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Fixed Drug Eruption Likely Triggered by Antitubercular Drugs During Tuberculosis Treatment: A Case Report

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Abstract

Tuberculosis (TB) remains a major global health challenge, contributing significantly to mortality rates around the world. Treatment with anti-TB first line drug can frequently lead to side effects Hepatotoxicity, GI Discomfort & skin rashes but the severe skin reaction are uncommon. A 38-year-old male patient presented to a private clinic with concerns about painful, fluid-filled skin lesions that were also causing significant itching. These symptoms began to manifest 7 weeks following the initiation of anti-tubercular treatment (ATT). The patient sought medical attention due to the persistent and distressing nature of these skin issues, which had become a prominent concern alongside his ongoing treatment regimen. The presentation of these symptoms raised the possibility of a drug-induced reaction, necessitating a thorough evaluation to determine the cause and appropriate management of his condition. Fixed drug eruptions can be linked to various medications. But there were limited literature available about ATT induce fixed drug eruptions It is important to remain vigilant for such reactions during anti-tubercular therapy (ATT), as current attention is primarily on hepatotoxicity and neurotoxicity. We should also include this type of reaction in our clinical evaluations to ensure a comprehensive assessment of potential adverse effects. [*Bangladesh Journal of Infectious Diseases, December 2024;11(2):209-213*]

Keywords: Adverse reactions; anti-tubercular therapy; fixed drug eruptions; hepatotoxicity; pharmacovigilance; skin lesions

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Introduction

Tuberculosis is one of the foremost contributors to infectious disease-related mortality among adults worldwide[1]. For patients with drug-sensitive tuberculosis, the conventional treatment protocol generally starts with a combination of first-line oral medications: Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), and Ethambutol (E)[2]. The multi-drug regimen used in antituberculosis treatment can lead to a wide variety of cutaneous adverse drug reactions (CADR), from mild conditions like pruritus and fixed drug eruptions and urticaria to severe, potentially life-threatening reactions such as acute generalized exanthematous pustulosis (AGEP), Ototoxicity, Neophrotoxicity, Neurotoxicity Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN)[2-3]. Fixed

drug eruption (FDE) term Described in 1889 by Bourns, the condition was later named "fixed drug eruption" or by Brocq in 1894, reflecting its characteristic presentation and consistent localization in response to specific drugs[4]. Fixed drug eruption (FDE) presents as one or more well-defined, erythematous patches that typically appear in response to a systemic drug exposure and often leave behind residual hyperpigmentation after healing[5]. In fixed drug eruption, immunological re-exposure to the offending drug triggers a local immune response mediated by memory CD8+ T-cells, which release cytokines like interferon-gamma that contribute to inflammation and damage to the epidermal basal layer, leading to the destruction of melanocytes and keratinocytes by infiltrating T-cells and neutrophils[6].

Case Presentation

A 38-year-old male patient weighing 73 kg came to a private clinic with complaints of painful, fluid-filled skin lesions accompanied by severe itching. Upon detailed history, it was noted that he was diagnosed with Pulmonary tuberculosis 2 months ago and is currently undergoing treatment for pulmonary tuberculosis with a daily regimen of rifampicin 450 mg+ isoniazid 300 mg + ethambutol 800 mg with pyridoxine 10 mg. Currently from the last 7-10 days he sought medical attention due to the persistent and distressing nature of these skin issues i.e. erythematous patches on anterior neck, lower abdominal region, which had become a prominent concern alongside his ongoing treatment regimen. The presentation of these symptoms raised the possibility of a drug-induced reaction, necessitating a thorough evaluation to determine the cause and appropriate management of his condition. As a patient in combinations ATT leading to challenges in pinpointing the responsible medication. As per Medical History they are sensetized with seasonal allergies. During the physical examination, the patient appeared to be in stable overall health. Blood samples were collected immediately and sent for further investigation (Table 1).

Their respiratory rate was noted to be 24 breaths per minute, and their oxygen saturation was recorded at 96%, pulse rate is 95 BPM, blood pressure- 130/75 mmHg, temperature normal, CVS- s1s2 +, Motor response obeyed on command, best verbal response was oriented. The patient was treated with intravenous administration of Chlorpheniramine, a first-generation alkylamine antihistamine, and 4 mg of dexamethasone administered intramuscular, Mupirocin 2% ointment twice daily.

Table 1: Haematological Report

Name of the Tests	FDE		Normal Range	Units
	Before	After		
Alanine Aminotransferase (ALT)	35	36	5–50	U/L
Aspartate Aminotransferase (AST)	23	29	10–40	U/L
Alkaline Phosphatase (ALP)	120	135	45–150	U/L
Gamma-Glutamyl Transferase (GGT)	36	39	9–50	U/L
Total Bilirubin	0.32	0.28	0.1–1.2	mg/dL
Direct Bilirubin	0.01	0.03	0.0–0.3	mg/dL
Indirect Bilirubin	0.85	0.89	0.1–1.0	mg/dL
Albumin	4.6	4.6	3.5–5.0	g/dL
Prothrombin Time (PT)	12	11.5	11–13.5	seconds
International Normalized Ratio (INR)	0.9	0.85	0.8–1.1	ratio
Hemoglobin (Hb)	14	13.2	14–18	g/dL
White Blood Cell Count (WBC)	12	32	4.5–11.0	x10^9/L
Platelets	175	120	150–450	x10^9/L
Mean Corpuscular Volume (MCV)	85	78	80–100	fL (femtoliters)
Mean Corpuscular Hemoglobin (MCH)	12	18	27–31	pg (picograms)
Mean Corpuscular Hemoglobin Concentration (MCHC)	20	19	32–36	g/dL
Red Blood Cell Count (RBC)	4.12	4.45	Men:4.5-6.0	x10^12/L
C-Reactive Protein (CRP)	2.5	20	< 3.0	mg/L
Erythrocyte Sedimentation Rate (ESR)	35	80	Men:0–15	mm/hr

Table 2: Naranjo Scale with interpretation

Sl.No.	Please answer the Following Questionnaire and Give the Pertinent Score	Yes	No	Don't know	Score
1	Are there previous *conclusive* reports on this reaction?	1	0	0	0
2	Did the adverse event occur after the suspected drug was administered?	2	-1	0	1
3	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	1	0	0	1
4	Did the adverse reaction reappear when the drug was readministered?	2	-1	0	0
5	Are there alternative causes (other than the drug) that could have on their own caused the reaction?	-1	2	0	2
6	Did the reaction reappear when a placebo was given?	-1	1	0	0
7	Was the drug detected in the (or other fluids) in concentrations known to be toxic?	1	0	0	0
8	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	1	0	0	0
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	1	0	0	0
10	Was the adverse event confirmed by any objective evidence?	1	0	0	1
Total					5
Interpretation					
	definite	if the overall score is 9 or greater			
	probable	for a score of 5 to 8			
	possible	for 1 to 4			
	doubtful	if the score is 0			

Due to this suspected reaction, the standard antitubercular regimen was promptly halted to prevent any further complications. Based on the ongoing therapy and clinical evaluation to determine the root cause and prevent further complications, we can conclude that ATT regimen is the primary cause for this type of eruption, according to the Naranjo adverse drug reaction probability scale score is 5 (Table2). The drug is a likely cause of the adverse reaction.

Discussion

Fixed Drug Eruptions (FDEs) remain a significant and increasingly recognized issue in clinical practice, with the list of potential offending drugs continually growing[7]. FDEs can be triggered by a range of medications, and cross-reactivity among drugs within the same class can provoke similar eruptions, making it crucial for physicians to exercise heightened vigilance when prescribing such medications.

While many cases of FDE are relatively benign and resolve with discontinuation of the offending drug, there are instances where the eruptions can cover extensive areas of the skin and may present as bullous lesions. In these more severe cases, the eruptions can lead to considerable discomfort and, in rare circumstances, pose serious health risks[8-9]. Thus, careful consideration and monitoring are essential to mitigate potential adverse effects and ensure patient safety.

Physicians must remain aware of the evolving list of drugs associated with FDEs and stay informed about potential cross-reactivity to manage and prevent these reactions effectively. Therefore, effective management of Fixed Drug Eruptions (FDE) necessitates identifying the specific drug or antigen responsible for the reaction[10-11]. It is crucial to avoid these causative agents to prevent recurrence of the eruption. Currently, the rechallenge test remains the most dependable method for confirming the offending drug; however, the use of skin tests for diagnosis is increasingly gaining prominence[12].

As advancements in diagnostic techniques continue, these skin tests are becoming a valuable tool in accurately identifying the triggers of FDE and guiding appropriate therapeutic strategies to ensure better patient outcomes and minimize the risk of future reactions.

Conclusion

Fixed Drug Eruption (FDE) is a notable yet underappreciated cutaneous adverse drug reaction, including its occurrence with anti-tubercular therapy (ATT). This case underscores the critical importance of timely recognition and intervention to avert complications. Discontinuation of the implicated medication, combined with targeted symptomatic management, facilitated the patient's recovery. Given the potential for FDE to mimic more severe dermatological conditions, heightened clinical awareness is imperative. Emerging diagnostic modalities, particularly skin testing, are proving invaluable in pinpointing offending agents with precision. Such advancements enable the formulation of safer treatment regimens, reducing recurrence risk and enhancing patient safety and therapeutic outcomes.

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Conflict of Interest
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Data Availability
Any questions regarding the availability of the study's supporti ng data should be addressed to the corresponding author, who can provide it upon justifiable request.

Ethics Approval and Consent to Participate
The written consent was secured from the patient's legal guardian for the publication of any potentially identifying details.

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