

Initial Presentation of Pain in Patients with Fibromyalgia

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ABSTRACT

Background: Fibromyalgia is characterized by diffuse musculoskeletal pain at the time of diagnosis, but many patients report their initial symptoms as being focal or local.

Objectives: To evaluate, prospectively, the initial location of body pain in recently diagnosed patients with fibromyalgia.

Methods: Non-selected patients from the rheumatology clinic who were recently diagnosed with fibromyalgia (≤ 2 years) with symptoms of < 4 years participated in our study. Demographic and clinical parameters were documented, as was the initial location of pain they had experienced. Sub-analysis of data according to gender and ethnicity was conducted using chi-square test.

Results: The study comprised 155 patients. Mean age was 39.8 ± 11.7 years; 85% were female. Mean duration of symptoms was 2.11 years and of diagnosis was 0.78 years. Six patients (3.9%) reported initial symptoms of pain as being diffuse from the start, 10 (6.5%) could not remember the location of their initial symptoms, and 139 (90%) reported initial focal pain. Hands were reported as the initial area of pain for 25.2% of the patients, 19.4% reported the back, and 11% reported both trapezial areas as the initial area of pain. In 90% of the patients (excluding patients with back, abdominal, or chest pain) the initial symptoms were bilateral and symmetrical. No significant difference in initial presentation was found among different gender or ethnic groups.

Conclusions: Pain in fibromyalgia patients usually presents as focal and symmetrical. Bilateral hand pain, followed by back pain, was the most common reported area of initial pain among fibromyalgia patients.

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KEY WORDS: fibromyalgia, focal pain, initial presentation, musculoskeletal pain

The male-to-female ratio is approximately 4:1 [1]. The pathogenesis of this syndrome is not fully understood. Central localization of pain is the leading theory, where the presumption is that pain perception at the brain level is exaggerated [4]. Treatment is usually symptomatic and periods of exacerbations and improvement are also common in this syndrome.

At the time of diagnosis, patients usually report diffuse musculoskeletal pain; however, many patients report initial pain being focal and evolving to diffuse symptoms of pain over time. Surprisingly, we found no studies in the literature about the initial areas of pain among patients with fibromyalgia.

In this study, we prospectively recruited patients at the rheumatology clinic who were recently diagnosed with fibromyalgia. We evaluated the location of initial area/s of pain in their body.

PATIENTS AND METHODS

Non-selected recently diagnosed patients with fibromyalgia (≤ 2 years) who attended the rheumatology clinics at different settings, including the Nazareth Hospital in Nazareth, Laniado Hospital in Netanya, as well as Maccabi and Meuhedet health services in northern of Israel, were prospectively asked to participate in our study. After obtaining written consent from patients, demographics, duration of symptoms and diagnosis, treatment, serology, radiologic, and electromyographic results were documented. These patients were asked if they remembered the first place in their body where pain started. Migraines or headaches were excluded from being initial symptoms of pain because migraines and headache have been found to precede other symptoms of fibromyalgia by years. Back pain was included as an initial symptom regardless of duration and existence of disc bulging or other mechanical problems. Patient responses of initial presentation at three or more different body areas, symmetrical or not, were considered as diffuse presentation. Response of presentation at two different body areas, symmetrical/bilateral or not, were considered as local, such as bilateral hands with bilateral elbows, or bilateral hands with left elbow.

Fibromyalgia is a common type of chronic pain syndrome [1]. It is mainly characterized by diffuse musculoskeletal pain, fatigue, and mood and sleep problems [2]. In addition, many patients have co-morbidities including migraines, irritable bowel syndrome, and discopathy [3]. Fibromyalgia affects approximately 3–5% of the general population, mostly women.

Inclusion criteria included patients who met the American College of Rheumatology Criteria from 2010 for the diagnosis of fibromyalgia with duration of symptoms less than 4 years and a diagnosis by rheumatologist.

Exclusion criteria included patients with fibromyalgia that developed after physical trauma, patients with sacroiliitis, patients with back pain developing directly after delivery or epidural procedure, patients with positive serology of antinuclear antibodies or rheumatoid factor, patients with elevated c-reactive protein > 1.5 the upper normal limit, patients with connective tissue disease, patients with primary osteoarthritis of the hands, patients with osteoarthritis of the knees, patients with carpal tunnel syndrome or any entrapment neuropathy, patients performing anaerobic sport activity, and/or patients with plantar fasciitis.

We retrospectively reviewed the charts of the patients to verify for the complaints and location of pain they reported.

Simple measures of frequency were used to calculate the different parameters. Chi-square test (two-tailed *P* value) was used for subgroup analysis to compare between genders and also between different ethnic groups.

RESULTS

Our study comprised 155 patients who qualified under the criteria of our study. Ten patients were unsure of the initial presentations; six reported that their initial pain symptoms were diffuse from the start; and 139 (90% of all patients) reported local areas as initial areas of pain, mostly bilateral, and symmetrical.

Table 1 summarizes the demographics and clinical parameters of all the patients. The mean age of patients was 39.8 ± 11.7 years; 85.6% were female. Mean duration of pain and time since diagnosis was 2.11 ± 1.16 and 0.78 ± 0.65 years, respectively.

Table 2 shows the distribution of location of initial pain symptoms based on patient reports. The most common areas were hands, mostly bilateral, followed by the back and trapezial areas. All patients with hand pain had hand X-rays without findings explaining the hand pain; 23 had negative electromyographic studies of the hands; 21 patients among those with initial presentation of back pain had magnetic resonance imaging (MRI) of the sacroiliac joints that was negative for sacroiliitis,

and 5 other patients had negative HLA B27 levels. All patients with knee pain had negative X-rays of the knees, 9 patients had negative ultrasound of the knees and 4 had negative MRI. All patients with feet and pelvic area pain had negative X-rays.

When reviewing the charts of the patients, we found information regarding initial pain in 88 patients (~57%). For 76 reports (~87%) the information was similar to that which the patients reported. Among the rest of the patients (13%), other places or pain in the extremity without specifying the exact location, were reported. In any case, we kept the distribution of pain as reported by the patients.

Table 3 and Table 4 show subgroup analysis based on gender and ethnic groups. No significant difference was found between male and female patients or between Jewish or Arab patients.

DISCUSSION

The most prominent finding in our study is that at least 90% of the patients reported that their initial symptoms of pain started in a local, mostly symmetrical area of the body, and not as a diffuse widespread pain.

Only 3.9% of the patients reported having diffuse musculoskeletal pain from the start. This phase of diffuse musculoskeletal pain seems to be a later phase developing apparently over months or years. The issue of the usual amount of time that it takes for a patient with fibromyalgia with local complaints, which then develop to wide spread pain, could not be answered in this study, but it seems to occur over a few months to a few years.

Bilateral hands were the most common initial body area of pain. Usually such complaints could allude to the possibility of inflammatory diseases such as connective tissue diseases, carpal tunnel syndrome, tendinopathy, or degenerative changes, and rarely raises the suspicion of fibromyalgia [5-7].

Back pain was second in the list, and the differential diagnosis here is mainly between mechanical pain such as discopathy or inflammatory diseases such as spondyloarthropathy [8,9]. Even patients with isolated back pain and lumbar discopathy may eventually develop fibromyalgia.

Patients who presented with bilateral knee pain had no evidence of synovitis or knee effusion but usually had prominent tenderness at the distal thigh areas close to the knee joint or at the anserine area.

The most classic area of musculoskeletal pain described by fibromyalgia patients is at the trapezial areas [10]. Complaints at these areas should raise real suspicion for fibromyalgia. However, in our study, it was the third most frequent place reported as the initial body pain area.

The bilateral epicondyle and trochanteric area are also classic areas of tendineal problems [11]. Complaints at these areas, although common in the general population, could remain as local problems and some of these patients may develop symptoms of fibromyalgia.

Table 1. Demographics and clinical parameters

Parameter	Result
Female : Male	132 : 23
Jews: Arabs	86 : 69
Age*	39.8 ± 11.7 (14-61)
Duration of pain*	2.11 ± 1.16 (0.3-4)
Duration of diagnosis*	0.78 ± 0.65 (0-2)

*Mean ± standard deviation, years (range)

Table 2. Distribution of initial location of pain in all our patients (N=155)

Parameter	Result (%)
Patient reporting diffuse pain from the start	6 (3.9)
Patients who could not remember	10 (6.5)
Hand/s + wrist/s	39 (25.2)
Hands, bilateral	21
Hand, right	6
Hand, left	1
Hands, bilateral and bilateral arms, elbows, Legs, or trapezial areas	4
Wrists, bilateral	4
Wrist, left	1
Finger, first, bilateral	1
Finger, left, fifth	1
Back	30 (19.4)
Low back	20
Neck area	5
Upper back	1
Mid-back	1
Coccyx	2
Trapezial area, bilateral	17 (11)
Knees, bilateral	13 (8.4)
Feet	8 (5.2)
Bilateral	4
Foot, left	1
Bilateral feet and bilateral trochanters	3
Legs	6 (3.9)
Bilateral	5
Legs + feet, bilateral	1
Trochanters, bilateral	6 (3.9)
Elbows	4 (2.6)
Bilateral	3
Elbow, right	1
Chest	3 (2)
Ankles	3 (2)
Bilateral	2
Ankle, right	1
Shoulder, right	2 (1.3)
Abdomen	2 (1.3)
Forearms, bilateral	1 (0.6)
Arm, left	1 (0.6)
Flanks, bilateral	1 (0.6)
Body pain and numbness, left side	1 (0.6)
Inguinal area, right	1 (0.6)
Mid pelvic, left	1 (0.6)

Table 3. Distribution of areas of initial pain among women vs. men

Parameter	Women	Men	P value
Hands + wrists	35	4	0.401
Back/neck	25	5	0.678
Trapezial areas	15	2	0.799
Knees	10	3	0.375

Table 4. Distribution of areas of initial pain among Jews vs. Arabs

Parameter	Jews	Arabs	P value
Hands+ wrists	22	17	0.885
Back	18	12	0.577
Trapezial areas	9	8	0.829
Knees	9	4	0.312

The lack of documentation of symptoms in 43% in the reviewed charts could be due the lack of report by the patients or lack of documentation by the treating physician. In any case, the documented findings in the majority of the patients had high correlation with their answers. As mentioned, we kept the location of initial pain as reported by the patients following our question. The documented information in the charts could also be affected and were biased by the nature of conversation or questions by the treating physician that were not documented.

When looking at both sexes, the distribution of the initial symptoms was quite similar. No significant difference was found also between two different ethnic groups, Arabs vs. Jews, in Israel.

It is not clear whether the beginning of fibromyalgia development in our study could be considered as the time of these initial local symptoms, or at the time of diffuse musculoskeletal pain. The answer to this question needs to be determined through prospective cohort studies from the general population, especially of young women and girls who report focal areas of pain. Such patients should be carefully followed and asked about the development of other co-morbidities and symptoms of fibromyalgia.

Regardless of the pathogenesis, many systemic diseases and inflammatory/autoimmune syndromes or non-inflammatory conditions could start with one finding only, accumulating more and more findings over time, leading eventually to the diagnosed of the disease. The interesting thing in our study is that it encompasses a majority of the patients with fibromyalgia, and not a minority, making our finding totally out of main stream research.

Fitzcharles and Yunus [12], who are world authorities in fibromyalgia, stated, "The typical patient is female in her 40s or 50s with a few years of ill-defined musculoskeletal pain. Onset of symptoms is usually gradual, but occasionally there may be a

sudden onset following an identifiable event, such as a medical illness, a mentally stressful incident or physical trauma" [12]. We could not find studies specifically addressing the evolution of fibromyalgia that can confirm that fibromyalgia is a widespread diffuse musculoskeletal pain from the start. This issue needs to be addressed.

Physicians, including rheumatologists who regularly follow fibromyalgia patients, often hear new complaints from these patients, including new areas of pain, dizziness, tinnitus or hearing loss that did not exist before. Patients with fibromyalgia may develop new symptoms and signs, and this fact could support the idea that the widespread musculoskeletal pain at the time of diagnosis could start as less widespread symptoms/signs, including focal or local pain, as in our patients.

It is not easy to explain our findings in terms of pathogenesis, but we think that those patients with early fibromyalgia, who present with few symptoms, are prone to present with hand pain since the hands contain the most active joints of the body followed by back/knee pain, which are subjected to enormous physical load.

LIMITATIONS

The main limitation was recall bias, especially among patients with fibromyalgia, where memory problems could be a real issue [13]. However, most of the patient answers were direct and without hesitations.

CONCLUSIONS

Pain in fibromyalgia patients usually presents as focal and symmetrical. Bilateral hand pain, followed by back pain, was the most common reported area of initial pain among fibromyalgia patients.

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Capsule

Pirfenidone in heart failure with preserved ejection fraction: a randomized phase 2 trial

In heart failure with preserved ejection fraction (HFpEF), the occurrence of myocardial fibrosis is associated with adverse outcome. Whether pirfenidone, an oral antifibrotic agent without hemodynamic effect, is efficacious and safe for the treatment of HFpEF is unknown. In this double-blind, phase 2 trial (NCT02932566), Lewis et al. enrolled patients with heart failure, an ejection fraction of 45% or higher and elevated levels of natriuretic peptides. Eligible patients underwent cardiovascular magnetic resonance and those with evidence of myocardial fibrosis, defined as a myocardial extracellular volume of 27% or greater, were randomly assigned to receive pirfenidone or placebo for 52 weeks. Forty-seven patients were randomized to each of the pirfenidone and placebo groups. The primary outcome was change in myocardial extracellular volume, from

baseline to 52 weeks. In comparison to placebo, pirfenidone reduced myocardial extracellular volume (between-group difference, -1.21%; 95% confidence interval, -2.12 to -0.31; $P=0.009$), meeting the predefined primary outcome. Twelve patients (26%) in the pirfenidone group and 14 patients (30%) in the placebo group experienced one or more serious adverse events. The most common adverse events in the pirfenidone group were nausea, insomnia and rash. In conclusion, among patients with HFpEF and myocardial fibrosis, administration of pirfenidone for 52 weeks reduced myocardial fibrosis. The favorable effects of pirfenidone in patients with HFpEF will need to be confirmed in future trials.

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