Dress Syndrome: Time to Define Treatment Guidelines?

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Abstracts: **Background:** DRESS (Drug rash with eosinophilia and systemic Symptoms) syndrome is a drug hypersensitivity syndrome which begins around 2- 6 weeks after exposure to a drug. If treated early, can recover completely and much of morbidity can be avoided. **Case:** A patient with history of taking carbamazepine for epilepsy, presented with typical features of maculopapular erythematous rash, exfoliative dermatitis and edema over upper and lower extremities, face, and trunk. He had eosinophilia, lymphadenopathy and elevated liver enzymes. His condition rapidly improved after withdrawing carbamazepine and starting steroids. **Discussion:** The rapid recovery with steroids in this case and in a few cases reported previously also suggests a need of RCT to assess steroids as an established modality for management of this severe but curable entity.[Muley A NJIRM 2014; 5(5):106-107]

Key Words: Dress Syndrome, Recovery, Steroids.

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Introduction: DRESS (Drug rash with eosinophilia and systemic Symptoms) syndrome is a drug hypersensitivity syndrome which begins around 2-6 weeks after exposure to a drug1. It is rare but a severe type of drug reaction which also mimics many other serious disease entities2. It occurs most commonly with aromatic anticonvulsants, some antibiotics, antiviral and immunotherapeutic agents3.

It usually presents with fever, maculopapular rash, generalized lymphadenopathy, hypereosinophilia and hypogammaglobulinemia (in early phase of reaction)4. Detailed medical history of systemic medications plays a central role. Before making the diagnosis, other eosinophilic disorders like rhinitis, asthma, allergic hypersensitivity reactions, hypereosinophilic syndrome, eczema, Well syndrome, eosinophilic fasciitis; pulmonary diseases like Churg-Strauss, eosinophilic pneumonia, eosinophilic gastroenteritis; malignancies like Hodgkins lymphoma, myeloproliferative disorders and parasitic infestations should be ruled out.

Case Report: A 40 year old male farmer presented with intermittent fever of moderate grade since 8 days, followed by maculopapularerythematous rash, exfoliative dermatitis and edema over upper and lower extremities, face, and trunk. Patient gave a history of suffering from recurrent seizures since last three months for which he was started on carbamazepine 200mg twice daily 6 weeks back. There was no history of chronic cough, burning micturition, skin allergies, altered bowel habits or joint pain. He also had a history of alcohol abuse since last 10 years.

On general examination, pulse was 82/min regular and BP was 110/70mm Hg. He was febrile on admission. Generalized lymphadenopathy (Right cervical, right axillary, and bilateral inguinal) was present. All lymph nodes were discreet, nonmatted, firm in consistency. Inguinal lymph nodes were tender. Erythematous maculopapular, pruritic rash, exfoliativedermatitis andedema were present over both upper and lower extremities, trunk and face (Fig.1). Examination of cadiovascular, respiratory, abdominal and nervous systems was unremarkable.

Lab investigations showed Hb 15.5gm%, TLC 30500 cell/cumm, DLC - neutrophils – 41%, lymphocytes – 33%, abnormal lymphocytes – 12%, monocytes – 2% and eosinophils – 12% , AEC 3744 cells/cumm, platelets 2.74 lacs/cumm. Peripheral smear showed normocytic, normochromic RBCs, leucocytosis, atypical lymphocytosis and eosinophilia (Fig.3). LFT revealed AST- 64 IU/L, ALT -256 IU/L, bilirubin (T) - 1.2 mg%, RFT showed Urea-44mg% and S.creatinine-1.2 mg% . Carbamazepine level was 4.6 mcg/ml. Total protein, S. Albumin and S. Globulin were 5.9g/dl, 3.5 g/dl and 2.4 g/dl respectively. Urine & Stool were normal. HBsAg, HIV, WIDAL , VDRL, MP, ANA and RA factor were all negative. Blood and urine culture showed no growth. USG abdomen showed hepatomegaly, but X-ray chest PA and MRI brain

were normal. FNAC of inguinal lymph node showed diffuse hyperplasia with mixed population of lymphoid cells, centroblast, centrodytes, tingible body macrophages and numerous eosinophils and paracorticalpostcapillaryvenular hyperplasia (Fig.4). A diagnosis of DRESS syndrome was made and carbamazepine was discontinued. IV dexamethasone was started. Skin rashes and other haematological investigations including total counts, eosinophil counts, and liver function tests improved remarkably in seven days (Fig. 2). There was a reduction in the number of palpable lymph nodes following treatment. Overall clinical condition improved and patient was discharged after tapering and stopping steroids.

Discussion: Although previously described as Drug induced hypersensitivity syndrome (DIHS), DRESS syndrome term was introduced in 1996 by Bocquetet al1. It appears acutely in first 2 – 6 weeks after initiation of drugs like phenobarbitone, carbamazepine, phenytoin, lamotrigine, minocycline, sulphonamide, allopurinol, dapsone, ethambutol, celecoxib etc3. Patient usually presents with fever, pharyngitis, lymphadenopathy, eosinophilia leucocytosis, elevated liver enzymes, renal failure, pneumonia and diarrhoea4. Exact pathophysiology of the condition is not known; however, it is postulated that eosinophil derived protein toxicity is involved in development of systemic symptoms6. Although the exact incidence is not known, it is rare, given the fact that the incidence with aromatic anticonvulsants is 1 in 5000-10,000. Nevertheless, as the incidence of this disease is very low and the disease is potentially life-threatening, there is no evidence based on randomized controlled trials. Therapy in most cases includes systemic corticosteroid in combination with rapid withdrawal of drug5.

Most of the features except pneumonia and renal failure were present in this patient. The rapid and complete recovery of this patient highlights the fact that it is important to recognize this entity early because it can mimic other pathologies which are potentially serious (with mortality as high as 10%)2 and treating it early can reduce morbidity and mortality to a great extent. Accidental re-exposure and drug provocation tests should be avoided; patient and their relatives must be informed about the causal drug and chances of crossreactivity with other medications. All cases of DRESS syndrome should be reported to local pharmacovigilancecenters. The rapid recovery with steroids in this case and in a few cases reported previously also suggests a need of RCT to assess steroids as an established modality for management of this severe but curable entity.

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