

Case Report

Ceftriaxone induced drug rash with eosinophilia and systemic symptoms

Vivek S. Guleria¹, Mukesh Dhillon¹, Shaman Gill¹, Nardeep Naithani¹

¹Department of Internal Medicine, Armed Forces Medical College, Pune, India

Received: February 2014
Accepted: March 2014

Corresponding author:
Dr. Vivek S. Guleria,
E-mail: viveksguleria@gmail.com

ABSTRACT

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a drug reaction commonly occurring in association with aromatic anticonvulsants and allopurinol. It is characterized by triad of fever, skin eruption, and systemic involvement. DRESS is rare with beta-lactam antibiotics and even rarer with ceftriaxone. We describe a case of pneumonia who developed ceftriaxone-induced rash, bicytopenia, eosinophilia, transaminitis and was eventually diagnosed and managed successfully as a case of DRESS.

Keywords: Ceftriaxone; Drug rash with eosinophilia and systemic symptom; Eosinophilia

INTRODUCTION

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is an acute, severe, unpredictable cutaneous reaction to drugs leading to skin eruptions and visceral involvement. The characteristic features include a diffuse maculopapular rash, facial edema, exfoliative dermatitis, fever, lymphadenopathy, visceral involvement (renal impairment, carditis, pneumonitis), hematological abnormalities (mainly eosinophilia, lymphocytosis and atypical lymphocytes).^[1] DRESS was first described by Chaiken *et al.* in 1950 with dilantin (phenytoin).^[2] It occurs with numerous drugs (e.g., anticonvulsants, sulphonamides, and allopurinol).^[3] DRESS with beta-lactam antibiotics has been also reported. Ceftriaxone, a cephalosporin is used for variety of infections. This drug is known to be associated with rare and mild side-effects such as urticaria, skin rash, diarrhea, vomiting, transient neutropenia, and hemolysis. However, ceftriaxone-induced DRESS is rare. To the best of our knowledge, there have

been only two cases reported in the literature.^[4] We report herein one case of DRESS induced by ceftriaxone.

CASE REPORT

A 33-year-old male was admitted (10, November 2013) with fever and dry cough of 4 days duration in a peripheral hospital. The patient had no known comorbidities and didn't give history of any drug allergy in the past. On examination, he was found to be febrile (100 F), had a pulse of 90/min, blood pressure of 126/80 mmHg, respiratory rate of 24/min and had crackles in right infrascapular region. Based on the clinical examination and chest X-ray, he was diagnosed to have pneumonia. His hematological and biochemical parameters were within the normal limit. He was started on injection of ceftriaxone (1 g, intravenous, every 24 h). On the 3rd day of admission, his fever dropped down and he was afebrile by day 6. Ceftriaxone was continued. On the 7th day, he developed transaminases elevation, alanine aminotransferase (alanine transaminase (ALT) =219 IU/L; aspartate aminotransferase (AST) =356 IU/L; alkaline phosphatase (ALP) =246 IU/L). On the 11th day, he had recurrence of high grade fever with maculopapular rash over trunk, extremities and swelling of wrist and ankles [Figures 1-3]. He was transferred to our center on day 11, with the following laboratory findings: Hemoglobin = 11.4 g%; total leucocyte count (TLC) =1900/cm³ with relative eosinophilia of 10%; platelets (Plt) count = 1,47,000/cm³

Access this article online



Website: www.jrpp.net

DOI: 10.4103/2279-042X.137077



Figure 1: Erythematous maculopapular rash over chest and abdomen



Figure 2: Erythematous maculopapular rash over back



Figure 3: Erythematous maculopapular rash over thigh

(previous Plt = 2,00,000/cm³). His peripheral blood smear showed leucopenia with relative eosinophilia, 6% atypical lymphocytes, Plt: 1,50,000/cm³ and no evidence of hemolysis and hemoparasite. His

liver enzymes were markedly raised as below: ALT = 766 IU/L; AST = 2424 IU/L; ALP = 162 IU/L, and lactate dehydrogenase = 3732 IU/L. His urea and creatinine were 46 and 1.7 mg/dL, respectively. Bone marrow aspiration/biopsy was done and presented to be normal. His hepatitis B surface antigen, antihepatitis C virus antibody, and human immunodeficiency virus antibody were all negative. Rapid diagnostic test for malaria and dengue serology were negative. A diagnosis of ceftriaxone-induced DRESS was made, based upon European Registry of severe cutaneous adverse reactions (RegiSCAR) criteria.^[5] Ceftriaxone was stopped and patient was treated with injection of dexamethasone 4 mg, thrice a day for initial 2 days and later oral prednisolone 60 mg/day, which was gradually tapered over 6 weeks. Only after 48 h of steroid therapy, patient started improving symptomatically and became afebrile after 72 h. His rash cleared over 5 days and his hematological and biochemical parameters started improving after 72 h and became normal by day 8 of starting steroids [Table 1].

DISCUSSION

Drug rash with eosinophilia and systemic symptoms syndrome is a life-threatening adverse reaction to a drug with associated mortality rate of about 10%. Proposed mechanism of pathogenesis of DRESS has been failure of drug detoxification pathways leading to accumulation of harmful metabolites which in turn activate CD4 + CD8 + T-cells. These cells release interleukin-5 which activates eosinophils and sets up an inflammatory cascade.^[6] Earlier, there was no consistent name for this syndrome and it was named after the culprit drug as phenytoin syndrome, allopurinol hypersensitivity syndrome, dapsone syndrome, etc., Bocquet *et al.*^[7] proposed the term drug rash with eosinophilia and systemic symptoms (DRESS) to simplify the nomenclature of drug-hypersensitivity syndromes. Since then, various criteria have been evolved to define DRESS [Table 2]. Among all the criteria being used to diagnose DRESS, RegiSCAR criteria^[5] is the most widely used.

Our patient was diagnosed as DRESS syndrome as he was fulfilling all Bocquet *et al.*^[7] proposed criteria and criteria 1, 2, 3, 4, 6, 7 of RegiSCAR.^[5] However, except for fever, no other Japanese consensus group criteria^[8] was being fulfilled, as the symptoms and signs had appeared early (11 days of ceftriaxone administration), there was leucopenia (TLC = 1900) rather than leukocytosis, and absolute eosinophil count was only 190/cm³ though there was relative increase in eosinophils (10% of TLC). Patient was treated as having ceftriaxone induced DRESS syndrome and he showed a uneventful recovery with steroids and cessation of the offending drug.

Table 1: Hematological and biochemical laboratory findings of the patient

Laboratory test	On admission	Day 7	Day 11	Day 13	Day 19
Hgb (g %)	13.0	12.8	11.4	12.6	12.2
TLC (/cm ³)	7400	5600	1900	2800	6600
DLC (P/L/E/M/B)	62/33/4/1/0	66/27/6/1/0	30/58/10/2/0	48/41/8/2/1	78/16/3/2/1
Platelets (/cm ³)	2.0 L	1.80 L	1.47 L	1.68 L	2.10 L
AST/ALT (IU/L)	27/22	356/219	2424/766	1098/438	34/28
Serum bilirubin (mg/dL)	0.8	1	Total: 2.3 Direct: 1.6	2.0	1.0
LDH (IU/L)	-	506	3732	1088	346
Urea/creatinine (mg/dL)	19/0.6	-	46/1.7	34/1.2	22/0.8

Hgb=Hemoglobin, TLC=Total leucocyte count, DLC=Differential leucocyte count, P=Polymorphs, L=Lymphocytes, E=Eosinophils, M=Monocytes, B=Basophils, ALT=Alanine aminotransferase, AST=Aspartate aminotransferase, LDH=Lactate dehydrogenase

Table 2: Scoring systems for diagnosis of DRESS

Bocquet <i>et al.</i>	RegiSCAR study group	Japanese consensus group
DRESS is confirmed by presence of 1 and 2 and 3	More than 3 of the criteria are required for the diagnosis of DRESS	Typical DRESS (presence of all 7 criteria); atypical DIHS (all criteria present except lymphadenopathy and HHV-6 reactivation)
1. Cutaneous drug eruption	1. Hospitalization	1. HHV-6 reactivation
2. Adenopathies >2 cm in diameter or hepatitis (liver transaminases >2 times upper limit of normal) (or) interstitial nephritis (or) interstitial pneumonitis (or) carditis	2. Reaction suspected to be drug related	2. Prolonged clinical symptoms 2 weeks after discontinuation of causative drug
3. Hematologic abnormalities Eosinophilia>1.5×10 ⁹ /L (or) atypical lymphocytes	3. Acute rash	3. Maculopapular rash developing>3 weeks after starting drug
	4. Fever above 38°C	4. Fever above 38°C
	5. Enlarged lymph nodes involving at least two sites	5. Lymphadenopathy
	6. Involvement of at least one internal organ	6. ALT>100 U/L or other organ involvement
	7. Blood count abnormalities Lymphocytes above or below laboratory limits	7. Leukocyte abnormalities (at least one) Leucocytosis (>11×10 ⁹ /L)
	Eosinophils above laboratory limits (in percentage or absolute count)	Atypical lymphocytosis (>5%)
	Platelets below laboratory limits	Eosinophilia (1.5×10 ⁹ /L)

DRESS=Drug rash with eosinophilia and systemic symptoms, RegiSCAR=European Registry of severe cutaneous adverse reactions, DIHS=Drug-induced hypersensitivity syndrome, HHV-6: Human herpesvirus 6, ALT=Alanine aminotransferase

The culprit drugs most commonly associated with DRESS are anticonvulsants, allopurinol, minocycline, sulfasalazine, dapsone, nevirapine, and abacavir.^[3] Ceftriaxone-induced DRESS is rare. To our knowledge, there have been only two cases of ceftriaxone-induced DRESS reported in the literature.^[4] Until date, ceftriaxone has not been included in the list of drugs causing DRESS. DRESS is generally treated with moderate-or high-dose corticosteroids, but response may be suboptimal and prolonged treatment with systemic glucocorticoid may be required. Other immunosuppressive agents, such as cyclosporine, have also been used.^[9]

REFERENCES

1. Kano Y, Shiohara T. The variable clinical picture of drug-induced hypersensitivity syndrome/drug rash with eosinophilia and systemic symptoms in relation to the eliciting drug. *Immunol Allergy Clin North Am* 2009;29:481-501.
2. 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.
3. Tetsuo Shiohara, Yoko Kano, Ryo, Takahashi. Current Concepts on the Diagnosis and pathogenesis of Drug-induced Hypersensitivity Syndrome . *JMAJ* 2009;52:347-52.
4. Akcam FZ, Aygun FO, Akkaya VB. DRESS like severe drug

rash with eosinophilia, atypic lymphocytosis and fever secondary to ceftriaxone. *J Infect* 2006;53:e51-3.

5. Kardaun SH, Sidoroff A, Valeyrie-Allanore L, Halevy S, Davidovici BB, 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* s2007;156:609-11.
6. Choquet-Kastylevsky G, Intrator L, Chenal C, Bocquet H, Revuz J, Roujeau JC. Increased levels of interleukin 5 are associated with the generation of eosinophilia in drug-induced hypersensitivity syndrome. *Br J Dermatol* 1998;139:1026-32.
7. 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.
8. Shiohara T, Iijima M, Ikezawa Z, Hashimoto K. The diagnosis of a DRESS syndrome has been sufficiently established on the basis of typical clinical features and viral reactivations. *Br J Dermatol* 2007;156:1083-4.
9. Zuliani E, Zwahlen H, Gilliet F, Marone C. Vancomycin-induced hypersensitivity reaction with acute renal failure: Resolution following cyclosporine treatment. *Clin Nephrol* 2005;64:155-8.

How to cite this article: Guleria VS, Dhillon M, Gill S, Naithani N. Ceftriaxone induced drug rash with eosinophilia and systemic symptoms. *J Res Pharm Pract* 2014;3:72-4.

Source of Support: Nil, **Conflict of Interest:** None declared.