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Imported African schistosomiasis and the potential risk of transmission in China

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KEYWORDS African schistosomiasis; *Schistosoma haematobium*; *Schistosoma mansoni*; transmission risk; China

1. Introduction

Schistosomiasis is an important global public health problem, and over 200 million individuals are estimated to be infected with *Schistosoma* spp. in 76 tropical and subtropical countries around the world [1]. In China, only *Schistosoma japonicum* was endemic. This species was once highly endemic in 12 provinces, and more than 10 million people were infected in the early 1950s [2]. Since that time, great progress has been made in the prevention and control of schistosomiasis. By the end of 2015, the transmission of schistosomiasis had been interrupted in five of the 12 former endemic provinces, and seven provinces had achieved transmission control in China (<1% prevalence of *S. japonicum* infection in humans and livestock, no autochthonous patients with acute schistosomiasis, and no infected snail hosts for consecutive 2 years) [3]. In 2015, it is estimated that there are 77,194 human cases, and no cases of acute schistosomiasis were reported in China [4].

African schistosomiasis is caused primarily by the blood flukes *S. haematobium* or *S. mansoni*. *S. hematobium* infection is endemic primarily in Africa and the Middle East, and causes urinary schistosomiasis. *S. mansoni* infection is distributed around the world, predominantly in Africa, the Near East, South America and the Caribbean, and produces intestinal schistosomiasis [1]. Both *Schistosoma* species are transmitted by intermediate host snails. Human infection is caused by skin contact with cercaria-contaminated freshwater during swimming, fishing or bathing. The principal clinical manifestations of *S. haematobium* infection are bladder irritation, hematuria, and urinal tract blockages, whereas the manifestations of *S. mansoni* infection are usually relatively mild, such as fever, abdominal pain, diarrhea, and weakness. Some patients may be mild or asymptomatic [5]. More than 90% of cases with African schistosomiasis occur in Africa, and China is a non-endemic area. However, an increasing number of Chinese citizens travel to Africa for work or leisure following the development of economic programs and tourism, the globalization of international trade, cultural exchange and China-aided projects in Africa. More than one million Chinese workers are working in Africa and approximately 900,000 Chinese people vacation in Africa each year [6]. There is an increasing trend for cases of African schistosomiasis in China. In this study, we report two cases of African schistosomiasis imported from Tanzania and Madagascar to China and discuss its potential transmission risk in China.

2. Case description

Case 1. A 48-year-old man from Dengfeng County in Henan Province of central China worked in a tin mine in the Mpanda district of Tanzania from November 2007 to December 2008. During that time, he and his fellow workers frequently swam, bathed, and fished in a local river. He experienced general debility, fatigue, abnormal sweating and blood in his urine soon after his return. He was treated for a suspected urinary tract infection at the local village clinic for 7 years because of his low income, but did not obviously improve. On December 17, 2015, he was admitted to a local hospital with aggravated symptoms and terminal hematuria. He was diagnosed with papillary papilloma of the bladder based on cystoscopy and histopathology and underwent surgical excision of a tumor. His hematuria transiently disappeared after surgery. However, progressive hematuria reappeared on July 6, 2017, and the patient was hospitalized in the First Affiliated Hospital of Zhengzhou University. The physical examination was unremarkable. Routine blood examination showed a normal white blood cell count of 8500 with eosinophilia (11.6%, 990 eosinophils/μl). Abdominal CT examination revealed irregular thickness of the left rear section of the top of the bladder wall, and an electrosurgical excision was performed. Due to the suspected parasitic infection, the patient was presented to our Department of Parasitology on 20 July.

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Urine samples were collected over 24 h and examined under a microscope after sedimentation, but no eggs were found. Histopathological sections of the surgical specimen of the bladder tissue revealed diffuse granulomas with intense inflammatory infiltrates. Many barrel- or spindle- shaped eggs were observed in granulomas. At higher magnification, the typical terminal spines of these eggs identified them as eggs of *Schistosoma haematobium* (Figure 1). This patient was treated with praziquantel (40 mg/kg/day in two doses for one day). Two weeks after treatment, the hematuria disappeared and eggs were no longer found in the patient's urine.

Case 2. On March 2, 2017, a 25-year-old student from Xiangchen city in Henan Province in central China presented to the Parasitology Department of Zhengzhou University. He had a 2-month history of persistent fever with a temperature of 37.6–39 °C, cough, abdominal pain and diarrhea. Inquiries revealed that he had been traveling in Madagascar from October to November 2016, where he often swam and bathed in small local rivers. The general reddish, itching skin rashes occurred the day after swimming, but the skin eruption disappeared after treatment with anti-allergic agents at a local clinic. On February 21, 2017, he was admitted to the local hospital. Initial laboratory examinations showed an elevated white blood cell count of 12,050 and marked eosinophilia (17.6%, 2120 eosinophils/μl). He also had increased C-reactive protein levels (15.13 mg/l). Chest CT examination revealed patchy infiltration in both lungs and a small amount of pleural effusion. The patient was treated with antibiotics for pneumonia but was not cured. He had aggravated symptoms of high fever (38.9–39.8 °C), abdominal pain and diarrhea with mucous bloody stool.

On March 1, the patient was transferred to the Affiliated Hospital of our university for further diagnosis. Routine blood examination revealed leukocytosis of 10,600, high eosinophilia (24.9%, 2640 eosinophils/μl), and elevated C-reactive protein levels of 33.9 mg/L. An agglutination test revealed that all antibodies against the antigens of typhi 'O' and 'H' and paratyphi A, B and C had negative titers less than 1:40. A colonoscopy showed erosion, submucosal bleeding spots and ulcers of the transverse colon. Histological sections of colon biopsy tissues revealed chronic mucosal inflammation together with acute inflammation and submucosal lymphocyte aggregation, but no eggs were found. Eggs were not observed via the direct stool smear, sedimentation and egg hatching methods. Serum antibodies against tissue-dwelling parasites (*Spirometra erinaceieuropaei*, *Taenia solium*, *Paragonimus skrjabini*, *Clonochis sinensis*, *Trichinella*

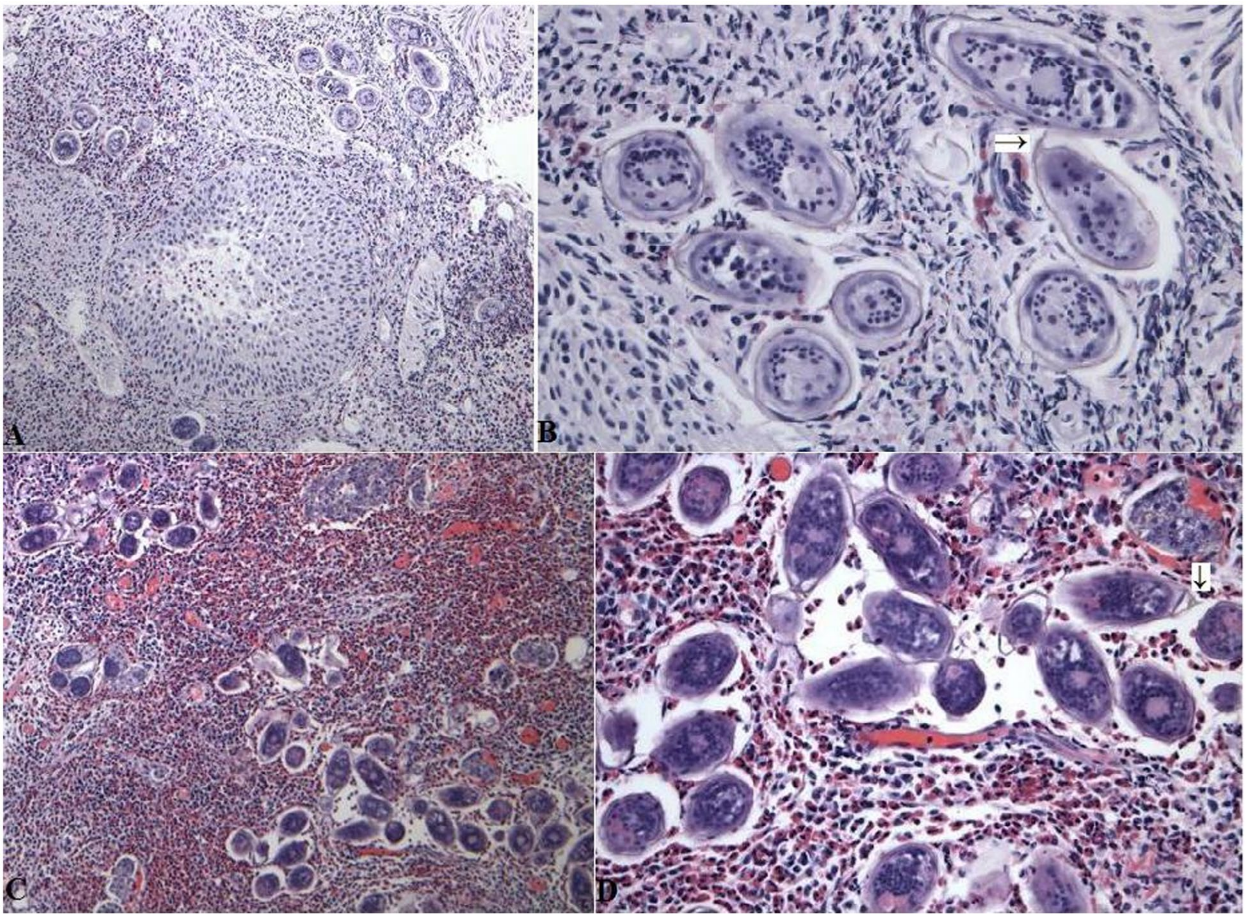

Figure 1. Histopathology of a bladder surgical specimen (hematoxylin and eosin stained). (A) and (C): Low-power view of bladder tissue shows granulomas with eggs (×100). (B) and (D): High-power view of *S. haematobium* eggs in granulomas. Note the characteristic barrel-shaped eggs with a terminal spine. The arrow (→) indicates the terminal spine (×400).

spiralis) were negative by enzyme-linked immunosorbant assay (ELISA) or immunofluorescence test (IFT) [7]. However, serum antibody IgG against *Schistosoma japonicum* was strong positive by indirect haemagglutination test (IHA) (Anji, Hefei, China) [8]. This patient was tentatively diagnosed with schistosomiasis caused by *S. mansoni*, as he had never been to the endemic areas of *S. japonicum* in China and other countries. He was treated with praziquantel as described in Case 1. Two days after starting treatment, his temperature began to decrease. One week after therapy, there was general improvement. The patient's fever declined to normal, but he still had leukocytosis of 12,060 and higher eosinophilia (29.7%, 3300 eosinophils/μl). Three weeks after treatment, the patient had no further symptoms, laboratory findings showed an almost normal eosinophil count (5.8%) and weakly positive anti-*Schistosoma* antibodies.

3. Discussion

African schistosomiasis has been imported to non-endemic countries in Europe, North America, Australasia and Asia [9–11]. In Europe, 1465 cases of imported schistosomiasis were reported between 1997 and 2010, and 95% of the cases were acquired in Africa [5]. In China, the development of economics and tourism, the globalization of international trade, the exchange of culture and science, and Chinese-aided projects in Africa have resulted in increasing numbers of Chinese people going to Africa for travel or work in recent years. It is currently estimated that there are over one million Chinese workers mining, building, exploring, paving roads or supplying water in Africa. More cases of African schistosomiasis will be imported into China. From 1979 to 2016, a total of 154 patients infected with *S. mansoni* and 291 patients infected with *S. hematobium* were reported in mainland China, and most patients had returned to China from Angola, Mozambique, Zambia, Congo, Liberia, South Africa, Mozambique, Yemen, Zanzibar, Tanzania, and so on [12–14].

Because African schistosomiasis is rare in non-endemic regions, clinicians, including pathologists, are unacquainted with its clinical manifestations and unaware of the possibility of schistosomiasis. When patients are exposed in Africa and present symptoms after returning from Africa to China, misdiagnosis usually occurs. This misdiagnosis might result in advanced disease and complications, as reported in Case 1 here. That patient had been successively misdiagnosed for more than 8 years and underwent two operations. Even after cystoscopy and histopathology, he was still misdiagnosed as having a bladder tumor. The clinical manifestations of *S. mansoni* infection are non-specific, and given the low positive identification rate from egg and serologic examinations, the infection is often undiagnosed and misdiagnosed. Out of 16 patients returning from Tanzania to Germany, eggs were found in only one patient [15]. Another study revealed that *S. haematobium* eggs were detected in only 6 of 184 patients returning from African countries (primarily Angola and Mozambique) to China, but 96% of patients were positive for anti-*Schistosoma* antibodies. Out of these patients, 61% had urinary symptoms and 39% were asymptomatic [16].

Once one case of African schistosomiasis is diagnosed in a non-endemic region, it should be regarded as a sentinel of this imported disease. Since infected people could be asymptomatic or might have only minor symptoms, they usually do not seek medical advice. Additionally, most Chinese patients returning from Africa come from rural areas in central and western China; these patients generally go to the village clinic due to their low incomes. As mentioned in Case 1, the patient was treated for a urinary infection at the village clinic from 2009 to 2015. This suggests that for every patient who returns from Africa, there may be many more individuals who, if similarly exposed, might remain asymptomatic, not seek care, and therefore remain at risk of the complications of chronic schistosomiasis. The number of diagnosed patients might reflect only the tip of the iceberg in terms of the actual number of patients with African schistosomiasis in China [17]. A history of contact with local river or lake water in people returning from Africa is highly suggestive of African schistosomiasis. Whether patients have the clinical manifestations, such as eosinophilia, or are asymptomatic, clinicians should be aware of the possibility of *Schistosoma* infection. The hematuria in patients with *S. haematobium* infection may disappear transiently after surgical excision of bladder lesions but could recur soon after if anti-*Schistosoma* treatment is not given. Direct pathogen and serological examination for *Schistosoma* infections should be conducted for all people returning from Africa. Praziquantel is the drug of choice for schistosomiasis and is effective against all *Schistosoma* species, and the recommended dose is 40 mg/kg/day in two doses for one day. The local governments, disease control centers and clinicians should implement public health education that advocates avoiding exposure to contaminated freshwater for people going to Africa.

The importation of African schistosomiasis might also have the environmental impacts, due to the possibility of introducing African schistosomes into local rivers and lakes, which poses a potential risk as an infection source for this disease in non-endemic regions. In 2013, an outbreak of *S. haematobium* infections occurred in Corsica in France, and more than 120 local inhabitants or tourists were infected. The introduction of this schistosomiasis is considered to be related to infected individuals arriving from an African endemic region and contaminating the local river with *S. haematobium* eggs discharged in urine, followed by the subsequent infection of freshwater snails [11]. Sequencing analysis further revealed that the *S. haematobium* specimens from Corsica were closely related to those from Senegal in Africa [18,19]. In China, the freshwater snail *Biomphalaria straminea*, which is an intermediate host of *S. mansoni*, was introduced into a river in Hong Kong via the import of tropical aquarium plants or fish by air from South America between 1970 and 1982 [20,21]. Subsequently, this snail was disseminated into rivers and ponds in Shenzhen in southern China as an invasive snail species [22]. This process suggested that this snail can survive, reproduce, spread through the river, and form new populations in natural environments in southern China. Recent surveys showed that *B. straminea* is the predominant snail population in many snail breeding sites of Shenzhen city and has spread through the river to Shenzhen, Dongguan and Huizhou in southern China, suggesting that this snail has a great dispersal capacity [23–25]. But, none of the *B. straminea* specimens collected from Hong Kong was found to be infected with *S. mansoni* by biopsy and PCR [26], and no *S. mansoni* infections were detected in *B. straminea* collected in southern China following exposure to the parasite cercariae in laboratory [27]. The results demonstrated that the invasive *B. straminea* snails seem to be incompatible with *S. mansoni*. Moreover, up to present, the intermediate hosts of *S. haematobium* are not detected in China, and there might be a low risk of transmission of African schistosomiasis in China. However, a morphological and DNA-sequence based phylogenetic study indicated that five of seven populations of *Biomphalaria* snails collected in Guangdong province of southern China clustered more closely with *Biomphalaria kuhniana* than with *B. straminea*. The displacement of *B. straminea* by *B. kuhniana* in Guangdong is considered as an explanation for the habitat changes observed among the snails between Hong Kong in the 1980s and the present. The potential risk of transmission of *S. mansoni* in China is more likely to come from parasite importation in the snail stage, than from transmission by migrant workers from Africa or South America [28]. Besides, although it is likely rare, the potential outbreaks of imported *S. mansoni* infection caused by importing infected snails might pose a threat to public health in the neighborhood of international container ports. Hence, the further investigation and surveillance of the presence of *B. kuhniana* around ports in southern China should be carried out.

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Disclosure statement

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