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Case Study
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A RARE DAPSONE-RELATED LIFE-THREATENING HYPERSENSITIVITY SYNDROME IN A LEPROSY PATIENT

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ABSTRACT

Leprosy is a chronic infectious disease resulting from infection with the bacterium Mycobacterium lepra. It remains a significant public health problem in many parts of the world, particularly in developing countries like India, Indonesia, Nigeria, Bangladesh. Dapsone is a sulfone derivative that has been a cornerstone of multidrug therapy (MDT) for leprosy treatment since the 1940s (Mungroo et al., 2020). Some common adverse effects of dapsone include methemoglobinemia, hemolytic anemia, agranulocytosis, and hypersensitivity reactions (HRS) (Schifff et al., 2006). Life-threatening hypersensitivity reactions to dapsone are a rare but serious complication that needs prompt recognition and management.

KEYWORDS: leprosy, DHS, Drug adverse effects.

INTRODUCTION

A severe and sometimes fatal reaction to dapsone, called dapsone hypersensitivity syndrome (DHS) is characterized by a range of symptoms from and rash to multi-organ failure. This uncommon but dangerous illness usually manifests itself week to months after starting dapsone medication. So the necessity of stopping dapson immediately along with supportive treatment to lessen its serious effects.

CASE REPORT

We report the case of a 52-year-old male leprosy patient who developed a severe, life-threatening hypersensitivity syndrome a month after initiating dapsone-based MDT therapy. The patient was admitted to our hospital, presenting with fever, chills, and rigors. He had jaundice, dark-colored urine, and diffuse abdominal pain for 7 days. One month prior, the patient was diagnosed with multibacillary (MB) Hansen's disease with lepromatous nodules. He was prescribed the WHO multidrug therapy (MDT) regimen, i.e., dapsone 100 mg once daily, clofazimine 300 mg on day 1 every month, followed by 50 mg once daily, and rifampicin 600 mg once a month. The patient was a social drinker and smoker with a history of 20 packs per year. On examination, he was toxic-looking, with icterus, skin rashes, and excoriation of all other body parts. There was tender cervical lymphadenopathy. He had a generalized maculopapular erythematous skin rash with scales.(Fig 1a,1b)

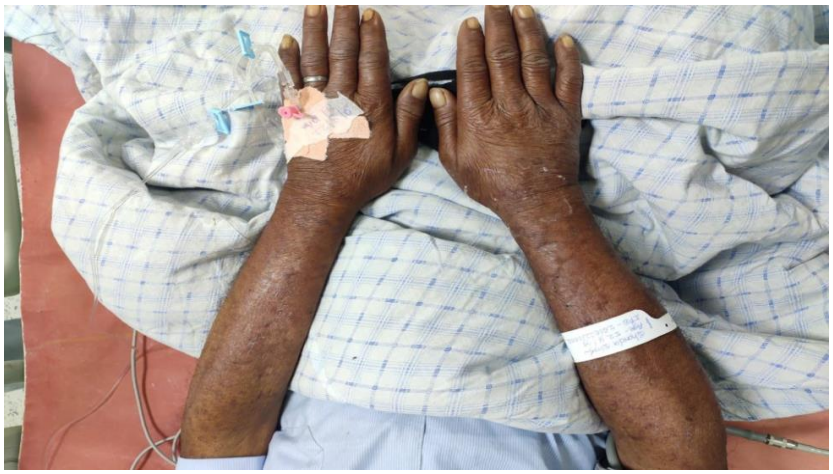

Fig-1 a.

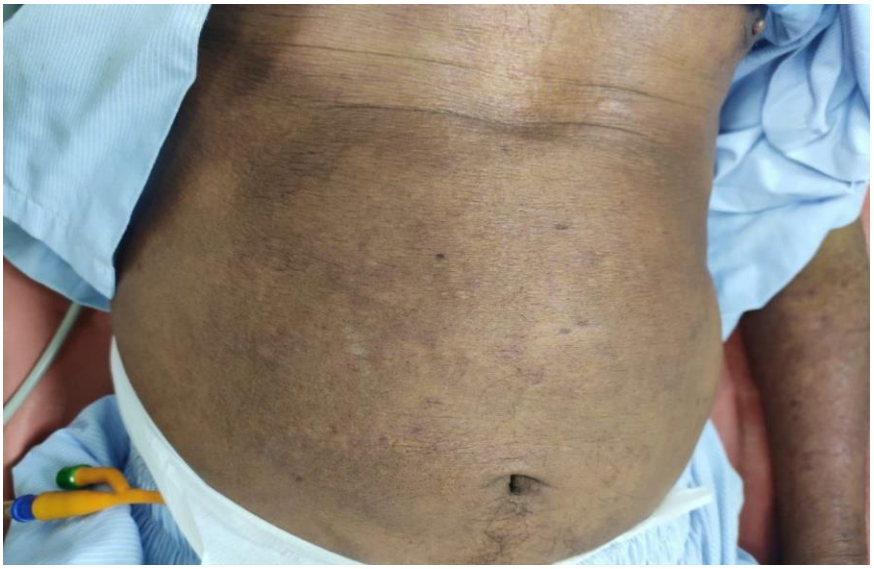

Fig 1: b.

Eyes and mucous membranes were not involved. There were ascites with pitting oedema along with right-sided testicular swelling. His blood pressure was significantly low at 80/54 mmHg, with a heart rate of 116 beats per minute, a temperature of 105°F, and an oxygen saturation of 90% on room air.

Table-1.

Parameters	Day 1	Day 7	Day 14
Hb	8.2 g/dl	8.6 g/dl	10.2 g/dl
WBC	20100/ microliter (N-65%, L-15%, M-8%, E-12%)	13400/ microliter	7500/ microliter
MCV	86.6 fl	87.9fl	92.6 fl
MCH	31.8 pg	32.9 pg	31.8 pg
RBC	3.13 mcL	2.61 mcL	2.66 mcL
PLATELETS	3.13 Lac/ cumm	2.3 Lac/ cumm	2.1 Lac/cumm
RDW	19.4%	21.5%	23%
Total bilirubin	14.73 mg/dl	6.9 mg/dl	2.00 mg/dl
Direct bilirubin	8.73 mg/dl	2.84 mg/dl	0.94 mg/dl
Indirect bilirubin	6.00 mg/dl	4.06 mg/dl	1.06 mg/dl
AST	97.1 U/L	60.21 U/L	34 U/L
ALT	60.5 U/L	52.46U/L	48 U/L
Alkaline phosphatase	854.0 UL	681.5 U/L	340.3 U/L
Total protein	5.05 g/dl	3.98 g/dl	5.34 g/dl
Albumin	2.40 g/dl	2.02 g/dl	2.88 g/dl
Serum creatinine	2.01 mg/dl	1.10 mg/dl	0.7 mg/dl
Blood Urea	86.1 mg/dl	54.40 mg/dl	37.9 mg/dl
Uric acid	7.5 mg/dl	5.65 mg/dl	4.02 mg/dl
Na	135 mmol/L		
K	4.9 mmol/L		
RBS	82.3 mg/dl		
Serum amylase	48 U/L		
Serum lipase	32 U/L		
Triglyceride	218 mg/dl		
HIV/ HCV/ HBsAg	Negative		
CRP	61.19 mg/dl		
LDH	461 U/L		

Table -2.

Urine examination	Day 1	Day 7
Colour	Dark yellow	Pale yellow
Glucose	Nil	Nil
Protein	++	Trace
Pus cell	1-2/hpf	2-4/hpf
Epithelial cell	1-2/hpf	0-1/hpf
Cast	Nil	Nil
Crystal	Nil	Nil
RBC	25-30	2-3

The abdominal examination could not be completed due to diffuse tenderness. The USG abdomen showed mild hepatomegaly with a grade 1 fatty liver and enlarged pancreas with multiple enlarged peripancreatic, pre- and para-aortic, and right iliac lymph nodes. The USG scrotum revealed hydrocele on the right side minimal with scrotal oedema. A peripheral blood smear showed microcytic hypochromic RBCs without any evidence of hemolysis. The blood parameter has a deranged liver and renal function test with both conjugated and unconjugated bilirubinemia. LFT has both obstructive and hepatocellular patterns. creatine was 2.01 mg/dl (Table-1). urine had 2+ protein with no abnormal cells or cast (Table-2). All cultures, along with Gram, ZN, and fungal strains for blood, were negative. All the tests for malaria, leptospirosis, typhus fever, CMV, and EBV were negative. Patent was immediately shifted to the ICU and was managed with IV fluid and the empirical antibiotics meropenem and clindamycin. In view of persistently low BP and decreased urine output, the vasopressor noradrenaline was started. He continued to have a fever despite being on antibiotics for 3 days. A diagnosis of dapsone-induced hypersensitivity syndrome was made on the basis of a history of dapsone intake followed by fever, skin rash, eosinophilia, lymphadenopathy, hepatitis, and nephritis. Dapsone was immediately stopped, and he was given IV prednisolone (1 mg/kg) on day 4, and IV antibiotics continued, IV fluids, oral antihistamines, multivitamin and mineral supplements, and petroleum jelly for topical application on the skin. He improved over the next two weeks with gradual absences of fever with gradual absence of fever jaundice and rashes. He was switched to oral prednisolone for one month and gradually tapered over six weeks with regular follow-up. Recovery was complete after one month. Clofazimine and rifampicin were continued. (Fig 2a,2b)

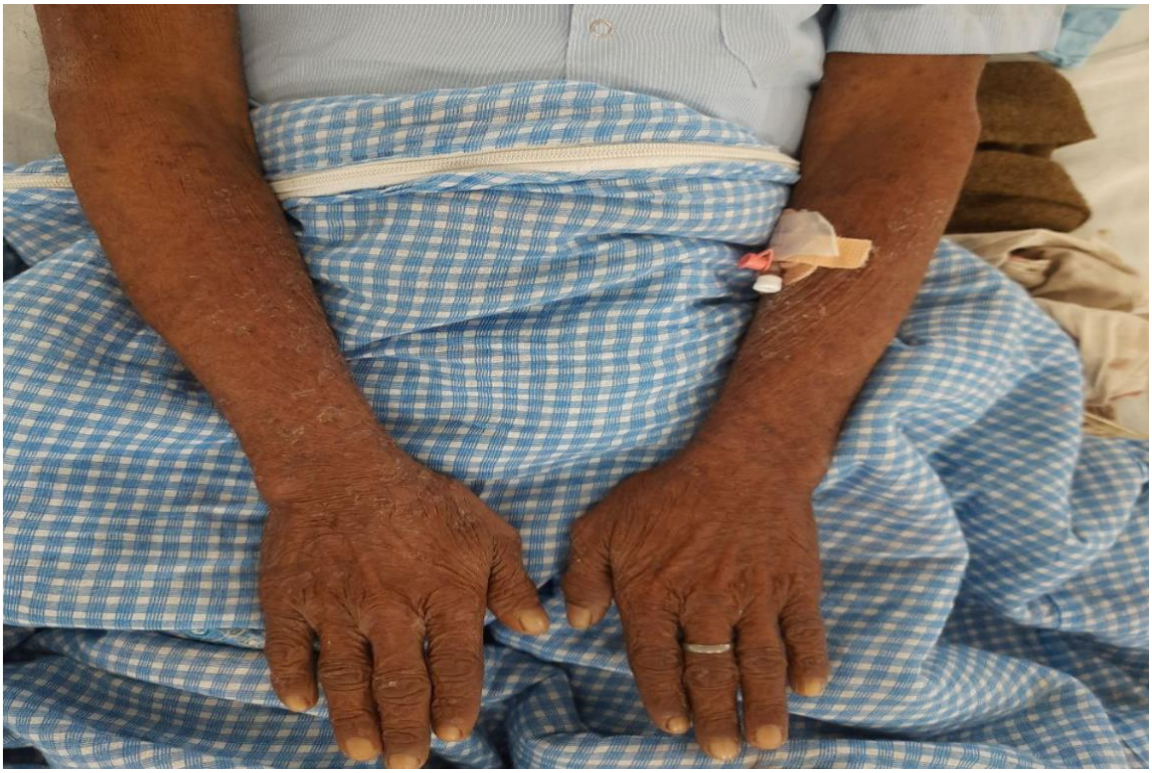

Fig- 2a.

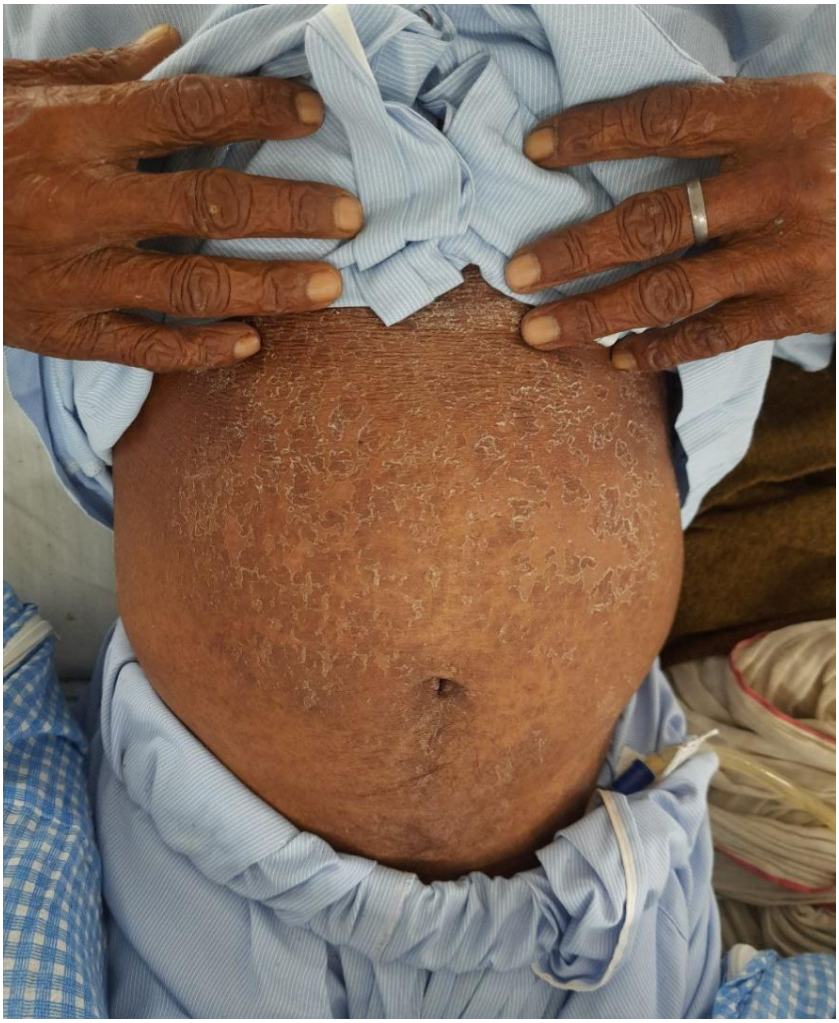

Fig-2b.

DISCUSSION

Leprosy is the oldest disease known to mankind. It remains a significant public health concern in many countries, particularly in India and other endemic regions across the globe. The burden of leprosy in India is at its maximum, and it accounts for 60% of global leprosy. Out of all leprosy cases, multidrug-resistant cases are 30%. Treatment of leprosy with multidrug therapy (MDT) involving dapsone, rifampicin, and clofazimine has proved to be highly effective. (Foss & Motta, 2012). Dapsone has potent anti-inflammatory and antimicrobial properties that have made it an important therapeutic agent in the management of various medical conditions, such as malaria, Pneumocystis carinii pneumonia, dermatitis herpetiformis, bullous pemphigoid, and leprosy (Falcone et al., 2016; Mungroo et al., 2020). In addition to therapeutic benefits, Dapsone has a range of adverse effects, from the most common, like methemoglobinemia, hemolytic anemia, and agranulocytosis, to life-threatening Dapsone hypersensitivity reactions. Dapsone-hypersensitivity syndrome (DHS) is a rare but potentially fatal adverse effect. It occurs in about 0.5% to 3% of patients exposed to the drug (Parkins & White, 2013). Diagnosis of DHS is often delayed because the initial clinical presentation may be nonspecific, with fever, rash, and internal organ involvement. The onset of symptoms can vary widely from a few days to several weeks after the initiation of dapsone therapy (Ditto, 2004; REES et al., 1985). The pathophysiology of the Dapsone hypersensitivity reaction is thought to be due to the formation of reactive metabolites of dapsone, which act as haptens and trigger a T-cell-mediated immune response, leading to the development of severe hypersensitivity reactions. (Mungroo et al., 2020).

In our case report, the patient developed dapsone-induced hypersensitivity syndrome about a month after starting multidrug therapy for leprosy. He was presented with fever, jaundice, skin rash, and lymphadenopathy. He had multi-organ involvement, presenting with eosinophilia, hepatic dysfunction, renal impairment, and hemodynamic instability. The temporal association between the initiation of dapsone therapy and the development of the characteristic signs and symptoms led to a diagnosis of dapsone-induced hypersensitivity syndrome. Immediate discontinuation of dapsone and prompt initiation of systemic corticosteroid therapy are essential for the management of dapsone hypersensitivity

syndrome. With appropriate treatment, the prognosis is generally good, with a mortality rate of 10% to 20%.

CONCLUSION

This case report highlights the importance of awareness and early recognition of dapsone-induced hypersensitivity syndrome, a potentially life-threatening adverse effect, in leprosy patients receiving multidrug therapy. Clinicians should be vigilant for the development of such reactions, especially during the initial phase of treatment, and should promptly discontinue dapsone and initiate appropriate management to ensure favorable outcomes.

Consent for publication

Not applicable.

Conflict of interest

None of the authors have conflicts of interest. This manuscript is original and has not been submitted elsewhere for publication.

REFERENCES

1. Ditto, A. (2004, February 1). Drug rash with eosinophilia and systemic symptoms (DRESS) secondary to anti-tuberculosis therapy with features of isoniazid toxicity. Elsevier BV, 113(2): S309-S309. https://doi.org/10.1016/j.jaci.2004.01.607
2. Falcone, E L., Petts, J R., Fasano, M B., Ford, B., Nauseef, W M., Neves, J F., Simões, M J., Tierce, M L., Morena, M T D L., Greenberg, D E., Zerbe, C S., Zelazny, A M., & Holland, S M. (2016, March 1). Methylotroph Infections and Chronic Granulomatous Disease. Centers for Disease Control and Prevention, 22(3): 404-409. https://doi.org/10.3201/eid2203.151265
3. Foss, N T., & Motta, A C F. (2012, December 1). Leprosy, a neglected disease that causes a wide variety of clinical conditions in tropical countries. Instituto Oswaldo Cruz, Ministério da Saúde, 107(suppl 1): 28-33. https://doi.org/10.1590/s0074-02762012000900006
4. Mungroo, M R., Khan, N A., & Siddiqui, R. (2020, December 1). Mycobacterium leprae: Pathogenesis, diagnosis, and treatment options. Elsevier BV, 149: 104475-104475. https://doi.org/10.1016/j.micpath.2020.104475.
5. Parkins, G., & White, B. (2013, March 8). DRESS syndrome presenting like septic shock. Oxford University Press, 106(7): 671-673. https://doi.org/10.1093/qjmed/hct050
6. REES, R S., ALTENBERN, D P., Lynch, J B., & King, L E. (1985, November 1). Brown Recluse Spider Bites. Lippincott Williams & Wilkins, 202(5): 659-663. https://doi.org/10.1097/00000658-198511000-00020
7. Schiff, D., Roberts, W., & Sue, Y. (2006, June 1). Methemoglobinemia Associated With Dapsone Therapy in a Child With Pneumonia and Chronic Immune Thrombocytopenic Purpura. Lippincott Williams & Wilkins, 28(6): 395-398. https://doi.org/10.1097/00043426-200606000-00015