

## Case Report



## Methotrexate-Induced Symmetrical Drug – Related Intertriginous and Flexural Exanthema: A Rare Cutaneous Reaction

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### ABSTRACT

Symmetrical Drug-Related Intertriginous and Flexural Exanthema (SDRIFE) is an uncommon cutaneous reaction that typically presents as a symmetrical erythematous rash following systemic drug exposure. Methotrexate, widely used for its anti-neoplastic, anti-inflammatory, and immunosuppressive properties, is generally well tolerated at low doses. However, accidental overdose can result in significant toxicity. We report a case involving a 40-year-old male who developed erythematous and hyperpigmented lesions over the groin, neck, arms, and legs, accompanied by odynophagia, following an inadvertent methotrexate overdose due to a dispensing error. Clinical findings were consistent with SDRIFE. Methotrexate was immediately discontinued, and calcium leucovorin was administered as an antidote. The patient responded positively to the intervention. This case emphasizes the need for vigilance in drug dispensing practices and raises awareness of SDRIFE as a potential manifestation of methotrexate toxicity. Early recognition and prompt treatment are essential for preventing serious outcomes.

**Keywords:** SDRIFE, baboon syndrome, methotrexate overdose, medication error, hypersensitivity.

### INTRODUCTION

Symmetrical drug related intertriginous and flexural exanthema (SDRIFE) is also called as baboon syndrome which is a rare, symmetrical erythematous rash that appears in skin folds, particularly the buttocks, inner thighs, and also may involve flexural area after exposure to certain systematic medications.<sup>1</sup> There are many other medicines associated with SDRIFE, including non-beta-lactam antibiotics, chemotherapeutic agents, analgesics, and antifungals.<sup>2</sup> Similarly, Methotrexate, an antimetabolite is used alone or together with other medicines to treat several types of cancer. It is also used to treat rheumatoid arthritis, severe psoriasis. When administered in appropriate doses, it is effective and generally well-tolerated; however, errors in administration can lead to severe toxicity.<sup>3</sup>

### CASE REPORT

A 40-y old man presented to dermatology OPD at HSK hospital, Bagalkot. A complaint of painful skin lesions on groin region, complaints of symmetrical skin lesions on arm neck and leg bilaterally as shown below in the [figure number 1, 2a and 2b] pt also complaints of difficulty in swallowing food in the past 2 days. The patient was on medication such as Itraconazole, Prednisolone and he had taken tab Leetrexate (Methotrexate) 7.5 mg once a day for 7 days. where the pharmacist was supposed to dispense Levolyte 5mg due to negligence of the pharmacist he dispensed Leetrexate 7.5 mg unfortunately, the patient experienced methotrexate toxicity because of an unintentional overdose caused by medication error i.e. dispensing error. Patient was diagnosed as symmetrical drug related intertriginous and flexural exanthemata's rash

based on drug history and clinical features. The reaction was managed by withdrawing the methotrexate and patient was treated with injections such as Dexamethasone, Inj Pheniramine Malate, Inj Multivitamin Inj Ceftriaxone were administered intravenously and only Inj Filgrastim was administered subcutaneous also antihistamine was administered to patient and topical applicants such as Propygenta and Dentogel for lesions in the mouth was treated. He was treated for the methotrexate overdose by calcium leucovorin{antidote} also topical corticosteroids were provided for symptoms relief.

The patient condition improved gradually after the drug was withheld as shown in fig 3 and 4 and an antidote inj calcium leucovorin was administered.

### DISCUSSION

#### Role of Methotrexate:

Methotrexate, although generally immunosuppressive, may in some individuals act as a **hapten**, forming a complex with skin proteins. This complex is then presented by **antigen-presenting cells** to **memory T-cells**, triggering a localized immune reaction.

#### Misuse or Overdose Enhances Risk:

In reported cases of methotrexate-induced SDRIFE, the reaction often followed inappropriate dosing or medication error, suggesting that dose-dependent toxicity may also amplify the immunological reaction.<sup>5</sup>



### Mechanism of Methotrexate-Induced SDRIFE:

Delayed-Type Hypersensitivity (Type IV): Methotrexate may act as a hapten, binding to host proteins and forming a neo-antigen. This can trigger T-cell activation and immune-mediated inflammation in specific areas of the skin, especially flexural and intertriginous zones.<sup>4</sup>

### Management of toxicity

Patterns of MTX-induced toxicity may be determined by the means and dose administered. Patients may experience diverse signs and symptoms, and could potentially need hospitalisation and intensive care monitored by physicians and nurses. Typically, the preferred primary approach is to discontinue the MTX administrations as well as the concomitant drugs and monitoring blood parameters, renal parameters, and liver parameters as the initial toxicity developed. The treatment approach should be determined by the clinical symptoms and signs. Usually, these patients can be treated with the following three standard approaches: (i) maintenance of the level of MTX serum; (ii) maintenance of body hydration.<sup>5</sup>

This case highlights how a seemingly minor error — such as dispensing the wrong drug—can lead to a serious and uncommon adverse reaction like SDRIFE. While methotrexate is generally safe at therapeutic doses, an overdose can activate immune mechanisms resulting in characteristic skin rashes. SDRIFE remains underdiagnosed due to its resemblance to other dermatoses. Increased awareness among healthcare professionals is essential for early recognition. Prompt withdrawal of the offending agent and appropriate supportive therapy often lead to full recovery. Pharmacists and clinicians must be especially vigilant in prescribing and dispensing high-risk medications like methotrexate. Documentation and reporting of such rare adverse events can help build stronger medication safety protocols.

### CONCLUSION

SDRIFE is a rare dermatological side effect that should be considered in the monitoring of skin lesions during administration of certain medications such as chemotherapeutic agents, non-beta-lactam antibiotics, analgesics, and antifungals. SDRIFE is a rare but noteworthy dermatological reaction that can arise from systemic

medications, including methotrexate. This case underlines the need for careful medication dispensing and encourages clinicians to include SDRIFE in the differential diagnosis when patients present with symmetrical intertriginous rashes following drug exposure.

### CONSENT TO PARTICIPATE

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that their names and initials will not be published and due efforts will be made to conceal their identity.

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