

DAPSONE HYPERSENSITIVITY SYNDROME - A CASE REPORT

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Abstract:

Dapsone is widely used for a variety of infectious, immune and hypersensitivity disorders. However, the use of dapsone may be associated with a plethora of adverse effects.

We are reporting a 6 year old who was treated with dapsone for one month. He presented to us with low grade fever and skin lesions all over body with normal systemic examination. He was evaluated and was diagnosed as having Dapsone Hypersensitivity Syndrome (DHS) and treated with steroids.

The incidence of DHS ranges from 0.5% to 3%. DHS can present as early as 7–10 days after administration of the drug upto 6 months into therapy DHS must be promptly identified, as

untreated the disorder could be fatal. This syndrome is best approached with the immediate discontinuation of the offending drug and prompt administration of oral or intravenous glucocorticoids. Since dapsone is used for various indications, the salient features about the syndrome and its management should be familiarized.

Keywords: Dapsone, Hypersensitivity, DHS, DRESS.

Introduction :

Dapsone has been the drug of choice for the treatment of leprosy but it is also used for the treatment of many dermatologic indications like dermatitis herpetiformis, vesicobullous dermatoses, cutaneous vasculitis, polyarteritis nodosa, nodulocystic acne and cutaneous mycetoma¹. It has antibiotic and anti-inflammatory property that makes it suitable drug of choice for the above mentioned conditions². Dapsone has been increasingly utilized in the chemoprophylaxis of *Pneumocystis carinii* infection in combination with trimethoprim/sulfamethoxazole in HIV patients. This has led to increasing incidence of dapsone-related complications. The various adverse effects include dapsone hypersensitivity

syndrome (DHS), which is characterized by fever, skin eruption and internal organ involvement several weeks to as late as 6 months after patients are given this drug. This case report emphasizes effects associated with DHS

and the discussion provide an overview of pathogenesis, clinical feature, diagnosis and management of DHS.

Case Report:

A six year old previously healthy boy diagnosed with lichen planus was treated with dapsone for one month (100mg quarter tablet once a day). He presented to us with low grade fever and skin lesions all over body due to which he discontinued the medication one week back. Initially the lesions were skin coloured and nonpruritic which soon became reddish pruritic lesions. Patient had loss of appetite and lethargy. There was no history of abdominal pain, vomiting, pallor, bleeding diathesis or cardio respiratory symptoms.

On examination, he had normal vitals and oxygen saturation. There were no pallor, jaundice, lymphadenopathy or cyanosis. There was no oral ulcers. There were multiple maculo papular rashes over the trunk, both upper and lower limbs in addition to few hyperpigmented plaque with scaling on bilateral knees, elbows and legs. Systemic examination was normal.

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Investigations revealed elevated transaminases (SGOT-386IU/L, SGPT-336IU/L), elevated alkaline phosphatase, mildly elevated Prothrombin time/INR and Renal function test was normal. Blood routine showed lymphocytic leucocytosis with normocytic anemia. The child was diagnosed as having Dapsone Hypersensitivity Syndrome and given treatment with oral steroids (1mg/kg/day) and supportive measures. Vitamin K was given for 3 days. Child was discharged on oral steroids. He was reviewed after two weeks. Rashes had reduced and there were no new lesions or systemic symptoms. The clinical presentation of our patient along with the clinical response to glucocorticoids strongly suggest a drug induced hypersensitivity.

Discussion:

The incidence of DHS ranges from 0.5% to 3%¹. DHS is characterized by a hypersensitivity response to dapsone. Dapsone (4, 4'-Diaminodiphenylsulphone) is a sulphone used mainly as an anti-inflammatory and anti-bacterial agent for the treatment of skin diseases. Many mechanisms explain the anti-inflammatory effects of dapsone. They are its interference with neutrophil chemotactic migration and adherence, suppression of neutrophil recruitment, inhibition of local production of toxic secretory products, and inhibition of prostaglandins and leukotrienes release by blocking their inflammatory effects¹. The side effects of dapsone are less if plasma concentration is below 5mg/l¹.

Molecular and Immunopathogenesis of DHS might be a combination of type I, type IV and type III hypersensitivity reactions and also a modified graft versus host disease mediated by activated T-lymphocytes².

After absorption from the gastrointestinal tract it is transported through the portal circulation to the liver where it is metabolized primarily via two pathways: N-acetylation and N-hydroxylation. N-hydroxylation is shown to be the initial step in the formation of toxic intermediate metabolites, such as nitrosamines and possibly other compounds, which can induce hemolytic anemia and methemoglobinemia. It is presumed that these molecules are also important in the pathogenesis of DHS. A reduction

in either quantity or activity of N-hydroxylation reduced the total clearance of dapsone³.

The classic triad of DHS consists of fever, skin eruption, and internal organ involvement. Fever, hepatitis, exfoliative dermatitis, lymphadenopathy and hemolytic anemia might be seen in varying combinations⁴. DHS can present as early as 7–10 days after administration of the drug up to 6 months into therapy⁴. Skin lesions can present as erythematous papules, plaques, pustules, and eczematous lesions, Steven Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN). Usually these lesions begin to resolve within 2 weeks of stopping dapsone. The severity of the cutaneous changes does not correlate with the extent of internal organ involvement. Some of the systemic findings are, infiltrative lung disease, hepatobiliary involvement, splenomegaly, pulmonary eosinophilia, photosensitivity, peripheral neuropathy, psychosis, pancreatitis, renal involvement (in the form of nephrotic syndrome and renal papillary necrosis)⁵.

The differential diagnosis includes DRESS syndrome (drug rash, eosinophilia and systemic symptoms) and its variants, Churg Strauss syndrome, Hypereosinophilic syndrome, TEN, SJS, Still's disease, hematological and lymphoreticular malignancy and certain connective tissue disorders.

The main treatment for DHS is immediate discontinuation of the drug with initiation of oral or parenteral glucocorticoids, depending on severity. Dapsone is found to persist in the body for up to 35 days hence, the glucocorticoids should be tapered gradually over a period of more than one month. Patients with viral hepatitis are at increased risk for the development of DHS, suggesting the need to perform a screening test for hepatitis B before starting dapsone⁶.

There is also a higher risk for the development of hypothyroidism after three months, considering thyroid replacement therapy if the patient develops clinical hypothyroidism as a delayed complication. Supportive measures like nutritional support, meticulous fluid and electrolyte balance, control and prevention of infectious

complications (cellulitis, sepsis) and skin care if necrotizing disease (TENS or SJS). For patients with dapsone-induced hemolysis, Vitamin E supplementation might be beneficial while in patients with methemoglobinemia co administration of cimetidine can have an ameliorative effect. Other therapeutic options that could be tried are

methotrexate, azathioprine, cyclosporine or hydroxychloroquin, though not extensively studied. In some patients, in spite of drug withdrawal and steroid therapy, a relapsing and chronic course might ensue.

A high index of suspicion is needed for early diagnosis and prompt treatment of DHS.

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