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# Generalized Bullous Fixed-Drug Eruption in a 15-Year-Old Child With Becker Muscular Dystrophy and Epilepsy

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## ABSTRACT

**Introduction:** Generalized bullous fixed drug eruption (GBFDE) is a potentially life-threatening condition, typically triggered by a range of medications. Its incidence in the pediatric population is exceedingly low.

**Case summary:** We present a 14-year-old boy with a complex medical history, including Becker muscular dystrophy and epilepsy, who experienced recurrent episodes of GBFDE over the past 2 years. The episodes culminated in a severe presentation resembling Stevens-Johnson syndrome. Detailed evaluation identified ibuprofen as the culprit drug. The patient was treated with prednisone, commencing at a dose of 0.5 mg/kg and tapered over a 2-week period, which resulted in a significant regression of lesions.

**Conclusion:** In cases with multiple potential drug triggers, it is essential to identify common drug classes associated with GBFDE and monitor the onset of symptoms post-ingestion. Our findings support the effective and safe use of prednisone, highlighting a generally positive prognosis for pediatric patients with this condition.

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## INTRODUCTION

Fixed drug eruption (FDE) is a common type of cutaneous adverse drug reaction that typically presents with the recurrence of single or multiple skin lesions at identical anatomical sites upon re-exposure to the offending agent. The most common triggers include antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, and anticonvulsants.[1,2] Lesions most commonly appear within 48 hours of drug administration and are characterized by erythematous to violaceous, well-defined plaques featuring a distinctive dusky-grey center, often resulting in post-inflammatory hyperpigmentation.[1,2] In some cases, patients can develop blisters, and, rarely, extensive skin detachment may occur, leading to a generalized bullous fixed drug eruption (GBFDE). GBFDE may be diagnosed when at least 10% of the body surface area is involved.[1,3] GBFDE is classified as a severe cutaneous adverse reaction (SCAR), with a potential for fatal outcomes.[4] Data and clinical experience regarding GBFDE are limited, particularly in the pediatric population.

## CASE SUMMARY

A 14-year-old boy exhibited a 48-hour history of rapid-onset skin lesions. The patient presented with the medical history of Becker muscular dystrophy, diagnosed at the age of 5 years, then he developed focal epilepsy at the age of 9 years, and he had mild intellectual disability.

On admission, dusky-erythematous macules were present on his face, trunk, and extremities, centered by flaccid bullae, and some had targetoid features (Figure 1A). A larger lesion with an atrophic center was present in his mandibular region (Figure 2A). There was no mucosal involvement, and the patient was hemodynamically stable. Laboratory investigations revealed a mildly elevated erythrocyte sedimentation rate (32 mm/h).

**FIGURE 1.** (A) Numerous erythematous macules, some of them having targetoid appearance, centered with flaccid bullae. (B) Residual hyperpigmented macules were present 6 months after the initial presentation.

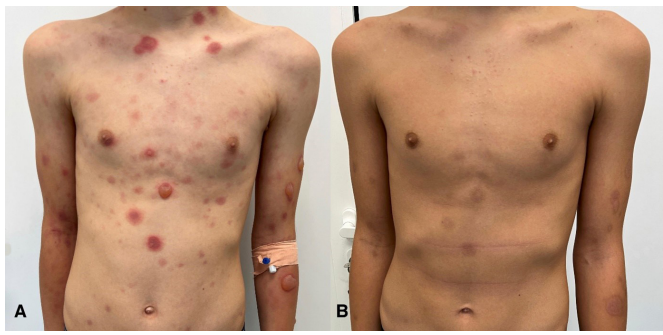


**FIGURE 2.** (A) Location of initial lesion with central atrophy due to the multiple recurrences of BFDE in this area. (B) Residual atrophy in the mandibular region at month 6 follow-up.

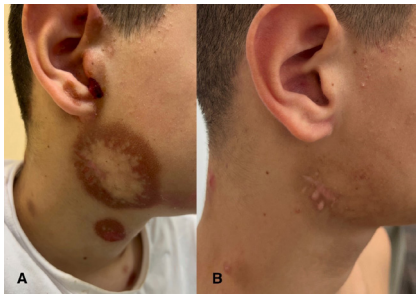
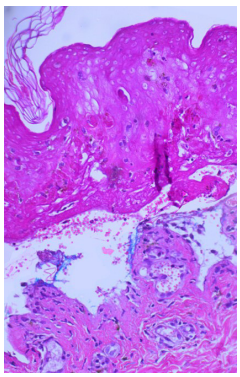



**FIGURE 3.** Histopathologic findings revealed full-thickness epidermal necrosis, subepidermal blister, mild lymphocytic infiltrate, and melanophages in the papillary dermis.



The patient's mother reported a prior history of similar cutaneous eruptions over the last 2 years, primarily affecting his mandibular area, neck, and upper trunk. Lesions resolved with residual hyperpigmentation and progressively increased in severity with each episode. Due to the suspected FDE, his neurologist attempted to modify the patient's anticonvulsant regimen, suspecting the connection to these medications. However, despite multiple adjustments, including carbamazepine, levetiracetam, clobazam, and valproic acid, the eruption of skin lesions was recurring.

Detailed history revealed that ibuprofen had been taken shortly before the episodes. The patient correlated each recurrence with intense physical activity, subsequent myalgia, and ibuprofen use, followed by a short latency until skin lesions appeared. A biopsy confirmed bullous FDE: full-thickness epidermal necrosis with sparse lymphocytic infiltration and melanophages (Figure 3).

Treatment with prednisone at 0.5 mg/kg was commenced. No new lesions developed, and the prednisone dose was gradually tapered, concluding at 0.2 mg/kg after 14 days, leaving residual hyperpigmented macules. On the follow-up visit, 6 months later, the patient did not report the occurrence of similar episodes (Figure 1B, Figure 2B). Patch test with ibuprofen (5% and 10% in petrolatum) was performed on the residual hyperpigmented lesion on the right mandibular area, with the normal skin as a control site. Skin reactions were evaluated on days 2, 3, and 7. Positive reaction (grade 2) to ibuprofen 10% was detected on days 3 and 7.

## DISCUSSION

Approximately 2.5% of children develop various adverse cutaneous drug reactions (ACDR), of which FDE accounts for about 11%. GBFDE is exceedingly rare in children.[5] Up to now, only 25 pediatric cases of GBFDE have been reported in the literature.[6]

Fixed drug eruption is mediated by CD8+ memory T cells that, upon re-exposure to the causative medication, activate and induce epidermal necrosis. After the resolution of lesions, these cells remain quiescent at the dermal-epidermal junction. A refractory period may occur, complicating drug identification.[7,8] In our patient, distinguishing the culprit drug, either daily clobazam, levetiracetam, valproic acid, and lamotrigine, or intermittent ibuprofen, was challenging, with the main focus leaning toward the patient's epilepsy and anticonvulsants rather than the exact timeline for other drugs that the patient consumed. In addition, it is well-known that macular FDE can evolve to bullous forms, particularly with continued/repetitive drug exposure, which was the case in our patient.[1]

Studies indicate antibiotics as the primary cause of FDE, with trimethoprim/sulfamethoxazole implicated in 73% of cases in a large Pakistani study.[9] NSAIDs were frequently associated in Tunisian and French studies.[10,11] Anticonvulsants, like phenobarbital and carbamazepine, were less frequently reported. In a systematic review of GBFDE in the pediatric population, the most frequently associated drugs were antibiotics, followed by acetaminophen, NSAIDs, and anticonvulsants.[6] This infrequency further complicated the culprit drug identification in our case, relying mostly on the patient's history.

The oral challenge test is the most sensitive method for confirming the causative drug, but it is contraindicated due to GBFDE risk.[12] Patch testing is a safer, less sensitive alternative, recommended at least 6 weeks post-resolution of the eruption, with positive reactions observed predominantly in NSAIDs in adults and anticonvulsants in the pediatric population.[6,13,14] Reaction to ibuprofen was confirmed by the positive patch test in our patient.

Management of GBFDE necessitates drug cessation and supportive care, including oral antihistamines, topical antiseptics, and systemic corticosteroids in severe cases.[1] Twelve of the 25 pediatric GBFDE patients needed administration of

oral corticosteroids.[6] Our patient responded rapidly to a 2-week tapering regimen of prednisone. Current literature lacks clinical trials comparing the efficacy of supportive care alone with corticosteroids or cyclosporine for GBFDE. Additionally, no fatalities were reported in the pediatric cases of GBFDE, further corroborated by the present case.[4]

This case of a very rare and severe clinical presentation in the pediatric population highlights the significance of time-based association with the suspected drug and, therefore, the necessity for a detailed medication history in a patient with multi-drug therapy and appreciation of the most probable drugs that might induce FDE. These measures could prevent unnecessary therapeutic modifications in complex patients with multiple comorbidities. We provide additional evidence that short courses of low-dose systemic corticosteroid therapy can prove efficient in the rapid resolution of skin lesions in GBFDE, without side-effect induction. Furthermore, we underscore the good prognostic outcome in pediatric patients with GFBDE, even in patients with multiple comorbidities.

## DISCLOSURES

None of the authors has any conflicts of interest to disclose.

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