DAPS ONE-INDUCED DRESS: A CASE REPORT

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ABSTRACT

Drug reaction with eosinophilia and systemic symptoms, is a very dangerous adverse drug effect causing rashes, eosinophilia, and multiple organ damage. Many drugs are implicated in causing DRESS with most common ones being antimicrobials and antiepileptics. Dapsone used in the treatment of Hansen's disease as a first-line agent is known for causing many side effects ranging from nausea, vomiting, insomnia, anaphylaxis, hypersensitivity reactions, rashes, muscle weakness, abdominal pain, and so on. Hence, we report a rare case of dapsone-induced DRESS in a tertiary care hospital in South India.

Keywords: Dapsone, Adverse effect, Liver toxicity, Rashes, Eosinophilia.

INTRODUCTION

Drugs are widely used because of their ability to affect the biological systems of the body. The use of these drugs may also carry certain unwanted or unintended effects [1]. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe adverse drug reaction usually characterized by rash, fever, lymphadenopathy, and single or multiple organ involvement [2]. The most commonly involved organ is the liver, leading to acute hepatitis-like condition. The reaction has a delayed onset, usually 2-6 weeks after the initiation of drug therapy. The estimated incidence of this syndrome varies from 1 in 1000 to 1 in 10,000 drug exposures [3]. The overall mortality associated with DRESS syndrome is about 10% and occurs usually in patients with severe multiorgan involvement [4]. The drugs most commonly causing this reaction are antiepileptics (phenobarbitone, phenytoin, carbamazepine, and lamotrigine), antimicrobials (minocycline, β-lactams, sulfonamides, abacavir, and nevirapine), and allopurinol, causing this reaction are antiepileptics (phenobarbitone, phenytoin, carbamazepine, and lamotrigine), antimicrobials (minocycline, β-lactams, sulfonamides, abacavir, and nevirapine), and allopurinol, sulfasalazine [5]. Here, we describe a case of dapsone-induced DRESS syndrome which was managed successfully using oral steroids.

CASE REPORT

Informed consent was taken from the patient. A 35-year-old male was referred to our hospital on 17/09/2013 with complaints of fever and jaundice for one week. He was diagnosed as having multicellular leprosy in an outside hospital and was started on dapsone 100 mg, clofazimine 50 mg daily, and rifampicin 450 mg single dose monthly on 20/08/2013. On 05/09/2013, he presented with fever, easy fatigability, giddiness, and jaundice. He was found to be anemic (Hb-5.6 mg/dl) and was given blood transfusion (2 units) there. After transfusion, his hemoglobin level rose to 10.1 g/dl (09/09/2013). The patient developed fever and deep jaundice following which he was referred here.

General examination of the patient at admission showed pallor, icterus, and lymphadenopathy with generalized papular eruptions. Ulnar nerve thickening and other leprotic hand changes were present. He also had mild hepatosplenomegaly and epigastric tenderness. The patient was conscious and alert and other systems’ examination were within normal limits. He is a reformed alcoholic and does not have any known drug allergies.

Laboratory investigations done on 17/09/2013 revealed the following. The patient had elevated total white blood cell count (42,800/mm³). Peripheral smear showed eosinophilia (13%) and atypical lymphocytosis (Table 1). The patient also had elevated liver enzymes - alanine aminotransferase 96 IU/L, aspartate aminotransferase 125 IU/L, alkaline phosphatase 1415 IU/L, gamma-glutamyl transferase 848 IU/L, and elevated bilirubin levels - total bilirubin 22.2 mg/dl and direct bilirubin 17.2 mg/dl (Table 2). Renal function tests were within normal limits. Chest radiograph was normal. Tests were negative for malaria, hepatitis B surface antigen and antibodies to hepatitis C virus (18/09/2013). Blood culture was sterile after five days of incubation (17/09/2013). The patient was also negative for antinuclear antibodies done on 27/09/2013.

A diagnosis of DRESS syndrome was made. All antileprotic medications were stopped. The patient was started on oral steroids and antibiotics with tablet methylprednisolone 8 mg 3-0-0, injection tazillin (piperacillin+tazobactam) 4.5 g total dissolved solids (TDS), and injection metronidazole 500 mg TDS. The patient was also given tablet cetirizine 10 mg OD and fusid cream (fusidic acid), Dermcare shampoo for the skin lesions. The patient was discharged on 04/10/2013 after hepatic parameters started resolving and the skin lesions subsided.

DISCUSSION

The acronym DRESS syndrome was first used by Bocquet et al. [4] to describe a potentially life-threatening syndrome usually presenting with cutaneous reaction following exposure to a drug (Dapsone in our case) associated with fever, hematologic abnormalities (eosinophilia and atypical lymphocytes), and internal organ involvement. 4,4’-diaminodiphenylsulfone (Dapsone) is widely used for a variety of infectious, immune and hypersensitivity disorders, with indications ranging from Hansen’s disease, inflammatory disease, and insect bites [6].

The exact pathophysiologic mechanisms involved in its development are not yet fully understood. Different mechanisms have been proposed such as defects in drug metabolism leading to accumulation

| Date       | Total WBC (/mm³) | Eosinophil counts (%) |
|------------|------------------|-----------------------|
| 17/09/2013 | 42800            | 13                    |
| 01/10/2013 | 7100             | 1                     |

Table 1: Laboratory investigations

WBC: White blood cell
Table 2: Laboratory data

| Date       | Total bilirubin (mg/dL) | Direct bilirubin (mg/dL) | AST (IU/L) | ALT (IU/L) | ALP (IU/L) |
|------------|-------------------------|--------------------------|------------|------------|------------|
| 17/09/2013 | 22.2                    | 17.2                     | 125        | 96         | 1415       |
| 19/09/2013 | 21.6                    | 16.8                     | 114        | 73         | 1057       |
| 26/09/2013 | 8.7                     | 7.3                      | 84         | 175        | 751        |
| 28/09/2013 | 6.1                     | 4.9                      | 61         | 137        | 632        |
| 01/10/2013 | 4.3                     | 3.2                      | 43         | 90         | 402        |
| 03/10/2013 | 3.5                     | 2.2                      | 42         | 73         | 334        |

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

Table 3: Adverse drug assessment

| Scaling     | Case |
|-------------|------|
| Naranjo’s   | Probable |
| Hartwig’s    | Moderate severity |
| Thornton’s  | Not preventable |

of toxic metabolites and subsequent immunological reactions, slow acetylation, viral reactivation (especially human herpesvirus 6, human herpesvirus 7, and Epstein–Barr Virus), and genetic predisposition with certain human leukocyte antigen alleles [7]. Dapsone after absorption is metabolized primarily by two pathways: N-acetylation and N-hydroxylation. N-hydroxylation yields a potentially toxic metabolite hydroxylamine which could be involved in the pathogenesis [8].

Among the different diagnostic tools available for DRESS syndrome, the Regi-severe cutaneous adverse reactions (SCAR) scoring system [9] and the Japanese study group of severe cutaneous adverse reactions to drugs (SCAR-J) [10] systems are the important ones. Our case meets both the Regi-SCAR and SCAR-J criteria for the diagnosis of DRESS syndrome as the patient had fever, liver involvement, and blood count abnormalities (leukocytosis, eosinophilia, and atypical lymphocytosis) in addition to the cutaneous manifestations persisting even after withdrawal of the offending agent. In addition, infectious and autoimmune conditions as the possible cause were ruled out.

Causality assessment was done using Naranjo’s scale [11], and a probable causal relationship was established in both the cases. Severity and preventability assessment was done using Hartwig’s scale [12] and Thornton’s scale [13], and it was found to be moderately severe and not preventable, respectively (Table 3)

CONCLUSION

Being a severe adverse drug reaction with considerable morbidity and mortality, a high level of suspicion is required to diagnose this entity early to improve outcome. Early diagnosis and treatment is of utmost importance as delay in treatment may lead to mortality. Prompt discontinuation of offending drug (Dapsone) and systemic steroids is the mainstay of treatment in DRESS along with other supportive treatment. Steroids should be tapered slowly; otherwise relapse of symptoms may occur.

REFERENCES

1. Antony A, Joel JJ, Shetty J, Umar NF. Identification and analysis of adverse drug reactions associated with cancer chemotherapy in hospitalized patients. Int J Pharm Pharm Sci 2016;8(7):448-51.
2. Cardoso CS, Vieira AM, Oliveira AP. DRESS syndrome: A case report and literature review. BMJ Case Rep 2011;2011. pii: Bcr0220113898.
3. Fizenson-Albala F, Auzerie V, Mahe E, Farinotti R, Durand-Stocco C, Crickx B, et al. A 6-month prospective survey of cutaneous drug reactions in a hospital setting. Br J Dermatol 2003;149(5):1018-22.
4. Bocquet H, Bagot M, Roujeau JC. Drug-induced pseudolymphoma and drug hypersensitivity syndrome (Drug Rash with eosinophilia and systemic symptoms: DRESS). Semin Cutan Med Surg 1996;15(4):250-7.
5. Ben m’rad M, Leclerc-Mercier S, Blanche P, Franch N, Rozenberg F, Fulla Y, et al. Drug-induced hypersensitivity syndrome. Clinical and biologic disease patterns in 24 patients. Medicine (Baltimore) 2009;88(3):131-40.
6. Lakshmi R, Liniya S, Vijayalakshmi S. Dapsone induced hypersensitivity syndrome revisited. Acta Derm Venereol 2003;83(5):422-4.
7. Bohan KH, Mannuri TF, Wilson NM. Anticonvulsant hypersensitivity syndrome: Implications for pharmacological care. Pharmacotherapy 2007;27(10):1425-39.
8. 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.
9. Kardaun SH, Sidoroff A, Valerye-Allanore L, Haley S, Davidovici BB, Mockenhaupt M, et al. Variability in the clinical pattern of cutaneous side-effects of drugs with systemic symptoms: Does a DRESS syndrome really exist? Br J Dermatol 2007;156(5):609-11.
10. Shiohara T, Iijima M, Ikezawa Z, Hashimoto K. The diagnosis of a DRESS syndrome has been sufficiently established on the basis of typical clinical features and viral reactivations. J Occup Med Toxicol 2006;1:9.
11. 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(2):239-45.
12. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm 1992;49(9):2229-32.
13. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm 1992;27(6):538.