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Acute Schistosomiasis in European Students Returning From Fieldwork at Lake Tanganyika, Tanzania

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Background. Schistosomiasis is common in many African regions and poses a risk for travelers and the local population. So far, schistosomiasis in travelers or expatriates returning from the Tanzanian bank of Lake Tanganyika has not been reported.
Methods. We report a group of students who sought treatment with signs of acute schistosomiasis after having returned from Lake Tanganyika, Tanzania. Information as to travel and exposure as well as clinical and laboratory data were collected.
Results. Schistosomiasis was diagnosed in 8 of 16 students from Berlin, Germany, who had returned from a 2- to 3-month stay of fieldwork in Kigoma District at Lake Tanganyika, Tanzania. All 16 students reported frequent freshwater exposure at the lake. Six patients showed signs of acute schistosomiasis and had fever, and some of them also had cough, weakness, headache, or abdominal pain. Eosinophilia was present in five of the six symptomatic individuals. Notably, two serologically enzyme-linked immunosorbent assay (ELISA)-positive individuals did not report or present with symptoms or abnormal laboratory parameters. *Schistosoma mansoni* eggs were found in one symptomatic and one asymptomatic individual each. Blood and stool samples from the other eight individuals who were equally exposed to freshwater yielded negative results.
Conclusions. This is the first report of an outbreak of acute schistosomiasis imported from the Tanzanian shore of Lake Tanganyika and highlights the risk for travelers and the local population of acquiring the infection in that part of Tanzania. It provides arguments for routine serological screening for schistosomiasis in individuals who had prior freshwater contact in endemic areas, irrespective of symptoms or other laboratory findings.

Schistosomiasis is common in many tropical and subtropical regions, with about 200 million persons infected worldwide.[1] Infection occurs by cercariae-contaminated freshwater contact. A few weeks after initial infection, acute schistosomiasis, also referred to as Katayama syndrome may occur. This is especially true in non-immune patients and is supposedly caused by the migration of schistosomula or early oviposition or both. Fever, cough, and eosinophilia together with the history of freshwater exposure in a disease-endemic area suggest acute schistosomiasis. The symptoms commonly regress spontaneously without treatment, but chronic infection may lead to severe, sometimes life-threatening complications.[2] Serological tests are used as an indirect diagnostic method in acute schistosomiasis, which often occurs in the prepatent period of the infection. In addition, polymerase chain reaction (PCR) has been proven to be a valuable diagnostic tool.[3] Schistosomiasis poses a significant burden on the Tanzanian population, but studies on schistosomiasis in Tanzania have focused mainly on regions around Lake Victoria.[4,5] In contrast, data from the Lake Tanganyika area, the world's longest lake (north–south extension 675 km) and home of millions of inhabitants and an emerging travel destination, are remarkably scarce. Recent data from a survey on hematuria used as a proxy marker for *Schistosoma haematobium* infection suggested endemicity of the disease in the local population.[6] In addition, there is one report on *Schistosoma mansoni* in the same area, however, in a baboon population in the Gombe National Park.[7]

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For the western bank (Democratic Republic of the Congo) of Lake Tanganyika, cases of schistosomiasis among Belgian military personnel and in travelers have been published.[8,9] Schistosomiasis in travelers or expatriates returning from the eastern, Tanzanian bank of the lake, however, has not yet been reported.

Materials and Methods

The study was approved by the Ethics Committee of Charité—Universtitätsmedizin Berlin.

We report a group of students and faculty from a Berlin university who sought treatment at the outpatient department of the Institute of Tropical Medicine and International Health, Charité—Universitätsmedizin Berlin in October 2011, after having returned from Tanzania. The entire 20 group members had designed and helped to construct an eco-lodge in Mwamgongo, a village in Kigoma district next to Gombe National Park, at the Tanzanian shore of Lake Tanganyika. The students had stayed between 2 and 3 months in Tanzania. After returning to Berlin, three students were initially diagnosed with acute schistosomiasis. Assuming an outbreak situation, their colleagues were informed and encouraged to come in for diagnosis and treatment. A total of 16 persons eventually presented at our outpatient department. These individuals had been lodged by local families, and all had repeatedly gone swimming in Lake Tanganyika at sites in Mwamgongo and in Kigoma (30 km away); three students had had few freshwater contacts as well in the neighboring Gombe National Park. None of the group members had been exposed to freshwater in schistosomiasis-endemic areas during previous travels. Patients were clinically examined and questioned regarding the duration of stay at Lake Tanganyika, number and dates of freshwater contacts, and the location where they were swimming. They were asked for symptoms consistent with acute schistosomiasis, specifically fever, cough, weakness, headache, and abdominal pain. They were also questioned for previous travels to schistosomiasis-endemic regions. Clinical examinations included a full body status. Control visits have been planned for 24 months after the last freshwater exposure and are ongoing.

Serum samples were tested for anti-*Schistosoma* antibodies by enzyme-linked immunosorbent assay (ELISA; *S mansoni* soluble egg antigen; DRG Instruments, Germany), indirect hemagglutination assay (IHA; *S mansoni* adult worm antigen; Siemens Health Care Diagnostics, Germany), immunofluorescence assay (IFA; Bernhard-Nocht-Institute, Hamburg, Germany), and for *Schistosoma* DNA by PCR as part of a prospective multicenter study for the diagnosis of acute schistosomiasis.[10,11] Additionally examined routine laboratory parameters included complete and differential blood count, and C-reactive protein (CRP). In symptomatic patients, thick and thin blood smear and an immunochromatographic rapid test (BinaxNow® Malaria; R-Biopharm AG, Darmstadt, Germany) were done to rule out malaria. Stool examinations for ova and parasites were done using the merthiolate-iodine-formaldehyde (MIF)-stool concentration technique[12] in all individuals. Twenty-four-hour urine collections were obtained from all symptomatic individuals and in those with a positive *Schistosoma* serology; samples were filtered and examined by microscopy.

Results

The 16 group members (7 women and 9 men) presenting to our outpatient clinic were 21 to 54 years of age (median, 24 years). They reported freshwater contacts in Tanzania that were dispersed over a median period of 7 weeks (range, 2–10). The median number of recalled freshwater contacts was 30 (range, 5–75). None of the patients were able to recollect any symptoms or showed signs of cercarial dermatitis. Symptoms of acute schistosomiasis were present in 6 of the 16 patients (38%). All six symptomatic patients presented with fever; further symptoms included cough in four and abdominal pain in two patients, as well as non-specific weakness in four and headache in three patients. The median time between first freshwater contact and first symptoms in the six symptomatic patients was 54.5 days (range, 31–97). Three patients developed symptoms during their stay at Lake Tanganyika and had further freshwater contacts after the first onset of symptoms. Acute schistosomiasis was not suspected and no further diagnostics or treatment was done in Tanzania. The other three symptomatic students developed symptoms 10, 12, and 27 days, respectively, after the last freshwater exposure. Median duration of symptoms in all symptomatic patients was 32.5 days (range, 3–61). Serum samples from four of the six symptomatic individuals tested positive for antibodies against *Schistosoma* by ELISA, IHA, and IFA, and positive for *Schistosoma* DNA by PCR. In the other two symptomatic and in two asymptomatic patients, only ELISA and IHA were performed, and the ELISA yielded positive results with all four samples while the IHA was positive in only two serum samples (Table 1). Samples from the other eight equally exposed individuals yielded negative results in ELISA and IHA. Eosinophilia was present in five of the six symptomatic patients [maximum absolute eosinophil counts (AEC): 952–9,853/μL]. Other laboratory parameters were normal except CRP, which was initially elevated in four of the six symptomatic patients (range, 18–63 mg/L; Table 1). Stool samples were obtained from all 16 individuals, but *S mansoni* eggs were detected in only one symptomatic and one asymptomatic patient more than 3 months after the most recent freshwater exposure. Twenty-four-hour urine collection samples were obtained at least once from all individuals with positive serological results and were negative for eggs. Seven patients received praziquantel (40 mg/kg body weight, daily for 3 days) at least 3 months after the most recent freshwater exposure when

Table 1 Clinical and laboratory data of the eight students diagnosed with schistosomiasis

Patient No.	Symptoms (days)	AEC/μL (initial/maximum)	CRP (mg/L)	ELISA+ (days)	IHA+ (days)	IFA+ (days)	PCR+ (days)	Ova* (days)
1	47	384/4,539	20	76	76	76	76	119
2	47	5,474/9,853	18	72	72	80	80	Negative
3	62	2,292/3,713	24	94	94	94	94	Negative
4	97	447/2,288	<5	196	330	196	196	Negative
5	69	938/952	63	341	341	ND	ND	Negative
6	31	<600	<5	238	Negative	ND	ND	Negative
7	No symptoms	<600	<5	184	184	ND	ND	184
8	No symptoms	<600	<5	229	Negative	ND	ND	Negative

*Ova, *Schistosoma mansoni* eggs in stool.
CRP, C-reactive protein; ELISA, enzyme-linked immunosorbent assay; IHA, indirect hemagglutination assay; IFA, immunofluorescence assay; ND, not done; AEC, absolute eosinophil count; (days), days after first freshwater exposure.

symptoms had resolved and treatment was considered to be effective. The patient who presented with the highest eosinophil count (maximum AEC, 9,853/μL) received early praziquantel treatment and additional corticosteroids 6 weeks after onset of associated symptoms (fever, weakness, cough, loose stools), and praziquantel treatment was repeated 3 months later because of persistent weakness and eosinophilia (AEC, 2,403/μL). Absolute eosinophilic counts decreased in all patients with eosinophilia. All stool examinations (1–7 per patient; median 2; maximum 8 months after treatment) were negative for *Schistosoma* eggs. Four group members did not present to our institute despite repeated invitations, and we consequently have no data as to their status and outcome. Reportedly, one of these individuals fell sick and had symptoms consistent with acute schistosomiasis in another European country and received treatment there.

Discussion

We report schistosomiasis in 8 of the 16 persons returning from the Tanzanian shore of Lake Tanganyika, an area for which data regarding this disease are virtually absent. Studies on schistosomiasis in Tanzania have focused mainly on regions around Lake Victoria, widely ignoring Lake Tanganyika.[4,5] These cases illustrate the risk of acquiring schistosomiasis not only for travelers to this area but also for the resident population considering their more intense and life-long exposure. Also, this outbreak underlines the usefulness of detecting disease activity by using travelers as sentinels.[9,13,14] Lake Tanganyika has erroneously been mentioned as a high-risk area for travelers for acquiring schistosomiasis.[13] We assume, however, that rather Lake Malawi was meant in that report since there is no "Lake Tanganyika in Malawi." Lake Malawi, in fact, is well known as a high-risk area for schistosomiasis in travelers and has been the most important source of acute schistosomiasis in travelers seen at the Hospital of Tropical Diseases, London, within a period of 14 years.[15] There is only one report on *S mansoni* in the Kigoma area, which focuses on the baboon population in Gombe National Park.[7] Although *S mansoni* infection is believed to be mainly restricted to humans, these primates might possess a potential role as a reservoir for *S mansoni* in this area. Further research including genomic analyses is warranted to answer that question. Our patients had repeatedly been exposed to freshwater over several weeks, so date of first infection and time frames, eg, from first infection to symptoms and seroconversion could not be exactly specified. In acute schistosomiasis, the suspicion of the diagnosis is mainly a clinical one after freshwater exposure, but the confirmation is often based on serological testing. However, this causes a diagnostic gap: seroconversion occurs in most cases around 6 weeks post infection and 4 weeks after first symptoms, respectively, or even later.[16,17] Since eggs are deposited usually within 5–10 weeks post infection, assays for the detection of eggs usually yield negative results in acute schistosomiasis.[16–18] Therefore, *Schistosoma* egg excretion is not a reliable marker during the early, acute phase of the disease for which PCR may become increasingly important as a diagnostic tool.[3,11] As observed in our patients, acute infection may be asymptomatic, and may evolve without abnormal laboratory parameters. This offers strong arguments to perform at least a schistosome antibody test at about 3 months after freshwater contact. Misdiagnosis in travelers may translate into increased risks of chronic infection and neuroschistosomiasis.[19] Praziquantel, the treatment of choice in schistosomiasis, acts primarily on adult worms. Praziquantel should not be administered in acute schistosomiasis because it does not kill schistosomula and may even be deleterious when given during the acute phase by inducing an allergic type of response to parasitic destruction.[17] Corticosteroids may alleviate the symptoms but may also reduce the plasma concentration of praziquantel if given at the same time.[17] Therefore, it is recommended to use praziquantel approximately 3 months after the last freshwater exposure.[17] Interestingly, eight persons remained uninfected although having been repeatedly exposed to freshwater in the same sites as the eight

infected individuals. No obvious differences in exposure habits were found, ie, they had been exposed to freshwater at the same locations, and the amount and duration of freshwater contacts were comparable. This infection rate of 50% may indicate a rather low density of cercariae in the water of that area. Our study also emphasizes the need for professional pre-travel advice, particularly for long-term travelers in schistosomiasis-endemic areas. Although repellents have been suggested to prevent penetration of the skin by the cercariae,[20,21] this only reduces the risk but does not provide full protection. Thus, the avoidance of freshwater contact remains the only effective preventive measure for travelers to disease-endemic areas. For the resident population, this is hardly a feasible option. In conclusion, this outbreak in returning travelers illustrates that *S mansoni* poses a thus far underestimated hazard for the local population living on the Tanzanian shore of Lake Tanganyika. Systematic investigations into the actual disease burden and the implementation or review of control measures are warranted.

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Declaration of Interests

The authors state they have no conflicts of interest to declare.

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