Case Report

ANTI TUBERCULOSIS THERAPY INDUCED DRESS SYNDROME

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ABSTRACT:

Background: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) represents a rare yet potentially fatal hypersensitivity reaction. Although various medications have been associated with this condition, rifampicin is an infrequent culprit.

Case Presentation: A 72-year-old male with hypertension and a history of spinal surgeries presented with fever, widespread pruritic rash, and edema following three weeks of empirical treatment with Rifampicin. Assessment using RegiSCAR criteria resulted in a score of 6, confirming a definitive diagnosis of DRESS syndrome. Laboratory tests indicated eosinophilia (30%), elevated liver enzymes, and increased serum IgE levels (409 IU/ml). The patient was treated with intravenous corticosteroids, followed by a tapering oral regimen, which resulted in significant clinical and biochemical improvement.

Conclusion: Timely identification and immediate cessation of adverse effect of drug are crucial for achieving favorable outcomes in DRESS syndrome. This case underscores the importance of clinical awareness, even with frequently prescribed medications such as Rifampicin.

Keywords: DRESS syndrome, Rifampicin, anti-tuberculosis therapy, hypersensitivity reaction, eosinophilia, RegiSCAR, systemic drug reaction, steroid therapy, dermatologic emergency, adverse drug reaction

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INTRODUCTION

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a potentially life-threatening, delayed, type 4 hypersensitivity reaction to drugs. It manifests with multisystem involvement, as well as cutaneous and hematological symptoms, appearing 2-8 weeks after the initiation of the implicated medications, with a mortality rate of 8-10 percent.[1] Although literature on this condition is limited and inadequate in the Pakistani context, the hematological symptoms typically include leukocytosis and significant eosinophilia, along with the presence of atypical lymphocytes. The liver is the most commonly affected organ, involved in 60-80 percent of cases.[2,3] Cutaneous symptoms may begin with prodromal signs such as itching, which can progress to a morbilliform or maculopapular rash, along with other skin manifestations that may persist long after drug exposure. The International Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) criteria are utilized worldwide for clinical diagnosis, relying on clinical signs and symptoms in conjunction with laboratory findings, including eosinophilia, elevated leukocyte counts, and abnormal liver enzymes.[2]

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A total of 44 drugs have been identified in the literature as potential triggers, including antipsychotics, antiepileptics, beta-lactam antibiotics, and antituberculosis medications, with Carbamazepine being the most frequently implicated.[4] Rifampicin is infrequently reported as a causative agent of DRESS Syndrome. We encountered a case of DRESS Syndrome where Rifampicin was determined to be the causative drug, as evidenced by the timing of symptom onset following the initiation of the medication.

CASE PRESENTATION

A 72-year-old male presented to the Emergency Department of Farooq Hospital (Westwood Branch, Lahore) with complaints of fever, generalized rash, generalized edema, and severe itching. He had a history of undergoing spinal fixation twice in the past due to spinal stenosis (Fig.1), which raised concerns for suspected osteomyelitis/infection. Consequently, he had spinal implant removal performed one week prior. The patient had also taken Rifampicin empirically for three weeks. On the third postoperative day, he returned to the hospital with the aforementioned complaints. Prior to this, during his admission for spinal implant removal, he exhibited a mild rash across his body (suspected Interstitial Nephritis secondary to Rifampicin), which nearly resolved by the time of discharge. However, the rash re-emerged with a severe flare-up affecting his entire body, including his face, accompanied by generalized and facial edema. Upon examination, the rash was morbilliform (Fig.3), covering approximately 70-80% of his body, with significant redness and edema. Given the patient's previous history of three weeks of Anti-Tuberculosis Therapy (Rifampicin) and the negative results for the following tests (Antinuclear Antibody, Extractable Nuclear Antigen, Complement component 3, Complement component 4, Mycoplasma Serology, Epstein-Barr Virus Serology, Human Herpes Virus-6 Serology, Varicella Zoster Virus Serology, Herpes Simplex Virus Serology, Hepatitis B and Hepatitis C Serology), a provisional diagnosis of DRESS SYNDROME was established. To confirm the diagnosis, the RegiSCAR scoring system was utilized, which categorizes cases as “negative case,” “probable case,” or “definitive case” of DRESS Syndrome.[2] In this instance, the score was determined to be “6,” thus classifying it as a “definitive case of DRESS Syndrome.” The causative drug was promptly discontinued, and the patient was admitted to the hospital. As fever was also one of the presenting complaints, blood cultures and sensitivity tests were conducted, along with all other baseline assessments, including Serum Immunoglobulin E levels. The patient's Eosinophil count was significantly elevated at 30%, and Serum Immunoglobulin E levels were also increased at 409 IU/ml. In contrast, his Procalcitonin level was recorded at 0.20. He commenced treatment with IV Dexamethasone at a dosage of 4mg every 8 hours for the first two days, after which the dosage was adjusted to 4mg every 12 hours until the fifth day post-admission. The patient was discharged on the fifth day post-admission, transitioning from IV Dexamethasone to oral Prednisolone (Tab Deltacortil) at a daily dosage of 45mg, administered as three tablets orally three times a day (5mg per tablet). Additionally, topical steroids were applied, including a mild topical steroid for facial application. It is noteworthy that this patient had a medical history of hypertension and allergic rhinitis. The DRESS SYNDROME experienced by the patient resulted in an exacerbation of acute asthma, accompanied by abnormalities in the liver profile, likely due to inflammatory changes in the bile ducts and lungs (refer to Fig.2), secondary to the DRESS SYNDROME. Following the prescribed treatment, the rash began to diminish, and the itching reduced significantly, with the rash decreasing by nearly 90% by the seventh day (see Fig.4). There was a marked improvement in his laboratory results, as detailed below:

Furthermore, his blood culture sensitivity indicated no bacterial growth. It is additionally intended to gradually reduce the dosage of Prednisolone on a weekly basis, aiming to reach the minimum dose by the eighth week, thereby discontinuing the steroids entirely. Furthermore, a sequential follow-up of Immunoglobulin E levels, C-Reactive Protein, Liver Function Tests, and Renal Function Tests will be conducted accordingly. Two days post-discharge, the patient showed significant improvement with a 90% recovery in the rash (Fig.4), along with all pertinent systematic profiles.

Table 1: Laboratory Investigations (day wise)

Parameter	Day 1	Day 2	Day 3	Day 4
Eosinophils (%)	30	4	6	9
Total Leukocyte Count (×10⁹/L)	15.0	11.8	10.4	7.6
C-Reactive Protein (mg/L)	178.0	97.2	40.9	36.4
Alkaline Phosphatase (U/L)	1092	1009	1174	987
Gamma Glutamyl Transferase (U/L)	986	1013	1246	1116
Serum Albumin (g/dL)	2.9	3.0	3.1	—
Serum Urea (mg/dL)	44	36	25	35
Serum Creatinine (mg/dL)	1.3	1.1	1.0	—

Table 2: Diagnosis of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS Syndrome) using Regi SCAR Scoring System

Criteria	Result in our case	Score
Fever (≥ 38.5 oC)	Yes	0
Enlarged lymph nodes	No/Unknown	0
Atypical Lymphocytes	Yes	+1
Eosinophilia	≥ 1500 cells or ≥ 20%	+2
Skin Rash Extent >50%	Yes	+1
At least two of: edema, infiltration, purpura, scaling	Yes	+1
Biopsy suggesting DRESS	No	-1
Internal Organ Involved	≥ 2	+2
Resolution in >15 days	No/Unknown	-1
Alternative diagnosis excluded (by ≥ 3 biological investigations) Yes +1		
Total Score=6 (Definitive Case)		

Table 3: Changings in Investigations (at the time of admission versus at the time of discharge)

Parameter	Normal Value Range	Value at the time of Admission	Value at the time of Discharge
Eosinophils	1-4 %	30%	2%
Total Leukocyte Count	4-11 x 109/L	15.0x109 /l	7.6x109 /l
C-Reactive Protein	Less than 0.700	178.0	36.4
Alkaline Phosphatase U/L	44-147	1092	987
Gamma Glutamyl Transferase U/L	10-40	986	1116
Serum Albumin g/dL	3.5-5.2	2.9	3.1
Serum Urea mg/dL	10-50	44	35
Serum Creatinine mg/dL	0.6-1.1	1.3	1.0

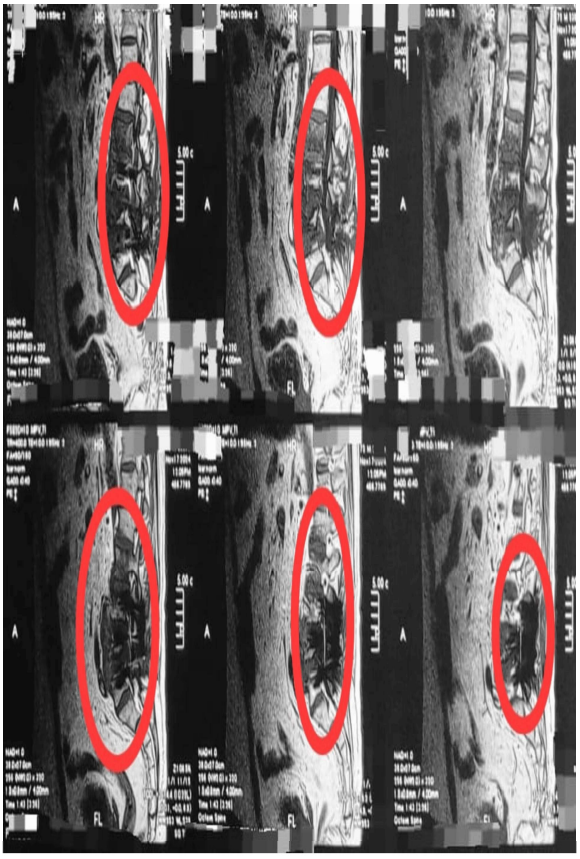

FIGURE 1: MRI Lumbosacral Spine: Stenosis

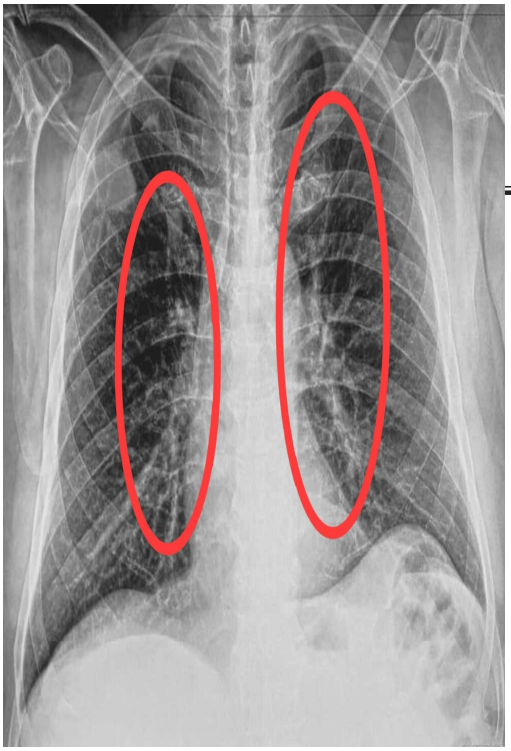

Figure 2: X-Ray Chest: Prominent Hilar Markings

Figure 3: Morbilliform Rash on the day of Presentation (Day 1)

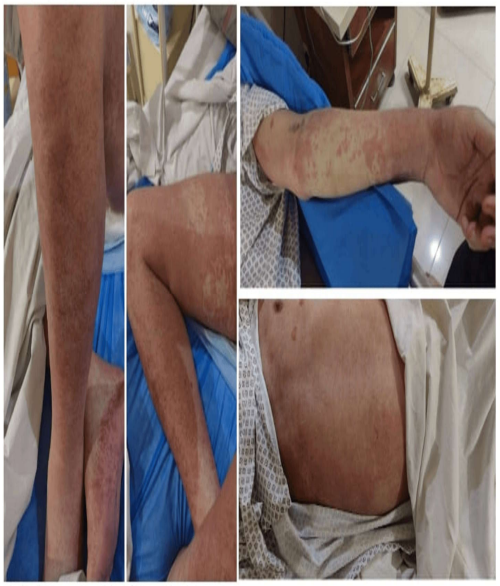

Figure 4: Rash on Day 7 (2 days after discharge); 90% recovery

DISCUSSION

DRESS Syndrome is classified as a Type IV B hypersensitivity reaction, which is marked by symptoms such as fever, an erythematous morbilliform skin rash, facial swelling, and eosinophilia, alongside the involvement of various internal organs, primarily the liver, lungs, and kidneys. Hematological findings typically include leukocytosis and eosinophilia.[3] The diagnosis is challenging due to the varying latency periods associated with different drugs and combinations, as well as the diverse presentation of symptoms. The diagnosis of DRESS Syndrome is established based on the widely accepted RegiSCAR Criteria.[3] The precise pathogenesis of DRESS Syndrome remains unclear; however, three key components involved in its pathogenesis include genetic predisposition linked to specific Human Leukocyte Antigens, the metabolic pathways of drugs, and the reactivation of latent viruses.[4,5] In the case presented, a 54-year-old male had a history of using an Anti Tuberculosis Therapy drug for over three weeks prior to his hospital admission for osteomyelitis, which resulted in DRESS Syndrome characterized by a rash covering more than half of his body, eosinophilia, and other systemic manifestations. This was diagnosed as a definitive case of DRESS Syndrome, with a score of 6 according to the RegiSCAR criteria. The common drug categories implicated in DRESS Syndrome include aromatic anticonvulsants, antimicrobials, antituberculosis agents, anti-inflammatory medications, antivirals, and herbal remedies.[6] Anti Tuberculosis Therapy is a fixed drug combination primarily utilized for tuberculosis; however, in this instance, the patient was using it as an empirical treatment for his spinal osteomyelitis. DRESS Syndrome resulting from first-line Anti Tuberculosis Therapy is exceedingly rare, and identifying the culprit drug is complicated due to the combination of therapies. All Anti Tuberculosis Therapy medications have the potential to induce DRESS Syndrome, but Rifampicin is the most frequently associated drug among first-line Anti Tuberculosis agents. Consequently, it is crucial to recognize the early signs and symptoms of DRESS Syndrome in patients undergoing Anti Tuberculosis Therapy who may be at risk of developing this syndrome.[6,7]

CONCLUSION

Timely identification and immediate cessation of adverse effect of drug are crucial for achieving favorable outcomes in DRESS syndrome. This case underscores the importance of clinical awareness, even with frequently prescribed medications such as Rifampicin.

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AUTHOR'S CONTRIBUTIONS

OF: Concept, Article writing

HJG: Abstract, Introduction

IMI: Case Description

US: Critical Approval

MRM: Data Analysis

MOR: Data Collection

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CONFLICT OF INTEREST

None

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