

Case Report

DDS- syndrome: a rare side effect of dapsone in leprosy patients

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Abstract A 35-year-old male suffering from mid-borderline leprosy was put on multidrug therapy. Six weeks after the commencement of therapy he developed features of DDS- syndrome. Dapsone was immediately stopped, he was put on oral steroids. The patient gradually improved and the liver functions became normal within few weeks. The steroids were gradually tapered off. Dapsone was replaced with quinolones.

Key words

Dapsone, DDS-, syndrome, jaundice, hepatotoxicity.

Introduction

Dapsone (DDS) first came into medicine as an antibacterial agent but was found to be less effective and more toxic than sulphonamides. Likewise its activity against tuberculosis was disappointing. Nevertheless, it has been the mainstay in the treatment of leprosy for many years because of its availability, low cost, low toxicity and susceptibility of strains of *Mycobacterium leprae* to very low concentration of the drug. However, it has also proved a very valuable drug in the management of a wide range of mainly uncommon dermatoses.

Toxicity is a considerable problem with dapsone but overall drug has probably fewer long-term side effects than do corticosteroids or sulphonamides. Toxic side effects are mediated through the

hydroxylamine metabolites. These include hemolysis, methemoglobinemia, and agranulocytosis. Less common side effects include peripheral neuropathy, drug rashes, renal damage, hypoalbuminaemia, cholestasis, psychosis and reversible male infertility. Very rarely it causes hypersensitivity syndrome commonly known as DDS-syndrome which is potentially a fatal condition. We report a case of this rare syndrome.

Case report

A 35-year-old male presented in department of dermatology with a 6-month history of dry scaly plaques over left elbow and buttock. On examination the plaques were punched out in appearance with loss of pin prick and fine touch. Right superficial cutaneous branch of radial nerve and both posterior tibial nerves were thickened and palpable. After thorough clinical examination and investigations, a diagnosis of mid-borderline (BB) leprosy was made. The patient was registered in Leprosy

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Hospital, Lahore and was put on multidrug therapy. After about 6 weeks of commencement of therapy, he started complaining of yellow discoloration of eyes, high colored urine, anorexia and nausea. These complaints gradually worsened and over the next few days he started having low grade intermittent fever, at times accompanied by shivering. Within next few days he developed a generalized maculopapular, severely pruritic rash over the body. On examination of the patient, he was looking toxic and lethargic, was febrile, deeply jaundiced, throat was congested. Cervical, retroauricular, jugulodigastric lymph nodes on left side were enlarged and palpable. They were tender, firm, mobile, discrete and smooth. Liver was palpable (5cm below right costal margin); it was firm, smooth, mobile but was moderately tender. The skin examination showed infectious mononucleosis-like rash all over the body. A provisional diagnosis of DDS-syndrome was made. Investigations showed raised bilirubin (113 $\mu\text{mol/l}$ – normal 8-17 $\mu\text{ mol/l}$) and disturbed hepatic enzymes (serum alanine transaminase 215 IU/l – normal 10-40 IU/l, serum alkaline phosphatase 431 IU/l – normal 148-280 IU/l). Ultrasonography of abdomen showed mild enlargement of liver. HBs Ag and anti-HCV antibodies were not detected. ESR was markedly raised (32mm at the end of 1st. hour - Westergren). Blood showed relative lymphocytosis (46%). Serum urea, creatinine, electrolytes, PT, PTTK were within normal range. Malarial parasite was not seen in peripheral smears. On the basis of clinical picture and investigations, a diagnosis of DDS-syndrome was made. The patient was 'put on systemic steroids (oral prednisolone 1 mg/kg body weight) and dapsone was stopped

immediately. Within few days the patient showed a marked improvement and became afebrile, rash subsided with desquamation. Jaundice also improved and settled gradually. The steroids were gradually tapered off and the patient became all right within few weeks. When the liver functions returned to normal, ofloxacin 200 mg bid was added as substitute for dapsone.

Discussion

Although toxicity is a considerable problem with dapsone but it is used by millions of patients without serious problems. There are several potentially devastating adverse effects of dapsone; however, it is incumbent that patients on this drug should be monitored carefully. Fixed eruptions occur in 3% of West Africans being treated for leprosy. Erythema multiforme¹ and exfoliative dermatitis² have been described during leprosy treatment. Another uncommon side effect is a hypersensitivity reaction (dapsone or sulphone syndrome), the syndrome generally begins 4-6 weeks after the initiation of treatment. The findings are similar to those of infectious mononucleosis. Common signs and symptoms associated with this process are morbilliform eruptions sometimes leading to exfoliative erythroderma with pruritus, fever, malaise, hepatitis, lymphadenopathy, anaemia and lymphocytosis with increased number of atypical lymphocytes³⁻⁹. Virtually all patients develop increased ESR and elevated liver enzymes.¹⁰ Reports of fatalities and spontaneous resolution are found in the literature. In Vanuatu, 24% of 37 patients treated with daily dapsone 100 mg, clofazamine, and monthly rifampicin and clofazamine for leprosy over 4 years,

developed the dapsone syndrome, with a fatality rate of 11%.¹¹ The increase in reactions may be related to a high starting dose of dapsone, probably enhanced by the combination with clofazimine and rifampicin and a genetic susceptibility of the Melanesian population. Immediate discontinuation of dapsone is recommended if symptoms arise and prednisolone given for several weeks. In most cases a favorable outcome is achieved.¹⁰

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