# Clinico-pathological features of the drug reaction with eosinophilia and systemic Symptoms syndrome: A case study

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## ABSTRACT

Drug reaction with eosinophilia and systemic symptoms syndrome is a syndrome with a varied spectrum of clinical features. The cutaneous manifestations can be an urticarial, maculopapular eruption also including, vesicles, bullae, pustules, purpura, target lesions, facial edema, cheilitis, and erythroderma. Systemic manifestations include lymphadenopathy, fever, and leukocytosis (often with eosinophilia or atypical lymphocytosis), as well as hepatitis, nephritis, pneumonitis, myositis, and gastroenteritis, in descending order. Diagnosis can be made on the basis of the clinical picture and the RegiSCAR (Registry of Severe Cutaneous Adverse Reaction group) scoring system. Here, we present the case of a 40-year-old male with a history of herbal medicine intake after which he developed a diffuse skin rash.

**Key words:** *Cutaneous, Drug reaction with eosinophilia and systemic symptoms, Rashes, Skin lesion*

Drug-induced hypersensitivity syndrome (DIHS) is a systemic drug reaction also known as drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, since eosinophilia is not always present [1]. DRESS syndrome is a syndrome with a varied spectrum of clinical features. The clinical manifestations usually appear 2–8 weeks after the introduction of the triggering drug [2]. Clinically, DIHS presents with a prodrome of fever and flu-like symptoms for several days, followed by the appearance of a diffuse morbilliform eruption usually involving the face [1]. Systemic manifestations include lymphadenopathy, fever, and leukocytosis (often with eosinophilia or atypical lymphocytosis), as well as hepatitis, nephritis, pneumonitis, myositis, and gastroenteritis, in descending order [1]. The cutaneous manifestations consist of an urticarial, maculopapular eruption including vesicles, bullae, pustules, purpura, target lesions, facial edema, cheilitis, and erythroderma [3]. The life-threatening potential of the DRESS syndrome is high and the mortality is estimated to be around 10% in multiple studies [4].

## CASE REPORT

A 40-year-old man, a resident of Shampur, Bengaluru, presented to the General medicine outpatient department (OPD) with complaints of skin lesions all over the body, fever, and burning sensation in the oral cavity for 20 days. The skin lesions were acute in onset; initially, the patient noticed them on his face which later progressed to involve bilateral upper and lower limbs, chest, back, and mouth. He also complained of fever which was of acute onset, moderate-grade, not associated with chills or rigors, associated with generalized body ache, and was relieved on medications. The fever lasted for 2–3 days and subsided after that. He also complained of a burning sensation while passing stools and urine. The patient gives a history of consumption of herbal medicines for weight loss, which was given to him by a friend, following which the patient developed his symptoms. He had no pre-existing medical conditions. The patient did not give a history of regular medication with any other drugs or allergy to any medications in the past. There was no eruption of similar skin lesions in the past. No history of the passage of blood-tinged stools, melena, loose stools, or abdomen pain.

On examination, the patient was conscious and oriented with a pulse rate of 94/min, blood pressure of 130/80 mmhg, and temperature of 101° Fahrenheit. Systemic examination was essentially normal but icterus was present. Local examination revealed raised scaly, maculopapular rash ranging from 1 to 2 cm, with a raised erythematous base over his face (Fig. 1), upper limbs (Fig. 2), lower limbs, trunk, and back. The lesions were pruritic and non-tender. Oral mucosa showed severe erythema but no ulcers were seen.

Laboratory investigations revealed an elevated leukocyte count of 21,680/cumm with eosinophils constituting 34.1% and the absolute eosinophil count was 7392/cumm. Peripheral smear showed a normocytic, normochromic picture, with severe eosinophilia, and no atypical cells were found. Total bilirubin was 4.5 mg/dl with direct bilirubinemia of 3.2 mg/dl. SGOT was

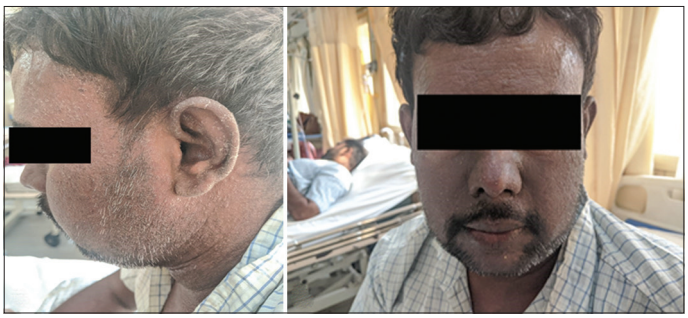

**Figure 1: Scaly macules and papules over the face, including the ear and the neck**

**Figure 2: Scaly macules and papules present on both the forearms**

437 U/L, SGPT was 891 U/L, alkaline phosphatase was 173 U/L, and serum GGT was 294 U/L. Prothrombin time was 19.8 s and INR was 1.47. The stool routine showed no ova or cysts. Ultrasonography of the abdomen revealed a hypoechoic liver, which was normal in size. Renal function tests, electrocardiogram, 2D- Echocardiography, and the chest X-ray were normal. The Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) score was 5, which came to a probable diagnosis of the DRESS syndrome.

The patient was started on systemic steroids, Inj. Hydrocortisone 100 mg 8 hourly, anti-histaminic drugs, and Tab Fexofenadine 120 mg OD, following which the erythema decreased. The patient was discharged after his fever subsided and serious systemic involvement was ruled out. The patient came for follow-up in the OPD, there was no reoccurrence of fever, and the rash over the trunk and back had resolved, and the rash over the face took more than 3 weeks to subside.

## DISCUSSION

The pathogenesis of the DRESS syndrome is thought to be the prototypical T-cell-mediated hypersensitivity reaction as suggested by *in vitro* demonstration of drug-specific T cells [5,6]. The association between Human Herpes Virus (HHV) and drug exanthems has been shown; most commonly, in the association of an ampicillin-induced exanthem arising in 80% of those with acute Epstein–Barr virus (EBV) infection. Reactivation of herpes viruses, especially EBV, HHV-6, and HHV-7, is a common finding and proposed as an explanation for flares in disease despite the withdrawal of the culprit drug [7,8]. Indeed, some authors have suggested that the detection of viral reactivation is a useful diagnostic marker of the DRESS syndrome [8].

Th2 environment during the DRESS syndrome may predispose towards the induction of regulatory T cells. This impairs host-virus control and results in viral reactivation followed by a surge in antiviral CD8+ T cells, which cause a secondary flare in the skin eruption [9]. An alternative hypothesis is that in the DRESS syndrome, a large proportion of proliferating CD8+ T cells from the skin, blood, or other organs are virus-specific and that the causative drugs specifically enhanced viral replication in the patient's B cells. This suggests that the induction of virus replication rather than drug-specific immune responses as the principal pathogenic feature of the DRESS syndrome [10].

The diagnosis of the DRESS syndrome is mainly clinical and one must consider the latency period, diversity of symptoms, and exclusion of similar non-drug-induced conditions. The RegiSCAR group suggested criteria for hospitalized patients with a drug rash to diagnose the DRESS syndrome [11]. RegiSCAR criteria [4] for the diagnosis of DRESS syndrome are as follows: hospitalization, reaction suspected to be drug-related, acute rash, fever >38°C, enlarged lymph nodes at a minimum of 2 sites*, involvement of at least one internal organ*, blood count abnormalities*, lymphocytes above or below normal limits, eosinophils above the laboratory limits, and platelets below the laboratory limits. Among these, three out of four asterisked (*) criteria are required for making the diagnosis.

DRESS syndrome must be recognized early and the causative drug should be withheld. Many reports suggest that the earlier the drug withdrawal, the better the prognosis [12]. Treatment is supportive and symptomatic management; corticosteroids though often used, have less evidence regarding their effectiveness [13]. Other immunosuppressants, such as cyclosporin, may also be required [14,15].

## CONCLUSION

The rationale of this study is that the DRESS syndrome should be suspected when a patient comes with widespread rashes, with a history of drug intake, and unknown supplements for weight loss. Due to the systemic involvement, the mortality of the patients is found to be about 10%. Early recognition and withdrawal of the offending drug are indicated. Diagnosis can be made on the basis of the clinical picture and the RegiSCAR scoring system.

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