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BRIEF COMMUNICATION

Diagnostic Issues of Acute Schistosomiasis With *Schistosoma mekongi* in a Traveler: A Case Report

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A Belgian traveler returning from Laos developed acute schistosomiasis. Feces microscopy and polymerase chain reaction (PCR) followed by sequence analysis revealed *Schistosoma mekongi*. Schistosome antibody test results and real-time PCR in serum were initially negative or not interpretable. A HRP-2 antigen test for *Plasmodium falciparum* and an enzyme-linked immunosorbent assay (ELISA) antibody test for *Trichinella* yielded false-positive results.

Schistosoma mekongi infection is exceptional in travelers. Even when diagnosis is suspected, confirming early stage infection may be complicated by insufficient sensitivity of schistosome antibody assays and by (false) positive antigen and antibody assays against other pathogens.

Case Report

A 27-year-old male Belgian traveler developed low grade fever, night sweats, and cough soon after returning from a 4 months' adventurous travel to Laos, Cambodia, and Yunnan province in south China. He had lost some weight but had neither diarrhea nor anorexia. He was a practicing vegetarian.

He had, together with his girlfriend, visited the "Four Thousand Islands" (Si Pan Don) region, a conglomerate of islets situated in the Mekong River straddling the Laos–Cambodian border, 5 weeks prior. He reportedly took a daily swim in the Mekong River for 1 week (D0 = first day of exposure), as well as in a sandy old river bend with stagnant water at the southernmost part of Khong Island, called Don Det, on one occasion. He did not report swimming in rivers or ponds elsewhere during his travel.

Symptoms started about 6 weeks after exposure (D45). The patient consulted his family physician 10 days later (D55) and was referred at the outpatient clinic of the Institute of Tropical Medicine, Antwerp, Belgium (ITMA) 5 days thereafter (D60), when symptoms had already subsided. Clinical signs were unremarkable. Ultrasound revealed a modest spleen enlargement, and the routine laboratory workup showed a marked hypereosinophilia (Table 1). Chest X-ray was normal.

Two serum antischistosome antibody tests were performed at the initial and the subsequent visits: an in-house enzyme-linked immunosorbent assay (ELISA) using a *Schistosoma mansoni* antigen (mixture of egg and adult worm extract), and an indirect hemagglutination inhibition assay (IHA), using a *S mansoni* adult worm extract (ELI.H.A Schistosoma, ELITech Group, Puteaux, France), with titration and cut-off at 1/80 (positive at ≥1/160). Up to 15 weeks after exposure (D105), the IHA could not be interpreted because of the presence of antibodies reacting with sheep RBC in the patient's serum. The result of schistosome ELISA antibody test was negative at the first visit (D60), while that of the *Trichinella* antibody test and the malaria HRP-2 antigen test were positive. Blood smear and polymerase chain reaction (PCR) for malaria, as well as the *Plasmodium falciparum* antibody test, were all negative.

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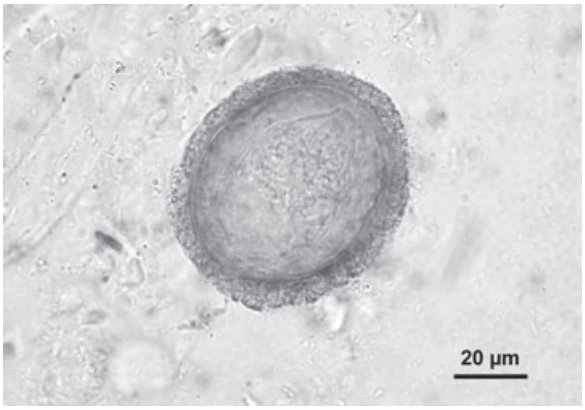

Figure 1 *Schistosoma mekongi* egg.

At D60, microscopy after enrichment for ova and parasites revealed 50 ova of *S mekongi* per gram of feces (Figure 1).

To confirm species identification, real-time PCR[2] and conventional PCR followed by sequence analysis were performed on a fecal sample on D60 and D225. DNA was extracted using a QIAamp DNA stool mini kit (Qiagen). Sequencing of the real-time PCR product and of the complete Internal Transcribed Spacer (ITS) rRNA region amplified by the conventional PCR demonstrated the presence of *S mekongi* DNA. The 733 bp sequence amplified using the ITS4 and ITS5 primers was identical to *S mekongi* from GenBank (accession number U82284 and SMU22169) with the exception of a single base pair transition.[3]

A real-time PCR using the Sm1-7 PCR test targeting the 121-bp tandem repeat sequence common to human schistosomes[4,5] revealed cell-free schistosome DNA in serum at D105 but not at D60, D72, and D225 (Table 1). Instead of using 10 mL of plasma as in the original setup, DNA extraction was performed on 1.5 mL of serum on D60 and D72 and on 2 mL of serum on D105 and D225, quantities that proved to be sufficient in *S mansoni* infections.[4,6]

The patient was given a single dose of praziquantel at D69, when symptoms had already subsided for 2 weeks. He declined concomitant corticosteroid treatment but was warned of a possible exacerbation of symptoms. He consulted 3 days later (D72) because of high-grade fever, severe and blood-stained diarrhea, abdominal colics, and some cough, starting a few hours after praziquantel ingestion. By that time the eosinophil count increased to 15.350/µL and the schistosome ELISA antibody test had turned positive. The patient was treated with oral corticosteroids (methylprednisolone 32 mg o.d. gradually tapering to nil in 14 days). Symptoms disappeared promptly after the first dose and never reappeared. At a control visit at D105, the patient was asymptomatic, eosinophil count had lowered dramatically, and a stool sample was negative for *S mekongi* eggs. A second treatment with praziquantel was given. No symptoms appeared thereafter. At a control visit 6 months later (D225), the eosinophil count had returned to normal, and PCR was negative both in feces and serum.

His companion had bathed at the same spot in the Mekong River, but never developed symptoms. A schistosome antibody test taken elsewhere 3 months after exposure showed a positive result, and she was reportedly treated without developing symptoms.

Table 1 Acute schistosomiasis with *Schistosoma mekongi*: clinical and laboratory data

Date	D45	D55	D60	D69	D72	D105	D225
Treatment*				PZQ	Steroids	PZQ	
Fever	+		−	−	+	−	−
Cough	+		−	−	+	−	−
Abdominal pain	−		−	−	+	−	−
Diarrhea	−		−	−	+	−	−
Eosinophil count (n/µL)		1,929	8,290		15,530	1,160	500
IgE (IU/µL)		n/a	593		472	395	n/a
Schistosoma ab IHA		n/a	n/exe		n/exe	n/exe	1/320
Schistosoma ab ELISA		n/a	−		+	+	+
S mekongi PCR; feces		n/a	+		n/a	n/a	−
Schistosoma sp. PCR; serum		n/a	−‡		−‡	+	−
Eggs in feces (epg)		−	50		n/a	−	−
Trichinella ab ELISA		n/a	+†		+†	−	−
Pf HRP-2 Ag test		n/a	+†		+†	+†	−

+ = positive; − = negative; n/a = not available; D45 = first day of symptoms, 45 days after first exposure; ELISA = enzyme-linked immunosorbent assay; IHA = hemagglutination inhibition assay; n/exe = not executed due to presence of anti-sheep RBC agglutinins in patients' serum; PCR = polymerase chain reaction; PZQ = praziquantel.

*Treatment: praziquantel (PZQ) single dose of 3 g (40 mg/kg).

†False-positive test result: interference with cross reacting antibodies in patients' serum.

‡Small serum sample size (<1 mL).

Discussion

Epidemiology

Infections with *S mekongi* have been reported in populations from the endemic region along the Mekong River for many years. Nevertheless, intensive population treatment has substantially reduced the morbidity and the prevalence of infection in the local population.[7] Infections with *S mekongi* are exceptional in travelers, and cluster cases are not unusual.[8] It was diagnosed in 12 Israelis in 2002 to 2006, including 4 of a cluster,[8] and in a Canadian traveler with neuroschistosomiasis who had swum in the Mekong River in Laos 2 years prior.[9] Khong Island (Si Pan Don, Four Thousand Islands) is a well-known endemic spot for *S mekongi* and an increasingly popular traveler destination. Just before crossing into Cambodia, the Mekong River splits into many branches, creating a multitude of islets and terminating in rapids of scenic beauty.

Diagnosis

Diagnosis of acute schistosomiasis was readily suspected because of the markedly raised eosinophil count and the exposure to a possible source of *S mekongi* 5 weeks prior.

Diagnosis was confirmed both by microscopy and by detecting *S mekongi*-specific specific DNA in a stool sample. Contrary to what we observed in a cluster of travelers infected with *S mansoni*, DNA could not be detected in the patient's serum during the acute phase.[6] This may be owing to interspecies variation in DNA sequences reactive with the chosen primer-probe set. The Sm1-7 PCR targeting the 121-bp tandem repeat sequence was proven successful in *S mansoni* diagnosis but not in *Schistosoma haematobium* infection (unpublished results). It has been evaluated for the first time in this study in a naturally acquired *S mekongi* infection. The poor performance of PCR for detection of schistosome species other than *S mansoni* illustrates the need for a genus-wide PCR protocol for clinical application that detects all human schistosome species with a similar level of sensitivity.

Diagnostic workup during the acute phase of the disease may occasionally be marred by serum antibodies cross-reacting with *Trichinella* antigen, and with sheep RBC, invalidating the IHA test result.[10] Similarly the HRP-2 *P falciparum* antigen test showed a false positive reaction persisting for at least 2 months.[11]

Treatment during the acute phase

When treating an asymptomatic patient during the acute phase of infection with praziquantel, it is not unusual to observe an exacerbation of symptoms shortly after ingestion.[6,12] This is thought to be the result of a sudden release of a vast amount of schistosome antigen. This may explain the substantial rise in eosinophil count. Symptoms may be spectacular, but subside readily with corticosteroid therapy.[6,12]

Caution has to be taken when considering praziquantel treatment during the acute symptomatic phase. This may in some circumstances lead to severe neurologic symptoms. Therefore, referring praziquantel treatment until after the acute symptoms have subsided (induced by corticosteroid treatment or spontaneously) is recommended.[13] On the other hand, referring praziquantel treatment for too long may increase the risk of neuroschistosomiasis that may occur during the late acute phase.[14]

Confirming the diagnosis of schistosomiasis soon after exposure is still elusive. Whether schistosome DNA is already detectable in serum, feces, or urine during the prepatent phase of schistosomiasis is still unclear. If so, it would offer a powerful tool to select recently exposed patients for early treatment with artemisinin derivatives because praziquantel treatment before schistosome maturation is ineffective.[15]

Declaration of Interests

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

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