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Fever with rash; Role of an untold history in clinching the diagnosis

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Abstract

Dapsone is a potent antimicrobial and anti-inflammatory compound, which is mainly used in the treatment of leprosy, neutrophilic dermatoses and a variety of blistering skin diseases. It is known to cause a severe adverse drug reaction presenting with fever, rash and multiorgan involvement known as Dapsone Hypersensitivity Syndrome (DHS). Here we report a case of near fatal fever, rash, and hepatitis secondary to dapsone.

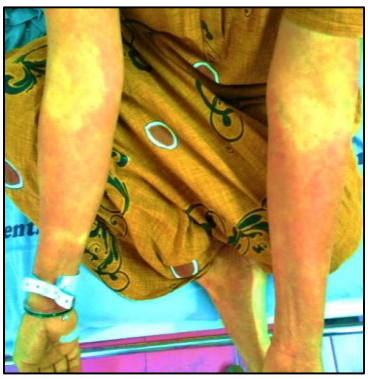
Keywords: Dapsone Hypersensitivity, Dapsone Syndrome, Leprosy, Multidrug Treatment

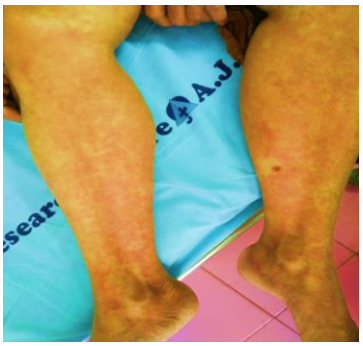
Introduction

Dapsone hypersensitivity reaction was reported as early as 1950 by Lowe and was so named by Allday and Barnes. Dapsone (DDS) syndrome is also called the "five week dermatitis", because it suddenly occurs five to six weeks after the administration of dapsone. It usually subsides on cessation of dapsone therapy.[(1)] This drug-induced hypersensitivity syndrome also known as "sulfone syndrome".[(2,3)] Apart from the cutaneous lesions which are always found, the other features may not necessarily be present in all cases.[(4,5)] With the advent of WHO Multidrug Therapy for leprosy, more cases of dapsone syndrome have been reported which is a potentially life-threatening reaction.

Case Report

A 51 year-old woman presented to us with history of high-grade fever of 5 days duration associated with pruritic rash. On admission, her temperature was 40°C, blood pressure was 130/90 mm Hg, and heart rate was 120 beats/ min. The rash was intensely pruritic, maculopapular exanthematous rash on the extremities, chest, trunk, back and face. There was no history of sore throat, coryza or redness of eyes. The other system examinations were unremarkable. On history and clinical examination we considered Viral hepatitis with rash, Infectious mononucleosis and Viral exanthematous fever as our differential diagnosis. Investigations revealed Hemoglobin - 10 g%; white blood cell count - 7100/mm^3, erythrocyte sedimentation rate of 35 mm in the first hour and a platelet count – 182,000 /mm^3. Reticulocyte count was 0.8%. Peripheral smear showed hemolytic anaemia with eosinophilia. Her liver function tests were abnormal with a direct bilirubin of 4.73 mg/dl, indirect bilirubin of 0.87 mg/dl, aspartate aminotransferase of 256 U/l, alanine aminotransferase - 146 U/l, alkaline phosphatase - 275 U/l, serum albumin - 3.10 g/ dl, and prothrombin time - 13 seconds. Viral hepatitis serology (IgM antibody to Hepatitis A antigen, Hepatitis B surface antigen, and Hepatitis C antibody) were negative. Methemoglobinemia was present. Paul Bunnel test was negative. The levels for urea, creatinine, uric acid, and electrolytes were within normal limits. HIV screening, blood culture, and urine culture were negative. Abdominal ultrasound showed enlarged portal hepatic lymph nodes. Chest x-ray was normal. On further probing patient revealed the history of intake of dapsone for Paucibacillary leprosy for more than a month (however this history was not revealed to us during the time of admission and there were no cutaneous lesions on the body which were suggestive of Hansens disease.) Finally, a diagnosis of Dapsone hypersensitivity syndrome (DHS) was thus made based on the patient's significant treatment history, clinical findings and deranged laboratory investigations. Dapsone was immediately stopped and corticosteroids given orally (prednisolone 30 mg/d). There was clinical improvement after two weeks and laboratory test results returned to normal levels within 3 weeks. The steroids were slowly tapered and stopped over a period of 1 month. She was continued on clofazimine and rifampicin to treat the leprosy.





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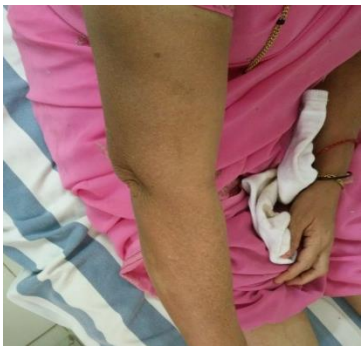

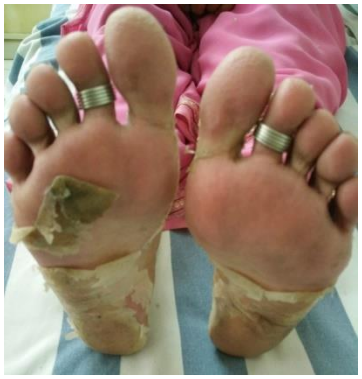

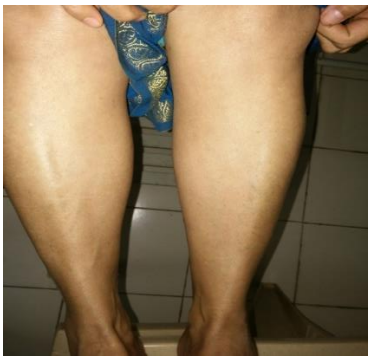

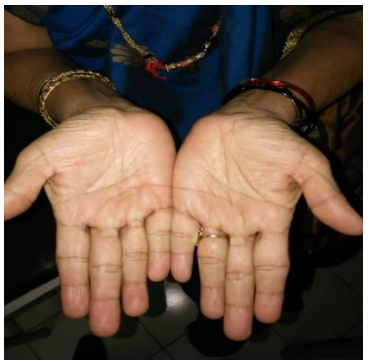

Day 15

Discussion

Dapsone Hypersensitivity Syndrome (DHS) appears in about 0.5-3.6% of persons treated with dapsone.[6] Richardus and Smith[7] have mentioned the following criteria to diagnose a case of Dapsone Hypersensitivity:

a. The symptoms appear within 8 weeks after commencement of dapsone and disappear after the discontinuation of the drug.
b. The symptoms cannot be ascribed to any other drug given simultaneously with dapsone.
c. The symptoms are not attributable to Lepra Reaction.
d. No other disease liable to cause similar symptoms is diagnosed.

Unlike other drug reactions this syndrome can begin within 10 days of initiating dapsone therapy or a prolonged exposure, which can be 6 months or more. This interval between drug introduction and reaction varies, although some generalizations can be made.

R. Zhang et al[8] found an association of HLAB*13:01 with DHS. The use of HLA typing in all patients receiving dapsone in clinical practice is still questionable. HLAB*13 is most frequent in Asians, highest in Indian population. Patch testing and intradermal skin test may be undertaken; however they are unreliable. Where facilities are available, lymphocyte stimulation test with dapsone can be carried out. Oral challenge test with dapsone may be dangerous in previously sensitized person, hence may be carried out under supervision.

The diagnosis of leprosy is made mainly clinically, besides that slit-skin smear examination to identify the bacilli and histopathology examination of lesioned skin can help support the diagnosis. In our patient there was a hypopigmented macule on the right buttock with loss of sensations (touch/pain/temperature), Right Ulnar nerve thickening was present (correct measurement could not be done), Wasting of the right-sided hypothenar muscles, Power- Grade 3, Card test-positive, Froment's sign- positive. Histopathology examination of the skin showed Epidermal thinning, Subepidermal Grenz zone had sheets of foamy

histiocytes sprinkled with few lymphocytes. Fite Farraco Stain was found to be positive in few areas.

Cimetidine, a metabolic inhibitor has the ability to reduce hepatic oxidation of dapsone to hydroxylamine,[9] methemoglobin formation can be controlled for almost 3 months, and the incidence of side effects such as headache and lethargy were significantly reduced. But in a case of already developed DHS its use has not been established. Hence, we refrained its use in our patient. Our patient was treated with systemic corticosteroids in tapering dose and adequately hydrated with oral and i.v. fluids, while dapone was stopped with immediate effect. The paucibacillary leprosy was treated with pulse rifampicin and regular clofazamine.

DHS can be life-threatening; hence it becomes crucial to consider this diagnosis in patients on regular dapsone therapy. It can be easily mistaken for progression of the primary disease. Currently, no tests are available to predict the risk and the progression of DHS. Patient awareness becomes imperative for early recognition of symptoms and signs suggestive of DHS.

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