



**CHRONIC BULLOUS DISEASE OF CHILDHOOD IN A RESOURCE-LIMITED
SETTING: A DIAGNOSTIC CHALLENGE**

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ABSTRACT

Chronic Bullous Disease of Childhood (CBDC) is a rare autoimmune blistering disease that predominantly affects young children. Its diagnosis is often challenging because of clinical overlap with infectious and other autoimmune blistering disorders, particularly in resource-limited settings where direct immunofluorescence (DIF), the diagnostic gold standard, is unavailable. Objective: To describe the diagnostic approach and management of a pediatric patient with CBDC using clinicopathological correlation and systematic exclusion of differential diagnoses in the absence of DIF. This case report was based on comprehensive history taking, physical examination, medical record review, laboratory investigations, histopathological examination, treatment evaluation, and clinical follow-up of a 4 year old girl presenting with generalized blistering lesions. The clinical and laboratory findings were analyzed descriptively through clinicopathological correlation, systematic comparison with relevant differential diagnoses, and assessment of the patient's clinical response to therapy. The patient presented with a one-month history of generalized tense bullae involving the forehead and extremities, with some lesions demonstrating the characteristic cluster of jewels pattern. Histopathological examination revealed subepidermal and intraepidermal blister formation with neutrophilic and eosinophilic inflammatory infiltrates. Although DIF could not be performed because of limited institutional resources, the diagnosis was established through clinicopathological correlation, systematic exclusion of differential diagnoses, and a favorable response to dapsone therapy. Marked clinical improvement was observed within two weeks after dapsone. A structured clinicopathological approach, combined with careful exclusion of differential diagnoses and therapeutic response, can facilitate timely diagnosis and appropriate management of CBDC in resource-constrained settings where immunopathological confirmation is unavailable.

Keywords: autoimmune blistering disease; chronic bullous disease of childhood; clinicopathological correlation; dapsone; differential diagnosis; pediatric dermatolog

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INTRODUCTION

Chronic Bullous Disease of Childhood (CBDC), also known as childhood linear IgA bullous dermatosis, is a rare autoimmune subepidermal blistering disease that predominantly affects children younger than five years of age. It is characterized by linear deposition of immunoglobulin A (IgA) along the epidermal basement membrane zone and represents the most common autoimmune blistering disease in children, despite its overall rarity (Menaldi et al., 2024; Pradhan et al., 2022). Clinically, CBDC presents with tense vesicles and bullae on an erythematous or normal skin base, often arranged in the characteristic “cluster of jewels” or “string of pearls” configuration. Lesions most frequently involve the perioral and perineal regions but may also affect the trunk, extremities, face, and mucous membranes (Tate et al., 2018). Although the disease generally has a favorable prognosis and frequently remits before puberty, delayed recognition may lead to prolonged morbidity and inappropriate treatment (Varo et al., 2017).

The exact pathogenesis of CBDC remains incompletely understood. Proposed triggers include infections, medications, vaccinations, ultraviolet radiation, and, less commonly, malignancy (Sulistianingrum et al., 2023). Antibiotics such as amoxicillin–clavulanate and

vancomycin have been most frequently implicated, while infectious triggers include upper respiratory tract infections, gastrointestinal infections, *Salmonella* enteritis, and Epstein–Barr virus infection (Patsatsi, 2018). Histopathological examination typically demonstrates a subepidermal blister with predominant neutrophilic infiltration; however, these findings are not specific and may overlap with those of other autoimmune blistering diseases. Consequently, direct immunofluorescence (DIF), demonstrating linear IgA deposition along the basement membrane zone, remains the diagnostic gold standard (Tate et al., 2018).

Despite these characteristic immunopathological findings, the diagnosis of CBDC remains challenging because of its rarity and its considerable clinical overlap with other pediatric blistering disorders, including bullous pemphigoid, dermatitis herpetiformis, epidermolysis bullosa acquisita, mucous membrane pemphigoid, erythema multiforme, and infectious bullous diseases (Pradhan et al., 2022). Furthermore, access to DIF is limited in many healthcare settings, particularly in resource-constrained environments, making diagnosis heavily dependent on careful clinicopathological correlation and systematic exclusion of differential diagnoses. Consequently, misdiagnosis or delayed diagnosis is not uncommon and may result in inappropriate management.

This case is noteworthy because it highlights the diagnostic challenges encountered in a child presenting with generalized blistering lesions that closely resembled several autoimmune blistering disorders. The report emphasizes a systematic approach to narrowing the differential diagnosis through comprehensive clinical assessment, histopathological evaluation, and clinicopathological correlation in the absence of immediate immunopathological confirmation. By presenting this case, we aim to improve clinicians' awareness of CBDC, facilitate its early recognition, and provide practical insights into distinguishing CBDC from other pediatric blistering diseases to enable timely and appropriate management

METHOD

This study was conducted as a case report describing the clinical presentation, diagnostic evaluation, management, and follow-up of a pediatric patient diagnosed with Chronic Bullous Disease of Childhood (CBDC). Clinical data were collected from the patient's medical records at Dr. Sitanala Hospital, Tangerang, including medical history, physical examination, laboratory investigations, histopathological findings, treatment, and clinical outcomes. The diagnosis was established based on clinicopathological correlation after systematic exclusion of other autoimmune and infectious blistering disorders. Owing to limited institutional resources, direct immunofluorescence was not performed. Written informed consent for publication of the case details and clinical photographs was obtained from the patient's parent or legal guardian

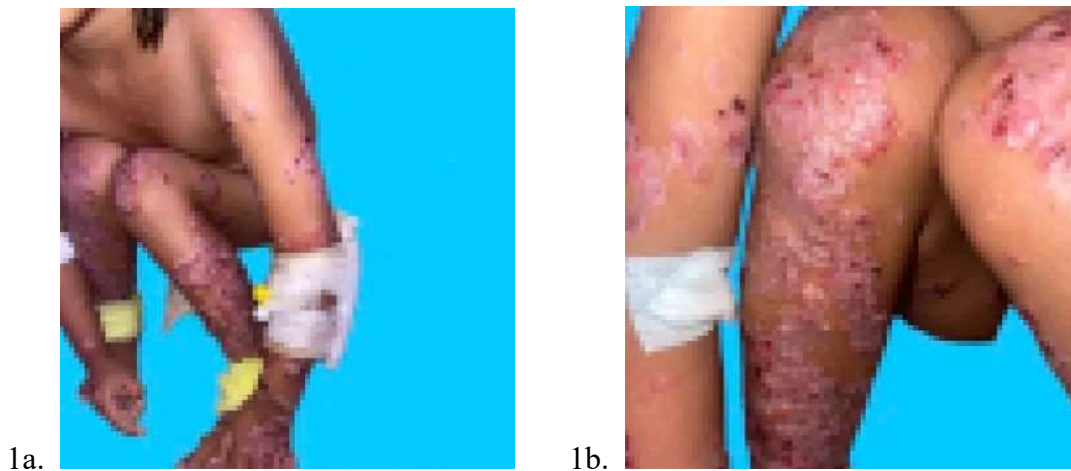
RESULT

A 4-year-old female pediatric patient presented with skin lesions on both lower extremities, upper extremities, and the forehead, characterized by the appearance of blisters for one month prior to hospital admission. Initially, the skin lesions appeared as erythematous macules on the forehead and lower extremities; however, they gradually became more widespread, and the erythematous macules progressed into vesiculobullous lesions. Some of the blisters ruptured, releasing clear fluid. The lesions were accompanied by pruritus in the affected areas. The patient also experienced fever since the onset of the rash. The patient's immunization status was incomplete. On physical examination, the patient appeared to be in good general condition, with vital signs within normal limits. Anthropometric assessment using the WHO growth charts revealed severe malnutrition, with a body weight of 11 kg and a height of 101 cm (Z-score < -3).

Dermatological examination of both upper and lower extremities revealed multiple tense bullae on an erythematous base, lenticular in size, well-demarcated, with some lesions forming a “cluster of jewels” pattern. Several bullae had ruptured, resulting in annular, dark crusts accompanied by

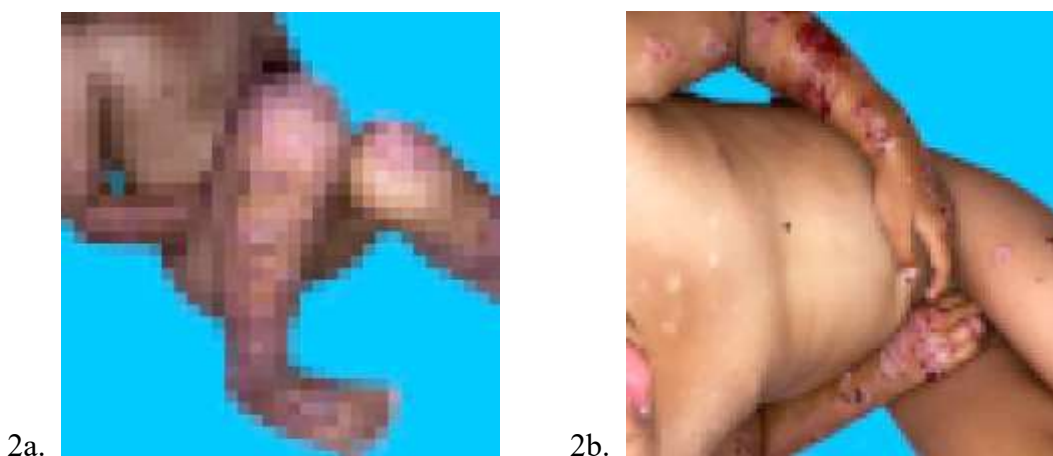
erosions (Figures 1a and 1b). On the face, multiple lenticular post-inflammatory hypopigmented macules were observed.

Laboratory investigations showed leukocytosis ($23.14 \times 10^3/\mu\text{L}$) and thrombocytosis ($665 \times 10^3/\mu\text{L}$). The initial diagnosis in this case was bullous impetigo in a severely malnourished patient. Treatment included intravenous ampicillin–sulbactam at a dose of 275 mg four times daily for three days, oral paracetamol 120 mg four times daily as needed for fever, and oral cetirizine 5 mg once daily. Aspiration of the bullae was performed, followed by application of rivanol wet dressings twice daily for one hour and topical mupirocin cream applied twice daily.



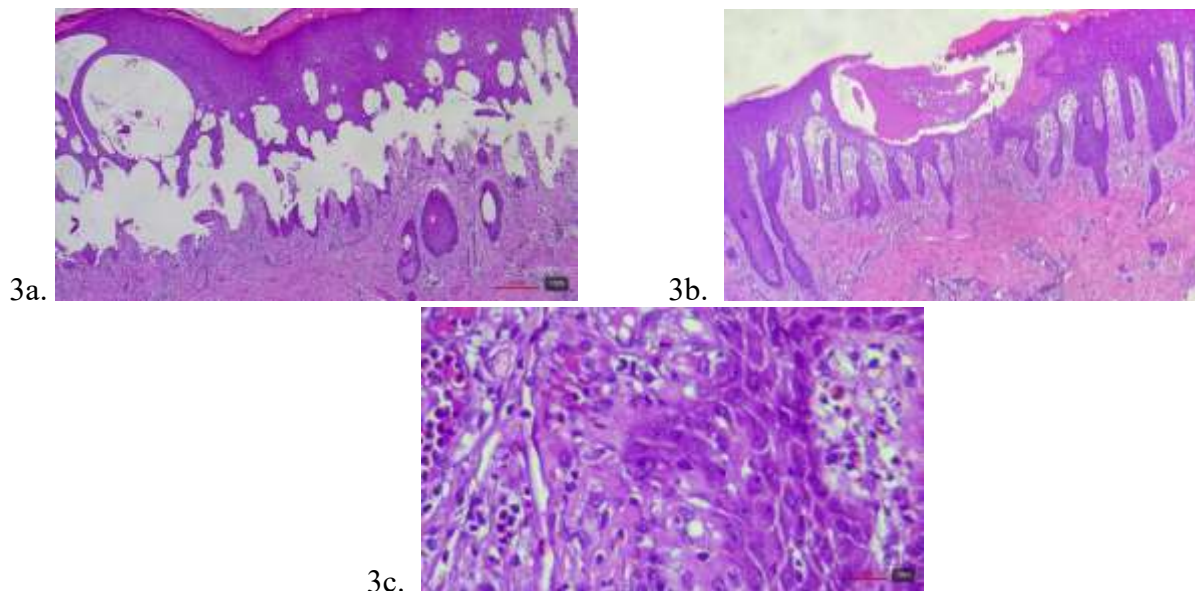
Figures 1a and 1b. (Day 3 of treatment) Multiple tense bullae with an erythematous base were observed on both upper and lower extremities. The lesions were lenticular in size with well-defined borders; some formed a cluster of jewels pattern, while others had ruptured, resulting in annular dark crusts accompanied by erosions.

During hospitalization, new bullae continued to appear until day 7 of treatment (Figures 2a and 2b). Leukocytosis improved to $15.99 \times 10^3/\mu\text{L}$, and a skin biopsy was performed on day 8 of hospitalization. The patient was discharged for outpatient follow-up with oral methylprednisolone 8 mg once daily, oral cefadroxil 150 mg twice daily, and topical gentamicin cream applied twice daily. The patient was advised to apply baby lotion three times daily, maintain personal hygiene, and bathe twice daily using soap.



Figures 2a and 2b. (Day 7 of treatment) Newly developed tense bullae were observed.

Histopathological examination revealed the presence of subepidermal bullae (Figure 3a) as well as intraepidermal bullae (Figure 3b), containing inflammatory cell infiltrates composed of neutrophils and eosinophils (Figure 3c). These findings may be observed in linear IgA dermatosis (CBDC) as well as other chronic bullous diseases, including bullous pemphigoid, dermatitis herpetiformis, epidermolysis bullosa acquisita (EBA), and mucous membrane pemphigoid. The pathologist recommended direct immunofluorescence examination to confirm the diagnosis; however, due to limited facilities, this test could not be performed.



Figures 3a, 3b, and 3c. Histopathological findings show subepidermal and intraepidermal bullae containing inflammatory cell infiltrates composed of neutrophils and eosinophils.

Based on clinical and histopathological findings, the patient was started on dapsone 20 mg once daily, with methylprednisolone 4 mg once daily continued. After two weeks, marked improvement of skin lesions was observed. Examination of the lower extremities revealed hypopigmented and hyperpigmented macules, some forming well-demarcated plaques with scarring, while multiple discrete tense bullae with crusts persisted (Figures 4a and 4b). The parents reported recurrence of bullae when therapy was discontinued. Dapsone was increased to 24 mg once daily, and methylprednisolone 4 mg was administered every other day, with gradual tapering until discontinuation.



Figures 4a and 4b. (After 2-weeks follow-up) On the lower extremities, hypopigmented and hyperpigmented macules were observed, some forming well-demarcated plaques with scarring. Multiple discrete tense bullae with overlying crusts were present on some lesions.

Table 1.
Differential Diagnosis of Chronic Bullous Disease of Childhood and the Clinical Findings
Supporting Diagnostic Exclusion in the Present Case

Differential diagnosis	Key clinical features	Findings in our patient	Reason excluded
Bullous impetigo	Superficial flaccid bullae, honey-colored crusts, responds to antibiotics ³	Progressive tense bullae despite antibiotics	Poor therapeutic response and compatible histopathology favored CBDC
DH	Herpetiform vesicles, gluten-sensitive enteropathy ^{2,3,6}	No herpetiform lesions or papillary microabscesses	Clinical and histopathological findings inconsistent
EBA	Trauma-prone sites, scarring, milia ^{2,3,6}	None present	Clinical presentation not compatible
BP	Elderly patients, flexural bullae ^{2,3}	Four-year-old child with extremity lesions	Age and clinicopathological findings inconsistent
MMP	Predominant mucosal involvement with scarring ^{2,3}	No mucosal lesions	Clinical presentation inconsistent

Note: Adapted from Fitzpatrick's Dermatology (Wolff et al., 2019; Pradhan et al., (2022); Sulistianingrum et al., (2023)).

Abbreviations: CBDC, Chronic Bullous Disease of Childhood; DH, dermatitis herpetiformis; EBA, epidermolysis bullosa acquisita; BP, bullous pemphigoid; MMP, mucous membrane pemphigoid; DIF, direct immunofluorescence.

DISCUSSION

Chronic Bullous Disease of Childhood (CBDC) is an uncommon autoimmune blistering disorder in children, and its diagnosis remains challenging because of its considerable clinical overlap with infectious and other autoimmune blistering diseases. In the present case, the patient was initially diagnosed with bullous impetigo because of generalized bullous lesions with ruptured erosions and crust formation. This initial impression is understandable, as bullous impetigo is considerably more common than CBDC in children and may present with flaccid bullae and superficial erosions. Similar diagnostic challenges have been reported in previous case reports. Goccev (2010) described a 3-year-old boy with a two-week history of widespread pruritic blistering eruptions that was initially misdiagnosed as bullous impetigo. Despite treatment with systemic and topical antibiotics together with antihistamines, the lesions continued to progress, ultimately leading to the diagnosis of CBDC. Anansiripun et al (2018) reported a 1-year-old boy presenting with generalized bullae and annular erythematous erosions involving the face, trunk, back, extremities, and perianal region, who was initially treated for bullous impetigo with intravenous cloxacillin and wet dressings. However, no clinical improvement was observed after three days of treatment, and subsequent skin biopsy revealed subepidermal blister formation consistent with CBDC. Similarly, our patient failed to improve with the initial management for bullous impetigo, prompting further investigation. The chronic disease course, progressive development of new lesions despite treatment, and the characteristic annular arrangement of tense bullae ("cluster of jewels") prompted reconsideration of the diagnosis. Collectively, these cases highlight that failure to respond to appropriate antimicrobial therapy should prompt clinicians to reconsider the diagnosis and evaluate for autoimmune blistering diseases such as CBDC, particularly when the clinical morphology and disease course are atypical for bullous impetigo.

The clinical manifestations observed in our patient were largely consistent with the reported spectrum of CBDC, including tense bullae on an erythematous base, pruritus, and the characteristic "cluster of jewels" configuration. Nevertheless, unlike the classic distribution involving the perioral and perineal regions, our patient predominantly exhibited lesions on the forehead and extremities. Previous case reports have demonstrated variability in the distribution of CBDC lesions. Varo et al (2017) reported that lesions predominantly involved the genital and buttock regions, although they also occurred on the trunk, extremities, and face. In contrast, Yadav et al (2025) described

symmetrical bullous lesions involving the face, scalp, and both the upper and lower extremities. Similarly, our patient presented with lesions predominantly affecting the forehead and extremities, highlighting the heterogeneous clinical distribution of CBDC beyond its classic predilection sites. Therefore, clinicians should maintain a high index of suspicion for CBDC even when lesions occur outside the classic predilection sites, particularly when the characteristic morphology is present.

Histopathological examination demonstrated subepidermal and intraepidermal blister formation accompanied by neutrophilic and eosinophilic inflammatory infiltrates, findings that supported the diagnosis of an autoimmune subepidermal blistering disease. Although direct immunofluorescence (DIF) remains the gold standard for confirming CBDC by demonstrating linear IgA deposition along the basement membrane zone, this investigation could not be performed because of limited institutional resources. The diagnostic challenges encountered in our case are comparable to those reported in other resource-limited settings. Wright and Rein (2025), in a case report from Central Africa, established the diagnosis of CBDC based on the characteristic clinical morphology, disease course, and favorable response to dapsone and corticosteroid therapy, as skin biopsy, direct immunofluorescence (DIF), and serological testing were unavailable. Similarly, Varo et al (2017), in a case report from southern Mozambique, emphasized that the diagnosis of CBDC remained primarily clinical because of limited diagnostic resources and required careful exclusion of other blistering disorders, including bullous pemphigoid, dermatitis herpetiformis, and erythema multiforme. Comparable challenges were also described by Mellyanawati et al (2021) reported a suspected case of CBDC in a 5-month-old infant in whom definitive diagnosis could not be established because direct immunofluorescence was unavailable and the family declined skin biopsy due to financial constraints. These reports, together with our case, highlight that the diagnosis of CBDC in resource-constrained settings often relies on careful clinical assessment, available histopathological findings when obtainable, and systematic exclusion of differential diagnoses. Our case differs from that of Wright and Rein and Mellyanawati et al. in that histopathological examination could be performed, providing additional diagnostic support despite the absence of immunopathological confirmation. Collectively, these cases emphasize that a structured clinicopathological approach remains essential for establishing a reliable diagnosis when direct immunofluorescence cannot be performed.

The principal diagnostic challenge in this case was distinguishing CBDC from other autoimmune blistering diseases with overlapping clinical and histopathological features. Bullous Impetigo, Dermatitis Herpetiformis (DH), Epidermolysis Bullosa Acquisita (EBA), Bullous Pemphigoid (BP), and Mucous Membrane Pemphigoid (MMP) were all considered during the diagnostic evaluation. However, several features favored CBDC, including the patient's age, the characteristic annular arrangement of bullae, the predominance of neutrophilic inflammation on histopathology, the absence of significant mucosal involvement, and the lack of clinical features suggestive of the alternative diagnoses. Rather than relying on a single diagnostic feature, this case highlights the importance of integrating clinical presentation, histopathological findings, disease evolution, and treatment response to achieve the most likely diagnosis.

Another important observation was the patient's rapid improvement following dapsone therapy. Dapsone is considered the first-line treatment for CBDC because of its potent inhibitory effects on neutrophil-mediated inflammation (Spalek et al., 2024). In our patient, new blister formation ceased and the skin lesions improved markedly within two weeks of treatment initiation. A similar therapeutic response has been reported in several published cases. Yadav et al (2025) described a 5-year-old boy with direct immunofluorescence-confirmed CBDC who demonstrated marked clinical improvement within five days after the initiation of oral dapsone (0.5 mg/kg/day), following initial treatment with oral prednisolone while awaiting glucose-6-phosphate dehydrogenase (G6PD) testing. Likewise, Anansiripun et al. (2018) reported significant clinical improvement after dapsone

was initiated once a normal G6PD level had been confirmed. Similarly, Wright & Rein, (2025), described sustained disease

control with dapsone (1 mg/kg/day), which enabled successful tapering of prednisone, with the patient remaining lesion-free at follow-up without treatment-related adverse effects. Although the time to clinical improvement varied among these reports, the consistently favorable response to dapsone further supports its role as the first-line treatment for CBDC. In our patient, the rapid clinical improvement after dapsone therapy further strengthened the working diagnosis of CBDC, although therapeutic response alone should not be considered diagnostic.

The coexistence of severe malnutrition in this patient deserves consideration. Although malnutrition has not been established as a direct cause of CBDC, impaired nutritional status may alter immune regulation and increase susceptibility to infections, several of which have been proposed as potential triggers for autoimmune blistering diseases (Patsatsi, 2018). Nevertheless, the relationship between malnutrition and CBDC remains speculative, and it is more appropriate to regard severe malnutrition as a concomitant condition rather than a causal factor (Jones et al., 2014).

The main limitation of this report is the absence of direct immunofluorescence, which prevented definitive immunopathological confirmation of the diagnosis. Nevertheless, this case demonstrates that, in settings where immunofluorescence is unavailable, a systematic diagnostic approach incorporating clinical morphology, histopathological findings, exclusion of differential diagnoses, and therapeutic response can provide sufficient diagnostic confidence to guide appropriate management. This experience underscores the importance of careful clinicopathological correlation in resource-limited settings and contributes to the limited literature describing the diagnosis of CBDC without immediate access to immunofluorescence.

CONCLUSION

Chronic bullous disease of childhood is a rare autoimmune blistering disorder that remains diagnostically challenging, particularly in resource-limited settings where direct immunofluorescence is unavailable. This case highlights the importance of integrating clinical presentation, histopathological findings, systematic exclusion of differential diagnoses, and therapeutic response to establish a reliable diagnosis. A structured clinicopathological approach can facilitate timely recognition and appropriate management of CBDC, even in the absence of confirmatory immunopathological testing.

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