Case Report: Nodular Lung Schistosomiasis Lesions after Chemotherapy for Dysgerminoma

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Abstract. We report an unusual case of pulmonary schistosomiasis in a traveler to Mali that was diagnosed 16 months after primary infection, one month after she finished chemotherapy for a malignant tumor. Serologic analysis showed marked eosinophilia. Our case emphasizes the need to detect parasitic infections in cancer patients with unexplained eosinophilia, particularly in immigrants and travelers to tropical countries.

Schistosomiasis is a trematode infection endemic in many tropical countries in Africa, Asia, and South America. It is estimated that more than 500 million persons live in areas at risk for this disease and 200 million persons have chronic infections.1 The infection is acquired through contact of intact skin with fresh water contaminated with schistosomal cercariae. During acute infection, severe but transient itching of the skin (swimmer’s itch) develops in some patients, which results from penetration by the parasites. Three to eight weeks after infection, Katayama syndrome, an acute immune-complex mediated inflammatory response to egg-laying by maturating females within the tissues, develops in a small proportion of patients. This syndrome is more frequent in travelers not exposed to the parasite and in persons with S. mansoni infection, although it can occur with other species. Chronic infection with Schistosoma spp. primarily affects the gastrointestinal tract (S. mansoni) or genitourinary system (S. haematobium) and is characterized by bloody diarrhea, hepatic fibrosis with portal hypertension (S. mansoni), and hematuria, prostatic lesions, or vesical malignancies (S. haematobium).1

The lungs can be affected at different stages of the infection. However, infection of these organs is not a paramount complication of the disease. Little is known about the effect of immunosuppression in patients with schistosomiasis. However, patients with acquired immunodeficiency syndrome and those with T cell dysfunction have decreased parasite egg output.2,3 After retroviral therapy, immune inflammatory reconstitution syndrome (IRIS) associated with parasitic infections, including schistosomiasis,4,6 can develop in patients infected with human immunodeficiency virus (HIV). These patients have active symptoms of infection related to granuloma formation because of reactivation of the immune system. We report an atypical case of pulmonary schistosomiasis in a traveler to Mali that was diagnosed 16 months after primary infection, one month after she finished chemotherapy for a malignant tumor.

CASE REPORT

A 34-year-old woman had a diagnosis of ovarian dysgerminoma, and a tumor was surgically excised. Four years later, a retroperitoneal lump (diameter = 8 cm) was detected in a routine computed tomography (CT) scan. Cytologic analysis confirmed a recurrence of dysgerminoma, and the patient was given chemotherapy (bleomycin, etoposide, and cisplatin) every three weeks for four cycles during a three-month period. A chest radiograph four weeks after completion of chemotherapy showed multiple nodular lesions (diameter = 4 mm) in both lungs. A CT scan confirmed the presence of these nodular lesions (Figure 1) but no treatment was given at that time. Seven months later, another CT scan showed the same nodular lesions and a positron emission tomography–transmission/attenuation correction scan showed a pathologically increased glycidic index (Figure 2). The retroperitoneal mass was dramatically decreased compared with its size in previous examinations. The patient was well and results of a physical examination were unremarkable. Hemogram showed marked eosinophilia (Figure 3).

An open lung biopsy was performed and pathologic study of the lung showed granulomatous lesions surrounding trematode structures (Figure 4). The total IgE level was 6,206 IU/mL. Urine was normal and no parasite eggs were observed in three examinations. Schistosome eggs were not detected in three feces samples. The result of a serologic enzyme-linked immunosorbent assay for Schistosoma spp. was positive. A review of the lung biopsy specimen showed deformed Schistosoma eggs surrounded by eosinophilic granulomas (Figure 5) and a pair of parasites within a pulmonary vessel (Figure 6).

Sixteen months earlier, the patient had traveled through rural Mali and visited the Dogon country. She reported walking barefoot through stagnant water pools. She had not visited any other countries in tropical regions. Her partner, who visited Mali with her, had a diagnosis of a urinary S. haematobium infection.

The patient was treated with praziquantel (40 mg/kg, 1,200 mg twice a day on two days one month apart) without complications. One month after treatment, a chest CT scan showed a marked reduction of lung nodules, and her eosinophil count decreased to a normal level (Figure 3).

DISCUSSION

Pulmonary signs and symptoms have been described in patients with acute, subacute, and chronic schistosomiasis. During Katayama syndrome, up to 70% of patients with S. mansoni infections may have respiratory symptoms (dry cough and wheezing).7 These symptoms are seen less frequently in patients with S. haematobium infections.8 A chest radiograph may show different abnormalities, including well-defined nodules or soft, diffuse micronodules, located predominantly in the lower lobes, bronchial wall thickening,9 and, rarely, alveolar consolidation. Symptoms and radiographic abnormalities seen in chest radiographs at this stage of the disease may be caused by an immunologic response to migrating immature schistosomulae, which may be a form of allergic alveolitis with eosinophilia and high levels of circulating...
immune complexes.\textsuperscript{10,11} Patients treated with praziquantel showed a transient worsening of respiratory symptoms, which has been attributed to the inflammatory reaction that follows release of antigen after death of the parasites.\textsuperscript{12}

A form of subacute lung disease has also been described in schistosomiasis, particularly in \textit{S. haematobium} infection.\textsuperscript{13} Eggs may be embolized in small pulmonary vessels and lung parenchyma and produce a granulomatous reaction of variable intensity. The clinical signs could be extremely variable and range from asymptomatic cases of severe disease with hypoxemia, cough, and lung edema. A chest radiograph may show large nodules, patchy infiltrates, or pleural effusions.\textsuperscript{14,15} Anti-schistosomal therapy might provoke worsening of pulmonary symptoms and abnormalities seen by radiography.

The lungs can also be affected in long-standing hepatosplenic infestation caused by \textit{S. mansoni}, \textit{S. haematobium}, and other species in residents of disease-endemic areas.\textsuperscript{16} In these cases, massive embolization of eggs in the pulmonary vasculature from the vesical plexus (in persons infected with \textit{S. haematobium}) or from the intestinal plexus (in persons infected with \textit{S. mansoni}) provokes granulomatous vasculitis and interstitial pulmonary schistosomiasis.\textsuperscript{17,18} As a result, pulmonary hypertension develops in 7–23% of the patients and cor pulmonale with right-sided heart failure develops in 5% of the patients.\textsuperscript{19} Chest radiographs of these patients show nodular or micronodular interstitial infiltrates, fibrosis, and lesions that may resemble tuberculosis or tumors.\textsuperscript{20}

Our case illustrates two features of schistosomiasis not previously described. The first feature is the effect of cancer chemotherapy in reducing the eosinophil count in patients with schistosomiasis. The percentage of eosinophils in our case was 20.1% at the time of tumor recurrence. This value decreased to 4.9% three months later while the patient was receiving chemotherapy, which indicated the inability of the immune system to activate eosinophils against the parasites. The second feature is that four weeks after cancer chemotherapy, IRIS might have occurred. This finding was demonstrated by the fact that the eosinophil count dramatically increased to 26%, and pulmonary nodular lesions were detected in CT and positron emission tomography–CT scans and confirmed by lung biopsy to be granulomatous reactions around \textit{Schistosoma} spp. egg parasites within the lung tissue.

Immune inflammatory reconstitution syndrome is a well-known phenomenon in HIV-infected patients after effective antiretroviral therapy is initiated. It has been shown to be associated to \textit{S. mansoni} infection.\textsuperscript{4–6} To the best of our
knowledge, this is the first case with morphologic documentation of *Schistosoma* spp. infection affecting the lungs in cancer patients with IRIS.

Another interesting finding was the presence of adult worms within pulmonary vessels. In patients infected with *S. mansoni* who have porto-pulmonary shunts, killed adult parasites might migrate from portal veins to lung vessels. In *S. haematobium* infections, adult parasites located in the perivesical plexus might migrate to the pulmonary vessels by the inferior cava vein. We speculate that cancer chemotherapy might have affected or killed adult worms and, in this case, they might have migrated to the lung vessels by this route.

In our case, despite extensive improvement in lung tissue pathology and several attempts to recover parasite eggs from urine and feces, we were not able to identify the schistosome species. However, we presume that the patient was infected with *S. haematobium* for several reasons. First, most cases of schistosomiasis reported from the Dogon country are *S. haematobium* infections.\(^{21-24}\) Second, the partner of the patient had a documented *S. haematobium* infection diagnosed by the presence of eggs. Third, adult worms within lung vessels did not have tubercles on their surfaces, which are characteristic of *S. mansoni* infection. Our case emphasizes the need to detect parasitic infections in cancer patients with unexplained eosinophilia, particularly in immigrants and travelers to tropical countries.

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