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DRESS Syndrome Following Anti-Tubercular Therapy: A Case Report

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Abstract

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a rare, severe cutaneous adverse reaction characterized by widespread rash, fever, hematologic abnormalities, and potential multi-organ involvement. It is most often associated with anticonvulsants, sulfonamides, and allopurinol, while anti-tubercular drugs (ATT) are rarely implicated. We report the case of a 66-year-old female with a history of tuberculous pericardial effusion who developed recurrent diffuse erythematous, blanchable maculopapular rashes with facial edema and systemic symptoms following re-exposure to anti-tubercular therapy. Her symptoms were temporally related to ATT administration, strongly supporting a diagnosis of ATT-induced DRESS syndrome. The patient's past medical history included hypothyroidism and cerebrovascular accident, but no significant drug allergies. Clinical evaluation revealed fever, facial swelling, generalized pruritic rash, and systemic complaints without significant abnormalities on chest or abdominal examination. Prompt discontinuation of ATT and supportive management led to clinical improvement.

This case underscores the importance of early recognition of DRESS, even with uncommon culprits such as anti-tubercular drugs. Given the global prevalence of tuberculosis, ATT-induced DRESS poses unique therapeutic challenges, particularly in balancing drug hypersensitivity management with effective tuberculosis treatment. Clinician awareness and timely intervention remain key to improving outcomes in this potentially life-threatening condition.

Keywords: Antitubercular therapy, DRESS, eosinophilia

Introduction

DRESS syndrome is a rare but potentially life-threatening severe cutaneous adverse reaction characterized by a constellation of clinical findings including extensive skin eruption, fever, hematologic abnormalities (eosinophilia or atypical lymphocytosis), and multi-organ involvement .[1,2] First described in the 1990s, its incidence is estimated to be between 1 in 1,000 to 1 in 10,000 drug exposures, with a reported mortality rate of up to 10%. The pathogenesis is not fully understood but is believed to involve a complex interplay of drug-specific immune responses, viral reactivation (particularly human herpesvirus-6), and genetic susceptibility, including associations with certain HLA alleles.[3,4]

DRESS typically presents 2–8 weeks after exposure to the offending drug, most commonly anticonvulsants, sulfonamides, allopurinol, and certain antibiotics.[5] Clinical recognition can be challenging, as symptoms often mimic infectious or autoimmune conditions. Early diagnosis and withdrawal of the culprit drug are crucial to reducing morbidity and mortality. [6] Although ATT is rarely implicated, reported cases have shown that these agents can trigger severe hypersensitivity reactions, posing significant therapeutic challenges, particularly in regions where tuberculosis remains highly prevalent. [7] Here, we present a case of DRESS syndrome secondary to anti-tubercular therapy, highlighting the diagnostic challenges and clinical course, and emphasizing the importance of prompt recognition and management.

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Case Presentation

A 66-year-old married female presented to the emergency department with a three-day history of fever, reaching up to 102°F, continuous in nature, and associated with chills and rigors. She also complained of progressive facial swelling, diffuse pruritic rashes (starting from right thigh) for 15 days, increasing shortness of breath, and tingling sensation of the mouth with difficulty in swallowing during meals. She had been diagnosed with tuberculous pericardial effusion (Figure 1) four months prior and was started on anti-tubercular therapy (ATT).

Within one week of initiating ATT, she developed generalized pruritic rashes (starting from right thigh to whole limg then to abdomen then to the face), leading to discontinuation of therapy. ATT was restarted after two weeks once the rashes had subsided, but she again developed similar rashes at the same sites with increasing severity. Her past medical history was significant for hypothyroidism, diagnosed 12 years earlier and managed with 125 mcg levothyroxine daily, and a stroke 8 years ago, resulting in residual left-sided weakness involving the face, upper and lower limbs. She was a non-smoker, consumed alcohol occasionally, and her family history was unremarkable. On examination, she was alert and oriented with a glassgow comma score of 15/15. Her vital signs were stable except for fever. There was no pallor, icterus, lymphadenopathy, or dehydration however mild edema was present. Cutaneous examination revealed diffuse erythematous, blanchable maculopapular rashes over the entire body including palm and sole, associated with facial edema. (Figure 2) however there was no mucousal involvement.

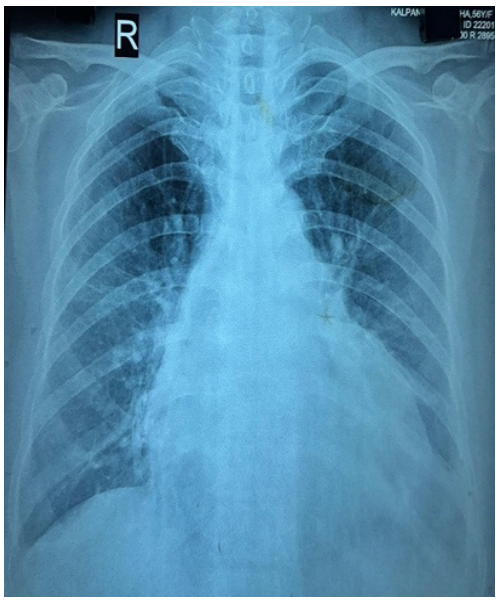

Figure 1: Chest X-ray (posteroanterior view) showing cardiomegaly with a globular cardiac shadow, suggestive of pericardial effusion.

Chest and abdominal examinations were unremarkable. The laboratory investigations revealed leukocytosis (TLC 14,700/cumm) with eosinophilia (8%), along with elevated liver enzymes (SGPT/ALT 189.72 U/L, SGOT/AST 72.37 U/L) and hyperbilirubinemia (total bilirubin 6.07 µmol/L), consistent with systemic involvement in DRESS syndrome. Based on the RegiSCAR criteria, our patient achieved a score of 5–7, consistent with a probable to definite diagnosis of DRESS syndrome secondary to anti-tubercular therapy. Based on the temporal association with ATT re-exposure, widespread rash, facial edema , and clinical course, a diagnosis of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome secondary to anti-tubercular therapy was made.

The patient was initially started on standard first-line anti-tubercular therapy (ATT) with 2HRZE + 4HR (two months of isoniazid, rifampicin, pyrazinamide,

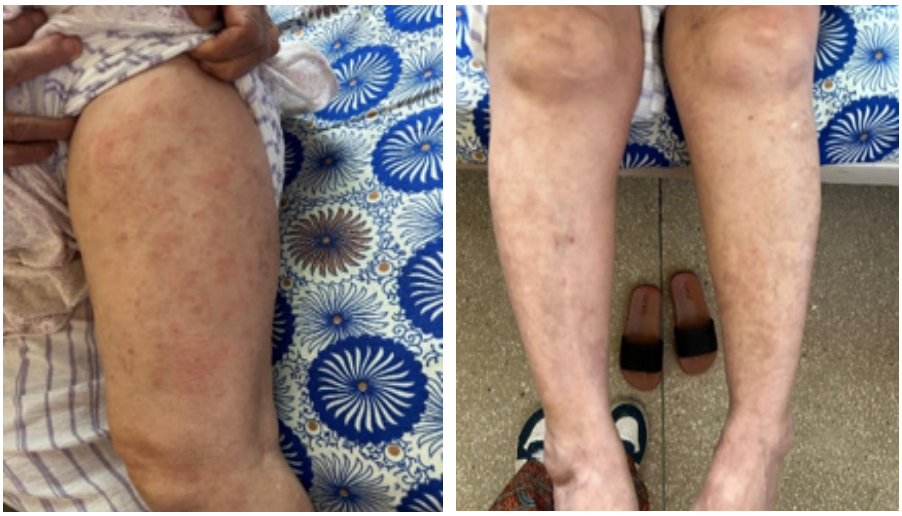

Figure 2a, 2b: Clinical photographs showing diffuse erythematous maculopapular rash involving the lower limbs. The lesions are widespread, non-blanchable, and confluent in areas, associated with mild edema. The rash demonstrates symmetrical distribution over both legs and thighs, consistent with a drug-induced hypersensitivity reaction.

and ethambutol followed by four months of isoniazid and rifampicin). However, within three weeks of initiation, the patient developed widespread rash, fever, and systemic symptoms consistent with DRESS syndrome, prompting immediate withdrawal of ATT. Supportive management was provided, including antipyretics, systemic corticosteroids, antihistamines, and monitoring of organ function. The patient showed gradual clinical improvement with resolution of fever, cutaneous lesions, and normalization of laboratory abnormalities over subsequent follow-up. Re-challenge with ATT was deferred, and the patient continues under regular clinical surveillance for tuberculosis control and drug hypersensitivity monitoring.

Discussion

DRESS syndrome is one of the most severe manifestations of drug-induced hypersensitivity, with a clinical course that can be prolonged and fatal if unrecognized. The syndrome is characterized by cutaneous eruptions, fever, hematologic abnormalities, and internal organ involvement. Mortality rates are reported between 2–10%, primarily due to fulminant hepatic failure, severe myocarditis, or multi-organ dysfunction .[1,2,4] The diagnosis of DRESS remains challenging due to its heterogeneous clinical presentation and overlap with other dermatologic and systemic disorders such as Stevens–Johnson syndrome, acute viral infections, and sepsis. [8] Several diagnostic criteria have been proposed, including those of the European Registry of Severe Cutaneous Adverse Reactions (RegiSCAR). According to RegiSCAR, the presence of fever, acute rash, lymphadenopathy, hematological abnormalities (eosinophilia or atypical lymphocytosis), and internal organ involvement strongly support the diagnosis .[9] In this case, the patient presented with fever, widespread non-blanchable maculopapular rash, facial edema, and systemic symptoms in close temporal relation to anti-tubercular therapy re-exposure, fulfilling the major diagnostic features.

The pathogenesis of DRESS is multifactorial and not completely understood. Proposed mechanisms include genetic predisposition, drug-induced immune dysregulation, and viral reactivation, particularly of human herpesvirus-6 and Epstein–Barr virus. Genetic associations, such as specific HLA alleles, have been implicated with certain drugs, although limited data exist for anti-tubercular agents .[6,10] Immunopathology is characterized by drug-specific T-cell activation and massive cytokine release, leading to systemic inflammation and organ dysfunction.[11] While most DRESS cases are associated with anticonvulsants, sulfonamides, allopurinol, and antibiotics, anti-tubercular drugs such as isoniazid, rifampicin, pyrazinamide, and ethambutol have also been implicated, albeit rarely. [5,7] Given the global burden of tuberculosis, recognition of ATT as a potential cause of DRESS is clinically important. Withdrawal of the offending drug remains the cornerstone of therapy, but re-initiation of ATT poses significant challenges, especially in endemic regions where alternative regimens may be limited. [12]

The first and most critical step in management is immediate discontinuation of the suspected drug. Supportive care includes systemic corticosteroids, which are widely used despite the lack of randomized controlled trials, and symptomatic management of cutaneous and systemic manifestations. [13] In refractory or relapsing cases, additional immunosuppressive therapies such as intravenous immunoglobulin (IVIG), cyclosporine, or mycophenolate mofetil have been reported. Our patient responded to discontinuation of ATT and systemic management, underscoring the importance of early clinical recognition. [14]

Conclusion

DRESS syndrome is a rare but potentially fatal adverse drug reaction that requires a high index of clinical suspicion for timely diagnosis. Although anti-tubercular drugs are infrequently implicated, this case illustrates that they can serve as important triggers, particularly upon re-exposure. Prompt recognition, immediate discontinuation of the offending drug, and initiation of appropriate supportive therapy remain the cornerstone of management. In tuberculosis-endemic regions, ATT-induced DRESS poses a unique therapeutic challenge, underscoring the need for individualized treatment strategies and multidisciplinary collaboration. Early intervention not only improves outcomes but also reduces the risk of life-threatening complications, highlighting the importance of clinician awareness of this rare but serious entity.

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