Fibromyalgia and Autoimmune Diseases: the Pain behind Autoimmunity

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Fibromyalgia syndrome is a commonly encountered disorder characterized by chronic widespread musculoskeletal pain and related symptoms along with multiple painful tender points [1]. The pathogenesis of fibromyalgia is not entirely understood, although the current concept views the syndrome as the result of central nervous system malfunction resulting in amplification of pain transmission and interpretation [1]. Recent evidence suggests that genetic and environmental factors may play a role in the etiopathology of fibromyalgia and other related syndromes [1,2].

Fibromyalgia syndrome is common in patients with autoimmune disease and may be the source of many of the symptoms and much of the disability in these patients [3,4]. In this review we focus on the co-morbidity of fibromyalgia and autoimmune diseases, its prevalence and clinical implications.

Fibromyalgia and autoimmunity

Two autoantibodies, the anti-68/48 kD and the anti-45 kD, have been reported as possible markers for certain clinical subsets of primary fibromyalgia and chronic fatigue syndrome and of secondary fibromyalgia/psychiatric disorders, respectively [5]. In particular, the anti-68/48 kD antibodies were considered to be closely associated with fibromyalgia/chronic fatigue syndrome patients presenting with hypersomnia and/or cognitive disorders.

Pamuk and Cakir [6] reported that thyroid autoimmunity in fibromyalgia patients was similar in frequency to that in rheumatoid arthritis patients but higher in frequency when compared to the control group. Although the frequencies of TPO antibodies (antithyroid peroxidase) in both fibromyalgia and RA patients were significantly higher than in the controls, the increase in the frequency of thyroglobulin antibodies (antithyroglobulin) was not significant. Thyroid autoimmunity, especially the presence of TPO antibodies, was found to be associated with the presence of migraine and tension headaches [6]. In a Danish study, fibromyalgia patients tended to have slightly higher antipolymer antibody levels than did controls when adjusted for symptom severity [7]. Smart et al. [8] found that 30% of 66 fibromyalgia patients were positive for antinuclear antibody, with a 75% preponderance of the speckled pattern.

Fibromyalgia and cytokines

Wallace and collaborators [9] found that fibromyalgia patients had increases over time in serum levels and/or PBMC-stimulated activity of soluble factors whose release is stimulated by substance P. It was hypothesized that because interleukin-8 promotes sympathetic pain and IL-6 induces hyperalgesia, fatigue and depression, they may play a role in modulating symptoms of fibromyalgia. Higher levels of IL-10, IL-8 and tumor necrosis factor-alpha were found in fibromyalgia patients than in controls [10].

A slight disturbance in the innate immune system of fibromyalgia patients was reported by Macedo et al. [11], suggesting enhanced adhesion and recruitment of leukocytes to inflammatory sites. However, another study indicated that dysregulation of cytokine production by circulating monocytes or non-monocytic cells (lymphocytes) is not a dominant factor in the pathogenesis of fibromyalgia/chronic fatigue syndrome [12].

Fibromyalgia and autoimmune diseases

Up to 65% of patients with systemic lupus erythematosus attending a rheumatology clinic met the American College of Rheumatology criteria for fibromyalgia [13]. Of 75 patients with SLE, 40% had coexistent fibromyalgia that adversely affected their quality of life [14]. In another study, 57% of patients with RA and 24% of those with psoriatic arthritis were found to have fibromyalgia [15]. Wolfe and Michaud [16] reported that fibromyalgia exists in a substantial number of patients with RA (17.1%) and that their RA is more severe by subjective and objective measures. Various rheumatic diseases were detected in 62% of patients with autoimmune thyroid disease, fibromyalgia being the most prevalent (in 31%) [17].

Clinical significance of autoimmunity in fibromyalgia

Although fibromyalgia is generally regarded as a non-inflammatory and non-autoimmune disease, some patients display autoimmunity features. The obvious question is: Do fibromyalgia patients have autoantibodies predisposed to develop autoimmune diseases?

Dinerman and team [18] found that 14% of fibromyalgia patients had a positive ANA test, 30% had a history of Raynaud's phenomenon, and 18% had symptoms of Sjögren's syndrome, but

RA = rheumatoid arthritis
PBMC = peripheral blood mononuclear cells
IL = interleukin
SLE = systemic lupus erythematosus
ANA = antinuclear antibody

none of them progressed to a classic connective tissue disease. Al-Allaf and co-authors [19] suggested that patients with fibromyalgia have the same rate of positive ANA as do osteoarthritis patients (8.8% and 8.9%, respectively). Results from their study did not show that ANA are a good predictor of the future development of connective tissue disease in fibromyalgia patients and the majority of ANA-positive patients became ANA negative on follow-up. Recently it was reported that there was no significant difference in the frequency of ANA or thyroid antibodies between fibromyalgia patients and controls, and that the risk of connective tissue diseases is not increased in fibromyalgia [20].

Is fibromyalgia an autoimmune disease

Since some fibromyalgia patients display autoimmunity and fibromyalgia is prevalent in autoimmune diseases, it may be speculated that it is in fact an autoimmune disorder. However, the reports on immunological markers in fibromyalgia are not consistent and there is no evidence for inflammatory mechanisms in this syndrome. Referring to fibromyalgia as an autoimmune disease is speculative at the present time. However, fibromyalgia may in some cases be an early sign of an autoimmune disease.

The association of fibromyalgia and autoimmune disease, specifically SLE, may pose diagnostic dilemmas. Although fibromyalgia does not correlate with SLE disease activity, the clinical features of fibromyalgia in these patients may contribute to misinterpretation is lupus activity.

Conclusions

Fibromyalgia is common in autoimmune diseases and there is some evidence for immunological aberration in fibromyalgia. Although it cannot be considered an autoimmune disease, recognition of the association between fibromyalgia and autoimmune diseases is relevant to every physician who treats patients with autoimmune diseases.

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I hope our wisdom will grow with our power, and teach us that the less we use our power the greater it will be

Thomas Jefferson (1743-1826), third U.S. president, and principal author of the Declaration of Independence.