Helminthic Therapy
A New Era in Immune-Mediated Diseases

To the Editor:

The epidemic of autoimmune diseases in developed industrialized countries is often explained by the “hygiene hypothesis” linking a decrease of infectious burden with rise of autoimmune diseases. Helminth therapy is suggested as potential therapy for autoimmune and inflammatory disorders in humans. We present a middle-aged woman with history of mixed connective tissues disease who was treated with helminthic therapy and showed good response.

A 33-year-old woman with history of mixed connective tissue disease presented for routine follow-up. She received a diagnosis at age of 22 years. Her presenting symptoms included polyarthritis, mouth sores, photosensitivity, malar rash, dry eyes and mouth, and Raynaud phenomenon. Laboratory workup was positive for antinuclear antibodies, antithrombin-3 antibodies, anti-double-stranded DNA antibodies, and hypocomplementemia. She was treated with meloxicam and hydroxychloroquine. Hydroxychloroquine was discontinued because of adverse effects, and azathioprine was added, which she self-discontinued after 6 months. Afterward, she experienced severe flare, which was treated with steroids. Belimumab infusions were started. She reported partial relief of symptoms, which prompted her to pursue alternative therapies including naturopathic medicine.

She started using helminthic therapy. She procured Necator americanus larvae and self-inoculated herself with nematodes. Initially, she inoculated 25 larvae every 3 months and subsequently prolonged interval to 6 months. She is gradually titrating up the number of larvae in increments of 10 with each dose to reach the goal of 100 larvae every 6 months. She is using 45 larvae at this time. The inoculations cause a mild itch within 5 minutes that disappears after a few days. She reports significant improvement in symptoms (joint pain, swelling, rash) after her second inoculation. Her routine laboratory tests include complete blood count and iron studies to monitor adverse effects. On this visit, she was asymptomatic. There was no evidence of rash or synovitis on examination. Complete blood count, comprehensive metabolic panel, C-reactive protein, erythrocyte sedimentation rate, and complement levels were within reference ranges. She was contented with helminthic therapy and wanted to continue it. She was advised to follow up regularly to monitor disease activity.

The hygiene hypothesis was introduced by Strachan1 for hay fever. It suggests that highly hygienic lifestyles and medical conditions affect immune modulation that increases risk of inflammatory and autoimmune disorders. This concept is also implicated in several other immunologic disorders such as asthma, diabetes mellitus type 1, cardiovascular diseases, multiple sclerosis, and inflammatory bowel disease.2-4 Although responsible factors for this correlation have not yet been clearly defined, protective factors of various agents such as helminths is suggested.

Parasitic helminths have transformed into highly efficient immune modulators through progressive evolution. This unique ability to alter immune responses has created interest among investigators to explore the possibility of using worms, or their products, as anti-inflammatory treatments.5 Exact pathophysiologic mechanisms of autoimmune disease development are not well understood, but it is attributed to inappropriate immunologic responses to innocuous antigens by the T_{H1}-type immune response.6 It results in increased production of cytokines associated with inflammation including interleukin 12 (IL-12), interferon γ, and tumor necrosis factor α. Helminths secrete immune-regulatory molecules that can shift the hyperactive T_{H1} proinflammatory response to T_{H2} response with reduced inflammation by down-regulating the production of IL-10, IL-4, IL-5, IL-13, and transforming growth factor β.7 This is one of the multiple proposed mechanisms that is widely accepted.

Multiple animal models and preclinical trials have suggested the beneficial effect of helmint infections in asthma, inflammatory bowel disease, multiple sclerosis, and systemic lupus erythematosus.7,8 In a prospective observational study, Correale et al.9 followed up 12 parasite-infected patients with multiple sclerosis for 4 years. Results demonstrated significantly lower number of exacerbations in parasite-infected patients compared with the control group. It was suggested that down-regulation of autoimmune response was associated with greater suppressive cytokines secretion by T regulatory cells in these patients. Similarly, Creoie et al.10 demonstrated significant improvement in quantitative disease indices in 9 patients with Crohn disease infected with N. americanus larvae. Helminth-derived immunoregulatory molecules have shown promising results with attenuation and amelioration of ulcerative colitis in several experimental animal studies.7,8 In 2 different murine model studies, Bashi et al.11,12 suggested the therapeutic role of tuftsin-phosphorylcholine (helminth-based compound) in rheumatoid arthritis and systemic lupus erythematosus.

Our patient’s good response to helminthic therapy supports ongoing research for developing helminth-based therapies. In recent years, substantial work is done to understand association between intestinal microbiota and autoimmune or inflammatory diseases, but many questions remain unanswered, which include their role as preventive therapy. However, current efforts may lead to a new era in development of anti-inflammatory drugs.

Jawad Bilal, MD
Department of Internal Medicine
University of Arizona
Tucson, AZ
jawadbilal@deptofmed.arizona.edu

Elly Varma, MD
Hem Desai, MD
Dominick G. Sudano, MD
Department of Internal Medicine
University of Arizona
Tucson, AZ

The authors declare no conflict of interest.

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