Disseminated tense bullae on newborn

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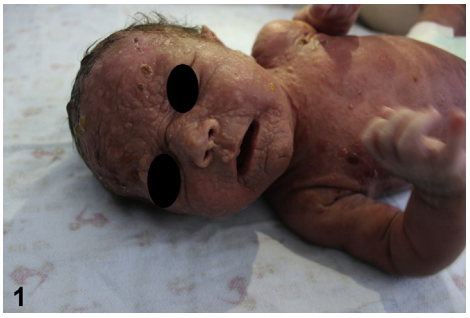

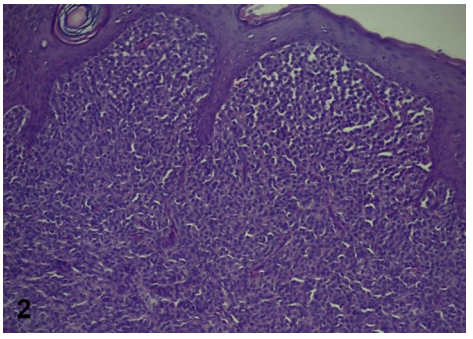

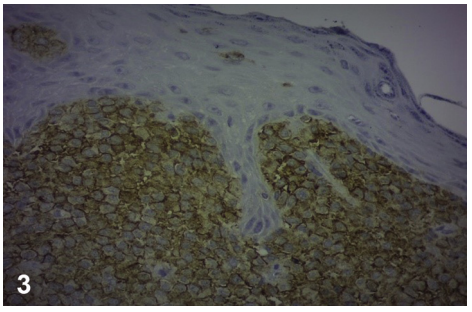

A newborn boy in the first 14 days of life was evaluated by the Dermatology service for bullous lesions on the face and scalp, hyperpigmented macules on the body, and persistent irritability. Antibiotic therapy was started, and analgesic medications (dipyrone and paracetamol) were used to improve the skin condition and irritability. The patient was treated with ibuprofen; however, after 8 hours he showed significant worsening with appearance of tense bullae and erosions on his body. His skin was considerably thickened, with leather appearance, and brownish, with a "peau d'orange" appearance (Fig 1). Moreover, we observed that friction led to mild urtication in our patient. On the other hand, he had no systemic involvement. Tests performed to rule out systemic involvement were chest X-ray and abdominal ultrasound. Virus serology results were negative for HIV, herpes simplex virus and Epstein-Barr virus. Representative images of the histopathologic and immunohistochemical (CD117) biopsy findings are shown in Figs 2 and 3, respectively.

Question 1: What is the most likely diagnosis?

A. Impetigo bullosa

B. Epidermolysis bullosa simplex

C. Diffuse cutaneous mastocytosis (DCM)

D. Staphylococcal-scalded skin syndrome

E. Erythema multiforme

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Answers:

A. Impetigo bullosa — Incorrect. Impetigo bullosa is a skin infection caused mainly by *Staphylococcus aureus*, with the rare appearance of intact vesicles or bullae. Typically, the lesions are copious, especially in the mouth and nose regions. Confirmation of the diagnosis can be obtained with Gram stain and culture.[1]

B. Epidermolysis bullosa simplex — Incorrect. Epidermolysis bullosa simplex is one of the main types of bullous epidermolysis, which is represented by fragility of the skin, and due to minor mechanical trauma, nonscarring blisters and erosions are formed. Its diagnosis is established through molecular genetic testing and skin biopsy.[2]

C. DCM — Correct. DCM is characterized by generalized infiltration of mast cells in the skin, with frequent formation of bullae. Bullous lesions are frequently observed, with reports of bullous lesion involvement in 62% to 69% of the patients, and may even be the first presentation of DCM. Bullae appear mainly on the trunk, scalp, and extremities, developing into erosions and thickening of the skin. Clinically, patients have pruritus, generalized erythema, pachydermia, and a darker skin color compared with that of normal-appearing skin. In order to assist the diagnosis, histologic examinations are typically performed. Frequent follow up and proper treatment are essential for significant improvement in overall clinical outcomes and disease control. Treatments include the use of antihistamines, systemic and topical corticosteroids, and mast cell stabilizers.[3]

D. Staphylococcal-scalded skin syndrome — Incorrect. Staphylococcal-scalded skin syndrome is a cutaneous infection that can cause bullae and erosions in newborns. The risk of skin infection is greater for premature and immunosuppressed newborns. Antibiotic therapy is administered in cases of suspected staphylococcal-scalded skin syndrome, in which thorough hygiene measures should be taken until the results of the tests are available. Its diagnosis is established by culture and sensitivity evaluation.[2]

E. Erythema multiforme — Incorrect. Erythema multiforme is a disease that manifests through blisters, macules, papules, and plaques on the body and that is caused by a reaction to infection or medication. In particular, there are often acral lesions, which can appear first on the limbs, head, and neck and subsequently spread elsewhere. Its diagnosis can be confirmed by clinical findings and histopathologic tests.[4]

Question 2: What is the name of the pathognomonic clinical sign of the disease?

A. Nikolsky sign

B. Asboe-Hansen sign

C. Pseudo-Darier sign

D. Cluster of jewels sign

E. Darier sign

Answers:

A. Nikolsky sign — Incorrect. The Nikolsky sign is a useful tool in the diagnosis of skin diseases, characterized by dislodgement of epidermis due to the application of tangential/lateral pressure on the skin or the border of a blister. The Nikolsky sign allows the differentiation of intraepidermal blisters from subepidermal blisters. It can often be observed in patients with staphylococcal-scalded skin syndrome, Stevens-Jonhson syndrome/toxic epidermal necrolysis, and pemphigus.[5] However, negative Nikolsky sign can be observed in some skin diseases, such as bullous pemphigoid, which is characterized by pruritic and tense blisters.

B. Asboe-Hansen sign — Incorrect. The Asboe-Hansen signal, also called the blister-spread sign, reflects the ability to extend a blister in the direction of the periphery through mechanical pressure applied to the roof of the intact bubble. It is important to analyze Stevens-Johnson syndrome/toxic epidermal necrolysis, pemphigus, severe bullous drug reactions, and other blistering diseases. This sign is similar to the Nikolsky sign.

C. Pseudo-Darier sign — Incorrect. Pseudo-Darier sign reflects temporary induration or piloerection on rubbing the lesions. It is elicited through transient induration with piloerection caused by stroking, being present in many conditions, including Becker nevus and smooth muscle hamartoma.[5]

D. Cluster of jewels sign — Incorrect. The cluster of jewels sign is associated with bullous disease, with the appearance of new lesions on the margins of the oldest lesions, resembling a cluster of jewels. It is also known as the string of pearls or rosette sign.[5]

E. Darier sign — Correct. The Darier sign is one of the main criteria for the diagnosis of DCM. The Darier sign is characterized by histamine release due to the friction of the lesions that cause

urtication.[3] It is related to transient erythema and edema production caused by rubbing the lesion. This sign is elicited through moderate pressure with a tongue spatula on the lesion around 5 times, developing a wheal-and-flare reaction of the lesion a few minutes later.[6] This sign can also be seen in proliferative conditions, which, however, is rare.

Question 3: Which mutation may be involved in this patient's condition?

A. TYR

B. VEGFR-3

C. KRT5

D. KIT

E. FBN1

Answers:

A. TYR — Incorrect. TYR is frequently associated with albinism.[7]

B. VEGFR-3 — Incorrect. VEGFR-3 is related to the Milroy disease.[7]

C. KRT5 — Incorrect. KRT5 is observed in patients with epidermolysis bullosa simplex.[7]

D. KIT — Correct. KIT is associated with mastocytosis. An activating mutation at codon 816 of KIT is often observed in these patients.[6]

E. FBN1 — Incorrect. FBN1 is observed in patients with systemic sclerosis.[7]

Abbreviation used:

DCM: diffuse cutaneous mastocytosis

Conflicts of interest

None disclosed.

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