

The Dapsone Dilemma: A Case Report

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Dapsone, a cornerstone drug in leprosy management, can rarely induce severe hypersensitivity reactions collectively termed dapsone hypersensitivity syndrome (DHS). This condition is characterized by fever, hepatitis, rash, lymphadenopathy, and hemolytic anemia, primarily attributed to genetic predisposition and toxic metabolite formation. We describe a case of a 37-year-old woman with lepromatous leprosy who developed diffuse exfoliative scaly plaques and persistent hepatic dysfunction following dapsone therapy. Clinical and biochemical resolution was achieved upon drug withdrawal and initiation of corticosteroids. This case illustrates a significant morphological variant of DHS showing exfoliative erythroderma with ichthyosiform scaling and deep fissuring and it highlights the risk of prolonged progression when diagnosis is delayed.

Keywords: Dapsone, Dapsone Hypersensitivity Reaction, Lepromatous Leprosy, DRESS

Introduction

Dapsone hypersensitivity syndrome also known as sulphone syndrome, is an uncommon idiosyncratic reaction with potentially fatal outcomes. It classically presents with fever, rash, and hepatic involvement occurring two to eight weeks after drug initiation. Hence the name “fifth-week dermatitis.” The estimated incidence is approximately 1% among patients receiving dapsone therapy (Ansah et al 2023). We report this case on account of its unusual cutaneous morphology — presenting as exfoliative erythroderma with ichthyosiform scaling and deep fissuring rather than the classical morbilliform eruption — and the notably

prolonged clinical course, compounded by a diagnostic delay that prevented timely initiation of corticosteroid therapy.

Case Report

A 37-year-old female homemaker presented with widespread erythematous scaly lesions and deep fissures. One month after starting World Health Organization (WHO) - recommended MDT for multibacillary leprosy, she developed generalized erythema, elevated liver enzymes, and malaise, leading to discontinuation of therapy. Despite cessation, lesions progressed to near-total body involvement with exfoliation over the following two months. During this period, the patient had sought care at an outside hospital under the

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department of general medicine, where DHS was not confirmed as the diagnosis. She was referred to our institution only after significant clinical deterioration. On examination, diffuse

erythema and exfoliative scaly plaques were noted, involving nearly 90% of the body surface, accompanied by ectropion and limb edema (Fig. 1 a–d).



Fig.1 : (a-b) Diffuse erythema accompanied by ichthyosiform scaling and numerous deep fissures was observed across the trunk.

(c-d) Multiple ichthyosiform plaques with deep fissuring were noted over the shoulder and left upper extremities.

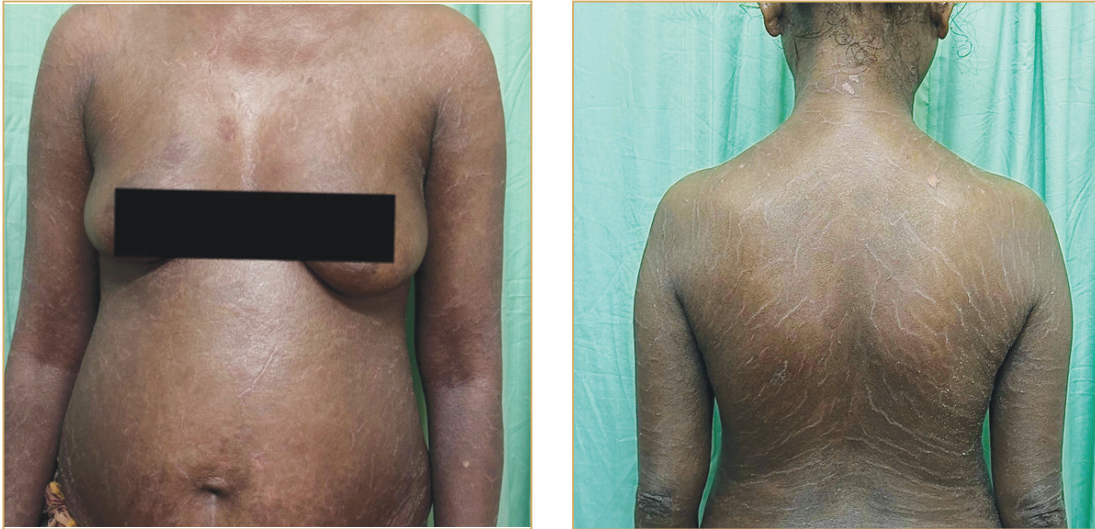


Fig. 2 : Two weeks after initiation of treatment.

Laboratory tests revealed extremely high transaminase levels, with aspartate aminotransferase (AST) at 1230 IU/L and alanine aminotransferase (ALT) at 1450 IU/L, along with anemia (Hb 9.8 g/dL) and leukocytosis (16,050 cells/cu mm). Blood culture yielded *Acinetobacter baumannii*. Histopathology revealed features of Hansen's disease, lepromatous leprosy type, with superimposed inflammatory changes and neutrophilic microabscesses. Fite stain demonstrated numerous bacilli. A slit-skin smear tested positive for acid-fast bacilli, indicating a bacteriological index (BI) of 4+ and a morphological index (MI) of 30%, confirming disease activity.

A diagnosis of DHS with secondary infection was made. She received intravenous corticosteroids, broad-spectrum antibiotics (piperacillin-tazobactam), and hepatoprotective therapy (N-acetylcysteine).

The AST and ALT later decreased to 42 IU/L and 98 for ALT, but the initial severity indicates a potential risk of liver failure. Upon stabilization, she was

switched to an ofloxacin and clofazimine-based alternative regimen, with marked improvement within two weeks (Fig. 2).

Discussion

Dapsone, or 4,4'-diamino-diphenyl sulfone, is the parent compound of sulfone drugs. Since the 1950s, it has served as a first-line treatment for leprosy. The FDA has approved dapsone for the treatment of leprosy, dermatitis herpetiformis, and acne vulgaris (Ghaoui et al 2020). Dapsone functions as a bacteriostatic agent against *Mycobacterium leprae*, leading to various adverse events that can be attributed to individual genetic susceptibility, intolerance, idiosyncratic reactions, and hypersensitivity (Gavilanes et al 2015).

Dapsone may cause adverse events such as mild hemolysis, peripheral neuropathy, fatigue, and headache. Among these, DHS is one of the most severe and life-threatening complications linked to dapsone.

Lowe first identified it in 1949 in a Nigerian patient with leprosy. In 1950, Lowe and Allday described

it as diamino-diphenyl sulfone (DDS) syndrome, also known as sulfone syndrome (Criado et al 2012). Currently, DHS is classified under drug reaction with eosinophilia and systemic symptoms (DRESS). However, some authors refer to it as drug-induced hypersensitivity syndrome (DiHS) because eosinophilia is not observed in every case (Gavilanes et al 2015). The cutaneous manifestations of this syndrome can vary widely, ranging from papular erythematous eruptions and erythroderma to erythema multiforme, toxic epidermal necrolysis, and Stevens–Johnson syndrome (Gavilanes et al 2015). Most frequent sign of DHS is a morbilliform rash. In contrast, our patient presented with persistent erythroderma accompanied by exfoliative scaling and deep fissuring - a severe and atypical morphological variant that diverges from the classic morbilliform pattern and posed a significant diagnostic challenge.

A similar case was documented in a 35-year-old male with multibacillary leprosy who developed exfoliative dermatitis, hepatitis, renal impairment, and severe anemia approximately six weeks after commencing multidrug therapy. Despite prompt discontinuation of dapsone, initiation of systemic corticosteroids, and supportive management, the patient's condition deteriorated, culminating in multiorgan failure and death (Ansah et al 2023).

Mortality rates as high as 11–13% have been reported in severe cases of DHS, underscoring the importance of maintaining a high index of suspicion for early diagnosis and prompt intervention to prevent fatalities and late complications.

Significant hepatic involvement was observed in the patient being reported in present report, with liver enzyme levels exceeding four times the normal range. The liver remains the most commonly affected extracutaneous organ in DHS.

Dapsone undergoes hepatic metabolism via the N-hydroxylation pathway, generating reactive metabolites such as hydroxylamine, which are implicated in hepatocellular injury and, in severe cases, acute liver failure (Hasan & Rabbani 2020).

Additionally, the concomitant use of rifampicin, a drug with known hepatotoxic potential, may exert a synergistic effect with dapsone, further amplifying hepatic stress and contributing to the marked transaminitis seen in this case (Gavilanes et al 2015).

Discontinuing the causative drug is the first step because it directly addresses the root cause. In this case, although dapsone was discontinued promptly upon symptom onset, the patients' late diagnosis led to a delayed initiation of systemic corticosteroids, during which the condition continued to deteriorate. This delay highlights a critical pitfall: DHS may not be immediately recognized outside dermatology settings, and the absence of prompt immunosuppressive therapy can allow the syndrome to progress to severe erythroderma.

Upon referral to our institution and initiation of systemic corticosteroids, rapid clinical improvement and a faster recovery were achieved. Supportive skin care further eased symptoms. However, relapse after steroid tapering remains a concern, underscoring the need for careful follow-up.

Conclusion

DHS though infrequent, poses a significant threat in endemic regions. Vigilant clinical monitoring during early weeks of therapy enables timely diagnosis and management, thereby reducing morbidity and mortality. This case underscores the importance of awareness among clinicians and the potential for prolonged recovery despite appropriate intervention.

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