QUIZ SECTION

Disseminated Erythema and Vesicles on the Trunk and Extremities in a Teenager: A Quiz

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A 13-year-old girl presented with widespread pruritic erythema and blisters for 1 month. The patient had no systemic symptoms, and her personal and family medical histories were unremarkable. Physical examination demonstrated disseminated oedematous, urticarial erythema with vesicles and tense bullae, some exhibiting a "string-of-pearls" pattern, on the scalp, trunk, and extremities (Fig. 1). Perioral vesicles, and erosions on the oral and vulvar mucosa, were also observed. Laboratory tests revealed elevated white blood cell count (11.61×10^9/L, reference: $3.5–9.5 \times 10^9$/L) and IgE (1520 IU/mL, reference: < 100 IU/mL). Other investigations, including renal/hepatic function, urinalysis, complements levels, and autoantibody profile, were all unremarkable. A skin biopsy and direct immunofluorescence (DIF) were also performed.

Histological examination revealed subepidermal blistering filled with neutrophils and eosinophils, liquefaction degeneration of basal cells, and a neutrophil infiltrate in the superficial dermis (Fig. 2). DIF showed linear deposition of IgG and C3 at the dermo-epidermal junction (DEJ), without IgA or IgM (Fig. 3A–B). Indirect immunofluorescence (IIF) on normal human skin demonstrated IgG anti-basement membrane zone (BMZ) antibodies, while saline-split skin (ss-IIF) testing showed IgG located on the dermal side (Fig. 3C–D). Further testing for serum antibodies associated with autoimmune bullous diseases (AIBDs), including antibodies against bullous pemphigoid (BP)180, BP230, desmoglein (Dsg)1, Dsg3, laminin 5, laminin γ1 (p200), and type VII collagen (COL7), revealed elevated anti-COL7 antibodies level at 92U/ml (reference: < 10.94U/ml).

What is your diagnosis?

1: Epidermolysis bullosa hereditarian
2: Linear IgA bullous dermatosis (LABD)
3: Bullous systemic lupus erythematosus (BSLE)
4: Epidermolysis bullosa acquisita (EBA)

See next page for answer.

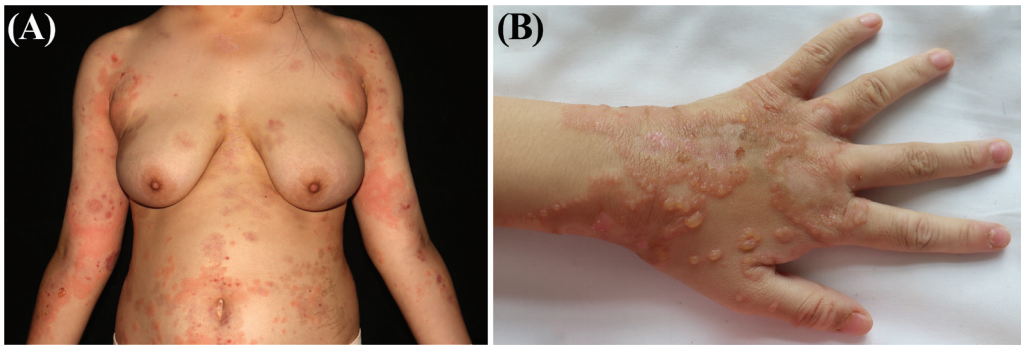

Fig. 1. (A) Disseminated oedematous, urticarial erythema with vesicles and tense bullae on the trunk and upper extremities. (B) Tense vesicles and bullae exhibit a "string-of-pearls" pattern on the dorsal hand.

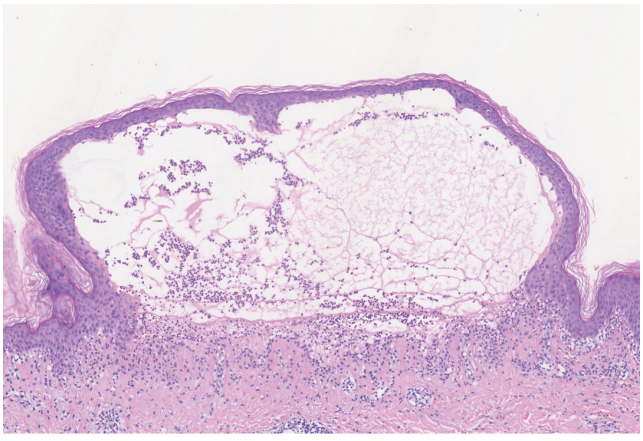

Fig. 2. Histopathology revealed subepidermal blistering filled with neutrophils and eosinophils, liquefaction degeneration of basal cells, and a neutrophil infiltrate in the superficial dermis (haematoxylin-eosin stain, original magnification×100).

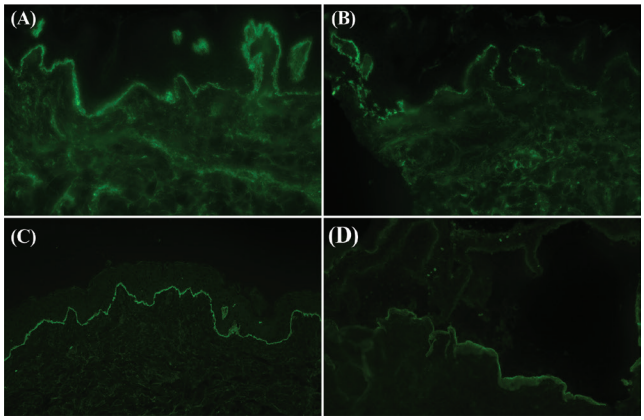

Fig. 3. (A, B) Direct immunofluorescence showed linear deposition of IgG and C3 along the dermo-epidermal junction. (C) Indirect immunofluorescence on normal human skin demonstrated IgG anti-basement membrane zone antibodies. (D) Indirect immunofluorescence on salt-split skin showed IgG located on the dermal side.

ANSWERS TO QUIZ

Disseminated Erythema and Vesicles on the Trunk and Extremities in a Teenager: A Commentary

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***Diagnosis*: Epidermolysis bullosa acquisita (EBA)**

EBA is an acquired autoimmune blistering disease that occurs rarely in childhood, with a prevalence of 1.2 cases per million children under 18 years old in Germany (1). It is classified into 2 major clinical phenotypes: the classical mechanobullous type and the inflammatory type (2). The classical type, typically observed in adults, is characterized by marked skin fragility, blisters, erosions, scarring, and milia formation, preferably in trauma-prone sites and on the extensor skin surface. The inflammatory type, which can mimic other AIBDs, is subclassified into BP-like, LABD-like, mucous membrane pemphigoid-like, and Brunsting–Perry pemphigoid-like EBA (2). Inflammatory EBA is predominantly found in children and presents with generalized inflammatory lesions resembling BP or LABD, like our patient. The most commonly and severely affected sites are the extensor surfaces of the extremities. Additionally, flexural or intertriginous areas of the trunk, such as the cleavage, navel, armpit, groin, and neck, are often involved (3). Mucosal involvement, including oral, ocular, genital, and trachea/larynx mucosa, is more frequent and severe in paediatric EBA compared with adults (3–5).

Histopathological and immunological features are crucial for diagnosing EBA. Histopathology typically shows subepidermal blisters, predominantly filled with neutrophils or a mixture of neutrophils and eosinophils in the inflammatory type, while the classical type shows scarce or absent lymphocytic infiltration (6). DIF reveals linear IgG and C3 deposition along the DEJ, with IgA or IgM less common (4). IIF detects IgG anti-BMZ antibodies, which bind to the dermal side in ss-IIF. Circulating anti-COL7 antibodies are a definitive diagnostic feature of EBA and can also be identified as a 290-kDa band by immunoblot analysis of normal human dermal extracts (3). Immunoelectron microscopy further confirms the diagnosis by showing IgG deposits within the lower lamina densa and/or sublamina densa zone at the DEJ(6).

Based on the clinicopathological and immunological findings, the diagnosis of paediatric inflammatory EBA was established for our patient. The differential diagnoses include epidermolysis bullosa hereditaria, BP, LABD, and BSLE. A negative family history of blistering diseases and immunological testing can exclude epidermolysis bullosa hereditaria. BP is typically characterized by autoantibodies against BP180 and BP230, with linear IgG deposition on the epidermal side of the blister. LABD is identified by linear IgA deposition along the DEJ. Although anti-COL7 antibodies are also specific to BSLE, the presence of a positive autoantibody profile, like anti-dsDNA and anti-Smith antibodies, along with multisystemic involvements, can help differentiate BSLE from EBA.

There is no standardized treatment for EBA. Systemic corticosteroids and dapsone serve as first-line treatment and demonstrate satisfactory efficacy in most paediatric EBA cases (5). Additional conventional therapies include methotrexate, cyclosporine, mycophenolate mofetil, azathioprine, and colchicine. In severe or refractory cases, intravenous immunoglobulin, plasmapheresis, extracorporeal photopheresis, and rituximab have been reported to induce complete remission (5). For our patient, initial treatment with methylprednisolone (40 mg/day), cyclosporine (150 mg/day), and high-potency topical steroids for 5 days resulted in poor disease control, with dozens of new blisters daily. The methylprednisolone dose was increased to 80 mg/day, and colchicine 0.5 mg/day was added (due to dapsone unavailability). After 10 days, the skin lesions showed some improvement, but over 10 new blisters continued to appear daily. To achieve better disease control and reduce corticosteroid dependence, the patient received 2 infusions of rituximab (500 mg each, 2 weeks apart). The patient responded well (Fig. S1) and achieved complete remission 3 months after rituximab therapy, with methylprednisolone tapered to 16 mg/day combined with colchicine 1 mg/day, and the level of anti-COL7 antibodies decreased to normal range (5 U/mL). At the 8-month follow-up after rituximab treatment, methylprednisolone was tapered to 4 mg/day and colchicine was discontinued. Only post-inflammatory hyperpigmentation and striae distensae remained on the patient's skin. Notably, rituximab has shown favourable treatment outcomes in refractory AIBDs, as observed in our case. Paediatric EBA usually exhibits better responsiveness to conventional therapies and has a more favourable prognosis than adult EBA (5).

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IRB approval status: Patient consent was obtained.

The authors have no conflicts of interest to declare.

REFERENCES

1. Hübner F, König IR, Holtsche MM, Zillikens D, Linder R, Schmidt E. Prevalence and age distribution of pemphigus and pemphigoid diseases among paediatric patients in Germany. J Eur Acad Dermatol Venereol 2020; 34: 2600–2605. https://doi.org/10.1111/jdv.16467
2. Prost-Squarcioni C, Caux F, Schmidt E, Jonkman MF, Vassileva S, Kim SC, et al. International Bullous Diseases Group: consensus on diagnostic criteria for epidermolysis bullosa acquisita. Br J Dermatol 2018; 179: 30–41. https://doi.org/10.1111/bjd.16138
3. Zhang Y, Dang J, Li R, Chen X, Zhu X, Wang M. Clinical features of paediatric inflammatory epidermolysis bullosa acquisita: a case series study. Acta Derm Venereol 2024; 104: adv11917. https://doi.org/10.2340/actadv.v104.11917
4. Iwata H, Vorobyev A, Koga H, Recke A, Zillikens D, Prost-Squarcioni C, et al. Meta-analysis of the clinical and immunopathological characteristics and treatment outcomes in epidermolysis bullosa acquisita patients. Orphanet J Rare Dis 2018; 13: 153. https://doi.org/10.1186/s13023-018-0896-1
5. Hignett E, Sami N. Pediatric epidermolysis bullosa acquisita: a review. Pediatr Dermatol 2021; 38: 1047–1050. https://doi.org/10.1111/pde.14722
6. Iranzo P, Herrero-González JE, Mascaró-Galy JM, Suárez-Fernández R, España A. Epidermolysis bullosa acquisita: a retrospective analysis of 12 patients evaluated in four tertiary hospitals in Spain. Br J Dermatol 2014; 171: 1022–1030. https://doi.org/10.1111/bjd.13144