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Case Series

Analyzing Fixed Drug Eruptions (FDES) Induced by Non-Steroidal Anti-Inflammatory Drugs (NSAIDS): A Case Series

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Abstract:

Background: Cutaneous adverse drug reactions (CADRs) account for 2-3% of all adverse drug reactions (ADRs), encompassing conditions ranging from mild rashes to severe manifestations like Stevens - Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). This study focuses on Fixed Drug Eruptions (FDEs), a subset of CADRs, particularly in the context of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).

Objectives: The primary aim of this study is to analyze the incidence and characteristics of FDEs in patients exposed to various NSAIDs. By examining these cases, the study aims to enhance understanding of the relationship between NSAID consumption and the development of FDEs.

Methods: Employing a case series approach, this study tracked patients treated with NSAIDs who subsequently developed FDEs. The data was gathered from Adverse Drug Reaction (ADR) reports submitted to the ADR Monitoring Center (AMC) affiliated with our institute over a six-month period from June to November 2023.

Results: In this period, six distinct cases of FDEs associated with NSAIDs were identified. These involved the following medications: Combiflam, injection Diclofenac, two cases with unidentified NSAIDs, a combination of Paracetamol and Aceclofenac, and finally, an injection of Paracetamol.

Conclusion: This study highlights the potential risk of FDEs in patients consuming NSAIDs. The findings highlight the need for heightened awareness among healthcare professionals regarding the cutaneous risks associated with NSAIDs. This case series contributes to the broader understanding of drug-induced dermatological reactions, emphasizing the importance of diligent ADR reporting and monitoring.

Keywords: Fixed Drug Eruptions, Non-Steroidal Anti-Inflammatory Drugs, Adverse Drug Reactions.

Introduction

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) represent a significant category in pharmacology, with a history dating back to the late 19th century [1]. The introduction of acetyl salicylic acid, more commonly known as aspirin, in 1899 marked the beginning of the NSAID era [2]. However, it wasn't until half a century later, in 1949, with the emergence of phenyl butazone, that the term 'NSAID' was formally coined. This class of drugs has since expanded to include well-known medications such as Paracetamol (introduced in 1955), Diclofenac (1970), Ibuprofen (1961), and Aceclofenac (1990), among others [3].

NSAIDs, as their name implies, are non-steroidal medications primarily used for their antipyretic (fever-reducing) and analgesic (pain-relieving) properties [4]. They have become some of the most commonly used drugs worldwide, often available over the counter (OTC), making them easily accessible for self-medication[5]. Their widespread use, however, brings to light the importance of understanding their potential adverse effects, particularly in the context of cutaneous adverse drug reactions (CADRs).

One such reaction is the Fixed Drug Eruption (FDE), a unique type of CADR. FDEs are characterized by recurrent, well-demarcated, lichenoid lesions that appear at the same skin or mucosal site upon re-exposure to the causative drug [6]. Their distinct nature makes them a critical area of study

in dermatological pharmacology. The recurrent nature of FDEs upon exposure to the same medication highlights the importance of identifying and understanding the offending agents, especially in commonly used drugs like NSAIDs [7].

The rationale behind this study is grounded in the need to enhance awareness among physicians and healthcare providers about the potential of NSAIDs to cause FDEs. Given the high prevalence of NSAID use for a range of common ailments, it is vital for healthcare professionals to be cognizant of this risk, which could significantly impact patient management and drug prescription practices.

The primary aim of this study is to evaluate the occurrence and characteristics of fixed drug eruption cases in patients taking NSAIDs. By doing so, we hope to shed light on the frequency, clinical presentation, and severity of FDEs associated with this class of drugs.

The objective is twofold: Firstly, to document in detail the spectrum of FDEs caused by the NSAID group, capturing the variety of clinical manifestations and the specific NSAIDs implicated. Secondly, to explore the association of these drug eruptions with any underlying morbidities or predisposing factors in patients, thus providing a comprehensive overview of the risk profile associated with NSAID-induced FDEs.

Methodology

Study Design: The research was structured as a retrospective case series study, focusing on a specific subset of adverse drug reactions.

Study Subjects: The subjects of this study were six documented cases of Fixed Drug Eruptions (FDEs) attributed to the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).

Study Setting: The research was carried out at the Adverse Drug Reaction Monitoring Centre (AMC), associated with the Department of Pharmacology at Sri Venkateswara Medical College and Sri Venkateswara Ramnarain Ruia Government General Hospital, located in Tirupati.

Study Period: The timeframe for this retrospective study was set from June 2023 to November 2023, a duration of six months. The study was done after approval of the institutional scientific and ethics committee.

Sample Size: The study focused on a sample of six case reports, all of which involved FDEs triggered by the use of NSAID medications.

Inclusion Criteria: The study included all reported cases of suspected adverse drug reactions from June 2023 to November 2023, specifically targeting those instances where FDEs were induced by NSAID use.

Exclusion Criteria: The research excluded other types of Cutaneous Adverse Drug Reactions (CADRs) that were related to NSAIDs or other drug groups. Additionally, cases of FDEs caused by drugs other than NSAIDs were not considered for this study.

Ethical Consideration: In this study, patient consent forms were diligently obtained, allowing for the publication of patient photos while safeguarding their privacy and rights. Moreover, the research adhered rigorously to ethical research standards, receiving approval from both the institutional scientific committee and the ethics committee, emphasizing our dedication to ethical research practices.

Study Methods: For this investigation, the suspected ADR reporting forms collected from June 2023 to November 2023 were meticulously reviewed. From these, six case reports detailing FDEs as a result of NSAID use were identified and selected for in-depth analysis. This methodology was designed to provide a focused examination of the relationship between NSAID use and the occurrence of Fixed Drug Eruptions, contributing valuable insights into this specific adverse reaction within the broader context of drug safety and patient care.

Case Report 1

A 30-year-old male patient with the identification number 24807 presented at the Dermatology Outpatient Department with hyperpigmented patches on his upper and lower limbs. These symptoms had appeared one day prior, on June 20, 2023. The patient's medical history revealed that he had taken a single dose of Combiflam (a combination of Ibuprofen and Paracetamol) to alleviate body pains. He reported a similar rash occurrence in the past following the intake of a painkiller. Combiflam was immediately discontinued on the day of presentation.

The patient was admitted for treatment, receiving oral Prednisolone, Betamethasone cream for topical application, and Cetirizine tablets. His recovery was successful, leading to the classification of this incident as 'probable' according to the WHO-UMC causality assessment scale. Upon complete recovery, the patient was discharged with the advice to avoid all Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in the future.

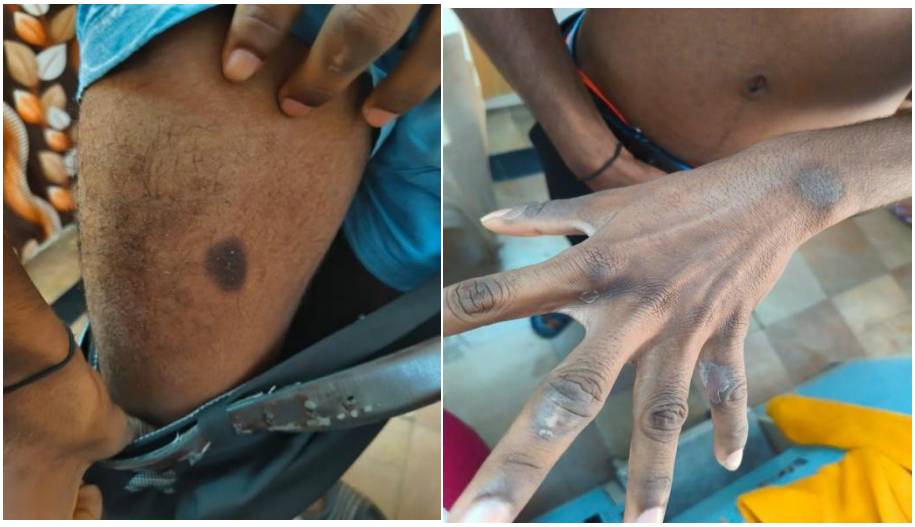

Figure 1:

Case Report 2

A 62-year-old female patient, registered under OP number 151674, visited the Dermatology Outpatient Department on August 7, 2023. She presented with hyperpigmented lesions on her forearms and legs, accompanied by itching. These symptoms manifested approximately 30 minutes after she received an injection of Diclofenac for trauma. The patient reported a similar rash in the past following the use of a painkiller, leading to the immediate discontinuation of Diclofenac. For treatment, she was prescribed oral Prednisolone, Cetirizine tablets, Azithromycin tablets, and Mupirocin ointment for topical application.

The patient was monitored through follow-up visits and subsequently recovered. She was advised to avoid all Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in the future. The incident was classified as 'Probable' on the WHO-UMC causality assessment scale.

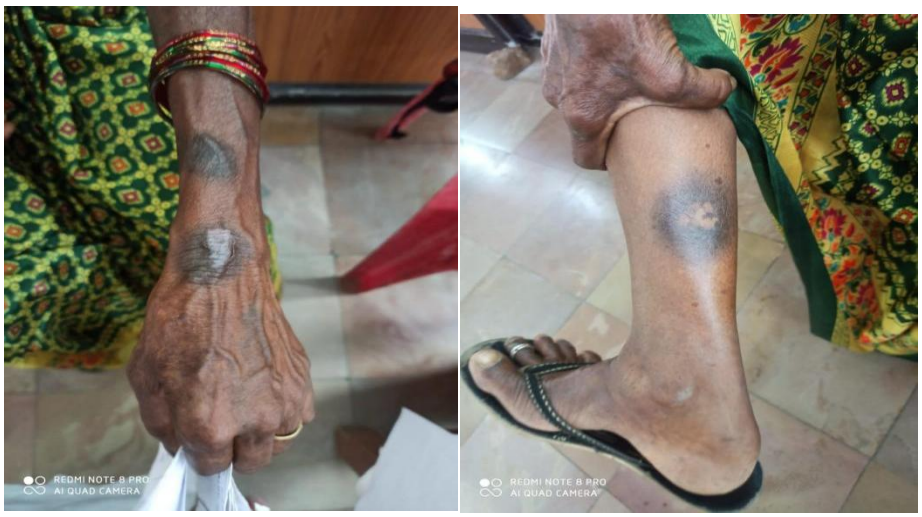

Figure 2:

Case Report 3

A 53-year-old female patient, bearing the OP number 163531, visited the Dermatology Outpatient Department on August 28, 2023. She reported hyperpigmented lesions on her chest, abdomen, arms, thighs, and legs, accompanied by itching. These symptoms occurred following the administration of an unidentified NSAID injection, given by a Registered Medical Practitioner (RMP) for toothache. The patient had a history of developing rashes after taking painkillers.

Upon evaluation, the patient was prescribed Cetirizine tablets, calamine lotion for topical use, and vitamin supplements. Following consistent follow-up appointments, she showed recovery from the lesions. The patient was advised to avoid all Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in the future. This case was assessed as 'Probable'

according to the WHO-UMC causality assessment scale.

Figure 3:

Case Report 4

A female patient aged 63 years, with IP no 31173, came to Dermatology OPD, on 25-09-2023 with complaints of generalised bullous lesions. on eliciting history, it was found that the patient was taken tablet paracetamol + aceclofenac combination for knee pain 2 days ago. On the same day of taking the drug, the patient developed painful, fluid filled lesions in the mouth, groin and external genitalis followed by multiple bullous eruptions occurred all over the body which ruptured spontaneously with serous fluid discharge.

Patient gave history that he developed rashes similarly when he took a painkiller The patient was hospitalised and put on Inj. Decadron, Tab. Cetrizine and Mupirocin ointment. Patient was discharged after recovery, with an advice of, not to take any NSAIDs in future. The causality assessment according to WHO-UMC scale for this case was Probable.

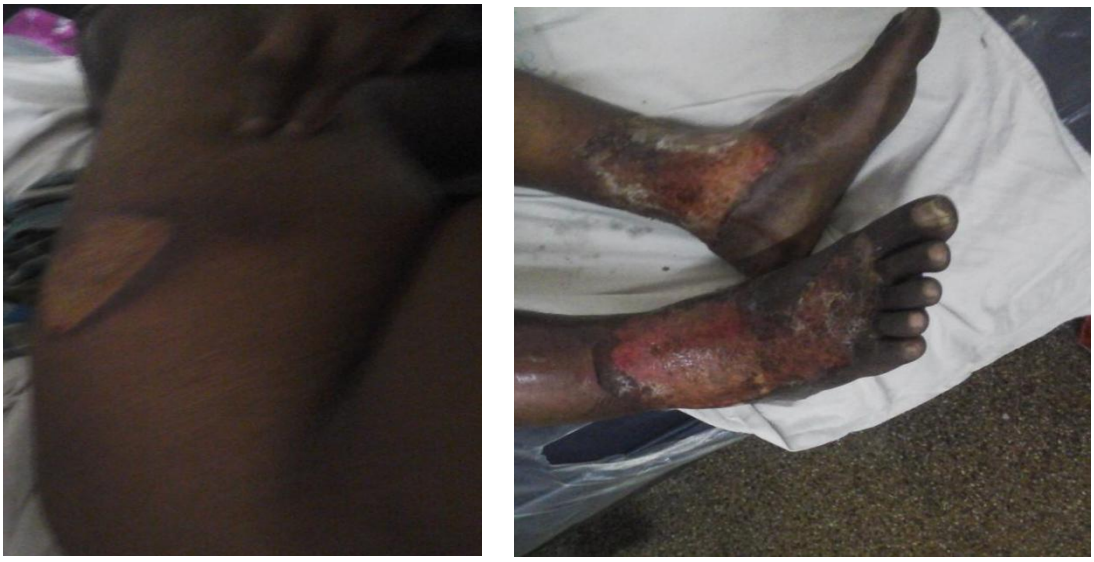

Figure 4:

Case Report 5

A 62-year-old male patient, with inpatient number 36698, presented to the Dermatology Outpatient Department on October 27, 2023. He complained of generalized bullous lesions, which appeared after taking an unspecified NSAID prescribed by a local Registered Medical Practitioner (RMP). Physical examination revealed well-defined hyperpigmented plaques and multiple ruptured bullae covering his lower limbs, buttocks, inguinal region, forearms, and trunk, with the scalp remaining unaffected.

The patient reported a history of developing similar rashes after using painkillers. He was admitted for treatment, receiving Prednisolone tablets, Cetirizine tablets, and Mupirocin ointment. Following treatment, he recovered from the condition. The incident was classified as 'Probable' in the causality assessment. He was advised to avoid taking any painkillers without prior consultation with a doctor.

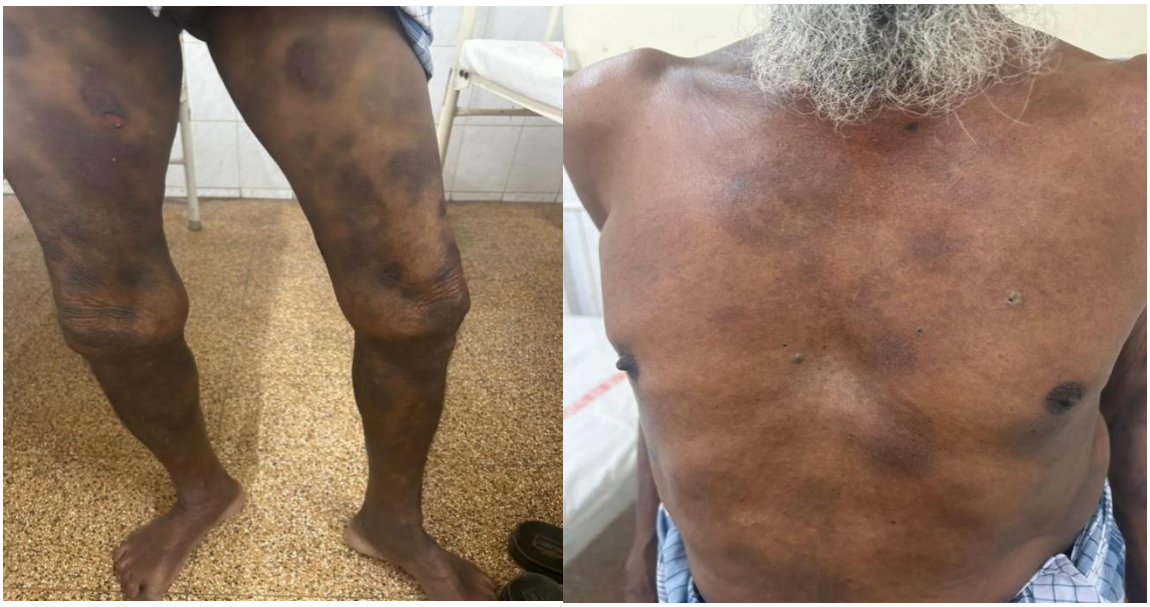

Figure 5:

Case Report 6

A 53-year-old male patient, with the inpatient number 39357, was admitted due to an acute febrile illness. On November 20, 2023, he was treated with an injection of Paracetamol. Subsequently, he developed drug eruptions on his left arm and the inner regions of both thighs. He had a history of similar rash occurrences after taking painkillers. To address these symptoms, the patient was treated with intravenous Decadron (Dexamethasone) and an injection of Chlorpheniramine.

After his recovery, he was discharged with the recommendation to avoid any Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in the future. This adverse drug reaction was classified as 'Probable' on the WHO-UMC causality assessment scale.

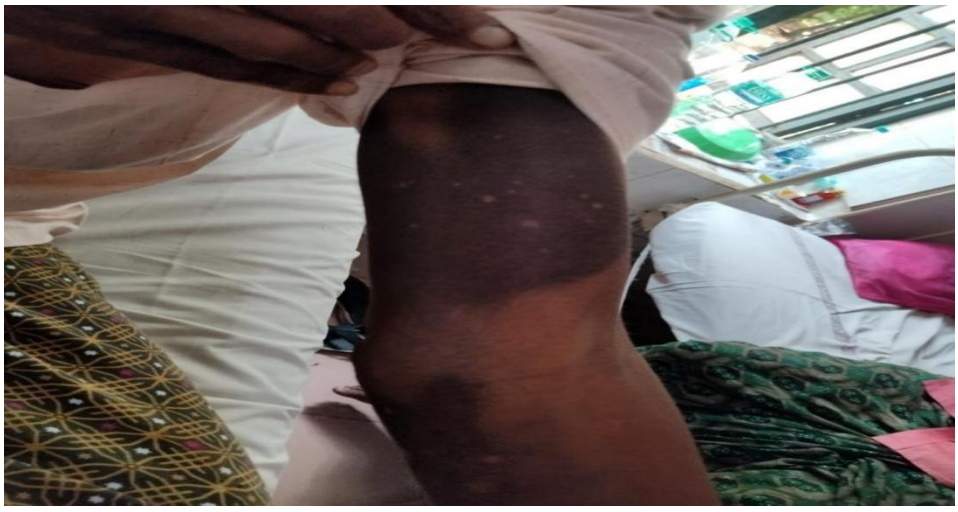

Figure 6:

Discussion

Fixed Drug Eruptions (FDE) represent a distinct category of Cutaneous Adverse Drug Reactions (CADRs) characterized by the development of round or oval erythematous patches at the same site upon reexposure to a specific drug. Various types of FDEs have been identified, including pigmented FDE, nonpigmented FDE, granular FDE, bullous FDE, oval FDE, vulval FDE, psoriasis-like FDE, eczematous FDE, urticarial FDE, linear FDE, erythema dyschromicum perstans type FDE, and cellulitis eruption FDE. Notably, all six cases reported in this series were diagnosed as bullous FDE [8,9].

It's worth mentioning that there is a scarcity of studies reporting FDE as case series specifically related to the exposure to Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). While isolated case reports exist, an article published in the Annals of SBV Journal in July-December 2018 (Volume 7, Issue 2) presented a case series of FDEs associated with drugs such as ceftriaxone, NSAIDs, cotrimazole, norfloxacin, and doxycycline [10,11]. Upon reviewing Adverse Drug Reaction (ADR) reports submitted to the ADR monitoring center, FDEs were sporadically encountered in cases involving ceftriaxone, ciprofloxacin, doxycycline, and tramadol. The morbidities associated with FDEs varied, ranging from painful blisters to hyperpigmented patches and scarring [12].

Treatment strategies for FDEs typically involve discontinuing the offending drug, using topical steroids, administering antihistamines, antibiotics, and, in some cases, oral steroids [13].

It's essential to note that other CADRs associated with NSAIDs include erythema multiforme, toxic epidermal necrolysis, and Stevens-Johnson syndrome. In all six ADR cases discussed here, causality assessment was categorized as 'Probable/Likely' according to the Uppsala Monitoring System of the World Health Organization. Due to ethical considerations, rechallenging with the suspected drugs was not performed, and thus, causality assessment as 'Certain' was not established [14].

Conclusion

Raising awareness about Fixed Drug Eruptions (FDEs) linked to NSAID exposure is crucial for healthcare providers. This knowledge enables swift identification and early intervention, mitigating the potential harm and complications associated with FDEs. Timely recognition and management can significantly reduce patient suffering and improve overall clinical outcomes.

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