Dapsone-Induced Fulminant Hepatic Failure and Death of a Young Male

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Abstract

Fulminant hepatic failure (FHF) is a serious complication of dapsone syndrome. In our case, the young male patient took dapsone for the treatment of his dermatitis herpetiformis. After 18 days of taking dapsone therapy orally, he developed dapsone syndrome including FHF, also known as acute hepatic failure. He admitted in our intensive care unit (ICU) with low Glasgow Coma Scale (GCS) score (E3 V2 M4), elevated serum bilirubin (2.3 mg/dL) and alanine amino transferase (ALT) (261 U/L) level. Finally, he was diagnosed as dapsone-induced hepatic encephalopathy with high level of serum bilirubin (12.9 mg/dL), ALT (2372 U/L) and ammonia (>500 µg/dL). After completing five sessions of plasma exchange, abnormalities of the liver biomarkers reduced, significantly, but GCS not improved. His brain death was declared and then he died. Dapsone syndrome-associated death is a very rare incidence and in our case, patient died from FHF-associated brain death.

Keywords: Dapsone; Fulminant Hepatic Failure; Bilirubin; Brain Death

Background

Fulminant hepatic failure (FHF), also known as acute liver failure (ALF), is characterized by severe functional impairment of a previously sound liver within a very short time with tremendous loss of its synthetic capacity, and the development of hepatic encephalopathy (HE), an advance-staged liver impairment-associated reversible diminution of brain function [1, 2]. Dapsone is the first-line drug for the treatment of leprosy and dapsone-induced hypersensitivity reaction, also known as dapsone syndrome, can be a life-threatening event [3]. FHF caused by dapsone is a rare incidence, and here we found a case of dapsone-induced FHF in a young male patients who died with brain death.

Case Description

A 23-year-old male patient came to our hospital emergency room (ER) with the complains of high grade fever for last 10 days; swelling of face; yellowish colored sclera and urine; swelling and ulceration of lips; fever (101° F); headache; few scattered maculopapular rashes all over the body and altered consciousness Figure 1-3. There was no history of vomiting, abdominal pain and loose motion. According to the statements of patient’s attendance, for his dermatitis herpetiformis treatment, doctor prescribed him dapsone (each 50 mg tablet, once daily for the first 5 days; and then twice daily). He started to take dapsone as per the doctor’s prescription. After 18 days of taking dapsone, he developed few rashes in his back, chest and legs; physical weakness; severe muscle pain and fever (102° F). Then he reported to a nearest healthcare center where dapsone was stopped by the doctor, and hepatomegal (through 2D ultra sonogram of whole abdomen) with increased serum bilirubin level (2.3 mg/dL) and alanine aminotransferase (ALT) (261 U/L) was detected. He was on treatment, but his physical condition was deteriorating there rapidly day-by-day and decided to shift for better treatment to our hospital. Immediately after completing ER procedures, he was shifted to intensive care unit (ICU). In ICU, his initially done lab investigation reports were- serum bilirubin 8.2 mg/dL; ALT 1721 U/L; alkaline phosphatase (ALP) 226 U/L; serum albumin 2.5 g/dL; total IgE 1284 IU/mL; serum ammonia 223 µg/dL; prothrombin time 23.4 seconds (INR 2.16); white blood cell (WBC) count 16.3 K/µL; eosinophils 8.4%; C-reactive protein (CRP) 76.5 mg/L; procalcitonin 0.65 ng/mL; platelet count 154 K/µL; haemoglobin 9.1 g/dL; serum creatinine 1.6 mg/dL; body temperature 104° F; blood pressure 130/80 mmHg; pulse rate 126 beat/minute; SPO2 95% in room air and Glasgow Coma Scale (GCS) score- E3 V2 M4. He was treated as per the conservative ICU protocol for dapsone syndrome-associated hepatic encephalopathy and initially methylprednisolone was administered intravenously. After 72 hours, his GCS reduced to E2 V2 M3; ALT, serum bilirubin and ammonia level increased to 2372 U/L, 12.9 mg/dL and >500 µg/dL, respectively. The serum level of bilirubin, ALT and ammonia reduced to 7.4 mg/dL, 138 U/L and 177 µg/dL, respectively after completing five sessions of therapeutic plasma exchange, but his GCS level and respiratory function extremely declined, and he was taken on full mechanical ventilation support. His brain death was clinically declared on his 12th ICU-day with a GCS score- E1 V1 M1 and he died one day later.
Figure 1: Yellowish sclera due to dapsone syndrome

Figure 2: Lip ulceration due to dapsone syndrome

Figure 3: Dapsone-induced maculopapular rashes (almost healed)

Discussion

The use of dapsone started from the middle of the 20th century in leprosy management, but now its use has been extended to dermatitis herpetiformis, cutaneous vasculitis, vesicobullous dermatoses, nodulocystic acne, cutaneous mycetoma, polyarteritis nodosa and even in the treatment of brown recluse spider bite [4]. Dapsone (4,4'-diaminodiphenylsulfone) is a sulfone and possesses anti-inflammatory and anti-bacterial activity [3]. Adverse reactions with dapsone, also termed as ‘dapsone syndrome’, first described as hypersensitivity vasculitis syndrome in 1999, is currently manifested by fever, hepatic impairment, cholangitis, splenomegaly, lymphadenopathy, skin lesions and hemolytic anemia generally developed within 3-6 weeks of taking dapsone [3, 4]. Adverse reactions with dapsone also termed as ‘dapsone syndrome’, first described as hypersensitivity vasculitis syndrome in 1999, is currently manifested by fever, hepatic impairment, cholangitis, splenomegaly, lymphadenopathy, skin lesions and hemolytic anemia generally developed within 3-6 weeks of taking dapsone [3, 4]. This syndrome is found among 0.2% – 0.5% of its users and can develop as long as 6 months of initiating dapsone therapy [5, 6]. Dapsone-induced hepatotoxicity is basically responsible for the development of hyper bilirubinemia and elevated ALT level indicates the hepatocellular injury [4]. In our case, patient developed dapsone syndrome within 3 weeks of taking dapsone orally and that was clinically justified by maculopapular rashes, hepatomegaly, high bilirubin and ALT level. The fatality of dapsone syndrome was mentioned in different studies and dapsone-associated FHF was first reported by Garcia et al in a 12-year old girl [3, 4, 6]. Dapsone is metabolized in the liver, yields toxic intermediate metabolites including nitrosamines and hydroxylamine (potential toxic metabolite) through N-hydroxylation pathway while N-acetylation pathway produces nontoxic metabolites. These toxic metabolites potentially cause hepatic impairment while initial glucocorticoids therapy effectively reverses the severity of the syndrome [3, 4]. Unfortunately, in spite of receiving steroid and therapeutic plasma exchange, our patient did not respond adequately as it was required within that short treatment period. HE followed by FHF is still an unknown phenomenon and HE-associated brain death a crucial situation triggered by elevated level of ammonia. In the United States, annually approximately 2000 people are experienced with FHF and about 60% of these are drug-induced. Brain glutamine concentration is increased significantly during hyper ammonemia, leading to brain impairment and ultimately results in death [2, 7]. Though dapsone-induced FHF-associated death is a very rare incidence, but in our case, the young patient developed hyperammonemia, hyperbilirubinemia and elevated
ALT level as a consequence of dapsone syndrome within a short period of time under extreme ICU support, severely turned into HE, and finally died from complete brain death (evaluated and declared by the doctors). Dapsone syndrome is a rare but life threatening event. In most of the cases, early effective treatment including steroid therapy is sufficient to reduce the severity of the reaction. However in our case, the patient did not respond well to therapies, rapidly developed dapsone-induced FHF which ultimately turned into HE and finally he died.

Limitations of the Study

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Declarations

Ethical approval and consent to participate: Patient written consent was taken from the patient’s party for the publication purpose.

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