International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 03 Issue 11 November 2023

Page No: 2641-2645

DOI: https://doi.org/10.47191/ijmscrs/v3-i11-19, Impact Factor: 6.597

Juvenile Bullous Pemphigoid with Similarity Clinical Features to Chronic Bullous Disease of Childhood

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ABSTRACT

Introduction: Autoimmune bullous disease (ABD) is a specific autoimmune skin disease characterized by subepidermal vesicles and bullae. In pediatrics, there is an autoimmune bullous disease controversy with clinical clusters of jewel on Chronic bullous disease of childhood (CBDC) but dominant IgG autoantibodies. A similar clinical presentation challenges diagnosis; thus, supporting studies on direct immunofluorescence (DIF) as a specific autoantibody factor are necessary.

Case: A 10-year-old boy with clinically tense-walled blisters with or without an erythematous base is itchy all over his body, with a predominance of palmoplantar, neck, inguinal, and axillary, presented by erosions, crusts, and a partial cluster of jewels lesion with mucosal involvement. A complete blood count shows leukocytosis and eosinophilia. Hematoxylin-eosin (HE) staining revealed a subepidermal cleft with eosinophil predominance, while direct immunofluorescence (DIF) revealed IgG deposits in the basal membrana and intercellular parts of the basal stratum.

Discussion: Histopathology reveals subepidermal blisters of eosinophil dominance, and direct immunofluorescence (DIF) examination reveals IgG autoantibody deposit dominance, verifying the diagnosis of juvenile bullous pemphigoid. Given that BP180 (BPAG2) is one of the autoantigens involved, there may be similarities between the histology and clinical presentation of Bullous pemphigoid (BP) and CBDC.

Conclusion: Autoimmune bullous diseases are difficult to differentiate clinically, histological studies and direct immunofluorescence are necessary to make a diagnosis.

KEYWORDS: Bullous pemphigoid, CBDC, Autoimmune, Immunofluorescence

ARTICLE DETAILS

Published On:
07 November 2023

Available on:
https://ijmscr.org/

INTRODUCTION

Autoimmune bullous disease (ABD) is a specific autoimmune skin disease defined by the presence of autoantibodies against the skin structure's target antigen, desmosome and hemidesmosome[1], manifesting in a subepidermal bullous and vesicles.[3] Based on the target antigens and locations of the bullous, the disease is classified into four types: pemphigus, pemphigoid, epidermolysis bullosa acquisita (EBA), and dermatitis herpetiformis (DH).[1] Chronic bullous disease of childhood (CBDC), bullous pemphigoid (BP), and dermatitis herpetiformis (DH) are the most frequent disorders in children.[3,4]

Bullous pemphigoid (BP) is an autoimmune disease with antigen targets BP180 and BP230 characterized by itching, a subepidermal blister predominantly eosinophils, and deposits of IgG or C3 in the basalis membrane. It occurs rarely in children.[5-7] Bullous pemphigoid in children is known as juvenile bullous pemphigoid (JBP) and shares clinical, histological, and immunopathological characteristics with BP in adults.[8] JBP occurs most frequently between the ages of 1.5 months and 14 years.[9]

Chronic bullos disease of childhood (CBDC) is an autoimmune disease that manifests as a cluster of jewels with linear continuous IgA autoantibodies in the dermo-epidermal basal membrane zone.[2,10] CBDC is a rare disease with a yearly frequency of 0.5–2.3 cases per million people.[11]

There is a lack of epidemiological data on autoimmune bullous in children. Concerning the controversy in the case of

children with a clinical cluster of jewels on CBDC but a predominance of IgG autoantibodies.[9] The majority of autoimmune bullous diseases are clinically similar and require histological examination as well as immunofluorescence studies (IMF).[1] The aim of this article is to discuss and identify juvenile bullous pemphigoid cases with clinical manifestations similar to chronic bullous disease of childhood utilizing histology and direct immunofluorescence. This article can help physicians enhance their clinical diagnosis and subsequent examination skills, allowing them to manage BP accurately.

CASE

A 10-year-old Brebes resident arrived at the Dr. Soeselo Hospital emergency room in Slawi, Tegal, complaining of severe blisters and itching over nearly his entire body for four months. The first blister, which was located close to the genitalia, itched and did not cause a fever. The patient complained about a week after undergoing a circumcision and taking medicine prescribed by a general practitioner. The medication included an unidentified capsule and sulfanilamide powder for the circumcision lesion. An oral treatment plan consisting of methylprednisolone 16 mg once daily, co-amoxiclav (amoxicillin 250 mg, clavulanic acid 62 point 5 mg) three times a day, and vitamin C 50 mg once daily was prescribed to a dermatologist at Brebes following an unspecific dermatitis diagnosis. Although the complaint subsided, the blister continued to reappear nearby or in a different location. After being sent to a dermatologist in Slawi, the patient was advised to visit the emergency department for Steven Johnson syndrome, also known as TEN. The patient is the second child of two brothers and sisters, and no other family or siblings have expressed any similar concerns.

A physical examination revealed that the patient was generally healthy, mentally conscious, had vital signs that were within normal ranges, weighed 25 kg, and had no enlargement of the lymph nodes. The folds of the thighs, palms, soles, and around the genitals at the dermato-venerological examination of almost the entire body appear to be tense-walled vesicles and bullous with a predominance over the skin base with or without erythema; multiples spread, and some appear confluent, partly with erosion and crust (**Figure 1**). **Figure 1A-B** shows how the region of the thigh, abdomen, and arms appear to be tightly converging, with the central brown-yellow crust appearing to be a cluster of jewels. Both milia and scar tissue were absent. Both the hands' and the feet's fingernails were normal, and the Nikolsky mark was negative. Juvenile bullous pemphigoid (JBP), chronic bullous disease of childhood (CBDC), and epidermolysis bullosa acquisita (EBA) are the different diagnoses in this case based on the history and physical examination.

Comprehensive laboratory blood tests identified monositosis, eosinophilia, and leukocytosis. Acantolytic cells were not detected by Tzanck's test, and neither bacteria nor polymorphonuclear leukocytes were detected by the Gram stain. Additionally, liver and kidney function were both within normal limits. The lesions and perilesions surrounding the jewel-like cluster in the right femur were used to collect a skin biopsy from the patient. Hematoxylen-eosin (HE) staining was used to perform a histological analysis, which revealed a vesicobulosis reaction in the skin tissue, basket weave orthoceratosis in the epidermis, and subepidermal blisters with a high eosinophil concentration and low lymphocyte and neutrophil numbers (**Figure 2A**). The dermis is thin, with a high proportion of eosinophils and lymphocytes and a low proportion of neutrophils, particularly in the perivascular vessels. Malignancy was not indicated. Direct immunofluorescence (DIF) examination revealed IgG deposits on the basal membrane and intercellular areas in the basal layer. No IgA deposits or C3 deposits were detected on the basal membrane (**Figure 2B**). The histopathological and DIF analysis are more suitable for bullous pemphigoid.

Therapy for patients included fluid aspiration, open compresses with normal saline in the erosion area, cetirizine tablets 10 mg once daily, silver sulfadiazine cream twice daily, and injection of methylprednisolone 24 mg once daily while sparing dapsone 25 mg once daily. Lesions are getting better, but more continue to develop.

Figure 1. Clinical presentation of juvenille pemphigoid bulosa. The tense-walled blisters in the entire body (A), the central brown-yellow crust appearing to be a cluster of jewels (B), blister on mucosal (C), and palmoplantar (D-E)

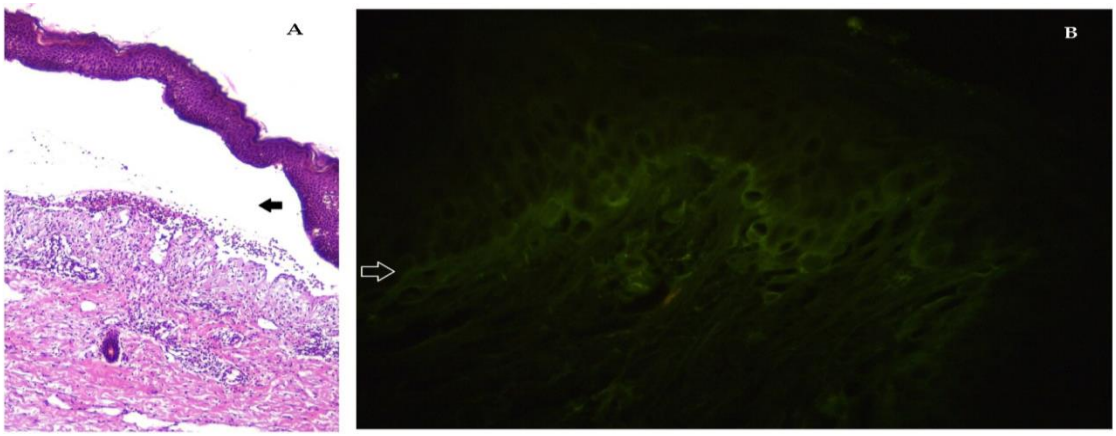

Figure 2. (A) Hematoxylen-eosin (HE) x100, revealed subepidermal blisters with a high eosinophil concentration and low lymphocyte and neutrophil number. (B) Direct immunofluorescence (DIF) x400, revealed IgG deposits on the basal membrane and intercellular areas in the basal layer.

DISCUSSION

Bullous pemphigoid, an autoimmune disease that primarily targets the BP180 and/or BP230 antigens, is most common in the elderly but can also occur in children and adolescents.[5,7,8] Clinically similar to BP in adults, facial and mucous involvement is more common in children.[12,13] The highest incidence occurs in infants aged 4 months and in childhood aged 8 years,[7] while according to Belzile et al., the age range is from 20 months old to 12 years old.[5] Infants have a predilection for lesions in the palmoplantar (79%) and face (62%), whereas in children, the genitalia are primarily affected by lesions.[2,5,7] Lesions are generalized in 60% of cases.[13] Juvenile bullous pemphigoid is characterized by tense-walled blisters that appear with or without an erythema base and are preferably located in the fold area (axillae and inguinals), flexor arms, and palmoplantar.[7,10,12] Blister eruptions are often preceded by severe itching and urticarial plaque or serpiginous erythema lesions with blisters in the periphery that may contain clear or hemorrhagic fluid. A new blister may appear at the edge of the old lesion, giving the appearance of a cluster of jewels like the CBDC. No Nikolsky sign was found. Temporary hyperpigmentation could be left behind by the lesions.[2,5,7] Leukocytosis, eosinophilia, or neutrophilia were found by a complete blood test.[5,14] The histopathological picture of JBP is identical to that of the adult; pathognomonic findings found subepidermal blisters without acantolysis with the eosinophil dominant inflammatory cells; occasionally found neutrophils as well as lymphocytes adapted to the progressive stage of the lesion.[2,5,10,15] Since it can be challenging to differentiate between ABDs histopathologically, a DIF examination—the Gold Standard for diagnosing ABDs and identifying autoantibodies in the skin and mucous membranes—is meant to provide a conclusive diagnosis.[1,13] In the DIF examination, JBP showed linear IgG deposits in almost all cases without C3 along the basement membrane.[2,7-9,12]

The patient case characteristics align with the onset of BP disease at 10 years of age. The disease manifests clinically as a clear, tense blister preceded by intense itching, with a preference for early dominant lesions in the genital area that extend to the flexion, palmoplantar, and eventually become generalisata. The slightly pathognomonic cluster of jewels and the dominating lesions of the tension blisters force a diagnosis for ranches based on their clinical appearance. The results of the complete blood count indicated eosinophilia, and the histological analysis using HE stain showed subcutaneous blisters without acantolysis and a predominance of eosinofil infiltrate. The CBDC pathognomonic lesions, or clusters of jewels, are the perilesional lesions used for the DIF examination. Although IgA autoantibodies were first thought to be the cause of the lesions, DIF revealed linear IgG deposition along the basement membrane. This is in line with the controversy surrounding the child who has clinically dominant clusters of jewels on the CBDC but shows dominant IgG on the DIF.[9] The clinical and histopathological picture of BP and CBDC could be similar since one of the autoantigens involved, BP180 (BPAG2), is the same[12,17] but the immunoglobulin involved is different: IgA in CBDC and IgG in BP. The criteria for JBP by Nemeth et al.[8] are: 1) age under 18 years; 2) clinical vesicle/tension blister; 3) histology shows subepidermal blister and eosinophilia; 4) linear IgG or C3 deposits in the basement membrane zone in DIF along with indirect immunofluorescence. In this case, BP reports that the histopathology, DIF, and clinical picture all meet the Nemeth et al. criteria.

The different diagnosis in this case is CBDC, or linear IgA bullous dermatosis, a rare but most common chronic autoimmune bullosis in children with the primary target protein antigen 180 kDa BPAG2 (BP180), which creates subepidermal blisters[11] and IgA deposits along the basement membrane.[16,17] The CBDC disease is an ABD with an onset of less than 5 years and a higher incidence in women than men.[2,11,17] affects the skin and mucous membranes, associated with non-specific prodormal symptoms such as acute fever accompanied by atritis, atralgia, and weakness. A mild pruritic symptom can be noted.[17] The clinical presentation is a tense-walled blister appearing on the normal

skin or on the erythema base with a pathognomony such as a cluster of jewels or string of pearls, which occurs as a result of the appearance of new blister lesions the edges of the old lesions which combine to form a polycyclic or arterial plate with a crust in the middle.[2,10,11] Lesions can develop locally or generally with a predilection; they most frequently appear on the face, particularly in the mouth region, and on the lower extremities, particularly in the palmoplantar, perineum, abdomen, and perigenital areas.[2,10] The histology of CBDC revealed subepidermal blister neutrophils as the main infiltrates, with eosinophils occasionally also present.[2,10] As a result of a normal skin biopsy and perilesions, the DIF examination revealed linear IgA deposits in the basement membrane zone. There might be fewer IgG, IgM, and C3 deposits.[10,11,16] In the case of this patient, who is male, a few lesions form clusters of jewels, which are in agreement with the CBDC diagnosis; however, the diagnosis of the JPB is supported by the histopathological examination and DIF.

Epidermolysis bullosa acquisita (EBA) is a rare chronic disease in children that affects the skin and mucous membranes and has autoantibodies against collagen type VII. In terms of clinical presentation, there are five different types of EBA: 1) Classic EBA, which includes mechanobulosa lesions with skin fragility, hemorrhagic blisters leaving scar tissue, milia, pigmentary changes, and nail atrophy, especially in the extensor muscle of the extremities, elbows, knees, fingertips, and crease areas; 2) Similar to BP without skin, scar tissue, and milia fragility; 3) Similar to sycatric pemphigoid with mucosal involvement (bucal, conjunctiva, palate, nasopharynx, esophagus, rectum, and genital area) and scarring tissue; 4) Similar to CBDC with mucosal involvement; 5) Similar to Brunsting-Perry pemphigoid with head and neck predilection. EBA has a subepidermal blister with a dominant neutrophilic and partially eosinophilic infiltrate as its histopathology. In the basement membrane zone, linear IgG and C3 deposits were discovered during the DIF analysis; IgA and IgM deposits may have been fewer.[18] Since IgG deposits were found in the DIF results, the diagnosis of an EBA can be ruled out even though the clinical presentation in this case is consistent with EBA types 2 and 4, while the histopatology does not even match an EBA.

CONCLUSION

A single pediatric case with a clinical cluster of jewels has been documented, but histology and DIF point to a JBP diagnosis. A diagnosis requires both a histological study and immunofluorescence studies using direct immunofluorescence because the majority of bullous autoimmune disease cases in children do not differ clinically.

REFERENCES

I. Heckler I, Hong M, Sinha A, Venkataraman I. Serological Biomarkers and Their Detection in Autoimmune Bullous Skin Diseases. *Dermatol Pract Concept.* 2022;12(2):e2022116.

II. Daniel BS, Murrel DF. Review of autoimmune blistering disease: the Pemphigoid disease. *JEADV*. 2019;33:1685-1694.

III. Kong YL, Lim YL, Chandran NS. Retrospective study on autoimmune blistering disease in paediatric patients. *Paediatr Dermatol*.2015; 326: 845-825.

IV. Gupta V. Clinicoepidemiological study of vesiculobullous disorders in pediatric age group. *Indian J Paediatr Dermatol*. 2015;16:9-16.

V. Faris Oumeish, Hamdi Hamad, Hussain Tukmatchy, Niall Scully and Mohammed Al Abadie, Bullous Pemphigoid in Children: Clinical Presentation, Pathology and Management. *Clin Res Dermatol Open Access.* 2021;8(1): 1-4.

VI. Biradar S.M, Dhanavidya S, Kavya P, Keerthi T, Sunanda N et al. Bullous Pemphigoid A Rare Autoimune Disease: A case Report. *International Journal of Medicine and Medical Research*. 2018;4:2:20-23.

VII. Denise Miyamoto, Claudia Giuli Santi, Valéria Aoki, Celina Wakisaka Maruta. Bullous pemphigoid. *An Bras Dermatol*. 2019;94(2):133-46.

VIII. Nemeth AJ, Klein AD, Gould EW, Schachner LA. Childhood bullous pemphigoid. Clinical and immunologic features, treatment, and prognosis. *Arch Dermatol*. 1991;127:378-86.

IX. Waisbord-Zinman O, ben-Amitai D, Cohen AD, et al. Bullous pemphigoid in infancy:Clinical and epidemiologic characteristic. *J Am Acad Dermatol*.2008;58:41-8.

X. Patsatsi A. Chronic Bullous Disease or Linear IgA Dermatosis of Childhood - Revisited. *J Genet Syndr Gene Ther.* 2013;4:151.

XI. Diaz M S, Morita L, Ferrari B, et al. Linear IgA Bullous Dermatosis: A Series of 17 Cases. *Actas Dermo-Sifiliograficas*.2019;110(8):673-80.

XII. Donna A. Culton DA, Liu Z, Diaz LA. Bullous pemphigoid. Dalam Sewon Kang, Masayuki A, Anna LB, Alexander HE, David JM, Amy JM.*Fitzpatrick's Dermatology in General Medicine 9th ed*. New York:Mc Graw Hill co.2019;54:944-59.

XIII. Sansaric F, Stein SL, Peronic-Rosic V. Autoimmune bullous disease in childhood. *Clin Dermatol*.2012;30:114-27.

XIV. Saenz AM, Gonzales F, Ciroco A, Tacaronte IM, Fajardo JE, Calebotta A. Childhood bullous pemphigoid: A case report and 10-year follow-up. *Int J Dermatol*.2007;46;508-10.

XV. Ghohestani R, Novotney J, Chaudary M, Agah RS. Bullous Pemphigoid: From the Beside to the Research Laboratory. *Clin Dermatol*.2001;19:690-6.

XVI. Gareth Edwards, Gilles FH Diercks, Marc AJ Seelen, Barbara Horvath, Martijn BA van Doorn, Jeffrey Damman. Complement Activation in Autoimmune Bullous Dermatoses: A Comprehensive Review. Frontiers in Immunology. 2019;10:1477.

XVII. Nicholas MW, Rao CL, Hall III RP. Linear Immunoglobulin A dermatosis and chronic bullous disease of childhood. In:Sewon Kang, Masayuki A, Anna LB, Alexander HE, David JM, Amy JM.*Fitzpatrick's Dermatology in General Medicine 9th ed*. New York:Mc Graw Hill co.2019;58:992-1001.

XVIII. Woodley DT, Chen M. Epidermolysis bullosa acquisita. In:Sewon Kang, Masayuki A, Anna LB, Alexander HE, David JM, Amy JM. *Fitzpatrick's Dermatology in General Medicine 9th ed*. New York:Mc Graw Hill co.2019;56:971-80.