Acute Pulmonary Schistosomiasis in Travelers Returning from Lake Malawi, Sub-Saharan Africa

G. S. Cooke, A. Lalvani, F. V. Gleeson, and C. P. Conlon

From the Infectious Diseases Unit, Nuffield Department of Clinical Medicine, John Radcliffe Hospital, and the Department of Radiology, Churchill Hospital, Oxford, England

We describe four cases of acute schistosomiasis presenting to the Infectious Diseases Unit of John Radcliffe Hospital (Oxford, England) during a 2-month period in autumn 1997. All four patients had swum in Lake Malawi, a freshwater lake in sub-Saharan Africa that is associated with Schistosoma haematobium and, less commonly, Schistosoma mansoni infections. All four patients had a severe acute illness and had prominent pulmonary involvement, both clinically and radiologically. This represents a change in the recognized pattern of presentation and could possibly reflect a new parasite variant in the lake.

Schistosomiasis is endemic in many parts of the tropics, with repeated and chronic infections leading to considerable morbidity and sometimes death in affected populations. Exposure to infection occurs in fresh water, through intact skin, and is a risk for travelers as well as for native populations. Although chronic presentations are more common, schistosomiasis may present acutely. Some people initially develop a transient dermatitis (swimmer’s itch) caused by the schistosomal cercariae penetrating the skin.

Later, acute schistosomiasis (Katayama fever) may develop in the previously unexposed host [1]. Typically this occurs 3–6 weeks after infection and is characterized by fever, urticaria, and occasionally bronchospasm. It is thought to be an immune complex disease following the onset of egg-laying by the maturing female worm and is more common with Schistosoma mansoni infections [2, 3]. Katayama fever is usually self-limiting and subsides over a few weeks, although a longer clinical course and occasional fatalities have been described.

The majority of infected travelers remain asymptomatic, as their infections are slight, with few adult worms and a small egg burden. Rarely, disastrous symptoms occur when eggs find their way to the CNS [4]. The increase in tourism to Africa has led to increased recognition of Katayama fever. The diagnosis of acute schistosomiasis can be difficult and is usually based on an appropriate exposure history, along with nonspecific symptoms such as fever, malaise, and myalgia in association with eosinophilia.

Pulmonary symptoms (coughing and wheezing) have been reported to occur in up to 70% of individuals infected by S. mansoni but are less commonly described in association with Schistosoma haematobium [5, 6]. We describe four patients presenting to the Infectious Diseases Unit of John Radcliffe Hospital (Oxford, England) between October and November 1997 whose only exposure to fresh water was in Lake Malawi at Cape Maclear, an area in sub-Saharan Africa where S. haematobium is endemic. All four had marked respiratory symptoms, had abnormalities evident on chest radiographs, and required hospitalization, a presentation we had not previously seen. In only one case were schistosomal ova detected, but all cases were serologically proven by means of a schistosomal ELISA that detects antibodies to soluble schistosomal egg antigens.

Patients

Case 1. A 20-year-old female student presented to another hospital 4 weeks after swimming in Lake Malawi (where her two companions both experienced classical symptoms of swimmer’s itch). She had a high fever and nasal stuffiness, but a physical examination revealed no other abnormalities. Laboratory investigations showed leukopenia (2.4 × 10^9 leucocytes/L), mild thrombocytopenia (134 × 10^9 platelets/L), and negative thick and thin malarial films. Liver function was mildly deranged (aspartate aminotransferase [AST] level, 55 U/L). Her symptoms resolved without treatment and she presented to our unit 4 weeks later with an urticarial rash over the arms and eosinophilia (0.5 × 10^9 eosinophils/L).

She remained well until 3 weeks later, when she developed a persistent cough and the rash worsened. The level of eosinophilia rose to 3.3 × 10^9/L over 3 days, but skin and rectal biopsies revealed no parasites. Chest radiography and CT of the lungs revealed pulmonary nodules. Empirical treatment with praziquantel (40 mg/kg as a single dose) was followed by low-grade pyrexia (temperatures to 37.5°C).

At follow-up the patient was well and had a normal eosinophil count and chest radiograph. Twelve weeks following treatment, a schistosomal ELISA was positive to level 3.
Case 2. A 22-year-old male student began experiencing fevers, headaches, and sweats 3 weeks after swimming in Lake Malawi. He was treated with halofantrine in Kenya for presumptive malaria and returned home 3 days later. On return he was mildly fatigued, but a physical examination revealed no abnormalities.

Laboratory investigations revealed eosinophilia (0.6 × 10⁹ eosinophils/L). He was seen again 4 days later with an eosinophil count of 2 × 10⁹/L, and in view of some mild alterations in bowel habits he was treated with mebendazole for a presumed intestinal helminthic infection, although stool microscopic findings were normal. His chest radiograph at this time was normal.

Ten weeks after swimming in Lake Malawi, he presented again because of the return of his initial symptoms, including fever and headaches. Chest radiography and CT revealed pulmonary nodules and eosinophilia, the level of which had risen to 2 × 10⁹/L. Schistosomal serology at this stage was negative, and biopsies of skin and rectum yielded no organisms. He was treated with praziquantel (40 mg/kg as a single dose), followed by albendazole, with no ill effects.

Ten weeks after initial presentation (14 weeks postexposure), the schistosomal ELISA was positive at level 4 and the chest radiographic changes had resolved. Antibodies to filariae and *Strongyloides* were not detected. One month later he was well and had a normal blood cell count.

Case 3. A 20-year-old female student became lethargic with fevers 2 weeks after swimming in Lake Malawi. Initial investigations revealed leukopenia (3.4 × 10⁹ leukocytes/L) and thrombocytopenia (102 × 10⁹/L), with mild derangement of liver function (alanine aminotransferase, 150 U/L; AST, 55 U/L). She was negative for schistosomal antibodies at this time and her condition improved. However, she presented again 1 month later with terminal dysuria, pelvic pain, and an urticarial rash over her lower abdomen. She had eosinophilia (4.1 × 10⁹ eosinophils/L) and stool microscopic findings were normal, while urine microscopy showed only pus cells.

Following treatment with praziquantel (a 40-mg/kg single dose), she became systemically unwell with high fevers, a troublesome cough, and a worsening urticarial rash. Her eosinophil count had risen to 8.4 × 10⁹. Rectal and skin biopsies yielded no organisms, but diffuse nodular infiltration was evident on a chest radiograph (figure 1, left) and on a CT image (figure 2).

Over the next 2 days her condition improved, and she has remained well. Schistosomal serology 10 weeks after initial exposure became positive to level 3, and a chest radiograph was normal (figure 1, right). Serological tests for a number of other pathogens, including filariae and *Strongyloides*, remained negative.

Case 4. A 20-year-old male student, the partner of patient 1, presented to his general practitioner because of mild lethargy.
A CT scan in case 3 confirmed the presence of pulmonary nodules.

8 weeks after swimming in Lake Malawi. *S. haematobium* was identified in a stool sample. Three days later he developed a dry cough and pruritic urticarial rash and was treated with praziquantel (40 mg/kg). Within 24 hours of treatment he experienced a systemic illness with high fevers that necessitated hospitalization.

Laboratory investigations revealed eosinophilia (absolute eosinophil count, 4 × 10⁹/L) and pus cells in the urine. Chest radiography revealed nodular shadows similar to those described in case 1. Ten weeks after initial exposure, schistosomal serology was positive to level 4. His condition improved without further treatment, and he remains well with a normal blood cell count.

**Discussion**

Acute schistosomiasis, which occurs mainly in nonimmune visitors to areas where the disease is endemic, can be difficult to diagnose with certainty, as ova may not be easily detected in the early stages of infection. Serological tests become positive only at a later stage in the illness (mean time to seroconversion, 1.6 months; range, 0–6 months) [6]. Diagnosis rests on recognition of the clinical syndrome in the setting of (usually) peripheral blood eosinophilia and an appropriate history of exposure to fresh water.

Typically the symptoms are mild and nonspecific, consisting of fever, lethargy, and malaise. Abnormal physical findings are uncommon but include hepatomegaly, splenomegaly, wheeze, rash, and urticaria. Pulmonary symptoms were described with regard to the majority of *S. mansoni* infections in a Brazilian series but in ~50% of *S. mansoni* cases from Mali [7, 8]. Chest radiographic changes have been described as occurring in *S. mansoni* infections, even in those without respiratory symptoms [9]. These include soft, diffuse micronodules tending to affect the lower lobes.

However, to our knowledge, pulmonary involvement in association with radiographic changes has not been described in reported *S. haematobium* infections. Pulmonary symptoms have previously been thought to be rare; in one series of 29 patients, only one was affected [2], although almost half of the patients in another series had coughs [6].

*S. haematobium* has become the leading cause of schistosomiasis in the United Kingdom [10]. This is thought to result from increased travel to sub-Saharan Africa. Studies suggest that of those infected in Lake Malawi, 96%–99% will have been infected by *S. haematobium* [11].

Our recent experience suggests a changing pattern of presentation of schistosomiasis, with more cases presenting as acute schistosomiasis. These patients had more severe symptoms than seen previously in our unit, and we have not previously found changes on chest radiographs. While *S. haematobium* was definitely confirmed to be present in only one patient, it is likely that this was the infecting agent in all the cases, as all the patients were exposed in the same part of Lake Malawi, known to be an area where *S. haematobium* is endemic.

Unfortunately, the schistosomal ELISA used, which detects antibody to soluble schistosomal egg antigen, cannot distinguish between species.

Although chronic infection with *S. mansoni*, probably because of shunting through fibrotic livers, can lead to egg deposition and granuloma formation in the lungs and subsequently to pulmonary hypertension, the transient lung problems in acute schistosomiasis are clearly different. In acute schistosomiasis, it is possible that the respiratory symptoms and the nodules seen on radiography result from an immune response to migrating immature schistosomulae.

The second feature of these cases is that three patients became transiently more unwell following praziquantel treatment. Although worsening of the clinical condition has been recognized following treatment for acute schistosomiasis, this may be underrecognized. It may be that patients such as ours with pulmonary involvement are more at risk of adverse reactions to praziquantel.

The mode of action of praziquantel is not known, but it is thought to affect the mature worm, with less activity against immature worms or the schistosomal ova. Why the drug should exacerbate the symptoms of acute infection is not clear. One postulate is that treatment kills migrating worms with the release of schistosomal antigens, leading to an intensified immune response similar to that already occurring naturally in response to the acute infection.

We cannot draw firm conclusions from only a handful of cases, but with the rising popularity of travel to sub-Saharan Africa, clinicians should be alert to the possibility of acute schistosomiasis and its pulmonary features. The reason for the emergence of what seems to be a new clinical variant of acute schistosomiasis due to *S. haematobium* is not clear. Although it may simply reflect a higher incidence of a rare but hitherto
unrecognized presentation as a result of increased travel to Lake Malawi, it is possible that this novel presentation may be due to a new parasite variant in the lake.

It is also not clear from our own experience or that described in the literature whether specific therapy with praziquantel affects the natural history of acute schistosomiasis. Some investigators advocate delaying treatment until the acute phase resolves, but this might increase the risk of rare but serious complications. Steroids have been used in this setting, although there is no proof of their efficacy [12].

It should also be recognized that steroids may reduce the efficacy of praziquantel [13]. Our experience and that of others with the worsening of symptoms following treatment suggests that it might be prudent to administer corticosteroids at the time of the first praziquantel dose and to consider a second dose of praziquantel when the acute symptoms have resolved.

References