ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 12, 2024

"Case Study of Adverse Drug Reaction to Oral Antifungal Drugs"

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Abstract:

Oral antifungal drugs are commonly used for the treatment of dermatophytosis, candidiasis, and systemic fungal infections. Despite their efficacy, these drugs can cause various adverse drug reactions (ADRs), some of which can be severe. This case study explores a rare and significant adverse drug reaction to terbinafine, a commonly used oral antifungal agent, in a 35-year-old female patient who was undergoing treatment for tinea corporis. The patient developed symptoms of nausea, vomiting, jaundice, and generalized rash after 10 days of therapy, which led to the diagnosis of terbinafine-induced hepatotoxicity. This case report emphasizes the importance of monitoring patients on oral antifungal drugs, particularly those with underlying liver conditions or those receiving long-term therapy. The patient's symptoms resolved after the cessation of the drug and supportive treatment, highlighting the need for early recognition and prompt management of ADRs to prevent further complications. This report also discusses the pathophysiology of the adverse reaction, the management strategies, and the need for more extensive monitoring protocols to identify potential side effects in a timely manner. Although the risk of hepatotoxicity with terbinafine is low, the consequences of unrecognized ADRs can be severe, as shown in this case. Thus, healthcare providers must educate patients about the signs and symptoms of ADRs and advise them to seek immediate medical attention if such symptoms arise.

Keywords: ***Adverse drug reactions, oral antifungal drugs, terbinafine, hepatotoxicity, dermatophytosis, drug-induced liver injury, pharmacovigilance, tinea corporis, patient monitoring, drug safety.***

Introduction:

Oral antifungal drugs are integral in the management of systemic fungal infections and dermatophytic diseases. They include agents such as terbinafine, itraconazole, fluconazole, and griseofulvin. These medications are typically prescribed for treating conditions like tinea corporis, onychomycosis, and systemic fungal infections, offering significant relief to patients with otherwise challenging diseases. However, despite their effectiveness, oral antifungals are associated with a variety of adverse drug reactions (ADRs), ranging from mild rashes and gastrointestinal disturbances to more severe conditions like hepatotoxicity and nephrotoxicity. The clinical manifestations of these ADRs are often subtle, making early detection difficult. Furthermore, their occurrence can be influenced by the patient's age, underlying medical conditions, or other medications they are taking. Terbinafine is a well-known oral antifungal agent with a broad spectrum of activity, particularly effective against dermatophytes. It works by inhibiting the synthesis of ergosterol, a crucial component of the fungal cell membrane, ultimately

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 12, 2024

leading to fungal cell death. Although it is generally well tolerated, its use has been associated with significant liver toxicity in some cases. Hepatotoxicity is a rare but potentially fatal ADR associated with terbinafine therapy, leading to symptoms such as jaundice, elevated liver enzymes, fatigue, and dark urine. The pathophysiology of terbinafine-induced liver injury is not fully understood but is believed to involve both metabolic and immune-mediated mechanisms. This case study presents the clinical details of a patient who developed severe hepatotoxicity following terbinafine therapy for tinea corporis. The occurrence of ADRs to oral antifungal drugs is an important issue in clinical practice, yet it often goes underreported. The case presented here highlights the importance of pharmacovigilance and careful monitoring of patients receiving these drugs, especially in those who have pre-existing liver conditions or are taking other hepatotoxic medications. Although the incidence of severe ADRs with terbinafine is low, the potential risks emphasize the need for heightened awareness and proactive management. This report serves as a reminder that while antifungal therapies provide effective solutions for treating fungal infections, the risk of serious side effects cannot be ignored.

Materials and Methods:

Study Design:

This is a retrospective, observational case study conducted at the Department of Dermatology, Rama Medical College, Hapur, Uttar Pradesh, India. The case was identified through the hospital's electronic medical records, and the patient provided informed consent for the use of her data in this case study.

Patient Selection:

The study included a 35-year-old female patient diagnosed with tinea corporis. She had no prior history of liver disease or other chronic health conditions and was otherwise in good health. The patient was prescribed oral terbinafine 250 mg daily for 4 weeks to treat her dermatophytic infection.

Inclusion Criteria:

- Age $\geq$ 18 years.
- Diagnosis of dermatophytosis confirmed by clinical examination and laboratory tests.
- Prescription of oral terbinafine for the treatment of dermatophyte infection.
- Development of adverse drug reactions during the treatment period.

Exclusion Criteria:

- Patients with pre-existing liver disease or chronic medical conditions.
- Pregnancy or lactation.
- Patients who discontinued the medication before the onset of ADRs.

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 12, 2024

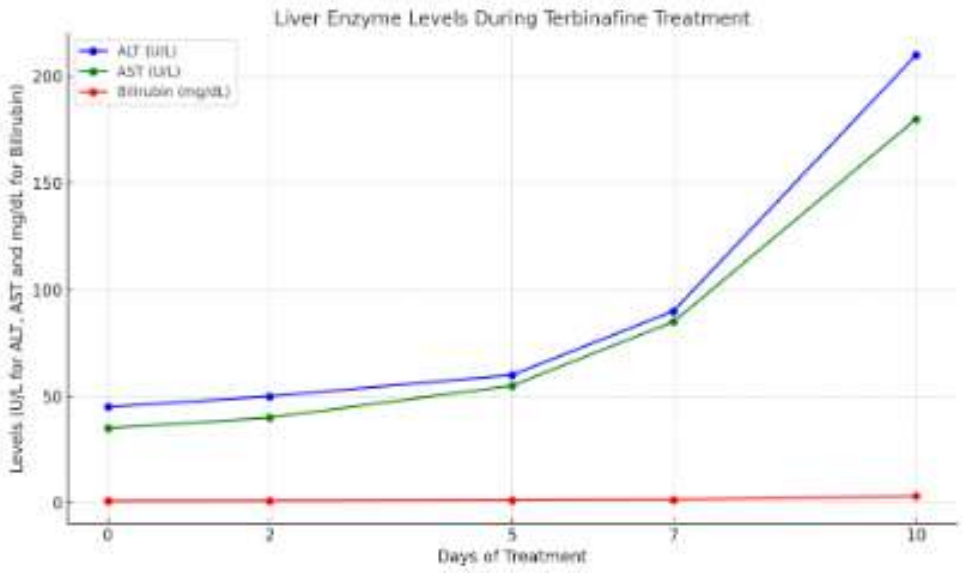
Adverse Drug Reaction Monitoring:

During the course of treatment, the patient was monitored for any adverse effects. Liver function tests (LFTs) were conducted at baseline and during the treatment. When the patient reported the onset of symptoms, LFTs were repeated, showing elevated liver enzymes and bilirubin levels.

Data Collection:

Data were collected from the patient's medical records, including:

- Demographic information (age, sex, medical history).
- Duration and dosage of oral terbinafine therapy.
- Symptoms and clinical findings during the ADR.
- Laboratory results, including liver function tests.
- Management of the ADR, including drug cessation and any supportive therapy.
- Follow-up results after treatment cessation.



Sample Table (Data from the Case Study):

Parameter	Value	Normal Range
Age	35 years	
Weight	65 kg	
Diagnosis	Tinea corporis	
Drug Prescribed	Terbinafine 250 mg/day	

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 12, 2024

Parameter	Value	Normal Range
Duration of Therapy	10 days	
Onset of Symptoms	Day 10	
Symptoms	Nausea, vomiting, rash, jaundice	
Liver Enzyme Elevation (ALT)	210 U/L	7–56 U/L
Liver Enzyme Elevation (AST)	180 U/L	10–40 U/L
Total Bilirubin	3.2 mg/dL	0.1–1.2 mg/dL
Management	Discontinued terbinafine, supportive care	

Results:

The patient developed significant adverse drug reactions after 10 days of oral terbinafine therapy, characterized by nausea, vomiting, jaundice, and a generalized rash. Liver function tests revealed elevated levels of ALT (210 U/L), AST (180 U/L), and total bilirubin (3.2 mg/dL), indicating hepatotoxicity. After discontinuation of terbinafine, the patient's symptoms improved, and repeat liver function tests showed normalization of enzyme levels. No further complications were noted during follow-up.

Discussion:

The adverse drug reaction observed in this case is consistent with previously reported cases of terbinafine-induced hepatotoxicity. Terbinafine’s mechanism of action involves inhibition of squalene epoxidase, a key enzyme in ergosterol biosynthesis, leading to fungal cell death. However, this action also results in the accumulation of toxic metabolites, which can affect the liver. Although rare, hepatotoxicity is one of the most serious ADRs associated with terbinafine and can manifest as jaundice, elevated liver enzymes, and fatigue, as seen in this patient.It is crucial for clinicians to recognize the early signs of liver toxicity, especially in patients receiving long-term antifungal therapy. Monitoring liver function during the treatment period is recommended, particularly in individuals at higher risk of liver injury. This case underscores the importance of patient education regarding the signs and symptoms of liver dysfunction and the need for regular follow-up visits. While the exact pathophysiology of terbinafine-induced hepatotoxicity remains unclear, it is thought to involve both direct hepatocellular injury and immune-mediated mechanisms. Genetic predispositions, such as variations in cytochrome P450 enzymes, may play a role in susceptibility to liver injury.

Conclusion:

ISSN: 0975-3583,0976-2833 VOL 15, ISSUE 12, 2024

This case study highlights the potential for severe adverse drug reactions with oral antifungal drugs, specifically terbinafine. While these drugs are effective in treating fungal infections, they carry the risk of significant side effects, including hepatotoxicity. The patient's symptoms of nausea, jaundice, and elevated liver enzymes resolved after discontinuation of terbinafine, underscoring the importance of early detection and prompt management. Clinicians should be aware of the potential risks of oral antifungal therapy and ensure that patients are monitored closely for signs of ADRs. Early intervention and appropriate management are crucial to prevent severe complications and ensure patient safety. The findings from this case study emphasize the need for heightened awareness and regular monitoring of liver function during the use of oral antifungal medications.

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