Fibromyalgia in children and adolescents: Clinical manifestations and diagnosis

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INTRODUCTION

Fibromyalgia is characterized by chronic and diffuse musculoskeletal pain, fatigue, and nonrestorative sleep, as well as several other typical symptoms that may vary from patient to patient. The etiology and pathogenesis of this disorder are unknown, although data indicate that a significant central sensitization component is at the root of the syndrome [1-3]. Initially described in adults, this disorder is often seen in children and adolescents and may be referred to as juvenile primary fibromyalgia when it occurs in childhood [4,5]. Adult data cannot always be extrapolated to those with juvenile fibromyalgia syndrome, since there are some distinct differences [6]. (See "Pathogenesis of fibromyalgia".)

The clinical manifestations and diagnosis of fibromyalgia in children and adolescents are reviewed here. The treatment and outcome of juvenile fibromyalgia and the clinical features, diagnosis, and treatment of the disease in adults are presented separately. (See "Fibromyalgia in children and adolescents: Treatment and prognosis overview" and "Clinical manifestations and diagnosis of fibromyalgia in adults" and "Initial treatment of fibromyalgia in adults".)

EPIDEMIOLOGY

Diagnostic variability makes reliable estimates difficult to ascertain, but limited data from population-based studies suggest that the prevalence of fibromyalgia syndrome in school-aged children and adolescents is between 2 and 6 percent [5,7,8].

The age of onset of fibromyalgia is typically in the early to middle adolescent years. One study using data from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry indicated that ages at baseline visit ranged from 9 to 20 years, with a mean of 15.4±2.2 years [9]. Fibromyalgia is thought to be rare in children under nine years of age and virtually nonexistent in children under four years of age.

Patients with fibromyalgia account for approximately 7 percent of all cases referred to tertiary pediatric rheumatology centers [10,11]. There is a strong female predominance in the pediatric population, similar to that seen in adults [9,12].

ETIOLOGY

Although the etiology of fibromyalgia remains unknown, it is considered to be a disorder of pain regulation, classified often under the term "central sensitization" [1]. One widely accepted hypothesis is that fibromyalgia is a disorder of pain regulation due to neuroendocrinologic changes in the central and peripheral nervous systems, which occurs in genetically susceptible individuals, possibly in response to environmental triggers. This results in heightened pain perception and hypersensitivity to numerous stimuli.

The following is a summary of the data from studies in adults with fibromyalgia that support this mechanism of central sensitization. They are discussed in greater detail separately. (See "Pathogenesis of fibromyalgia".)

- The increased incidence of fibromyalgia in first-degree relatives of patients with this condition supports genetic susceptibility.
- Alterations in pain processing with increased levels of pain mediators and increased activation of pain-sensitive areas of the brain as detected by magnetic resonance imaging are observed in patients with fibromyalgia.
- Neurohumoral abnormalities are observed in the hypothalamic-pituitary-adrenal axis at baseline and after provocative testing in patients with fibromyalgia.
- Sleep and mood disturbances are noted in the majority of patients, suggesting underlying central nervous system dysfunction.
- Autonomic nervous system dysfunction (eg, orthostatic hypotension) is seen more frequently in patients with fibromyalgia compared with the normal population.

There is also evidence that small-fiber polyneuropathy underlies fibromyalgia in some patients, but these data are preliminary. A study of 15 adolescent to young adult patients diagnosed with fibromyalgia indicated that 53 percent had low epidermal neurite density in

contrast with 4 percent of controls, data that parallel similar studies in adults [13]. While these findings are of interest, it is unclear exactly what they mean, and it is premature to conclude that small-fiber neuropathies are the cause of fibromyalgia [14]. In fact, fibers that are less functional or of smaller diameter should decrease rather than increase sensitivity and pain [15]. Additional systematic research is needed [13,16].

The relationship between fibromyalgia syndrome and postural orthostatic tachycardia syndrome (POTS) continues to be elucidated [17,18]. In addition, there is a strong association between joint hypermobility and central sensitization [19,20]. Lastly, genetic polymorphisms in various pain and neurochemical pathways have been identified in some series of patients with fibromyalgia and have been suggested as risk factors for the development of this disorder. (See "Pathogenesis of fibromyalgia".)

There is increasing recognition that fibromyalgia may occur in patients with other diagnosed rheumatologic conditions [21]. Fibromyalgia may also co-occur with a number of other syndromes, including migraine headache [22,23], temporomandibular joint disorder [24,25], gastrointestinal disorders such as irritable bowel syndrome and possibly celiac disease [26-28], and gynecologic disorders such as endometriosis and vulvodynia [29,30]. There is increasing evidence that many "functional" pain problems and related symptoms, including orthostatic intolerance, sleep disturbance, mood issues, and hypermobility, may have common etiologic roots [31].

CLINICAL FEATURES

Fibromyalgia is characterized by chronic, widespread pain and the presence of tender points. Other common symptoms include fatigue, headache, depressed and/or anxious mood, and disturbed sleep. (See 'Classification and diagnostic criteria' below.)

Data collected through the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry provided insights into coexisting symptoms that accompany juvenile fibromyalgia syndrome [9]:

- Widespread musculoskeletal pain – 91 percent
- Frequent headaches – 68 percent
- Nonrestorative sleep – 52 percent
- Frequent awakenings – 42 percent
- Increased sleep latency – 41 percent
- Numbness and tingling of extremities – 32 percent
- Hypermobility on exam – 28 percent
- Subjective soft tissue swelling of extremities – 22 percent
- Irritable bowel symptoms – 16 percent

- Hypersomnia – 14 percent

Pain — The cardinal manifestation of fibromyalgia is diffuse musculoskeletal pain involving the arms, legs, back, and neck. Not all parts of the body may be affected simultaneously, but it is important to recognize that this is not a localized phenomenon. Affected patients frequently say, "I hurt all over" or "Everything hurts."

The pain may be described as an ache or an achy feeling, but terms as varied as "dull," "sharp," "shooting," "excruciating," and "burning" also are used by patients to describe the pain. It is usually constant and chronic, not intermittent, and may vary in intensity. It may wake patients from sleep, but, as a rule, the disturbed sleep characteristic of fibromyalgia is not caused by pain. The pain is not usually relieved by nonsteroidal antiinflammatory drugs (NSAIDs).

Although patients may describe joint pain and stiffness, they will also complain of pain and aching in the muscles, one characteristic that distinguishes fibromyalgia from arthritis. In addition, patients with fibromyalgia do not have swollen or inflamed joints on physical examination, although many will describe subjective perception of joint swelling. (See 'Differential diagnosis' below.)

In both the Yunus and Masi [4] and American College of Rheumatology (ACR) [32,33] criteria for fibromyalgia, chronic pain is a required finding, with the ACR definition specifying a minimum duration of three months (table 1). (See 'Classification and diagnostic criteria' below.)

Tender points — The second common finding in patients with fibromyalgia is the presence of multiple tender points (figure 1) [4,32,33]. These are highly localized areas of the body ("points") that are consistently sensitive to pressure. Palpation of these specific tender points in patients with fibromyalgia usually elicits pain causing a significant reaction in the patient, such as wincing and a withdrawal response [34]. Patients are usually not aware of the presence of the tender points as areas that are particularly painful. Although the presence of tender points is used clinically in adults to make the diagnosis of fibromyalgia, they are no longer a requirement in the revised ACR classification system [33]. (See 'Diagnosis' below.)

Children with fibromyalgia tend to have fewer tender points than adults [4]. The exact number of tender points present in a child with possible fibromyalgia is not as important in making the diagnosis of juvenile fibromyalgia as whether the child's constellation of symptoms is consistent with the diagnosis (ie, persistent, chronic, widespread pain associated with other symptoms such as sleep disturbances), provided that no other disease process is evident. (See 'Diagnosis' below.)

The presence of tender points in the absence of chronic pain does not appear to be predictive of later development of fibromyalgia in children [35].

Fatigue — Fatigue is a common and key complaint in children with fibromyalgia, similar to adults with this disorder. The prevalence of fatigue in series of children with fibromyalgia has ranged from as little as 20 percent [36] to 80 to 100 percent [4,9,37].

Headache — Frequent headaches occur in a majority of patients with fibromyalgia. The reported incidence ranges from 55 to 80 percent of patients [4,38-40].

Sleep disturbance — Disturbed or interrupted sleep occurs in at least two-thirds of children with fibromyalgia [10,39,41-45]. Patients most often describe difficulty in falling asleep. Despite complaints of severe fatigue, these children often take an hour or more to fall asleep. Even when they do fall asleep, many have difficulty maintaining sleep and wake up during the night. There may be overlap with restless legs syndrome [39]. Nonrestorative sleep (feeling tired or exhausted even after getting a full night's sleep) is a common complaint in children with fibromyalgia. (See "Restless legs syndrome and periodic limb movement disorder in children" and "Assessment of sleep disorders in children".)

Psychosocial impact — Children often suffer from fibromyalgia for many months, sometimes years, before the diagnosis is made. As a consequence, their day-to-day life may be greatly disrupted. Standardized measures can be used to assess the impact of juvenile fibromyalgia on function and quality of life [46].

Some children with fibromyalgia sleep during the day after not being able to sleep at night because of sleep disturbances. School attendance is often inconsistent or poor, or the child is switched to home schooling. Enabling these dysfunctional children to improve adaptive functioning and to attend school regularly should be primary goals for the patient, caregiver(s), and the health care provider.

In addition, dietary habits may deteriorate, and many patients fail to participate in any form of exercise and become deconditioned. This may perpetuate the cycle of pain. (See "Fibromyalgia in children and adolescents: Treatment and prognosis overview".)

Comorbid psychiatric conditions — Several comorbid psychiatric conditions are associated with fibromyalgia in both children and adults. It would not be surprising that these conditions are more prevalent in children with fibromyalgia if the underlying pathogenesis of fibromyalgia is indeed related to neuroendocrine changes in the central and peripheral nervous systems in response to environmental triggers in genetically susceptible individuals. (See 'Etiology' above.)

Psychiatric comorbidities include depression [4,47,48] and anxiety, mood, and behavioral disorders [47,49]. It is important to rule out primary psychiatric conditions, especially

depression, when considering a diagnosis of fibromyalgia since signs of dysphoria may mimic symptoms of fibromyalgia. Children with fibromyalgia are more likely to have temperamental instability and increased vulnerability to stress [38].

The interactions among these conditions may contribute to the breadth and severity of symptoms seen in children with fibromyalgia [38]. However, it is unclear whether there is a causal relationship between fibromyalgia and any of these disorders and, if so, whether fibromyalgia is a cause or an effect [42,50].

LABORATORY AND OTHER STUDIES

There are no specific laboratory or imaging tests that are diagnostic of fibromyalgia. All laboratory testing and imaging tests should be normal unless a child has an associated underlying autoimmune disease in addition to fibromyalgia. Thus, we do not advocate performing extensive blood and/or imaging tests in patients who clinically have typical features of fibromyalgia and who do not have symptoms or signs suggestive of another disorder.

Minimal laboratory, imaging, and other studies may be performed as part of the initial evaluation. Normal results of complete blood counts, acute phase reactants, urinalyses, chemistry profiles, and thyroid studies are expected. Antinuclear antibodies (ANA) and rheumatoid factor (RF) testing should be obtained only in patients who have symptoms and physical examination findings that suggest lupus or inflammatory arthritis. These tests are not helpful in patients with typical signs and symptoms of fibromyalgia, because a small percentage of patients have a nonpathologic-positive test for ANA, reflecting the underlying presence of incidental positive ANA tests in the general population. A basic set of screening radiographs of a few affected areas/joints is rarely indicated unless there is a concern about other disease processes or a history of past injuries. Sleep studies and polysomnography are not generally recommended in children, unless there are symptoms suggestive of obstructive sleep apnea, primary sleep disorders, or restless legs syndrome.

CLASSIFICATION AND DIAGNOSTIC CRITERIA

The diagnostic criteria for fibromyalgia in children and adolescents have been controversial. While many continue to rely on the Yunus and Masi criteria to diagnose children with fibromyalgia, the 2010 American College of Rheumatology (ACR) criteria, especially when coupled with a physical exam, is a sensitive and specific tool in the diagnostic process for adolescent patients [51].

Yunus and Masi criteria — In 1985, criteria for diagnosing fibromyalgia in children were published based upon a review of 33 children (mean age 14.7 years, range 9 to 17 years) (table 1) [4]. These criteria (referred to as the Yunus and Masi criteria) differ from those of the American College of Rheumatology (ACR) 1990 criteria in requiring fewer tender points (5 versus 11), as well as clinical findings beyond diffuse pain. The other major clinical findings include the absence of another underlying condition or cause and normal laboratory test results.

ACR criteria — Several different classification schema have been proposed in adults. The most frequently used diagnostic criteria were published by the American College of Rheumatology (ACR) in 1990 [32] and revised in 2010 [33]. The original ACR criteria include widespread pain for at least three months' duration and the presence of at least 11 tender points at 18 potential sites. The revised ACR criteria do not require tender points for diagnosis but do require the presence of generalized widespread pain for at least three months and a scale based upon the degree of fatigue, nonrestorative sleep, and/or cognitive symptoms in addition to a number of somatic symptoms. These criteria are usually not used clinically in practice but are useful for research and epidemiologic purposes.

The original criteria were based upon the evaluation of 293 adult patients (mean age of 44.7 years), and the subsequent criteria were based upon evaluation of 196 patients with current fibromyalgia and 67 patients with prior fibromyalgia (mean age of 54.6 years). At no juncture has the application of these criteria to children been validated [5].

One study examined the applicability of the 2010 ACR criteria to children with juvenile fibromyalgia and found that it had a high specificity and sensitivity and, therefore, may be used as an alternative to the older Yunus and Masi criteria [51]. Additionally, this pediatric study found that a few symptoms included in the ACR symptom severity scale were rarely reported by children, whereas a few others (such as tenderness to touch and sensitivity to sounds, lights, and smells) were more commonly reported and need to be included into future validation studies.

DIAGNOSIS

The diagnosis of juvenile fibromyalgia is made clinically and is based upon the presence of the typical clinical features outlined in the section above (see 'Clinical features' above) and the exclusion of other pathologic processes.

In our practice and those of many pediatric rheumatologists, we use the Yunus and Masi diagnostic criteria (table 1), which includes multiple common signs and symptoms seen in children with fibromyalgia [4]. Others are evaluating use of an adapted 2010 ACR criteria in

the diagnosis of juvenile fibromyalgia [51]. (See 'Yunus and Masi criteria' above and 'Clinical features' above.)

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for juvenile fibromyalgia includes other pain syndromes, particularly complex regional pain syndrome (CRPS) type 1; chronic fatigue syndrome (CFS), also known as CFS/myalgic encephalomyelitis (ME); and rheumatic diseases. Differences in clinical features distinguish fibromyalgia from these other disorders, which also present with musculoskeletal pain.

Complex regional pain syndrome type 1 — CRPS type 1 (formerly known as reflex sympathetic dystrophy, posttraumatic sympathetic dystrophy, and Sudeck's atrophy) typically presents with moderate-to-severe pain that is usually localized to an extremity. There are specific diagnostic criteria for this syndrome, which include continuing pain disproportionate to an inciting event, hyperalgesia and allodynia (severe pain with even light stroking of the skin of the affected area), edema, sweating, and changes in color or temperature in the affected limb [52]. These changes may be subtle early in the disease process or extreme, with severe atrophy and trophic changes of the skin, hair, and nails and significant dysfunction of involved muscles and joints. As with fibromyalgia, CRPS occurs more frequently in females than males and is much more common in adolescents than in younger children.

Patients with CRPS are easily distinguished from patients with fibromyalgia because they have localized pain (compared with the diffuse pain that occurs in many parts of the body in fibromyalgia), and they usually do not have tender points. In addition, sleep disturbance, fatigue, headaches, and other features of fibromyalgia are not cardinal features of CRPS. (See "Complex regional pain syndrome in children".)

Growing pains — Growing pains are common in children, but they are usually seen in school-aged children and not adolescents, as is more commonly the case with fibromyalgia. Growing pains typically affect both legs and sometimes the arms and other areas of the body, almost always occur at the end of an active day or in the middle of the night, and may wake a child at night.

Children with growing pains are easily distinguished from patients with fibromyalgia because they have localized rather than diffuse or widespread pain; their pain is intermittent, only occurs at night, is self-limited rather than chronic and persistent, and is not characterized by tender points. In addition, they do not have other associated symptoms. Growing pains are also far more likely to be relieved by nonsteroidal antiinflammatory drugs (NSAIDs). (See "Growing pains".)

Chronic fatigue syndrome or myalgic encephalomyelitis — CFS/ME is not a pain syndrome. However, at times, patients with this syndrome can have diffuse pain in addition to severe fatigue, indicating possible overlap between CFS and fibromyalgia. Studies have sought to elucidate common etiologies but typically do not include younger adolescents [53]. Nonetheless, there is strong evidence that the two syndromes often coexist, making a determination as to which is primary or secondary a challenge [54]. (See "Clinical features and diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome".)

Rheumatic diseases — Juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), and other rheumatic diseases are usually easily differentiated from fibromyalgia because of the presence of objective physical findings consistent with joint and systemic inflammation and laboratory abnormalities. (See "Oligoarticular juvenile idiopathic arthritis" and "Polyarticular juvenile idiopathic arthritis: Clinical manifestations, diagnosis, and complications" and "Systemic juvenile idiopathic arthritis: Clinical manifestations and diagnosis" and "Classification of juvenile idiopathic arthritis" and "Childhood-onset systemic lupus erythematosus (SLE): Clinical manifestations and diagnosis".)

The rheumatic disease most commonly confused with fibromyalgia is JIA because the symptoms of musculoskeletal pain and joint stiffness can be quite similar in the two diseases. Patients with fibromyalgia will often have joint tenderness and pain on motion of the joint, which may be confused with the inflammatory synovitis of JIA. However, they will also have tenderness of the muscles in areas away from the joints, have tender points, and will lack the objective signs of synovitis such as true joint swelling and loss of motion that occur in patients with arthritis. In addition, back pain is common in fibromyalgia, but it does not occur in most children with JIA, except in those with enthesitis related arthritis (or spondyloarthropathy).

Secondary fibromyalgia can coexist or develop in children with rheumatic diseases such as JIA and SLE, so it is possible for patients to have both [55,56]. In such cases, differentiating pain due to a flare of the underlying disease from pain due to fibromyalgia may be particularly challenging.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Fibromyalgia".)

SUMMARY AND RECOMMENDATIONS

- Fibromyalgia is one of a group of chronic pain disorders that is characterized by chronic and diffuse musculoskeletal pain, severe fatigue, nonrestorative sleep, and the presence of tender points. (See 'Introduction' above.)

- The etiology of fibromyalgia is unknown, although the suspected mechanism is disordered pain regulation due to neuroendocrinologic changes in the central and peripheral nervous systems that occur in genetically susceptible individuals, possibly in response to environmental triggers. (See 'Etiology' above and "Pathogenesis of fibromyalgia".)

- In children with fibromyalgia, clinical features include diffuse pain, headache, sleep disturbances, fatigue, depression, and the presence of tender points. (See 'Clinical features' above.)

- The diagnosis of juvenile fibromyalgia is made clinically and is based upon a history of chronic, generalized pain and associated features (eg, fatigue, sleep disturbances, headache, and depression); a physical examination that may demonstrate the presence of tender points and also excludes other diagnoses that may present similarly; and negative or normal laboratory tests. (See 'Diagnosis' above and 'Classification and diagnostic criteria' above.)

- The differential diagnosis for juvenile fibromyalgia includes other pain disorders (eg, complex regional pain syndrome type 1 [CRPS]); growing pains; chronic fatigue syndrome (CFS), also known as CFS/myalgic encephalomyelitis (ME); and rheumatic diseases. Differences in clinical features usually distinguish fibromyalgia from these other disorders, which also present with musculoskeletal pain. However, there may be considerable overlap, and more than one condition may coexist in individual patients. (See 'Differential diagnosis' above.)

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GRAPHICS

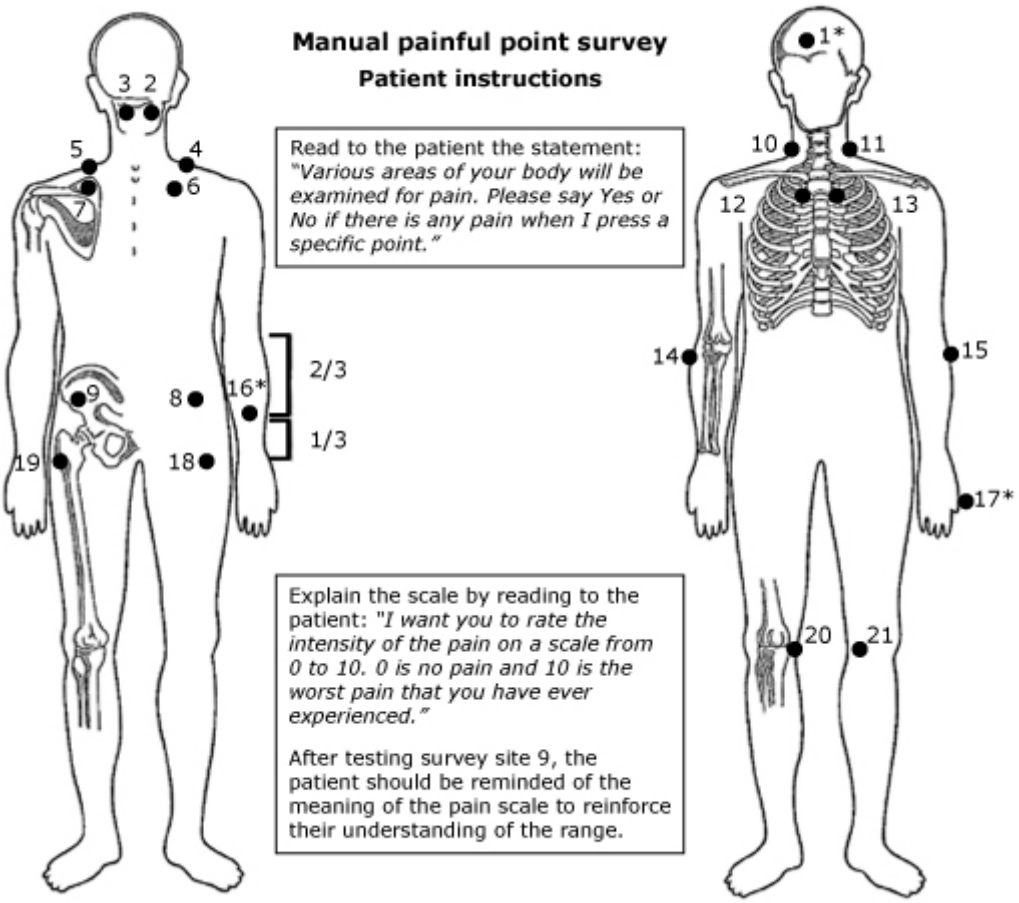
Yunis and Masi criteria for juvenile primary fibromyalgia

The diagnosis for juvenile primary fibromyalgia is based upon all 4 major criteria plus 3 of the 10 minor criteria
Major criteria
1. Generalized musculoskeletal aching at ≥3 sites for at least 3 months
2. Absence of an underlying condition or cause (eg, arthritis or trauma)
3. Normal test results
4. Five tender points
Minor criteria
1. Chronic anxiety or tension
2. Fatigue
3. Poor sleep
4. Chronic headaches
5. Irritable bowel syndrome
6. Subjective soft tissue swelling
7. Numbness
8. Pain modulation of physical activity
9. Pain modulation by weather factors
10. Pain modulation by anxiety and/or stress

Modified from: Yunis MB, Masi AT. Juvenile primary fibromyalgia syndrome. A clinical study of thirty-three patients and matched normal controls. Arthritis Rheum 1985; 28:138.

Graphic 69755 Version 4.0

Diagram of painful points in fibromyalgia



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Graphic 79397 Version 2.0

Contributor Disclosures

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