NAMS Practice Pearl

Fibromyalgia Screening in Patients With Unexplained Chronic Fatigue

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Women often complain of symptoms of fatigue and generalized aches and pains around menopause. Even though fibromyalgia is more prevalent in midlife women, not all women presenting with aches and pain and disrupted sleep meet diagnostic criteria for fibromyalgia. This* Practice Pearl *addresses the distinction between chronic fatigue syndrome and fibromyalgia and the management of fibromyalgia in perimenopausal and postmenopausal women.

Fatigue is a symptom frequently reported by menopausal women. Chronic fatigue is diagnosed after the fatigue has been present for at least 6 months, and it has a very wide differential diagnosis. A focused history and physical examination are an important part of the evaluation of chronic fatigue. Initial laboratory work-up typically includes a complete blood count, electrolytes, creatinine, transaminases, HIV testing, and thyroid-stimulating hormone level. Select patients may need focused additional testing as dictated by their histories and examinations. Unfortunately, comprehensive testing may identify the cause of the fatigue only in about 1 in 20 cases.[1] The presence of chronic undifferentiated fatigue is not synonymous with chronic fatigue syndrome, which is a distinct clinical diagnosis.

When to suspect chronic fatigue syndrome or fibromyalgia. Postexertional malaise—characterized by a prolonged and disproportionate increase in fatigue symptoms after physical, emotional, or cognitive stress—is a feature of fatigue suggestive of either myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) or fibromyalgia. Myalgic encephalomyelitis/chronic fatigue syndrome is a poorly understood condition characterized by debilitating fatigue that is otherwise unexplained and minimally relieved by rest, unrefreshing sleep, severe postexertional malaise, orthostatic intolerance, and cognitive impairment (ie, brain fog). Fibromyalgia, on the other hand, is a central sensitization syndrome typified by amplification of pain signals out of proportion to sensory inputs (hyperalgesia) and the generation of pain signals from otherwise innocuous sensory stimuli such as touch (allodynia).[2] Both fibromyalgia and ME/CFS have been associated with postviral syndromes, including coronaviruses.

The diagnostic criteria for fibromyalgia and ME/CFS overlap significantly—up to 70% of patients with fibromyalgia will meet criteria for ME/CFS, whereas 35% to 70% of patients with ME/CFS will meet criteria for fibromyalgia.[3] Despite the symptom and diagnostic criteria overlap, fibromyalgia and ME/CFS represent two distinct clinical syndromes. The peak incidence of ME/CFS is bimodal, during the teen years and the 30s.[4] The typical age of onset for

fibromyalgia is between 20 and 50 years, with increasing prevalence with age. The prevalence is also about two to three times higher in women.[5]

A biologic explanation of the sex differences in the prevalence of fibromyalgia has not been established; however, links between a decline in estrogen and menopause in enhancing chronic pain symptoms have been suggested.[6] Clinical evidence suggests that women may report worsening in their fibromyalgia symptoms around the final menstrual period, or they may report new-onset aches and pains that may meet diagnostic criteria for fibromyalgia. However, limited evidence has not demonstrated improvement in fibromyalgia-associated pain with hormone therapy (HT).[7]

Fibromyalgia is not considered a diagnosis of exclusion, and in fact, it frequently coexists with other conditions associated with myofascial and joint pains.[8] American College of Rheumatology (ACR) fibromyalgia diagnostic criteria in 1990 have evolved from allodynia (pain from a stimulus that typically would not cause pain) at 11 of 18 tender points on examination to a 2016 self-reported survey of widespread pain and severity of related symptoms including fatigue, cognitive symptoms, and sleep quality. Pain generally must be present above and below the waist and on both sides of the body. The pain does not need to be consistently present—the 2016 ACR criteria qualifies pain needing to be present in 1 of 19 body sites within the last week. Because pain in fibromyalgia can be migratory, monitoring specific pain regions may not be necessary unless the site is a primary pain generator undergoing focused treatment. The 2016 ACR criteria's self-reported symptom survey can be adapted to a paper screening tool for general use. Referral to a rheumatologist or general internist can help confirm a suspected diagnosis.

Fibromyalgia onset is often gradual, taking months to years to fully develop, and symptoms can wax and wane in response to physical, emotional, and environmental stressors. Consequently, mean time to fibromyalgia diagnosis from symptom onset has been found to be about 6.4 years.[9] Conversely, patients who develop ME/CFS abruptly fall from high functional levels to severe functional limitations over a short period of time after some "triggering event." Chronic fatigue secondary to fibromyalgia may not have a clearly identifiable triggering event, and as with the characteristic pain symptoms, it comes on more gradually. Pain is not uncommon in ME/CFS, but severe postexertional fatigue is the primary functional limitation of this condition.

Central sensitization and sensory hypervigilance. Fibromyalgia frequently occurs concurrently with other central sensitization syndromes: chronic headache syndromes, irritable bowel syndrome, painful bladder syndrome/interstitial cystitis, postural orthostatic tachycardia syndrome, pelvic pain syndromes, temporomandibular joint pain, and multiple chemical sensitivities. In central sensitization syndromes, sensory output is generally amplified, producing a broad range of symptoms that are often not associated with structural pathology. Amplified sensory processing is not restricted to painful stimuli—often patients will report heightened sense of smell, light sensitivity, sound sensitivity, temperature sensitivity, fatigue, and sensitivities to medication adverse events in addition to pain. Sensory hypervigilance can magnify the intensity and effect of common menopause symptoms, including hot flashes, night sweats, and sleep disruption.

Fibromyalgia and menopause. Menopause has been associated with onset of fibromyalgia symptoms in some women and also with worsening pain, fatigue, and sleep disruption in patients with existing fibromyalgia**.** There have been suggestions of a link between a decline in estrogen and increased reports of chronic pain symptoms.[6] However, research on this topic is sparse in

general, and the limited existing evidence has not shown considerable benefit of HT on fibromyalgia symptoms.[7] That being said, anecdotal evidence suggests that women report improvement in aches and pains with HT use after menopause. Further research in this area is needed for clarification of these conflicting observations. Additionally, vasomotor symptoms (VMS) of menopause can be amplified by the temperature sensitivity that is characteristic of fibromyalgia-further research focusing on the effect of fibromyalgia on VMS frequency and intensity is warranted.

***Management of fibromyalgia in postmenopausal women*.** Women with fibromyalgia may experience more bothersome VMS, and therefore HT use may be indicated to reduce VMS burden and improve sleep quality**.** Graded exercise has the strongest evidence for managing fibromyalgia-associated pain, with weaker evidence for fatigue mitigation.[10] Cognitive-behavior therapy, mindfulness-based therapy, and multicomponent therapies also have weak evidence for pain reduction but may reduce the sensory hypervigilance that contributes to VMS burden in menopause. Some nonhormone treatments for VMS, such as gabapentinoids and serotonin-norepinephrine reuptake inhibitors, also reduce pain in fibromyalgia and may be reasonable alternatives or supplements to HT for their pain-relieving effects.[2] Current FDA-approved medications for fibromyalgia are limited to duloxetine, pregabalin, and milnacipran; other medications with similar mechanisms of action are frequently used off-label.

Pearl. Fibromyalgia is more common in midlife women. Screen for fibromyalgia in perimenopausal and postmenopausal women with unexplained fatigue and postexertional malaise with delayed recovery. The 2016 ACR diagnostic criteria can be adapted to a self-reported survey to facilitate screening of patients with undifferentiated fatigue. The presence of widespread pain out of proportion to tissue injury, age at onset, and the tempo of symptom development can be useful to differentiate fatigue secondary to fibromyalgia from chronic fatigue syndrome. Graded exercise therapy has strong evidence for pain reduction but only weak evidence for fatigue reduction. Some pharmacologic therapies used for treatment of VMS in menopause are also effective therapies for fibromyalgia-associated pain.

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Disclosure

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