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ID CASE

A Woman With Chronic Lower Abdominal Pain, Vaginal Discharge, and Infertility After a Stay in Mali

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A 28-year-old Belgian women presented with hypogastric pain, vaginal discharge, menorrhagia, dysmenorrhea, dyspareunia, and fatigue, which persisted over 8 years. These complaints started a few weeks after an accidental fall in the Niger river during a trip to Mali, after which she had noticed an itching rash localized on the abdominal wall. There were no urinary complaints. Various attempts to conceive in the previous 2 years had failed. She also reported intermittent hematochezia but no diarrhea. During the past 8 years, the patient consulted several gynecologists and had extensive investigations, including a hysterosalpingography without diagnostic yield.

There was no significant medical history except for hay fever for which no maintenance treatment was required. Further travel history revealed a 1-month stay in Ecuador 10 years ago where the patient had swum in rivers.

At physical examination, palpation of the hypogastrium was moderately painful. External genitalia had a normal appearance. There was light cervical motion tenderness during bimanual vaginal examination. A speculum examination showed no vaginal or cervical inflammation or friability. Digital rectal examination was normal. Blood tests showed a hemoglobin of 12.6 g/dL, a total leucocyte count of 7.600/μL with 50% neutrophils, 35% lymphocytes, 6% eosinophils, 2% basophils, and 7% monocytes, and a platelet count of 328.000/μL. Tests for syphilis, human immunodeficiency virus, *Chlamydia trachomatis*, and gonorrhea were negative. Urinary sediment showed 18 erythrocytes/μL, no leucocytes, and the presence of mucus. No proteinuria was detected. Atypical inflammation was reported on a Pap smear, and a cervical biopsy was performed by the treating gynecologist and showed calcified structures within nonnecrotic granulomas (Figure 1).

WHAT IS YOUR DIAGNOSIS?

ANSWER: GENITAL SCHISTOSOMIASIS

The biopsy of the cervix showed calcified *Schistosoma* eggs in the center of granulomas containing eosinophils and other inflammatory cells (Figure 1). We performed cervical,

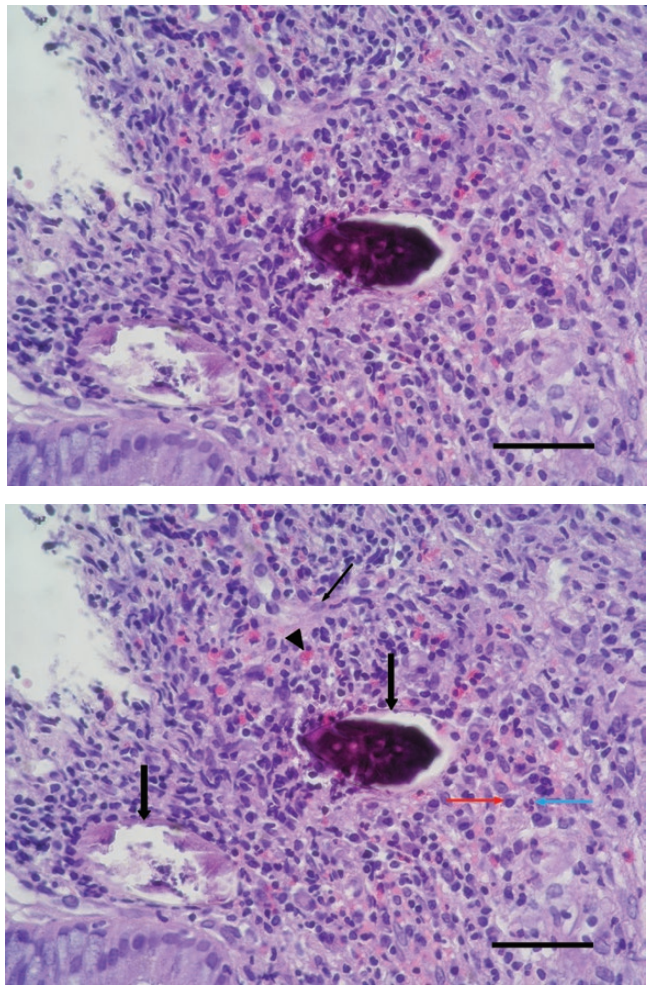

Figure 1. Hematoxylin and eosin stain on a cervical biopsy. Two calcified *Schistosoma* eggs (thick arrows) are seen within a nonnecrotic granuloma composed of histiocytes (thin arrow) and mixed inflammatory cells including eosinophils (arrowhead), lymphocytes, neutrophils (blue arrow), and plasma cells (red arrow). The parasite in the lower left granuloma is partially resorbed. Scale bar indicates 50 μm.

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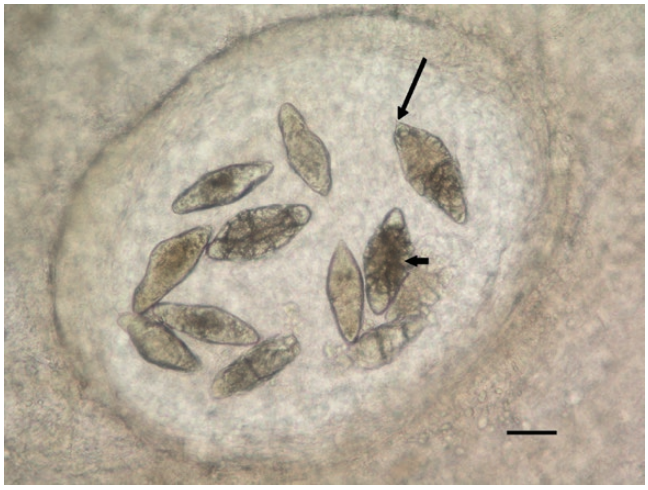

Figure 2. Rectal snip, unstained wet mount preparation. A cluster of *Schistosoma* eggs with different stages of calcification (short arrow indicates advanced calcification) having inconspicuous terminal spines (long arrow) and equatorial bulges. Scale bar indicates 50 µm.

vaginal, and rectal snips. Calcified *Schistosoma* eggs (average size 106 × 42 µm) with a terminal spine were seen in the rectal and cervical snips (Figures 2 and 3), suggesting an infection with a member of the *Schistosoma haematobium* group. Egg shape is polymorphic with some types resembling *Schistosoma intercalatum* because of the equatorial bulge, or the *S haematobium* × *Schistosoma bovis* hybrids that have been reported in Senegal, Corsica, and Mali [1]. However, *S intercalatum* is only reported in the Democratic Republic of Congo [2], and the size of *S intercalatum* eggs ranges between 140 and 240 µm and is thus much larger than the eggs found here.

Enzyme-linked immunosorbent assay and indirect hemagglutination test for *Schistosoma* were both positive (ratio 2.26 with reference range <1.00 and 1/320 with reference range <1/160, respectively). A real-time polymerase chain reaction (PCR) targeting the *S haematobium* complex-specific *Dra I* sequence [3] and the *Schistosoma* genus-specific *28S* gene [4] was positive on the cervical smear and rectal and cervical snips, whereas a real-time PCR detecting the *Schistosoma mansoni* complex-specific *Sm1-7* sequence [1, 5] was negative. Sequencing of the partial 28S PCR product (225 base pairs [bp]) could not distinguish between *S haematobium*, *S bovis*, or *S intercalatum/Schistosoma guineensis*. A rapid diagnostic multiplex conventional PCR (RD-PCR [6]) on the cervix biopsy showed a strong *S bovis* band and a weak *S haematobium* band. Subsequent sequencing of the *S bovis* fragment (258 bp) showed a 100% match to *S bovis* (GenBank accession number of best match: MK757177.1).

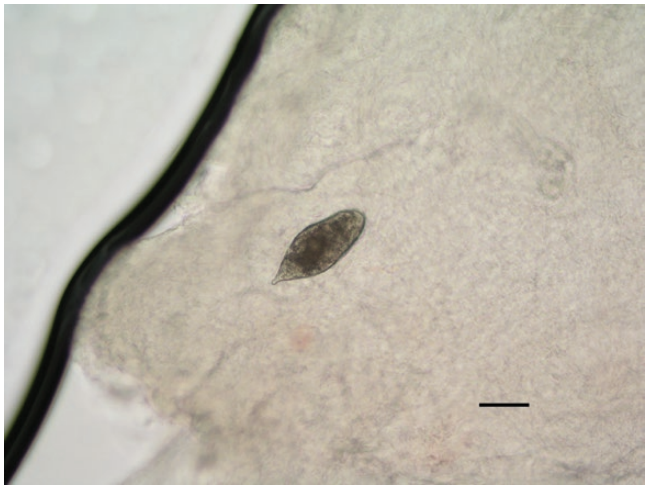

Figure 3. Cervical snip, unstained wet mount preparation. A calcified *Schistosoma* egg with terminal spine. Scale bar indicates 50 µm.

A partial cytochrome oxidase subunit I (COI) fragment (417 bp) was also sequenced for the rectum biopsy and showed 99.76% identity with *S haematobium* from GenBank (accession number of best match: MK333538.1). These results indicate either a mixed *S bovis* and *S haematobium* infection or an infection with hybrid forms of these species. The latter scenario is supported the most given the egg morphology reported above. In addition, *S haematobium* × *S bovis* hybrids have already been reported in a Nigerian village that is also situated in the Niger River basin [6].

The patient was given a treatment of 20 mg/kg praziquantel 3 times for 1 day only, which was repeated 1 month later. After this treatment, only temporary relief of the abdominal pain and dyspareunia was noticed. Five months after diagnosis and treatment, serum *Schistosoma* circulating anodic antigen was slightly positive at 1.44 pg/mL (normal value <1.0 pg/mL). No baseline value was available at diagnosis. An additional single dose of praziquantel 40 mg/kg was given.

Schistosomiasis is an infection caused by trematodes from the genus *Schistosoma*, affecting approximately 230 million persons worldwide [7]. After leaving their intermediate host, freshwater snails, cercaria penetrate the skin, which can lead to a rash called cercarial dermatitis or swimmers itch. In retrospect, the abdominal rash in our patient, the day after falling into the Niger River, was suggestive of swimmers itch. After 2–10 weeks, juvenile (larval) worms migrate to the mesenteric or perivesical veins. During this migration, symptoms of acute schistosomiasis (or Katayama syndrome) can develop in nonimmune travelers; the symptoms are characterized by fever, cough, urticaria, myalgia, and/or abdominal symptoms combined with eosinophilia. Adult worms survive in blood vessels for years excreting hundreds to thousands of eggs daily. Late complications are caused by a chronic granulomatous reaction on *Schistosoma* eggs trapped in tissues, followed by a fibrous scarring process. *Schistosoma mansoni*, *S intercalatum*, *Schistosoma japonicum*, and *Schistosoma mekongi* usually cause hepatointestinal schistosomiasis, sometimes leading to periportal fibrosis with portal

hypertension, whereas *S haematobium* causes urogenital complications [7].

Genital schistosomiasis is a rare diagnosis in returning travelers. In a 2016 publication, researchers found 44 genital schistosomiasis cases ever reported in female migrants and travelers coming from *Schistosoma*-endemic countries with less than half of them being returning travelers [8]. Other possible clinical presentations of genital schistosomiasis include perineal or vaginal lesions, cervicitis, endometritis, salpingitis, infertility, and fistulae [8]. In the above-mentioned series, only 1 patient had a combined genital and rectal localization [9], presenting with a rectovaginal fistula. Our patient mentioned hematochezia, the reason why we performed rectal snips, showing *Schistosoma* eggs. *Schistosoma haematobium* infections usually have a genitourinary location, and *S bovis* infection is only found in the intestines. A hybrid infection explains both localizations at the same time in our patient, which led to the final diagnosis.

CONCLUSIONS

Five months after the last dose of praziquantel, the complaints in our patient had completely disappeared with the exception of intermittent genital itching. She is currently scheduled for follow-up appointments at a fertility center. With increasing tourism to areas where *Schistosoma* is endemic, more cases of genital schistosomiasis might be encountered in returning travelers. Our case illustrates that diagnosis can be missed for years if there is no clinical awareness.

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