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Case Report

Not uncommon but often under-recognized: case report of fixed drug eruption in a child

Kaysha-Lin Lexminarayana*, Ming Lee Chin, Su Yuen Ng

Department of Pediatrics, Raja Permaisuri Bainun Hospital, Ipoh, Malaysia

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***Correspondence:**
Dr. Kaysha-Lin Lexminarayana,
E-mail: kaysha.lin@gmail.com

ABSTRACT

When re-exposed to the offending drug, fixed drug eruptions (FDEs), a distinctive type of mucocutaneous drug reaction, typically recur in the same places. Often, these eruptions are benign in nature, however the recurrence and appearance of these lesions may be a cause of worry to patients, and in the pediatric population, to their caretakers as well. Lack of awareness among clinicians coupled with suboptimal history taking pertaining to drug usage are the key factors leading to delayed and under-diagnosis of FDEs. We discuss the case of a child whose fixed drug eruption was misdiagnosed as an insect bite for more than a year. This led to parental anxiety, as well as trial of multiple avenues of treatment to no avail. This article aims to raise awareness of the importance of prompt recognition of FDEs, as identification and discontinuation of the offending drug will alleviate the eruptions and prevent recurrence of the condition.

Keywords: Fixed drug eruption, Pediatric, Adverse drug reaction

INTRODUCTION

Fixed drug eruptions (FDEs), which have an array of differential diagnoses, are a frequent diagnostic challenge for clinicians.[1] Because they commonly occur in the same location as prior reactions, a history of previous lesions in the same area should prompt the consideration of FDE. Despite the benign nature of these lesions, pruritus, pain, and appearance may result in distress.[2]

We discussed the case of a child who had his fixed drug eruption mistaken for an insect bite for over a year. This caused his caregivers a lot of anxiety, due to the recurrent nature of the lesion. We got a review the varying presentations of FDEs, diagnosis, as well as treatment.

CASE REPORT

A two-year-old boy was referred from a local healthcare facility for hyperpigmentation over his left anterior chest wall for the past one year. When first noticed, the lesion measured 0.5 cm in diameter, and was thought to be an insect bite. It was not raised or pruritic in nature. According to the child's parents, it gradually became larger in size and darker in color.

Over the span of one year, attempts to treat the lesion with topical agents were futile. Parents self-purchased virgin coconut oil, as well as plant body oil, however these products brought no improvement despite constant application. Upon seeking medical treatment, he was diagnosed with post-inflammatory hyperpigmentation secondary to the initial insect bite. He was prescribed with daily hydrocortisone 1% cream, but it did not make a difference either. On further history, it was disclosed that the lesion would become erythematous and raised whenever he had a febrile illness. This was followed by peeling of the skin when the temperature abated. Interestingly, however, the lesion would reappear at the exact same site during each febrile illness, but with an increase in size. There was no mucosal involvement otherwise. The child was otherwise thriving, with no other systemic symptoms. He had no known prior food or drug allergies.

On examination, he appeared alert, clinically pink, and was not septic looking. His height and weight were between the 75th to 90th percentile for his age. Systemic examination was unremarkable. A well-circumscribed, circular patch was noted over his left anterior chest wall. It measured 4.5 cm in diameter, and had central hyperpigmentation surrounded by a rim of lighter shade.

It was fortunate that he visited only two health clinics whenever he was unwell, hence a detailed drug history was successfully obtained, as listed in Table 1.

Table 1: Detailed drug history.

Duration	Drug
May 2022	Oral paracetamol
	Oral dexamethasone
September 2022	Oral paracetamol
	Oral cetirizine
	Oral carbocisteine
	Oral amoxicillin-clavulanic acid
November 2022	Oral paracetamol
March 2023	Oral paracetamol
	Oral erythromycin
	Benzydamine spray
April 2023	Oral paracetamol

All drug doses were checked and confirmed to be appropriate for his weight.

Based on history and physical examination, he was diagnosed with fixed drug eruption, likely due to paracetamol. This was because paracetamol was the constant drug consumed during all febrile episodes. He was referred to a tertiary center for a dermatology consult.

Two days prior to his appointment, the child developed an upper respiratory tract infection, and was prescribed with paracetamol by a local clinic. Unsurprisingly this time, the lesion over his left anterior chest wall became raised and erythematous. Pictures taken by his parents revealed a targetoid lesion, with a central dusky red area of skin, a paler pink surrounding ring, and a bright red outermost ring. This time around, child developed a new, similar lesion over his left cheek as well. Parents were advised to immediately stop serving paracetamol.

Upon dermatology review, the lesions over the child's left anterior chest wall and left cheek were back to being hyperpigmented patches, the former 4.5 cm in diameter and the latter 1.5 cm in diameter. An allergy card for paracetamol was issued, and ibuprofen was suggested as an alternative for future febrile illnesses. Parents were not keen to proceed with patch test or oral rechallenge at that point in time.

He was reviewed in our clinic two months later. During this period, he had an episode of acute tonsillitis and was prescribed with Ibuprofen as anti-pyretic. The patches over his left anterior chest wall and left cheek no longer became erythematous after consumption of Ibuprofen. His parents were happy and relieved to finally have a diagnosis for their child.

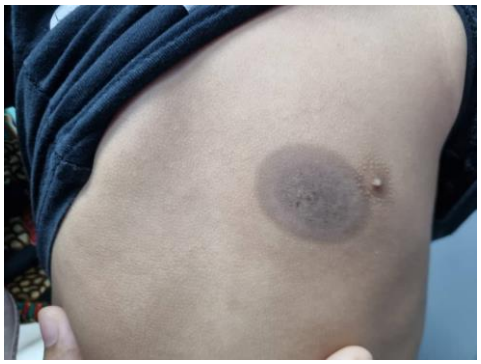

Figure 1: Well-circumscribed hyperpigmented patch measuring 4.5 cm in diameter over child's left anterior chest wall.

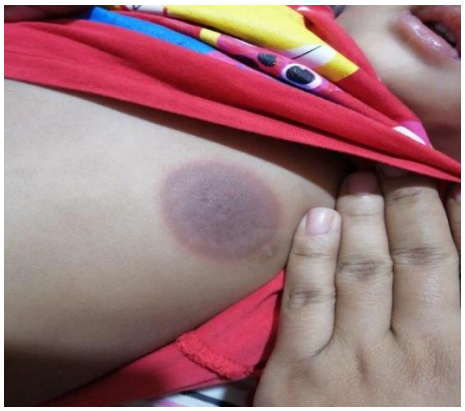

Figure 2: Raised, erythematous targetoid lesion over child's left anterior chest wall during febrile illness.

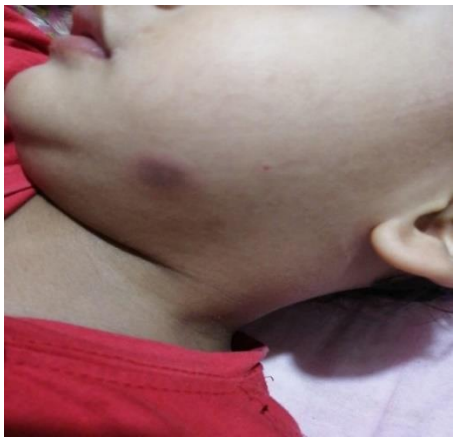

Figure 3: Similar lesion seen over child's left cheek.

DISCUSSION

FDEs are a specific type of mucocutaneous drug reaction in which lesions typically recur in the same locations upon

re-exposure to the offending drug. In the pediatric age group, FDEs account for approximately 5 to 22% of cutaneous drug reactions.[1,2] However, the actual incidence may be higher as FDEs are often underdiagnosed, frequently being mistaken for other conditions, namely insect bites and urticaria. Clinicians are often unfamiliar with this condition as there are multiple presenting variants of FDEs, coupled with the fact that FDEs are one of the less commonly occurring drug reactions.[3] FDE is a delayed type 4 hypersensitivity reaction following exposure to an offending drug. The exact pathogenic mechanisms remain unknown. However, it is postulated that intraepidermal CD8+ T cells play a key role in mediating the localized epidermal lesion that characterizes FDE. Exposure to the offending drug is thought to induce local reactivation of memory T-cell lymphocytes.[4,5]

Typically, FDE manifests in the form of well-defined, circular to oval, dark red to brown/black macules that may go on to evolve into edematous plaques with or without vesiculation or blistering. Commonly, these develop over the lips, hands, feet, genitalia, and perianal area, but may also occur anywhere on the body.[6] There is ordinarily a close temporal association with ingestion of an offending drug. Less commonly, generalized bullous FDE (GBFDE) may mimic other skin disorders such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN); but this can be differentiated by less than 2 mucous membrane involvement and absence of systemic symptoms.[7]

Upon administration of the offending drug, acute lesions conventionally appear in 30 minutes to 8 hours, but can occur up to 14 days later.[7] When the drug is discontinued, lesions generally resolve spontaneously in 7 to 10 days, leaving residual post-inflammatory hyperpigmentation. Upon re-exposure to the offending drug, lesions typically recur in the same location within 24 hours. In some instances, new lesions or a more severe generalized eruption may result.[8]

Making a diagnosis of FDE entails detailed and thorough history taking, as well as a high degree of suspicion by the clinician. The differential diagnosis of FDE includes lichen planus pigmentosa, post-inflammatory hyperpigmentation, acute urticaria, bullous pemphigoid, cellulitis, discoid lupus erythematosus, drug eruption, and dermatologic manifestations of SJS and TEN.[9] Clinicians may employ scoring systems such as the Naranjo algorithm, a questionnaire for determining the likelihood that an adverse drug reaction is actually due to the drug rather than the result of other factors.[10]

The diagnosis of FDE is made based upon typical history and lesion morphology. Provocation tests in the form of systemic testing (oral challenge) or topical testing (patch testing) are methods to further establish diagnosis.[4]

Oral provocation testing is considered the ‘gold standard’ for identifying the causative drug due to its high sensitivity and specificity. The main purpose of a rechallenge is to induce a similar eruption in a mild form, and a sub-therapeutic dose would be generally sufficient to do this.[12] Recommendations state that initiation with a sub-therapeutic dose is advisable, with a slow increase to therapeutic dosing if no reaction occurs.[12]

However, a consensus on the appropriate dose of the suspected drug sufficient to induce a mild reaction or the timing of the test after the resolution of the initial eruption has not been reached yet.[13] In a prospective series of 93 patients with FDE, oral challenge was started with one-half of the therapeutic dose; if no reaction was elicited, a full dose was given.[14] A flare-up reaction occurring within 30 min to 8 hours of the oral challenge within a resting FDE lesion is considered a positive test response.

Patch testing can be used if oral testing cannot be performed, or if the patient/caregiver is not keen for an oral challenge. However, there is no standardized method for patch testing in FDE, and it can be technically and logistically difficult. Patch testing also has limited sensitivity, whereby the positive reaction rate is only 40% .[15] Peri-lesional presence of memory T cells is exceedingly low; hence positive results would only yield when patch testing is performed on previously involved skin.

A skin biopsy may be performed when the patient has an ambiguous presentation, particularly in variants of FDE such as GBFDE or the non-pigmenting subtype.[16]

In managing FDE, it is imperative to discontinue the offending drug, following which, lesions typically resolve without treatment. There is very limited data on the efficacy of symptomatic therapies in the treatment of FDE. Current recommendations suggest the use of medium- to high-potency topical corticosteroids and systemic antihistamines to provide symptomatic relief. However, clinicians should exercise caution in using Levocetirizine and cetirizine, as these antihistamines have been reported to cause FDEs.[17]

It is important to check for Paracetamol intolerance in all children with cross-intolerance to NSAIDs because there is no other approved medication for the treatment of fever or inflammation.[18]

FDE carries an excellent prognosis; patients generally make a full recovery upon discontinuation of the offending agent.[19] Residual post-inflammatory hyperpigmentation typically fades away after a duration of several months. It is advised to practise sun protection, covering of affected areas and the use of sunscreen to expedite pigmentation resolution and prevent darkening.

CONCLUSION

It is crucial to recognize fixed drug eruptions, as recurrence may cause significant distress to the patient and caregivers, as evident in this case. A detailed drug recall, along with history of lesion appearing on the same site on

re-exposure to the specific drug, are of utmost importance. This can lead to early recognition of FDE and discontinuation of the offending medication, which is the mainstay of treatment.

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REFERENCES

1. Khaled A, Kharfi M, Ben Hamida M, El Fekih N, El Aidli S, Zeglaoui F, et al. Cutaneous adverse drug reactions in children. A series of 90 cases. La Tunisie medicale. 2012;90(1):45-50.
2. Sharma VK, Dhar S. Clinical pattern of cutaneous drug eruption among children and adolescents in north India. Pediatric dermatology. 1995;12(2):178-83.
3. Shaker G, Mehendale T, De La Rosa C. Fixed Drug Eruption: An Underrecognized Cutaneous Manifestation of a Drug Reaction in the Primary Care Setting. Cureus. 2022;14(8):e28299.
4. Shiohara T, Mizukawa Y. Fixed drug eruption: a disease mediated by self-inflicted responses of intraepidermal T cells. Eur J Dermatol. 2007;17(3):201-8.
5. Shiohara T. Fixed drug eruption: pathogenesis and diagnostic tests. Curr Opin Allergy Clin Immunol. 2009;9(4):316-21.
6. Korkij W, Soltani K. Fixed drug eruption. A brief review. Arch Dermatol. 1984;120(4):520-4.
7. Lipowicz S, Sekula P, Ingen-Housz-Oro S, Liss Y, Sassolas B, Dunant A, et al. Prognosis of generalized bullous fixed drug eruption: comparison with Stevens-Johnson syndrome and toxic epidermal necrolysis. Br J Dermatol. 2013;168(4):726-32.
8. Brahimi N, Routier E, Raison-Peyron N, Tronquoy AF, Pouget-Jasson C, Amarger S, et al. A three-year-analysis of fixed drug eruptions in hospital settings in France. Eur J Dermatol. 2010;20(4):461-4.
9. Montazer F, Jahani Amiri K, Mofarrah R, Ahmadi A, Nouripour B, Mofarrah R. A first case of fixed drug eruption due to Tamsulosin. Journal of cosmetic dermatology. 2020;19(5);1143-5.
10. Heelan K, Shear NH. Cutaneous drug reactions in children: an update. Paediatr Drugs. 2013;15(6):493-503.
11. Mahboob A, Haroon TS. Drugs causing fixed eruptions: a study of 450 cases. International journal of dermatology. 1998;37(11):833-8.
12. Lee AY. Fixed drug eruptions. Incidence, recognition, and avoidance. Am J Clin Dermatol. 2000;1(5):277-85.
13. Kidon M, Blanca-Lopez N, Gomes E, Terreehorst I, Tanno L, Ponvert C, et al. EAACI/ENDA Position Paper: Diagnosis and management of hypersensitivity reactions to non-steroidal anti-inflammatory drugs (NSAIDs) in children and adolescents. Pediatr Allergy Immunol. 2018;29(5):469-80.
14. Miah MA, Ahmed SS, Chowdhury SA, Begum F, Rahman SH. Fixed drug eruptions due to cotrimoxazole. Mymensingh Med J. 2008;17(2):S1-5.
15. McClatchy J, Yap T, Nirenberg A, Scardamaglia L. Fixed drug eruptions - the common and novel culprits since 2000. J Dtsch Dermatol Ges. 2022;20(10):1289-1302.
16. Anderson HJ, Lee JB. A Review of Fixed Drug Eruption with a Special Focus on Generalized Bullous Fixed Drug Eruption. Medicina. 2021;57:925.
17. Jhaj R, Asati DP, Chaudhary D. Fixed drug eruption due to levocetirizine. J Pharmacol Pharmacother. 2016;7(2):109-11.
18. Zambonino MA, Torres MJ, Muñoz C, Requena G, Mayorga C, Posadas T, et al. Drug provocation tests in the diagnosis of hypersensitivity reactions to non-steroidal anti-inflammatory drugs in children. Pediatr Allergy Immunol. 2013;24(2):151-9.
19. Khaled A, Kharfi M, Ben Hamida M, El Fekih N, El Aidli S, Zeglaoui F, et al. Cutaneous adverse drug reactions in children. A series of 90 cases. Tunis Med. 2012;90(1):45-50.

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