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A FATAL CASE OF SULONE SYNDROME

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Summary:

An unusual fatal case of Sulfone syndrome is presented. The other three fatal cases are compared.

Introduction:

Leprosy is a very common disease and is most often treated with dapsone. Various toxic reactions to dapsone have been described. The incidence of Sulfone syndrome is far less than 0.5%. [13] It consists of fever, exfoliative dermatitis, lymphadenopathy, hepatocellular jaundice, anemia, leucopenia, and mononucleosis occurring within the first six weeks of Sulfone therapy representing a reaction of generalized hypersensitivity. It may appear in an incomplete form as hepatitis or dermatitis alone. Though frequently reported about 30 years ago [1,6,8,9], virtually no reports followed later on, except one report each in 1956[7] and 1967[10] and two in 1981.[5,13] On scrutiny of literature, no reports could be found from India, despite dapsone being the mainstay of treatment in so many leprosy patients. Only three deaths have been attributed to dapsone in the United Kingdom over the past seventeen years[4]. We could find only twenty reported cases (and 2 % incidence of dermatitis but no hepatitis, in over five hundred of Lowe's cases)[9] of Sulfone syndrome, and only three fatal cases [1,5,7] in the available literature. A fourth fatal case is presented here.

Case Report:

A 30-year-old well-built nonalcoholic watchman of the poor socio-economic class was diagnosed as leprosy grade 3+ (Dharmendra classification[2]) and was started on oral dapsone 50 mg/day along with Chloroquine phosphate 750 mg/day and dexamethasone 2 mg/day on March 22. He was taking this treatment regularly and also received aspirin, paracetamol, and

diazepam intermittently for non-specific aches and pains and vitamins and minerals continuously during further treatment. On April 21 (31st day) he was noted to be having malaise, weakness, pyrexia (41^0C), erythematous rash over trunk, forearms, and legs, icterus, bilirubinuria (2+), and hepatomegaly (5 cm, firm, tender). He was hospitalized at a peripheral dermatological center in Bombay for four days, dapsone and dexamethasone were continued and paracetamol (3 gm for one day), diazepam (5 mg hs for 3 days), aspirin (1800 mg/day for 4 days), tetracycline (1 gm/day for 2 days orally), iron, and vitamins were given.

On admission at our hospital on May 1(without any record of clinical findings from April 25, but no drugs taken except dapsone and dexamethasone) patient appeared ill, was febrile, anemic, and deeply icteric with generalized lymphadenopathy, erosions of the oral mucosa, and generalized erythematous maculopapular rash with scaling, but sparing soles and palms. The liver was 4 cms-palpable, firm, and non-tender. The spleen was 1 cm palpable, firm, and non-tender. There was no evidence of encephalopathy.

The laboratory data were as follows: Haemoglobin 8 gm/dl, hematocrit 25, red cell count 2.2 x 10^{12}/L, normal red cell morphology, reticulocytes 0.5%, platelets 8 x 10^{11}/L, white cell count 4.1 x 10^9/L, polymorphs 64%, lymphocytes 36%, ESR 53 mm at the end of the first hour (Wintrobe), bilirubin 427.5 micromol/L (direct 301 micromol/L), SGOT 100.3 IU, SGPT 222.2 IU/L, alkaline phosphatase 25.6 2 IU/L, total proteins 7.6 g/l, albumin 2.8 g/l. Other biochemical parameters were within normal limits. Methemoglobin and HBsAg were not detected. VDRL was negative. The ear lobule smear was positive for acid-fast bacilli.

The patient had a fulminant course over the next 36 hours with rapidly progressive hepatic encephalopathy and gastrointestinal bleeding and expired on May 3 (33rd day). A postmortem liver biopsy was done which showed normal hepatic architecture. Many hepatocytes showed swelling with granular and vacuolated cytoplasm. Groups of hepatocytes showed necrosis. No appreciable mononuclear infiltrate or biliary stasis was seen.

Discussion:

Although the case could not be fully investigated in the available time, we strongly feel that there are sufficient circumstantial and clinical grounds for the diagnosis of Sulfone syndrome. The presentation did not match in any manner with that of viral hepatitis as described in text books[12]. No evidence of Epstein-Barr and other viruses has been found in recent case reports [5,13]. Aspirin[11] and paracetamol[14] are hepatotoxic only in large doses whereas tetracycline[3] is hepatotoxic only on intravenous administration in larger doses. Diazepam[14] can cause cholestatic jaundice which was not evident in this case. Chloroquine[14] is not hepatotoxic. In all cases of Sulfone syndrome described so far, none of these drugs were used. For these reasons, we consider these other drugs to be highly unlikely to be causative of the clinical picture in this case.

Sulfone syndrome is supposed to be due to hypersensitivity and an immunologic mechanism has been speculated[5]. The high incidence of Sulfone syndrome in the 1950s has been attributed to high initial doses of dapsone. In a recent case[13], dapsone was used in the dose of 50 mg/day and prednisolone was used during treatment of the reaction. This patient recovered totally. In another recent but fatal case[5], steroids were continuously given since the initiation of dapsone therapy in a higher dose of 100 mg/day. While treating the reaction, the dose of steroids was stepped up. In the earlier reported cases, concomitant steroids were probably not used. In our case, the dose of dapsone was not high, and as in another case[5], concomitant steroid therapy could not prevent hypersensitivity reaction. Thus, out of four fatal cases, two[1,7] received very high initial doses of dapsone, one[5] received a high dose of dapsone along with steroids and our case received a moderate dose of dapsone along with steroids. It is thus possible that a high initial dose of dapsone as well as concomitant use of steroids can cause a severe reaction that may be fatal.

References:

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