IJD Case Report

Childhood vesiculobullous eruptions: a case report of a rare conundrum

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Received: 6 September 2023
Accepted: 17 May 2024

Pemphigus vulgaris is a severe autoimmune disorder with blistering of the skin and mucous membranes due to antibodies targeting desmoglein 3. It typically manifests in adults between 40 and 50 years of age, with a higher prevalence in females. Presentation in children is rare and poses greater challenges in diagnosis and management. Childhood pemphigus vulgaris, a variant affecting children under 12 years old, accounts for a small proportion of vesiculobullous eruptions in the pediatric population. The most common condition in the differential diagnosis of childhood vesiculobullous eruptions is chronic bullous disease of childhood (CBDC). Here, we describe a seven-year-old girl who presented with vesicles, flaccid bullae, and erosions with crusting over the body, accompanied by oral mucosal involvement. Skin biopsy revealed the characteristic suprabasal cleft with a tombstone appearance, while direct immunofluorescence demonstrated a fishnet pattern, confirming the diagnosis of childhood pemphigus vulgaris. She was successfully treated with intravenous antibiotics, tapered systemic corticosteroids, and azathioprine.

Keywords: pemphigus, childhood, azathioprine, direct immunofluorescence

Iran J Dermatol 2025; 28: 294-298

DOI: 10.22034/ijd.2024.413921.1751

INTRODUCTION

The differential diagnosis for vesiculobullous lesions in the pediatric age group includes a wide range of disorders like infections (human herpes virus, chikungunya rash, bullous impetigo, staphylococcal scalded skin syndrome), autoimmune disorders (chronic bullous disease of childhood, pemphigus group disorders, epidermolysis bullosa, bullous systemic lupus erythematosus), drug reactions (Stevens-Johnson syndrome, bullous fixed drug eruption, erythema multiforme), and nutritional causes [1]. Here, we describe a seven-year-old child presenting with extensive vesiculobullous lesions with mucosal involvement.

CASE PRESENTATION

A seven-year-old girl, born to a non-consanguineous marriage, presented with multiple fluid-filled lesions on the trunk and upper and lower limbs, which ruptured to form erosions over the past 10 days. She also reported oral intolerance to spicy food. There was no history of fever, joint pain, photosensitivity, erosions at trauma-prone sites, burning micturition, ocular redness, recent drug intake or vaccination, or similar complaints in the past or among other family members.

On examination, her vital signs were stable, with no pallor, icterus, cyanosis, or edema. Systemic examination was unremarkable. Dermatological

Please cite this article as: Belgaumkar VA, Raj R, Pradhan Sh, Nile S, Bhale G. Childhood vesiculobullous eruptions: a case report of a rare conundrum. Iran J Dermatol. 2025; 28(4): 294-298.

examination revealed multiple vesicles and flaccid bullae arranged in a circinate pattern, surrounded by erythema and erosions, with thick brownish-black adherent crusts over the face (predominantly involving the perioral and perinasal areas) as well as the trunk and bilateral upper and lower limbs (Figure 1). Extensive erosions were present on the scalp with matting of the hair. Direct and marginal Nikolsky's signs were positive. The Asboe-Hansen sign showed an irregular angulated border. Mucosal examination revealed a few erosions on the buccal mucosa, inner aspect of the lip, vulval and perianal regions. Genital and ocular mucosa were within normal limits. The palms, soles, hair, and nails

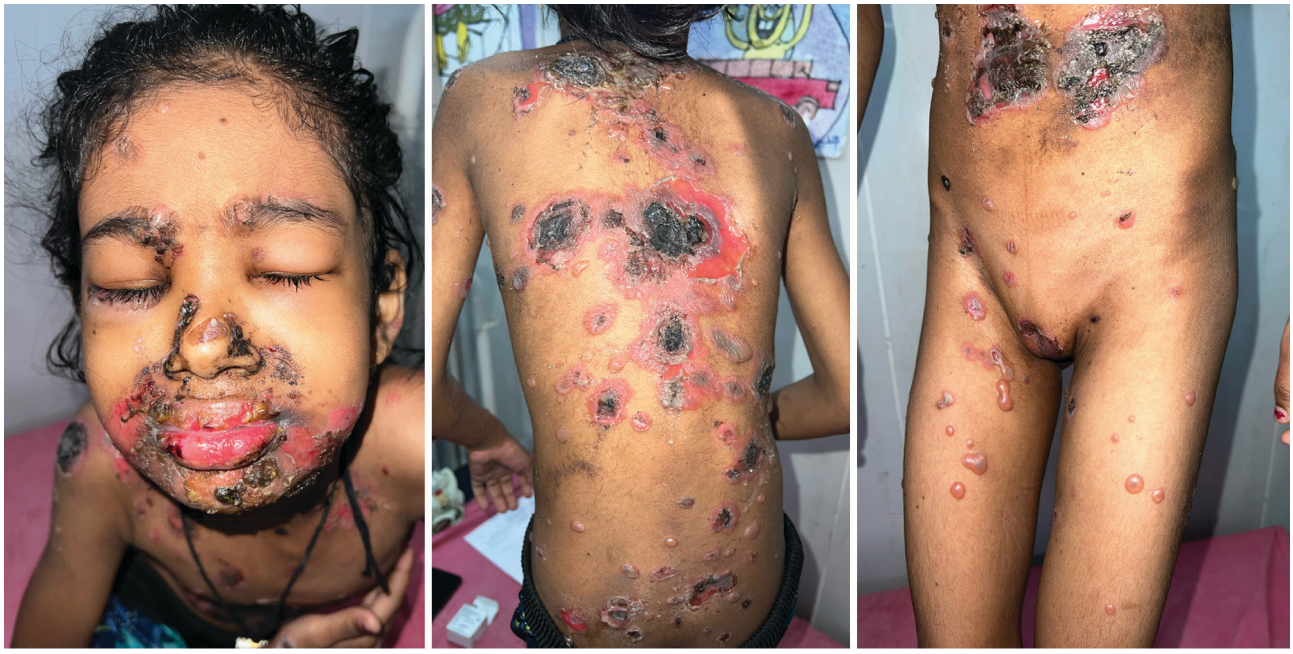

Figure 1. Multiple crusted erosions, a few vesicles, and flaccid bullae over the perioral area, forehead, trunk, and lower limbs.

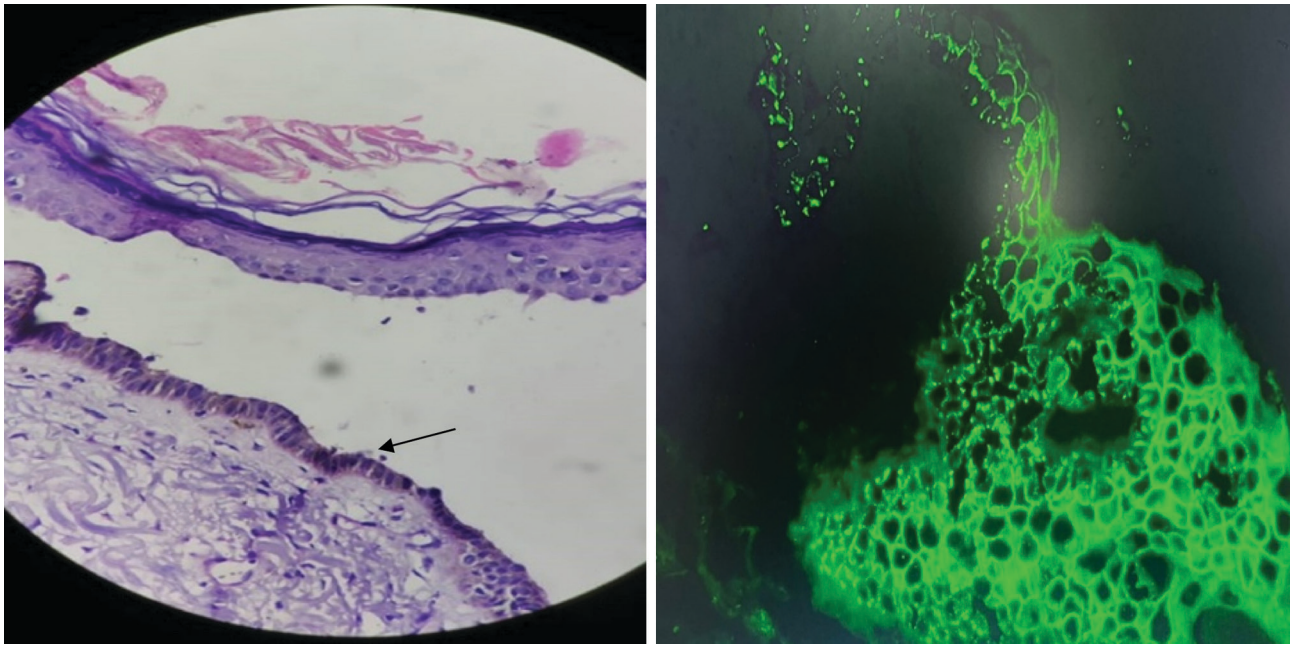

Figure 2. Photomicrograph of a vesicle (H&E, 40×) showing a suprabasal split with a tombstone appearance (black arrow). Photomicrograph (Direct Immunofluorescence) showing an intraepidermal fishnet pattern.

were unremarkable. Clinical differential diagnoses included pemphigus vulgaris and chronic bullous disease of childhood.

Complete hemogram, renal and liver function tests, and urine routine microscopy were within normal limits. The Tzanck smear showed giant acantholytic cells. Serological viral markers—including Human Immunodeficiency Virus, Hepatitis C Virus, and Hepatitis B surface antigen—were negative. Radiological investigations and electrocardiogram (ECG) findings were unremarkable. A skin biopsy from the vesicle showed a suprabasal cleft with a row of tombstone appearance of basal layer. Direct Immunofluorescence showed an intraepidermal fishnet pattern (Figure 2) with IgG positivity, while IgM and IgA were negative. Based on these findings, a final diagnosis of childhood pemphigus vulgaris was made.

She was treated with intravenous antibiotics (cephalosporins), dexamethasone injections (1 mg/kg/day, equivalent to prednisolone), oral azathioprine 25 mg once daily, local care including topical antibiotics and normal saline compresses, triamcinolone buccal paste 0.1% applied locally for oral lesions, multivitamins, and calcium supplements. The lesions gradually improved within three weeks. Steroids were tapered over two weeks, and she was transitioned to oral prednisolone (15 mg/day). Complete resolution of the existing lesions (Figure 3), with no new lesions appearing, was achieved by the end of four weeks. She is currently under regular follow-up and is being maintained on gradually tapered doses of prednisolone and azathioprine with stringent monitoring.

Ethical considerations

Written informed consent for the publication of this case report has been obtained from the guardians of the patient.

DISCUSSION

The word pemphigus is derived from the Greek word “pemphix” which means “blister”. Pemphigus vulgaris (PV) is the most common variant within the pemphigus group of disorders. It is an autoimmune disease with mucocutaneous blistering as a consequence of antibodies directed against desmoglein 3. The peak incidence occurs between the fourth and fifth decades of life, mostly affecting individuals aged 40 to 60 years, with a female predominance. The disease shows racial predilection and is more commonly observed in Ashkenazi Jewish populations and in Eastern countries such as India, Malaysia, China, and Japan.

It is rarely seen in children, with an incidence reported to be 0.1 to 0.5 cases per 100,000 inhabitants per year [2]. The exact incidence in the Indian subcontinent has not been documented to date. The

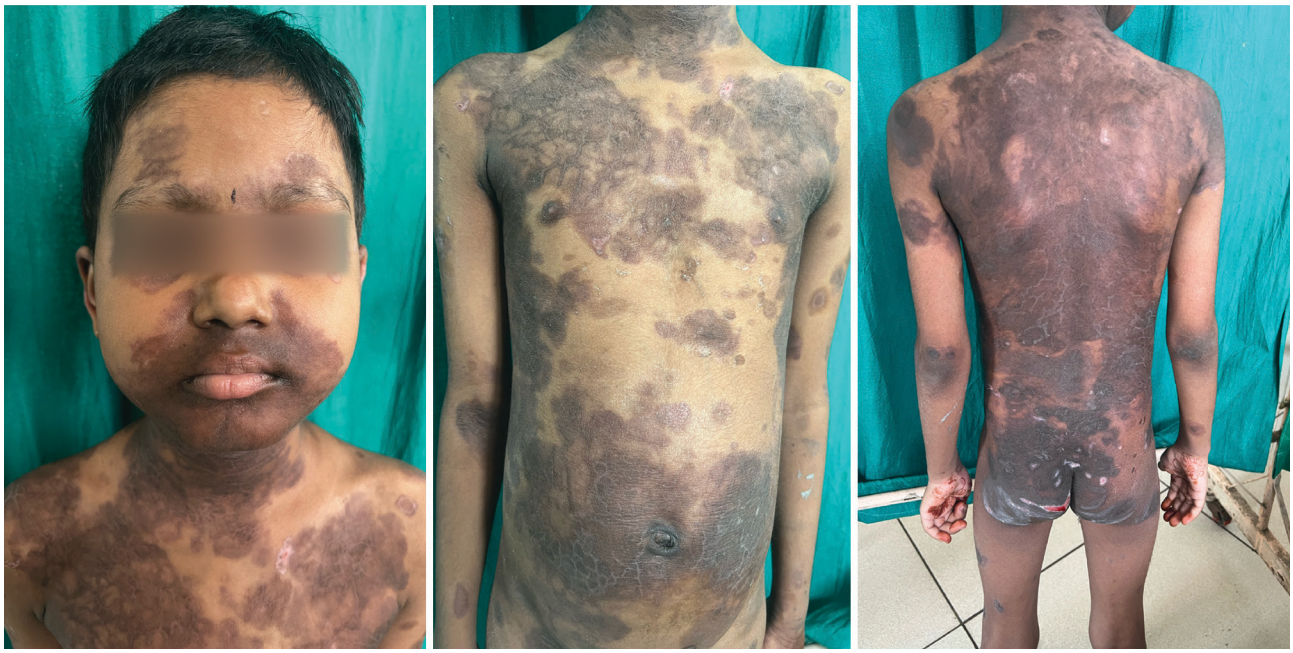

Figure 3. Post-inflammatory hyperpigmentation on the face, chest, abdomen, back, and buttocks.

pediatric variant is classified into childhood PV (CPV), occuring in children under 12 years, and juvenile PV (JPV), seen in individuals aged 12 to 18 years [3]. CPV accounts for around 1.4% to 3.7% of cases and is rare in children under 10 years of age [4]. Unlike adult cases, CPV affects males and females equally. A transient form of pemphigus is mostly observed in Ashkenazi Jewish neonates due to the transplacental transfer of antibodies [5].

Pemphigus vulgaris accounts for a small proportion of vesiculobullous disorders in the pediatric population. The condition most commonly considered in the differential diagnosis of childhood vesiculobullous eruptions is chronic bullous disease of childhood (CBDC), a subepidermal disorder characterized by IgA antibodies targeting epidermal and dermal-associated antigens with molecular weights of 285 kDa and 97/120 kDa, respectively. CBDC typically presents with the abrupt onset of asymptomatic or itchy tense vesicles or bullae on normal or erythematous skin, arranged in a "cluster of jewels" or "string of pearls" appearance. Sites of predilection include the perioral area, lower trunk, gluteal region, thighs, and perineal surfaces, with minimal mucosal involvement. In our case, the circinate configuration of vesicles and bullae on an erythematous base resembled CBDC, posing a clinical diagnostic challenge. However, the presence of a positive Nikolsky's sign, large spreading erosions, and extensive mucosal involvement favored a diagnosis of pemphigus vulgaris over CBDC. Furthermore, characteristic histopathological features such as a suprabasal split with tombstoning and the intraepidermal fishnet pattern observed on direct immunofluorescence confirmed pemphigus vulgaris. In contrast, CBDC shows a subepidermal bulla with neutrophilic collections along the basement membrane and linear IgA deposition on direct immunofluorescence.

The triggering factors for pemphigus vulgaris include various antigenic agents such as herpes virus, bacterial infections, drugs like enalapril and monteleukast [6], and vaccination with diphtheria-tetanus toxin, and malignancy (none of these triggers were identified in our patient). In some cases, a strong genetic association has been found with HLA alleles DRB1*04 and *14, as well as DQB1*0503 and *0302, in several populations [7]. IgG autoantibodies against desmoglein 3 are responsible for the loss of intercellular adhesion between epidermal cells, resulting in acantholysis and causing blistering of the skin, mucous and membrane. The presence of anti-desmoglein 1 antibodies in pemphigus vulgaris is considered a poor prognostic factor [2]. Recently, a new pemphigus antigen, desmoglein 4, along with other non-desmoglein antigens such as the human α9-acetylcholine receptor and keratinocyte annexin-like molecules that bind acetylcholine—termed pemphaxin and catenin—are thought to play a role in its etiopathogenesis [8].

The most commonly affected areas are the skin, or oral mucous membranes, and other mucosal sites such as the ocular, genital, nasopharyngeal, and esophageal regions. Pediatric pemphigus differs from adult-onset pemphigus in that it has a higher incidence of genital and ocular mucosal involvement, the oropharynx, nasopharynx, larynx, oesophagus and genital mucosa, as observed in our patient. However, adults are more likely to have associated autoimmune diseases like type 1 diabetes, rheumatoid arthritis, thyroid disease, hematological conditions, and oropharyngeal malignancies compared to pediatric cases [9].

Since this disorder is infrequent in the pediatric population, no evidence-based treatment guidelines are available. Corticosteroids (prednisolone 1–2 mg/kg) remain the mainstay of treatment for disease control during the acute phase [2]. Various immunosuppressive agents, such as azathioprine, cyclophosphamide, methotrexate, cyclosporine, and mycophenolate mofetil, are required for maintenance therapy. Other steroid-sparing agents, including dapsone, sulfapyridine, gold, erythromycin, and antimalarials can be administered concomitantly to allow a reduction in steroid dosage. Intravenous immunoglobulin (IVIG) is a safe and effective treatment option. Rituximab and plasmapheresis are reserved for severe, recalcitrant cases. The specific challenges in managing our patient included administering the optimal dose of immunosuppressives—considering the risk-benefit ratio—while vigilantly monitoring the clinical course and tolerability. Fortunately, she responded satisfactorily to corticosteroids and azathioprine without any major adverse effects.

Pediatric pemphigus has a better prognosis compared to adults, although it often follows a relapsing course. Rarely, it can be fatal due to sepsis and treatment-related side effects such as growth

retardation, osteopenia, and cataracts. However, mortality rates in children (2.9%) are reported to be lower than those in adults [10].

CONCLUSION

Being a relatively rare disorder, CPV presents challenges in both diagnosis and management. A high index of clinical suspicion, supported by appropriate investigations, facilitates early diagnosis, thereby minimizing morbidity and improving outcomes. Here, we elaborate on the overall disease presentation, treatment, and prognosis of CPV.

Acknowledgment

Department of Pediatrics.

Authors' contributions

Acquisition of data: **VB**, **RR**, **SN**, and **GB**; analysis and interpretation of data: **VB**, **SN**, **RR**, and **SP**; drafting of the manuscript: **VB**, **RR**, and **SN**; critical revision of the manuscript for important intellectual content: **VB**; administrative, technical, and material support: **VB** and **SP**.

Funding source

None.

Conflict of interest: None declared.

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