Acute edema blisters in a hereditary angioedema cutaneous attack

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ABSTRACT

Hereditary angioedema is a rare autosomal dominant disease characterized by recurrent episodes of acute edema affecting the skin and the respiratory and digestive tracts. Acute edema blisters or hydrostatic bullae develop after rapid accumulation of interstitial fluid usually associated to cardiac insufficiency. Lesions contain sterile fluid and break up easily resolving without scars. Blisters disappear when fluid accumulation resolves. We describe a patient developing recurrent acute edema blisters as a consequence of cutaneous hereditary angioedema attacks.

Key words: acute, angioedema, blisters, bullae, hereditary.

INTRODUCTION

Numerous skin diseases are characterised by the presence of blisters. In some of them, blistering is their main manifestation while in others this is an infrequent finding. Most of these diseases are associated with substantial morbidity and some of them can cause death. Thus, an appropriate differential diagnosis and prompt and correct treatment is mandatory. Bullae characteristics like location, spread and itching and mucus membrane affectation help to pinpoint specific diseases. Moreover, accompanying systemic symptoms, previous exposition to drugs, insects or other sick people add to the differential diagnosis[1]. Acute edema blisters rarely develop in older patients presenting with acute cardiac insufficiency or renal failure, but they have not been described in hereditary angioedema, another very uncommon cause of acute and massive edema formation.

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CASE REPORT

A 52-year-old Caucasian man known to be affected with type I hereditary angioedema attended the clinic with a severe angioedema attack involving his left arm. The skin was very tense and the swollen area was covered by erythematous mottling and erythema marginatum (fig. 1). Over the ensuing hours, several small blisters formed on the folds of the flexural skin of the elbow (fig. 2). The bullae unroofed on the next day and the ulcers cured leaving a transitory pigmented scar. The patient admitted that on another occasion blisters developed on his right elbow and on a third time on his groin. Skin lesions cured without longstanding marks.

DISCUSSION

Patients with acute fluid overload may present with blister formation, especially on the extremities

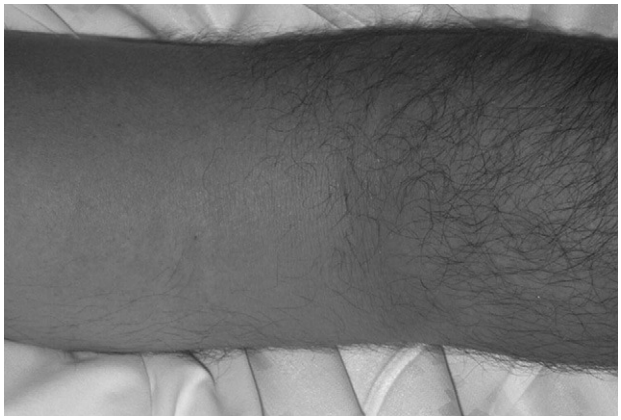

Fig. 1.—Ventral aspect of patient's elbow showing edema, mottling erythema and erythema marginatum.

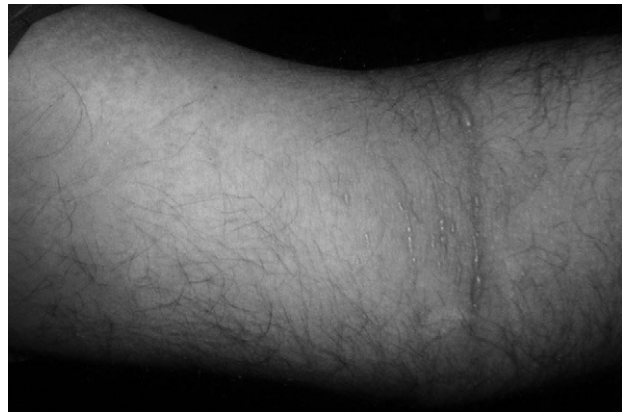

Fig. 2.—Tense blisters developed on elbow skin folds.

such as occurred in this patient. Blisters in the context of acute edema have been named "acute edema blisters" or "hydrostatic bullae". In all cases when the cause of the underlying edema is treated, the blisters subside. Bullae that form because of edema contain sterile fluid and a thin roof and usually break within a few days. It has been suggested that acute edema blisters develop when capillary filtration rate exceeds lymphatic drainage and where tissue compliance is low and skin is lax, like in skin folds. Once the fluid imbalance is corrected, these blisters resolve without recurrence[2]. If they are located on a distal portion of the lower extremities, elevation of the legs can reduce the edema and subsequent blister formation. The colocation and temporal association of acute edema and blister formation help to differentiate these lesions from other bullous diseases like bullous pemphigoid, pemphigus vulgaris, herpes zoster, drug eruptions and contact dermatitis[3].

Hereditary angioedema (HAE) is an autosomal dominant disease occurring with an estimated frequency of 1: 10,000 to 1:50,000 persons. It has been reported in all races with no sex predominance. The disease often begins in childhood and is caused by partial deficiency of the plasma protein C1-inhibitor (C1 INH). Mutations in the gene coding for this protein cause two variants of the disease. Type I with low detectable C1-INH serum protein (85 % of cases) and type II with normal to high protein levels but low C1-INH function (15 % of cases). The pathogenesis of the acute edema attacks of HAE is not completely known but recent data suggest that bradykinin is the most important mediator[4]. HAE is clinically characterised by recurrent and self-limiting episodes of marked edema of the skin, gastrointestinal tract, and larynx. Fluid accumulation occurs over several hours, persists for 10 to 12 hours and resolves spontaneously during 2 to 4 days. Cutaneous angioedema is described as nonpruritic and nonpitting. It is characterised by circumscribed swelling located mostly on the extremities, the face, or the genitals. During attacks, patients may have erythematous mottling, erythema multiforme or erythema marginatum, always mild and transient, that inconstantly heralds or attends their angioedema[5].

The temporal association of edema and blisters in this patient, without bulla formation outside HAE attacks supports the diagnosis of acute edema blisters. This is the only patient that has ever had bullae out of 47 that we care for. Moreover, we witnessed only one blistering episode out of 165 attacks that we have treated in the last two years. To our knowledge, this is the first description of spontaneous edema blisters in HAE.

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