A 26-year-old female with a past medical history of anxiety disorder presented for evaluation of a three-month history of daily generalized pruritic hives intermittently associated with lip and periorbital swelling. She did not have symptom-associated fevers, joint pain, shortness of breath, or painful or bruising urticaria. She was not taking any new medications, and did not have any known food or medication allergies. She had a family history of Hashimoto’s disease. Examination revealed diffuse red wheals without dermatographism.

Chronic urticaria is present when hives occur regularly for greater than six weeks. Hives can occur alone in 40 percent of patients, with angioedema in 40 percent of patients, or in 20 percent of cases, angioedema can occur alone. Angioedema affects the lips, face, hands, feet, or scrotum. Angioedema can affect the pharynx and tongue, but almost never involves the larynx.

Chronic urticaria is often idiopathic; however, other etiologies should be considered, including dermatographism and physical urticaria (e.g., cold, cholinergic, pressure, vibratory, solar, and aquagenic), or autoimmune (40 to 45 percent of patients have circulating IgG antibodies directed against the IgE receptor or IgE). Additionally, in a subset of patients, urticaria and angioedema can be a manifestation of an underlying connective tissue disease, systemic vasculitis, or thyroid disease.

A thorough history and physical examination assesses for symptoms/signs that may indicate vasculitis or other connective tissue disease. If evaluation is not suggestive of an underlying systemic condition, routine laboratory testing is not indicated. If systemic disease is suspected, testing includes erythrocyte sedimentation rate, antinuclear antibodies, thyroid antibodies, or skin biopsy. Hereditary angioedema is not associated with urticaria; therefore, in patients with urticarial, testing of complement or C1 inhibitor is not indicated.

The mainstay of treatment includes use of nonsedating antihistamines such as fexofenadine or cetirizine. However, in severe cases, the usual recommended dose of antihistamines may not be beneficial. Therefore, use of doses as high as four times the standard dose is indicated in these patients and has been shown to be effective.

In recalcitrant disease, other treatments are added in a step-wise manner to achieve remission. Following maximal doses of nonsedating antihistamines, the addition of a first-generation sedating antihistamine (e.g., hydroxyzine or doxepin) or H2 receptor blockade (e.g. ranitidine) is considered. Approximately 15 percent of histamine receptors in the skin are H2 subtype, and therefore, the addition of H2 blockade can augment inhibition of the wheal-and-flare reaction. If urticaria persists despite maximal histamine blockade, other therapeutic options include: leukotriene receptor antagonists, long-term corticosteroids, and steroid sparing agents such as colchicine, sulfasalazine, hydroxychloroquine, dapsone, mycophenolate, cyclosporine, and omalizumab.

The patient was started on fexofenadine 360 mg twice daily (four times standard dose) without change in urticaria. In a step-wise manner, doxepin 10 mg at bedtime was started followed by ranitidine 150 mg twice daily without a change in her symptoms. Given her family history of thyroid disease, an evaluation of TSH and thyroid antibodies revealed a diagnosis of Hashimoto’s disease, and she was started on thyroid replacement with gradual improvement of urticaria and angioedema. Currently, antihistamines are being reduced as tolerated by her symptoms.