

SHORT COMMUNICATION

Acute Edema Blisters on a Skin Swelling: An Unusual Manifestation of Hereditary Angioedema

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In most patients, hereditary angioedema (HAE) is caused by a deficiency of functionally active C1 inhibitor (C1-INH) in plasma (HAE-C1-INH), due to mutations of the C1-INH gene (1). HAE-C1-INH is clinically characterized by recurrent episodes of edema at various body sites, followed by disease-free intervals of variable duration. Skin swellings, abdominal pain attacks and laryngeal attacks are the most frequent symptoms. Laryngeal attacks are potentially fatal and can lead to airway obstruction and death by asphyxiation (2). We report here a patient with HAE-C1-INH who developed blisters on her skin swelling as a rare complication of HAE-C1-INH.

CASE REPORT

A 47-year-old Caucasian woman attended the clinic with severe swelling of her left forearm. A few hours after onset of the swelling multiple blisters developed on the skin at the site of the swelling (Fig. 1). The lesions were not accompanied by inflammatory signs or fever. There were no blisters on other body parts and the patient had no subjective complaints. The regional lymph nodes were not painful or enlarged. Three days later, the swelling had completely subsided, but remnants of the blisters were visible for approximately one week.

The patient's family history revealed that her father and brother had died of asphyxiation from laryngeal edema and that her son had had recurrent skin swellings, abdominal pain attacks, and laryngeal edema. The patient had previously experienced mild recurrent skin swellings, mostly located on her forearms, several abdominal pain attacks, and one mild laryngeal edema. Initial symptoms started at the age of 15 years and since then, she had experienced one attack every 2 or 3 years.



Fig. 1. Multiple blisters on a skin swelling of hereditary angioedema.

Laboratory results showed C1 inhibitor protein 8.9 mg/dl (normal 15–35 mg/dl), C1 inhibitor activity 25% (normal 70–130%), and C4 9 mg/dl (normal 20–40 mg/dl). Consequently, HAE-C1-INH type 1 was diagnosed.

DISCUSSION

In our patient, the blisters followed a massive skin swelling and were not typical for a bullous erysipelas or a blistering phytophotodermatitis with lymphangitis. Since the blisters were confined to the site of the skin swelling, we assume that they were “acute edema blisters” (AEB), arising from the underlying edema of an HAE-C1-INH attack. This is an extremely rare presentation of HAE-C1-INH. In a study of HAE symptoms, 196 (97.5%) of 201 patients with 65,102 skin swellings reported a total of 59,095 (90.8%) swellings at the extremities (3). Of these, only 3 patients (1.5%) with more severe swelling reported blister formation: 2 patients had blisters in the crook of the elbow and one patient developed blisters at the instep, one day after onset of the attack. As in the case described here, all 3 patients experienced only one episode of blistering. We are aware of only one case in which a patient's HAE-C1-INH skin swellings were accompanied by blisters on more than one occasion (4). Only recently, another patient with HAE-C1-INH was described, who developed painful blistering upon acute edema exacerbation (5). In this case, however, the blisters were not located at the site of the skin swelling.

AEB are caused by high interstitial fluid pressure that leads to the separation of the dermo-epidermal junction, resulting in subepidermal blister formation in the absence of inflammatory signs. AEB have only been reported in patients with severe swelling and are most frequently observed on the lower leg (“hydrostatic bullae”). They are usually associated with chronic venous insufficiency and edema due to cardiac insufficiency (6). Blistering sometimes occurs in cutaneous mastocytomas. The current report shows that AEB may occur due to severe skin edema of HAE-C1-INH.

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