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CASE REPORT

A comprehensive case report on dapsone hypersensitivity syndrome

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Abstract: Dapsone is an antimicrobial agent with anti-inflammatory properties used commonly in the treatment of leprosy. However, it can rarely cause a severe adverse drug reaction known as dapsone hypersensitivity syndrome (DHS). The main objective of this case report is to highlight the challenges in diagnosis and management of this potentially life-threatening DHS. We present a case of a patient who developed DHS after long-term dapsone therapy. The clinical features, laboratory and radiological investigations, differential diagnosis and treatment are described. The patient presented with fever, skin rash and involvement of multiple organs. DHS was confirmed based on diagnostic criteria. Dapsone was immediately discontinued and the patient was started on corticosteroids. Other potential causes were ruled out. DHS is a rare but serious reaction to dapsone. It can mimic other conditions making diagnosis challenging. Awareness of this adverse effect is important for healthcare professionals prescribing dapsone, especially long-term, to promptly identify and manage the condition. Our case highlights the key aspects in diagnosis and management of DHS.

Keywords: Drug hypersensitivity; Adverse drug reaction; Dapsone syndrome; Leprosy

1. Introduction

Dapsone (4,4'- diamino – diphenyl sulfone) is a sulfone derivative with potent antimicrobial and anti-inflammatory properties. It works by inhibiting the biosynthesis of folic acid through competitive inhibition of dihydropteroate synthetase. Due to its activity against pathogens like Mycobacterium leprae and Pneumocystis jirovecii, dapsone remains an important first-line therapy for leprosy and Pneumocystis pneumonia prophylaxis [1,2]. It is also used in the treatment of dermatitis herpetiformis and various bullous dermatoses like pemphigus vulgaris. However, dapsone is known to cause severe adverse drug reactions [3-5]. One such reaction is dapsone hypersensitivity syndrome (DHS), previously known as drug reaction with eosinophilia and systemic symptoms (DRESS). First reported in 1950, it typically manifests 1-2 weeks after initiation of dapsone therapy [6,7]. Clinically, DHS is characterized by a triad of fever, skin eruption and end-organ involvement. The liver and hematopoietic system are most commonly involved, with rates of hepatic involvement ranging from 34-94% in various case series [8-10]. Presentation can range from mild abnormalities in liver enzymes to fulminant hepatitis.

The incidence of DHS is estimated to be approximately 1 in 1000 dapsone exposures [9]. Diagnosis is challenging due to its variable manifestations and similarity to other conditions. It carries significant morbidity and mortality if not recognized and managed promptly. While DHS was initially associated with antiepileptics, it is now recognized with a variety of drugs including dapsone, sulfonamides, allopurinol and metronidazole. Immediate withdrawal of the culprit drug along with supportive measures forms the mainstay of treatment [10, 11]. Here we describe a case of biopsy-proven DHS that developed in a patient receiving long-term dapsone therapy. Through this report, we aim to enhance awareness of this serious adverse reaction among healthcare workers to facilitate early identification and management of DHS

2. Case report

2.1. Subjective evidence

A 14-year-old female patient presented to the paediatric ward of a tertiary care hospital with chief complaints of high grade fever for one week and jaundice involving the skin and eyes for one week. Her past medical history was significant for Henoch Scholien

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Purpura for which she had been prescribed tablet Dapsone and oral prednisolone 10 mg. However, she had discontinued these medications one week ago when the fever started.

Upon examination, the patient had intermittent high fever without diurnal variation which responded to antipyretics. She also exhibited jaundice involving the skin as evidenced by yellowish discoloration as well as the eyes. Additionally, her urine had turned yellow in colouration. She had experienced a similar episode of yellowish discolouration of skin at the age of 6 years for which she had received traditional treatment. On presentation to our facility, a detailed history was obtained and physical examination was done noting the signs of fever and jaundice for further evaluation and management.

2.2. Observation

On physical examination, the patient's vital signs were as follows: blood pressure 100/60 mmHg, pulse rate 108/min, respiratory rate 20/min and temperature 101.9°F. Oxygen saturation was 98% room air. Cutaneous examination revealed erythematous macules and papules involving the bilateral upper and lower limbs along with purpuric lesions on the lower limbs (Figure 1). Systemic examination was otherwise unremarkable. Hematological investigations showed hemoglobin of 9.9 g/dL, red blood cell count of 3.81 million/cu.mm, white blood cell count of 12,900 cells/cu.mm with differential counts of 40% neutrophils, 55% lymphocytes (outside normal range of 20-40%) and 1% eosinophils and 4% monocytes. Platelet count was 1.23 lakh/cu.mm. Peripheral smear ruled out malaria. Erythrocyte sedimentation rate was elevated at 50 mm/Hr. Urine analysis and blood groups were normal. Liver function tests revealed elevated total bilirubin of 7.4 mg/dL with direct bilirubin of 5.1 mg/dL, aspartate transaminase of 470 IU/L, alanine transaminase of 540 IU/L and alkaline phosphatase of 202 IU/L. Serum proteins, electrolytes and renal function tests were otherwise within normal limits. C-reactive protein level was elevated at 27.7 mg/dl. Widal test was positive for Salmonella typhi antigens).

Figure 1. Skin condition before treatment

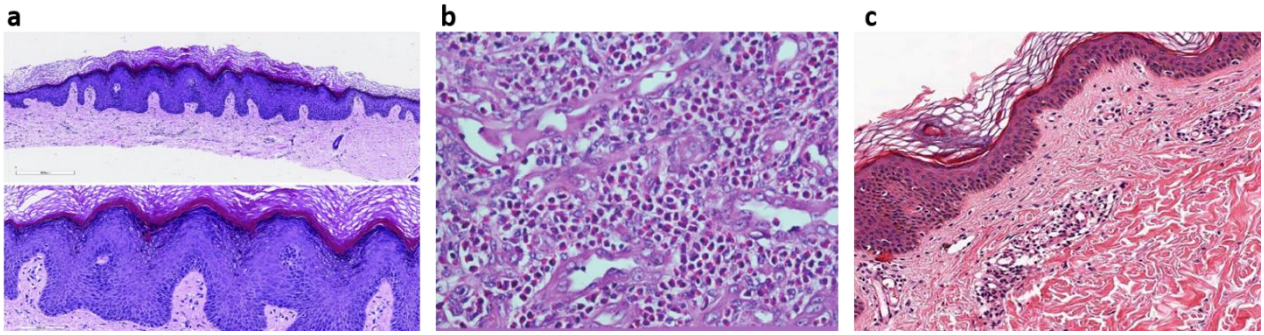

Figure 2. Skin Biopsy microhistograms showing a. Mild orthokeratosis b. Perivascular lymphocytic infiltrate c. Few extravasated RBC

Abdominal ultrasound showed mild hepatosplenomegaly with increased echogenicity of the portal vein, suggestive of drug-induced/infective hepatitis. The gallbladder was minimally distended with edematous wall changes, likely reactive. Minimal ascites was also noted.

Skin biopsies from the limbs revealed mild orthokeratosis on histopathological examination (Figure 1a). In the dermis, there was a minimal perivascular lymphocytic infiltrate seen (Figure 1b) along with few extravasated red blood cells (Fig 6). No fibrin deposition was observed (Figure 1c).

Antinuclear antibody testing showed a strong homogenous staining pattern for nRNP/Sm and Sm antigens, with borderline reactivity for SSA and PLNA. Based on the patient's history of Henoch–Schönlein purpura on dapsone therapy, physical findings, investigative reports and radiological findings, a diagnosis of dapsone hypersensitivity syndrome was made. Treatment initiated included oral prednisolone, pantoprazole, paracetamol, ursodeoxycholic acid, rifaximin, levocetirizine, lactulose along with topical lactobacillus formulation and supportive care. Significant clinical improvement was observed with this standardized management protocol.

2.3. Treatment

The patient was admitted and started on the following standardized treatment protocol [12]:

- Oral prednisolone 30mg once daily
- Pantoprazole 40mg once daily
- Paracetamol 650mg as needed for fever
- Ursodeoxycholic acid 150mg twice daily
- Rifaximin 200mg three times daily
- Levocetirizine 5mg twice daily
- Topical lactobacillus formulation at night
- Oral lactulose 20ml twice daily as required

Dapsone was discontinued immediately. Significant recovery was observed with resolution of skin lesions (Figure 3) during hospital stay with this management.

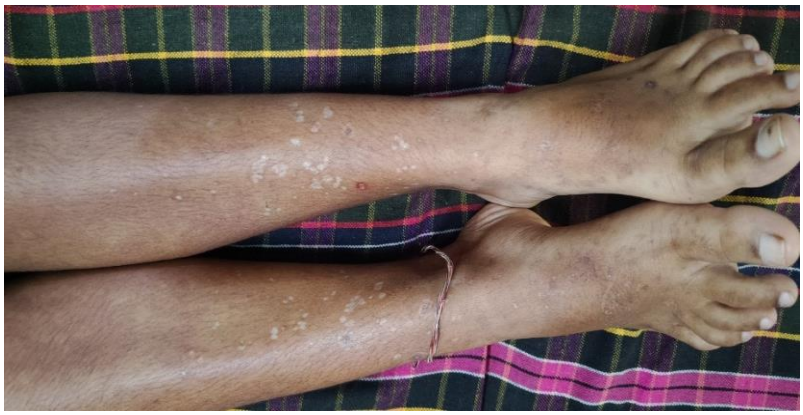

Figure 3. Skin condition after treatment

At discharge, the following tapering regimen was prescribed:

- Prednisolone 30mg for 1 week, 20mg for 1 week, 10mg for 1 week
- Rifaximin 200mg three times daily for 9 days
- Ursodeoxycholic acid 150mg twice daily for 7 days
- Topical calamine lotion twice daily
- Topical lactobacillus formulation at night
- Lactulose 20ml for 1 week

A follow up after 1 week was advised to review clinical progress.

3. Discussion

This case highlights dapsone hypersensitivity syndrome (DHS), a rare but potentially life-threatening adverse drug reaction. The patient was on long-term dapsone therapy for Henoch Schönlein purpura which is known to increase the risk of DHS development. Clinically, she presented with fever and jaundice, consistent with DHS. Laboratory investigations revealed elevated liver enzymes,

suggesting drug-induced hepatic involvement [3,4]. Abdominal imaging showed hepatosplenomegaly and portal vein changes compatible with a drug-induced hepatotoxicity picture [5]. A temporal association between initiation of dapsone therapy and symptoms, supported by investigations confirming multi-organ involvement led to the diagnosis of DHS in this patient [6,7]. Immediate withdrawal of the culprit drug is crucial for managing DHS [8]. In addition, she was started on systemic steroids and symptomatic treatment based on established protocols, to which she responded well clinically [9,10]. Though rare, DHS carries risks of mortality if unrecognized [11-14].

4. Conclusion

This case highlights the importance of considering DHS in patients on long-term dapsone presenting with compatible symptoms. A high index of clinical suspicion, prompt diagnosis and standardized management can help mitigate risks as seen here. Dose titration and monitoring during the tapering phase also likely aided recovery without relapse. In conclusion, this report enhances awareness of DHS, an adverse reaction that can potentially mimic other conditions. It reinforces the need for vigilance among clinicians to facilitate early identification and management of this serious drug-induced hypersensitivity syndrome.

Compliance with ethical standards

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Conflict of interest statement

All authors declare that there is no conflict of interest.

Statement of informed consent

Informed consent was taken from the patient.

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