

**CASE REPORT ON PARACETAMOL INDUCED CUTANEOUS DRUG ERUPTION**

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**ABSTRACT**

Analgesic and antipyretic drug paracetamol is widely prescribed as an over-the-counter drug worldwide in all age groups of patients. paracetamol is obtained in several different forms, including syrup, regular tablets, effervescent tablets, injections, suppositories, and other forms. Comparatively, it is a safer non-steroid anti-inflammatory drug (NSAID). Almost all drugs cause adverse reactions. Cutaneous ADRs are quite common and some of them are very severe, leading to significant comorbidities. Early identification of the disease as well as the causative drug and its discontinuation at the earliest possible time is the key to management and avoidance of a more severe reaction. In our country, some common drugs that cause CADR are antimicrobials, mainly  $\beta$ -lactams, fluoroquinolones, and sulfonamides. We report a case of a 52-year-old female patient who presented with cutaneous drug eruption after ingestion of paracetamol. Our case reports aim to raise awareness among health professionals about this widely used drug and its rare side effects.

**KEYWORDS:** Paracetamol, Non-steroidal anti-inflammatory drugs, Cutaneous drug eruption.**INTRODUCTION**

In the world of pharmaceuticals, paracetamol (acetaminophen, Anatomical Therapeutic Chemical Classification code N02BE01) is one of the most widely used and widely available analgesics and antipyretic drugs that is available without prescription throughout the world.<sup>[1]</sup> Acetaminophen directly acts on CNS and inhibits the synthesis of prostaglandins by inhibiting two COX isoforms, COX-1 and COX-2. As well as having a lack of anti-inflammatory effects in the peripheral areas, it regulates the fever by directly acting on the hypothalamic heat-regulating center in the brain.<sup>[2]</sup> Non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated in patients with gastric ulcers, hypersensitivity to aspirin, impaired blood coagulation, pregnant women, nursing mothers, and children with fevers associated with disease.<sup>[3]</sup> The most common ADRs that occur due to the usage of acetaminophen are Liver and kidney damage, hemolytic anemia, neutropenia, leucopenia, pancytopenia, thrombocytopenia, jaundice, and hypoglycemia. In rare cases, paracetamol can cause angioedema, urticaria, maculopapular exanthema and skin rash.<sup>[4]</sup> The term cutaneous adverse drug reactions (CADR) refers to the clinical manifestations of the skin, mucosae, and adnexa caused by a drug or its metabolites. Most drug reactions occur in the skin, which may affect up to 10% of hospitalized patients and 1–3% of multi-medicated patients.<sup>[5]</sup> Approximately 2–3% of hospitalized patients experience skin drug eruptions as a result of drug therapy. Non-Steroidal Anti-Inflammatory Drugs

(NSAIDs), antibiotics, and antiepileptics have drug eruption rates approaching 1–5%.<sup>[6]</sup> Antibiotics, antimicrobials, NSAIDs, sulfa drugs, biopharmaceuticals, chemotherapy agents, anticonvulsants, and psychotropic drugs are the most prevalent drug classes responsible for causing cutaneous conditions. Several drugs, including digoxin, aluminum hydroxide, multivitamins, acetaminophen, bisacodyl, aspirin, thiamine, prednisone, atropine, codeine, hydrochlorothiazide, morphine, insulin, warfarin, spironolactone cause cutaneous drug eruptions less often.<sup>[7]</sup> This case report was conducted to observe cutaneous adverse drug reactions following paracetamol administration.

**Case Presentation**

A 52-year-old female patient has been suffering from high-grade fever associated with chills and rigor, loose stool, vomiting, and abdominal discomfort for 7 days. So, she was taking paracetamol 500 mg (orally, three times daily), ondansetron 4 mg (orally, once daily), and pantoprazole 40 mg (orally, one time daily) medication from the local medical store for 5 days. 2 days later she developed rashes on her skin. After that, she came to Gandhi Hospital.

On examination, the patient was drowsy and afebrile. The patient's pulse rate was 90 beats per minute. BP was 110/90 mmHg. No pain on palpation of the abdomen. Dermatological examination revealed multiple hyperpigmented maculopapular lesions and scaling in the

abdomen, bilateral upper and lower limbs shown in **figure.2**. Diffuse scaling appeared on the scalp. Several erythematous vesicles were present over the hand palates and a painful oral ulcer was seen in the mouth, shown in **figure.1**.

The patient had no other complaints and no other relevant past medical history. Laboratory investigations such as hemoglobin, complete blood count, and blood sugar level were found to be within normal limits. Ultrasound of the abdomen shows no pathology. An allergy screening test by serum radioimmunoassay was done and that showed an allergy to paracetamol.

#### ADR analysis

Based on the patient's past and current medication history, drug-induced cutaneous eruptions were suspected. In analyzing the ADR profile, it was found that acetaminophen produced cutaneous drug eruption.

Based on Naranjo's causality assessment scale, it falls into the "Probable" category of adverse drug reactions.<sup>[8]</sup> Based on the causality assessment scale of the WHO-Uppsala Monitoring Centre, it is classified as a probable/likely adverse drug reaction.<sup>[9]</sup> Hartwig and Siegel severity assessment scales described it as moderate adverse drug reactions.<sup>[10]</sup> In Table 1, we show all causality assessments.

**Table 1: Causality assessment of Suspected ADRs by using the various assessment scales.**

Causality assessment scales	Score	Assessment
Naranjo's Scale	6	Probable
WHO-UMC scale	7	probable
Hartwig & Seigel scale	Moderate severity with Level 3	



**Figure 1: Rash and Oral ulcer around the mouth.**

#### Management of ADR

ADRs are generally managed with withdrawal/suspension, dose reduction of suspected drugs, and supportive therapy. Here the suspected drug was not administered to the patient for further management.

#### Treatments

In the hospital, the patient receives the following treatment

1. Levocetirizine 10mg OD
2. Liquid paraffin local application
3. Benzocaine gel for local application (30 min before food)
4. Tess gel (Triamcinolone 0.1% W/W) for local application (30 min after food)
5. Betadine Gargle ( povidone iodine 2% w/v)
6. High rich protein diet

5 days later, the patient's oral mouth ulcer was subsided and all the hyperpigmented maculopapular lesions and scaling in the abdomen, bilateral upper and lower limb, face, scalp, and Few erythematous vesicles over the hand palates were subsided. The patient was discharged from the hospital and instructed not to take paracetamol.



**Figure 2: Multiple hyperpigmented maculopapular lesion on the bilateral upper limb.**

## DISCUSSION

Paracetamol is a widely used over-the-counter analgesic-antipyretic agent and known to have a safety profile with a very low incidence of side effects. A variety of clinical presentations can accompany these cutaneous drug eruptions, which appear as oval, erythematous patches. It may occur anywhere on the body, including the face, tongue, hands, feet, torso, extremities, and genitalia.<sup>[11]</sup>

In our patient, multiple hyperpigmented maculopapular lesions and scaling were seen in the abdomen, bilateral limbs, and face. Diffuse scaling was present on the scalp. A few erythematous vesicles were observed over the hand palates, as well as an oral ulcer after paracetamol use. Based on various clinical evaluations and causality assessments using the Naranjo ADR probability scale, WHO-UMC causality system, Karcha, and lasagna scale, Modified hartwig and Siegel severity assessment scale, and predictability scale, find that acetaminophen produces cutaneous drug eruption.

Cutaneous drug eruption has no known pathophysiology. Memory T cell survival mediated by interleukin. Site-specific lesions are caused by interleukin-20. The local tissue damage is attributable to distinct CD8-positive T cell intraepidermal clusters. After activation, resting T cells destroy nearby keratinocytes, releasing cytokines including interferon-gamma. CD8+ T cells, CD4+ T cells, and neutrophils contribute to tissue damage in cutaneous drug eruption.<sup>[12]</sup>

We initially stopped paracetamol and started antihistamine treatment (levocetirizine 10 mg) for our patient. Following five days of treatment, our patient was cured of all dermatological manifestations and discharged from the hospital. We advised our patient not to take paracetamol again and come to the hospital for further evaluation.

## CONCLUSION

In this case report, we show how an over-the-counter drug (paracetamol) can cause cutaneous adverse drug reactions. In this way, more awareness should be raised regarding the over-the-counter drug. The fastest

recovery can be achieved with prompt diagnosis, history taking, early recognition, and discontinuation of the causative drug with symptomatic treatment and an antihistamine combination. Healthcare professionals should be aware of drugs that can cause cutaneous drug eruption before prescribing them

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