

***Salmonella-S. mansoni* ASSOCIATION IN PATIENTS WITH ACQUIRED IMMUNODEFICIENCY SYNDROME**

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SUMMARY

Two young men with *Salmonella* bacteraemia, active schistosomiasis and the acquired immunodeficiency syndrome are reported. The clinical presentation comprised nonspecific signs and symptoms, such as fatigue, malaise, weight loss, diarrhoea, prolonged fever, and hepatosplenomegaly. In one patient, liver biopsy showed poorly formed granulomata around *Schistosoma mansoni* eggs and hepatitis. Treatment of schistosomiasis alone induced consistent clinical improvement with eventual cure of both *Salmonella* and *S. mansoni* infections. Recognition of the *Salmonella-S. mansoni* association in patients with AIDS is important because treatment of schistosomiasis makes a difference, improving the prognosis of this otherwise, recurrent, potentially fatal bacteraemia.

KEYWORDS: Schistosomiasis; *Salmonella*; AIDS; Acquired immunodeficiency syndrome

INTRODUCTION

Salmonella bacteraemia occurs with increased frequency in infants, in the elderly and in patients with diseases associated with hemolysis (such as sickle cell diseases, malaria, and bartonellosis), with lymphoma, with leukemia, and with systemic lupus erythematosus⁴. Patients with AIDS develop recurrent, relapsing *Salmonella* bacteraemia that is difficult to cure with antibiotics¹⁰. In Subsaharan Africa gram-negative bacteraemia is second only to tuberculosis as a cause of death among HIV-infected individuals³. Chronic persistent *Salmonella* bacteraemia has also been described in association with *S. mansoni* infection. The most common characteristics of the clinical syndrome are^{7,11}: I) a long history of a febrile disease; II) bacteraemia with one of many species of the genus *Salmonella*; III) chronic active schistosomiasis. We report two patients with AIDS and *Salmonella* bacteraemia that have been cured of the *Salmonella* infection after treatment for schistosomiasis with oxamniquine.

CASE REPORTS

Patient 1: A 24-year-old, previously healthy white man, was hospitalized with fever, diarrhoea, and a 10-kg weight loss over three months. Physical examination showed an ill, pale, and wasted man with a temperature of 39.8 °C, with patchy alopecia, generalized lymphadenopathy and oral candidiasis. His abdomen was protuberant with hepatosplenomegaly and ascites. The right lobe of the liver was tender to palpation and extended 4 cm below the right costal

margin. The spleen was palpable 6 cm below the left costal margin. Edematous infiltration of the skin, and pedal edema were also observed. Initial laboratory investigations showed pancytopenia (haemoglobin, 8.1 g/dl; white blood cells, 3000/cu mm; platelets, 65,000). His serum albumin was 1.7 g/dl; globulin, 4.5 g/dl. Three blood cultures grew *Salmonella* serogroup D. He tested HIV-positive by ELISA and western blot analysis. TCD4+ count was 265 cells/ μ l and TCD8+ was 1088 cells/ μ l. Serologic tests for cytomegalovirus, toxoplasmosis, hepatitis B and C, and a VDRL slide test were all negative. Liver biopsy specimens obtained during laparoscopy revealed poorly formed granulomata around *S. mansoni* eggs with scattered lymphocytes, plasma cells, and eosinophils; several areas of spotty necrosis of hepatocytes with lymphocyte and macrophage infiltration were documented.

The patient was easily irritable and aggressive, and left the hospital prematurely, against medical advice. Just before dismissal, though, he was treated for schistosomiasis with oxamniquine (15 mg/kg, body weight, single dose). He did not accept the diagnosis of AIDS and refused treatment with antiretroviral drugs. Notwithstanding, during his occasional visits to the outpatient clinic a consistent clinical improvement was observed. The patient's fever and diarrhoea subsided 20 days after being discharged from the hospital. In the following two months his weight increased 15 kg. The ascites and oedema of the lower limbs vanished and he continued to improve for the next five months. There was an involution of the liver and spleen, the latter being just palpable. Three consecutive blood cultures remained sterile. His hemoglobin was 12.1 g/dl; white blood cells, 5600/cu mm, and platelets,

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288,000. Serum albumin was 3.4 g/dl and globulin, 2.1 g/dl. There was no significant increase in the lymphocyte subset counts on the occasion (TCD4+ = 273; TCD8+ = 1442). Cure of schistosomiasis was ascertained by 9 negative stool examinations for parasite ova performed along the 10 months of follow up after treatment. He was seen last time 18 months after the initial treatment for schistosomiasis and was asymptomatic.

Patient 2: A 26-year-old man with a history of homosexual activity was admitted with diarrhoea, fever, fatigue and weight loss of 11 kg over the last four months. For some time he rejected medical attention. Twenty days earlier, he was treated for schistosomiasis with oxamniquine in another hospital. He noticed significant clinical improvement after treatment but loose bowel movements and low fever persisted.

Axillary temperature on admission was 36.8 °C. His abdomen was flat but the right lobe of the liver and the spleen were easily palpable and painful to palpation. *Salmonella enteritidis* was recovered from three blood cultures and two stool cultures. In the fragments obtained by rectal biopsy viable eggs of *S. mansoni* were seen. The hemoglobin level was 10.8 g/dl. His serum albumin was 2.4 g/dl and globulin was 4.8 g/dl. His serum tested HIV-positive by ELISA and western blot analysis. TCD4+ count was 40 cells/ μ l and TCD8+ was 667 cells/ μ l. He remained afebrile during the time (15 days) that he stayed in our hospital.

He was seen at the outpatient clinic two months later and was asymptomatic. His spleen was not palpable and his weight increased 10 kg. Serum albumin was 4.3 g/dl and globulin 4.2 g/dl. TCD4+ count increased to 202 cells/ μ l and TCD8+ to 1317 cells/ μ l. Three parasitological stool examinations remained negative for *S. mansoni* ova 60 days after treatment; a rectal biopsy taken around the same time did not show viable eggs of the worm. Ten months after the first admission to hospital he is feeling well and have had no recurrences of the bacteraemia.

DISCUSSION

This is the first description of the *Salmonella-S. mansoni* association in patients with AIDS. *Salmonella-S. mansoni* association occurs most commonly in males between the ages of 10 and 30 years. The response to antibiotic therapy is dramatic⁸. However, recurrent *Salmonella* bacteraemia is common if the underlying schistosome disease is not treated.

It is interesting to note that patients with AIDS and *Salmonella* bacteraemia, without concurrent schistosomiasis, also show a very similar clinical picture to that presented by our patients, except for the good response to treatment with oxamniquine. Previous in vitro work has demonstrated that oxamniquine is not active against the bacteria^{7,9}. Hence, the most probable explanation for the clinical improvement of our patients after receiving oxamniquine is that treatment of schistosomiasis cured the *S. mansoni* infection and indirectly the *Salmonella* bacteraemia. Data on the behaviour of schistosomiasis mansoni in the immunosuppressed host are rather few².

Depression of cell-mediated immune response in the host diminishes granulomatous response to *S. mansoni* eggs¹. Mice experimentally infected with *S. mansoni* and immunosuppressed by drugs or thymectomy develop diffuse and severe hepatitis. Liver tissue of patient 1 showed diminished granulomatous response to *Schistosoma mansoni* eggs and areas of hepatocyte necrosis.

There is no clear explanation as to why *Salmonella-S. mansoni* association has not been seen by other investigators in patients with AIDS. The association may help to explain the high proportion of *Salmonella* bacteraemia reported in AIDS patients from Africa^{3,5}. It is probable that infection with *S. mansoni* may not even be considered by the physician examining a patient with AIDS and *Salmonella* bacteraemia.

In addition, the routine use of active drugs against *Salmonella*, in AIDS patients, like sulfametoxazol-trimethoprim or zidovudine may further distort the clinical features of this peculiar association⁶.

It is also worth mentioning that egg output decreases sharply in mice experimentally infected with *S. mansoni* and immunosuppressed by drugs or thymectomy¹. A well formed granuloma seems to facilitate the migration of eggs in the host tissues. Without granuloma formation, *S. mansoni* eggs do not reach (or only in small numbers) the gut lumen. Diagnosis of schistosomiasis, based on stool microscopy, in this context, should be reexamined. Rectal or liver biopsies, and ELISA tests for circulating antigens would represent an alternative to stool examination in such cases. Studies in patients with schistosomiasis and AIDS and low TCD4+ cell counts are mostly needed either to confirm or exclude this interesting hypothesis.

RESUMO

Associação *Salmonella-S. mansoni* em pacientes com a síndrome da imunodeficiência adquirida

Apresentam-se os casos de dois jovens com bacteriemia por *Salmonella* associada a esquistossomose mansoni ativa em pacientes com a síndrome da imunodeficiência adquirida. A apresentação clínica incluiu sintomas e sinais inespecíficos como fadiga, perda de peso, diarréia, febre prolongada e hepatoesplenomegalia. A biópsia hepática em um paciente revelou granulomas mal formados em torno de ovos de *S. mansoni* e hepatite de intensidade moderada. O tratamento da esquistossomose com a oxamniquine induziu melhora clínica progressiva culminando com a cura da salmonelose e da esquistossomose. O reconhecimento da associação *Salmonella-S. mansoni* em pacientes com AIDS mostra-se importante nesses casos pois o tratamento da esquistossomose melhora o prognóstico da bacteriemia por *Salmonella* que pode tornar-se recorrente e fatal nos pacientes com AIDS.

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