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Ciprofloxacin–Tinidazole-Induced Anaphylactoid Reaction: A Case Report

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Abstract

Adverse drug reactions (ADRs) are a significant cause of morbidity and healthcare burden. Anaphylactoid reactions are acute hypersensitivity responses that mimic anaphylaxis but occur via non–IgE-mediated mechanisms. We report a case of a 21-year-old female who developed generalized pruritus, urticaria, hypotension, and respiratory discomfort shortly after the first dose of a ciprofloxacin-tinidazole fixed-dose combination. The suspected drugs were discontinued, and the patient showed rapid and complete recovery with supportive management. Causality assessment indicated a possible association, and the reaction was classified as mild and not preventable. This case highlights the importance of early recognition and management of hypersensitivity reactions, even with commonly prescribed antibiotics, and underscores the role of pharmacovigilance in improving drug safety.

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Introduction

Anaphylactoid reactions are acute, systemic hypersensitivity responses that clinically resemble anaphylaxis but occur via non-IgE-mediated mechanisms, often involving direct mast cell and basophil activation with subsequent release of vasoactive mediators such as histamine. These reactions are characterized by the rapid onset of cutaneous manifestations (e.g., flushing, pruritus, urticaria), along with potential cardiovascular and respiratory involvement, and may occur even on first exposure to the offending drug [1-2].

The fixed-dose combination (FDC) of ciprofloxacin and tinidazole is widely prescribed for the management of gastrointestinal infections, including infectious diarrhea and dysentery caused by bacterial and protozoal pathogens. Ciprofloxacin, a fluoroquinolone antibiotic, exerts its bactericidal action by inhibiting bacterial DNA gyrase and topoisomerase IV, thereby disrupting DNA replication. It demonstrates potent activity against Gram-negative organisms such as Escherichia coli, Salmonella, Shigella, and Neisseria species. Tinidazole, a synthetic imidazole derivative, is effective against protozoal infections such as amoebiasis, giardiasis, and trichomoniasis, and also exhibits activity against anaerobic bacteria [3-4].

Ciprofloxacin is well absorbed orally, with a bioavailability of approximately 70-80% and a peak plasma concentration achieved within 1-1.5 hours. While generally well tolerated, it has been associated with adverse effects ranging from mild gastrointestinal disturbances to serious reactions such as QT prolongation, dysglycemia, and hypersensitivity reactions. Notably, both anaphylaxis and anaphylactoid reactions have been reported with ciprofloxacin, including cases occurring after the first dose. Similarly, tinidazole, although less commonly implicated, has been associated with hypersensitivity reactions, including severe systemic manifestations upon re-exposure [5-9].

In the context of acute infectious diarrhea, this combination is particularly advantageous due to its dual antimicrobial coverage against both bacterial and protozoal pathogens [10]. However, the potential for immediate hypersensitivity reactions necessitates careful monitoring, especially given that anaphylactoid reactions can progress rapidly and may be life-threatening if not promptly recognized and managed [1-2].

According to vigiaccess database, although there are a lot of ADRs with hypersensitivity reaction and other associated skin disorders, however the occurrence of anaphylactoid reaction is very scantly. In the present case, the patient developed features consistent with an acute anaphylactoid reaction shortly after administration of the ciprofloxacin–tinidazole combination. The rapid onset of pruritus, erythematous wheals, and early systemic symptoms underscores the importance of early identification of such adverse drug reactions (ADRs).

Case Presentation

This case was documented as part of a pharmacovigilance elective conducted under the Department of Pharmacology at Christian Medical College and Hospital, Ludhiana, an Adverse Drug Reaction (ADR) Monitoring Centre. The case was reported from the Department of Medicine and entered into the VigiFlow database under the identification number IN-IPC-301228122.

A 21-year-old female patient (initials: AS), weighing 60 kg, presented with a 48-hour history of acute gastroenteritis. Following clinical evaluation, she was initiated on a fixed-dose combination (FDC) of ciprofloxacin 500 mg and tinidazole 600 mg, administered orally twice daily for seven days. Omeprazole 20 mg twice daily was also prescribed for gastroprotection. Within a short interval after administration of the first dose on October 16, the patient developed sudden onset of generalized pruritus accompanied by diffuse erythematous wheals over the bilateral wrists and lower extremities. This was followed by progression of symptoms, including facial flushing, a sensation of throat tightness, mild difficulty in breathing, and lightheadedness.

On examination, the patient had widespread urticaria with wheals and facial erythema. Vital signs revealed mild hypotension and tachycardia. Respiratory examination showed no wheeze; however, the patient appeared mildly dyspneic. There was no evidence of cyanosis, stridor, angioedema, or mucosal involvement. Based on the acute onset of cutaneous and early systemic manifestations shortly after drug exposure, a diagnosis of an acute anaphylactoid reaction was considered. The suspected offending agents-ciprofloxacin and tinidazole-were immediately discontinued.

Supportive management was initiated promptly, following which the patient demonstrated rapid clinical improvement, with resolution of pruritus, cutaneous lesions, and systemic symptoms over the next few hours. Complete recovery was achieved within the same day. Re-exposure to the suspected drugs was avoided due to the risk of recurrence with potentially increased severity. The clear temporal association, rapid onset of symptoms, and complete resolution following drug withdrawal (positive dechallenge) strongly support a causal relationship between the ciprofloxacin–tinidazole combination and the observed adverse drug reaction, consistent with an anaphylactoid mechanism.

Causality and Severity Assessment

The suspected adverse drug reaction was reported to the Pharmacovigilance Programme of India (PvPI) and assessed using standardized pharmacovigilance tools. Causality assessment using the Naranjo Adverse Drug Reaction Probability Scale yielded a score of 4, indicating a possible adverse drug reaction [10]. This was based on the temporal association between drug administration and onset of symptoms, improvement following drug withdrawal (positive dechallenge), and the absence of re-exposure.

The severity of the reaction was evaluated using the Modified Hartwig and Siegel Severity Assessment Scale, which classified the event as Level 1 (mild severity). The reaction required drug withdrawal but did not necessitate intensive medical intervention, oxygen support, or prolonged hospitalization. Preventability assessment using the Schumock and Thornton criteria suggested that the reaction was not preventable, as it occurred on first exposure and could not have been anticipated based on prior history [11-12].

A summary of these assessments is presented in Table 1.

Table 1: Summary of ADR Assessment

Assessment Tool	Criteria Applied	Result	Interpretation
Naranjo Probability Scale[10]	Temporal relationship, improvement on withdrawal, no re-exposure.	Score = 4	Possible ADR
Modified Hartwig & Siegel Scale[11]	Drug withdrawal required, no hospitalization or oxygen support needed.	Level 1	Mild severity ADR
Schumock & Thornton Scale[12]	Could the reaction be prevented by a different dose or monitoring?	No	Unpreventable ADR (First exposure)

Discussion

Adverse drug reactions (ADRs) are defined as noxious and unintended responses to medications administered at therapeutic doses and represent a significant clinical concern in routine practice. ADRs can significantly impair patients' quality of life and place an increased burden on healthcare systems. If not promptly recognized and effectively managed, ADRs remain a major public health concern, contributing substantially to global morbidity and mortality [13-14].

Hypersensitivity reactions to antibiotics constitute an important proportion of ADRs. In the present case, the clinical presentation-characterized by rapid onset of pruritus, erythematous wheals, hypotension, and respiratory discomfort-is consistent with an acute anaphylactoid reaction, a form of immediate hypersensitivity that clinically resembles anaphylaxis but occurs through non–IgE-mediated mechanisms [1-2].

Unlike classical Type I hypersensitivity reactions, which require prior sensitization and IgE-mediated mast cell activation, anaphylactoid reactions can occur on first exposure to the offending agent. The underlying mechanism involves direct activation of mast cells and basophils, leading to rapid release of vasoactive mediators such as histamine, leukotrienes, and prostaglandins. These mediators increase vascular permeability, induce vasodilation, and produce smooth muscle effects, resulting in clinical manifestations including urticaria, flushing, hypotension, and respiratory symptoms. Although mechanistically distinct, anaphylactic and anaphylactoid reactions are often clinically indistinguishable at presentation. Consequently, both conditions are managed as medical emergencies requiring prompt recognition, discontinuation of the offending drug, and initiation of appropriate supportive therapy, including administration of epinephrine when indicated [1-2].

In the present case, the onset of symptoms shortly after the first dose of the ciprofloxacin-tinidazole combination supports a non–IgE-mediated immediate hypersensitivity reaction. Ciprofloxacin has been well documented to cause both anaphylactic and anaphylactoid reactions, including severe presentations occurring soon after administration. Similarly, tinidazole, although

less frequently implicated, has been associated with hypersensitivity reactions ranging from mild cutaneous manifestations to severe systemic reactions, particularly upon repeated exposure [7-9].

Previous reports have described cutaneous and systemic hypersensitivity reactions associated with ciprofloxacin, including urticaria, pruritus, and systemic involvement. Additionally, nitroimidazoles such as tinidazole have been reported to cause hypersensitivity reactions of increasing severity with repeated exposure, highlighting the importance of avoiding re-challenge. The use of fixed-dose combinations, although beneficial in providing broad antimicrobial coverage, may complicate causality assessment, as it becomes difficult to identify the individual offending agent. This is particularly relevant in the present case, where both ciprofloxacin and tinidazole are known to be associated with hypersensitivity reactions [7-9].

This case underscores the importance of maintaining a high index of suspicion for acute hypersensitivity reactions, even with commonly prescribed and generally well-tolerated antibiotic combinations. Early recognition, prompt discontinuation of the suspected drugs, and avoidance of re-exposure are essential to prevent recurrence and progression to potentially life-threatening complications.

Limitations

This case report has certain limitations. As a single-patient observation, the findings cannot be generalized to a broader population. The use of a fixed-dose combination limits the ability to identify the individual causative agent, as both ciprofloxacin and tinidazole are known to be associated with hypersensitivity reactions. Rechallenge with the suspected drugs was not performed due to ethical concerns, thereby limiting definitive confirmation of causality. Additionally, objective laboratory parameters such as serum tryptase levels were not measured, which could have provided further support for the diagnosis of an anaphylactoid reaction.

Future Directions

Further research is required to better understand the incidence and mechanisms of anaphylactoid reactions associated with commonly used antibiotic combinations. Large-scale pharmacovigilance studies and real-world data analysis may help identify risk factors and susceptible patient populations. There is also a need to develop standardized monitoring protocols for early detection of hypersensitivity reactions in patients receiving antimicrobial therapy. Increased awareness among clinicians regarding the potential for immediate reactions, even on first exposure, can improve early recognition and management. Strengthening pharmacovigilance systems and encouraging systematic reporting of such cases will enhance the understanding of rare adverse drug reactions and contribute to safer prescribing practices.

Conclusion

This case demonstrates an acute anaphylactoid reaction following administration of the ciprofloxacin-tinidazole fixed-dose combination. Despite being widely prescribed and generally well tolerated, these agents can rarely produce immediate hypersensitivity reactions, even upon first exposure. The case emphasizes the need for heightened clinical vigilance when prescribing commonly used antibiotics. Early identification, prompt discontinuation of the offending agents, and timely supportive management are crucial for favorable outcomes. Furthermore, reporting such cases contributes to pharmacovigilance efforts and enhances awareness of rare but clinically significant adverse drug reactions.

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