A Rare Case of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS): Glimepiride, the Unlikely Culprit

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ABSTRACT
Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare and challenging entity which can be life threatening and is associated with many medications. Yet, Glimepiride has never been reported as offending agent.

We present here the first case of Glimepiride induced DRESS syndrome. A 40-year-old male with type 2 diabetes mellitus was prescribed Glimepiride. One month later, the patient presented with diffuse rash, fever, swelling of extremities and jaundice. The leucocyte count at presentation was 22,000 cells/µL and absolute eosinophil count 5,400 cells/µL, with no atypical cells on peripheral blood smear. Skin biopsy was non-specific. Other sources of infections such as parasitic infections, HIV, viral hepatitis were ruled out. Patient improved symptomatically on discontinuation of Glimepiride and improved dramatically on steroids. DRESS syndrome as a possible complication of Glimepiride should be considered by clinicians. According to RegiSCAR, our case was categorized as definitive with score of 7. In the vast majority of reported cases, they are classified as probable cases.

Keywords: drug reaction, Glimepiride, RegiSCAR.

INTRODUCTION
Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare and challenging adverse drug reaction, which can be life threatening. It presents with fever, variable skin eruptions, hematological abnormalities and involvement of multiple organs. The estimated incidence of DRESS syndrome seems to vary between 1 in 1000 to 1 in 10,000 drug exposures (1). There is a latency period of two weeks to two months between drug administration and onset of symptoms (2). In 1996, Bocquet et al. identified and proposed DRESS as a syndrome, which was believed to be associated with many medications, most commonly anticonvulsants, allopurinol and sulfonamides (3). Early recognition and timely intervention represent the cornerstone of management as the associated mortality is as high as 10% (4). In a recent review of the published cases of DRESS in PubMed/Medline from January 1997 to May 2009, done by Cacoub et al., a total of 44 drugs were found to be involved, but Glimepiride was not mentioned as an offending agent in the literature (5). We are
presenting a rare case of Glimepiride induced DRESS syndrome in a 40-year-old male.

**CASE REPORT**

A 40-year-old male was diagnosed with type 2 diabetes mellitus and was prescribed Glimepiride, which he continued to take for a month. After one month, he presented with a six-day long high-grade fever (102 degree F), pruritic rashes on skin of the face, trunk and extremities (Figures 1 and 2), swelling over the lower limbs (Figure 3) and yellowish discoloration of eyes. On physical examination, jaundice was present along with enlarged non-tender lymph nodes of around 1.5 cm in size in the cervical, axillary and inguinal regions. Skin of the face, trunk and extremities showed lesions suggestive of erythematous rash along with scaling. On admission, his leucocyte count was 22,000 cells/µL and the absolute eosinophil count 5400 cells/µL.

His total bilirubin was 12 mg/dL, SGOT 112 IU and SGPT 126 IU. There were no atypical cells on peripheral smear examination. Skin biopsy revealed perivascular and peri-adnexal inflammatory infiltrates comprised of neutrophils, eosinophils and lymphocytes. The inflammatory
infiltrate is focally invading the vessel wall with extravasation of red blood cells. Serum immunoglobulin E and complement levels were normal. Blood culture and urine cultures were sterile. Stool studies did not reveal any abnormality. Anti-nuclear antibody was found to be negative. Work up was done for fever, jaundice and lymphadenopathy, and possible causes of malaria, dengue, enteric fever, infectious mononucleosis, viral hepatitis, HIV and leptospirosis were ruled out.

Glimepiride was discontinued upon admission and supportive treatment in form of antipyretics and fluids were given. Patient’s symptoms started to improve. Steroid was added in view of organ involvement. Patient’s condition improved dramatically following the addition of steroid and he was discharged 10 days later. On follow up after 10 days of discharge, the patient was asymptomatic with leucocyte count of 8900 cells/µL and absolute eosinophil count of 324 cells/µL, with normal liver function.

**DISCUSSION**

Pathogenesis of DRESS syndrome is not completely understood and is said to be multifactorial, which may involve the immunological mechanism and pathway of drug detoxification (6). Its occurrence would be determined by combination of exposure to a drug capable of causing adverse reaction given in sufficient dosage and for a definite period of use in a susceptible individual (7). Also, predisposition with certain HLA allele has been identified along with associated reactivation of herpes virus family (8). Some patients may have visceral organ compromise and chronic complications, which can lead to a mortality rate of approximately 10%.

Prompt withdrawal of the culprit drug constitutes the only irrefutable way to treat the syndrome (9). The reliability of diagnosis depends on the clinical and laboratory features along with exclusion of other diseases. Antipyretics should be used for lowering fever, and skin care may involve the use of topical steroids and emollients. When exfoliation is present, the management is similar to that of burns, including electrolyte correction, adequate hydration and prevention of sepsis (9).

The role of corticosteroids in DRESS is controversial. As internal organ involvement may be due to accumulation of eosinophils, it may play a role in its management. A dramatic response in both clinical and laboratory findings has been reported. It may be used in case of organ or life-threatening disease (10).

Diagnostic criteria are based on the clinical and laboratory findings. Biopsy may be helpful, but it is not specific. The European Registry of Severe Cutaneous adverse reaction (RegiSCAR) study group has devised a scoring system to help the diagnosis of DRESS syndrome and classify the cases as no case, probable, possible and definitive case (11).

Based on RegiSCAR, our patient had a fever greater than 38.5 degrees Celsius (0 Points), enlarged lymphnodes >1 cm at three sites (1 point), more than 20% eosinophils (2 points), skin rash involving >50% of body (1 point), with edema and scaling (1 point), involvement of liver (1 point) and investigations to rule out other causes (1 point). With a cumulative score of 7, our case was a definitive case of DRESS.

**CONCLUSION**

DRESS syndrome is an unpredictable and challenging entity, which clinicians should keep in mind. DRESS syndrome with Glimepiride as the culprit drug has not been previously reported. Hence, Glimepiride, as an inciting drug causing DRESS syndrome, may be included in the list of probable culprit drugs; so, there is a great need for early diagnosis and intervention, which could help to reduce the significant mortality associated with the use of the incriminated drug.

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