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Case Report

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Paracetamol Induced Fixed Drug Eruption in a Child

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Abstract

Paracetamol, also known as acetaminophen, is widely regarded as safe by both healthcare professionals and the public. However, it is important to recognise that all medications have the potential to cause adverse reactions. Skin reactions are among the most common types of adverse drug reactions, with a hospitalisation rate of 2–3%. Non-steroidal anti-inflammatory drugs, antibiotics, and antiepileptics are known to cause drug eruptions at rates ranging from 1–5%. We report an interesting case involving an 11-year-old child who developed a fixed drug eruption a few hours after ingesting paracetamol syrup.

Keywords: Paracetamol, Acetaminophen, Fixed drug eruption, Adverse reaction

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INTRODUCTION

Fixed drug eruptions (FDE) are a specific type of adverse drug reaction (ADR) that occur in individuals who have previously been sensitised to a particular medication.[1] Paracetamol, also known as acetaminophen, is a widely used analgesic and antipyretic, available over the counter in various formulations.[2] Although adverse reactions at therapeutic doses are uncommon, skin-related side effects can range from mild itching and rashes to severe conditions such as Stevens-Johnson syndrome and toxic epidermal necrolysis.[3]

FDEs associated with paracetamol are relatively uncommon compared to those caused by other medications, such as non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotics—particularly sulfonamides and tetracyclines. These reactions are more frequently observed in children and adolescents and are relatively rare in the elderly. In Brunei Darussalam, there have been no previously documented cases of paracetamol-induced FDE in children. This case report describes an 11-year-old boy who developed FDE affecting the perioral region, eyelids, and palms following intermittent exposure to paracetamol. Symptomatic treatment was administered, and the lesions gradually resolved over time.

CASE REPORT

An 11-year-old previously healthy male presented for evaluation due to noticeable lip swelling and discolouration involving the eyelids and perioral region. The lesions ranged in appearance from erythematous to hyperpigmented and extended to both lips as well as the left palm. These symptoms had persisted for approximately five days.

One week prior to presentation, the patient had developed a fever and presented to the outpatient clinic and was prescribed paracetamol by the general practitioner. He denied taking any other medications. Within 24 hours of taking paracetamol, he experienced swelling of the lips and the development of reddish-brown lesions around the mouth, which subsequently spread to the upper eyelids and the left palm. He also reported oral soreness and the formation of blisters on his tongue, but denied any burning sensations or pruritus. There was no involvement of the genital region.

Upon further assessment, the patient's parents reported the patients had two previous episodes involving similar skin locations. One month earlier, the patient developed mild lip swelling approximately 30 minutes after ingesting paracetamol for a headache. The swelling resolved spontaneously by the following morning, although residual post-inflammatory hyperpigmentation remained. A year prior, following oral paracetamol administration for fever, he experienced swollen lips, along with blisters and ulcers in the mouth and on the tongue within a few hours. This episode was initially misdiagnosed and treated as a herpes simplex infection; however, serological tests for herpes simplex virus (IgG and IgM) were negative. Interestingly, the sites of skin involvement was similar to the latter episodes. There was no significant family history of drug allergies.

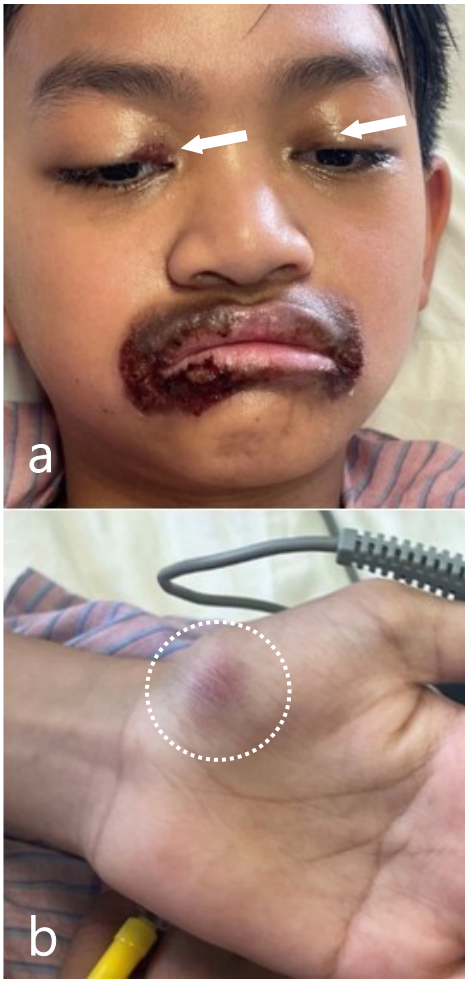

Figure 1: a) Fixed drug eruption showing lips swelling, dusky erythematous crusted patches on perioral skin, and hyperpigmented patches on eyelids (arrows), and b) dusky erythematous crusted patches on the left hypothenar area of the palm (dotted circle).

On clinical examination, the patient had well-defined hyperpigmented macules with erythematous borders in the perioral region. Crusted patches were present at the corners of the mouth, and vesicles were observed on the tip of the tongue (Figure 1a). Reddish-brown oval patches were noted on both eyelids (**Figure 1a**) and the left hypothenar region of the palm (**Figure 1b**). The child was in stable condition with normal vital signs. Laboratory investigations, including complete blood count and biochemical profile, revealed no significant abnormalities.

Based on the history of recurrent lesions following paracetamol ingestion and the clinical presentation, a diagnosis of FDE due to paracetamol was established. The treatment regimen included intravenous fluids, oral antihistamines (chlorpheniramine syrup 2 mg twice daily for five days), topical steroid cream

hydrocortisone 1% twice daily applications for two weeks), a moisturiser 50 50 paraffin ointment twice daily applications for wo weeks), and mouth gargles (chlorhexidine mouthwash for two weeks). Paracetamol administration was discontinued, and the parent was advised to avoid paracetamol for any future febrile episodes or other uses.

It is important to note that a skin biopsy was not performed, as the parents did not provide consent. Additionally, an oral provocation test was not conducted due to the limited availability of the test at our facility.

After 10 days of treatment, the erythematous and scabby patches in the perioral area had resolved. The ulcers on the tongue, lip swelling, and oral soreness had also subsided (**Figure 2a**). The reddish-brown patches affecting the hand had evolved into residual hyperpigmentation (**Figure 2b**).

DISCUSSION

FDE is a relatively common reaction that can occur with more than 100 different medications.[4] It is characterised by the recurrence of skin lesions at the same site following exposure to a specific drug.[4] FDEs may account for approximately 16-21% of all cutaneous drug eruptions.[2] These eruptions can occur in individuals of any age and affect both genders equally, representing between 5% and 22% of cutaneous drug reactions in children.[5]

A study by Fathallah et al. reported that paracetamol induced FDE accounted for less than 1.5% of all documented cases.[6] These eruptions are particularly prevalent in children, accounting for 14% to 22% of cutaneous drug reactions.[7] Raipurkar et al reported a case of bullous FDE caused by paracetamol syrup in a child as young as two years old.[2] To date, there have been no report of paracetamol leading to site-specific FDE in the literature in Brunei Darussalam.

In FDE lesions, intraepidermal CD8+ T cells cause epidermal damage upon re-exposure to the triggering drug.[8] Initially inactive, these T cells become activated, releasing interferon-gamma and cytotoxic granules, with mast cells enhancing this process through tumour necrosis factor-alpha production.[8] Other immune cells contribute to tissue damage in advanced lesions, while regulatory T cells (Tregs) help modulate the response.[8] Most activated T cells undergo apoptosis, but some persist as memory cells due to interleukin-15 signals from basal keratinocytes.[8]

FDEs are classified as type IV hypersensitivity reactions.[9] They typically appear within one week after the initial drug exposure, although they can also develop within minutes upon re-exposure.[9] It is essential to consider the possibility of a drug-induced reaction if a patient suddenly develops a symmetrical cutaneous eruption while taking a medication.

Clinically, FDEs are characterised by well-defined, round or oval erythematous patches, plaques, or less frequently, bullae that may feature a dusky-grey centre.[9] The drugs most commonly associated with FDEs include acetaminophen, NSAIDs, anticonvulsants, and antibiotics.[9] The lesions frequently appear on the lips, anogenital area, and other sites of previous trauma.[9]

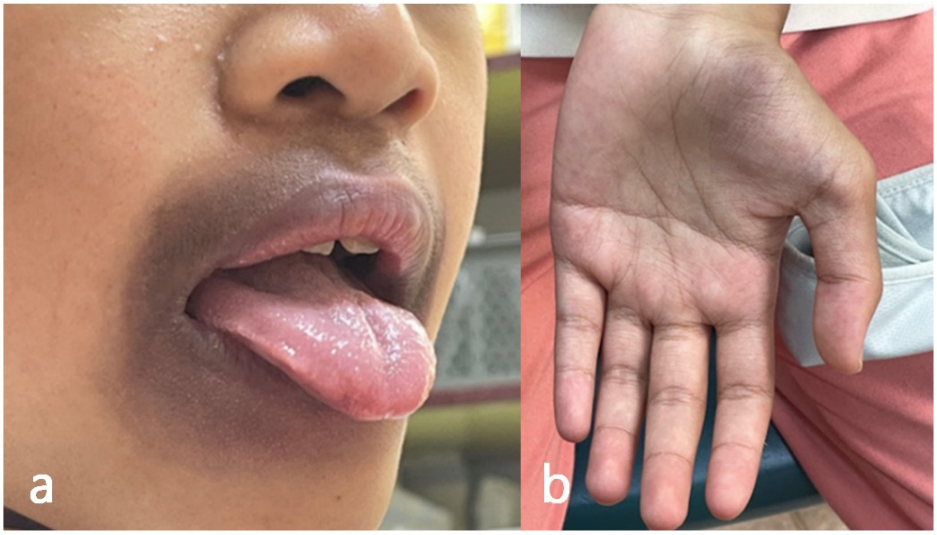

Figure 2: After 10 days of treatment, a) residual hyperpigmentation of fixed drug eruption of the perioral area and, b) residual hyperpigmentation on the left hypothenar area of the palm.

Commonly implicated medications include [9]:

1 - Antibiotics: Tetracyclines, penicillin, trimethoprim-sulfamethoxazole, metronidazole, ciprofloxacin, clarithromycin.

2 - NSAIDs: Ibuprofen, naproxen, etoricoxib.

3 - Anticonvulsants: Barbiturates, phenytoin, carbamazepine.

4 - Others: Cetirizine, omeprazole, pseudoephedrine, sulphasalazine, vaccinations.

5 - Food additives: Tartrazine, Quinoline Yellow.

The diagnosis of drug reactions is primarily clinical; however, confirming the specific drug involved may require skin biopsies, patch tests, or lymphocyte transformation tests.[9] Oral challenge testing is generally discouraged due to the associated risks, making patch testing the preferred method.[9]

The primary treatment for FDEs involves identifying and eliminating the causative agent.[9] This process includes reviewing the patient's medication history, any chemical exposures, and previous episodes.[9] Discontinuing the offending drug usually results in the resolution of lesions within a few days, although post-inflammatory hyperpigmentation may persist.[10] In our case report, the parents decided against drug challenges, and limited resources hindered patch testing, leading to a clinical diagnosis. The boy presented with FDE, exhibiting swelling and redness around the mouth. Following the discontinuation of paracetamol, his symptoms improved significantly within a week, although some residual hyperpigmentation persisted.

Since FDEs cannot be reversed and pigmentation may persist indefinitely, prevention is crucial. This can be accomplished through increased awareness of common causative drugs and the likelihood of recurrence with the same or similar medications. When possible, using alternatives is advisable.[4] Patients and their families should be advised to avoid the offending drug and any chemically related medications and be provided with a written list of both the generic and brand names of these drugs.

CONCLUSION

This case underscores the importance of recognising FDE as a potential adverse reaction to paracetamol in children. It serves as a reminder that even common medications can cause significant side effects. Healthcare providers should be diligent in educating patients and guardians on how to recognise and report such reactions. Notably, this is the first documented case of FDE induced by paracetamol in children in Brunei Darussalam.

Abbreviations

FDE	Fixed drug eruption
ADR	Adverse drug reaction
NSAIDs	Non-steroidal anti-inflammatory drugs

Declarations

Conflict of interests

The authors declare no conflict of interests.

Consent

Consent has been obtained from patient's parents for publication.

Acknowledgement

None.

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