An Outbreak of Acute Schistosoma mansoni Schistosomiasis in a Nonendemic Area of Brazil: A Report on 50 Cases, Including 5 With Severe Clinical Manifestations

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Background. Acute schistosomiasis is a systemic hypersensitivity reaction against the migrating schistosomula and eggs. In this report, we describe an atypical outbreak of the disease with severe cases. Transmission occurred in a nonendemic area of Brazil, which became a new focus of transmission due to the in-migration of infected workers.

Methods. From December 2009 to March 2010, the 50 patients with acute schistosomiasis (group 1) bathed in a swimming pool supplied by a brook on a country estate in the outskirts of São João del Rei, Brazil. Thirty other subjects (group 2) living in the same area, who denied having contact with the swimming pool, volunteered to participate in the study. All participants were submitted to clinical, laboratory, and ultrasound examinations.

Results. Five of 50 (10%) patients were admitted to the hospital: 1 with myeloradiculopathy, 1 with diffuse pulmonary micronodules, and 3 with diarrhea and dehydration. All 5 had hypereosinophilia and prolonged fever. Group 1 patients more frequently had cercarial dermatitis ($P = .01$), blood in the stool ($P = .04$), and intrabdominal lymph nodes ($P = .001$). All group 1 patients were treated with praziquantel; 1 patient with myeloradiculopathy also received oral prednisone (60 mg/day) for 6 months with complete recovery.

Conclusions. This report describes the first time that patients from an outbreak of acute schistosomiasis have been compared to controls. Five subjects (10%) had severe manifestations of schistosomiasis. Diagnosis of the disease and its severity was delayed because physicians did not consider that an epidemic of schistosomiasis might emerge in a nonendemic area.

Keywords: acute schistosomiasis; outbreak; myeloradiculopathy; pulmonary nodules; fever of unknown origin.

Schistosomiasis caused by Schistosoma mansoni was first described in Brazil by Pirajá da Silva in 1908. Unfortunately, this disease is still considered a major public health problem, owing to the large extent of the transmission area [1]. Moreover, because of the disease’s varied and severe presentation, including upper digestive bleeding, neuroschistosomiasis, glomerulonephritis, and pulmonary hypertension, control and elimination of this disease is a top priority of the Brazilian government [2–4].

An estimated 4–6 million people in Brazil are currently infected with S. mansoni. The disease is prevalent in 519 of the 853 municipalities (61%) in Minas Gerais State (in southeast Brazil); an estimated 1 000 000 people are infected among the 10 870 063 who live in the endemic areas of this state [3].

Acute schistosomiasis is a systemic hypersensitivity reaction against the migrating schistosomula and eggs.
A diversity of clinical manifestations appears during the migration of schistosomes in humans, including cercarial dermatitis, fever, pneumonia, diarrhea, hepatomegaly, splenomegaly, intraabdominal lymph node adenopathy, liver abscesses, skin lesions, brain tumors, and myeloradiculopathy [5–7]. Hypereosinophilia is common and is suggestive of a schistosomiasis diagnosis.

Here, we report on an atypical outbreak of the disease with severe cases. Transmission occurred in a nonendemic area of Brazil, which became a new focus of transmission due to the in-migration of infected workers. Snails of Biomphalaria glabrata (the intermediate host of S. mansoni) had not been found to be infected with cercariae in the area on previous occasions. Workers from out of state were temporarily hired to build houses in the neighborhood of a country estate in the outskirts of São João del Rei (SJDR), Brazil, where locals became infected. Clinical, laboratory, and ultrasound findings were compared between study participants with and without acute schistosomiasis.

METHODS

Patients
São João del Rei is a city located in the southeast of Minas Gerais State in Brazil. It has 85,503 inhabitants and a high human development index (0.816) compared to the whole country (0.710). Except for Matosinhos, a small district of SJDR, schistosomiasis transmission has not been reported in the area since 1971. From December 2009 to March 2010, 50 individuals (group 1) who have always lived in SJDR bathed in a swimming pool supplied by a brook in a country estate in the outskirts of the city. Two months later, a patient with paraplegia was examined at a reference center for schistosomiasis in a general hospital in Belo Horizonte (the capital of Minas Gerais State), and the diagnosis of schistosomal myeloradiculopathy was confirmed [8, 9]. This patient reported that others in the same area, including her husband and daughter, had symptoms consistent with acute schistosomiasis.

After news spread about the schistosomiasis outbreak, local health authorities identified 30 volunteer controls who lived in the neighborhood of the country estate where the first group was infected but who denied bathing in the swimming pool (group 2). Physicians and laboratory technicians from Belo Horizonte investigated the outbreak. A standardized questionnaire containing sociodemographic, epidemiologic, and clinical data was given to study participants from groups 1 and 2. All participants voluntarily agreed to participate in this study and signed an informed consent waiver prior to data collection. This study was approved by the Ethical Committee of the Universidade Federal de Minas Gerais, Brazil.

Malacologic Survey
One month after being informed of the outbreak, a specialized team from the Minas Gerais State Health Department visited the area to identify possible foci of contamination and to
conduct a systematic collection of water snails in the area surrounding the country house. The 200 collected mollusks were sent to a reference laboratory of helminthiasis and medical malacology for both morphologic [10] and molecular identification [11]. Biomphalaria glabrata was the only species of snail identified in the area.

Parasitologic Examination
Coproscopic analysis of 2 stool samples from each of the 80 individuals in groups 1 and 2 was performed. Two slides per sample were analyzed using quantitative and qualitative methods [12, 13]. Stools for examination were collected between 3 and 4 months after the date of contact with waters. Individuals positive for schistosomiasis were treated with a single oral dose of praziquantel (50 mg/kg body weight). A patient with myeloradiculopathy also received prednisone (60 mg/day) for 6 months [8] according to the recommendations of the Brazilian Ministry of Health.

Clinical Examination
Group 1 individuals were submitted to anamnesis and clinical examination by one of the authors (JRL). Particular attention was given to the abdominal examination: The right hepatic lobe was examined on the anterior axillary line, and the left hepatic lobe was examined on a line passing through the xyphoid process. The spleen was palpated and measured under the left costal margin with the patient in dorsal decubitus during deep inspiration. Ten milliliters of venous blood was obtained from each patient for further serologic tests. The medical files of 5 patients admitted to hospitals in SDJR were revised, and clinical details of the cases, including blood tests and radiologic films, were consulted after permission was obtained from patients and local authorities.

Imaging Techniques
All participants were submitted to an abdominal ultrasound using a portable Medison Sonoace 1500, 3.5 MHz apparatus (Samsung, Korea) and examined according to the World Health Organization’s proposed protocol for ultrasound assessment of schistosomiasis-related morbidity [14]. The longitudinal diameter of the liver and spleen were measured, and the presence of lymph nodes adenopathy was ascertained [15]. One patient underwent magnetic resonance imaging (MRI) of the spinal cord performed for the diagnosis of paraplegia; the MRI was obtained using a 1.5T unit (GE Sigma unit, General Electric) [16]. A computed tomographic (CT) scan of the lungs was obtained for 1 patient, and 5 patients underwent chest radiography [16].

Schistosomiasis Serology
Sera from the 80 individuals (groups 1 and 2) were tested for schistosomiasis using enzyme-linked immunosorbent assay (ELISA) for surface worm antigen (SWAP). The ELISA-SWAP was performed in microtiter plates from MaxiSorpTM Surface (NUNC, Denmark) sensitized with 100 μL/well of 1 g/mL of SWAP diluted in a 0.05 M carbonate-bicarbonate buffer at a pH of 9.6. The samples were incubated for 16 hours at 4°C. The plates were washed 3 times with 0.15 M phosphate-buffered saline (PBS) at a pH of 7.2 with 0.05% Tween 20 (LGC Biotechnology; washing buffer). The nonspecific sites were blocked with 10% fetal bovine serum in the washing buffer at 37°C for 1 hour. After additional washing steps, 100 μL of each of the human serum samples diluted 1:50 in PBS were added in triplicate into each well, and the plates were incubated at room temperature for 1 hour. Afterward, the plates were submitted to the washing steps and incubated at room temperature for 1 hour with conjugated anti–immunoglobulin G (IgG) human peroxidase (Southern Biotech) diluted 1:60 000 in washing buffer. The plates were washed again, and 100 μL of substrate 3,3′,5,5′-tetramethylbenzidine solution (TMB/H2O2; Invitrogen) was added to each well. After 20 minutes of incubation in the dark, the reaction was stopped by adding 50 μL/well of 2N sulfuric acid. The results were obtained as absorbance values at 450 nm in a microplate reader (Bio-Rad Laboratories 3550) [17].

Diagnosing Acute Schistosomiasis
Diagnosis of acute S. mansoni schistosomiasis was based on epidemiologic data (recent contact with stream water in an endemic area), clinical data (cercarial dermatitis, acute enterocolitis, fever, cough, malaise, paraplegia, pulmonary involvement, hepatomegaly and/or splenomegaly), laboratory assays (eosinophilia, IgG antibodies against SWAP, eggs in the stools or in rectal biopsy fragments), and imaging techniques (ultrasound with liver and/or spleen enlargement and lymph node adenopathy, MRI showing spinal cord injury). To be considered as having acute schistosomiasis in the present study, the participants had to have 1 or more of the symptoms/signs described above, evidence of an infection (parasitologic or serologic), and reported contact with contaminated waters of the swimming pool [7, 17]. An MRI and CT scan helped in diagnosing complications of the disease in 2 patients, but they were not considered in the statistical analysis.

Statistical Analysis
This is a case-control study. Information obtained from patients in groups 1 and 2 was stored in a database using EpidaData 3.1 (Epidata Association, Odense, Denmark), and the analysis was performed using the Statistical Package for Social Sciences (SPSS), version 15.0 (IBM SPSS, Chicago, Illinois). Tables were constructed, and the percentages, medians, and means were calculated. To assess statistically significant differences between cases and controls regarding clinical signs and symptoms, the χ² test was used.
RESULTS

Group 1 patients fulfilled the criteria for the case definition of acute S. mansoni schistosomiasis. They comprised 50 subjects, including 31 men (62.0%) and 19 women, whose age ranged between 4 and 75 years with a mean age of 33.3 (SD, 18.5) and a median age of 48.5 years. Group 2 (normal controls) comprised 30 subjects, including 31 men (62.0%) and 16 women, whose age ranged from 2 to 82 years with a mean age of 37.5 (SD, 17.7) and a median age of 32 years (t test for age in years, P = .84). In group 2, no patients tested positive in the serologic test used in this study. Frequency of signs and symptoms in groups 1 and 2 were compared (Table 1), and a statistically significant difference was observed for cercarial dermatitis (P = .01), blood in the stool (P = .04), and lymph node adenopathy (P = .001) evidenced by ultrasound. Weight, height, and systemic arterial blood pressure were not significantly different between groups 1 and 2.

Case Reports

Case 1

A 14-year-old girl was admitted to the hospital in São João del Rei reporting fever, abdominal pain, diarrhea, cough, and dyspnea, which had started 30 days earlier (Table 2). She recalled having disseminated pruritus after bathing in a swimming pool in a country estate in the outskirts of her hometown. A palpable spleen and liver were noticed by the attending physician. Chest radiography revealed lungs with a nonspecific interstitial pattern of involvement. She was treated with antibiotics (ciprofloxacin and metronidazole) without improvement. Her family decided to seek help in another hospital. A new hemogram revealed leukocytosis with eosinophilia (3900 cells/mL), a CT scan of the lungs showed the presence of diffuse micronodules in both lung fields (Figure 1), and the CT scan of the abdomen reported hypodense nodules over the liver with intra-abdominal lymph nodes. A lung biopsy via bronchoscopy was performed, and microscopy found no specific diagnosis. Schistosoma mansoni eggs were found in her stool. She was treated with praziquantel (50 mg/kg body weight) and improved slowly. Nowhere in her medical records was the diagnosis of acute schistosomiasis considered.

Case 2

A 27-year-old woman reported the onset of lumbar pain radiating to her left leg, which progressively evolved into paraparesis, paraplegia, and fecal and urinary retention 2 months after swimming in a pool in the periphery of SJDR. She also complained of daily fever and diarrhea. Stool examination was negative for S. mansoni, but a rectal biopsy revealed inflammation and the presence of viable eggs of the worm in the examined fragments. According to the patient, her husband and her 8-year-old daughter were also sick. A routine hemogram showed eosinophilia (930 cells/mL). A sample of her cerebral spinal fluid revealed 70 lymphocytes/mm³ and increased protein concentration (1440 mg/mL). Magnetic resonance imaging of the spinal cord showed dilation of the conus medullaris (Figure 2). She was treated with praziquantel (50 mg/kg body weight, single dose) and prednisone (60 mg/kg/day for 6 months) with complete recovery of the neurologic signs and symptoms.
DISCUSSION

This outbreak has atypical characteristics. A possible explanation for the presence of *S. mansoni* was developed during the preliminary investigation into the causes of the epidemic. Men coming from endemic areas of the northeast of Minas Gerais State were employed by home builders to work in the construction of country houses, restaurants, and hotels. As temporary workers, they lived in improvised shelters without sanitary facilities. The workers used local waters for bathing and feces disposal; unexpectedly, those waters supplied a swimming pool where the local population was infected. This area had been considered by health authorities as nonendemic for schistosomiasis for the last 20 years [1, 3].

To our knowledge, this is the first time that a group of volunteers (controls) was used to compare signs and symptoms in an outbreak of acute schistosomiasis. This was important in the present study because only cercarial dermatitis, blood in the stools, and the presence of lymph node adenopathy diagnosed by ultrasound proved to be statistically significant. The use of a control group shows that many complaints in outbreaks may not be caused by the disease itself; once people become aware of the disease in an acquaintance, they may be influenced by the acquaintance’s complaints and start to feel sick themselves. In addition, the signs and symptoms presented by the subjects of our study were obtained by physical examination and by a standardized questionnaire. For signs and symptoms, such as fever, the answer was restricted to “yes” or “no”; this approach has limitations. The complaints were not properly discriminated, and this dichotomization may have distorted the evaluation of the clinical presentation of acute schistosomiasis. This problem occurs in investigation of outbreaks due to limitations of the data collection methods: one physician is responsible for physical examination, a second physician is responsible for questionnaire application, and the obtained data are transferred to a database to be analyzed at another occasion. A comprehensive view on what specific data are obtained is usually delayed, and analysis of the data may be dispersed to multiple researchers.

Five patients (10%) had a severe form of the disease. All were admitted to the hospital with a preliminary diagnosis of fever of unknown origin [18], and 1 patient developed paraplegia with fecal and urinary retention, which was later diagnosed as schistosomal myeloradiculopathy [19]. Such a high number of patients with severe complications of schistosomiasis has only occasionally been reported [20–23].

Additionally, in previous reports, severe cases of the disease may have been unnoticed because patients sometimes seek care in hospitals far from the area of infection. Moreover, it is not easy to obtain permission from patients to be examined by government investigators, particularly if they have a high standard of living and are admitted to private hospitals.

Eosinophilia, a reliable marker of acute schistosomiasis, was present in all 5 patients with severe manifestations of the disease. Unfortunately, a leukocyte count was not obtained for other subjects in groups 1 and 2 due to logistical problems. Furthermore, SJDR, an important historical city in Minas Gerais State, attracts tourists from other states and countries, and some tension with locals was noted because they feared that news about the outbreak in the press would result in a decrease in tourism and economic losses.

Blood in the stools, cercarial dermatitis, and lymph node adenopathy have already been described in patients with acute schistosomiasis and were therefore expected to be more frequently found in the patients [7, 20–27]. Surprisingly, the frequency of fever, diarrhea, cough, and a palpable liver and spleen were not significantly different between the groups. We have considered some hypotheses to explain our findings: (1) Except for the 5 patients with severe complications, the remaining group exposed to waters in the swimming pool had minor symptoms and did not find it necessary to seek medical help, which may be related to the difficulty in finding medical help in rural areas of Brazil; (2) there was a large proportion of children in both study groups, and other bacterial and/or viral diseases may explain some of the complaints/findings in the control group; (3) although they denied having contact with the waters in the area, part of the control group may have had contact with the waters but were afraid of telling the truth to a group of investigators representing nonlocal health authorities. A combination of these explanations also seems probable.

CONCLUSIONS

We report an outbreak of acute *S. mansoni* schistosomiasis in 50 subjects who bathed in a swimming pool supplied by a local brook; this previously nonendemic area became a new focus of transmission due to the in-migration of infected workers from endemic areas. Five patients (10%) developed severe complications associated with the disease. Physicians working in the area did not consider the possibility of an epidemic of schistosomiasis in a nonendemic area. Health authorities seek to prevent epidemics of acute schistosomiasis in areas known to be endemic, and those areas are usually held under surveillance; this outbreak shows, however, that even nonendemic regions should be prepared for schistosomiasis. Water may periodically become contaminated with an infected intermediate host, and this area could become a new focus of schistosomiasis transmission to susceptible hosts.

Notes

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