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Case Report

A case report of aceclofenac induced drug induced hypersensitivity syndrome

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ABSTRACT

Drug-induced hypersensitivity syndrome (DIHS) is an unusual, potentially life-threatening, multi-organ adverse drug reaction. DIHS usually develops 2-6 weeks after drug initiation. We report a case of 21 years old female with maculopapular rash associated with fever and generalised lymphadenopathy, 15 days after intake of aceclofenac. Treatment with intravenous corticosteroids, antibiotics and fluids along with cessation of the offending drug resulted in successful resolution.

Keywords: DIHS, Drug reaction with eosinophilia and systemic symptoms, Aceclofenac, NSAIDs

INTRODUCTION

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, also known as DIHS is a potentially life-threatening adverse drug reaction. Dermatologic manifestations of DIHS can be diverse, with morbilliform rash being the most common presentation. It may have a significant multisystemic involvement.[1] Viral reactivation characteristically follows onset of the disease.[2] DIHS is considered a severe drug reaction with a case fatality rate of 10-20%, most commonly from fulminant hepatitis with hepatic necrosis.[3,4] The disease usually starts abruptly with morbilliform exanthema with fever of >38 °C, 2-3 weeks after the introduction of the culprit drug.[2]

CASE REPORT

A 21 years old female, presented to our OPD with history of generalized swelling over her face spreading caudally for 7 days. The patient had an episode of high-grade fever associated with arthralgia 15 days back. The patient took Aceclofenac 100 mg tablet twice daily for the same and after which she developed generalized swelling. There was no history of preceding itching, redness, or trauma on the affected site prior to the onset of lesion. The patient also complained of abdominal pain and development of erythematous rashes over her face and body for 5 days. There was no history of cough, weight loss, loss of appetite and night sweats before and during the disease course. There was no previous personal or family history of similar lesions.

On dermatological examination, an erythematous morbilliform skin eruption involving >75% body surface area associated with facial edema and tender generalised lymphadenopathy. No visible oozing and crusting were noticed from lesions. No mucosa or scalp involvement.

Clinical investigations such as complete blood count, random blood sugar levels, electrolytes, liver function tests, kidney function tests, viral markers, blood cultures, peripheral blood smear, skin biopsy and urine routine examination etc. were done.

On the day of admission, CBC showed bicytopenia with a hemoglobin of 10.7 g/dl and platelet count of 36000/mm^3. Total leucocyte count was 96100 with 65% Eosinophils on differential. Peripheral blood smear

showed bicytopenia with normocytic normochromic anemia with eosinophilic leucocytosis. Absolute eosinophil count was 48500. PT/INR along with ALT, AST, total bilirubin, GGT, urea, uric acid, creatinine, total IgE and CK-MB were raised. USG abdomen was suggestive of Hepatomegaly, Bilateral echogenic kidneys (reactionary to ascites). Viral markers, ANA and blood cultures were negative.

Skin biopsy showed basket weave keratin covered epidermis. Underlying dermis shows superficial and deep mild perivascular inflammatory infiltrate of lymphocytes, histiocytes with few admixed eosinophils.

RegiSCAR score was calculated to be 8; RegiSCAR and Brocquet et al criteria confirmed DIHS, while JSCAR criteria was suggestive of DRESS.

Patient was treated with injectable, oral and topical agents. Platelet transfusion, intravenous fluids, injection methylprednisolone 40 mg and injection meropenem 500 mg 12 hourly, injection tramadol 1 amp 8 hourly was given. Orally, tablet febuxostat 40 mg once daily, tablet paracetamol 650 mg thrice daily and tablet levocetrizine 5 mg twice daily were given. Topically mometasone 0.1% cream mixed with emollients twice a day was applied over the lesions. Patient was discharged after 14 days with a complete resolution of the skin lesions and normal blood investigations on oral methylprednisolone which was gradually tapered.

Figure 1: Facial edema with maculopapular rash over the face and neck.

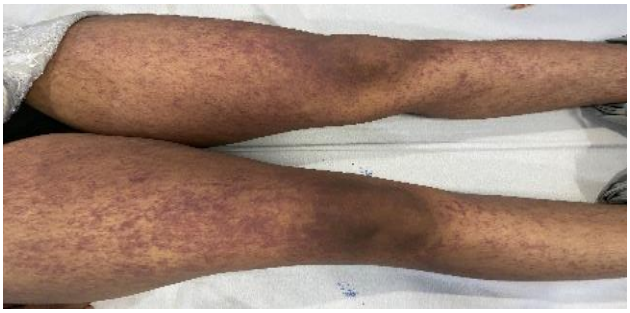

Figure 2: Maculopapular rash over the bilateral legs.

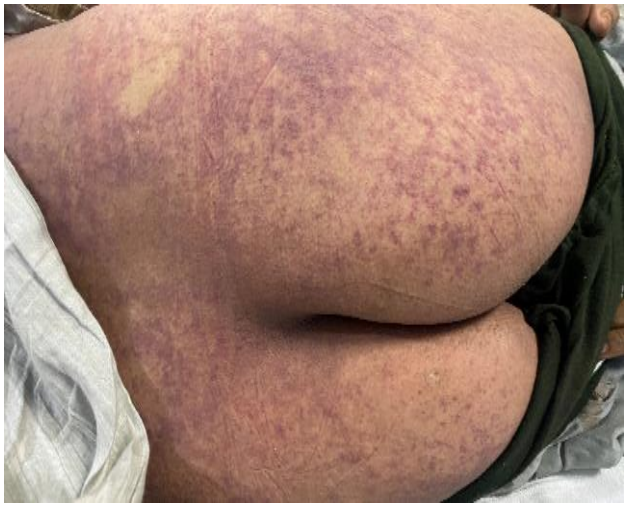

Figure 3: Morbilliform rash over lower back and buttocks.

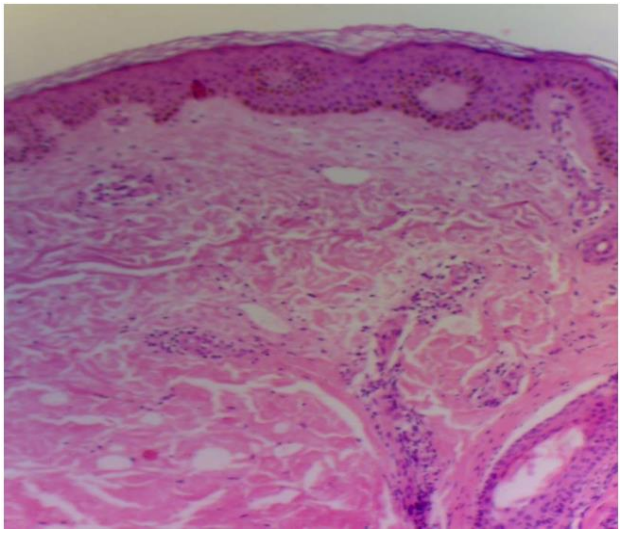

Figure 4: Histology from the lesion.

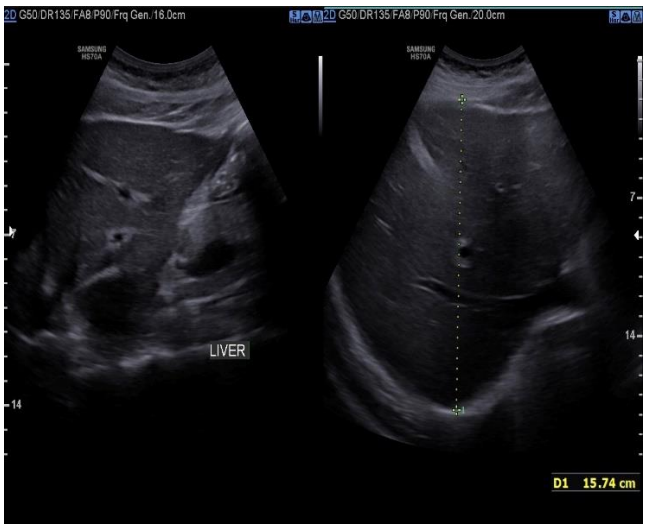

Figure 5: USG whole abdomen suggestive of hepatomegaly.

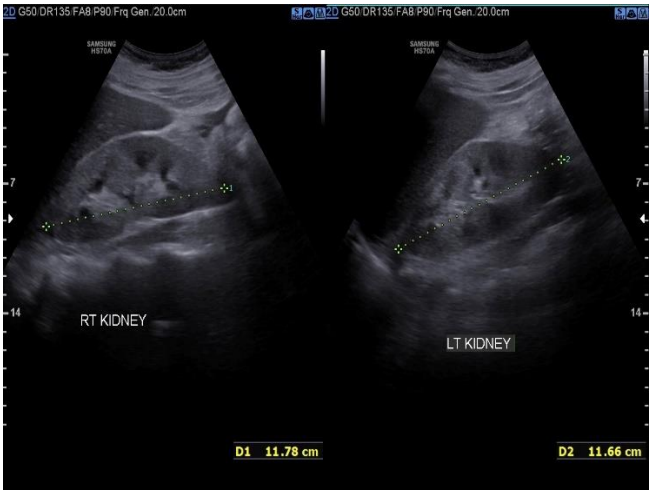

Figure 6: USG whole abdomen suggestive of bilateral echogenic kidneys (reactionary to ascites).

DISCUSSION

DIHS, or DRESS, is a multiorgan systemic disease characterized by fever, skin rash, lymphadenopathy, leucocytosis with eosinophilia and atypical lymphocytes, and liver dysfunction.[5] Necessary elements for DIHS are the drug; the virus; and their interplay with the immune system. DIHS has been associated with HHV-6 infection, human herpesvirus 7 (HHV-7), EBV and CMV.[6] It is triggered by a drug (usually an antiepileptic drug) started 3 weeks to 12 weeks before the onset of symptoms.[7] DIHS/DRESS is frequently associated with only a few drugs, like carbamazepine, phenytoin, phenobarbital, lamotrigine, dapsone, mexiletine, salazosulfapyridine, allopurinol, and minocycline.[5] However, it is less commonly associated with NSAIDs.

Clinically, DIHS usually starts with fever, which is followed by a cutaneous rash, lymphadenopathy and pharyngitis over the next 1-2 days. This is followed by systemic involvement, most commonly the liver, although hematologic, renal or pulmonary impairment may also occur.[8]

Symptoms usually develop 2-8 weeks after exposure to the drug, but earlier onset may be seen in patients with previous exposure to the offending agent. The most common presenting symptoms are fever and morbilliform rash. Systemic involvement is often present and may manifest as transaminitis, renal insufficiency, pneumonitis, myocarditis, or neurologic abnormities. A majority of patients of DIHS present with either localized or generalized lymphadenopathy. Peripheral blood abnormalities, including leucocytosis with reactive lymphocytosis and/or eosinophilia, are common.[9]

There is presently no gold standard for the diagnosis of DIHS.[1] Bocquet et al were the first who proposed criteria for DIHS.[3] Bocquet's criteria require meeting the following features: skin eruption, eosinophilia ($>1.5\times10^3/\mu L$) or atypical lymphocytes, and internal organ involvement, including lymphadenopathies (>2 cm in diameter), hepatitis (liver transaminases level more than twice the upper normal limit).[10]

The European registry of severe cutaneous adverse reaction study group has proposed a scoring system named as the RegiSCAR scoring system. The RegiSCAR's scoring system classifies DIHS cases as "no," "possible," "probable," or "definite" case.[1]

The Japan severe adverse reaction (JSCAR) research group has also proposed a validation score on the basis of clinical and laboratory features for DIHS. Typical or definite DIHS requires fulfilment of all seven criteria, while the diagnosis of atypical or probable DIHS is made in the presence of typical clinical features in the absence of evidence for HHV-6 reactivation.[11]

The differential diagnosis may include SJS/TEN, Acute generalized erythematous pustulosis angio-immunoblastic lymphadenopathy, erythroderma (lymphoma, eczema, psoriasis), vasculitis, acute viral infection.[12]

DIHS should be managed in an intensive care or burn unit for proper care and infection control. Withdrawal of causative drug, commencement of systemic corticosteroids, and supportive care are the mainstay of treatment of DRESS. Other immunosuppressive drugs have also been tried and show promise in future therapy.[13]

The French society of dermatology has outlined a consensus on the management of DRESS. They recommend the use of prednisone at a dose equivalent to 1 mg/kg/day in patients with any sign of severity including: transaminases level more than five times normal, renal involvement, pneumonia, hemophagocytosis, or cardiac involvement. They further recommend the use of IVIG at a dose of 2 g/kg over five days for a patient with life-threatening signs such as renal failure or respiratory failure.[14]

CONCLUSION

The diagnosis of DRESS should be highly suspected with the presence skin rash, liver involvement, fever, hyper-eosinophilia, and lymphadenopathy. The high rate of HHV-6 and other herpes virus reactivation associated with DIHS implies that it has a complex immunopathogenesis. Immediate withdrawal of causative drug, institutional treatment, and supportive measures, standard skin care, multidisciplinary approach, and prompt initiation of systemic steroid as indicated can reduce the morbidity and mortality to minimum.

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