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Internal Medicine

DAPSONE HYPERSENSITIVITY SYNDROME

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ABSTRACT One of the most serious side effects of Dapsone is Dapsone Hypersensitivity Syndrome (DHS). It can be potentially fatal without timely intervention. Moreover, it's hepatic/systemic manifestations may be mistaken for other disorders as it happened in our patient. We hereby, present a case report of middle-aged female who was initially presumed to have an Autoimmune disorder and on further diagnosis was found to have Dapsone Hypersensitivity Syndrome. This case is being reported to emphasize the need for detailed history taking, review of prior medication usage in general along with timely diagnosis and prompt treatment of this rare complication for favourable outcomes.

KEYWORDS : Dapsone Hypersensitivity syndrome, skin rash, drug reaction

INTRODUCTION:

Dapsone (4,4'-Diaminodiphenylsulphone) is an anti-inflammatory and anti-bacterial agent used in the treatment of various skin diseases as well as bacterial and fungal infection [1]. Its interference with neutrophil chemotactic migration and adherence is considered to be the reason for its anti-inflammatory action [1]. It can result in a number of adverse effects. Dapsone Hypersensitivity Syndrome (DHS) is one such adverse effect characterized by a triad of fever, skin eruption, and internal organ (lung, liver, neurological and other systems) involvement, which can occur several weeks to as late as 6 months after the initial intake of the drug. Prompt identification of DHS is vital as untreated, the disorder could be fatal.

CASE REPORT:

A 35 years old Female, with no known comorbidities, presented with history of developing erythematous itchy rash over her abdomen and extremities during her third trimester. She was started on symptomatic treatment with anti-histamines and moisturizers. Diagnosis of Polymorphic eruption of Pregnancy was made and she was advised to continue conservative management. But as she continued to have the rash in the post-partum period, she has consulted a doctor locally 3 months after delivery and she has taken a course of T.Dapsone 100mg twice a day for 1 week as prescribed by her local doctor for her skin rash. There was a dramatic response and the skin rash has resolved completely.

After a month, she has developed complaints of low-grade fever associated with diffuse joint and muscle pain along with new onset erythematous skin rash. She was also found to be hypoxic with SpO2 ~ 87 to 90%. She was admitted at a local hospital with the above complaints and on evaluation she was found to have anemia (Hemoglobin-9g%), Eosinophilia (10%), transaminitis (ALT-239, AST-300) with indirect hyperbilirubinemia. She also tested positive for Coomb's test (++), ANA (low titre) and ASMA. In view of the above picture, she was diagnosed to have Hemolytic anemia and Autoimmune hepatitis. She was initiated on oral steroids and other conservative management by her treating physician. Within 3 days of steroid therapy, her symptoms resolved.

She came to our hospital for further follow-up and management. She was on T. Methyl Prednisolone 4mg twice a day since 2 weeks while she presented to our hospital. She was symptomatically feeling better except for minimal fatigue and joint pain. On examination, she was conscious, oriented, afebrile and had SpO2 of 96% in Room air. General examination was significant for mild pallor. Rest of the general and systemic examination were normal. There wasn't any skin lesion as well when she presented to us. Baseline investigations done here showed mild anemia, resolving transaminitis (compared to outside report), mildly elevated inflammatory markers. Her autoimmune profile including ANA, ds-DNA, AMA, AMSA, RA and anti-CCP turned out to be negative. Her C3 and C4 levels were also normal. USG abdomen showed Grade I fatty liver. Chest X Ray was normal. Rheumatologist ruled out the possibility of any underlying autoimmune disorder as the possible cause for her symptoms.

Her current symptoms of low-grade fever, borderline hypoxia, joint pain has occurred 4 weeks later.

Patient was counselled to taper and stop the steroid therapy in view of the current diagnosis of Dapsone Hypersensitivity Syndrome. She felt relieved to have ruled out the complex diagnosis and management. Patient on follow up after 1 month, was symptom-free with resolved blood parameters including Liver Function Test.

Parameter	Result	Normal Value
Hemoglobin	11g%	11.5 to 16.5 g%
White Blood Cells	10730 cells/mm3	4000 – 11000 cells/mm3
Differential count	Neutrophils-71%, Lymphocytes-16%, Monocytes-7% Eosinophils-6%	40 – 80%, 20 – 40%, 2-10% 1-6%
ESR	26 mm/hour	0 – 20 mm/hour
CRP	6.74 mg/L	Less than 5mg/L
Urea	22 mg/dL	13 – 43 mg/dl
Creatinine	0.6 mg/dL	0.6 – 1.1 mg/dL
Random Blood Sugar	94 mg/dL	<140 mg/dl
Total Bilirubin	0.3 mg/dL	0 – 1.3 mg/dL
Serum Albumin	3.9 g/dL	3.5 – 5.2 g/dL
Serum Globulin	2.4 g/dL	2 – 3.5 g/dL
ALT (SGPT)	41 U/L	< 34 U/L
AST (SGOT)	23 U/L	< 31 U/L
GGTP	70 U/L	< 36 U/L
Alkaline phosphatase	90 U/L	< 98 U/L
Complement level – C3	126 mg/dL	84 – 175 mg/dL
Complement level – C4	25.4 mg/dL	15 – 50 mg/dL
Anti CCP, Rheumatoid Factor, ANA, ds-DNA, AMA, ASMA	Negative	

DISCUSSION:

DHS is characterized by a hypersensitivity reaction to Dapsone. The incidence of DHS ranges from 0.5% to 3% [2]. The classic triad of DHS consists of fever, eruption, and other organ involvement [2]. Fever, hepatitis, exfoliative dermatitis, adenopathy and hemolytic anemia might be seen in varying combinations and sequences. Studies have shown that this syndrome may begin as early as 7–10 days after administration of the drug or as late as 6 months into therapy with dapsone [2].

Manifestations of DHS include high grade fever, skin rash, lymphadenopathy, eosinophlia, hepatitis, acute pneumonitis, neurological and other systemic features of multi-organ dysfunction. Our patient had anemia, cholestatic pattern of hepatitis along with elevated inflammatory markers. Although acute pneumonitis (eosinophilic pneumonia) with hypoxia and pleural effusion has been reported in DHS, no overt pulmonary manifestation was seen in this patient when she reported to us.

The diagnosis of DHS is based on clinical findings of fever, skin rash, hepatitis and other systemic features, along with history of prior dapsone exposure. Skin biopsy findings are non-specific and hence usually aren't carried out. In our case, the diagnosis was based on typical clinical manifestations following 4 weeks of dapsone intake, after excluding other drug exposures and close differential diagnoses-namely viral hepatitis, autoimmune hepatitis and other tropical infections. This was further supported by prompt response to systemic steroids. Rechallenge with dapsone is not recommended, as it can be hazardous.

Pathogenesis of DHS is unclear but proposed mechanisms implicate metabolites of dapsone, which form haptens with the production of anti-dapsone antibodies [3]. The management involves prompt discontinuation of dapsone, systemic steroids (oral prednisolone 1 mg/kg/day or intravenous methylprednisolone in equivalent doses) with supportive care. Gradual tapering of prednisolone (over more than a month) is recommended considering the persistence of dapsone in the body up to 35 days [4]. Mortality as high as 12-23% has been reported in severe DHS [5]. Thus, a high index of suspicion for early diagnosis, along with prompt treatment initiation is essential.

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