Successful Sulfasalazine Treatment of Severe Chronic Idiopathic Urticaria Associated with Pressure Urticaria

Sir,

Chronic urticaria is a common cutaneous disease, but its pathogenesis is still poorly understood. We report on a patient with corticosteroid-dependent chronic idiopathic urticaria associated with pressure urticaria who failed to respond to treatment with antihistamines, a leukotriene receptor antagonist, and PUVA, but showed stable improvement after administration of sulfasalazine.

CASE REPORT

A 31-year-old male patient suffered for 5 years from recurrent episodes of hives and swellings often associated with shortness of breath. Weals occurred spontaneously and after pressure application. The patient repeatedly suffered from pronounced weals that developed after working in his profession as a moving packer, or from plantar swellings after long-distance walks. Whereas pressure testing with an 8-kg weight placed on the patient's thigh for 20 min failed to induce wealing over an observation period of 24 h, repeated strong grasping of an object for 10 min evoked prominent palmar hives. Routine laboratory tests, including serum electrolytes, total blood cell count, erythrocyte sedimentation rate, blood sugar level, antinuclear antibodies, anti-streptolysin titer, and urine analysis, failed to reveal any abnormalities, besides a mildly elevated gamma-transaminase level that was attributed to the regular alcohol consumption of the patient. Intracutaneous injection of autologous serum did not induce wealing (1) and food-associated urticaria was ruled out by food allergy testing and an elimination diet for 10 days. Based on these results, we diagnosed chronic idiopathic urticaria and pressure urticaria associated with shortness of breath.

Various antihistamines, such as loratidine, cetirizine, terfenadine, and ranitidine as well as systemic PUVA treatment failed to improve the symptoms. To control repeated episodes of shortness of breath and severe swellings, intravenous corticosteroids were needed at least 3 times monthly. As a consequence, the patient started to develop signs of Cushing's syndrome, with a significant increase in body weight. The leukotriene receptor antagonist montelukast was then administered, but failed to be effective. Subsequently, we started treatment with sulfasalazine at a dosage of 500 mg/day, which was slowly increased to a maximum of 3 g/day over a period of 3 months. After only a few days of treatment, the patient experienced a substantial improvement. At a dosage of 3 g/day he achieved complete resolution of the urticaria symptoms. Repeated testing demonstrated that wealing could no longer be induced even by strong grasping. Using a visual analogue scale with a range of 1–10, where 1 indicated no wealing and 10 extensive wealing, the patient ranked the wealing as being initially 9 and improving to 1 after beginning treatment with sulfasalazine. Furthermore, he denied any occurrence of wealing associated with walking. During 6 months of treatment with sulfasalazine, no adverse reactions were observed and regular laboratory follow-ups were unremarkable. After 6 months of successful sulfasalazine treatment, we tried to reduce the dosage to 2 g/day, which resulted in an increase in pressure-related symptoms. Therefore, the patient subsequently received 3 g of sulfasalazine per day, leading again to an improvement in clinical symptoms. After 1 year of treatment, the patient is free of weals with 3 g/day of sulfasalazine.

DISCUSSION

Urticaria is referred to as "chronic" if symptoms last for >6 weeks. Definable causes of chronic urticaria include allergens, drugs, exercise, physical factors, systemic disorders, and autoantibodies against the high affinity receptor for IgE, Fc epsilonRI, or against IgE (1). However, in up to 80% of patients with chronic urticaria, the etiology of the disease remains unknown. Whereas chronic idiopathic urticaria usually responds to H1 antihistamines, pressure urticaria is often difficult to treat. Corticosteroids have to be used in spite of the well-known side effects when they are administered over a long period of time.

Sulfasalazine belongs to the group of antifolates. It has been in use for >50 years as a treatment for inflammatory bowel diseases and rheumatoid arthritis. Side effects include hepatotoxicity, nephrotoxicity, and bone marrow toxicity. Therefore, careful monitoring of the complete blood count, liver function tests, and urine analyses are required (2).

The mechanism of action of sulfasalazine in the context of urticaria is still only partially understood. Although the subject of some controversy (2, 3), sulfasalazine may affect the IgE-mediated release of histamine from mast cells. In addition to histamine, sulfasalazine may also modulate other inflammatory mediators. In fact, it has been shown that the drug decreases the activity of prostaglandin synthetase (4).

To the best of our knowledge, there are only two reports on the treatment of severe, corticosteroid-dependent urticaria with sulfasalazine. In one study, marked improvement of chronic idiopathic urticaria with sulfasalazine was observed in 3 patients (5). Another group demonstrated that 2 patients with delayed pressure urticaria and angioedema achieved complete resolution of symptoms after treatment with sulfasalazine (2).

Our experience of rapid improvement of severe symptoms with sulfasalzine treatment in a patient with chronic idiopathic urticaria associated with pressure urticaria confirmed these observations. Sulfasalazine may thus be considered as an alternative corticosteroid-sparing drug for severe forms of urticaria. However, prospective clinical trials will still be needed to evaluate the effectiveness of sulfasalazine for treatment of the different forms of chronic urticaria.

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