Dengue fever in a patient with dapsone hypersensitivity syndrome: a diagnostic dilemma

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Background

It is a challenge to diagnose and manage a patient presenting with multiple life threatening conditions. The patient described here presented with dapsone hypersensitivity syndrome and dengue fever occuring at the same time which was further complicated with clinical sepsis.

Introduction

Dapsone is a drug which is widely used in dermatology to treat leprosy, vasculitis, vesicobullous dermatoses etc. It is 80% bio available and has a half life of 24-30 hours. Dapsone is metabolized by N-acetylation and N-hydroxylation in the liver. N-acetyldapsone leads to an equilibrium with dapsone in the body. N-hydroxydapsone formed through hydroxylation via cytochrome P450 oxidative pathway is believed to be responsible for majority of side effects. Dapsone hypersensitivity is an emergency requiring prompt treatment. The condition is characterized by fever, rash, lymphadenopathy and liver damage. As dapsone metabolites persist for about one month in circulation, management should be continued until liver enzymes return to normal.

Dengue fever is a mosquito borne viral fever prevalant in Sri Lanka mostly during rainy seasons, transmitted by mosquitoes within the genus Aedes, principally Aedes aegypti. Patients can present with fever and skin eruption, jaundice and multisystem involvment is seen in the more severe forms namely dengue haemorrhagic fever and dengue shock syndrome.

Case report

A previously healthy 33 year old patient presented with a large hypopigmented patch over the right forearm of three years duration. Loss of hair, sweating and pain sensation confirmed a clinical diagnosis of borderline tuberculoid leprosy.

Skin biopsy was compatible with borderline tuberculoid leprosy. As microbiological and haematological investigations were normal patient was commenced on multi drug therapy (MDT). As the lesion was large it was decided to start him on MB.

After completing one month's treatment, patient presented with fever, headache, athralgia, myalgia, tiredness, abdominal pain, loose stools, nausea, vomiting and dark coloured urine.

Examination revealed a febrile, ill looking patient with pallor and icterus.

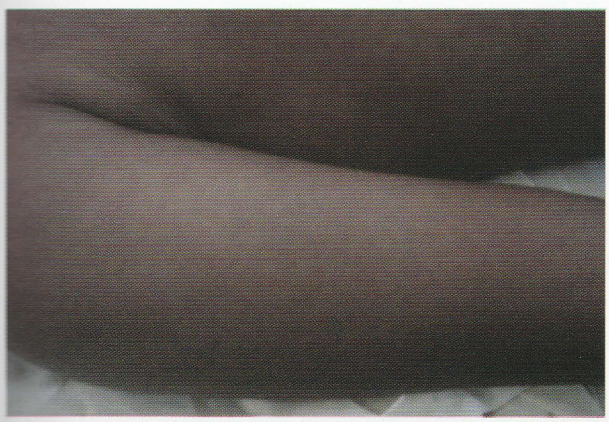

Figure 1.

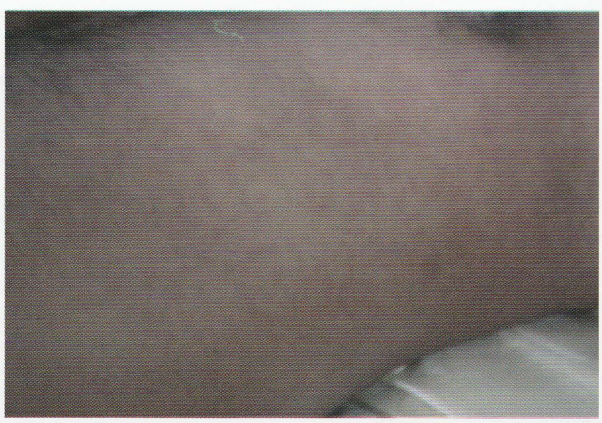

Figure 2.

Fig. 1 and 2. *Erythematous maculopapular rash.*

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Genaralized blanching maculopapular rash was present with generalized lymphadenopathy. A tender hepatomegaly and splenomegaly was noted.

Investigations

Patient had a Hb of 7g/dl and blood film revealed features of oxidant induced haemolysis. Liver profile showed high bilirubin and liver enzymes compatible with drug induced acute liver damage. Dengue antibodies were negative on 5th day of the fever.

Skin biopsy showed parakeratosis, mild focal acanthosis, band like lymphocytic infiltrate with epidermotrophism and prominent perivascular and interstitial inflammatory infiltrate with eosinophils.

Patient was treated as dapsone hypersensitivity syndrome. MDT-MB treatment was omitted.

Treatment was commenced with oral prednisolone 1mg/kg supplemented with symptomatic treatment. But the patient deteriorated and developed further symptoms with abdominal distension, tachycardia and dyspnoea. Steroid dose was reduced as an infective cause was suspected and investiga-tions were carried out to find a specific cause. Patient needed management in the Intensive care unit.

Screening tests for viral hepatitis, typhoid fever, leptospirosis and malaria were negative. Full blood count WBC - $23x10^9$/L with 70% neutrophils and severe thrombocytopenia. C reactive proteins -170mg/l. Blood culture - Negative. Urine culture - Negative. ANA - Negative. INR - 1.06. Blood urea - 3.9mmol/l. Serum electrolytes - normal. Serum creatinine - 89umol/l. Dengue antibodies IgM - positive on day 10. IgG - negative.

Ultrasound scan of the abdomen showed hepatosplenomegaly,free fluid in the gallbladder bed and pelvis, cholecystitis and cholangitis, sluggish peristalsis and inflammatory changes in the bowel wall.

Chest x ray showed B/L pleural effusion. ECG - normal. 2D echocardiogram - normal. Liver biopsy revealed histological features of chronic hepatitis and cholestasis with eosinophilic infiltrate compatible with drug induced hepatitis.

Treatment

Patient was treated in the intensive care unit with intravenous meropenem, metronidazole and amikacin. Initially prednisolone dose was reduced because of dengue positivity and clinical sepsis. After completing antibiotics prednisolone dose was increased to manage dapsone hypersensitivity syndrome.

Restarting antileprosy drugs were delayed for few months till his liver enzymes were normalized. His treatment was completed with ofloxacin instead of dapsone.

Discussion

Our patient had dapsone hypersensitivity and dengue fever which was proved by the investigations. Dengue fever is commoner than dapsone hyper-sensitivity. Both conditions can have similar clinical and biochemical features. Management is different in both conditions.

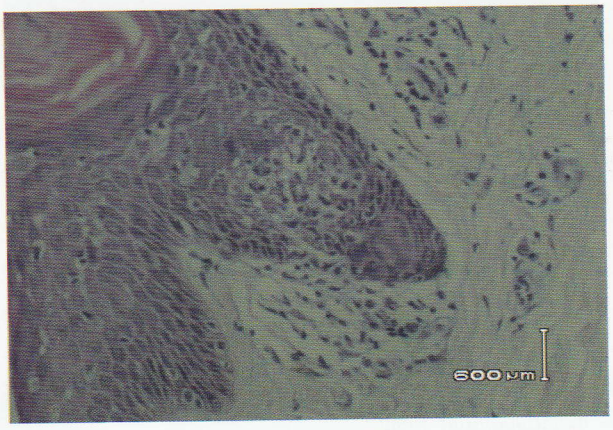

Figure 3.

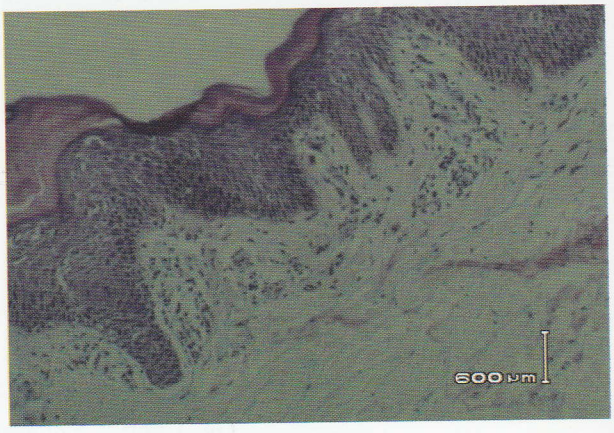

Figure 4.

Fig. 3 and 4. *Band like lymphocytic infiltrate with epidermotrophism and prominent perivascular and interstitial inflammataory infiltrate with eosinophils.*

Dapsone hypersensitivity syndrome is a well known serious adverse effect of dapsone. The illness present at the beginning of 2nd month of treatment. As fever is a well known manifestation of dapsone hypersensitivity syndrome other causes are often overlooked. Our case highlights this fact very well. Luckily our patient had only primary dengue fever without shock or haemorrhage.

Acknowledgements

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References

1. Stephen Wolverton and Marc Darst. Systemic drugs in Bolognia JL, Jorizzo JL, Rapini RP. Dermatology Mosby Publications. First edition 2003; 2077-8.

2. Breathnach SM. Drug reactions in Burns T, Breathnach S, Cox N, Griffiths C in Rook's textbook of Dermatology 8th edition Blackwell Science publications 75.63.

3. Langenbeck's Archives of surgery; *Clinical Sepsis and Septic Shock* 2008; **393**(6): 817-24.