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CASE REPORT

DAPSONE HYPERSENSITIVITY SYNDROME IS A RARE CAUSE OF NON-LEPROSY INDUCED PYREXIA OF UNKNOWN ORIGIN

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ABSTRACT

Introduction: *Pyrexia of unknown origin is a common cause of fever that requires admission and extensive workup for diagnosis and management in both the intensive care unit and the general ward. We present a case of a 35-year-old male with a past history of Lichen Planus under Dapsone therapy who presented with fever associated with chills and rigor, headache, skin rash, multiple swellings all over the body, shortness of breath, and hypotension. The patient was started on fluids and broad-spectrum antibiotics. Laboratory investigations, radiological investigation were done, and diagnosed as Dapsone hypersensitivity syndrome. The patient was treated with prednisone and antibiotics. He was discharged after 10 days of hospital admission. The patient was advised to follow up at 2 weeks, and prednisone was gradually tapered off during the visit. Drug history should be part of the history that helps in treating patients presenting with pyrexia of unknown origin.*

Keywords: *Dapsone, Hepatitis, Hypersensitivity*

INTRODUCTION

Pyrexia of unknown origin (PUO) is a common cause for admission in hospital that requires careful history, examination for diagnosis and treatment. Drug-associated fever is a common cause of PUO, which is often underdiagnosed. Dapsone is used in many diseases for treatment and prophylaxis due to its anti-inflammatory and antibiotics effect.[1] It causes multiple local and systemic side effects.

Dapsone Hypersensitivity Syndrome is an idiosyncratic reaction which is rare occurs in 0.5-3%) but potentially life-threatening adverse reaction to dapsone, which typically appears 4-6 weeks after starting the drug. It typically presents with a triad of fever, skin eruptions and internal organ (lungs, liver, neurological, and other system) involvement and may resemble DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) Syndrome. This syndrome can be best managed by timely diagnosis and immediate discontinuation of the offending drug, along with administration of oral or intravenous glucocorticoids in order to prevent further organ damage.

CASE SUMMARY

A 35 years old male, with a past history of Lichen Planus under Dapsone therapy for 2 month presented to the Emergency department with a chief complain of Fever with chills and rigor for 4 weeks, headache, swelling all over the body, skin lesion for 6 days and shortness of breath for 3 days after being referred by a primary physician from a local hospital where patient had received treatment for 10 days without any improvement in sign and symptoms. At a presentation in the Emergency Department, Glasgow Coma Scale

(GCS) was 15/15, pulse rate 114 beats/per min, blood pressure (BP) 80/40 mmHg, respiratory rate 26 breaths/min, temperature 101^{0}F, generalized lymphadenopathy and oxygen saturation 84% in room air. Abdominal and Cardiovascular examinations were normal. Chest examination showed bilateral crepitation in the infra-scapular and interscapular regions and maculopapular rash at the left supra-mammary region (Figure 1).

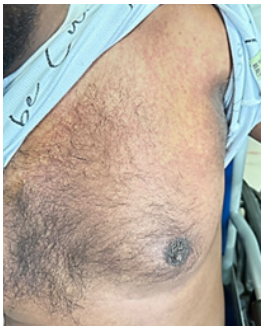

Figure 1: Maculopapular rash at the left supra-mammary region.

He was immediately resuscitated with 2 liters of Normal saline, and Noradrenaline was started at 0.2 microgram per kilogram per minute, and oxygen was started at 10 liters per minute via face mask. Chest X-ray (Figure 2) showed bilateral lower zone infiltrates. He was started on meropenem one gram intravenously every eight hours, Doxycycline 100 mg intravenously every twelve hours and Hydrocortisone 50 mg every six hours.

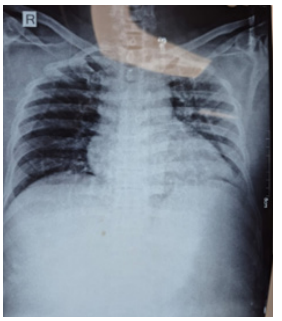

Figure 2: Chest X-ray PA View showing bilateral basal infiltrates

His blood investigation profiles were Total leucocyte count (TLC) - 18000/mm^3 Neutrophil 63%, lymphocyte 20% and Eosinophil 15% Platelets-120000/mm^3, Hemoglobin (Hb)-10gm/dl, Urea-58 mg/dl, Creatinine-1.3 mg/dl, Sodium, and Potassium are within normal limits. Total bilirubin 3.4mg/dl, in which direct 2.4mg/dl, Total protein 5.6mg/dl, of which albumin 3.2mg/dl, Alanine aminotransferase (ALT) 646 U/L, Aspartate aminotransferase (AST) 419 U/L, Alkaline phosphatase (ALP) 410 U/L Prothrombin time (PT) 18 seconds, International normalized (INR) ratio 1.5. Cerebrospinal spinal fluid analysis was normal. Computed Tomography (CT) of the head, and abdomen was normal. CT of the chest showed bilateral ground-glass opacities in the lower zone. Peripheral blood smear showed eosinophilia with normocytic normochromic anemia. Fine needle aspiration cytology of the left cervical lymph node showed features suggestive of reactive lymphadenitis. Serology for Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis E, Human Immunodeficiency virus, salmonella, scrub, dengue, malaria, kalazaar, and brucella was normal. Routine examination of urine was normal. Sputum, urine, and blood culture were normal.

Blood pressure gradually improved, and noradrenaline was stopped on the 4th day and Liver function test gradually improved over 2 weeks. The patient was diagnosed with Dapsone hypersensitivity syndrome. Prednisone was started at 60 mg/day on the 5th day. Patient was discharged on the 14th day of admission and was advised to follow up in seven days with gradual tapering of prednisone. He was followed every 14 days for 2 month and every 1 month for 6 month and did not show any complication.

DISCUSSION

Pyrexia of unknown origin is defined as persistent fever above 38.3°C (100°F) that evades diagnosis for at least 3 weeks, including 1 week of investigation in hospital. It has diagnostic challenges for the physician. The cause of PUO can be infective, inflammatory, neoplastic and miscellaneous. Diagnosis and workup require different strategies for diagnosis and has further classified PUO as classical, nosocomial, neutropenic, and HIV related. Our patient was having a classical and inflammatory cause of PUO.[3]

Dapsone Hypersensitivity Syndrome (DHS) is a hypersensitivity vasculitis syndrome characterized by fever, rash, hemolytic anemia, exfoliative dermatitis, lymphadenopathy, eosinophilia, and multiple systemic involvement that occurs as early as 2 to 6 hours as late as 6 months after starting Dapsone.

Our patient developed DHS after 2 months of Dapsone which is similar to a study by Kolli S et al[4] while other studies have shown that it occurs within 1 week – 12 weeks[1,2,5-7] of starting Dapsone. This variability of the latency time may be due to the variability of the acetylators, difference in the dose, and the modality of treatment. This wide variability of the latency period suggests a multi-organ hypersensitivity reaction, but the exact mechanisms are unclear.

Eosinophilia was present in our present while other studies[1,2,5-7] have shown that lymphocytosis was predominant in their patients. These differences may

be due to difference in the study population and the presence of other bacterial or viral infections in other patients.

Eosinophilic pneumonitis is most common in DHS which was present in our patients while in a study by Kinehara Y et al[8] pneumonitis was present without eosinophilia. This difference may be due to different in the patient population and the unclear pathophysiology of DHS.

Hepatitis is a common part of systemic involvement in DHS was present in our patients.

Maculopapular rash was only present in our patients while in other studies [2,6,7] severe manifestations like Stevens-Johnson Syndrome, exfoliative dermatitis and Toxic epidermal necrolysis were present. This difference may be due to a difference in the severity of presentation.

DHS most commonly occurs in the treatment of Leprosy with Dapsone, but DHS can occur in non-Leprosy patients, which was present in our patients and in a study by Zhu HQ et al.[9]

Treatment of DHS is corticosteroid with supportive therapy, which was done in our patients

Drug history should be taken in patients presenting with pyrexia of unknown origin.

To conclude, large scale studies are required to identify the cause and pathophysiology of Dapsone induced DHS.

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REFERENCES:

1. 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. doi:https://doi.org/10.1186/1745-6673-1-9 PMCID: PMC1524788

2. Vinod KV, Arun K, Dutta TK. Dapsone hypersensitivity syndrome: A rare life threatening complication of dapsone therapy. J Pharmacol Pharmacother. 2013;4(2):158-60.doi:https://doi.org/10.4103/0976-500x.110917 PMCID: PMC3669581

3. Fernandez C, Beeching NJ. Pyrexia of unknown origin. Clin Med (Lond). 2018;18(2):170-4. doi:https://doi.org/10.7861/clinmedicine.18-2-170 PMCID: PMC6303444

4. Kolli S, Suhagiya S. Dapsone induced hypersensitivity syndrome: a case report. International Journal of Basic & Clinical Pharmacology 2020;9(10):1609-11. doi:https://doi.org/10.18203/2319-2003.ijbcp20204106

5. Grace M. An unusual case of dapsone syndrome. Indian Dermatol Online J. 2011 ;2(2):88-90. doi:https://doi.org/10.4103/2229-5178.85999 PMID: 23130233

6. Ansah R, Arkoh EA, Quao BO, Groger M. Lack of Suspicion of Dapsone Hypersensitivity Syndrome in a Leprosy Patient: Case Report with Fatal Outcome. Res Rep Trop Med. 2023;14:135-9. doi: https://doi.org/10.2147/RRTM.S434947 PMID: 38170098

7. Kesari HV, Gawali UP, Agharia MAM, Dapsone hypersensitivity syndrome: A Potentially Fatal Condition- case report. Journal of Clinical and Diagnostic Research 2017;1(12):1-3. doi:https://doi.org/10.7860/JCDR/2017/30842.10927

8. Kinehara Y, Kijima T, Inoue K, Hirata H, Takeuchi Y, Fukushima K et al. Dapsone hypersensitivity syndrome-related lung injury without eosinophilia in the bronchoalveolar lavage fluid. Intern Med. 2015;54(7):827-31. doi:https://doi.org/10.2169/internalmedicine.54.3406 PMID: 25832951

9. Zhu HQ, Jiang SH, Song GL. Non-leprosy related dapsone hypersensitivity syndrome: A case report and literature review. Medicine (Baltimore). 2025 ;104(27): e43073. doi:https://doi.org/10.1097/MD.0000000000043073 PMID: 40629627