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A Case of Dapsone Hypersensitivity Presenting as Mimicker of Sepsis: Is It Really Uncommon?

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Introduction

Dapsone induced hypersensitivity syndrome also referred to as 'sulfone syndrome' is increasingly being recognized in clinical practice these days. It can present with varied local and systemic manifestations involving organ dysfunction. We hereby are presenting a case of hypersensitivity of this drug which presented in a similar fashion as that of sepsis.

Case Report

41 years male, resident of A.P, farmer by profession, with no past comorbidities, presented with chief complaints of skin lesions over his abdomen x 2 months, high grade intermittent fever with chills x 12 days, nausea with vomiting x 12 days and yellowish discoloration of urine x 12 days. The skin lesions over anterior aspect were hypo pigmented and patchy in nature and initially one to start with and gradually increased in number and size. There was associated h/o unquantified weight loss and decreased appetite. The lesions were non-itchy and were not associated with any altered pain or touch perception over skin lesions. He used to consume alcohol (40 gms/day) and had a history of high-risk behavior, about 4 years back. He was diagnosed by a local practitioner to have some skin disease (? Leprosy) and was started on combination drug therapy (Rifampicin, Clofazimine, Dapsone) which he took for about 1 month and had stopped around 2 weeks back when he developed high fever, gastrointestinal symptoms and increased skin lesions over abdomen. He had recent admission at outside hospital where he was being evaluated for febrile jaundice. On examination, he was febrile, tachycardic, B.P- 130/80 mmHg. He had marked icterus, pallor and generalized (cervical, axillary, groin) lymphadenopathy. On abdominal examination, hypo pigmented patches were seen (Fig.1) and his liver was palpable. On evaluation : Hb- 9.5, TLC- 15,030, DLC- P50,L28,E12,M04, Plt- 1.30 L, CRP- 2.8, INR- 1.2, PBS- Reactive lymphocytes +, Bil- 9.5 (direct- 6.2), OT/PT-66/82, ALP- 489, GGT-184, Alb-2.5, Glb-2.7, LDH-335, amylase-19, lipase-6. His viral markers were negative and tropical screen was also negative. His CT ABDOMEN showed acute acalculous cholecystitis, hepatomegaly, and splenomegaly, para aortic, pericardial and inguinal nodes. Trucut biopsy of cervical lymph node was done which on staining and HPE (Fig.2) was non-contributory. Also, he underwent skin biopsy (Fig.3) from his abdominal lesions which showed features s/o drug induced injury. He was opined to

have dapsone hypersensitivity and started on Inj. dexamethasone and hepatoprotectives after which he had a dramatic improvement and his LFT started normalizing. He was discharged after he showed a good clinical recovery, though his skin lesions were persisting. On follow up later as outpatient, he was much better symptomatically and his skin lesions had also improved.

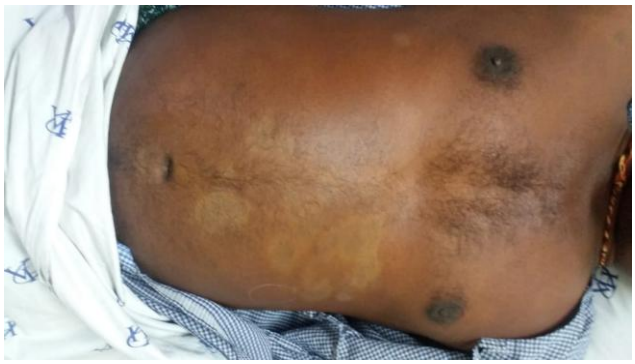

Fig 1 Hypo pigmented skin patches over abdomen

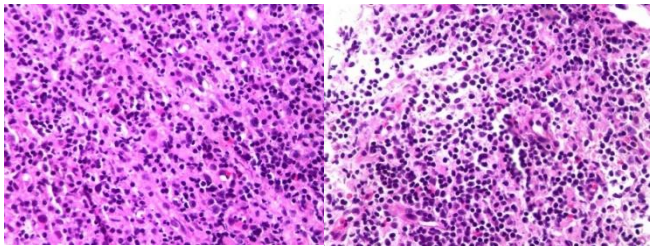

Fig 2 HPE of Lymph node biopsy (neck)

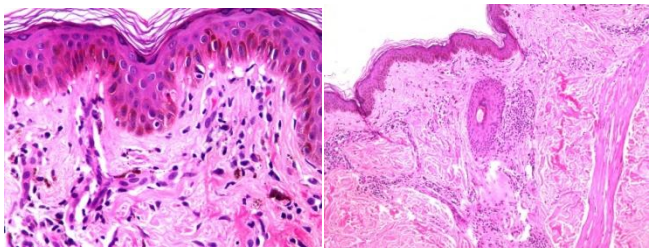

Fig 3 HPE of skin biopsy of abdominal lesions

Discussion

Dapsone has been used for the prophylaxis or treatment of various infections (leprosy, Pneumocystis jirovecii pneumonia, toxoplasmosis, cutaneous mycetoma, malaria), in several dermatological conditions and in immune thrombocytopenic purpura.

DHS, or dapsone hypersensitivity syndrome, is a form of idiosyncratic adverse effect of the drug. It is not dose-related buta cell-mediated hypersensitivity which range from mild cutaneous manifestations to severe life-threatening complications. Lowe and Smith first reported it in 1949 when they noted it in Nigerian leprosy patients[1]. The development of DHS varies from several weeks to as long as six months after treatment initiation and its incidence ranges from 0.5% to 3%[2]. It is known to be the cause for permanent organ damage or even death also if not recognized early and delay in management[3]

The main features are fever, skin rash, lymphadenopathy, and eosinophilia, pulmonary, hepatic and other systemic manifestations[2], along with antecedent history of dapsone exposure. Skin eruption, fever and involvement of internal organs comprises the classic triad of **DHS**. The cutaneous manifestations can vary from erythematous papules to pustules, plaques and eczematous lesions[4].

The pulmonary manifestations of this syndrome include the development of eosinophilic pneumonia, hypersensitivity pneumonia or even pleural effusion[5]. Gastrointestinal involvement usually include hepato-biliary dysfunction (manifesting as jaundice, hepatomegaly or cholangitis) and splenomegaly[6]. The cause of jaundice in DHS is partly attributed to hemolysis and partly due to hepatotoxicity per se. In the latter, both cholestatic and hepatocellular injury pattern has been seen. Other manifestations may include involvement of hematological, neurological or renal system. Our case mainly presented with fever, generalized lymphadenopathy, mild eosinophilia, hepatosplenomegaly and liver dysfunction. The skin rash over trunk was an old one and there were no new drug related eruptions.

Other conditions to be considered as a differential diagnosis in such situation should include: **DRESS** (Drug reaction with eosinophilia and systemic symptoms) syndrome, Hypereosinophilic syndrome, Churg Strauss Vasculitis, TEN (Toxic epidermal necrolysis), Still's disease, Steven Johnson Syndrome, hematological diseases (leukemia, lymphoma),

paraneoplastic disorders and some autoimmune or connective tissue disorders. **DHS** may also be thought of as a variant of the **DRESS** syndrome.

The standard line of therapy for **DHS** is to immediately discontinue the drug followed by starting glucocorticoids (either oral or parenteral, depending upon the severity of the illness)[7]. We should taper glucocorticoids slowly over a span of more than one month because dapsone has been found to remain in human body even for a period of 35 days.

Conclusion

Dapsone hypersensitivity is an important cause of morbidity which is usually under-rated and less thought of, though it is often seen in appropriate clinical settings. It is a great mimicker of sepsis and its early recognition is important for proper management and preventing further organ damage.

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