

## Case Report

# Dapsone hypersensitivity syndrome-rare complication of dapsone therapy

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**Received:** 28 January 2017

**Revised:** 09 February 2017

**Accepted:** 04 March 2017

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### ABSTRACT

Among several other adverse effects of dapsone therapy, dapsone hypersensitivity syndrome is extremely rare but most life-threatening complication. Here we report a case of severe dapsone hypersensitivity syndrome in a 27-year-old female student diagnosed as immune thrombocytopenic purpura on dapsone therapy who was admitted with remittent fever, lymphadenopathy and skin rash and was managed successfully with drug withdrawal and systemic glucocorticoid therapy. The idea of reporting this case is to recognise the rare potentially life threatening adverse effect of dapsone therapy, its timely diagnosis and favourable outcome with systemic glucocorticoid therapy.

**Keywords:** Dapsone, Hypersensitivity, Immune thrombocytopenic purpura, Lymphadenopathy, Skin rash

### INTRODUCTION

Dapsone (4,4'-diaminodiphenylsulfone) is used to treat various infections, hypersensitivity and immunological diseases.<sup>1</sup> The most commonly reported adverse effects of dapsone include idiosyncratic hypersensitivity skin reactions and dose dependant haemolytic anaemia and methemoglobinemia. Dapsone hypersensitivity syndrome (DHS) is a rare life threatening idiosyncratic complication characterised by fever, skin rash, lymphadenopathy, eosinophilia and several systemic complications involving hepatic, pulmonary and other systems leading to irreversible organ damage and death if not recognised early and managed promptly.<sup>2-5</sup>

### CASE REPORT

A 27-year-old female student from a rural area of Kashmir India was admitted in medical ward of Shri Maharaja Hari Singh Hospital, associated hospital of Government Medical College Srinagar, Jammu and Kashmir, India with complaints of remittent type of fever

associated with rigors and chills and pruritic skin rash of 1 week duration. Patients medical records revealed her of being a diagnosed case of immune thrombocytopenic purpura for which patient was put on dapsone 25 days earlier. Her examination on admission revealed patient had a high-grade fever (104°F), icterus, significant multiple discrete, mobile firm to hard lymph nodes involving posterior triangle of neck and bilateral axillae, diffuse confluent maculopapular non-blanchable rash involving face, neck, trunk, upper and lower extremities characteristically sparing palms and soles. Patient was hemodynamically stable and systemic examination was unremarkable except mild splenomegaly. Laboratory workup revealed leukocytosis, eosinophilia and thrombocytopenia (Hb-12.0g/dl, leucocytes-17600/μl, differential count: Neutrophils-56%, Lymphocytes-30%, Eosinophils-14%, platelets-57,000/μl), hepatitis (bilirubin: 3.2mg/dl, AST-134IU/l, ALT-114IU/l, ALP-98IU/l), hypoalbuminemia-3.2g, normal coagulogram. Renal function and urine examination. Work up for hepatitis A, B, C and E, typhoid, leptospirosis, malaria, typhus fever, CMV, EBV and HIV was negative. Septic

screen including repeated blood cultures and skin swab cultures were sterile. Chest X-ray, abdominal sonography and echocardiography was normal. Antinuclear antibodies were negative. Bone marrow work up revealed megakaryocytic hyperplasia which was consistent with diagnosis of immune thrombocytopenic purpura. Bone marrow gram staining and culture work up was unremarkable. Lymph node biopsy was reported as reactive lymphadenopathy.

Based on patient being on dapsone for over 3 weeks, with fever, eosinophilia, characteristic skin rash, lymphadenopathy and hepatitis with negative alternative work up, diagnosis of dapsone hypersensitivity syndrome was considered. With offending drug already discontinued on the day of admission, patient was started on oral steroid therapy (prednisolone 1mg/kg) on day 5 of the illness and showed a dramatic response to the therapy. Steroids were continued in full doses for a month and subsequently tapered off with complete resolution of clinical and laboratory abnormalities

## DISCUSSION

Dapsone is indicated for treatment or prophylaxis of several infections, skin disorders and immune disorders like immune thrombocytopenic purpura. DHS is a rare dose independent hypersensitivity adverse effect which can occur within weeks or months of initiation of dapsone therapy with reported incidence of 0.5-3.0%.<sup>1</sup> In our patient symptoms appeared 3 weeks after starting dapsone therapy.

The exact pathogenesis of DHS is not known however it is believed that metabolites of dapsone produce haptens resulting in anti-dapsone antibody production.<sup>6</sup>

Clinical manifestations include fever, lymphadenopathy, cutaneous manifestations like exfoliative dermatitis, pustular eruptions, erythema multiforme, Stevens-Johnson syndrome and toxic epidermolysis necrosis, eosinophilia, hepatitis pneumonitis, neurological manifestations and multi-organ dysfunction.<sup>7</sup> Our patient had high grade fever, severe exfoliative dermatitis, lymphadenopathy, eosinophilia and hepatitis. No pulmonary and neurological involvement was seen in our patient.

Differential diagnosis includes viral hepatitis, CMV, EBV infections, rickettsial diseases, leptospirosis, complicated malaria and other drug exposures. Diagnosis is ascertained by exclusion of above mentioned diseases with characteristic clinical findings along with antecedent

exposure to dapsone. Prompt response to steroid therapy supports the diagnosis.

Management of DHS involves discontinuation of the offending drug, Systemic steroids oral or intravenous and supportive care.<sup>8</sup> Steroid therapy should be tapered over a period of more than a month because dapsone persists in body for up to 35 days.<sup>8</sup> Early recognition and prompt treatment are essential as mortality in severe DHS has been reported to be as high as 12-23%.<sup>5</sup> Physicians and dermatologists prescribing dapsone need to be aware of this rare potentially life threatening complication to ensure early diagnosis and prompt management

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

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**Cite this article as:** Maqbool M, Wani FA, Koul RK, Shah PA. Dapsone hypersensitivity syndrome-rare complication of dapsone therapy. *Int J Res Med Sci* 2017;5:1700-1.