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Paracetamol Induced Bullous Fixed Drug Eruption

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ABSTRACT

We present a rare case of Bullous Fixed Drug Eruption triggered by the administration of Zerodol SP (aceclofenac 100 mg, serratiopeptidase 15mg, paracetamol 325 mg) to a 35-year-old female patient prescribed for fever and bodyache at a government hospital. Fixed drug eruption (FDE) is a distinctive type of cutaneous drug reaction that characteristically recurs in the same locations upon re exposure to the offending drug.[1] In the United States, drug eruptions occur in approximately 2-5% of inpatients and in more than 1% of outpatients. Internationally, drug eruptions occur in approximately 2-3% of inpatients.[2]The term bullous fixed drug eruptions refers to adverse drug reactions that result in fluid-filled blisters or bullae. Blistering can be due to various medications, prescribed or over-the-counter, natural or synthetic. Blistering may be localized and mild, or widespread and severe, even life-threatening.[3] FDE is a type IV hypersensitivity reaction where memory CD8+ T cells remain resident in previously affected epidermal sites and are reactivated upon re-exposure to the offending agent.[4] Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), antibiotics and anti- epileptics, have drug eruption rates approaching 1–5%.[5] Paracetamol is one of the common drugs prescribed as analgesic–antipyretic agent in all age group of patients. FDE is a well reported, but uncommon side-effect of paracetamol.[1]

Keywords: CD8+ T, Cutaneous drug reaction, Antipyretics, Type IV hypersensitivity reaction

Introduction

Cutaneous reactions to paracetamol are uncommon and include anaphylaxis. Urticaria, maculopapular rashes, and fixed drug eruptions (FDE). Dermatological side effects like erythematous skin rashes associated with paracetamol have been reported but are rare. Paracetamol induced FDE is reported in the literature in less than 1.5% of all cases of FDEs. Paracetamol is generally a well-tolerated drug with a good safety profile and low incidence of side effects at the recommended dose. Prolonged daily use can lead to serious side effects like kidney or liver damage, and long term side effects like increased risk of gastrointestinal bleeding.[6] Fixed drug eruption is a delayed type IV hypersensitivity reaction. In the initial phase memory CD8+ T cells at the dermo-epidermal junction release interferon-gamma when activated by the medication antigen causing epidermal basal layer damage. Recruited T-cells and neutrophils damage melanocytes and keratinocytes. During the resolution phase, dermal macrophages collect the melanin resulting in the typical post-inflammatory hyperpigmentation. Regenerating basal keratinocytes release interleukin-15 leading to the formation of resident memory CD8+ T-cells which remain quiescent but in a primed state ready to respond to the chemical antigen again.[7]

The skin lesions typically appear within 30 minutes to 8 hours of drug ingestion and are often misattributed if patients fail to disclose over-the-counter medication use.[4]

Patient Presentation:

A 35-year-old female with known hypothyroidism on tablet Thyronorm 50 mcg presented with multiple fluid-filled lesions over both hands and feet for one day, associated with burning sensation and pain. The onset was insidious and progressive. She had experienced one similar episode over the past year. Notably, she had a history of allergic reaction to paracetamol which presented as a rash with itching over similar sites in the body for a short period and which resolved without any medications. One day prior to the current eruption she took a combination NSAID tablet (aceclofenac + paracetamol + serratiopeptidase) for fever and bodyache.

Diagnostic Work-up:

On examination, multiple bullae present over dorsal aspect and medial border of bilateral feet, multiple bullae present over bilateral wrist and lateral border of thumb on both hands (Figure 1-4), mucosal involvement –lips affected, oral erosions over the palate. No oral or genital mucosal involvement was seen.

Treatment:

The suspected drug was withdrawn and she was managed with systemic corticosteroids, antihistamines, proton-pump inhibitor, analgesic, topical antibiotics, compresses and supportive therapy. The lesions ceased appearing and began to heal without systemic complications.

After few days on cutaneous examination: Multiple ulcer present on dorsal aspect of B/L foot of size 5x6 cm ,with sloping edges, well-defined margins ,healthy granulation tissue present, base firm, non-indurated, minimal tenderness present, serosanguinous discharge present.

Laboratory investigations such as haemoglobin, complete blood count, blood sugar level, serum electrolytes and Liver function tests were found to be within normal limits.

Causality outcome:

The causality assessment indicated that the adverse reaction was **probable** according to the WHO-UMC criteria, as the symptoms reappeared upon re-exposure to paracetamol and resolved after its discontinuation. Based on **Naranjo's scale**, a score of 6 further supported a probable adverse drug reaction. According to the **Modified Hartwig and Siegel Severity Scale**, the reaction was categorized as **Level 4(b)**, indicating moderate severity that required withdrawal of the drug and specific treatment, with the ADR being the primary reason for hospital admission. The **Schumock and Thornton Preventability Scale** classified the reaction as **definitely preventable**, given the patient's known history of paracetamol-induced fixed drug eruption and the availability of safer alternatives. Based on the **Predictability Scale**, the ADR was considered **predictable** due to the prior allergy or documented reaction to the drug.

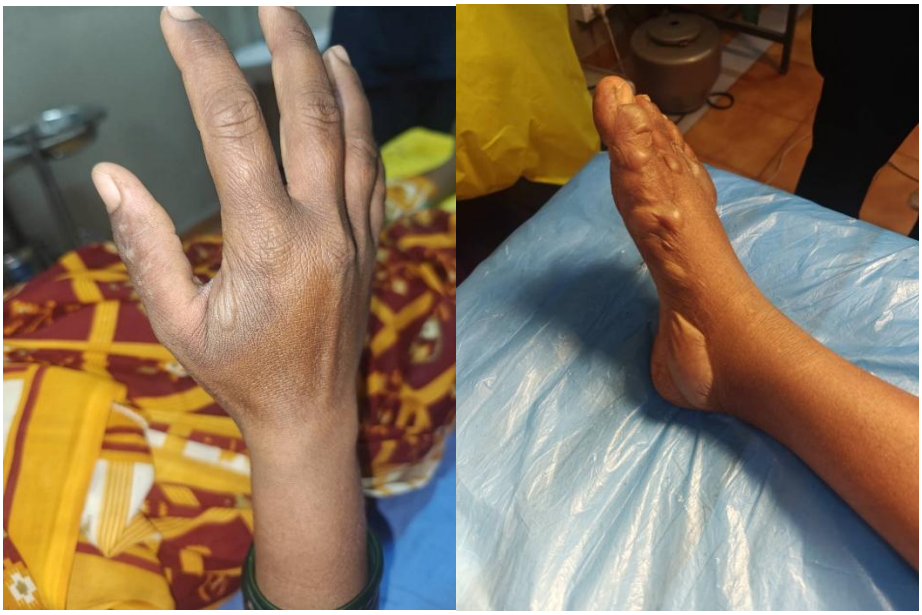

Figure 1 and 2: Fluid filled lesions on both right hand and foot.

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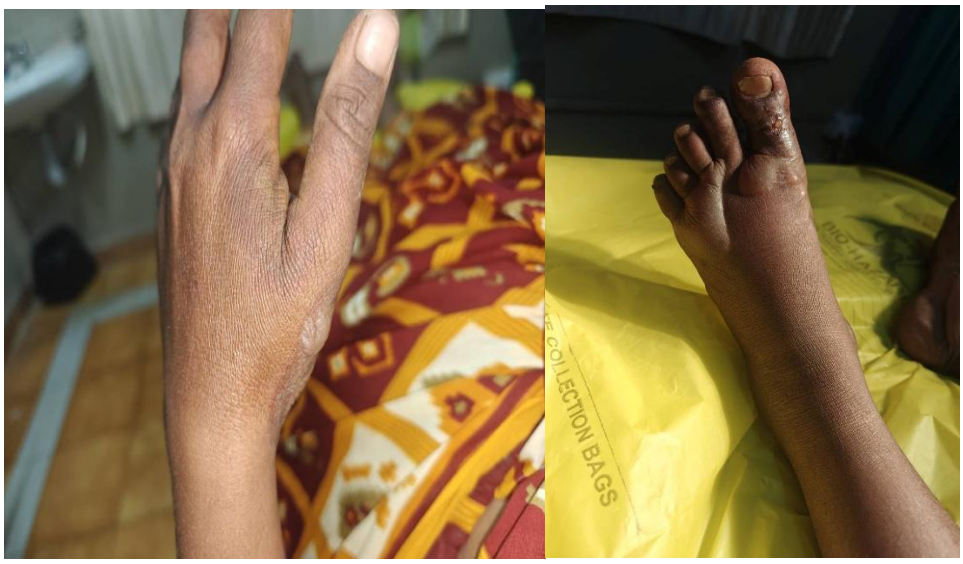

Figure 3 and 4: Fluid filled lesions on both left hand and foot.

Discussion

Pathologically, migration and residence of drug-specific effector-memory CD8+ T-cells in the epidermal side of the dermo-epidermal junction of the affected area account for the recurrence of eruption at the same site. Upon drug re-exposure, quiescent CD8+ cells become activated and secrete interferon-γ and cytotoxic granules into the local microenvironment. Paracetamol is one of the most common causes of FDE, as are mefenamic acid, ibuprofen, and aspirin.[8]

FDE results from activation of CD8+T cells within the skin by drug antigens, leading to the release of cytokines that recruit immune cells and attack keratinocytes and melanocytes. The presence of resident memory CD8 + T cells during the regeneration of basal layer keratinocytes is associated with FDE recurrence at the same site. CD8 + T cells play a key role in inflammation by recognizing drug antigens associated with specific MHC Class I molecules found on keratinocytes. Several HLA-A or HLA-B genes corresponding to MHC Class I molecules have been linked to FDE.[9]

The reason that **paracetamol-induced bullous fixed drug eruption** is seen more in certain populations (e.g., reported more in Asian/Indian literature) is **not** because paracetamol is inherently more dangerous in those populations, but because of **genetic predisposition (HLA/immune factors) + higher/excessive exposure + reporting/recognition bias.**

There are many drugs which causes fixed drug eruprion, they are, sulphonamides (cotrimoxazole), tetracyclines, penicillin, erythromycin, clarithromycin, rifampicin, NSAIDs, barbiturates, banzodiazepines, fluconazole, cetrizine, lamotrigine, omeprazole, lansoprazole, ACE inhibitors, and hormonal preparations.

Peak age for FDE is 21-30 years, although it may vary. Ratio of male:female is generally equal. Genetic predisposition occurs in cases who have family history of diabetes mellitus, atopy and drug allergy.[10]

Conclusion

Patients allergic to certain antipyretics may tolerate another brand or formulation if the reaction is caused by excipients rather than the drug itself. Management options include switching to a different formulation, avoiding all antipyretics if symptoms are mild, attempting desensitisation under supervision, or using alternatives such as low-dose paracetamol, COX-2 inhibitors, or pre-medication with antihistamines and leukotriene receptor antagonists.

Comprehensive efforts are required to prevent such reactions. Documenting prior drug responses in medical records and advising patients to avoid over-the-counter use are crucial steps. To prevent re-exposure, patients should receive drug allergy cards or mobile warnings. Pharmacogenetics testing for paracetamol-induced FDE is not yet conventional. However, improvements in immunogenomics may allow for preventative screening for drug hypersensitivity syndromes in high-risk or immunocompromised groups in the future.

Effective patient education, proper medical record-keeping, and caution when prescribing are essential for preventing recurrence. Future preventive measures may be further improved by pharmacogenetics' expanding involvement. Reexposure to paracetamol should be avoided in these situations and drug withdrawal is required. Future occurrences of these reactions could be avoided by using drug alert cards.

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Conflict of interest

The authors declare that there is no conflict of interest.

Reference

1. Dr. Payal Dashrath Nikose, Dr. Abhishek Jain, Dr. Prabha Khaire, Dr. Shilpa Pawar, Dr. Jalaja Bhandhekar International Journal of Medical Science and Current Research | May-June 2023 | Vol 6 | Issue 3
2. **Thomas N Helm, Brandon Ng** Drug Eruptions Updated: Oct 31, 2024
3. Dr Delwyn Dyall-Smith FACD, Dermatologist, 2009.
4. Surbhi Jain, Irfan Ahmad Khan, Mohammad Adil. Journal of Pharmacovigilance & Drug Safety 2025 Volume-22 | Issue-1
5. Raju Niraula1*, Punnam Chandar Thoutoum2 , Anuja Devkota3 , Sangita poudel1A Prospective Study of Drug Induced-Skin Reactions: Patient Approaching Department of Dermatology in Secondary Care Hospital Journal of Infectious Diseases & Preventive Medicine 2022 Vol.10 Iss.5 No:1000271
6. Dr. Asha Dattatraye Jadhav*, Dr. Prapti Persis Bathani, Dr. Tina Priscilla, Dr. Sumana Sen, Dr. Dilip Mathai. International Journal of Modern Pharmaceutical Research *2022, 6(4), 113-115*
7. Dr Amanda Oakley, Dermatologist, Hamilton, New Zealand, 2001; Updated: Dr Christine Condon, Resident Medical Officer, St Vincent's Hospital Melbourne, Australia; A/Prof Rosemary Nixon AM, Dermatologist, Skin Health Institute, Carlton, Australia. Copy edited by Gus Mitchell. March 2021
8. QU Lee * Hypersensitivity to antipyretics: pathogenesis, diagnosis, and management Hong Kong Med J | Volume 23 Number 4 | August 2017
9. Yuanyuan Wang, Huan Xue, Hejun Dai, Lianjuan Yang. Cross-Reactivity: a Case of Paracetamol-Induced Generalized Bullous Fixed Drug Eruption Followed by Dipyrone-Induced Fixed Drug Eruption. Clinical, Cosmetic and Investigational Dermatology 2025:18
10. Dr. Priyanka Sharma, Dr. Dinesh Kumar Yadav, Dr. Nidhi Sanwalka. PARACETAMOL-INDUCED FIXED DRUG ERUPTION: A CASE SERIES International Journal of Medical and Biomedical Studies Volume 5, Issue 2; February: 2021;

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