Case Report

Elevated Liver Transaminase Levels as the Principal Characteristic of Drug Eosinophilia and Systemic Symptoms (DRESS) Syndrome: A Case Report

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Abstract

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is a detrimental reaction of drug presenting as fever, skin eruptions, and internal organs involvement. DRESS has an increased mortality rate, estimated at 3 to 10%, primarily because of organ failure and sepsis. A female aged 24 years, attended the hospital complaining of pruritus and widespread red maculopapular rash covering her entire body, accompanied by fine yellowish scaling. The patient also exhibited jaundice, passed melena stools that later turned pale, and had dark tea-colored urine. Laboratory results revealed a high white blood cell count of 11.280. The patient's SGOT was 358 (N:<35), SGPT 524 (N:<41), total bilirubin 23.61 (N:0.1-1.2), indirect bilirubin 14.90, and direct bilirubin 8.71. Based on the J-Scar and Regis-Scar diagnostic criteria, this case was categorized as probable. Severe DRESS Syndrome symptoms pose a life-threatening risk due to their multi-organ involvement. Clinical manifestations encompass erythematous lesions, facial edema, high fever, lymphadenopathy, leukocytosis accompanied by eosinophilia. The more severe presentations involve visceral symptoms such as hepatitis, encephalitis, pneumonitis, hemophagocytic syndrome, and multi-organ failure. Therefore, effective treatment methods are very important for managing DRESS. To conclued, this case represents a probable diagnosis of DRESS Syndrome according to the J-Scar and Regis-Scar criteria. Organ involvement in this case primarily affected the liver, as revealed by elevated transaminase levels. If the patient makes a full recovery, a favorable prognosis is anticipated in terms of their overall quality of life.

Keywords: Aminotransferases; Drug-Related Side Effects and Adverse Reactions; Drug Hypersensitivity Syndrome; Liver Function Tests; Multiple Organ Failure

Introduction

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is an adverse reaction to a drug, that is relatively rare but can be severe in nature. It is characterized by symptoms such as fever, skin eruptions, and involving single or multiple internal organs in the body.[1,2] DRESS is has many names, including Drug-Induced Hypersensitivity Syndrome (DIHS) and Drug-Induced Multiorgan Delayed Hypersensitivity Syndrome (DIDMOHS).[3] The prevalence of DRESS is low, occurring in only 1 in 1.000 to 1 in 10.000 exposures. It tends to occur more frequently in women than in men.[3,4] DRESS can have a high mortality rate, estimated at approximately 3% to 10%, with the majority of deaths attributed to organ failure and sepsis.

This syndrome is a drug-induced hypersensitivity reaction and often presents as skin eruptions, hematological abnormalities (such as eosinophilia and leukocytosis), lymphadenopathy, and involving internal organs, including the liver and kidneys. Skin eruptions can manifest as a widespread morbilliform exanthem, often accompanied by fever.[4] A comprehensive case series of DRESS, found a significant proportion of patients (91%) experienced involvement of internal organ, with liver damage as highly prevelant visceral manifestation (75%).[5] To better understand the case report and the characteristics of DRESS related to elevated transaminase levels, we present and discuss an analysis of these transaminase levels, their association with DRESS, and any other pertinent factors.

Case Report

A female patient aged 28 years, attended our hospital complaining of itching with a maculopapular rash accompanied by fine yellowish scales covering her entire body (Figure 1 and Figure 2). Additionally, she had multiple, sudden-onset, and progressively increasing ulcerative lesions. The patient reported that these symptoms had been present for the past three weeks. Initially, redness appeared on her abdomen and subsequently spread to her arms, legs, and face. She also reported experiencing intermittent fever over the past three weeks. Notably, the patient had undergone a caesarean section one week before eruption of the red rash on her body. Over the past month, she had been taking various medications following the surgery, including vitamin B complex, cetirizine, cefadroxil, mefenamic acid, amoxicillin, paracetamol, dexamethasone and herbal extract to facilitate breast milk. The patient denied having any known allergies to specific medications. She further reported pale-colored stools and concentrated dark tea-colored urine. In the last three days, her eyes had also begun to turn yellow.

The patient, a homemaker, had not returned to work and had given birth one month earlier. Upon arrival, the patient appeared moderately ill with a Glasgow Coma Scale (GCS) score of 15. Her temperature 38.6 celcius, blood pressure on admission noted to be 120/80 mmHg , her pulse rate was 80 beats/minute, and her respiratory rate was 20 breaths/minute.

Laboratory tests performed on the patient revealed leucocytosis of 11.280 (N: 3.500-11.000) and elevated liver function markers and bilirubin levels indicative of acute transaminitis. Her SGOT level was 358 (N: <35), SGPT was 524 (N: <41), total bilirubin was 23.61 (N: 0.1-1.2), indirect bilirubin was 14.90, and direct bilirubin was 8.71. Hepatitis B and HIV was non-reactive. A complete set of laboratory results is provided in Table 1.

The patient was treated with corticosteroid and other supportive therapy. After three days of hospitalization in our secondary hospital, the patient did not show improvement and was then referred to a higher tertiary hospital to receive more advance care.

Table 1. Laboratory results of the patient

Laboratory	Day-1	Normal
Haemoglobin (g/dl)	11.7	11.7 – 15.5
MCV (fl)	81.9	80.0 – 100.0
MCH (pg)	27.5	26,0 - 34,0
MCHC	33.6	32,0 - 36,0
Leucocyte (/µl)	11.280	4.700 – 11.300
Hematocrit (%)	34.8	35.0 – 47.0
Thrombosit (/ul)	243.000	150.000 - 440.000
Diff count (%)		
- Eosinophil	0.1	0 – 4
- Basophil	0.5	0 – 1
- Neutrophil	46.7	51 – 67
- Lymphocyte	47.6	25 – 33
- Monocyte	5.1	2 – 5
SGOT	358	< 31
SGPT	524	< 31
Total Bilirubin (mg/dl)	23.61	0.1 -1.2
Direct Bilirubin (mg/dl)	8.71	
Indirect Bilirubin (mg/dl)	14.90	
BUN	10.8	7-20
Cr	0.7	0.7-1.2
Na	131	136-150
K	3.8	3.5-5.5
Cl	103	96-110

Table 2. J-Scar score

J-Scar Score
1. A maculopapular rash developing > 3weeks after drug initiation
2. Clinical symptoms continuing >2weeks after stopping therapy
3. Fever > 38oC
4. Liver abnormalities (SGOT>100 IU/L) or other organ involvement
5. Haematology abnormalities:
● Leucocytosis (>11*109/L)
● Atipical limphocytes (>5%)
● Eosinophilia (>1.5*109/L)
6. Limphadenopaty
7. HHV-6 reactivation
Total score:
7=Typical DRESS
5=Atypical DRESS
<5=Consider other diagnosis

Table 3. RegiSCAR-Score

Variable	No	Yes	Unknown
Fever (≥38,5oC)	-1	(0)	(-1)
Enlarged lymph nodes (≥2 sites, ≥1 cm)	0	1	0
Atipical lymphocyte	0	(1)	0
Eosinophilia	(0)		0
700-1499 or 10%-19,9%		1	
≥1500 or ≥20%		2	
Rash skin	0	◯	0
Extend >50%	0	1	0
At least 2 of: edema, infiltration, purpura, scaling	(-1)	(1)	0
Biopsy suggesting DRESS	-1	0	0
Internal organ involvement	0	◯	0
One		1	
Two or more	0	(2)	
Resolution in ≥ 15 days	(-1)	0	-1
Alternative diagnoses excluded (by ≥3 biological investigations)	0	1	0
Final score: <2=No case; 2-3=Possible; 4-5=Probable; >5=Definite			

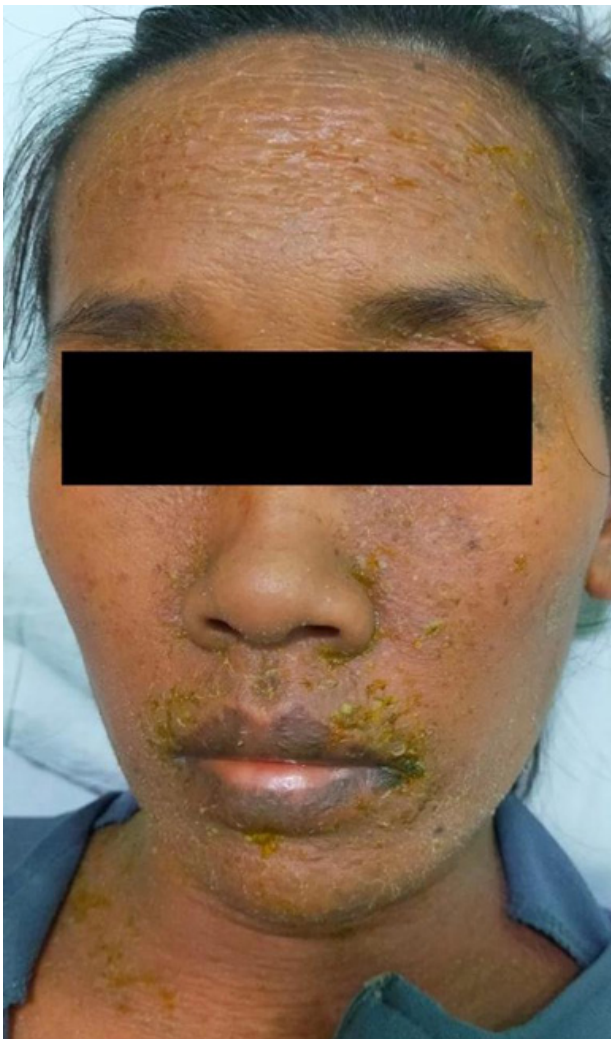

Figure 1: The patient's face that covered with yellowish scales

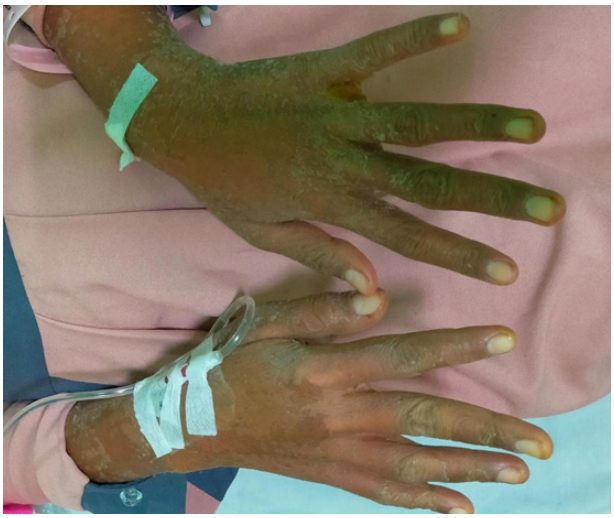

Figure 2: The patient's hands that also covered with yellowish scales

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Discussion

DRESS, or Drug Reaction with Eosinophilia and Systemic Symptoms, is a severe drug-induced reaction with a delayed clinical onset.[6] The key diagnostic features of DRESS include an elevated eosinophil count and systemic disturbances characterized by an increased number of lymphocytes and dysfunction in various viscera including the lungs, kidneys, liver, heart, nervous system, gastrointestinal system, and endocrine system. In the present case, DRESS was identified with elevated levels of liver transaminases. Sharma et al. wrote that in 90% of cases liver was frequently involved internal organ, followed by kidney involvement in 28% of cases.[7]

The estimate of incidence of DRESS, in general population is higher than one case per 10.000 persons exposed to drugs. Other data suggests an incidence of 0.9 per 100.000 individuals and 10 cases per million in the general population.[3,4] DRESS diagnosed on the basis of calculation of both J-Scar and RegiSCAR scores. Upon calculating these scores (Table 2 & 3), the J-Scar Score in this case is 5, indicating an Atypical DRESS presentation. Meanwhile, according to the Regis-Score, the case has a score of 3, classifying it as a "possible" case.

To diagnose DRESS using the RegiSCAR scoring system, eosinophilia is not an absolute requirement, but it is the most significant contributing factor for the diagnosis.8 In this case, the patient did not have elevated eosinophils, but the diagnosis of DRESS was still applicable due to the presence of other contributing factors.

In this particular case, the patient exhibited a red maculopapular rash with yellowish fine scales covering the entire body, resembling DRESS symptoms. Elevated liver function markers (SGOT: 358; SGPT: 524) were observed. Additionally, the patient displayed jaundice in the eyes, pale-colored stools, and dark, concentrated tea-colored urine. These findings align with the research by Sharifzadeh et al. described the common clinical features of DRESS, including widespread red skin rashes, fever, and frequently involving internal organs, especially the liver and kidneys.[3]

Up to 90% of DRESS patients exhibit the involvement of at least one organ. The liver is the most frequently involved organ, seen in 60-80% of cases. Typically, it presents as asymptomatic hepatitis besides hepatomegaly and jaundice, in severe cases, could cause fulminant liver failure.[6,10] Liver function tests may show abnormalities, including an increase of more than two times the normal value of alanine aminotransferase (ALT) and a value greater than 1.5 times that of alkaline phosphatase (ALP). Aforementioned changes are mild and last transiently. However, elevated liver enzyme levels can persist for several days after discontinuation of the offending drug and may take months to resolve.[6]

DRESS is a Type IV hypersensitivity reaction triggered by the response of Th2 lymphocytes and CD8+ cells. Th2 cells lead to Type IVb hypersensitivity affecting the skin. The release of T cells through the release of cytokines and chemokines such as IL4, IL5, and IL 13 activates and recruits eosinophils. In the immune response, Th-2 and Thymus activation-regulated chemokine (TARC) play crucial roles by recruiting polarized T lymphocytes capable of inducing eosinophilia and attracting type 2 innate lymphoid cells (ILC2s) to the skin through their specific T2 receptor. On the other hand, CD8+ cells contribute to internal organ damage.[3]

In this case, it is evident that every DRESS case is accompanied by organ damage, including liver involvement. Early recognition by healthcare professionals is crucial to promptly address DRESS syndrome and minimize the potential for further organ damage.

Conclusion

This case represents DRESS Syndrome with probable diagnosis according to the J-Scar and Regis-Scar criteria. Organ involvement in this case primarily affected the liver, as evidenced by elevated transaminase levels. If the patient makes a full recovery, a favorable prognosis is anticipated in terms of their overall quality of life.

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Authors' Contribution Statement

DY contributed to the conception, design, acquisition, analysis, interpretation of data, drafting of the manuscript, critical review of the manuscript, and final approval of the version to be published. JBP contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. SA contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. P contributed to the design, acquisition, interpretation of data, and critical review of the manuscript. RA contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. All authors are accountable for their work and ensure the accuracy and integrity of the study.

Conflict of Interest

Authors declared no conflict on interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.