Abstract

The diagnosis of bullae can be a challenge. The proper diagnosis and prompt treatment is mandatory because most of these diseases are associated with a significant degree of morbidity. The authors present the case of a 76-year-old woman admitted for treatment of anasarca. She also exhibited a bullous eruption localized to the right upper limb.

Keywords: blister, edema, renal insufficiency edema; edema bullae

Introduction

Bullae may be part of a primary condition or an infrequent finding in other systemic disease [1]. The vesicobullous dermatoses cover a wide variety of entities, including autoimmune bullous diseases and mechanobullous genetic diseases [2]. However, there are other diseases that can present with blisters in the clinical picture: bullous diabeticorum, coma blister, friction blister, hydrostatic blister, small vessel vasculitis, fixed drug eruption, allergic reaction to insect stings, thermal burns, among others [1,3].

Location, spread, symptoms, and involvement of mucous membranes can guide the investigation of specific diseases [1]. Rapid diagnosis and prompt treatment is mandatory because most of these diseases are associated with significant morbidity [2,3]. The authors present a 76-year-old woman, who was hospitalized owing to worsening renal function and anasarca. She exhibited a bullous eruption on the right forearm and we discuss the differential diagnosis, histopathology, and treatment.

Case synopsis

A 76-year-old woman with a history of coronary artery disease, hypertension, and diabetes mellitus, was admitted to the emergency department owing to anuria, abdominal pain, and dyspnea. At admission, she had edema of upper and lower limbs and abdomen without signs of pulmonary congestion. Owing to anasarca, venoclysis was difficult, requiring many attempts to peripheral venous puncture. Admission laboratory tests showed nitrogen retention (urea 217 mg/dl; creatinine 8.16 mg/dl) and anemia (RBC 2.58 million/mm³, hemoglobin 7.9 g%, hematocrit 23.8%); coagulogram, and total proteins within the normal standard. Nephrology departmental consultation was requested, and owing to worsening renal function, fluid overload, and uremia, double-lumen catheter insertion was carried out and hemodialysis began.
The day after admission, she had ecchymoses on the extensor surface of the right upper limb and tense blister (Figure 1a). There was no erythema and the patient reported that the lesions were asymptomatic. After 24 hours of onset, new hemorrhagic vesicobullous lesions emerged in the right upper limb, which coalesced and expanded in the ecchymoses area (Figure 1b, 1c). A Gram stain and culture of the fluid of two bullae were negative. A biopsy was performed adjacent to a vesicle. Histopathological examination showed no inflammatory infiltrates, but significant interstitial edema in the middle dermis (Figure 2).

Figure 1. (a) Tense blisters and bruising in the distal third of the right arm, right antecubital fossa, and proximal region of the right arm - the areas of bruises correspond to the locations of multiple attempts to venipuncture; (b) Blisters without signs of inflammation in the middle third of the right forearm are observed; (c) Hemorrhagic content of blisters on the area of ecchymosis.

Figure 2. Histopathological findings: absence of inflammatory infiltration, interstitial edema with formation of negative spaces, and uncoated endothelium in the upper and middle dermis. (hematoxylin and eosin staining; (a) 40X, (b) 100x, (C) 100x, (D) 400x).
The diagnosis of hydrostatic blister or edema blister was established, and the treatment included the replacement of her antihypertensive diltiazem, a calcium channel blocker that can aggravate edema, and optimization of clinical treatment.

**Discussion**

The pathophysiology of edema is complex and multifactorial and it develops when the capillary filtration rate exceeds the lymphatic drainage [1,3] (Figure 3). The primary cause could relate to heart failure, renal disease, liver cirrhosis, hypoalbuminemia, vein occlusion (thrombosis) or drug use, in particular, calcium channel blockers [1,3-5]. Edema blisters occur mainly in the extremities of patients with fluid overload in the interstitial space [1,4,5], especially in the elderly, as in our patient. In a study of 13 patients, the average age of onset of lesions was 74 years [4].

Clinically it begins with vesicles, which may coalesce, often giving rise to large bullae that may reach even a few centimeters in diameter [1,4,5]. The blister fluid is sterile and usually clear, but may be serous or hemorrhagic [3,4]. In patients with anasarca, the lesions tend to have a more widespread distribution [1]; the trauma from our patient’s venipuncture may have produced a predisposition for the bullae to localize to the arm. Histopathology is characterized by epidermal spongiosis, dilated dermal blood vessels, mild inflammatory infiltrate, dermal edema with wide separation of collagen bundles, and, in some cases, subepidermal blister [1,4]. Direct immunofluorescence is negative [1].

Veins used for venipuncture for sample collection or administration of solutions can be damaged by these procedures. Blood extravasation, which can cause ecchymoses and bruising, and/or extravasation of fluids may cause edema or even tissue necrosis. Because of the edema in our patient, it was difficult to obtain peripheral venous access, which caused damage to the punctured vessels in the right upper limb. This may have triggered the onset of vesicobullae, which initially emerged near the area of puncture attempts where there was increased local swelling and bruising. Although the patient had edema similar in the contralateral upper limb and lower limb, bullae did not arise in these areas.

The main conditions in the differential diagnosis are bullous diabeticorum, fixed drug eruption, friction blister, erythema multiforme, coma-induced bullae. One might also consider localized bullous pemphigoid or acquired epidermolysis bullosa in the appropriate setting [1,2,6-8]. The blisters associated with diabetes (bullosis diabeticorum) are characterized by spontaneous appearance, presence of minimal inflammation and location in acral regions, especially in the distal third of the lower limbs; its histopathology is non-specific [1]. There was no suggestive history for friction blister in our patient [1,8]. The clinical evolution of this case associated with the presence of interstitial edema with formation of clear spaces in the middle dermis allowed us to establish the correct diagnosis. Typically, blisters disappear quickly once the cause of edema is adequately treated [1]. Other measures include elevation of the limb, hypoproteinemia correction, diuretics, suspension of calcium channel blockers, compression bandages, and prevention of secondary infection [3-5].

![Figure 3](image-url)
Edema bullae, although relatively common in inpatient dermatology practice, are underreported in the literature [4]. Early recognition allows reassurance of the patient and treating physicians and allows the avoidance of unnecessary investigations.

References