

Short Report: Acute Schistosomiasis in Travelers: 14 Years' Experience at the Hospital for Tropical Diseases, London

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Abstract. We report 79 cases of acute schistosomiasis. Most of these cases were young, male travelers who acquired their infection in Lake Malawi. Twelve had a normal eosinophil count at presentation and 11 had negative serology, although two had neither eosinophilia nor positive serology when first seen. Acute schistosomiasis should be considered in any febrile traveler with a history of fresh water exposure in an endemic area once malaria has been excluded.

Acute schistosomiasis was first described in 1847 in the prefecture of Katayama, Hiroshima district, Japan.¹ Women brought to the region to be married were found to become acutely unwell with a fever after they had been exposed to fresh water. Acute schistosomiasis, or Katayama fever, is classically seen among travelers to regions where the disease is endemic. It is thought to be an immune-complex phenomenon, precipitated by the onset of egg-laying by newly matured adult female schistosomes. This occurs between 2 and 12 weeks after exposure²; the syndrome is seen almost exclusively among people who have no history of previous exposure to the infection. The symptoms of Katayama may include fever, cough, an urticarial rash, and diarrhea, with an elevated eosinophil count as a characteristic laboratory finding²; not every individual will have all of these. We report the clinical and laboratory features of acute schistosomiasis among 79 travelers who presented to the Hospital for Tropical Diseases (HTD) in London between 1998 and 2012.

Acute schistosomiasis is often a clinical diagnosis at the time of presentation and may only be confirmed later in the illness once a serological test has had time to become positive. We therefore defined cases according to the following five pre-defined criteria, with each case fulfilling all five.

1. Presence of at least one: fever, cough, rash, diarrhea.
2. A recent history of fresh water exposure in an area where schistosomiasis is endemic.
3. Positive schistosomal serology, either at presentation or follow-up.
4. Raised eosinophil count at some point during the illness.
5. Symptoms not attributable to any other condition.

Cases were identified from three sources: a database of schistosomiasis cases and two prospective databases of both inpatients and outpatients seen at HTD. Clinical notes and laboratory data were reviewed using a standard proforma.

Time from exposure to symptoms was taken as the first date of potential exposure to the date of symptom onset. Laboratory results were obtained from the appropriate clinical laboratories in University College London Hospitals. The schistosomal serology is an “in-house” enzyme-linked immu-

nosorbent assay (ELISA) detecting antibody to *Schistosoma mansoni* soluble egg antigen; once positive this test may remain so for years despite successful treatment. Positive results are reported as levels (bands of optical density from 1 to 9) with a result of one or more regarded as positive.³ The serology test has a sensitivity of 96% for *S. mansoni* and 92% for *Schistosoma haematobium*, whereas the reported specificity is 97%.³ Statistical analyses were performed using Graphpad/Prism version 5 for Mac OSX 2007. Spearman's ranked correlation or Mann-Whitney *U* tests were performed where appropriate.

Seventy-nine cases fulfilled the criteria and had case notes available for review. Because this was a retrospective study, some data were missing (as indicated in Table 1) and patients were investigated at the discretion of individual physicians rather than according to a systematic protocol. Most were men (56, 70%) and the median age of the cohort was 25 years (range 17–59). Sixty-six (84%) were born in Europe or Australasia. Ten were born in Africa (South Africa, Zimbabwe, Nigeria, and the Ivory Coast). One was born in Iran, one in Bangladesh, and for one the country of birth was unknown.

Lake Malawi was the commonest site of exposure (42, 53%). Most of the other cases were from West Africa, with only 10 (13%) acquiring their disease in East Africa, one in North Africa (Libya), and two in the Middle East (Saudi Arabia, Yemen). Most were on holiday (54, 68%) with 13 (16%) working as volunteers. There were five cases in British expatriates, four in new entrants to the UK, although the reason for travel was unclear in three.

Fever was the most common symptom (57, 72%) followed by cough (50, 63%). Most (59, 75%) reported at least two symptoms. A rash was described by 28 (35%) but only 10 (13%) had the classic triad of fever, cough, and rash. Thirteen (16%) remembered suffering swimmer's itch immediately after leaving the water.

Twelve cases had a normal eosinophil count at presentation (15%) and in 11 the serology was negative when first tested (14%) (Table 1). Two cases (3%) had both a normal eosinophil count and negative serology at presentation. There was a significant correlation between the schistosomal serology level and time since exposure ($r = 0.29$ 95% confidence interval [CI]: 0.05–0.5, $P = 0.01$), however no significant association with eosinophilia. There were no other significant correlations between variables including duration of symptoms and eosinophilia, although the presence of fever tended to be associated with a higher eosinophil count. Eight had

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TABLE 1
Clinical characteristics

	Median	Interquartile range	Range	Number of patients with normal results at presentation
Time from first exposure to symptoms (days) n = 64	37	21–55	14–100	
Duration of illness (days) n = 73	18	10–38	4–182	
Eosinophil count at presentation ($\times 10^9/L$) n = 79	1.17	0.6–2.5	0.0–10.2	12 (15%)*
Schistosomal serology at presentation (level) n = 79	3	1–4	0–6	11 (14%)†

* $\leq 0.4 \times 10^9/L$.

†Negative serology result.

eggs of *S. haematobium* in their urine and six had *S. mansoni* eggs in their stool.

Almost all patients (78, 99%) were treated with praziquantel during their acute illness at a dose of 40 mg/kg, given in two divided doses. Nine (11%) were also prescribed prednisolone. No adverse reactions were recorded.

Forty-one (52%) were seen at follow-up, 32 (78%) of whom were prescribed further praziquantel. Twenty-two (54%) of those followed up had a persistent eosinophilia. Two of these were found to have *Strongyloides* co-infection and another had atopic conditions (asthma and allergic rhinitis). Three had prolonged symptoms after treatment that required further follow-up, two because of cough and one chronic diarrhea. All of the patients ultimately made a complete recovery.

These data are consistent with previously published series of acute schistosomiasis among travelers in terms of the demographics, country of acquisition, and time to presentation.^{4–10} Katayama is not uncommon as a cause of fever in patients returning from sub-Saharan Africa; in a prospective study from Antwerp, it was the third most common cause of febrile illness in travelers from this region.⁶ Lake Malawi was the commonest site of exposure in our series, accounting for 53% of cases. The lake is a popular destination for travelers and has been the principal site of exposure in several previous series of both acute and chronic schistosomiasis.^{4,5,8,9} Men accounted for 70% of the cases, which may reflect risk-taking behavior rather than a true gender difference.¹⁰

Cercarial dermatitis, or swimmer's itch, is a useful symptom to elicit and was reported by 16%. However, it is probably only reported when patients are questioned directly. Fever and cough were the most common symptoms among this cohort. The presence of these and an urticarial rash are considered to be the classical features of acute schistosomiasis but were only seen in 13%. It has been suggested that cough is an early manifestation of the disease, with altered bowel habit or urinary symptoms occurring later. We found no correlation between symptoms and either time from exposure or duration of illness. Similarly, there was no demonstrable relationship between eosinophilia and either duration or severity of symptoms.

There was a significant correlation between the serology result and time since exposure reflecting the antibody response over time. Positive serology is not always seen in acute schistosomiasis, because it takes up to 3 months after exposure for detectable immunoglobulin G (IgG) antibodies to appear. In one series of 13 patients, the ELISA was positive at first presentation in nine (69%) where schistosomal DNA was detected.¹¹ In our series, 68 (86%) patients had a serology result of equal to or greater than level one, all of whom were tested within a few days of first presenting. The standard ELISA is therefore a useful test to perform during the acute illness as a "rule-in" rather than "rule-out" test. However, there were a proportion

of patients who had both a normal eosinophil count and negative serology when they first presented, suggesting that many cases of acute schistosomiasis among travelers may be missed.

Use of adjunctive steroids for treatment of acute schistosomiasis is an area of some debate. In this series, clinicians usually chose to offer praziquantel to patients with acute disease despite its relative lack of activity against immature flukes. No adverse reactions were recorded in any case. This is in contrast to other series and may reflect either use of a lower dose of praziquantel or failure to report or record adverse reactions^{6,9,11–13}; only nine were prescribed steroids, which may have been caused by the relatively mild nature of the symptoms experienced by this cohort of patients.

Over half were seen for follow-up and 41% of these were given a second dose of praziquantel to treat any residual schistosomes. Forty-six did not receive a second dose of praziquantel, mainly because they did not attend. This was not surprising, as patients with acute schistosomiasis are often young and only passing through London. Practice at HTD has now changed and patients are prescribed a second dose when first seen with instructions to take it 8 weeks later.

This series is limited by its retrospective nature. It is, however, the largest series of acute imported schistosomiasis seen at a single center and provides important insights into the demographics, presenting features, and epidemiology of the disease among travelers.

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