CASE REPORT

Fulminant hepatic failure in a 15 year old boy with borderline lepromatous leprosy and Type 2 reaction

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Summary The liver is the most frequently affected visceral organ in leprosy, particularly in the multibacillary group. Administration of hepatotoxic drugs may also affect liver function. We report the case of a male patient, diagnosed as borderline lepromatous leprosy with Type 2 reaction, who was managed with multibacillary multidrug therapy and steroids, and who then developed acute hepatitis and succumbed to sudden cardiac death. Although erythema nodosum leprosum has been described as a rare cause of death in the literature, such an occurrence in the present era when leprosy has been eliminated needs a special mention.

Introduction

Leprosy is a systemic disease involving skin, nerves and the reticuloendothelial system, the liver being the commonest internal organ affected. Hepatic involvement in leprosy may occur in both tuberculoid and lepromatous disease but is clinically more evident during lepra reactions, (mainly Type 2), and is characterised by focal lymphocytic infiltrate and degenerative changes in the hepatocytes, which constitute the most frequent histopathological findings. Fulminant hepatic involvement in leprosy is extremely rare. We report fatal, fulminant hepatic failure in an Indian adolescent boy who had borderline lepromatous (BL) leprosy with severe erythema nodosum leprosum (ENL). Our case exhibits two interesting features namely, the presence of necrotic ENL which is rarely encountered in children, and severe unremitting hepatic involvement which culminated in hepatic failure and death.

Case Report

A 15 year old boy having BL leprosy with recurrent ENL on multibacillary multi-drug therapy (MB-MDT) and oral prednisolone (10-30 mg/day) for the past 6 months, presented with papulo-pustular lesions, along with abdominal pain, vomiting and loss of appetite for the
previous 15 days. There were no complaints suggestive of motor weakness or any other systemic involvement. There was no history of alcohol consumption or previous liver disease. A provisional diagnosis of BL with Type 2 lepra reaction was made and his oral prednisolone was increased to 40 mg/day.

On examination he was mildly febrile (38 °C) and icteric. Lymphadenopathy was absent. Cutaneous examination showed multiple papulo-pustular lesions with ulceration and necrosis on both extremities and back (Figure 1).

The right posterior tibial nerve, and the ulnar, radial cutaneous and common peroneal nerves on both sides were enlarged. Systemic examination did not reveal any abnormality. Slit skin smear showed a bacteriological index of 5+ with solid and fragmented bacilli. Histopathological examination of papulo-pustular lesions confirmed ENL.

In view of the above, BL with infective hepatitis, ENL induced hepatitis or MDT induced hepatic damage were considered as possible diagnoses. MDT was withheld while oral prednisolone was increased to 40 mg/day.

The patient continued to develop fresh ENL lesions, along with high grade fever and worsening of the abdominal pain and vomiting. Laboratory reports showed anaemia, hypoproteinaemia, hyperbilirubinaemia of 5.7 mg/dl (normal, 0.3-1.3 mg/dl), AST 677 IU/l (normal, 12-38 IU/l), ALT 931 IU/l (normal, 7-41 IU/l), ALP 122 IU/l (normal, 33-96 IU/l), Total Leucocyte Count 19.7 × 10³ cells/mm³ (normal, 3.54-9.06 × 10³ cells/mm³), platelets 355,000/mm³ (normal, 150,000-400,000/mm³), deranged coagulation profile (PT- control 12.08 s, test 26.6 s; INR 2.27; PTTK- control 29 s, test 33.8 s) and electrolyte imbalance (Na⁺/K⁺ 117/4 mmol/l; normal, 136-146/3.5-5 mmol/l). Renal function tests, G-6PD, HIV and viral markers were normal. Peripheral smear for malarial parasite, Widal test, blood and urine culture, and abdominal ultrasound examination were normal. The patient also developed altered sensorium (Glasgow coma scale 9/15) with hepatic encephalopathy and was shifted to Medical ICU. Non-contrast computerised tomography of the head was normal. ANA/RF/ASO were negative while CRP was elevated. Hepatic encephalopathy was managed medically with intravenous fluids, hydrocortisone and antibiotics. However, a liver

Figure 1. Skin lesions seen on presentation.
biopsy could not be done. As the patient was showing improvement in his liver function, he suffered a sudden cardiac arrest and succumbed to the same.

Discussion

In moving from polar tuberculoid to polar lepromatous leprosy one finds a sharp increase in the prevalence of leprous lesions in the liver.\(^2\)

Mechanisms of liver involvement in leprosy include: infiltration of the liver by leprous granulomas, immune complex mediated injury in lepra reactions (Type 2) and drug induced (MDT) hepatic injury. Hepatotoxic drugs employed in MDT such as rifampicin and dapsone can induce hepatitis. Drug induced hepatitis shows temporal association with initiation of drugs and usually manifests within the first 4-6 weeks of starting MDT, however, if patients receive steroids for neuritis or reaction from the start of MDT it may present much later. The drug induced hepatic damage can be seen in the entire spectrum of leprosy. We excluded MDT as the cause of severe hepatitis in our patient as he had already completed six pulses of MB-MDT without any adverse effect. Moreover, serial monitoring of liver function tests during follow up visits in the past did not reveal any liver related adverse effects.

During ENL, the liver is frequently involved and shows a similar histopathological appearance to that of ENL seen in the skin.\(^3\) The most probable cause of liver damage in our patient was immune complex mediated liver injury after excluding viral and drug induced hepatitis. Severe ENL reactions include numerous ENL nodules with high fever or neuritis, ulcerating and pustular variants, recurrent episodes or involvement of other organs (eyes, testes, lymph nodes, joints, liver and kidney). The severity of the cutaneous lesions may not always be a true predictor of visceral involvement as seen in our patient also. This patient had a few necrotic, pustular lesions with mild fever without any neuritis, iridocyclitis, orchitis or glomerulonephritis yet he developed fulminant hepatic failure.

Our patient had been having recurrent ENL (chronic ENL) for the past 6 months and we assume that some degree of subclinical hepatic malfunction was already present (although not confirmed by liver histopathology in this case). It is also quite likely that uninterrupted administration of hepatotoxic drugs (dapsone and rifampicin) during the entire period of chronic ENL led to further deterioration of hepatic function and eventually to the development of a superimposed pustulonecrotic, acute ENL over and above the chronic ENL, which was instrumental in precipitating the fulminant hepatic failure. This case illustrates the point that patients with multibacillary (MB) disease, with a high BI (\(> 3\)), who require MDT for > 1 year and also suffer recurrent ENL attacks, are ‘High Risk’ cases for developing hepatic damage as they already have some degree of subclinical hepatic damage. In addition to the importance of regular monitoring of liver function tests in these patients, this case highlights the need for a high risk approach to manage pustulonecrotic Type 2 reactions, which can cause severe immune complex mediated damage to vital organs such as liver and kidney.

Ferrari et al. reported a 70 year old patient with lepromatous leprosy and Type 2 reaction with liver involvement showing raised serum transaminases levels (AST-145 IU/l, ALT-166 IU/l, GGT-60 IU/l), 5 times the upper reference value and serological tests for viral markers were negative. Lepromatous leprosy associated with severe Type 2 reaction was considered as the main diagnostic hypothesis and the patient responded to treatment with prednisone 1 mg/kg/day.
The literature on hepatic involvement in leprosy supports the observation that there is a mild increase in the levels of aminotransferases.\textsuperscript{4} Values 2-3 times higher than normal are quite uncommon and are considered pathological. On the other hand, extremely high levels of serum aminotransferases were observed in our case (about 22 times the upper reference value for AST and nearly 45 times for ALT), which have hitherto not been reported in LL with ENL. These high levels are suggestive of profound, widespread immunological damage to the hepatocytes which was unresponsive to standard dose of corticosteroids of 1 mg/kg/day thus resulting in hepatic failure. The rapid downhill course of hepatitis in this patient could possibly be attributed to an interplay between some undetected, pre-existing liver pathology and superimposed viral or bacterial infection causing precipitation of ENL with resultant immune complex mediated liver damage.

This case underscores the importance of an active search for any systemic abnormality coupled with regular, more frequent screening tests and timely management of intercurrent infections which may contribute to liver damage in tropical countries like India. Cases which develop a severe hepatic involvement possibly require aggressive management with higher doses of steroids (60-80 mg/day preferably parenteral) in order to achieve rapid halt of the ongoing immune damage. We surmise that although severe hepatitis or hepatic failure is a rare occurrence, it remains a lurking possibility in the ‘High Risk’ category of patients as discussed above. A proactive search for underlying liver disease, regular monitoring of liver function and a cautious approach to management of severe ENL can avert a sinister outcome.

References