Case Report: Early Detection of *Schistosoma* Egg-Induced Pulmonary Granulomas in a Returning Traveler

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Abstract. We report the case of a French traveler who developed acute pulmonary schistosomiasis 2 months after visiting Benin. He presented with a 1-month history of fever, cough, and thoracic pain. Initial investigations revealed hypereosinophilia and multiple nodular lesions on chest computed tomography scan. Lung biopsies were performed 2 months later because of migrating chest infiltrates and increasing eosinophilia. Histological examination showed schistosomal egg-induced pulmonary granulomas with ova exhibiting a prominent terminal spine, resembling *Schistosoma haematobium*. However, egg shells were Ziehl-Neelsen positive, raising the possibility of a *Schistosoma intercalatum* or a *Schistosoma guineensis* infection. Moreover, involvement of highly infectious hybrid species cannot be excluded considering the atypical early pulmonary oviposition. This case is remarkable because of the rarity of pulmonary schistosomiasis, its peculiar clinical presentation and difficulties in making species identification. It also emphasizes the need to consider schistosomiasis diagnosis in all potentially exposed travelers with compatible symptoms.

INTRODUCTION

Schistosomiasis is one of the most common neglected tropical diseases. In 2013, an estimated 261 million people were infected worldwide.¹ In endemic areas, the chronic phase of the disease causes significant morbi-mortality among local populations, while the acute phase is responsible for a non-negligible morbidity in travelers. According to the GeoSentinel Surveillance Network, 410 schistosomiasis cases were diagnosed among ill travelers between 1997 and 2008, mostly acquired in Africa.² We present a rare case of pulmonary schistosomiasis in a traveler to Benin, who was diagnosed 4 months after suspected contamination.

CASE PRESENTATION

In April 2013, a 21-year-old French man presented to a private clinic for a 1-month chief complaint of cough and thoracic pain. He returned from a 3-week trip to Republic of Benin (February 2013) where he bathed several times into rivers nearby Natitingou and Djougou (Atakora and Donga departments, respectively). Six weeks after returning home, he reported a febrile episode with pulmonary symptoms including dry cough, chest pain, and a brief pruritic rash (< 24 hours).

The blood tests showed hypereosinophilia (1.3 G/L) and elevated C-reactive protein (55 mg/L). Chest radiography was unremarkable. Amoxicillin was empirically given, as well as a short course of corticosteroids, to treat a hypothetical community-acquired pneumonia. Thoracic computed tomography (CT) revealed multiple bilateral lung nodules with irregular shapes, without ground-glass halos, reticular opacities, or mediastinal lymphadenopathies (Figure 1).

Considering both pulmonary abnormalities and increasing eosinophil count (1.8 G/L), a transbronchial biopsy was

performed. Unfortunately, it led to nonrelevant results (non-specific edematous and congestive changes without any malignant sign). Another chest CT scan was performed on May 2013 and showed a distinctly different distribution of pulmonary nodules. Suspecting an infectious/inflammatory etiology, a lung biopsy was carried out (June 2013). Histological examination revealed several epithelioid granulomas around *Schistosoma* eggs, associated with eosinophilic infiltrates (Figure 2A). Some eggs exhibited a prominent terminal spine, resembling *Schistosoma haematobium* (Figure 2B). Neither schistosomula nor adult worms were detected. No vasculitis or malignant criteria were noticed. Meanwhile, a modified Ziehl-Neelsen stain performed on tissue sections resulted positive (Figure 2C), raising the possibility of a *Schistosoma intercalatum*, *Schistosoma guineensis*, or hybrid species involvement.

In July 2013, the patient was referred to hospital for complementary investigations. Schistosomiasis serology was positive using commercial indirect hemagglutination assay [IHA] (titer of 1:160, threshold = 1:160) (Fumouze Diagnostics, Levallois-Perret, France) and enzyme-linked immunosorbent assay [ELISA] (optical density = 1.65, threshold = 0.37) (Bordier Affinity Products, Crissier, Switzerland). Microscopic examination of stool and urine samples that were collected once following specialized consultation resulted negative for ova and parasites. Eosinophilia decreased gradually on complete blood count. The patient received praziquantel 40 mg/kg once daily.

After 3 months, no more symptoms were reported, physical examination was unremarkable, and lung opacities on chest CT scan disappeared. Eosinophil count was within normal limits (0.5 G/L) and serological markers (IHA and ELISA) remained stable.

DISCUSSION

Acute schistosomiasis is a clinical picture occasionally observed during the early course of infection with *Schistosoma* sp.³ It may occur a few weeks after cutaneous penetration of cercariae and is characterized by nonspecific symptoms including fever, cough, headache, and urticaria, commonly associated

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FIGURE 1. Computed tomography scan of the chest (axial plane) showing a well-defined lung nodule in the right lung.

with eosinophilia. Oviposition, which characterizes the chronic phase of the disease, classically occurs weeks later. The symptomatic acute phase, mostly limited to nonimmune subjects, may include pulmonary manifestations mimicking other helminthic diseases (e.g., Loeffler syndrome).⁴⁻⁷ Pavlin and others⁸ identified, over a retrospective chart review, 89 cases of acute pulmonary schistosomiasis (APS) in travelers. Patients reported dry cough with dyspnea, wheeze, or chest pain, occurring within 2–8 weeks after exposure and healing within a few weeks/months. Chest X-rays and CT-scan usually showed bilateral nodules with ground-glass halos, more or less diffuse and transient. Pulmonary involvement is more common with *Schistosoma mansoni* than *S. haematobium* infection, but it remains a major sign of *S. haematobium* infection, even more frequent than fever.⁸

Schistosome eggs are exceptionally found in the lungs during APS. Indeed, ectopic oviposition, corresponding to eggs trapped in tissues outside the perivesicular or mesenteric plexuses (i.e., excluding the urinary tract, liver, and intestine), is mainly reported after a postmortem examination, especially with *S. mansoni*. Interestingly, Gonçalves and others showed that among 313 autopsy-proven *S. mansoni* infections, the lungs were the most common ectopic site (29.7%), but almost all organs can be affected.⁹ A case of pulmonary mansonic schistosomiasis diagnosed in a migrant who underwent a lung biopsy because of multiple nodules in both lungs was recently published.¹⁰ However, schistosome eggs were also found in liver and stool samples together with periportal fibrosis, defining the chronic stage of schistosomiasis. By contrast, Baharoon and others reported a case of APS confirmed by a biopsy in a traveler showing similar imaging features, only 10 weeks after exposure: laboratory tests revealed hypereosinophilia and a positive schistosomiasis serology, while a *Schistosoma* ovum was detected in tissue sections.¹¹ Similarly, in our case, the initial picture (symptoms, eosinophilia, and CT scan features) was consistent with APS. Moreover, anatomopathological study of persistent lung lesions, approximately 4 months after bathing, showed unexpected egg-induced granulomas.

Early pulmonary oviposition raises some questions. It could attest to a fast and massive egg laying into perivesicular or mesenteric plexuses, with egg's migration from portal and caval veins to the lungs. Nonetheless, urine and stool analysis were both negative for ova and parasites, and no rectal biopsy was performed in the absence of urinary or digestive functional signs. Portal hypertension with intrahepatic portacaval shunts, allowing the embolization of ova from the portal system to the pulmonary arterial tree is a well-known mechanism.¹² However, this theory should be discarded in our case because: 1) the patient did not suffer from any portal hypertension

FIGURE 2. Histological examination of a biopsy specimen from a lung lesion. (A) *Schistosoma* egg surrounded by granulomatous inflammation and eosinophilic reaction (hematoxylin and eosin stain, magnification $\times 100$); (B) *Schistosoma* egg exhibiting a prominent terminal spine (hematoxylin and eosin stain, magnification $\times 400$); (C) strongly positive acid-fast egg's shell (modified Ziehl-Neelsen stain, magnification $\times 400$).

symptoms; 2) histopathology does not evoke *S. mansoni* (lateral-spined eggs), and unlike this species, other schistosomes (e.g., *S. haematobium*, *S. intercalatum*, or *S. guineensis*) are exceptionally involved in periportal or “Symmer’s pipestem” fibrosis^{13,14}; 3) hepatic fibrosis and portal venous system destruction generally settle down gradually, it is thus highly improbable that our patient would have developed a portosystemic shunt within 4 months; 4) congenital hepatic portal venous fistula or spontaneous aneurysmal portal-hepatic venous shunts do exist, but it remains extremely rare.¹⁵ Erratic adult worm migration into pulmonary circulation with straight egg laying could also be a valid possibility, but no adults were found in lungs.

Species-level identification was difficult. Morphological analysis on hematoxylin-eosin stain (terminally spined egg group) associated with epidemiological data suggested a *S. haematobium*. Indeed, this species is largely distributed through the country in many areas, with some of them located nearby our patient’s bathing places.¹⁶ However, a real-time PCR targeting a *S. haematobium*-specific sequence resulted negative on biopsy containing schistosome eggs. A *Schistosoma bovis* infection could also be discussed. This terminally spined egg species is mainly responsible for cattle infections but can occasionally be found in humans.^{17–19} Ziehl–Neelsen stain questions this possibility. Actually, positive acid-fast shell of terminally spined eggs theoretically rules out *S. haematobium* or *S. bovis*,^{20,21} whose differential diagnosis includes *S. intercalatum* and *S. guineensis*, two very close species. Their eggs’ morphometry is characterized by a lozengic shape (instead of a round shape), a higher length (up to 250 µm), and a long slightly curved terminal spine.²² Transmission of these two anthrophilic species occurs almost exclusively in restricted areas of central Africa.^{23–26} Sporadic cases among travelers have also been reported across west Africa (Burkina Faso, Tchad, Mali, and Nigeria), but no transmission focus was precisely identified. To our knowledge, *S. intercalatum* has never been reported in Benin, whereas *S. guineensis* was mentioned in only one publication.²⁶ A similar case—of uncertain diagnosis—was described in Gabon in 2005 by N’Dong and others, but the authors concluded to a *S. haematobium* lung disease considering epidemiological, pathophysiological, and morphological criteria, in the absence of molecular study and despite the positive Ziehl–Neelsen stain.²⁷ Ultimately, the possibility of a hybrid species involvement such as *S. haematobium/S. bovis*, *S. haematobium/S. guineensis*, or *S. haematobium/S. intercalatum* cannot be ruled out. In fact, some hybrids have shown, during experimental designs, greater cercarial productivity from intermediate hosts, as well as higher infectivity and longevity, compatible with rapid and atypical lung damages.^{28,29} In Cameroon, a *S. haematobium/S. intercalatum* hybrid was detected in human stool and urine specimens.^{23,24} More recently, Huyse and others have demonstrated by egg genotyping (collected from human stool and urine samples) that hybridization between schistosomes species is not a rare phenomenon.³⁰ Furthermore, interestingly, the molecular evidence of hybridization between *S. haematobium* and *S. guineensis* was described for the first time in Benin in 2012.²⁶

In conclusion, this case is remarkable for the rarity of pulmonary schistosomiasis, its peculiar clinical presentation, and the difficulty to identify the species. Because the exact genetic nature of the eggs was not determined, we cannot exclude the possibility of an infection with *S. intercalatum* (never

reported in Benin) or with a hybrid species such as *S. haematobium/S. guineensis* (occasionally described in Benin), the atypical evolution preferentially supporting the latter. In both cases, it would be—to our knowledge—the first description of pulmonary schistosomiasis involving these aforementioned species. Such report also emphasizes the need for clinicians working in non-endemic areas to consider schistosomiasis diagnosis in all potentially exposed travelers presenting with compatible symptoms.

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