

Oxcarbazepine-induced drug rash with eosinophilia and systemic symptoms syndrome presenting as exfoliative dermatitis

Mahimanjan Saha, Surajit Gorai¹, Vaswatee Madhab

Department of Dermatology, Silchar Medical College, Silchar, Assam, ¹Department of Dermatology, Burdwan Medical College, Burdwan, West Bengal, India

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ABSTRACT

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a type of severe adverse cutaneous drug reaction characterized by fever, skin eruption, hematological abnormalities, and internal organ involvement. Although anticonvulsant drugs are mainly implicated in DRESS, newer anticonvulsants such as oxcarbazepine-induced definite cases of DRESS syndrome are rare and oxcarbazepine-induced DRESS syndrome presenting as exfoliative dermatitis is even rarer. We report a case of a 35-year-old male who developed DRESS syndrome presenting as exfoliative dermatitis after taking oxcarbazepine for 3 weeks.

Key words: Drug rash with eosinophilia and systemic symptoms, exfoliative dermatitis, oxcarbazepine

INTRODUCTION

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is an acute, potentially life-threatening, idiosyncratic, severe cutaneous adverse drug reaction characterized by fever, skin eruption, hematological abnormalities including eosinophilia or atypical lymphocytes, and internal organ involvement.^[1] The most commonly involved internal

organ is the liver, followed by the kidney and lungs.^[2] Although the estimated incidence of this syndrome varies from 1 in 1000 to 1 in 10,000 drug exposures, its true incidence is unknown because of variable presentation and inaccurate reporting.^[3] Aromatic anticonvulsant drugs such as phenytoin, carbamazepine, and phenobarbital are mainly implicated in DRESS.^[1,4] Newer antiepileptic drugs such as oxcarbazepine-induced DRESS are reported a few,^[5,6] whereas definite oxcarbazepine-induced DRESS presenting as exfoliative dermatitis is rare in literature. Here, we present a case of a 35-year-old male who developed DRESS syndrome presenting as exfoliative dermatitis after taking oxcarbazepine for the past 3 weeks.

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Address for correspondence:

Mahimanjan Saha, Department of Dermatology, Silchar Medical College, Silchar - 788 014, Assam, India.
E-mail: mahimanjan@gmail.com

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CASE REPORT

A 35-year-old male was admitted with generalized scaling and erythema of the whole body for the past 5 days. He was on tablet oxcarbazepine for the past 3 weeks for seizure disorder diagnosed recently. He was not known to have allergy to any drug in the past.

On examination, the patient was toxic, febrile (101°F), icteric, with tachypnea (25/min), tachycardia (110/min), conjunctival congestion, and cervical and inguinal lymphadenopathy. There was a diffuse swelling of the face with pitting edema of both the legs [Figure 1]. Brown-to-black semi-adherent scaling was present on more than 90% of the body surface area with the underlying erythema giving rise to the dull red appearance of the skin [Figure 2]. Palms and soles were also involved. Flexures were fissured and macerated with oozing. There were diffuse crepitations over both lung fields with tender hepatomegaly.

Initial investigation revealed leukocytosis (total leukocyte count = 12,440/cm³) with eosinophilia (absolute eosinophil count - 2488/cm³) and platelet count was 150,000/cm³. Peripheral blood smear showed leukocytosis, eosinophilia with 6% atypical lymphocytes. There was no evidence of hemolysis and hemoparasites. His liver function test was deranged with elevation of bilirubin (total bilirubin - 5.6 mg/dl) and liver enzymes (alanine transaminase = 784 IU/L; aspartate aminotransferase = 1324 IU/L; and alkaline phosphatase = 184 IU/L). His urea and creatinine were 65 and 1.8 mg/dl, respectively. Bone marrow examination did not reveal any abnormalities. Blood culture was sterile. Serological test for hepatitis A virus, hepatitis B virus, hepatitis C virus, human immunodeficiency virus, chlamydia, and mycoplasma was negative. Rapid diagnostic serological test for malaria and dengue was also negative. Blood for antinuclear antibody was negative. Based on the European Registry of

Severe Cutaneous Adverse Reactions (RegiSCAR) criteria,^[7] a definitive diagnosis of oxcarbazepine-induced DRESS was made. Oxcarbazepine was stopped, and the patient was treated with injection dexamethasone 1 ml (4 mg/ml), twice a day for initial 5 days with antihistaminic, topical corticosteroids, and emollient lotion. Prednisolone 40 mg/day was started orally and gradually tapered over 6 weeks. After 48 h of treatment, the patient started improving clinically and became afebrile after 72 h. Skin eruption gradually cleared over 10 days and his hematological and other laboratory parameters started improving after 72 h and became normal after 18 days of starting treatment.

DISCUSSION

A systemic severe allergic reaction to anticonvulsant therapy was first described by Chaiken *et al.* in 1950 and was named as “anticonvulsant hypersensitivity syndrome,” which was associated with phenytoin therapy.^[8] Since then, it has been also known as drug hypersensitivity syndrome and now popularized as DRESS syndrome which was coined by Bocquet *et al.*^[9] in 1996 characterized by fever, skin eruption, hematological abnormalities including eosinophilia or atypical lymphocytes, and internal organ involvement (hepatitis, nephritis, pneumonitis, myocarditis, and colitis).^[1]

Aromatic antiepileptic drugs such as phenytoin, carbamazepine, and phenobarbital are the most common causes of DRESS although other drugs such as lamotrigine, valproic acid, allopurinol, minocycline, sulfasalazine, dapsone, gold salts, nonsteroidal anti-inflammatory drugs and antiretroviral drugs such as nevirapine, abacavir, and beta-lactam antibiotics may also cause DRESS.^[1,2,4]

The pathogenesis proposed is a failure of detoxification of the drugs led to the accumulation of toxic metabolites and arene oxides which may trigger immunological cascade through CD4+ T and CD8+ T cells which, in turn, releases



Figure 1: Diffuse facial edema with scaling and erythema over the face and upper trunk



Figure 2: Brown-to-black semi-adherent scaling with underlying erythema involving most of the body parts

interleukin-5 leading to the activation of eosinophil.^[1,2] Reactivation of herpes virus, including Epstein–Barr virus and human herpes virus-6, 7, is also implicated in the pathogenesis of DRESS.^[1,2]

The diagnosis is difficult and challenging and often confuses the treating physician as symptoms mimic various infections, intoxication, neoplasia, and rheumatological diseases. To properly evaluate and diagnose DRESS, different criteria have been framed and among all, RegiSCAR criteria scoring system^[7] is most widely accepted now [Table 1].

Oxcarbazepine is a relatively new drug which is a structural derivative of carbamazepine, with a ketone in the place of the carbon–carbon double bond on the dibenzazepine ring at the 10th position (10-keto)^[10] [Figure 3].

Table 1: Registry of Severe Cutaneous Adverse Reactions criteria for diagnosing drug rash with eosinophilia and systemic symptoms

Criteria	No	Yes	Unknown/ unclassifiable
Fever ($\geq 38.5^{\circ}\text{C}$)	-1	0	-1
Lymphadenopathy (≥ 2 sites; > 1 cm)	0	1	0
Circulating atypical lymphocytes	0	1	0
Peripheral hypereosinophilia	0		0
0.7-1.499 $\times 10^9/\text{L}$ -or-10-19.9%*		1	
$\geq 1.5 \times 10^9/\text{L}$ -or- $\geq 20\%$ *		2	
Skin involvement			
Extent of cutaneous eruption $> 50\%$ body surface area	0	1	0
Cutaneous eruption suggestive of DRESS**	-1	1	0
Biopsy suggests DRESS	-1	0	0
Internal organ involved***	0		0
One		1	
Two or more		2	
Resolution in ≥ 15 days	-1	0	-1
Laboratory results negative for at least three of the following (and none positive)			
ANA	0	1	0
Blood culture			
HAV/HBV/HCV serology			
Chlamydia and mycoplasma serology			

Final score < 2 no case; 2-3 possible case; 4-5 probable case; > 5 definite case, *If leukocytes $< 4 \times 10^9/\text{L}$, **At least two of the following: edema, infiltration, purpura, scaling, ***Liver, kidney, lung, muscle/heart, pancreas, or other organs and after exclusion of other explanations. DRESS=Drug rash with eosinophilia and systemic symptoms, HAV=Hepatitis A virus, HBV=Hepatitis B virus, HCV=Hepatitis C virus

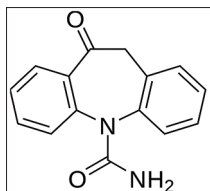


Figure 3: Structure of oxcarbazepine

DRESS is a well-known adverse drug reaction with other anticonvulsants, definite oxcarbazepine-induced DRESS is reported a few,^[5,6] and definite oxcarbazepine-induced DRESS presenting as exfoliative dermatitis is very rare in literature, to our knowledge.

Our patient fulfilled all the RegiSCAR criteria and had a score of 9, so he was marked as the definite case. As per Naranjo scale^[11] for assessing the causality of adverse drug reaction, the case was marked as probable. The patient was treated as oxcarbazepine-induced DRESS syndrome, and he showed uneventful recovery with steroids and on discontinuation of the offending drug.

Early withdrawal of offending medication or dechallenge is the first and foremost step of the treatment. Glucocorticoids still remain the most widely used agent for the treatment of DRESS syndrome although relapse can occur during tapering of glucocorticoids.^[12] Response is usually slow and it may last for several weeks to months. Other modalities such as the use of intravenous immunoglobulins^[13] and N-acetylcysteine^[14] are also reported in literature.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Cacoub P, Musette P, Descamps V, Meyer O, Speirs C, Finzi L, *et al.* The DRESS syndrome: A literature review. *Am J Med* 2011;124:588-97.
2. Giri PP, Roy S, Bhatyacharya S, Pal P, Dhar S. Dress syndrome with sepsis, acute respiratory distress syndrome and pneumomediastinum. *Indian J Dermatol* 2011;56:763-5.
3. Fiszenson-Albala F, Auzeur V, Mahe E, Farinotti R, Durand-Stocco C, Crickx B, *et al.* A 6-month prospective survey of cutaneous drug reactions in a hospital setting. *Br J Dermatol* 2003;149:1018-22.
4. Shiohara T, Kano Y, Takahashi R. Current concepts on the diagnosis and pathogenesis of druginduced hypersensitivity syndrome. *JMAJ* 2009;52:347-52.
5. Bosdure E, Cano A, Roquelaure B, Reynaud R, Boyer M, Viard L, *et al.* Oxcarbazepine and DRESS syndrome: A paediatric cause of acute liver failure. *Arch Pediatr* 2004;11:1073-7.
6. D'Orazio JL. Oxcarbazepine-induced drug reaction with eosinophilia and systemic symptoms (DRESS). *Clin Toxicol (Phila)* 2008;46:1093-4.
7. Kardaun SH, Sidoroff A, Valeyrie-Allanore L, Halevy S, Davidovici BB,

Saha, *et al.*: Oxcarbazepine-induced DRESS syndrome

- Mockenhaupt M, *et al.* Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: Does a DRESS syndrome really exist? *Br J Dermatol* 2007;156:609-11.
8. Chaiken BH, Goldberg BI, Segal JP. Dilantin sensitivity; report of a case of hepatitis with jaundice, pyrexia and exfoliative dermatitis. *N Engl J Med* 1950;242:897-8.
 9. Bocquet H, Bagot M, Roujeau JC. Drug-induced pseudolymphoma and drug hypersensitivity syndrome (drug rash with eosinophilia and systemic symptoms: DRESS). *Semin Cutan Med Surg* 1996;15:250-7.
 10. Porter RJ, Meldrum BS. Anti seizures drug. In: Katzung BG, editor. *Basic and Clinical Pharmacology*. 13th ed. New York: McGraw-Hill; 2015. p. 396-420.
 11. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30:239-45.
 12. Kaminsky A, Moreno M, Díaz M, Charas V, Bravo G, Kien C. Anticonvulsant hypersensitivity syndrome. *Int J Dermatol* 2005;44:594-8.
 13. Fields KS, Petersen MJ, Chiao E, Tristani-Firouzi P. Case reports: Treatment of nevirapine-associated dress syndrome with intravenous immune globulin (IVIG). *J Drugs Dermatol* 2005;4:510-3.
 14. Gabay C, De Bandt M, Palazzo E. Sulphasalazine-related life-threatening side effects: Is N-acetylcysteine of therapeutic value? *Clin Exp Rheumatol* 1993;11:417-20.