RESEARCH PAPER

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome with Transfusion Challenges: A Transfusion Medicine Perspective

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ABSTRACT

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a serious and potentially fatal form of hypersensitivity reaction characterized by a delayed onset of symptoms and multisystem involvement. It is frequently associated with hematological abnormalities and immune dysregulation, which can complicate clinical management. Immunohematological challenges may significantly impact compatibility testing and delay transfusion support. In such scenarios, transfusion of least incompatible red cell units with close clinical monitoring may be required. Early recognition, withdrawal of the offending agent, and a multi-disciplinary approach are critical and should be used to better patient outcomes.

Keywords: DRESS syndrome, Eosinophilia, Transfusion challenges, Immunohematology, Hypersensitivity reaction, Compatibility testing.

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Introduction:-

Drug reaction with eosinophilia and systemic symptom (DRESS) or drug-induced hypersensitivity syndrome is a severe, T-cell-mediated, hypersensitivity reaction caused by drugs [1]. It is a potentially life threatening disorder with a mortality rate of about 10% reported [2]. Though the precise pathogenesis is not completely understood, it has been linked to certain drugs, specific human leukocyte antigen (HLA) alleles, and altered immune response[2,3].

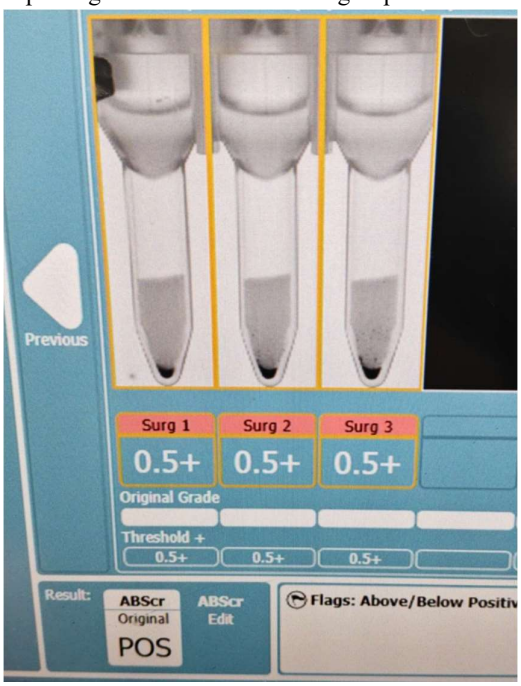
Antimicrobial agents like linezolid have been reported as potential triggers of DRESS syndrome, although considerable rare [3]. A positive direct antiglobulin test (DAT), the formation of autoantibodies and signs of immune-mediated hemolysis due to the systemic production of immunoglobulins are all potential outcomes of the immunohematological workup of DRESS syndrome [4]. However, this syndrome may also present with severe and potentially life-threatening complications such as acute gastrointestinal bleeding [5]. Diagnosis can be difficult and may be based on clinical judgment with the assistance of scoring systems, like the RegiScar (Registry of Severe Cutaneous Adverse Reactions) criteria [6].

Rarely but clinically important complications are acute kidney injury (usually secondary to interstitial nephritis), myocarditis, pneumonitis, and hematological dysfunction, which contribute significantly to morbidity and mortality. The laboratory and imaging results are usually dependent on the degree of organ involvement with hepatic injury being among the most common and severe manifestations [7–9]. Corticosteroids remain the mainstay of treatment, while additional immunosuppressive therapies are reserved for severe or refractory cases [10–12].

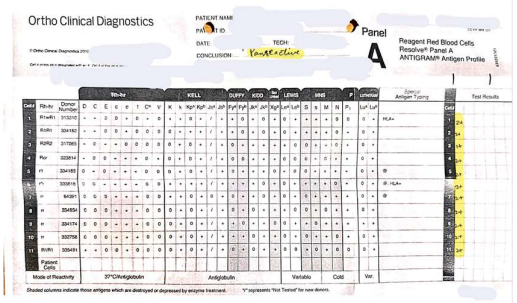
CASE REPORT:-

A 59-year-old male previously diagnosed case of DRESS syndrome before 2 weeks on ongoing corticosteroid therapy, was admitted with persistent fever and systemic symptoms including malaise, anorexia, generalized weakness, diffuse maculopapular rash with facial edema, and signs of multiorgan involvement, particularly hepatic and renal dysfunction. Initial laboratory evaluation revealed hemoglobin of 11.5 g/dL, AEC 700/µL leukocyte count of 10,220/µL, and platelet count of 178 ×10⁹/L. Renal function was deranged with elevated creatinine, while imaging studies were largely unremarkable. During hospitalization, the patient developed methicillin-resistant *Staphylococcus aureus* (MRSA) septicemia and was treated with appropriate antibiotics, including piperacillin–tazobactam and subsequently linezolid based on culture sensitivity. The patient later developed a progressive decline in haemoglobin (Hb-7g/dl) and platelet count (53 × 10⁹/L). Hematological evaluation demonstrated normocytic normochromic anemia with eosinophilia, a platelet count of 53,000/µL, a reticulocyte index of 0.07 suggestive of hypoproliferative marrow, elevated lactate dehydrogenase (551 U/L), and no evidence of indirect hyperbilirubinemia. Linezolid-induced myelosuppression was suspected, and the drug was discontinued; however, anemia persisted, necessitating transfusion support.

On routine immunohematological workup, ABO and Rh(D) blood grouping by column agglutination technique (CAT) determined his blood group to be A Rh(D) positive, with no grouping discrepancies and no previous history of blood transfusions. Pre-transfusion testing showed significant problems. Antibody screening was done using both the column agglutination technique (CAT) and the manual gel card method. The three cell antibody screening was performed using both CAT and manual gel card method showed a positive result with the following reactivity: Panel I: 0.5+, Panel II: 0.5+, and Panel III: 0.5+ as shown in (Tab/Fig-1), positive auto-control (1+), positive indirect Coombs test (1+), and strongly positive direct antiglobulin test (DAT, 3+), suggestive of autoimmune hemolysis or drug-induced immune hemolytic anemia in the context of DRESS syndrome. Antibody identification (ABID) using an 11-cell panel revealed pan-reactivity across all cells (Tab/Fig-2).6 units were crossmatched out of that 6 were incompatible (4 units-0.5+, 2 units-1+). In view of symptomatic anemia (hemoglobin 7 g/dL), a hematology opinion was sought prior to transfusion, and the decision was made to proceed with least incompatible red cell unit .Transfusion was given using least incompatible packed red blood cells (PRBCs) 0.5+ following careful risk–benefit assessment.The patient received a slow transfusion of one unit of least incompatible PRBC under close monitoring for transfusion reactions, with steroid coverage, using a freshly collected triple-bag unit of the same blood group.



Tab/Fig-1: Positive Antibody Screen with Weak Pan-reactivity Suggestive of Autoantibody Interference in DRESS Syndrome



Tab/Fig-2: Pan-reactive Antibody Screen (ABID) with Positive DAT in DRESS Syndrome

The patient showed steady clinical improvement after stopping the offending drug linezolid, continuing corticosteroid therapy targeted antimicrobial treatment and supportive care including transfusion, evidenced by resolution of

fever, improvement in rash and facial edema, stabilization of hemodynamic status, and recovery of hematological parameters, with hemoglobin improving from 7 g/dL to 8.5 g/dL, LDH decreasing from 551 U/L to 300 U/L, reticulocyte index increasing from 0.07 to 1%, and platelet count rising from 53 ×10⁹/L to 120 ×10⁹/L. Renal biopsy confirmed acute interstitial nephritis consistent with systemic involvement of DRESS syndrome, and creatinine levels improved with steroid therapy. No transfusion reactions were observed after PRBC transfusion and the patient was clinically stable at discharge.

Discussion:-

DRESS syndrome is a severe hypersensitivity reaction involving multiple organ systems with a delayed onset, a wide spectrum of clinical manifestations and a high degree of morbidity. It's often difficult to diagnose because of its heterogeneous presentations and overlap with infectious and autoimmune diseases . Previous studies have consistently described delayed onset, multiorgan dysfunction, and diagnostic difficulty in DRESS syndrome [13,3]. The latency period and systemic involvement observed in our patient are consistent with antibiotic-induced DRESS, where symptoms typically develop within 2–9 weeks of drug exposure and commonly involve hepatic and renal systems [13].

Antibiotics are among the most common reported causes of DRESS syndrome. Antibiotic-induced DRESS has been well described, particularly with multiple drug classes, making it more difficult to identify the offending agent in patients receiving polypharmacy [3]. A broad spectrum of antibiotics, including oxazolidinones, have been shown to cause DRESS syndrome with systemic involvement, while being less frequently identified than anticonvulsants. This shows the increasing number of triggering drugs [14]. In our case, linezolid exposure is notable, as it has been increasingly associated with DRESS syndrome presenting with systemic involvement [15]. Linezolid is generally well tolerated and has rarely been implicated in DRESS syndrome, most likely due to delayed T-cell-mediated hypersensitivity mechanisms induced by antibiotic exposure [16]. Other antibiotics, including antitubercular drugs and glycopeptides, have also been implicated, highlighting the broad spectrum of causative agents [17].

Hematological abnormalities are common in DRESS syndrome, most frequently eosinophilia and atypical lymphocytosis, however, cytopenias and immune-mediated complications may also occur. In one case report of DRESS syndrome complicated by severe acute hemolytic anemia, marked anemia and elevated lactate dehydrogenase were seen, which are similar to our patient's findings [18]. In addition, immune dysregulation in DRESS has been associated with secondary autoimmune phenomena, including the development of autoantibodies leading to red cell destruction [19].

From a transfusion medicine perspective, the presence of pan-reactive antibodies and a positive auto-control in our patient suggesting IgG antibody with or without complement activation, this significantly complicates compatibility testing. Similar immunohematological challenges have been described by Et al.Abu [20] where patients with DRESS syndrome and immune-mediated hemolysis, were distinguishing autoantibodies from underlying alloantibodies is critical prior to transfusion. In such cases, transfusion of least incompatible red cell units is often necessary when anemia is severe or symptomatic, as demonstrated in our patient.

Treatment of DRESS syndrome is mainly withdrawal of the offending drug. Administration of systemic corticosteroids remains the cornerstone of therapy. Adjunctive therapies such as intravenous immunoglobulin and therapeutic plasma exchange have been applied in severe or refractory cases Peña-Blanco L Et al. [21]. Plasma exchange may be particularly beneficial by removing circulating immune complexes and inflammatory mediators, thereby reducing disease severity. Therapeutic plasma exchange for DRESS syndrome is categorized as Category III in the American Society for Apheresis recommendations, indicating an unclear role and the requirement for individualized clinical decision-making.

Additional case reports have highlighted similar severe systemic involvement and therapeutic challenges in DRESS syndrome, reinforcing the need for individualized management strategies [22]. The coexistence of drug-induced marrow suppression and immune-mediated hemolysis, particularly in the setting of sepsis and multiple drug exposures, further complicates clinical decision-making, as seen in our patient.

The absence of advanced immunohematological workup, including adsorption studies (auto- and alloadsorption), elution testing, and molecular genotyping, limits definitive characterization of the underlying antibody specificity.Finally, previous reports have demonstrated that transfusion of least incompatible units can be performed safely under careful monitoring in patients with complex serological profiles, including those with autoimmune hemolysis [23]. The absence of transfusion reactions in our case further supports this approach and underscores the critical role of transfusion medicine specialists in managing such challenging scenarios. In the presence of pan-reactive autoantibodies, transfusion of 'least

incompatible' or best-matched red cell units is an accepted approach after exclusion of underlying alloantibodies, as complete serological compatibility may not be achievable while still ensuring adequate oxygen delivery with minimal transfusion risk [24,25].

Conclusion:-

DRESS syndrome presents significant diagnostic and therapeutic challenges due to its multisystem involvement and immune dysregulation. This case underscores the complexity of managing transfusion in the presence of pan-reactive autoantibodies and positive serological findings. Transfusion of least incompatible red cell units, when clinically indicated, can be safely performed with appropriate precautions and monitoring. Early recognition along with prompt withdrawal of the offending drug, and timely initiation of corticosteroid therapy are essential for positive outcomes. A coordinated, multidisciplinary approach integrating clinical, laboratory, and transfusion support is essential to optimize patient care in such complex scenarios.

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