



Resolution of chronic urticaria coincident with vitamin D supplementation

Recent studies have suggested that vitamin D may play a role in the balance of the innate and adaptive immune systems and may contribute to the pathogenesis of chronic urticaria (CU), atopic dermatitis, and other allergic diseases.^{1,2} We present a patient with longstanding CU in the setting of vitamin D deficiency, whose symptoms markedly improved after adequate vitamin D supplementation.

A 58-year-old man was referred to our Allergy/Immunology clinic for daily generalized hives of 4 months duration. He reported similar urticarial lesions 10 years prior that were associated with severe epigastric pain. Esophagogastroduodenoscopy at that time demonstrated *Helicobacter pylori* infection and angioedema of the gastroesophageal junction. The patient was treated with a combination therapy of lansoprazole, amoxicillin, and clarithromycin for 2 weeks and symptomatically improved until 4 months before the recent evaluation. Laboratory testing during the first presentation was significant for vitamin D deficiency with a 25-hydroxy vitamin D level of 4.7 ng/mL (normal, >30 ng/mL). He was diagnosed with osteopenia during that time, and supplemented with cholecalciferol 400 international units (IU) and calcium citrate 800 mg daily.

During the recent visit, the patient reported epigastric pain and daily hives for 4 months. A repeat esophagogastroduodenoscopy confirmed recurrent angioedema of the gastroesophageal junction, and fexofenadine 60 mg twice daily was initiated by his primary care physician. The abdominal pain persisted, and the patient continued to have daily urticaria despite medication compliance; he was therefore referred to our allergy clinic.

On examination, our patient had unremarkable vital signs and normal physical examination results, and his skin was without rashes or urticarial lesions. His daily medications in addition to fexofenadine included aluminum/magnesium antacid, cholecalciferol 400 IU daily, and calcium citrate 800 mg daily. Percutaneous skin testing with a battery of common food and environmental allergens was negative. The patient was diagnosed with CU, and daily fexofenadine was continued. Subsequently the abdominal pain resolved; however, he continued to have intermittent CU during the next 2 months. During this time, the patient followed up with his endocrinologist, and cholecalciferol was increased to 2,000 IU daily after a repeat dual-energy X-ray absorptiometry demonstrated worsening osteopenia. Of note, the patient ran out of antihistamine tablets several weeks later, but noticed complete resolution of his epigastric pain and urticaria despite not taking fexofenadine. Repeat 25(OH)D testing revealed normal (65 ng/mL) levels. The patient continues to take daily cholecalciferol and has not had a recurrence of symptoms.

Vitamin D is a secosteroid, and its main source is through de novo synthesis in the skin.³ Vitamin D deficiency is most commonly observed in countries with less ultraviolet light during the winter

months.⁴ The optimal level for 25(OH)D for bone health begins at 30 ng/mL, but the level required for optimal immune system homeostasis has not been established.⁵

Once vitamin D is produced in the skin or obtained in food, it requires chemical conversion in the liver and kidney to the physiologically active form of vitamin D, 1,25(OH)₂D₃. Recent studies have proposed several immunoregulatory activities for 1,25(OH)₂D₃, which interact with the immune system by directly and indirectly participating in the regulation and differentiation of distinct immune system components.⁵ Vitamin D deficiency has been associated with higher levels of immunoglobulin E sensitization in children and adolescents.⁶ Vitamin D also has been suggested as an immunomodulator of allergic skin diseases because of its role in regulating cathelicidin expression in the skin of patients with atopic dermatitis.² In a study performed by Thorp et al,¹ subjects with CU showed significantly reduced vitamin D levels compared with controls.

Although no studies of using vitamin D as treatment for CU have been published, supplementation with vitamin D has been therapeutically effective in distinct animal models such as autoimmune encephalomyelitis, collagen-induced arthritis, type 1 diabetes mellitus, inflammatory bowel disease, autoimmune thyroiditis, and systemic lupus erythematosus.^{3,5,7} While more studies are still needed, clinicians may consider screening CU patients for vitamin D deficiency if standard therapy fails. In patients who are found to be deficient, we recommend initiating vitamin D supplementation with subsequent monitoring of serum 25(OH)D levels. Even though our single case report does not establish a cause and effect, we hope it encourages a prospective trial regarding vitamin D supplementation as a treatment option in chronic urticaria.

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