Abstract:
DRESS (Drug Rash with Eosinophilia and Systemic Symptoms syndrome) is an idiosyncratic reaction to medication with a long latency characterised by rash, fever, involvement of internal organs, lymphadenopathy and hematological abnormalities, eosinophilia, thrombocytopenia, atypical lymphocytosis with synonyms of AHS (Anticonvulsant Hypersensitivity Syndrome), DIHS (Drug-Induced Hypersensitivity Syndrome) DIDMOHS (Drug-Induced Delayed Multiorgan Hypersensitivity Syndrome) Drug-Induced Pseudolymphoma. I present a case of DRESS syndrome secondary to administration of hydroxy chloroquine.

Keyword: Adverse reactions - DRESS syndrome - Eosinophilia - Hydroxy chloroquine

INTRODUCTION:
Drug hypersensitivity syndrome (DHS) refers to a severe, potentially life-threatening, drug reaction. To better individualize this drug reaction, the term "Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome" has recently been used. DRESS syndrome was first introduced in 1996 by Bocquet et al. (1). Fever, rash, lymphadenopathy, and internal organ involvement with marked eosinophilia constitute the main manifestations. The most frequently involved organ is the liver, followed by the kidney and lungs. The most frequently incriminated drugs are anticonvulsant, sulfonamides, dapsone, allopurinol, minocycline, and gold salt. The pathophysiology of DRESS syndrome remains unclear, but a defect in detoxification of causative drug, immunological imbalance, and infections such as human herpes virus type 6 (HHV 6) have been suggested (2). The overall mortality in DRESS is about 10% and occurs in patients with severe multi-organ involvement (1).

Case report:
Eight year old female child born out of non-consanguinous marriage had presented with
complaints of Fever for 1 month which was high grade and intermittent. Skin lesions which were urticarial rashes from day 4 of fever with itching and peeling for 25 days, Yellowish discoloration of eyes & passing high colored urine for 21 days. Pain both lower limbs, Puffiness of face, pedal edema and abdominal distension, oliguria for 20 days. Previously this child had lesion over the left thigh and knee joint pain on and off since 2 years for which the child was treated with native treatment given initially then for the past 3 months was treated with haloderm cream, Multivitamin Syrup and Tab. Hydroxychloroquine 200mg o.d. On examination child was conscious, oriented, afebrile, icteric; mild pallor, periorbital puffiness, bilateral pedal edema, generalized peeling of skin with dryness and scaling and erosions over lower limbs, gluteal region, lips, oral mucosa were noted. Genitalia, hair and nail were normal. Oral Candidiasis was present and there was no lymphadenopathy. Dry sclerotic lesion over left thigh was noted. Vitals were stable. Liver enlarged 3 cm, spleen just felt. No free fluid. Bilateral crepases were heard in the chest. Investigations showed; WBC Total Count - 23000/cu.mm. Differential Count: Polymorphs - 57%, Lymphocytes - 35%, Eosinophil - 8%. Hb: 9.8 g%. Platelets: 4.67 L /cu.mm. Absolute eosinophil count: 1800 / cu.mm. Peripheral smear revealed atypically lymphocytes. ESR was normal. Renal function tests, urine routine examination & culture were normal. Blood culture did not reveal any growth. LFT; Total bilirubin – 8.9 mg/dl. (Direct 4.5) SGOT – 153 IU, SGPT – 130 IU, ALP – 188 IU, CRP – positive. Coomb’s negative, HIV – negative. ANA – negative, CPK-MB – normal. Hepatitis screening – negative. CXR was normal. X-ray both thighs and knees was normal. USG abdomen – hepatosplenomegaly with altered liver echoes. No pleural and ascitic fluid. USG thigh showed skin & subcutaneous edema and muscles were normal. Initially patient was stabilised with Inj. Cefotaxime, Inj. Vancomycin, T. UDCA Antipyretics & supportive therapy. Later Inj. Dexamethasone was started and continued for 14 days. The skin lesions started resolving from Day 2 of starting steroids. By 7th day skin lesions were cleared. LFT was showing downward trend though the liver span remained the same. The child was discharged after 16 days with oral steroids. On follow up the child was on oral steroids for 2 weeks. No recurrence of symptoms after stopping steroids. Repeat LFT after 45 days showed T. bilirubin – 1.1 mg/dl (Direct 0.6). SGOT – 61 IU/L. SGPT – 50 IU/L
Pictures 1, 2, 3 of the patient (DRESS syndrome) show exfoliative dermatitis before treatment.

Pictures 4, 5 show resolved skin lesions (exfoliative dermatitis) after treatment.

**DISCUSSION:**

Hydroxy chloroquine sulphate is a synthetic antimalarial medication that inhibits the actions of toll-like receptors involved in B cell activation (2), widely used in Rheumatology due to its immune suppressive properties. Antimalarials are well known to cause adverse reactions, ocular and cutaneous side effects being the most frequent. The most frequently noted cutaneous manifestation is skin pigmentation. Already one reported case of DRESS syndrome caused by hydroxychloroquine, citation: Clin Rheumatol[2008] 27:537-539DOI10.1007/SDRESS syndrome was coined in 1996 to describe a rare, but serious hypersensitivity reaction to medications that involved fever, rash, lymphadenopathy, and internal organ involvement along with peripheral eosinophilia. It has been more commonly reported with anticonvulsants, sulfasalazine, allopurinol, nonsteroidal anti-inflammatory drugs, and antibiotics such as sulfonamides and minocycline. DRESS syndrome typically occurs 1 to 8 weeks after exposure to the offending drug and a chronic papulo-pustular skin eruption is often seen which can progress to exfoliative dermatitis. Hepatitis, interstitial nephritis, myocarditis, pneumonitis, and colitis are some of the systemic manifestations of DRESS syndrome. Several investigators have proposed that human herpesvirus-6 infection or reactivation may...
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trigger the onset of DRESS syndrome and contribute to internal organ involvement and the relapse of symptoms observed long after discontinuation of the causative drugs. Antiviral T cells are generated that may cross-react with the offending drug, reactivating human leukocyte antigen molecules and play a key role in DRESS syndrome similar to graft-versus-host disease. B cells are also likely involved as transient hypogammaglobulinemia has been observed at the onset of DRESS syndrome and drugs that have been implicated in this syndrome inhibit differentiation of B cells to immunoglobulin-producing cells in vitro. Central to this case is the distinction between DRESS and a typical drug eruption. Drug eruptions or “drug rashes” are by far the most common adverse drug reactions affecting the skin. The drug rash often occurs between 4 and 14 days after beginning a new drug, and can even occur 1 to 2 days after cessation of the drug. The onset can be more abrupt in the setting of a repeat exposure to a previously offending drug. It consists of erythematous macules or papules that are often symmetric, begin on the trunk or upper extremities, and become confluent. Although the eruptions may be polymorphous, they do not typically affect mucous membranes, and do not involve organ dysfunction. The key issue with DRESS syndrome to note is that the rash does not simply resolve with discontinuation of the drug; systemic corticosteroids (prednisone 0.5 – 1 mg/kg/d) and monitoring of laboratory tests for visceral involvement are indicated. The most common organ to be involved in DRESS syndrome is the liver and mortality for the syndrome is approximately ten percent especially in patients with severe multi-organ involvement. Care must be taken not to mistake DRESS syndrome for infectious diseases such as measles and infectious mononucleosis. The differential diagnosis should also include drug-induced lupus erythematosus, Kawasaki syndrome, serum sickness-like reaction, hypereosinophilic syndrome, drug-induced pseudolymphoma, and staphylococcal toxic shock syndrome. Significant morbidity with the DRESS syndrome may occur because serious internal organ involvement may go undetected due to its great variability and severity and it may be observed even several months post onset of the rash.

REGISCAR INCLUSION CRITERIA 1.
Hospitalisation. 2. Acute rash. 3. Fever > 38 c. 4. Lymphadenopathy in at least 2 sites. 5. Involvement of at least one internal organ. 6. Blood count abnormalities (lymphopenia, lymphocytosis, eosinophilia, thrombocytopenia). SCORE > 5 denotes Definite DRESS syndrome.

JAPANESE CONSENSUS GROUP DIAGNOSTIC CRITERIA;
MANAGEMENT; 1. Withdrawal of the offending drug. 2. Systemic corticosteroids. 3. i.v Immunoglobulins, interferon – Second line drug. 4. Symptomatic management.


REFERENCES


