

Schistosomiasis mansoni and severe gastrointestinal cytomegalovirus disease in a patient with acquired immunodeficiency syndrome

Esquistossomose mansoni e doença gastrointestinal grave pelo citomegalovírus em paciente com a síndrome da imunodeficiência adquirida

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ABSTRACT

The behavior of the Schistosoma mansoni infection in patients with AIDS has not been explored. The case of a young woman with schistosomiasis mansoni, AIDS, and cytomegalovirus disease is reported. The authors suggest that the helminth was not a bystander in this case, or rather, by interfering with the host's immune response, it set the stage for the development and/or aggravation of the viral infection.

Key-words: Schistosomiasis. Schistosoma mansoni. AIDS. Cytomegalovirus. Immunodeficiency. Lymphocytes.

RESUMO

O comportamento da infecção pelo Schistosoma mansoni não foi explorado em pacientes com AIDS. Relatamos aqui o caso de uma paciente com esquistossomose mansoni, AIDS, e doença pelo citomegalovírus. Os autores sugerem que o helminto não foi apenas um espectador neste caso, mas, que, ao interferir na resposta imune do hospedeiro, promoveu o surgimento e/ou agravamento da infecção causada pelo citomegalovírus.

Palavras-chaves: Esquistossomose. Schistosoma mansoni. AIDS. Citomegalovírus. Imunodeficiência. Linfócitos.

It has been estimated that 4-6 million people are infected by *Schistosoma mansoni* in Brazil, and 600 thousand by the human immunodeficiency virus (HIV-1). Reports on the association of schistosomiasis and AIDS are scarce but they have begun to appear in the literature. In Africa, a group of investigators found evidence that schistosomiasis may have an effect on plasma HIV concentration in coinfecting individuals and also on the density of HIV-1 coreceptors CCR5 and CXCR4 on the surfaces of CD4⁺ cells¹⁷.

In Brazil, patients who died with AIDS and were found at autopsy to also be coinfecting with *S. mansoni*, unveiled some interesting data¹⁵: 1) small and incomplete granulomas were observed around the eggs deposited in the tissues; and 2) a miliary distribution of eggs occurred in many organs (liver, spleen, lungs, intestine, pancreas and testes). The inferences derived from these cases and based on previous experimental

work^{3 4 5 8}, were of two kinds: a) without well formed granulomas the eggs do not reach the gut lumen and diagnosis of schistosomiasis based on stool examination is not possible; and b) without good immunity, the worms are not confined to the mesenteric vessels, migrate to unusual places in the body and lay their eggs in different organs⁹.

Cytomegalovirus (CMV) is the most common opportunistic viral infection in patients with AIDS. Autopsy studies have shown that up to 81% of HIV-infected patients presented clinical and pathologic evidence of CMV disease at the time of their death. Gastrointestinal involvement in CMV infection accounts for 5-10% of HIV-infected patients and occurs when the CD4⁺ T cell count falls below 100/mm³. This disease is an erosive or ulcerative process that can occur at any location in the gastrointestinal tract, from the mouth to the rectum^{1 6}.

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Herein, the case of a patient with AIDS, severe gastrointestinal cytomegalovirus disease and who also proved to be coinfecting with *S. mansoni*, after examination of part of the intestine removed during surgery, is reported.

CASE REPORT

A 32-year-old woman was admitted to hospital reporting a 15kg-weight loss over the previous 3 months. She also complained of malaise, diarrhea, abdominal pain and odynophagia. Clinical examination upon admission revealed an emaciated young woman with severe oral candidiasis. Blood tests disclosed anemia and lymphocytopenia (T CD4+ = 61 cels/mm³). ELISA for HIV proved positive, with a plasma viral load of 24,000/ml. Upper endoscopy confirmed the diagnosis of esophageal candidiasis and also revealed multiple ulcers on the esophagus. Under light microscopy, biopsies of the ulcers showed cells with inclusion bodies suggestive of CMV esophagitis. Ultrasound of the

abdomen was normal, except for a thickening of the wall of the distal ileum. Stool examinations were negative for eggs of helminthes or other parasites. Ten days after admission she developed sudden and severe intestinal hemorrhage followed by refractory shock. A colonoscopy performed during the episode showed numerous shallow bleeding ulcerations throughout the large bowel and distal ileum (Figure 1); the lesions were more intense in the right colon, cecum and distal ileum. The patient was operated on and the right colon and distal ileum were excised (Figure 2). Histopathology revealed several ulcers extending deep into the bowel wall. Endothelial cells of arterioles, venules and capillaries showed inclusion bodies suggestive of CMV infection (Figures 3 e 4). A large number of viable eggs of *S. mansoni* were described in the lamina propria and, characteristically, they were not surrounded by granulomas or any other inflammatory cells (Figure 4). After surgery the patient was transferred to an intensive care unit (ICU) and improved rapidly. Treatment for schistosomiasis with praziquantel (50mg/kg, body weight) was begun. She was placed on total parenteral nutrition, received intravenous

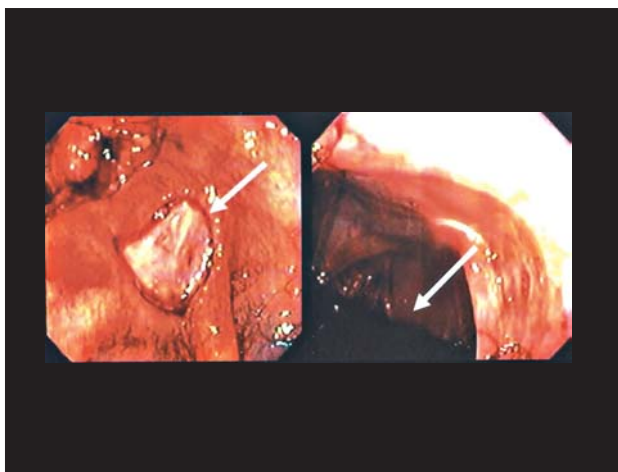


Figure 1 - Colonoscopy showing a bleeding ulcer on the left (arrow) and blood in the intestinal lumen on the right (arrow).

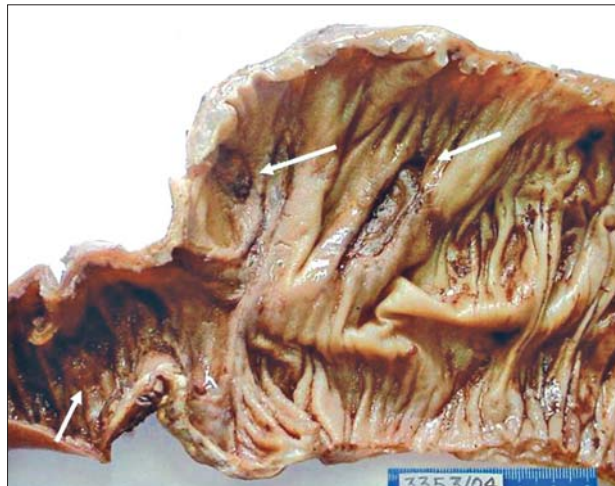


Figure 2 - Macroscopic appearance of the colon and distal ileum showing several sharply acute ulcers (arrows) extending deep into the bowel wall.

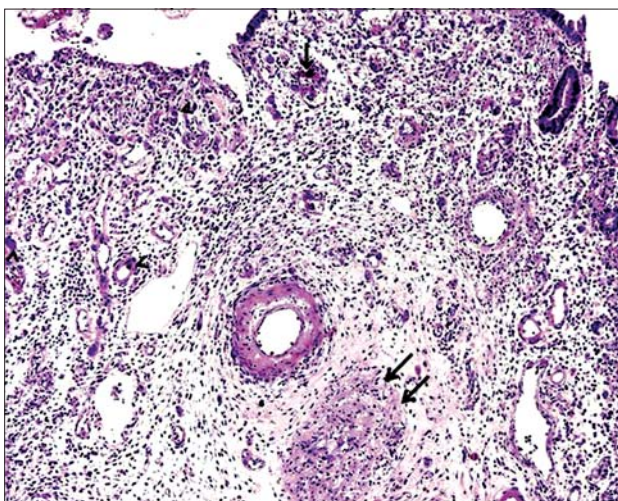


Figure 3 - Base of CMV ulcers showing mild inflammation, granulation tissue, vasculitis and thrombus formation with vascular occlusion (arrows). Cytomegalic inclusions occurred in endothelial cells of arterioles, venules and capillaries (arrow-heads).

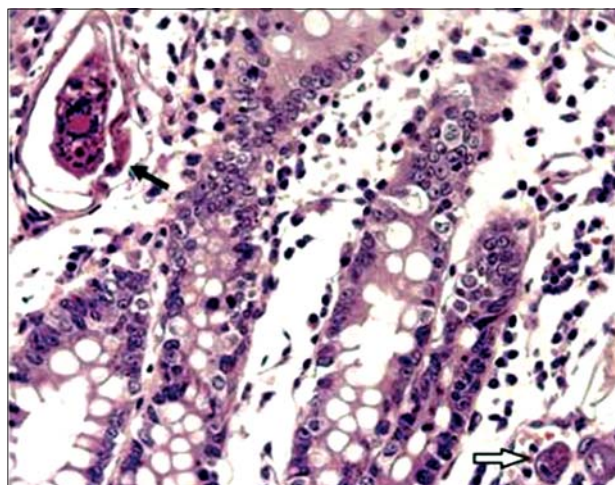


Figure 4 - Schistosoma mansoni viable egg in lamina propria without any inflammatory reaction on the upper left hand corner (black arrow). Enlarged and prominent endothelial CMV-infected cell (cytomegalic cell) with granular basophilic cytoplasm and containing one eosinophilic intranuclear inclusion surrounded by a halo (white arrow).

ganciclovir for cytomegalovirus infection and a highly active antiretroviral regimen for the treatment of AIDS. She was discharged from the ICU 5 days after admission and stayed in the infirmary for a further two months. One year later she was reexamined at the outpatient clinic and was feeling well. Her T CD4+ cell count was 224/mm³ and the HIV viral load was not measurable.

DISCUSSION

No inflammatory response around viable eggs of *S. mansoni* was observed in the patient herein reported, who presented with a severe disruption of the immune system. This is consistent with experimental work carried out on murine schistosomiasis, which showed that mice immunosuppressed by drugs or thymectomy plus irradiation, did not form granulomas around *S. mansoni* eggs deposited in tissues²⁻³. Granuloma formation is immune mediated and T CD4 + lymphocytes, particularly of the Th2 subset, play a central role in the inflammatory response to eggs of the parasite²⁻¹³. Parasitological stool examinations in this patient failed to reveal *Schistosoma mansoni* eggs. This was expected, because a fully formed granuloma is important in the extrusion of eggs from the intestinal mucosa into the stools.

Data from human studies support the hypothesis that people with helminth infections are more susceptible to HIV-1 infection and/or experience increased viral replication. Cells from individuals with schistosomiasis, intestinal helminthes, or filariasis are more susceptible to HIV-1 infection *in vitro*, than are cells from individuals without helminth infection. In addition, some authors have shown that HIV-1 replicates more readily in T helper 2 cell (Th2) environments, such as those caused by schistosome infection¹³. Similarly, the deviation of the immune system to a Th2 response caused by the worm would facilitate the state of chronic staphylococci carrier in the nasal mucosa and the eventual formation of pyogenic abscesses of the liver and muscles⁷⁻¹¹⁻¹⁶.

The patient developed a severe gastrointestinal cytomegalovirus disease, which was the reason for her admission to hospital and that almost caused her death. To control viral infections, the host depends mostly on mounting a solid Th1 immune response. Given the above information, it is possible to speculate that schistosomiasis may have played a contributing role in the severe evolution of the cytomegalovirus infection in this patient.

It also seems appropriate to comment here on the *Salmonella-S. mansoni* association, described mostly in Brazil and Africa. Lambertucci and Neves (1993) reported the case of a patient with this association who died and whose coinfection with tuberculosis in its miliary form was found during autopsy⁹. At this point, *S. mansoni* eggs were described in many organs, with incomplete granuloma formation around them. This is an example of the fact that different diseases evolving with severe immunosuppression will eventually present a similar pathological picture. On another occasion, two other patients with AIDS were also coinfecting with *Salmonella* and *S. mansoni*. Treatment of schistosomiasis

alone with oxamniquine cured the *Salmonella* bacteremia, produced a rapid improvement in the clinical picture and increased the T CD4 + cell counts to a level where treatment with highly active antiretroviral chemotherapy was no longer required¹⁰.

Oxamniquine and praziquantel have been used in Brazil for a long time now and are equally successful in the treatment of schistosomiasis mansoni. However, the efficacy of both drugs has been shown to be immunodependent⁵⁻⁸. Thus, a natural anxiety and preoccupation regarding the efficacy of both drugs in the treatment of schistosomiasis in patients with AIDS occurred. In our patient, schistosomiasis was diagnosed only by histology. After treatment with praziquantel, parasitological stool examinations have been repeated at the outpatient clinic up to one year after release from the hospital, and, so far, they remain negative for *S. mansoni* eggs.

In short, the case of a patient with AIDS, severe gastrointestinal cytomegalovirus infection and intestinal schistosomiasis mansoni is reported. The authors suggest that the worm was not a bystander in this case, or rather, by interfering in the host's immune response, it set the stage for the development and/or aggravation of the viral infection.

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