

### Chronic diarrhea and malabsorption caused by *Leishmania donovani*

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Chronic diarrhea and malabsorption are uncommon in immunocompetent patients with visceral leishmaniasis. We report two immunocompetent patients with visceral leishmaniasis where the predominant presentation was chronic diarrhea. One of them had clinically overt malabsorption and duodenal mucosa was loaded with *Leishmania donovani* bodies. The other patient had diffuse colonic aphthous and discrete ulcerations and *Leishmania donovani* bodies were seen in the crush smears of the colonic mucosa. With amphotericin B, there was reversal of malabsorption and healing of colonic ulcers. [*Indian J Gastroenterol* 2006;25:309-310]

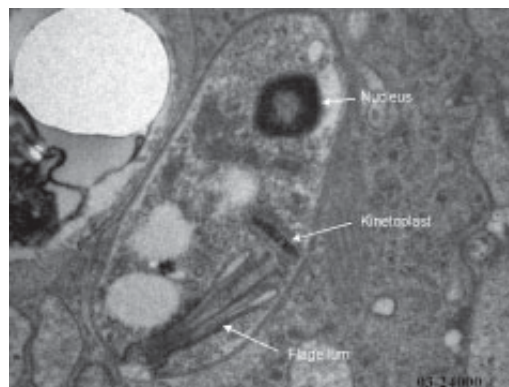
The incidence of visceral leishmaniasis (VL) is high in patients with HIV infection. Gastrointestinal involvement is a prominent feature of VL among individuals with HIV infection.<sup>1</sup> In people with no obvious immunodeficiency, VL is characterized by fever, weight loss and large splenomegaly. Although the prevalence of diarrhea ranges from 5%-26% in patients with VL,<sup>2,3</sup> presentation with chronic diarrhea and malabsorption is rare. Symptomatic colonic involvement and colonic ulcerations has not been described in these patients.

*Case 1:* A 29-year-old man from the state of Uttaranchal presented with chronic diarrhea, recurrent intestinal colic, fever and easy fatigability of 1-year duration. He passed 7-8 large-volume, frothy, and foul-smelling stools per day. He lost 21 Kg during this period. Since 9 months, he noticed a progressively increasing lump in the left upper quadrant of his abdomen. His appetite was normal and he did not have skin rashes, joints pain, oral ulcers or respiratory symptoms. His past medical history was non-contributory. He was a nonsmoker, social drinker, and had no

contact with commercial sex workers. He was treated with a course of antibiotics at the onset of his illness and received blood transfusion once for severe anemia. He was febrile and anemic at admission. His body mass index was 18 Kg/m<sup>2</sup> and he had acneform eruptions on his face. He did not have lymphadenopathy or icterus. Systemic examination revealed massive splenomegaly and mild hepatomegaly.

*Investigations:* hemoglobin 6.7 g/dL, leukocytes 1900/mm<sup>3</sup> (polymorphs 44%, lymphocytes 56%), platelets 92,000/mm<sup>3</sup>; prothrombin time 16.4 s (control 11); serum creatinine 1.3 mg/dL; total bilirubin 0.5 mg/dL, serum total protein 9.7 g/dL (albumin 2.5), AST 33 U/L, ALT 15 U/L, serum alkaline phosphatase 102 U/L. Serum protein electrophoresis revealed polyclonal gamma globulin, and there was no M band. There were no ova or cysts on multiple stool microscopic examinations, and modified acid-fast stain was negative for isospora, cyclospora, and cryptosporidium. Repeated stool culture did not grow any pathogens. Urine d-xylose excretion over 5 hours after 5 g d-xylose ingestion was 0.21 g (normal >1). Esophago-gastro-duodenoscopy revealed normal duodenal mucosa. Duodenal biopsy showed normal crypt-villus ratio and infiltration of lamina propria by chronic inflammatory cells. There were numerous *Leishmania donovani* (LD) bodies in the macrophages and few of them were seen lying extracellularly. The presence of LD bodies was confirmed by electron microscopic examination of the duodenal mucosal biopsy (Fig). Splenic aspirate was strongly positive (6+) for LD bodies. Bone marrow examination also showed macrophages containing numerous LD bodies. Contrast-enhanced CT revealed hepato-splenomegaly and dilated terminal ileum; however, the terminal ileum and colon appeared normal on colonoscopic examination. Serologic tests for HIV 1 and 2, HBsAg, and anti-HCV were negative. The aldehyde test was positive. CD<sub>4</sub> and CD<sub>8</sub> counts were normal. Twenty-four-hour urinary excretion of albumin was 2.5 g and 2.3 g on two occasions.

With a diagnosis of VL with malabsorption syndrome, he was treated with amphotericin B deoxycholate 50 mg daily intravenously for 25 days. He became afebrile, stool frequency decreased to 1-2/day, and spleen size regressed to 6 cm at the completion of treatment. Repeat urine



**Fig: Case 1: Electron microscopy of *L. donovani* body showing nucleus, flagellum and kinetoplast in duodenal biopsy**

d-xylose test improved to 1.12 g/5 g/5 h. Repeat duodenal mucosal biopsy at 6 weeks and 12 weeks revealed marked decline in parasite load. Twenty-four-hour urine albumin excretion also improved to 0.32 g after completion of treatment. One year later, he was asymptomatic, and there was normalization of hemoglobin.

*Case 2:* A 35-year-old lady was referred from the state of Bihar for chronic diarrhea for 2 years and intermittent fever for 6 months. She passed 7-10 moderate-volume stools per day, with no blood or mucus. She complained of generalized weakness and significant weight loss. Review of investigations done elsewhere revealed hypercellular bone marrow with megaloblastic changes. She had received antimalarials and antibiotics, to which there was no response. At admission, she had severe pallor, pedal edema, large splenomegaly and mild hepatomegaly.

*Investigations:* hemoglobin 4.5 g/dL, leukocytes 1300/mm<sup>3</sup> (polymorphs 54%, lymphocytes 46%), platelets 92,000/mm<sup>3</sup>; serum creatinine 1.1 mg/dL; serum proteins 8.1 g/dL (albumin 1.8 g/dL), AST 43 U/L, ALT 18 U/L, alkaline phosphatase 142 U/L. There were no ova or cysts on multiple stool microscopic examination, and modified acid-fast stain was negative for isospora, cyclospora and cryptosporidium. Repeated stool culture did not grow any pathogens. The urine d-xylose excretion over 5 hours after 5 g d-xylose ingestion was 1.08 g. Serology was negative for HIV and positive for aldehyde test. CT showed splenomegaly with thickened sigmoid, descending and proximal right colon. Colonoscopic examination revealed multiple aphthous ulcers scattered all over the colon and discrete ulcers in the rectum and cecum. Biopsies from the cecum showed inflammatory granulation tissue with increase in inflammatory cells in lamina propria. Crush smears from the biopsy tissue revealed LD bodies. The duodenal mucosa appeared normal and histological examination showed normal crypt-villus pattern. Bone marrow examination also showed LD bodies (3+) using Giemsa and acridine orange stains.

She was diagnosed to have VL along with involvement of the colon. She was given 3 units of packed red blood cells at admission and later treated with amphotericin B deoxycholate 50 mg IV daily for 20 days. She became afebrile by day 5 and stool frequency decreased to 2/day by day 7. At the time of discharge, spleen regressed to 7 cm, hemoglobin increased to 12 g/dL, and serum globulin declined to 5.6 g/dL. At 12 weeks' follow up, spleen was not palpable, hemoglobin was 12 g/dL, leukocytes 5500/mm<sup>3</sup>, globulin 4.9 g/dL, and urine d-xylose increased to 1.8 g/5 g/5 h. Colonoscopic examination after 8 weeks and 1 year showed normal colonic mucosa.

Intestinal involvement and overt malabsorption in VL is reported more frequently in those with concomitant HIV infection.<sup>2</sup> In one study,<sup>4</sup> of 10 patients with VL with no diarrhea, 7 had impaired vitamin A malabsorption. Although urine d-xylose was abnormal in only one patient, the mean d-xylose levels after treatment were significantly higher than the pre-treatment levels. Sub-clinical malabsorption of

nutrients is seen commonly in patients with VL with no diarrhea. In early studies, Sen Gupta *et al*<sup>5</sup> found avitaminosis A, B and C in Indian patients with leishmaniasis.

The exact mechanism of malabsorption caused by *Leishmania donovani* is not known. Although mechanical occlusion of the mucosa by parasites may be important, parasite load does not correlate with the severity of diarrhea and malabsorption. The other possible mechanisms include villous atrophy, competition between host and parasite for nutrients, altered motility, bacterial overgrowth, bile salt deconjugation and lymphatic blockade.<sup>4</sup>

Postmortem studies of VL in humans have shown parasitization and cellular infiltration of the intestinal mucosa and mesenteric lymph nodes.<sup>6</sup> Although both our patients had normal crypt-villous ratio, partial villous atrophy is known to occur even in those with no overt diarrhea. Parasites are mostly seen in macrophages, located mainly on villous tips, although a few of them can be seen lying extracellularly. LD bodies need to be differentiated from a variety of other micro-organisms including histoplasma, cryptococcus and *Mycoplasma avium complex*.

In summary, chronic diarrhea and malabsorption may be a presentation in patients with visceral leishmaniasis. Both small and large intestinal involvement can lead to diarrhea, and anti-leishmanial therapy results in rapid clinical and biochemical response.

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