormone release in response to corticotropin-releasing challenge, and abnormal diurnal rhythmicity in the secretion of cortisol and other hormones[1,2].

Changes have been noted in growth hormone (GH) axis that suggest abnormal hypothalamic function. Bennett and

associates[16] have demonstrated that insulin like growth factor-I (IGF-1) is low in about a quarter of FM patients. The defect in GH secretion that leads to the low IGF-1 appears to be hypothalamic in origin[16].

Autonomic Nervous system:

Just as with studies of neuroendocrine function, though, only a subset of FM patients have abnormal autonomic function[1]. Various studies have demonstrated that subsets of persons with FM as well as other similar disorders such as CFS, display low baseline sympathetic tone and an inability to respond to stressors [7,17].

Psychiatric, psychologic and Behavioral factors:

There has been a long standing debate about the role of psychiatric, psychologic, and behavioral factors in FM[1].

Approximately 20-40 percent of individuals with FM seen in tertiary care centers have an identifiable current mood disorder, such as depression or anxiety disorders[18].

The lifetime incidence of psychiatric comorbidities in FM patients from tertiary care centers ranges from 40-70%[1,2].

Clinical Features

To fulfill the criteria for FM published by an ACR committee in 1990, and individual must have a history of chronic widespread pain involving all four quadrants of body (and axial skeleton) and the presence of 11 of 18 “tender points” on physical examination. These classification criteria were never intended to be applied to individual patients for the purpose of diagnosis. At least half of the individuals who have the clinical diagnosis of FM will not fulfill this definition[2].

The patient most likely to be diagnosed as having FM is women between 25-50 years of age[6].

In addition to pain and tenderness, most individuals, experience a high prevalence of nondefining symptoms.

For example, most people with FM experience fatigue, and at least half of individuals who meet ACR criteria for FM also will meet criteria for chronic fatigue syndrome[2].

Patients with FM and related illness also display a wide array of allergic symptoms ranging from adverse reactions to drugs and environmental stimuli to reactions to drugs and environmental stimuli to higher than expected incidences of rhinitis, nasal congestion, and lower respiratory tract symptoms[12]. Heaving ocular, and vestibular abnormalities have been noted, including a high incidence of sicca symptoms, a decreased painful sound threshold, exaggerated nystagmus and ocular dysmotility, and asymptomatic low frequency sensorineural hearing loss[1,2].

People with FM wake up feeling like they need eight more hours of sleep. Another frequent complaint is swelling of the hands that is not obvious to the examiner, but the patient is clearly able to discern a difference, regardless of weather the swelling effects the ability to wear jewelry, clothing, and can be shown to not effect the shape and size of the fingers[6].

On physical examination exclusion of other conditions is the priority. Beside severe tenderness of the skin and muscle tissue there are few objective findings.

Bowel sounds are almost always increased, and there may be mild diffuse abdominal tenderness in varying locations and these sites change during the course of the examination[6].

The physical examination generally is unremarkable in FM, except for tender points. The tenderness may occur in virtually any part of the body, and is not confined to the vegions identified in the ACR criteria[1,2].

Diagnosis

It is difficult to diagnose a problem that has mostly subjective finding and few objective ones. FM is a diagnosis of exclusion. It takes an average of 5 years for the diagnosis to be made in a person because of the need to exclude 50 many other diagnosis[6].

The two criteria that need to be met for the diagnosis of FM to be made include pain on the left and right side of the body, both above and below the diaphragm. The pain must also present for a minimum of there months. There should also be areas of tenderness checked in 18 areas of the body[6].

Laboratory testing should be used judiciously in the evaluation of patients with clinical features consistent with FM. IF symptoms have been present for years and physical examination is unrevealing except for tenderness, a minimal workup is necessary. At the other end of the spectrum, a much more aggressive evaluation is warranted in the patient who present with acute or subacute onset of symptoms. Even in this setting, though, ordering serologic assays such as an antinuclear antibody titer should generally be avoided unless there is strong evidence for an autoimmune disorder[1,19].

Workups of the patients with sign and symptoms of FM include compete blood count, TSH, Hepatitis panel, ESR, chemistry profile, creatin in kinas and a urinalysis. If rheumatologic disorders like SLE, Polymyalgia Rheumatica (PMR), Rheumatoid arthritis (RA) and polymyositis need to be considered then an ANA and RF should also be done. Sleep studies are also a useful test, but must be done by a sleep center that evaluated for FM, and not just pulmonary problems that arise from sleep disturbances[6].

Aggrevating and Alleviating factors:

It is accepted that cold weather, humid weather or a rapid change in temperature can bring on an exacerbation of FM. Lifestyle patterns involving sleep, exercising past the point of exhaustion, anxiety, remaining inactive for long periods of time, missing sleep or meals, and allowing oneself to become severely physically or mentally fatigued can cause a flare-up in the syndrome[20].

Other triggers include surgery, medical illness, hypothyroidism, even the activation/infection of HIV or lyme disease can trigger FM[6].

Differential diagnosis

Table 2 lists the disorders that can simulate fibromyalgia. The two conditions that most closely simulate FM are hypothyroidism and polymyalgia rheumatica. For this reason, determination of thyroid stimulation hormone and erythrocyte sedimentation rate is suggested as in every person in whom the diagnosis of FM is being entertained[1].

Treatment

Non pharmacologic modalities:

Education patients with FM seen to be comforted once the diagnosis is confirmed by a health care professional[6].

Some patients who present with symptoms of FM nothing more than to be told that this is a non progressive condition.

Table 2. Misdiagnoses that may be Given to patients who Eventually are found to have the fibromyalgia syndrome.

Systemic lupus erythematosus, rheumatoid arthritis
Early spondlyoarthropathy
Multiple sclerosis
Depression
Hypochondriasis
Somatoform pain disorder
Malignering
Hypothyroidism
Inflammatory bowel disease
Sciatica
Neuropathy
Interstitial cystitis
Metabolic myopathy
Inflammatory myopathy
Alzheimer's disease
Meniere's disease
Polymyalgia rheumatica

Exercise relaxation and breathing exercise can be used to help a person maintain there functional ability at work[6].

Biofeed back there are a number of studies that show biofeed back successfully lessening the number of tender points, decreasing morning stiffness[6].

Hypnosis-Hypnosis has shown promise in relieving pain symptoms. Hypnosis was shown to be more effective than physical therapy in relieving pain in a controlled study of 40 patients with FM[21].

Physical therapy modalities-heat, stretching, massage, meditation, body work, can all be used to maintain the functional ability of a person with FM[6].

Manipulation people with FM both subjectively and objectively have been shown to benefit from manipulation[22].

Cognitive behavioral therapy focuses mainly on relaxation and coping strategies. There are strong positive reinforcements for healthy behaviors. Compliance with this therapy has been poor[23].

Pharamcological Modalities:

Tricyclic antidepressants: low dose of amitryptylline and trazodone have been shown to help with sleep, but have minimal effect of the pain symptoms. Initial dose of amitryptyllin is 10mg given at bed time. Symptom improval may take 4-6 weeks and a course of at least three months should be tried before a full evaluation of the therapy can be done[24].

Fluoexetine is most widely studied and has some medication is a minimum of two months[25].

Seratonin/ norepi reuptake inhibitor: evelafaxine is the only medication in this class and at high dose it does increase norepi and dopamine level in the serum. Anecdotally it has been very successful, but no double blind trials have been conducted yet[6].

Benzodiazepines: when used in combination with NSAIDS have shown benefit in reducing pain[26]. The chronic nature of FM makes benzodiazepines a difficult medication to choose[6].

Analgesic: tramadol in injectable form has been shown to be as effective as acetaminophen with codeine for treatment of pain without the side effect and abuse problem[27].

Calcitonin: nasal administration of calcitonin has been shown to decrease pain. Calcitonin is a serotonin precursor[6].

Muscle relaxants: cyclobenzaprine (Flexil) has been shown to help a person maintain stage four sleep and wake up more rested. A five my dose 1-2 hours before bedtime. It has also been shown to reduce pain particularly in the late evening [6,28].

Opoids: effective pain relievers but potentially dangerous medication to be using in FM(6).

Steroid injection in to trigger points: this therapy has been shown to increase a persons functional ability by increasing range of motion[6].

References:

1. Daniel J.C. Fibromyalgia. In Kelley's text book of Rheumatology. Sixth edition. WB Saunder's Company, 2001.

2. Daniel J.C. Fibromyalgia and diffuse pain. In Jobn H.Klipple, Primer on the Rheumatic disease. 12th edition. Arthritis foundation Co.2001.

3. Wolfe, Smyth, Yunus MB, et al: The American college of Rheumatology 1990 Criteria for the classification of fibromyalgia. Report of the multicenter criteria. Arthritis Rheum 33: 160, 1990.

4. Granges G, Little John G: Pressure pain threshold in pain free subjects, in patients with chronic regional pain syndromes, and in patients with fibromyalgia. Arth Rheum 36: 642, 1993.

5. Friedberg F, Jason LA,: Chronic fatigue syndrome and fibromyalgia: Clinical assessment and treatment. Journal of psychology, 57(4), 433-455, 2001.

6. Cymet TC: A practical approach to fibromyalgia Journal of the National Medical Association, 95(4), 278-285, 2003.

7. Clunw DJ, Chronsos GP: Chronic pain and fatigue syndrome: Overlapping clinical and neuroendocrine features and potential pathogenic mechanisms. Neuroimmunomodulaton 4: 134, 1997.

8. Yunns MB. Towards a model of pathophysiology of fibromyalgia: aberrant central pain mechanisms with peripheral modnlation. J Rheumatol. 19: 846-850, 1992.

9. Chronsos GP, Gold PW. The concepts of stress and stress system disorders. Overview of physical and behavioral hemostasis. JAMA 267; 1244, 1992.

10. Sorensen J, Benytssom A, Backman E, et al. Pain analysis in patients with fibromyalgia. Effect of intravenous morphine, lidocaine, and ketamine. Scand J Rheumatol 24: 36, 1995. Pubmed Abstract.

11. Bradley LA, Alberts KR, Alarcon GS: Abnormal brain regional cerebral blood flow and cerebrospinal fluid levels of substance P in patients and non-patients with fibromyalgia. Arth. Rheum 39(95):1109, 1996.

12. Welin M, Bragee B, Nyberg F, et al. Elevated substance P levels are contrasted by a decrease in met-enkephalin-argphe levels in CSF from fibromyalgia patients. J Musculoskeletal pain 3:3, 1995.

13. Elevated B, Nilsson CG, Lindh G, et al: Chronic fatigue syndrome differs from fibromyalgia. No evidence for elevated substance P levels in cerebrospinal fluid of patients with chronic fatigue syndrome pain. 78: 153, 1998. PubMed Abstract.

14. Ressell IJ, Vaeroy H, Javors M, et al. Cerebrospinal fluid biogenic amine metabolites in fibromyalgia/ fibrositis syndrome and Rheumatoid Arthritis. Arthritis Rheum 35: 550, 1992.

15. Crofford LJ: Neuroendocrine abnormalities in fibromyalgia and related disorders. Am J Med Sci, 315: 359, 1998. PubMed Abstract.

16. Benett RM, Cook DM, Clark SR, et al: Low somatomedin-C in fibromyalgia patients: An analysis of clinical specificity and pituitary/ hepatic responses. Arthritis Rheum, 36(95): 62, 1993.

17. Elam M, Johansson G, Willin BG: Do patients with primary fibromyalgia have an altered muscle sympathetic nerve activity? Pain , 48: 371, 1992. PubMed Abstract.

18. Biossevain MD, McCain GA: Toward an integrated understanding of fibromyalgia syndrome II. Psychological and phenomenological aspects. Pain : 239, 1991. PubMed Abstract.

19. Bates DW, Buchwald D, Lee J, et al. Clinical laboratory test findings in patients with chronic fatigue syndrome. Arch Intern Med 155: 97, 1995. PubMed Abstract.

20. Hench PK. Evaluation and differential diagnosis of fibromyalgia. Aproach to diagnosis and management Rheum Dis Clin North America. 1989; 15: 19-20.

21. Haaen HC, Hoenderdone HI, Van Romunde et al. Controlled trial of hypnotherapy in the treatment of refractory fibromyalgia. Am J Med. 104: 227-231, 1998.

22. Loks, Knchera ML, Peterson SC, et al. Osteopathic manipulative treatment in fibromyalgia syndrome JAOA. 92(9): 1177-1181, 1992.

23. Vlaeyen JWS, Teeken – Grwben N JN, Goosens MEJB et al. Cognitive educational treatment of fibromyalgia. A randomized clinical trial. I clinical effects. J Rheumatol, 23: 1237-1245, 1996.

24. Clauw D. Fibromyalgia: more than just a musculoskeletal disease. American family physician, 52(3), 843-851, 1995.

25. Arnold LM, Keek PE, Wlge JA. Antidepressant treatment of fibromyalgia a meta-analysis and review. Psychosomatics, 41(2); 104-113, 2000.

26. Russell IJ, Fletcher EM, Michaleak JE, et al. Treatment of primary fibrosis / fibromyalgia syndorem with ibuprofen and alpraz, lam a double blind placebo controlled study. Arthritis Rheum 34: 552-560, 1991.

27. Leventhal LJ. Management of fibromyalgia. Annals of internal Medicine, 131(11): 850-858, 1999.

28. Jeanne K, Tofferi, Jeffery L, et al. Treatmetn of fibromyalgia with cyclobenzaprine : A meta analysis Arthritis and Rheum . 51(1); 9-13, 2004.