



Letter

Contemplating the etiology of chronic urticaria and the implications of current guidelines

Chronic urticaria (CU) is a disorder defined as the presence of pruritus and urticaria for 6 weeks or longer.¹ Currently, a cause of CU is identified in only 5% to 20% of patients.^{1–3} Although most specialists treating patients with symptoms of chronic urticaria pursue basic laboratory investigations to find an explanation for chronic urticaria, the recent American Board of Internal Medicine and American Academy of Allergy, Asthma, and Immunology Choosing Wisely Guidelines state that clinical history and physical examination are necessary for the diagnosis of CU but that laboratory evaluation has limited diagnostic utility.⁴ Therefore, laboratory testing is only recommended when clinically indicated based on the presence of signs or symptoms beyond urticaria and pruritus. We describe one adult patient and one pediatric patient with CU and no other associated symptoms who were found to have autoimmune liver disease on further laboratory evaluation.

The first patient is a 44-year-old woman with a history of Hashimoto thyroiditis who presenting with daily pruritus and urticaria for 6 weeks. The rash was refractory to treatment with over-the-counter antihistamines but resolved after starting methylprednisolone therapy. Because the rash recurred 1 week after discontinuation of corticosteroid therapy, additional laboratory evaluation was pursued. The patient was prescribed colchicine, 0.6 mg twice daily, because of sedation from both first- and second-generation antihistamines with the plan to titrate the dose to 0.6 mg 3 times daily. The patient experienced complete resolution of her pruritus and urticaria within 1 month.

Initial laboratory workup revealed a normal complete blood cell count with differential, normal erythrocyte sedimentation rate, normal hepatic panel (including γ -glutamyl transpeptidase), and negative basophil histamine release assay. The thyroperoxidase antibody level was 306 IU/mL (reference range, <20 IU/mL), the C-reactive protein level was 0.69 mg/dL (reference range, <0.8 mg/dL), the antinuclear antibody titer result was mildly positive at 1:40, and the antimitochondrial antibody titer result was positive at 1:640. On subsequent testing, the mitochondrial M2 antibody level was significantly elevated at 131 IU/mL (reference range, <20 IU/mL). Given the positive antimitochondrial and M2 antibody titer results, the patient underwent liver biopsy and was found to have granulomatous portal inflammation and bile duct inflammation that consisted of epithelioid cells, histiocytes, and rare giant cells consistent with primary biliary sclerosis stage 1 to 2. She was prescribed ursodeoxycholic acid and has maintained normal liver function test results and control of her urticaria and pruritus.

The second patient is a male adolescent presenting at the age of 17 years with daily pruritus and urticaria that began 8 months before this visit. His symptoms were unassociated with angioedema, abdominal pain, or respiratory symptoms, and the patient underwent autologous serum skin testing with appropriate positive and negative controls, which revealed a 20-mm wheal with associated flare. Thyroid function test and basophil histamine release assay results were negative. He was diagnosed as having CU and prescribed carbinoxamine, 4 mg twice daily, and ranitidine, 150 mg twice daily. Within a month, his urticarial resolved; however, he continued to have severe pruritus, so cyproheptadine, 4 mg twice daily, and hydroxyzine, 75 mg twice daily, were also given during the next several months without resolution of his pruritus. Subsequently, liver function tests were performed.

Aspartate aminotransferase and alanine transaminase levels were elevated at 101 U/L (reference range, 12–32 U/L) and 112 U/L (reference range, 8–46 U/L). The total bilirubin level was 1.6 mg/dL (reference range, 0.2–1.1 mg/dL). The results of his hepatitis panel and cytomegalovirus and Epstein-Barr virus titers were all negative. His γ -glutamyl transpeptidase level was elevated at 397 U/L (reference range, 15–85 U/L), and his alkaline phosphatase level was elevated at 485 U/L (reference range, 48–230 U/L). Because his liver function test results remained abnormal on subsequent testing, he underwent liver biopsy, which revealed marked bile duct proliferation, focal cholangitis, and advanced fibrosis consistent with autoimmune hepatitis and possible overlapping sclerosing cholangitis. Subsequent magnetic resonance cholangiopancreatography ruled out sclerosing cholangitis. He began taking daily prednisone, 60 mg, and azathioprine, 100 mg, with complete resolution of his urticaria, pruritus, and elevated liver function test results. His maintenance therapy now consists of azathioprine alone.

Case reports in the medical literature are extremely limited regarding the presentation of autoimmune liver disease in patients presenting with CU and pruritus without additional clinical signs.^{5–7} Previous case reports cite clinical symptoms of arthralgias or fatigue in addition to chronic urticaria and pruritus or the development of skin involvement of urticarial lesions after diagnosis of a concurrent autoimmune condition.^{5–7} We describe 2 patients who presented with CU and pruritus without additional clinical signs or symptoms found to have autoimmune liver processes on further laboratory testing and biopsy. Current recommendations suggest minimizing laboratory evaluation in uncomplicated cases of CU; however, these cases suggest the broader laboratory assessment pursued by most specialists is still appropriate in patients with CU even in the absence of other signs or symptoms.

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Disclosures: Authors have nothing to disclose.

<http://dx.doi.org/10.1016/j.anai.2014.12.025>

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