

An unusual case of dapsone syndrome with a prolonged remitting and relapsing course lasting eight months: a case report

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Abstract Dapsone hypersensitivity syndrome is a well established entity which has been reported in literature since the 1950's. A unique case of dapsone syndrome which had a very prolonged course of eight months is reported with no similar precedence in literature. With the wide use of dapsone in many medical conditions, clinicians should be aware that dapsone can cause a prolonged clinical syndrome of dapsone hypersensitivity which might mimic other sinister conditions.

Key words

Dapsone hypersensitivity syndrome, granulomatous hepatitis, exfoliative dermatitis, leprosy, dapsone.

Case report

A 40-year-old female came with a 3 month history of fever, nausea, right hypochondrial pain, generalized pruritic skin rash and frothy urine, after the complete withdrawal of antileprosy treatment which was commenced 3 weeks preceding the onset of her symptoms, after being diagnosed with paucibacillary leprosy. Anti leprosy treatment comprised of 100 mg of dapsone daily with monthly rifampicin, only one dose of the latter had been taken prior to discontinuation. Low doses of prednisolone had been repeatedly prescribed to treat her symptoms which were attributed to dapsone syndrome however with poor response. She had never taken any herbal treatment or

other forms of native treatment. Exposure to heavy metals was excluded. She had not been on any other medication preceding her symptoms. Examination revealed a diffuse maculopapular exfoliative skin rash with alopecia, dependant edema and fever. Jaundice, pallor and lymphadenopathy were absent. The mucosae were normal. Cardiovascular respiratory and neurological system examination findings were unremarkable. A 2cm smooth, regular, nontender hepatomegaly was detected but abdominal examination was otherwise normal.

Laboratory investigations at this stage revealed Hb 14.8 g/dl, WBC 18700/mm³, DLC neutrophils 57%, lymphocytes 16%, eosinophils 24%. Blood picture showed eosinophilia. Liver function tests revealed total bilirubin 15 µmol/l with a direct fraction of 8 µmol/l, AST 400 U/L, ALT 877 U/L, alkaline phosphatase 131 U/L, serum albumin 32 g/l and a prothrombin time of 13s against a control of 12 s. Serological tests for hepatitis A virus (anti-HAV IgM), hepatitis B virus (HBsAg), hepatitis C virus (anti-HCV)

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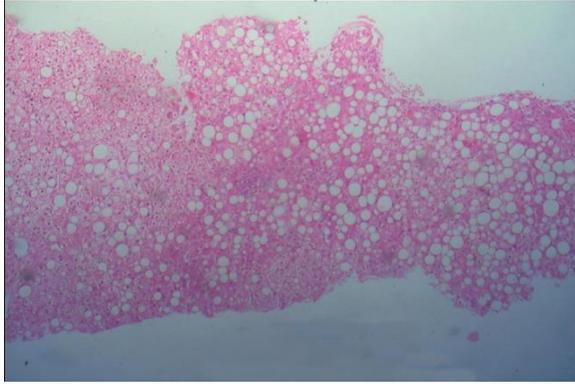


Figure 1 Liver biopsy shows mononuclear cell infiltrates with formation of vague granulomas composed of epithelioid histiocytes (10X).

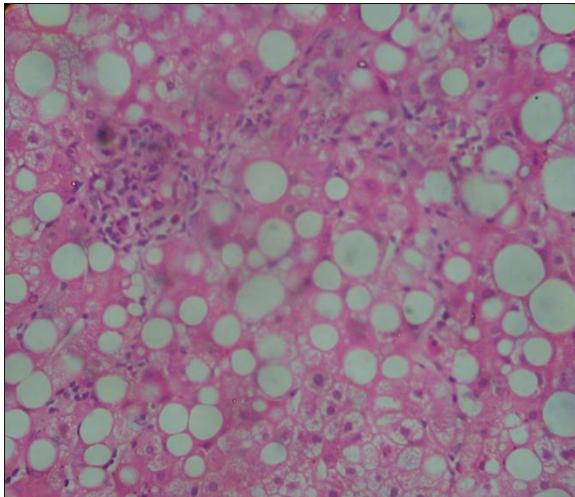


Figure 2 Liver biopsy exhibit mononuclear cell infiltrate with formation of vague granulomas composed of epithelioid histiocytes and admixed eosinophils with micro- and macrovesicular steatosis involving 50% of hepatic parenchyma suggestive of drug induced granulomatous hepatitis with steatosis (40X).

were negative. Blood for LE cells and serum ANA were negative. Ultrasound abdomen showed mild uniform enlargement of liver with normal echo-texture, and no evidence of portal hypertension or biliary dilatation. Urine full report showed 25-30 pus cells per high power field. Serum creatinine was 67 $\mu\text{mol/l}$. Blood and urine cultures were sterile. The skin biopsy was concluded as being compatible with exfoliative dermatitis. Liver biopsy showed intact parenchymal architecture. Portal tracts

revealed mononuclear cell infiltration with formation of vague granulomas of epithelioid histiocytes and admixed eosinophils. There was no bile duct abnormalities or interface hepatitis. Hepatic parenchyma demonstrated micro- and macrovesicular steatosis without any fibrosis. The biopsy was concluded as being highly suggestive of drug-induced granulomatous hepatitis.

The patient was treated with antipyretics, and intravenous hydrocortisone followed by high dose oral prednisolone (1mg/kg/d), topical steroids, emollients. Antihistamines were prescribed for pruritus. Antimicrobial cover was commenced until the negative cultures were received. Fever resolved within 4 days of commencement of high dose steroids and liver enzymes showed a declining trend. Although there was clinical and biochemical improvement of her condition with steroids, she relapsed frequently during the initial 3 months, whenever a steroid taper was attempted, and therefore, she was treated with a prolonged course of slowly tapering prednisolone for almost 8 months with bone protection. Her recovery was complicated by transient steroid-induced diabetes mellitus which was controlled with dietary measures and medication. But this subsequently resolved with reducing doses of steroids. She completely recovered and is currently not on any medications. On review at 9 months she was free of dermatological, hepatic or other systemic complaints or signs, and her blood counts, liver enzymes, blood sugars and urine full report parameters were all within normal limits.

Discussion

Dapsone is one of the mainstay drugs in the treatment of leprosy.¹ It is also used in many other conditions.² 'Dapsone syndrome' is a generalized hypersensitivity reaction that occurs

in patients on dapsone therapy.³ The cardinal features are fever, exfoliative dermatitis, lymphadenopathy, lymphocytosis, methemoglobinemia, hemolytic anemia and hepatotoxicity. Dapsone syndrome is a type of drug rash with eosinophilia and systemic symptoms (DRESS) syndrome.⁴

Hyperbilirubinemia when present in dapsone syndrome occurs due to haemolysis⁵ in addition hepatocellular and cholestatic liver injury.⁶ Liver biopsy shows either hepatitis, cholestasis or noncaseous granulomas⁷ though it is usually not performed routinely. The single dose of rifampicin which the patient had received is unlikely to have been the causative agent. Exfoliative dermatitis is more common with dapsone than other implicated agents.

Our case had the typical features of dapsone syndrome without an apparent alternative etiology for the presentation. The symptoms appeared within a month of starting of dapsone with sterile pyuria from renal involvement.⁸

Drug-induced liver granulomas are seen with numerous pharmacologic agents.⁹ The classical histological feature of drug induced liver damage firmly supported the diagnosis after exclusion of other likely causatives including herbal medications.

Treatment is withdrawal of dapsone and high dose steroids. Dapsone persists in the body for well over 35 days therefore glucocorticoids are best tapered slowly.¹⁰ However, this patient had an unusually prolonged dapsone hypersensitivity

syndrome persisting for 8 months following the withdrawal of dapsone. Literature search failed to reveal documented precedence of a similar prolonged course. The authors conclude that clinicians need to be aware of a prolonged clinical course in dapsone syndrome.

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