Indian J Lepr 2024, 96 : 87-89

http://www.ijl.org.in

Case Reports

Dapsone Induced Agranulocytosis – A Report of Two Cases

S Veeranna[1], S Rohith[2], PK Ashwini[3], Vinutha R[4], P Dugar[5]

Received: 01.08.2023 Revised: 16.10.2023 Accepted: 09.12.2023

Dapsone is associated with many adverse effects, some of which are severe and can be fatal. Agranulocytosis is a rare idiosyncratic reaction seen with dapsone. We report two cases, one with leprosy and one with hidradenitis suppurativa who developed agranulocytosis following dapsone administration. Early detection and immediate withdrawal of the drug are essential steps in the management of this severe adverse drug reaction.

Keywords : Dapsone, Agranulocytosis, Leprosy, Hidradenitis Suppurativa

Introduction

Dapsone holds unique pharmacological properties where it serves as both as anti-inflammatory and antimicrobial agent. Dapsone is primarily used in leprosy but is also useful in several dermatological conditions. Even though side effects are rare, dapsone can be associated with severe adverse effects like haemolytic anemia, methhemoglobinemia, agranulocytosis and dapsone syndrome (Bhat & Radhakrishnan 2003).

Agranulocytosis is rare, idiosyncratic reaction, and generally presents within the first 3 months of treatment with an absolute neutrophil count less than 0.5×10^9 per L (Andersohn et al 2007). Onset is gradual, occurring within 2–16 weeks of starting therapy (Sardana et al 2020). We are reporting 2 cases of agranulocytosis due to dapsone used in different indications.

Case 1:

A 24 year old female diagnosed as hidradenitis suppurativa was on dapsone 100mg once daily since 5 weeks, presented with fever, painful swelling in the inguinal area and genitals of 5 days duration. On examination there was diffuse swelling of labia majora extending up to thighs with bilateral inguinal lymphadenopathy. Temperature was 101° F, BP-90/60 mm Hg. Blood counts showed Hb-9.8 gm/dl, WBC -1300 cells/mm^3 (normal-4000-11000 cells/mm^3), neutrophills- 2.2% (40-75%), lymphocytes 93.7% (20-50%), platelets-1.6 cells/mm^3 (1.5-4.5 cells/mm^3). She was diagnosed as drug induced agranulocytosis with sepsis. She was treated with inj granulocyte-colony stimulating factor (G-CSF) 300mcg sc for 5 days, inj meropenem, inj linezolid, inj metronidazole.Surgical drainage of abscess was done. Her blood counts became

[1] Dr. Veeranna S, MD, Dept of Dermatology, JSS Medical College, Mysuru
[2] Dr. Shastri Rohith, MBBS, Rohith Skin Clinic, Mysuru
[3] Dr. Ashwini PK, MD, Dept of Dermatology, JSS Medical College, Mysuru
[4] Dr. Vinutha R, MD, Dept of Dermatology, JSS Medical College, Mysuru
[5] Dr Dugar P, MBBS, Dept of Dermatology, JSS Medical college, Mysuru.
Department of Dermatology, JSS Medical College & Hospital, JSS Academy of Higher Education & Research (JSSAHER), Mysuru, Karnataka- 570004, India
Corresponding author: Professor (Dr) Veeranna S, **Email:** veerannashastry9@gmail.com

normal after 6 days and was discharged after 15 days.

Case 2:

A 35-year-old female presented with 4 days history of fever, sore throat and easy fatigability. She was diagnosed as borderline leprosy 6 weeks before and was started on MB -MDT drugs (dapsone 100 mg, rifampicin 600 mg once a month and clofazamine 300 mg once a month and 50 mg daily). On examination she had multiple hypoaesthetic, hypopigmented patches with thickening of ulnar and radial cutaneous nerves. Her blood examination showed Hb -6.4 gm/dl, WBC count-360cells/mm^3 (normal-4000-11000 cells/mm^3), neutrophils-13.9% (40-75%), lymphocytes-82.9% (20-50%). Chest X ray showed bilateral mild pleural effusion with underlying lung collapse/consolidation, Sputum culture showed *Klebsiella pneumoniae* sensitive to colistin. Blood culture was negative. She was diagnosed as leprosy with dapsone induced agranulocytosis. She was treated with inj G-CSF 300µg sc for 5 days, inj cefepime and inj colistin. She recovered from pneumonia and was discharged after 14 days. She was restarted on MDT without dapsone (rifampicin, clofazimine, ofloxacin and minocycline). Her blood counts became normal after six days of follow-up.

Discussion

Drug induced agranulocytosis is a rare side effect of dapsone, however, this adverse reaction can be severe and fatal. It is an idiosyncratic reaction and the exact mechanism is not known. The drug metabolite hydroxylamine is cytotoxic to bone marrow cells and may play a role in this reaction (Coleman 2001). Dapsone induced agranulocytosis presents with the fever, sore throat or odynophagia, skin rash, cutaneous infections, malaise, cough, headache, chills, and confusion (St Claire et al 2021). Fatality rate of 20% has been reported and is secondary to sepsis. Dapsone therapy requires monitoring of blood counts, weekly for a month then bimonthly for next 2 months and there after periodically. However, given the severity of agranulocytosis and the unpredictable time of occurrence, these routine testing guidelines may not be able to detect this adverse reaction in early stages (St Claire et al 2021).

It is known that several millions of leprosy patients have been favourably treated with dapsone, with the incidence of serious side effects including agranulocytosis being very low. However, agranulocytosis is reported commonly, when dapsone is used in other conditions like dermatitis herpetiformis, autoimmune blistering diseases and malaria prophylaxis (Coleman 2001). This could be because of factors like pharmacogenomics, immunological, different dosage and co-administration of other drugs.

Both of our patients never had agranulocytosis and were not on any other drug which could have caused this reaction. Blood counts done prior to dapsone were normal. In both cases dapsone was given for the first time. Causality assessment using Naranjo scale showed dapsone as the probable cause of the reaction. Our patients developed agranulocytosis between 5-6 weeks after starting therapy. The cell counts normalised within 5 days of stopping the drug and administering G-CSF. Both patients recovered completely.

Patients on dapsone need to be monitored for early detection of this severe reaction. Patients have to be educated regarding the early signs like fever, sore throat and skin rash. A written instruction will help in early reporting. Immediate withdrawal of the drug and administering G-CSF, broad spectrum antibiotics as per management of febrile neutropenia would be life-saving.

References

1. Andersohn F, Konzen C, Garbe E (2007). Systematic review: agranulocytosis induced by nonchemotherapy drugs. *Ann Intern Med*. **146**: 657–665.

2. Bhat M R, Radhakrishnan K (2003). A case report of fatal dapsone induced agranulocytosis in an Indian mid borderline leprosy patient. *Lepr Rev*. **74**: 167-170.
3. Coleman MD (2001). Dapsone-mediated agranulocytosis: risks, possible mechanisms and prevention. *Toxicology*. **162 (1**): 53–60.
4. Sardana K, Bhushan P, Khurana A (2020). Treatment of leprosy. In: *Jopling's Handbook of Leprosy* (Sardana K, Khurana A, editors), 6th edition, CBS Publishers & distributors, New Delhi, pp 245-246.
5. St Claire K, Kaul S, Caldito EG et al (2021). Dapsone-induced agranulocytosis: symptoms may alert more reliably than the current blood monitoring protocol. *Br J Dermatol*. **184 (5**): 962-963.

How to cite this article : Veeranna S, Rohith S, Ashwini PK et al (2024). Dapsone Induced Agranulocytosis – A Report of Two Cases. *Indian J Lepr.* **96**: 87-89.