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*RESEARCH ARTICLE*

# CASE REPORT ON DRESS SYNDROME INDUCED BY ANTITUBERCULOSIS DRUGS

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## *Abstract*

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe adverse drug reaction characterized by an extensive skin rash in association with visceral organ involvement, lymphadenopathy, eosinophilia, and atypical lymphocytosis. We report a rare case of DRESS Syndrome secondary to anti tubercular treatment (ATT). A 53 year old male with pulmonary tuberculosis (TB) presented with fever, facial puffiness, bilateral pedal edema, itchy exfoliative rashes over face, thorax, abdomen, and extremities for 15 days after about 4 months of starting FDC of ATT. On examination there was hypotension (BP-80/60 mm Hg) and bilateral diffuse symmetrical exfoliative dermatitis over face, chest, abdomen, all 4 extremities sparing flexor aspect of thighs and legs. Investigations revealed eosinophilia, leucocytosis (predominantly lymphocytosis), raised alkaline phosphatase and acute kidney injury. FDC was withheld, skin biopsy was performed and the patient was managed as DRESS syndrome fulfilling diagnostic criteria with oral steroids (prednisolone 1mg/kg/day) and other supportive medications. The patient improved gradually with improvement in most of the symptoms and progressive return of laboratory parameters towards normal level. Individuals diagnosed with pulmonary TB who are undergoing treatment with FDC of ATT have a heightened susceptibility to DRESS. The timely identification and cessation of the offending agent can effectively mitigate mortality.



## Introduction:-

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe adverse drug reaction characterized by an extensive skin rash in association with visceral organ involvement, lymphadenopathy, eosinophilia, and atypical lymphocytosis. The clinical presentation is heterogeneous, and the disease course is typically prolonged. Despite the cessation of the offending drug, flares of disease may continue to occur. The latency between drug initiation and onset of disease is prolonged, typically between two to eight weeks. Drug reaction with eosinophilia and systemic symptoms (DRESS) is the most widely used term; drug-induced hypersensitivity syndrome (DIHS) is also frequently used. DRESS is estimated to occur in 0.9 to 2 per 100,000 patients per year. In hospitalized patients, DRESS accounts for 10 to 20 percent of all cutaneous adverse drug reactions. DRESS syndrome results from T cell-mediated hypersensitivity triggered by drugs in 80% of cases, with high-risk medications including anticonvulsants and antibiotics. Genetic factors, particularly HLA polymorphisms, and drug metabolism variations also contribute to susceptibility. We report a case of DRESS syndrome secondary to anti-TB drugs.

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**Case Report:**
A 53 year old male patient presented to casualty with complains of fever, facial puffiness, both lower limb swelling, itchy exfoliative rashes over face, thorax, abdomen, and extremities for 15 days. The patient was diagnosed as a case of pulmonary TB (though sputum-reports not available) by an outside physician 4 months ago and started on FDC as recommended by the NTEP. Patient had completed the course of intensive phase and currently taking continuous phase regimen. The patient had no other comorbidities.

**Figure 1:-**

On examination, patient was hypotensive (BP-80/60 mmHg), rest other vitals were stable. He had dry skin with bilateral diffuse symmetrical exfoliative dermatitis over face, chest, abdomen, all 4 extremities sparing flexor aspect of thighs and legs [Figure 1]. There was no mucosal, conjunctival involvement or lymphadenopathy. The findings of the examination of abdominal, cardiovascular, repiratory and central nervous system were unremarkable.

Lab investigations revealed that the patient had eosinophilia (Absolute Eosinophil Count – 2081), leucocytosis (predominantly lymphocytosis), raised alkaline phosphatase and acute kidney injury with low urine output [Table 1]. On peripheral smear, the patient had a normocytic normochromic anemia with eosinophilia with a few reactive lymphocytes [Figure 2]. Serology for dengue, widal, HIV, HbsAg and HCV were all negative. Blood culture revealed no growth. Autoimmune profile also came back negative. Chest X-ray PA view showed non homogenous opacities in the left upper zone [Figure 3].

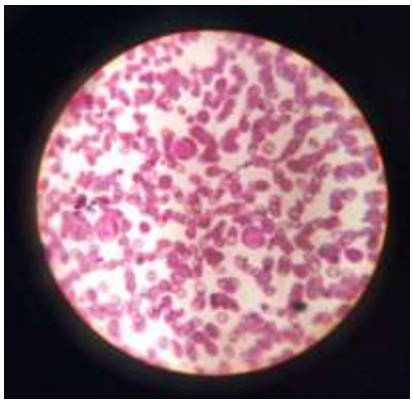

**Figure 2**

**Figure 3:-**

The patient's antitubercular (ATT) was put on hold after the lab investigations. He was treated for hypotenion and AKI with inotropes, started on IV broad-spectrum antibiotics, and for dermatitis, Dermatologist opinion was sought and emollients and anti histaminics were given accordingly. Once the patient was stabilized, patient underwent skin biopsy, which was reported as sub acute dermatitis with diffuse lymphocytic and eosinophilic infiltrates [Figure 4]. After ruling out other possible causes, diagnosis of DRESS Syndrome was made (with a cumulative score of 7 on RegiSCAR DRESS Scoring System) and anti-tubercular drugs were suspected to be the cause of this severe drug reaction.

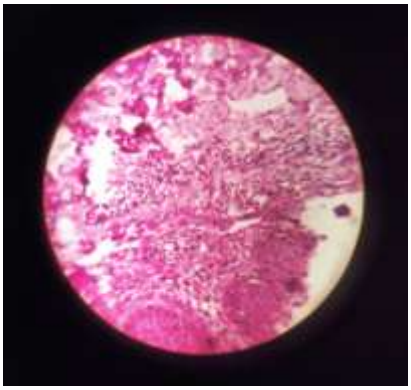

**Figure 4:-**

The patient was given prednisolone 1 mg/kg daily for 20 days. Later, the dose was gradually tapered and stopped over 4 weeks. Fever lasted for 5 days, rash gradually resolved after 10 days and renal function started to improve. The patient was discharged home after 21 days and advised to follow-up with repeat investigations.

**Table 1:-** Laboratory values in the course of the disease.

| **Day** | **WBCs** (per cmm) | **Neutrophils** (%) | **ALP** (U/L) | **Blood Urea** ( mg/dL) | **S. Creatinine** (mg/dL) |
|---|---|---|---|---|---|
| Day 1 | 15230 | 40 | 509 | 70 | 2.5 |
| Day 3 | 13720 | 42 | 513 | 71 | 2.4 |
| Day 7 | 11170 | 47 | 365 | 54 | 1.9 |
| Before Discharge | 10290 | 52 | 169 | 45 | 1.4 |

## Discussion:-

Anti TB therapy, especially the FDC therapy, is said to be more efficacious and more tolerable by the patient. As much as the usefulness of the regime, and the potential it has to save lives, there is an undeniable prominence of adverse reaction that occurs due to these drugs.

DRESS syndrome is one such manifestation. which is a severe adverse drug reaction characterized by an extensive skin rash in association with visceral organ involvement, lymphadenopathy, eosinophilia, and atypical lymphocytosis. Mortality ranges from 8% to 10% in this condition especially if there is liver involvement; hence early diagnosis and treatment are crucial. Aromatic anticonvulsants (phenytoin, phenobarbital, carbamazepine) are the most common cause of DRESS. But, DRESS syndrome following ATT is very rare and there are only a few case reports in thee literature. Furthermore, there have been fewer case reports from India that have shown DRESS syndrome secondary to ATT.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is primarily triggered by specific drugs, with about 80% of cases having a clear causative agent. Genetic factors, including HLA haplotypes, predispose individuals to developing DRESS with certain medications. The syndrome is characterized by a T cell-mediated immune response, involving CD4+ and CD8+ T cells producing inflammatory cytokines. Concurrent reactivation of Herpesviridae, particularly HHV-6, occurs in many cases, potentially influenced by drug-induced immune dysregulation. The exact relationship between drug-specific immune responses and viral reactivation remains under study. DRESS underscores the importance of considering both drug exposure and genetic susceptibility in its pathogenesis and management.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome typically starts 2-8 weeks after drug initiation, presenting with fever, lymphadenopathy, and a maculopapular rash that progresses to erythema. Mucosal involvement is mild. Systemic symptoms include eosinophilia, leukocytosis, and organ involvement (commonly liver, kidneys, lungs, and heart). Severe cases may lead to acute organ failure, particularly liver and kidneys, requiring intensive care. Prognosis varies; reactivation of herpes viruses may worsen outcomes.

There is no conclusive or specific test to diagnose DRESS syndrome. The Registry of Severe Cutaneous Adverse Reaction (RegiSCAR) group suggested criteria for hospitalized patients with a drug rash to diagnose DRESS syndrome [Table 2]. The diagnosis of DRESS syndrome is made based on the total score: <2 points – no case; 2-3 points - possible case; 4-5 points – probable case; >5 points – definite case for diagnosing DRESS syndrome.

**Table 2:-**

| Clinical parameters | Score | | | Comments |
|---|---|---|---|---|
| | −1 | 0 | 1 | |
| Fever ≥101.3°F (38.5°C) | No/unknown | Yes | | |
| Lymphadenopathy | | No/unknown | Yes | >1 cm, at least 2 sites |
| Eosinophilia $\geq 0.7 \times 10^9$ or ≥10% if leukopenia | | No/unknown | Yes | Score 2 points if $\geq 1.5 \times 10^9$ |
| Atypical lymphocytes | | No/unknown | Yes | |
| Skin rash | | | | |
| ▪ Rash suggestive of DRESS | No | Unknown | Yes | Suggestive features: ≥2 facial edemas, purpura, infiltration, desquamation |
| ▪ Extent ≥50% of BSA | | No/unknown | Yes | |
| Skin biopsy suggestive of DRESS | No | Yes/unknown | | |
| Organ involvement | | No | Yes | 1 point for each organ involvement, maximum score: 2 |
| Disease duration ≥15 days | No/unknown | Yes | | |
| Exclusion of other causes | | No/unknown | Yes | 1 point if 3 of the following tests are performed and are negative: HAV, HBV, HCV, mycoplasma, chlamydia, ANA, blood culture |

The mainstay of treatment for this remains to be an immediate withdrawal of the offending drugs and treating the patient symptomatically, with corticosteroid (topical/oral – depending on the symptoms). Adjunctive measures include gentle skin care with emollients and warm baths/wet dressings.

## Conclusion:-

DRESS syndrome, an important clinical condition that occurs as a triad of fever, rash, and eosinophilia with the involvement of systemic organs, is rarely reported secondary to anti-TB therapy, as in the present case. Knowledge, identification of the condition, and removal of the offending drug are of utmost importance. There is no specific diagnostic test that can confirm DRESS syndrome. Patients should avoid re-exposure. Suitable treatment alternatives have to be found. Physicians who prescribe ATT need to be aware of this severe hypersensitivity reaction to anti-TB drugs. General awareness of DIHS/DRESS is very important due to the severity and life threatening potential of this type of drug reaction.

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