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Case Report

Dapsone induced photosensitivity in Indian women: a rare case

Yashika Garg[1]*, Rajeshwari Gore[1], Sourabh Jain[2], Arun Kumar[1]

[1]Department of Pharmacology, [2]Department of Dermatology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

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***Correspondence to:**
Dr. Yashika Garg,
Email:
dr.yashika22@gmail.com

ABSTRACT

Dapsone, a potent antileprotic anti-inflammatory drug is used in treatment and prophylaxis of many dermatological and non dermatological conditions. Cutaneous adverse reactions to dapsone are uncommon ranging from mild maculopapular rash to fatal toxic epidermal necrolysis. We report here a case of 40-year-old, housewife treated for leprosy with paucibacillary multi drug therapy who presented with red itchy skin lesions over exposed areas of skin which worsened on exposure to sunlight. The patient was diagnosed as a case of dapsone-induced photosensitive dermatitis which was confirmed by improvement of symptoms on withdrawal of dapsone and recurrence of similar lesions on rechallenge with dapsone in reduced dose. Photosensitivity as adverse drug reaction to dapsone is rare and very few reports are available in the literature.

Keywords: Cutaneous adverse drug reaction, Dapsone, Leprosy, Photosensitivity

INTRODUCTION

Dapsone is the main constituent of anti-leprosy treatment used for various dermatological and non-dermatological conditions since the 1940s. Documented cutaneous adverse effects of dapsone range from pustular and acneiform skin eruptions, generalised maculopapular rash to erythema multiforme, erythema nodosum and rarely exfoliative dermatitis or toxic epidermal necrolysis.[1] Dapsone-induced photosensitivity is a rare, non-dose-related adverse effect of the sulfone experienced by patients of inflammatory skin disorders treated with dapsone. Only 13 cases have been reported in the literature to date.[2-7] Here, we report a case of dapsone-induced photosensitivity in an Indian patient on paucibacillary multidrug therapy (PB-MDT).

CASE HISTORY

A 40 year old housewife, resident of Delhi came to Dermatology outpatient department (OPD) of our hospital with raised red asymptomatic lesion on the forehead since 6-8 months. It was insidious in onset and gradually progressive. On physical examination, a well-defined shiny erythematous indurated plaque with smooth surface (3×2 cm in size) was noted. There was no sensory impairment, thickening of nerves or regional lymphadenopathy. Other physical examination was within normal limits. A provisional diagnosis of granulomatous dermatitis was made and a skin biopsy was done. The histopathological examination revealed thinned out epidermis and well-defined discrete epitheloid cell granulomas with multinucleate giant cells and foamy macrophages surrounded by lymphocytes in

upper and mid-dermis. Fite stain for acid fast bacilli did not demonstrate any organisms. Granulomatous dermatitis of possible mycobacterial etiology was suggested. On the clinico-pathological co-relation, a diagnosis of Borderline Tuberculoid (BT) Hanson's disease was made and patient was prescribed WHO recommended Multi Drug therapy (MDT) for Paucibacillary Leprosy comprising of tablet Dapsone 100mg once daily and Cap. Rifampicin 600mg once a month. Two weeks later, patient noticed pain and swelling in left side of her neck. On examination, a red, tender, soft, mobile 2×1cm swelling was felt in left posterior cervical triangle. Fine needle aspiration cytology (FNAC) of the neck swelling revealed reactive lymphadenitis. However, Hansen's disease plaque showed signs of improvement such as decrease in erythema, induration and flattening. Patient was advised cefixime 200mg and diclofenac 50 mg twice daily for 5 days, along with MDT for the primary disease. After four days, patient returned with the complains of fever, headache, swelling on face, itching, burning sensation and redness over exposed areas of the body widely distributed over face, 'V' area of the neck, posterior aspect of the neck, upper back, both hands and extensor aspect of the forearms and feet) which worsened on exposure to sunlight. Covered skin was spared. On examination, erythema, flushing and swelling was noted on malar prominences and chin. There was no pallor, icterus or hepatosplenomegaly. Routine urine, hematological and biochemical parameters including liver function tests, glucose 6 phosphate dehydrogenase and porphyrin levels, antinuclear antibodies, and chest X-ray were within normal limits. Human Immunodeficiency virus, hepatitis B surface antigens were negative. She denied the recent use of new soaps, new creams, or alcohol, different foods and prolonged exposure to sunlight than usual. There was no history of any drug intake other than that prescribed above (i.e.: MDT, cefixime and diclofenac) nor any photosensitivity before this episode. Patient was told to stop all drugs except the MDT and prescribed prednisolone (systemic corticosteroid) and fexofenadine (antihistaminic) in view of possible drug induced hypersensitivity reaction. One week later, the lymph node swelling and pain subsided, but the patient did not get any relief in hypersensitivity symptoms. Now, dapsone was stopped along with continuation of the conservative treatment. Two days after stopping dapsone, patient noticed improvement in her condition and the skin lesions started clearing. On examination, there was decrease in intensity of facial swelling and erythema with complete clearing in two weeks. In view of necessity of MDT for her primary disease, a rechallenge test with single half strength dose of 50 mg dapsone was done after taking necessary precautions and informed consent of patient on complete resolution of lesions. The rechallenge test along with exposure to sunlight led to erythema and burning sensation over photo exposed areas within 24hrs similar to previous episode thus confirming the diagnosis of dapsone induced photosensitivity, reaction.

Now, Dapsone was withdrawn and the patient was prescribed alternate antileprosy treatment with Ofloxacin 400 mg once daily. After 4 weeks of treatment, patient tolerated the treatment well and did not experience any symptoms of drug induced hypersensitivity. There was no recurrence of photosensitive eruption during follow up visits. The causality assessment for dapsone was "certain" on WHO-UMC causality assessment scale; whereas "probable" on Naranjo's scale (Score 8). The severity of ADR was found to be "moderate (level 3)" as per the modified Hartwig and Siegel Scale.

Figure 1: Erythema and swelling on sun-exposed skin - malar prominences, cheeks, forehead and chin.

DISCUSSION

Dapsone (diaminodiphenyl sulphone or DDS) is the most commonly used antileprosy drug since the 1940s. It is one of the main constituents of multidrug therapy (MDT) in leprosy by virtue of its anti-mycobacterial properties by interference with folate metabolism. Also, it acts it acts as a potent anti-inflammatory agent due its inhibitory effect in neutrophil chemotaxis and neutrophilic oxygen burst. It is also used in treatment of dermatitis herpetiformis, erythema elevatum diutinum and other dermatoses. Documented cutaneous adverse effects of dapsone include generalised maculopapular rash, exfoliative dermatitis, toxic epidermal necrolysis, erythema multiforme, erythema nodosum, pustular and acneiform skin eruptions.[8] Photosensitivity is a relatively rare adverse effect of dapsone.

Photo-induced drug eruptions are adverse drug events due to cutaneous reaction resulting from drug induced sensitization of the skin to ultraviolet/visible radiation. They represent 8% of reported drug induced cutaneous ADRs.[9] Photosensitivity may be phototoxic or

photoallergic reaction. Phototoxic disorders have a higher incidence than photoallergic disorders. The action spectra for most photoallergens and phototoxins lie in the ultraviolet A range.[10] The phototoxic reaction is based on a non-immunological mechanism and can be provoked in the majority of people on first exposure, if the concentration of substance or its metabolite and the amount of radiation of the appropriate wavelength are present. On the other hand, photoallergic reaction is based on immunological mechanism and can be provoked by UV radiation in a minority of people, who have been sensitized to the photosensitiser by previous exposure. It is a delayed (type IV) hypersensitivity and cell-mediated immune response similar to contact allergy occurring mainly on sun-exposed areas reflecting direct cellular damage on the skin produced by the photochemical reaction between the appropriate radiation and a photosensitizer usually a drug or a chemical or its metabolites independent of dose and duration of exposure.[11] Drugs implicated in causing photosensitive eruptions are sulphonamides, tetracycline, doxycycline, chloroquin, nalidixic acid, fluoroquinolones, griseofulvin, voriconazole, amiodarone, hydrochlorothiazide, naproxen, piroxicam, amisulpride, chlorpromazine and thioridazine.[12,13] Both topical and systemic sulphonamides are known sensitisers for photoallergic reactions. The characteristic sulphone group (C-SO2-C) as well as its metabolites are perpetrators. By oral route dapsone is mainly metabolized to monoacetyldapsone (MADDS) and hydroxylamine dapsone (DDS-NOH).[14]

Our patient had typical dapsone-induced photoallergic reaction with redness and itching over exposed skin which showed worsening on sun exposure within four weeks after starting dapsone. Dapsone was stopped and supportive therapy with topical emollients and oral antihistaminics alongwith avoidance of sunexposure led to significant improvement within 1 week. Onset of symptoms after the drug intake, type of rash, absence of prior photosensitivity, improvement on withdrawal of drug, and recurrence on rechallenge test led to the diagnosis drug induced photoallergic reaction. The patient was now prescribed alternative MDT for leprosy with Ofloxacin 400 mg. Although dapsone is being used in the treatment of leprosy and prophylaxis of pneumocystis carinii in AIDS patients from last six decades, dapsone-induced photosensitivity is very rare. In another Indian study, dapsone syndrome was reported in about 1.3% of about 700 leprosy patients on MDT which reports similar case presentation as that of our case.[15] Till date, there are 13 reported cases of dapsone-induced photosensitivity. Majority are from Asian continent, could be due to high exposure to sunlight.[1-5]

Drug-induced photosensitivity should be differentiated from other skin reactions mimicking it such as polymorphous light eruption, chronic actinic dermatitis, and rarely by porphyria cutanea tarda, viral exanthemata including infectious mononucleosis and lupus erythematosus. Dapsone-induced photosensitivity should also be differentiated from pellagra which shows darkening of involved skin area as compared to exfoliation and fading of involved skin in photosensitivity. Dapsone-induced photosensitivity can also be a part of dapsone hypersensitivity syndrome, where the patient has systemic symptoms and signs of fever, jaundice, hepatosplenomegaly, generalised lymphadenopathy in addition to exfoliative dermatitis, pruritus.[16]

It is important to recognize the cutaneous ADRs to dapsone, so that severe adverse reactions can be identified and managed promptly. It is equally important to continue MDT in minor CADRs weighing the risk of photosensitivity against it's potential benefit. So that patients suffering from leprosy can be cured and rendered non infectious as early as possible from uninterrupted MDT along with prevention of development of drug resistance.

With this case report, we aim to create awareness about photoallergy as an adverse drug reaction with dapsone. Immediate withdrawal of offending drug along with supportive measures carries excellent prognosis. Hence, cautious use of dapsone can help in early identification and management of this adverse drug reaction, thereby decreasing the incidence and associated morbidity

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