JAMA Dermatology Clinicopathological Challenge

Recurrent Blistering in an Infant

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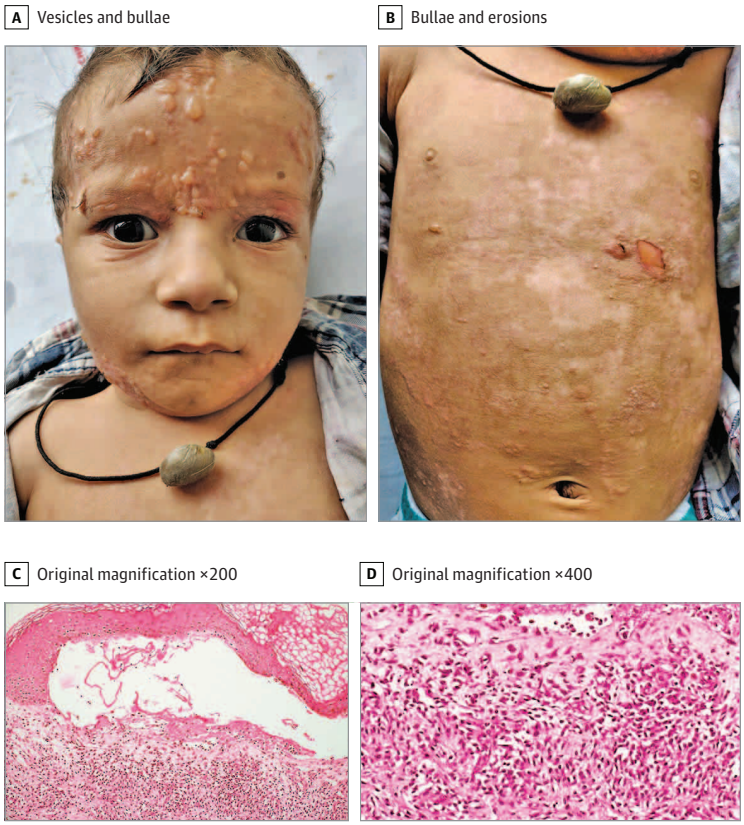

Figure. A, Multiple angulated vesicles and tense bullae over the forehead and chin. Background erythema can be appreciated. B, Tense bullae over the trunk with superficial erosions and postinflammatory hypopigmentation, which are healing with scarring and discrete milia formation. Few urticated papules and plaques can also be appreciated. C, Subepidermal bulla with bandlike mast cell infiltrate in the upper dermis (hematoxylin and eosin stain). D, Higher magnification showing dense infiltrate of mast cells in the upper dermis. Mast cells can be identified by ovoid to spindle-shaped nuclei (hematoxylin and eosin stain).

An infant boy, born to a nonconsanguineously wed couple, presented to the dermatology outpatient clinic with recurrent skin blisters since age 2 months. The lesions initially started over the trunk and subsequently progressed to involve the face, hands, and feet. The episodes of skin blisters were accompanied by pruritus and redness all over the body. There was no history of oral erosions or difficulty in feeding. Bowel and bladder movements were normal. The child had an older sibling who had no skin ailments, and none of the other family members were affected.

On examination, multiple tense, angulated vesicles and bullae on a background of erythema were seen over the face, trunk, and extremities (**Figure**, A and B). Few urticated papules and wheals were seen in isolation over the trunk. The ruptured bullae were healing with hypopigmentation with accompanying scarring and discrete milia formation. The mucosae and nails were normal. No contractures or webbing of fingers was noted. There was no organomegaly. A punch biopsy from a vesicle was subsequently performed (Figure, C and D).

WHAT IS YOUR DIAGNOSIS?

- **A.** Dystrophic epidermolysis bullosa
- **B.** Chronic bullous disease of childhood
- **C.** Bullous mastocytosis
- **D.** Congenital erythropoietic porphyria

Diagnosis

C. Bullous mastocytosis

Discussion

Darier sign, urtication, and erythematous halo produced in response to rubbing and scratching was diffusely positive over the trunk. The skin biopsy from the vesicle revealed clefting at the dermoepidermal junction containing fibrin. Upper dermis showed band-like inflammatory infiltrate comprising of mast cells that had ovoid- to spindle-shaped nuclei. Some scattered eosinophils were also noted (Figure, C and D). The mast cells stained positive for CD117 and toluidine blue. Results of immunofluorescence studies from perilesional skin were negative. The diagnosis of bullous mastocytosis was thus confirmed.

Complete blood cell count and liver function test results were found to be normal. Ultrasonography did not reveal any organomegaly. Owing to lack of any evidence of systemic involvement, bone marrow studies were not done. The child was prescribed hydroxyzine syrup, 0.5 mg/kg, per day with topical fluticasone propionate cream, 0.05%, to be applied twice daily. The episodes were well controlled while the child took antihistamines with mild flare-up during episodes of upper respiratory tract infections. The parents were told the necessary precautionary measures such as avoidance of extreme temperatures, rubbing of the skin, insect bites, and physical trauma and were also provided with a detailed safe drug list that avoided the mast cell–degranulating agents. The possible perioperative complications and instructions were also provided to them.

Diffuse cutaneous mastocytosis is a rare entity that occurs exclusively in infants. Two distinct presentations have been described. One is diffuse yellowish orange infiltration of the skin (leathery skin) with papules and nodules, with vesicular lesions noted occasionally. The other less common variant presents with extensive blistering as the initial sign accompanied by generalized erythema as seen in the index case.[1,2] Presence of widespread blisters in an infant can lead to a possibility of various other pediatric dermatoses. There are reports of infantile bullous mastocytosis that were initially misdiagnosed as epidermolysis bullosa,[1,3] staphylococcal scalded skin syndrome, bullous impetigo, and erythema multiforme.[4,5] Because of the early age of onset, recurrent nature, and presence of milia, the possibility of congenital epidermolysis bullosa was considered in the index case. However, blisters in epidermolysis bullosa are noninflammatory, involve the mucosae, and predominantly occur over pressure sites. On histopathology, there is lack of inflammatory infiltrate and the diagnosis can be established by immunofluorescence antigen mapping.[3] Chronic bullous disease of childhood usually presents after infancy with pruritic papules and vesicles characteristically arranged in an annular pattern (string of pearl) in the perioral and perineal region. Background erythema is generally present. Histopathology will show a subepidermal bulla with neutrophilic infiltrate, and linear deposition of IgA at basement membrane zone on immunofluorescence is pathognomonic.[6] Bullous porphyrias, namely congenital erythropoietic porphyria and rarely type III porphyria cutanea tarda, can present in infancy with generalized blistering over the photo-exposed areas that heals with atrophic scarring. Additional clinical features include hypertrichosis, erythrodontia, and reddish discoloration of urine. Skin biopsy shows subepidermal bulla with festooning of dermal papillae into the floor and periodic acid–Schiff–positive hyaline material in the perivascular areas. Direct immunofluorescence reveals deposits of IgG around the upper dermal vessels. Diagnosis can be confirmed by spectrofluorometry.[7]

Most pediatric cutaneous mastocytosis without systemic involvement are usually benign with spontaneous resolution by adolescence. Systemic involvement can manifest as hepatosplenomegaly and lymphadenopathy. Elevated serum tryptase levels and presence of c-Kit mutations can be used as an indicator for systemic involvement.[8] Bone marrow biopsy is indicated in case of recurrent systemic symptoms and evidence of organ involvement.[5]

The mainstay of treatment is parental counseling to avoid the triggering factors. The parents must be provided with a comprehensive list of drugs that are safe and that do not trigger mast cell degranulation. Antihistamines and topical steroids are first-line treatments. Mast cell-stabilizing agents such as sodium cromoglycate and ketotifen can also be used. Phototherapy (psoralen–UV-A) has been used for extensive disease. For systemic mastocytosis, targeted therapies directed against downstream signaling pathways of KIT are the mainstay of treatment.[9]

ARTICLE INFORMATION

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