National Journal of Physiology, Pharmacy and Pharmacology

CASE REPORT

Dapsone hypersensitivity syndrome - A case report

Selvalaxmi Gnanasegaran, Mangaiarkkarasi Adhimoolam, Srija Gopal

Department of Pharmacology, Sri Venkateshwaraa Medical College Hospital and Research Centre, Puducherry, India

Correspondence to: Mangaiarkkarasi Adhimoolam, E-mail: mangai.pink@yahoo.in

Received: October 18, 2017; **Accepted:** November 08, 2017

ABSTRACT

Dapsone is widely used for the treatment of leprosy and other immunological and inflammatory dermatological conditions such as dermatitis herpetiformis, vesiculobullous dermatoses, and pustular psoriasis. Dapsone hypersensitivity syndrome (DHS) is a rare reaction associated with fever, skin eruptions, and internal organs involvement. We report a case of DHS who presented with fever, productive cough, dyspnea, skin rashes, and jaundice. Leukocytosis, eosinophilia, and altered liver enzymes were observed in laboratory investigations and patient improved with conservative management.

KEY WORDS: Dapsone Hypersensitivity Syndrome; Fever; Skin Eruptions; Leprosy

INTRODUCTION

Dapsone is broadly used for the treatment of leprosy and other dermatological inflammatory diseases such as dermatitis herpetiformis, vesiculobullous dermatosis, malaria prophylaxis, and pustular psoriasis.[1] The common side effects associated are nausea, dizziness, fatigue, insomnia, paresthesia, hepatitis, and psychosis, whereas methemoglobinemia and hemolytic anemia are dose-related effects. The other rare reactions include dapsone hypersensitivity syndrome (DHS), Stevens–Johnson syndrome or toxic epidermal necrolysis, exanthematous eruption, agranulocytosis, pneumonitis, and nephritis. DHS is an idiosyncratic reaction appears to occur in 0.5%–3% patients, which is characterized by fever, skin rash, lymphadenopathy, eosinophilia, and several systemic complications involving pulmonary, hepatic, neurological, and other systems leading to irreversible organ damage and death when not recognized and managed promptly.[2,3]

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2017.7.1042308112017	

CASE REPORT

A 21-year-old male was admitted to the hospital with the complaints of fever, productive cough, rashes over the trunk and arm, dyspnea, and loss of appetite. A history revealed that he had consulted the dermatologist in our hospital 2 weeks before for the complaints of hypopigmented, hypoanesthetic patch over the left shoulder and was diagnosed as lepromatous leprosy and was initiated on the World Health Organization (WHO)-multidrug therapy. On examination, the patient was febrile (temp-104°F), icteric, conscious, and well oriented with increased pulse rate. Cyanosis and cervical lymphadenopathy were present with multiple erythematous rashes over the trunk and both arms. Bilateral basal crepitations were present. Laboratory investigations showed leukocytosis, eosinophilia, elevated liver enzymes, and prolonged prothrombin time with normal renal parameters. Complete blood count showed hemoglobin-13.3 g/dl, total leukocyte count-18000 cells/cu.mm, and absolute eosinophil count-540 cells/cu.mm; liver function test-serum bilirubin: Total-3.2 g/dl, direct-1.6 mg/dl, indirect-1.6 mg/dl, aspartate aminotransferase-239 IU/L, and alanine aminotransferase-19 U/L; total protein-5.5 g%, albumin-3.0 g/dl, and globulin-2.5 g%; prothrombin time-18 s. Renal function test showed blood urea, serum creatinine, and serum electrolytes within the normal range. Investigations were performed on the day of admission and repeated after 3 days [Table 1]. Chest X-ray showed bilateral lower zone

Table 1: Laboratory investigations on the day of reaction and after 3 days of treatment

Parameters	On the day of drug reaction	3 days after treatment
Hb (%)	13.3 g	11.5 g
Total leukocyte count	18000 cells/cu.mm	10700 cells/cu.mm
Serum bilirubin (total)	3.2 mg/dl	1.5 mg/dl
Serum bilirubin (direct)	1.6 mg/dl	1.0 mg/dl
Serum bilirubin (indirect)	1.6 mg/dl	0.5 mg/dl
Total protein (%)	5.5 g	4.7 g
Albumin (%)	3.0 g	2.7 g
Globulin (%)	2.5 g	2.0 g
AST	239 IU/L	78 IU/L
ALT	325 IU/L	24 IU/L
ALP	190 IU/L	90 IU/L

Hb: Hemoglobin, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase

reticulonodular pattern. DHS was confirmed based on above clinical features and laboratory investigations. Dechallenging was done immediately and the patient was treated with tablet. Paracetamol 500 mg tid/day, injection ceftriaxone 1 g i.v bid/day, injection hydrocortisone 100 mg i.v tid/day, and injection pheniramine maleate 25 mg i.v bid/day.

Symptoms resolved gradually and blood parameters improved from the 3rd day of treatment. As the patient responded well with the treatment, he was discharged after 10 days and this adverse event was reported to the adverse drug reaction monitoring center.

In this case, Naranjo algorithm was used to determine a plausible reaction due to dapsone.[4] The following criteria were considered: There were previous conclusion reports on this reaction (+1); the adverse event appeared after dapsone was administered (+2); adverse event improved when dapsone was discontinued (+1); adverse event reappeared when dapsone was readministered (0); alternate causes that could solely have caused the reaction (+2); the reaction reappeared when a placebo was given (0); drug detected in the blood (or other fluids) in a concentration known to be toxic (0); the reaction was more severe when the dose was increased or less severe when the dose was decreased (0); the patient had a similar reaction to dapsone in the previous exposure (0); and the adverse event confirmed by objective evidence (+1). Based on the total score of 7, this reaction was categorized as "probable" reaction to dapsone administration. According to the WHO-Uppsala Monitoring Centre causality assessment system, the adverse reaction was found to be "probable/likely" reaction to dapsone.[5]

DISCUSSION

DHS is typically characterized by fever, rash, hemolytic anemia, exfoliative dermatitis, lymphadenopathy, atypical lymphocytosis, hepatitis, agranulocytosis, nephritis, pneumonitis, hypothyroidism, and other systemic symptoms which may occur individually or in combination.[3] It was reported initially in 1950 by Lowe and was named by Aldday and Barnet.[6] Typically, the DHS symptoms begin within 2–6 weeks of the starting of therapy. However, it can appear as early as 6 h in a previously sensitized individual or as late as 6 months also after dapsone therapy.[7] Our patient showed moderate clinical symptoms and laboratory findings consistent of DHS which appeared after 2 weeks of dapsone therapy with high-grade fever, skin rashes, lymphadenopathy, eosinophilia, hepatitis, and pulmonary involvement.

The pathogenesis remains unknown and it was presumed that metabolites of dapsone, could form haptens with the production of anti-dapsone antibodies.[8] Metabolic differences in the production (e.g., increased activity or quantity of polymorphic enzymes of cytochrome P450) and detoxification of reactive metabolites could also play an important role in hypersensitivity reactions.[9] Significant enterohepatic circulation and high plasma protein binding of the drug and its metabolite (monoacetyl dapsone) makes the drug remains longer time in the body of up to 35 days.[10-12] Serum dapsone levels stabilize after 8–10 days of oral therapy, and hence, laboratory investigations should be done at baseline and every 2 weeks after the beginning of therapy. The laboratory investigations may predict possible onset of DHS, allowing prompt withdrawal of the drug, and thus preventing a greater number of cases.[6] Prompt withdrawal of the offending drug, supportive measures, corticosteroid therapy, and minimal use of other drugs is recommended as treatment guidelines because the mortality reported to be as high as 12–23% in DHS.[12] Our patient responded well with supportive management, steroids therapy and discharged after 10 days.

CONCLUSION

Our case reported a rare hypersensitivity reaction to dapsone, and hence, it is imperative for the physicians and dermatologists to have a watchful eye over the patients on dapsone to ensure timely diagnosis and appropriate management. The prompt withdrawal of the offending drug and supportive management leads to rapid recovery of our patient.

REFERENCES

1. Zhu YI, Stiller MJ. Dapsone and sulfones in dermatology: Overview and update. J Am Acad Dermatol 2001;45:420-34.
2. Pandey B, Shrestha K, Lewis J, Hawksworth RA, Walker SL. Mortality due to dapsone hypersensitivity syndrome complicating multi-drug therapy for leprosy in Nepal. Trop Doct 2007;37:162-3.
3. Kosseifi SG, Guha B, Nassour DN, Chi DS, Krishnaswamy G. The dapsone hypersensitivity syndrome revisited: A potentially fatal multisystem disorder with prominent hepatopulmonary

manifestations. J Occup Med Toxicol 2006;1:9.
4. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.
5. Meyboom RH, Royer RJ. Causality classification in pharmacovigilance centres in the European community. Pharmacoepidemiol Drug Saf 1992;1:87-97.
6. Aldday EJ, Barnes J. Toxic effects of diaminodiphenylsulphone in leprosy. Lancet 1951;2:205-6.
7. Kumar RH, Kumar MV, Thappa DM. Dapsone syndrome - A five year retrospective analysis. Indian J Lepr 1998;70:271-6.
8. Thappa DM, Sethuraman G. Dapsone (sulfone) syndrome (CME). Indian J Dermatol Venereol Leprol 2000;66:117-20.
9. Rieder MJ, Uetrecht J, Shear NH, Cannon M, Miller M, Spielberg SP. Diagnosis of sulfonamide hypersensitivity reactions by *in-vitro* "rechallenge" with hydroxylamine metabolites. Ann Int Med 1989;110:286-9.
10. Johnson DA, Cattau EL Jr., Kuritsky JN, Zimmerman HJ. Liverinvolvement in the sulfone syndrome. Arch Int Med 1986;146:875-7.
11. Grace M. An unusual case of dapsone syndrome. Indian Dermatol Online J 2011;2:88-90.
12. Kim GW, Park HJ, Kim HS, Kim SH, Ko HC, Kim BS, *et al*. Dapsone hypersensitivity syndrome that occurred during treatment of pediatric patient with erythema elevatum diutinum. Ann Dermatol 2011;23 Suppl 3:S290-5.

How to cite this article: Gnanasegaran S, Adhimoolam M, Gopal S. Dapsone hypersensitivity syndrome - A case report. Natl J Physiol Pharm Pharmacol 2018;8(4):616-618.

Source of Support: Nil, **Conflict of Interest:** None declared.