

An unusual case of dapsone hypersensitivity syndrome in a leprosy patient

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Abstract Dapsone (4, 4'-diamino-diphenyl sulfone, DDS) is a sulphone drug. Dapsone works through its antimicrobial and anti-inflammatory properties therefore it is useful for treating wide variety of infectious and inflammatory dermatological conditions including Hansen's disease. Its low cost and easy availability in India, makes it more common in use by the clinicians. It has adverse side effects with usual common doses, and can cause skin, nervous system, gastrointestinal, hepatic, renal, pulmonary and hematological toxicities. Serious side effects may sometimes occur and may present as Steven-Johnson syndrome, toxic epidermal necrolysis or dapsone hypersensitivity syndrome (DHS). DHS is a severe idiosyncratic adverse reaction with multiorgan involvement. It is a rare side effect which occurs 5-6 weeks after initial administration of drug which sometimes results in an unpredictable outcome. Hereby, we report a case of severe, life threatening DHS in a 14-year-old female patient suffering from Hansen's disease which was managed successfully with oral corticosteroids.

Key words

Dapsone, DDS, dapsone hypersensitivity syndrome.

Introduction

Robert Cochrane was the first to introduce dapsone for the treatment of leprosy patients in 1947 in Chingelput, South India.¹ Since then, dapsone has been effectively used as an anti-leprotic drug. Among many varieties of adverse and toxic effects associated with dapsone therapy, DHS is a very rare hypersensitivity reaction with unpredictable outcome.² DHS was referred as 'glandular fever' by Lowe and Smith in 1949.³ Allday and Barnes in 1951 gave it the name 'dapsone syndrome'.⁴ We herein describe a case of DHS in an adolescent female leprosy patient.

Case Report

A 14-year-old female patient presented in our skin OPD with complaints of generalized itchy rashes, jaundice and diffuse hair loss associated with high grade fever for 5 days. There was a history of intake of MDT (PB) drug five weeks prior for the treatment of Hansen's disease consisting of rifampicin (600mg) one capsule empty stomach, supervised dose and dapsone (50mg) in daily dose. General examination revealed that she had a pale look, confused with high grade fever (102°F), icterus, severe pallor, palpable lymph nodes in the cervical and axillary regions with enlargement of liver. There was no edema over face and extremities. Cutaneous examination revealed diffuse hair loss over scalp, generalized skin erythema and extensive scaling - suggesting exfoliative dermatitis (**Figure 1**). There was cheilitis, but oral mucosa and genital mucosa were normal. Few hypopigmented patches were seen over

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Figure 1 At the time of admission, female patient showing severe pale look with hair loss over scalp, generalized skin rashes and cheilitis. Few hypopigmented patches over lower extremities are present.



Figure 2a and 2b At 3 months of treatment most of the skin lesions have resolved and the patients health was restored.

her lower extremities. Detailed history suggested that these were postinflammatory hypopigmented marks.

Laboratory evaluation revealed severe anemia, leucocytosis with eosinophilia (Hb: 6.8 g/dl, leucocytes: 10,800/ μ l, platelets: 2,10,000/ μ l, differential count: neutrophils 74%, lymphocytes 30%, eosinophils 11%), hepatitis [bilirubin: 9.5 mg/dl, AST: 210 IU/l, ALT: 320 IU/l, alkaline

phosphatase: 422 IU/l]. Urine examination showed presence of bilirubin while renal function tests were normal. Tests for malaria, ELISA for HIV-1 and 2, hepatitis A, B, and C were negative. Chest radiography was unremarkable. Ultrasonography of abdomen suggestive of severe hepatomegaly.

With the above constellation of findings, we made the diagnosis of dapsone hypersensitivity syndrome. Dapsone was withheld immediately. She was started with oral prednisolone 30 mg/day (1 mg/kg) and was tapered in two weeks interval given for one month. Symptomatic treatment including antipyretics, antihistaminic (H1 blockers), emollients along with fluid and nutrition were given. Higher antibiotics were added to control infections. To combat anemia three units of blood transfusion was done. Later she was given rifampicin (600mg) once a month supervised dose along with ofloxacin (400 mg) and minocycline (100mg) in daily doses for 6 months. She was followed up later at regular intervals (**Figure 2a** and **2b**).

Discussion

DDS causes common adverse effects like hemolytic anemia in G6PD deficient patients, methemoglobinemia, agranulocytosis, hepatitis, peripheral neuropathy, insomnia and psychosis. It may sometimes lead to Stevens-Johnson syndrome or toxic epidermal necrolysis.

DHS may be considered as a rare yet important serious side effect. It is an idiosyncratic skin hypersensitivity syndrome also called the 'five weeks dermatitis' because it occurs suddenly five to six weeks after administration of dapsone therapy.^{5,6} It consists of exfoliative dermatitis, generalized lymphadenopathy, hepatosplenomegaly, fever and hepatitis.⁷ The drug hypersensitivity syndrome associated with **Drug Rash, Eosinophilia and Systemic**

Symptoms, as similar to our case, is called **DRESS** syndrome.⁸ The severity of skin symptoms and severity of internal organ involvement may not correlate.⁹ In our case only hepatic involvement was seen (as suggestive of laboratory findings) with no changes in spleen and in other organs.

The exact incidence of DHS is unclear due to the lack of a worldwide monitoring system for DHS. But according to the studies in different areas, the incidence is about 1-4% in WHO/MDT patients.^{10,11,12} This increased incidence of DHS may be due to two factors - first, the introduction of free MDT (blister packs) by WHO to the leprosy patients and second the increased awareness among physicians and yearly reporting of the cases of DHS.

Correct approach to treatment in proper time is very important in DHS. The first and foremost should be discontinuation of the dapsone. Most patients usually improve after prompt withdrawal of dapsone, but some still need systemic corticosteroid with supportive treatment including fluid and electrolyte balance, proper body temperature regulation, nutritional support, antibiotics.

To conclude, as dapsone is commonly used for various skin diseases, therefore clinicians including dermatologists need to familiarize themselves with the salient features of the syndrome and its management especially among leprosy patients who are newly treated with an MDT regimen containing dapsone.

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