CASE REPORT OPEN ACCESS

Unraveling a Rare Dermatological Conundrum: Bullous Pemphigoid Unveiled in a Pediatric Patient with a Familial Twist

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Abstract

Bullous Pemphigoid is an autoimmune, blistering skin disorder that is rarely seen in infants and children. Diagnosing Bullous Pemphigoid in children is challenging due to its rarity in this age group. Bacterial and parasitic infections can trigger bullous and blistering lesions in individuals with underlying Bullous Pemphigoid. We report a 5-year-old child who presented with pruritic blisters and bullous lesions, initially attributed to scabies. Porphyria Cutanea Tarda was also considered based on blistering skin and family history. Although immunofluorescence studies were not performed, the diagnosis of Bullous Pemphigoid of Childhood was confirmed through skin biopsy. The patient was treated with corticosteroids after addressing the scabies infection. This case highlights the importance of a comprehensive diagnostic approach in distinguishing between autoimmune and infectious skin condition.

Keywords: Bullous pemphigoid, childhood, scabies, bullous scabies, pruritis, bullous, blisters, autoimmune, immunobullous, skin biopsy, corticosteroids, Porphyria Cutanea Tarda, rare disease.

1. INTRODUCTION

Immunobullous diseases are a class of dermatological diseases caused by pathological autoantibodies binding to protein targets within the epidermis of the skin. The most common is Bullous Pemphigoid (BP), an autoimmune blistering disorder, that usually affects the elderly >65 years of age, equally seen in both males and females [1]. The incidence of BP is around 4.5 and 14 new cases per 1 million per year in Central Europe. Bullous Pemphigoid in children is a rarity. The first case of bullous pemphigoid in a child was described in 1970 and in an infant in 1977 [2].

Immunobullous diseases are a group of dermatological disorders characterized by pathological autoantibodies binding to protein targets within the epidermis. Bullous Pemphigoid (BP) is the most common of these conditions and typically affects individuals over 65 years of age [1], with an incidence of 4.5 to 14 new cases per 1 million per year in Central Europe. Bullous Pemphigoid in children is extremely rare, with the first cases documented in 1970 and 1977 [2].

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The main clinical features of childhood Bullous Pemphigoid include severe pruritus, subepidermal blisters, tense blisters, and eosinophilia on histology [3]. Due to its rarity in pediatric patients, it can be mistaken for other conditions like Bullous Scabies, Porphyria Cutanea Tarda, and Erythropoietic Protoporphyria [4]. Scabies, caused by Sarcoptes scabiei, typically presents as pruritic papules and burrows but can also manifest as bullous lesions due to secondary bacterial infection [5]. Differentiating Bullous Pemphigoid from Bullous Scabies is challenging due to their similar presentations, which include pruritis and fluid-filled vesicles [5]. Although immunofluorescence studies are important for distinguishing these conditions, in the absence of such studies, a thorough clinical and histopathological evaluation remains crucial.

2. CASE REPORT

A 5-year-old girl from Karachi presented to the Family Medicine Health Centre, Ziauddin, Karachi, Pakistan, with complaints of hypopigmented macules, blisters, and scabs all over her body for the past year. The blisters, ranging from 0.5 cm to 5 cm in diameter, were progressively enlarging. Upon rupturing, they released clear fluid without pus or blood, eventually healing into hyperpigmented macules, which would then become hypopigmented.

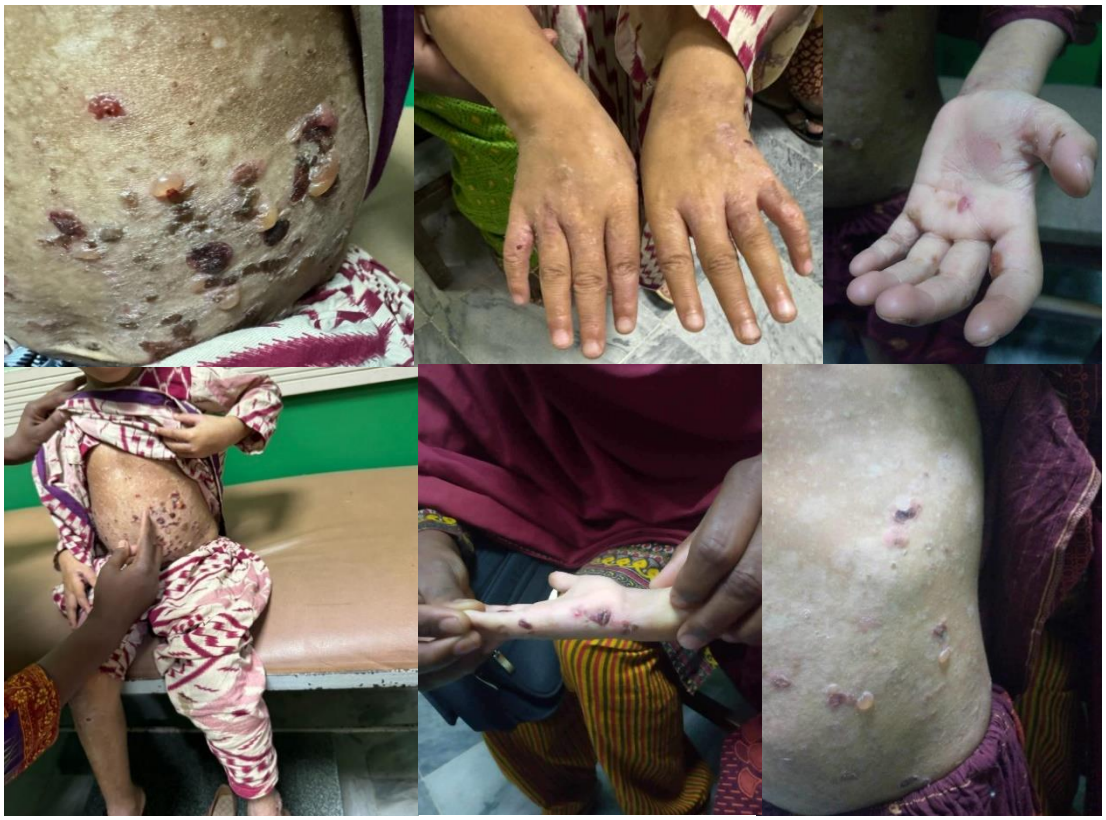

Figure 1: Multiple widespread crusted erosions and vesicles with post-inflammatory hypopigmentation distributed on trunk, arms and legs along with the involvement of hands and feet.

3. DISCUSSION

The term pemphigoid was first coined by Lever to describe a group of bullous diseases that present as subepidermal blistering. Bullous Pemphigoid (BP) being the most common out of all the bullous diseases [1].

Bullous Pemphigoid is an immunological disorder presenting with subepidermal blisters, eosinophilia, and pruritis. It is caused by autoantibodies against the self-antigens of the basement membrane zone. The antigens affected are BP180 and BP230; components of the hemidesmosome, an adhesive that allows adherence between the epidermis and the dermis. The binding of IgG autoantibodies against BP180 and BP230 induces neutrophilic chemotaxes, complement activation and release of mediators such as elastase and protease, which disrupt the hemidesmosome and hence the basement membrane, giving rise to blister formation [1].

Bullous Pemphigoid classically presents with intense pruritis and fluid-filled tense blisters. Mucosal lesions are generally not seen in Bullous Pemphigoid. The lack of mucosal lesions in BP, helps differentiate Bullous Pemphigoid from Pemphigus Vulgaris (PV), an immunobullous disease, which begins with flaccid blisters and erosions on the oral mucosa that spreads to involve other areas of the body [6]. Our patient had no evidence of oral or other mucosal lesions, allowing us to rule out Pemphigus Vulgaris as a cause of her symptoms. The histopathology of the skin biopsy also showed the presence of subepidermal blisters instead of subepithelial blisters seen in Pemphigus Vulgaris, effectively ruling out PV as a differential [7].

Another differential that was considered in our patient was Bullous Scabies. The patient presented with burrows and pruritic blisters on an erythematous base coinciding with the bullas, in accordance with a positive family history of scabies, prompting consideration as to whether Bullous Scabies was masquerading as pemphigoid [8]. It is hard to differentiate between Bullous Pemphigoid and Bullous Scabies, since both conditions present as pruritis, and fluid filled bullous lesions [9]. It is also important to note that bullous lesions are a rare manifestation of scabies and can morphologically and histopathologically mimic Bullous Pemphigoid [8, 9]. On histopathology, both conditions demonstrate subepidermal blisters with inflammatory infiltrates usually containing eosinophils; neutrophils and lymphocytes are also seen [8]. Linear IgG and C3 deposition at the basement membrane on Direct and indirect Immunofluorescence is the diagnostic hallmark for Bullous Pemphigoid. Around 58% of patients with Bullous Scabies have shown features similar to BP on Direct

Immunofluorescence, and around 21% of patients on Indirect Immunofluorescence, hence proving the importance of Indirect Immunofluorescent study to differentiate between the two conditions [9, 10].

A few theories have been hypothesized in the development of bullous lesions seen in scabies. On one hand superimposed staphylococcal infection can trigger bulla formation by the same mechanism seen in Bullous Impetigo. On the other hand, long standing scabies mite can cause injury to the basement membrane zone (BMZ) antigens through the production of lytic enzymes. This can alter the chemistry of the BMZ antigens and stimulate autoantibody production. Alternatively, antigens in the scabies mite can cross-react with the basement membrane antigens leading to autoantibody production in response to this antigenic similarity. The subsequent antibody production in both circumstances will cause complement activation, chemotaxis of neutrophils, eosinophils, and other inflammatory cells, along with the release of enzymes, that would induce subepidermal blister formation [11].

The bullous lesions in our patient first developed on the 6th day of her life, and have been recurring ever since then, indicating a more genetic/ immunological cause behind the disease, making Bullous Pemphigoid of Childhood in accordance with scabies infection a more likely diagnosis. The co-existence of both diseases in our patient makes it harder to differentiate whether the bullae were caused by scabies or induced by the underlying immunological disorder. It can also be postulated that the long-term untreated scabies infection could have triggered the underlying Bullous Pemphigoid as a Koebner phenomenon [12, 13]. In addition to the chronology of lesion occurrence, another notable point of differentiation between the two conditions lies in the clinical course. Infected Bullous Scabies, when adequately treated with 5% Permethrin cream, topical antibiotics, and in severe instances oral Ivermectin, demonstrates a tendency not to recur, contingent upon the maintenance of proper hygiene practices [8, 14]. Conversely, Bullous Pemphigoid exhibits a propensity for recurrence persistently until the initiation of sustained long-term therapy involving topical and oral corticosteroids. Steroid-sparing agents can also be considered for long-term treatment; Dapsone being the drug of choice not only for Bullous Pemphigoid but also for other immunobullous diseases [2, 15].

Blisters, bullae, erosions, and hemorrhagic crusts are also a manifestation of Porphyria Cutanea Tarda (PCT), a metabolic disorder of heme biosynthesis caused by decreased levels of uroporphyrinogen decarboxylase [16]. A deficiency of this enzyme induces a build-up of porphyrins in the skin, whose reaction with sunlight causes blistering and development of bullous lesions, specifically on sun-exposed areas such as hands, face, scalp, ears, legs, and soles [16]. These patients tend to have fragile skin, and minor trauma of the skin can cause blistering; hyperpigmentation develops after rupture and healing of these blisters [17]. Our patient had soft, friable skin with hyper and hypopigmented zones, hence, it was presumed that the friction of the skin due to continuous pruritis caused by the scabies infestation might have induced the generalized blistering and bulla formation attributable to the undiagnosed Familial Porphyria Cutanea Tarda. In addition, the patient's family originated from Khanpur Katora, a village in Punjab, Pakistan, and her parents had a consanguineous marriage, providing a genetic basis of the disease. Taking into consideration that other members of the family did not have similar complaints, PCT as a differential was viewed with scepticism. On histopathology, Familial PCT is characterised by cell-poor subepidermal bullae, festooning of dermal papillae, dermal sclerosis, hyalinization of dermal blood vessel walls, and perivascular infiltration of mononuclear cells in the upper dermis [18]. This differs from the histopathological picture of Bullous Pemphigoid and findings of the skin biopsy in our patient, hence ruling out PCT as a differential.

In our case, Direct Immunofluorescence (DIF) on salt-split skin, revealing IgG on the blister roof (epidermal side of split skin), would have been definitive for diagnosing bullous pemphigoid. However, due to resource limitations, we could not perform DIF. Despite this, the patient's clinical presentation and response to anti-scabetic treatment strongly indicated bullous scabies.

The primary objective of our study was to document the clinical and histopathological features of bullous scabies. The patient's clear clinical improvement with anti-scabetic therapy supports this diagnosis. We acknowledge the limitation of not using DIF and have emphasized the need for such diagnostic tools in similar future studies.

A variety of immunological diseases are present in a similar manner and most of them have differing treatment modalities; hence, it is important to carefully evaluate any patient that presents with pruritis, tense blisters and bullous lesions. Certain infections might trigger underlying, obscured immunological diseases, necessitating the importance of detailed history, examination, and diagnostic modalities for proper assessment of dermatological skin conditions. Our case on Bullous Pemphigoid is a prime example of a dilemmatic situation prompting in depth investigation into a clinical matter.

CONFLICT OF INTEREST

The authors declare no competing interests.

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PATIENT'S CONSENT

Inform consent was taken from the patient prior to the study.

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AUTHOR'S CONTRIBUTION

IIA, FJ and TS were involved in solving the case and writing the manuscript. TS did the skin biopsy. NB proofread the manuscript.

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