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## Case Report

# Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome induced by ceftriaxone with successful treatment — A case report and literature review

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## ABSTRACT

Drug reaction with eosinophilia and systemic symptoms is a rare and potentially life threatening condition characterised by hypersensitivity reactions to a drug with prolonged latency, in the form of skin rashes, hyper eosinophilia and systemic features like fever, lymphadenopathy, leucocytosis, internal organ involvement (liver, kidney, lung). Though it can occur in response to many drugs but very few cases has been described in relation to one of the most commonly used antibiotic ceftriaxone. Here we have described a case of DRESS in a patient who has been treated with ceftriaxone outside our hospital for sore throat.

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## 1. Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) is rare, often an unpredictable response to a drug characterised by skin eruptions, eosinophilia, systemic manifestations like fever, internal organ involvement (like hepatitis, carditis, renal and lung involvement), haematological manifestations like leucocytosis with atypical lymphocytes besides eosinophilia. In most of the cases fulfilling the criteria of DRESS, a drug can be attributed, but in 10 to 20 percent cases, a relationship with drug cannot be established.<sup>1</sup> There were numerous terms for this particular syndrome like drug hypersensitivity syndrome, dapsone syndrome, dilantin syndrome but it was Boucekt et al. who coined the term DRESS in 1963.<sup>2</sup> There are many drugs to which relationship with DRESS has been well established like antiepileptic drugs (phenytoin, phenobarbital, carbamazepine, lamotrigine), urate lowering

drugs (allopurinol, febuxostat), sulfa drugs (dapsone, sulfasalazine, sulfamethoxazole), nevirapine, olanzapine, strontium ranelate, beta lactam antibiotics.<sup>3</sup> There are very few cases of DRESS caused by ceftriaxone, one of the most commonly used antibiotic. Here we report one of such cases of DRESS caused by ceftriaxone,<sup>4,5</sup> a very commonly used antibiotic.

## 2. Case Report

A 18 years old girl, with total duration of illness of 5 days, presented with chief complaints of generalised swelling and redness of body associated with itching, starting from face, progressing to both upper limbs, trunk followed by both lower limbs; fever for 5 days which was low grade, intermittent and without chills and rigor; rest and exertional breathlessness; and 2 to 3 episodes of vomiting per day, unrelated to food. There was no history of similar illness in the past. She had no previous illness like asthma or any drug allergies. She had taken injection Ceftriaxone 1g 12

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**Table 1:** Different criteria for diagnosing DRESS

<b>Bocquet et al (2)</b>	<b>RegiSCAR study group (6)</b>	<b>Japanese consensus group(8)</b>
DRESS is confirmed by presence of 1, 2, 3	More than 3 criteria required for DRESS	Typical DRESS (all 7 criteria), atypical DRESS (all criteria except lymphadenopathy and HHV-6 reactivation)
1. Cutaneous drug eruption	1. Hospitalisation	1. HHV-6 reactivation
2. Adenopathies more than 2 cm in diameter or hepatitis or interstitial nephritis or interstitial pneumonitis or carditis	3. Reaction suspected to be drug related	2. Prolonged clinical symptoms 2 week after discontinuation of causative drug
4. Hematological abnormalities like eosinophilia( $1.5 \times 10^9/l$ ) and/or atypical lymphocytes	2. Acute rash	3. Maculopapular rash
-	3. Fever above $38^{\circ}C$	4. Fever above $38^{\circ}C$
-	4. Enlarged lymph nodes involving at least 2 sites	5. Lymphadenopathy
-	6. Involvement of at least 2 internal organs	6. ALT>100 U/L or other organ involvement
-	7. Blood count abnormalities like lymphocytosis or lymphopenia, eosinophilia above laboratory limits or platelets below laboratory limits	Leucocyte abnormalities (at least one) like leucocytosis ( $11 \times 10^9/l$ ), atypical lymphocytes (>5%), eosinophilia ( $1.5 \times 10^9/l$ ).

hourly, tablet Paracetamol 650 mg and vitamin B complex for fever and sore throat, 3 weeks before presentation. On examination patient was sick looking, with generalised erythematous confluent rash present all over the body with puffy face. Patient was febrile, there was tachycardia and tachypnea with blood pressure of 92/60 mm Hg in right arm supine position. General examination showed generalized lymphadenopathy and bilateral pitting type of pedal oedema. On systemic examination, no abnormality could be detected except mild right hypochondrial tenderness. On laboratory investigation, arterial blood gas analysis showed arterial oxygen saturation of 92.4%, alkaline PH (7.46),  $PCO_2$  35.8 mm Hg,  $HCO_3$  24 mmol/l, with normal anion gap. Her haemoglobin was 10.5 gm/dl, total leucocyte counts were  $54,800/\mu l$  with differential count of neutrophil 37.3%, lymphocytes 46.6%, and eosinophil 9.2%. Total platelet count was 1.9 lakhs/ $\mu l$ . Her absolute eosinophil count was  $4,968/\mu l$ . Peripheral smear showed moderate leucocytosis, neutrophils mild shift to left, few atypical lymphocytes and occasional plasmacytoid cells. Her Liver function test showed transaminitis and SGOT and SGPT were 345 IU/L, 237 IU/L respectively. Total bilirubin was 2.0 g/dl with indirect fraction 1.6mg/dl, serum alkaline phosphatase was 932 IU/L. Renal function test, routine urine microscopy, troponin levels, ECG and chest x-ray were normal. Monospot test for Epstein Barr virus, Hepatitis B antigen, anti HCV and HIV ELISA were negative.

A diagnosis of ceftriaxone induced DRESS was made based on European registry of severe cutaneous adverse reactions criteria. Patient was given injection chlorpheniramine and injection hydrocortisone 200mg intravenously stat, which was later shifted to oral prednisolone 40mg/day. Following 5 days of treatment,

patient became afebrile, rash disappeared and edema subsided with improvement in general condition and laboratory parameters. Prednisolone was gradually tapered over 6 weeks and discontinued.

### 3. Discussion

An immune reaction to drug or its metabolite is key factor in pathogenesis of drug reaction with eosinophilia and systemic symptoms. DRESS is strongly associated with activation of CD4 + CD8 + T-cells. These cells release interleukin-5 (IL-5) which activates eosinophils and sets up an inflammatory cascade.<sup>6</sup> In this case there was fever, rash, lymphadenopathy, blood count abnormality (leucocytosis, atypical lymphocytes, eosinophilia), lung involvement (tachypnea and falling  $O_2$  saturation), liver involvement (elevated liver enzymes); these findings fulfilled Bocquet et al. criteria,<sup>2</sup> European registry of severe cutaneous adverse reactions criteria<sup>7</sup> and Japanese consensus group criteria,<sup>8</sup> (except reactivation of HHV-6) (Please refer to table no 1), in the background of exposure to ceftriaxone 3 weeks back. Retrospective studies have reported a mortality rate of 5-10 % from DRESS syndrome.<sup>1</sup> The main causes of death are acute liver failure,<sup>9</sup> multiorgan failure,<sup>10</sup> or fulminant myocarditis.<sup>11</sup> Autoimmune diseases have been reported in some cases following resolution of drug reaction.<sup>12</sup>

### 4. Conclusion

To our knowledge, there have been very few cases of ceftriaxone-induced DRESS reported in the literature. 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 glucocorticoids may be required. Other immunosuppressive agents such as cyclosporine, have also been used.<sup>13</sup>

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## 6. Conflict of Interest

None.

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