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Case Report

Severe fatal form of dapsone hypersensitivity syndrome: a case report

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ABSTRACT

Dapsone is widely used for Hansen's disease, dermatitis herpetiformis and other immune and hypersensitivity disorder rarely used in children, can cause fatal severe form of adverse reaction with multiorgan involvement. Dapsone Hypersensitivity Syndrome (DHS) typically presents with a triad of fever, skin eruption, and internal organ (lung, liver, neurological and other systems) involvement, that occurs during first 2 to 8 weeks of initiating the treatment. The incidence of DHS ranges from 0.5% to 3%. We present an eight year child who developed this uncommon condition following two week of dapsone therapy. Child was presented with erythematous skin rash with severe hemolysis and deranged liver profile. With initial treatment child was not responded and required systemic glucocorticoids for long duration. It is emphasized that the clinician must be aware of the syndrome and promptly identified, as it can cause irreversible organ damage or death if untreated early.

Keywords: Dapsone, DHS, Immune and hypersensitivity disorder, Dapsone therapy

INTRODUCTION

DHS is a delayed hypersensitivity reaction of dapsone. One of the distinguishing features between it and other common drug allergies is its longer latent period. It is characterized by a hypersensitivity response to the drug dapsone, first described by Allday, Lowe, and Barnes as a hypersensitivity vasculitis syndrome. Dapsone has anti-inflammatory and immunomodulatory effects which are thought to come from the drug's blockade of myeloperoxidase. There has been an increased incidence of DHS in the past three decades worldwide, which may be due to several points. First, the introduction of free MDT to leprosy patients from WHO. Second, increased awareness of DHS among physicians and the rate of reporting is increasing yearly. The management of DHS included discontinuation of dapsone, systemic corticosteroid, hepatic protection, vitamins, topical glucocorticosteroid cream, and is individualized according to the severity of DHS.

CASE REPORT

A 8 year male child who is a known case of chronic ITP (Idiopathic thrombocytopenic purpura) was treated with dapsone for 2 week, presented with red erythematous rash involving trunk, limb and mucous membrane for 20 day, fever for one week and severe pain all over body for one day.

On examination child was febrile, had generalized erythematous, maculopapular rash over trunk and limb with exfoliation of mucous membrane of lips. There was generalized lymphadenopathy and bilateral pedal edema was noted. He had also hepatomegaly, with normal cardiovascular and respiratory system.

At admission haemogram revealed haemoglobin of 9.7 gm%, total leucocyte count of 65820/mm^3 (neutrophil 75%, lymphocyte 28%, monocyte 5%, eosinophil 2%), platelet count 14000/mm^3, erythrocyte sedimentation rate 50 mm in first hour. His liver function test was deranged (total bilirubin 1.23 mg/dl, aspartate aminotransferase 186 U/L, alanine aminotransferase 205 U/L, alkaline phosphatase 523 U/L, serum albumin 2.9 g/dl). Kidney function and serum electrolyte were within normal limit.

Child was treated with prednisolone, cetirizine, antibiotics ceftriaxone. Child required inj. tramadol for severe pain. After four days of treatment there was no clinical improvement, and investigation showed haemoglobin fall to 4.5 gm/dl (peripheral smear showed features of haemolysis), total leucocyte count increase to 90610/mm^3, total serum bilirubin increased to 3.21 mg/dl (indirect bilirubin 2.52 mg/dl). Following that he was started inj. methyl prednisolone, antibiotic changed to piperacillin with tazobactam and packed cell transfusion was given. On this treatment his clinical and hematological condition improved and child was discharged after 12 days of admission.

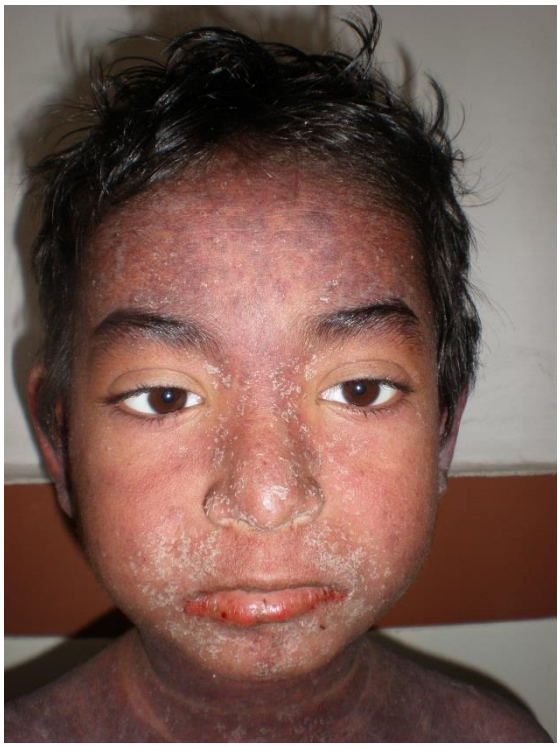

Figure 1: Child with chronic idiopathic thrombocytopenic purpura.

DISCUSSION

Dapsone (4, 4'-diamino-diphenyl sulfone) is the parent compound of sulfone drugs, synthesized in 1908, though its antibacterial properties were discovered in 1937. Dapsone has been used as a first-line treatment for leprosy since the 1950s. It is also the drug of choice for the management of dermatitis herpetiformis. Dapsone is metabolized in two pathways, N-acetylation and N-hydroxylation (oxidation). The formation of toxic intermediate metabolites such as nitrosamines and possibly other compounds through N-hydroxylation pathway are thought to be responsible for the haemolytic anemia, methemoglobinemia and dapsone syndrome.[3] However, the production and detoxification of toxic metabolites of dapsone is influenced by a number of genetic and environmental factors.[4] Due to significant enterohepatic recirculation of the dapsone it has a long elimination half-life averaging between 24 and 30 hours. Strong protein binding of the drug itself (70-90%) and its major metabolite, monoacetyl dapsone (99%), contribute to that long half-life in body up to 35 days.[5]

DHS was first noted by LOWE in 1949, in Nigerian leprosy patient who developed a rash within 2 to 5 weeks of recommended treatment,[6] and the term DHS was coined by Allday and Barnes in 1951.[7] The classic triad of DHS consists of fever, rash, and internal organ involvement (most commonly liver). Hepatitis, exfoliative dermatitis, lymphadenopathy and hemolytic anemia might be seen in varying combinations and sequences[8] Cutaneous manifestations may occur in the form of erythroderma, maculopapular eruption, erythema multiforme, Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson syndrome.[9] This syndrome can be considered a manifestation of the so-called Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, which has been reported in association with various other drugs, such as anticonvulsants, sulphonamides, allopurinol, minocycline and gold salts.[10] Hypersensitivity reactions is not related with dose and even it can cause dangerous reaction in a previously sensitized person. Exact pathophysiology is not clear although Positive lymphocyte stimulation test and predominantly activated cytotoxic T cells in the dermis of a DHS patient with skin involvement have suggested an allergic rather than idiosyncratic reaction.[11] The hematologic toxicity of dapsone (methemoglobinemia, hemolysis and agranulocytosis) is mediated by cytochrome P-450 induced metabolism of dapsone to hydroxylamines.[12] In the management of DHS it is very important to rule out hypothyroidism as it is well known after 3 month of dapsone therapy. The etiology attributed seems linked to the presence of autoantibodies, including antimicrosomal antibodies.[13] Treatment constitutes cessation of drug, early systemic corticosteroid therapy supportive management which lead to rapid recovery.

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