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OPEN ACCESS CASE REPORT

DRESS Syndrome – A Case Report with Learning Points

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ABSTRACT

Background: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a critical drug-induced hypersensitivity, often associated with antiepileptic drugs.

Case Report: A 21-year-old male with epilepsy developed DRESS syndrome after 8 weeks of phenytoin treatment. Symptoms included fever, widespread erythematous rashes, lymphadenopathy, and gastrointestinal discomfort. Laboratory findings showed leukocytosis, eosinophilia, and elevated liver enzymes, with high serum phenytoin levels. The Regi SCAR score was 7, confirming the diagnosis. Management involved discontinuing phenytoin, starting alternative antiepileptics, and administering corticosteroids and immunosuppressants, leading to patient improvement.

Discussion: This case emphasizes the necessity of early recognition and management of DRESS syndrome in patients on antiepileptic medication. It highlights the importance of the RegiSCAR criteria for diagnosis and the need for vigilant drug level monitoring. The variable presentation of DRESS syndrome, often leading to misdiagnosis, is also discussed.

Conclusion: DRESS syndrome is a life-threatening condition requiring prompt diagnosis and treatment. Awareness among clinicians is essential for early intervention and improved patient outcomes.

Key Words: *DRESS Syndrome, Phenytoin, Drug Hypersensitivity, Eosinophilia, Antiepileptic Drugs*

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INTRODUCTION:

Drug reaction with eosinophilia and systemic symptoms syndrome,also known as drug induced hypersensitivity syndrome, is a hypersensitive drug reaction most frequently encountered with anti epileptic drugs, antibiotics, antiviral drugs, allopurinol and sulfonamides. It is characterized by the presence of fever, rash and eosinophilia. Some patients may also show involvement of various organs like liver, kidney, lung, pancreas etc. Among the criteria used for the diagnosis of DRESS Syndrome, European Registry of Severe Cutaneous Adverse Reaction to Drugs and Collection of Biological Samples (RegiSCAR) Criteria is the most commonly used one.(1) Adverse Drug reactions including rashes, fever and eosinophilia started to get reported after the introduction of hydantoins.(2) The term DRESS syndrome was introduced by Bocquet et al.(3) This syndrome can cause clinical symptoms from 2-8 weeks after initiation of the offending drug. The incidence of DRESS syndrome is approximately 1 in 1000 to 1 in 10000 exposures.(4) In a recent record-linkage study, the risk for developing a hypersensitivity within 60 days of the first or second prescription in new users of Phenytoin or Carbamazapine was estimated to be 2.3-4.5 per 10,000 and 1-4.1 per 10,000, respectively.(5) The severity of cutaneous changes does not co-relate with the severity of internal organ involvement. Here we present an interesting case report of DRESS syndrome within 2 months of introduction of the drug (phenytoin) in an epileptic patient.

Case report:

A 21 year old male patient, a known case of epilepsy presented with complains of intermittent episodes of fever associated with chills. The patient was diagnosed with epilepsy and was started on phenytoin 100 mg bid for last 8 weeks. The patient had developed generalized erythematous rashes all over the body. The macular rashes were accompanied with nausea, vomiting and dull aching abdominal pain. The patient was febrile, normotensive with regular, feeble pulse of 98 bpm. He had generalised lymphadenopathy involving bilateral axillary lymph nodes and left supraclavicular group of lymph nodes.

The laboratory investigations showeda total leucocyte count 9700/mm^3, differential leucocyte count revealed polymorphs-68%, lymphocytes -15%, eosinophils -15%, monocytes -2%, and elevated CRP of 163.85 mg/L. The liver function tests showed elevated enzymes SGOT 303U/L, SGPT 218U/L, GGT 375U/L. ESR was 45 mm/hr. All other investigations including septicemia profile, Weil Felix test,peripheral smear for Malaria and serology for viral hepatitis were negative. Urine cultures showed growth of Enterococcus species and antibiotics were escalated accordingly. Serum Phenytoin levels were sent which was 37 mcg/ml (normal therapeutic range-10-20mcg/ml). Phenytoin was stopped and anti epileptics were changed to Benecetam 500 mg bid and Lacosamide 100 mg bid. Patient over the days developed dry cough and did not subside to antitussives.HRCT thorax was negative for Pneumonia with multiple enlarged bilateral axillary lymph nodes. USG guided FNAC of the left axillary and supraclavicular lymphnode was done which showed features suggestive of reactive lymphadenopathy. Application of Regi SCAR scoring system yielded a score of 7.

Patient was started on Dexamethasone 8 mg bid and later on immunosuppressant Cyclosporin 100 mg bid. Regular monitoring of blood parameters was done. The patient improved and was later discharged on day along with a course of corticosteroids and immunosuppressants.

Figure 1: Macular rashes over chest and neck region.

Discussion:

DRESS syndrome is a syndrome with a bread spectrum of clinical features. The clinical manifestations usually begin 2-8 weeks after the introduction of triggering drug. The common features consist of fever, rash, haematological findings (eosinophilia, leukocytosis) and abnormal liver function tests, which can mimic viral hepatitis.(6)

A systematic review of articles published during the past 20 years concerning all psychotropic drugs linked to DRESS syndrome, detected 1072 cases of psychotropic drug induced DRESS syndrome, most commonly implicated with carbamazepine, lamotrigine, phenytoin, valproate, and phenobarbital.(7) Other drugs include minocycline, sulphonamides, sulphasalazine, trimethoprim, allopurinol, abacavir, nevirapine, mexiletine, isoniazid, gold salts, diltiazem, atenolol, captopril, azathioprine and dapsone. The cutaneous manifestations typicallyconsists of maculopapular eruptions, urticaria and can occationally progress to vesicles, bullae, pustules. There can also be associated facial edema, cheilitis and erythroderma. The visceral involvement can occur in the form of hepatitis, pneumonitis, myocarditis, pericarditis, nephritis and colitis. The involvement of these organs resposible for morbidity and mortality. Although abdominal pain, nausea, vomiting and diarrhoea were common presinting symptoms when hepatic involvement is present. Hepatic involvement in the form of hepatocellular necrosis was the most frequent one.(6) The RegiSCAR group suggested criteria for hospitalized patients to diagnose DRESS syndrome include table 1.

Table 1: RegiSCAR Study group criteria for DRESS syndrome

RegiSCAR Study group criteria for DRESS syndrome
Reaction suspected to be Drug related
Acute rash
Fever> 38 degree Celsius
Enlarged lymph nodes at a minimum of 2 sites
Involvement of at least one internal organ
Blood count abnormalities
A) Lymphocytes above or below normal limits
B) Eosinophils above the laboratory limits
C) Platelets below the laboratory limits
Any of these three with suspected drug reaction is indicative of DRESS syndrome in hospitalized patients

Table 2: Criteria proposed by Japanese consensus group

1. Maculopapular rash developed >3 weeks after starting treatment with a limited number of drugs
2. Prolonged clinical symptoms after discontinuation of the causative drug
3. Fever
4. Liver abnormalities (Alanine transaminase >100 U/l) or other organ involvement
5. Leukocyte abnormalities (at least one present) A) Leukocytosis (11,000 cells/ mm3) B) Atypical lymphocytosis (>5% on peripheral smear) C) Eosinophilia (>1500 cell/ml)
6. Lymphadenopathy
7. HHV-6 reactivation
All seven criteria present : typical DRESS
All expect lymphadenopathy and HHV-6 reactivation present: Atypical DRESS syndrome

DRESS syndrome is a T cell mediated delayed type of hypersensitivity reaction. The pathogenesis of DRESS syndrome remains unknown, the proposed hypothesis include presence of specific HLA alleles.(8) These HLA allele association has significant implication for identifying the drug causing DRESS syndrome. The other contributing factor the role of viral infection causing DRESS syndrome. There are numerous publications demonstrating Human Herpesvirus-6 (HHV6), as well as HHV7, Epstein-Barr virus (EBV), and Cytomegalovirus (CMV) reactivation, or even sequential reactivation of several of these herpes family viruses in DRESS syndrome, though the incidence of virus reactivation is highly variable across studies.(8)The most common differential diagnoses for DRESS syndrome are Stevens-Johnson syndrome/toxic epidermal necrolysis, hypereosinphillic syndrome and Kawasaki disease.

The most important intervention in DRESS syndrome is the immediate discontinuation of causative drug.(9) corticosteroids are currently used as first line drugs in the management. When DRESS with life threatening signs such as hepatitis, renal failure, respiratory failure and bone marrow failure occurs along with systemic steroids, immunosuppressants, and intravenous IgG can also be used. When DRESS is confirmed with viral reactivation antivirals such as Gancyclovir can be used along with systemic steroids.

Conclusion:

DRESS syndrome is a severe adverse drug reaction and has high mortality rates. Clinicians should be aware of this diagnosis when patients on anticonvulsantspresent with fever, rash and eosinophilia (sepsis-like syndrome).Management includesrecognizing the presence of this syndrome, discontinuation of the causative drugs, use of systemic corticosteroids and immunosuppressants.

Conflicts of interest – None
Patient consent - Obtained.

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