SHORT COMMUNICATION

Portal Hypertension with Visceral Leishmaniasis

RAJNITI PRASAD*, UTPAL KANT SINGH, O P MISHRA*, BP JAISWAL AND SUNIL MUTHUSAMI

*From Department of Pediatrics, Nalanda Medical College, Patna, Bihar; and *Department of Pediatrics, Institute of Medical Sciences, Banaras Hindu University, Varanasi; India.*

Correspondence to:
Dr Utpal Kant Singh,
8, Rajendra Nagar,
Patna 800 013, Bihar, India.
utpalkant.singh@yahoo.co.in
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We conducted this study to observe evidence of portal hypertension in children with visceral leishmaniasis (VL). Eighty-eight consecutive cases (50 male) of VL were subjected to ultrasonography. Those with evidence of portal hypertension also underwent upper gastrointestinal endoscopy and liver biopsy. Eight patients had portal hypertension as evidenced by dilated caliber of portal and splenic veins. Two patients had periportal, splenic and peripancreatic collaterals and one patient had cavernous transformation of portal vein. Out of eight patients, four patients had esophageal and gastric varices. Liver biopsy was done in four patients and revealed hepatic sinusoidal dilations without any evidence of fibrosis. Portal hypertension may be an independent manifestation of VL and remain undiagnosed unless a physician maintains a high index of suspicion.

Key words: *India, Kala-azar, Portal hypertension, Ultrasonography, Visceral leishmaniasis.*

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L. donovani infections are associated with a wide spectrum of clinical manifestations, commonly described in India as visceral leishmaniasis (VL)(1-3). While the association of portal hypertension with parasitic diseases like schistosomiasis and malaria is well recognized, this has been only rarely reported with VL. This prospective study on children with VL was done to look for evidence of associated portal hypertension.

METHODS

The study was conducted between July 2004 to September 2008 at a tertiary hospital in eastern India located in the endemic area of VL. Ethics committees approved study protocol and consent form. Written informed consent was taken from legal guardians of children. All consecutive children aged 1 to 14 years, presenting with fever, splenomegaly and positive LD body in bone marrow or splenic aspirates examination were enrolled for the study.

Renal function, liver function tests, complete hemogram, PT/APTT, general blood picture were done in all the children. Bone marrow aspiration and microscopic examination was performed in all the children to detect *L. donovani* (LD) bodies and other hematological affections. Splenic aspiration was performed in bone marrow negative cases after correction of any existing derangement of coagulation profile. Children with significant lymphadenopathy also underwent lymph node aspiration and cytology.

All patients were subjected to color doppler study of hepatobiliary system before starting treatment. Those with significant portal (>13 mm)/splenic vein dilation(4) were further evaluated for gastric/esophageal varices by upper gastrointestinal endoscopy. Hepatitis B surface antigen and anti-HAV IgM antibody were also looked for in all these patients. Liver biopsy was performed in these cases. Patients with esophageal varices of grade II/IV were also subjected to sclerotherapy, particularly in those with

hematemesis and malena and put on propranolol prophylaxis (1mg/kg/day tid).

The parasitological analyses of bone marrow/ splenic aspirates and color doppler study were performed at completion of therapy, and after 1 month and 6 months. The density of parasites was graded from 0 (no parasite/10000 high power field) to 6 (>100 parasites/ field). The cure was defined as an absence of parasites at the end of therapy and no relapse during six months of follow up. Confirmed case of VL were treated with either Sodium stibogluconate (20 mg/kg/day intramuscularly for 30 days) or Amphotericin B at a dose of 1 mg/kg intravenously after sensitivity testing to a total cumulative dose of 15 mg/kg. During therapy, patients were monitored daily for vital signs, splenic size and adverse events.

RESULTS

We identified 88 children (38 females) in the age group of 1 to 14 (mean: 9.2±3.7) years with microscopically and serologically proved VL. Bone marrow aspirates were positive in 73 cases (82.9 %) and the remaining 15 (17.1%) cases showed LD bodies in the splenic aspirate. Significant lymphadenopathy was observed in 23 cases (26.1%), but LD bodies could be demonstrated in five cases on lymph node aspiration cytology. One child had concomitant pulmonary tuberculosis (sputum positive for AFB) and another was admitted with concomitant severe falciparum malaria (peripheral smear positive for malarial parasite). Of 88 patients, 68 had received sodium stibogluconate but 20 of them showed relapse after one month of follow up, which was treated with amphotericin B. Remaining children received amphotericin B as the initial therapy. None of the patient treated with amphotericin B relapsed. ***Table* I** depicts the clinicopathological profile of children who demonstrated features of portal hypertension. None of the children in our study had fulminant hepatic failure.

Portal hypertension was present in 8 children as evidenced by dilated caliber of the portal and splenic veins and splenic/peri-pancreatic collaterals. Two children had evidence of periportal, splenic and peripancreatic collaterals, and another child showed cavernous transformation of the portal vein. Liver biopsy showed sinusoidal dilation without hepatic fibrotic changes in four children, among whom esophageal and gastric varices were seen in two.

At follow-up, one month and 6 months later, ultrasonography of hepatobilliar system of eight children with portal hypertension showed no change in calibre of portal vein, splenic veins and splenic/ peripancreatic collaterals.

DISCUSSION

Portal hypertension has not been previously reported in pediatric visceral leishmaniasis. Pahwa, *et al*.(5) reported two children with fulminant hepatic failure who succumbed to the illness. In our series, although none presented with fulminant hepatitis, we detected

TABLE I HEMATO-BIOCHEMICAL CHARACTERISTICS OF CHILDREN WITH PORTAL HYPERTENSION

No	Age (y)	Hb (gm/dL)	TLC (mm^3)	APC (mm^3)	Total bilirubin (mg/dL)	Direct bilirubin (mg/dL)	ALT (IU/L)	AST (IU/L)	Serm albumin (g/dL)
1	6	9.9	5000	112000	1.0	0.5	40	30	2.8
2	5	1.8	2400	95000	0.62	0.21	12.6	31.1	2.2
3	8	11	6000	220000	0.6	0.1	42	76	3.0
4	10	5.1	2500	110000	4.3	0.9	24	34	2.6
5	11	9.3	3200	250000	0.8	0.2	64	44	2.0
6	10	6.3	3800	106000	0.7	0.2	20	54	2.6
7	11	6	10000	150000	1.0	0.4	77	174	2.4
8	10	8.1	3200	180000	0.9	0.2	16	29	2.2

ALT: *Alanine aminotransferase*; *AST*: *aspartate aminotransferase*; *TLC*: *total leucocyte count*; *APC*: *average parasite count.*

evidence of portal hypertension in 8 children, which had persisted on follow up at 6 months. Datta, *et al.*(6) reported three adult males with portal hypertension in VL and Prakash, *et al.*(8) reported an adult with leishmanial hepatitis with portal hypertension. Thus, with the present findings, it is evident that portal hypertension could not conclusively be ascribed to hepatitis as suggested(6). Aggarwal, *et al.*(8) in their study of sixty VL cases concluded that portal hypertension and cirrhosis of liver do not occur as a consequence of VL.

The findings on liver biopsy in our study indicate that in the absence of any significant hepatic cirrhotic changes in four cases, the cause of portal hypertension in this population may not be secondary but a primary involvement of the splanchnic vasculature. Cytokines and chemokines are known to play key roles in mediating the outcome of VL(9), but the precise sequence of events that determines the outcome of infection has not been fully elucidated. The chronicity and low grade persistent nature of the disease state in VL(10) lends support to the probability that portal hypertension is a gradually evolving event in VL.

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