Case Report: Testicular Swelling Due to Lymphatic Filariasis after Brief Travel to Haiti

Luis A. Marcos,* Nathan P. Shapley, Mark Eberhard, Jonathan I. Epstein, LeAnne M. Fox, Alan Magill, and Thomas B. Nutman

Infectious Diseases, Hattiesburg Clinic, Hattiesburg, Mississippi; Urology Clinic, Wesley Medical Center, Hattiesburg, Mississippi;

Division of Parasitic Diseases and Malaria, CDC, Atlanta, Georgia; Pathology Department, Johns Hopkins University,

Baltimore, Maryland; Malaria, Global Health Program, Bill and Melinda Gates Foundation, Seattle, Washington;

Laboratory of Parasitic Diseases, National Institutes of Health, Bethesda, Maryland

Abstract. After 6 months of a trip to Haiti, a 25-year-old healthy man presented with a 6-week history of a very slow progressive intermittent bilateral testicular pain and swelling. The biopsies in both testicles revealed the presence of a dead filarial parasite. Polymerase chain reaction products of the DNA from the biopsy were shown to have a 100% identity to *Wuchereria bancrofti*. Despite being uncommon in travelers, this presentation of *W. bancrofti* highlights the possibility of acquiring *W. bancrofti* during short-term trips to highly endemic regions of the world (i.e., Haiti).

CASE PRESENTATION

A 25-year-old healthy man presented with a 6-week history of a very slow progressive intermittent bilateral testicular pain and swelling. Symptoms started with moderate diffuse pain in the suprapubic area, radiating to both inguinal areas. Two weeks later, a persistent bilateral scrotal swelling along with severe intermittent pain (more in the right than left) continued for the next 4 weeks. Although there were no leukocytes present in the urinalysis, a presumptive clinical diagnosis of epididymo-orchitis was made and a 7-day course of fluoroquinolones was prescribed empirically by the primary care provider, without improvement. At the end of the 6 weeks, the testicular swelling started to decrease and finally resolved but a painless nodule in each testicle was noticed by the patient. He denied any fevers, sweats, or chills. An ultrasound revealed a small hypoechoic nodule about 11 mm in diameter in each testicle with some internal calcifications. An outpatient follow-up visit in 4 weeks was scheduled to assess the growth of these nodules but repeated ultrasound did not reveal any changes. Because of the poor response to antibiotics along with the progression of symptoms, bilateral testicular biopsy to remove both nodules was scheduled. He denied any prior medical condition. He drank only pasteurized milk, denied tuberculosis contacts, or unprotected sexual activity. He was born and raised in rural Mississippi where he has lived all his life. His only travel overseas was about 6 months ago when he went to Léogane, Haiti for 7 days for a missionary/volunteer trip, had several mosquito bites, and did not use personal protective measures. He did not receive pre-traveling counseling. On physical examination, both testicles had a single nodule with very mild swelling and tenderness on palpation around the epididymis. Some small inguinal lymphadenopathies were palpable bilaterally. Eosinophilia was absent. The histopathology examination showed acute inflammation with focal necrosis and structures of a parasite (Figure 1).

DIAGNOSIS

The biopsies in both testicles revealed the presence of a dead filarial parasite that was thought to be either a zoonotic

Brugia spp. or *Wuchereria bancrofti* (Wb). Both parasites have been found in testicular tissues. The size of the worm was 120 μ m in diameter. The worm was a non-gravid female in which two reproductive tubes and the intestine were visible (Figure 1); in some sections the cuticle appeared thicker over the lateral chords, a finding that suggests a *Brugia* spp. rather than *W. bancrofti* (Figure 1). Although *W. bancrofti* more commonly infects the genital tract, because of the unusual nature of the case, we entertained the possibility of this being a zoonotic *Brugia* infection acquired in Mississippi.

However, about 3 months after the onset of symptoms a Bm14-based IgG4 immunoassay (ELISA) performed at the Centers for Disease Control and Prevention (CDC) was negative.¹ To clarify the species of the filarial worm found on biopsy, DNA was extracted from an unstained paraffin-embedded tissue section and real-time polymerase chain reaction (PCR) was performed at the Laboratory of Parasitic Diseases, NIAID, NIH; using two separate Wb-specific primer/probe sets targeting the Wb LDR repeat and the Wb intergenic transcribed spacer (ITS), as described previously.^{2,3} Both assays were positive for *W. bancrofti* DNA at threshold cycle (Ct) values between 27 and 29. In addition, using PCR to amplify the ITS in the 5S rRNA gene,³ the product was sequenced and shown to have a 100% identity to *W. bancrofti* (GenBank accession no. U31644). One year after the onset of symptoms, when antifilarial IgG and IgG4 was performed at the National Institutes of Health, both were positive (IgG = 63.6 μ g/mL; normal range 0–14 μ g/mL; IgG4 = 509 ng/mL; normal 0 ng/mL).⁴ The patient received 12 days of diethylcarbamazine at a dose of 6 mg/kg/day per CDC recommendations and tolerated the medicine well. Evolution of clinical presentation and serological tests are illustrated in Figure 2.

FINAL DIAGNOSIS: BILATERAL TESTICULAR NODULES CAUSED BY *W. BANCROFTI* IN A TRAVELER

DISCUSSION

Lymphatic filariasis (LF), a chronic devastating parasitic disease, affects an estimated 120 million people in 73 countries worldwide.⁵ The acquisition of LF by a traveler to an endemic area is uncommon. According to the GeoSentinel Surveillance Network, a global network of specialized travel/tropical medicine clinics on six continents, filarial infections represent only 0.6% of the total individual patient encounters. Of reported filarial infections, those caused by *Onchocerca*

*Address correspondence to Luis A. Marcos, Hattiesburg Clinic, #4 Medical Boulevard, Hattiesburg, MS 39402. E-mail: marcoslrz@yahoo.com

FIGURE 1. Photomicrograph section of excisional biopsy of testis showing intense tissue reaction around a dead female filarial worm. Two uterine reproductive tubes (asterisks) containing infertile eggs and gut (arrow) are present. Scale bar = 50 μ m.

volvulus (37%) are the most common, followed by *Loa loa* (25%) and *W. bancrofti* (25%).⁶ In these analyses, the majority of those infected with *W. bancrofti* had durations of exposure > 6 months.^{6,7} In contrast, the patient described had only a one week stay in Haiti. Interestingly, his entire stay was in Léogane, an area formerly known to be hyperendemic for *W. bancrofti* despite seven rounds of mass drug administration, which had been carried out. It is known, however, that transmission of *W. bancrofti* has not been interrupted there yet.⁸ Furthermore, this patient helps elucidate the natural history of *W. bancrofti* infection (Figure 2). Indeed, the time of exposure to the time of development of a juvenile adult worm was 6 months with his symptoms occurring for the subsequent 6 weeks. Later, the testicular swelling resolved, but

testicular nodules harboring the adult parasites as shown by pathological examination were noted.

Classic histopathologic findings in *W. bancrofti* infection can include a range of conditions, from viable adult worms with minimal host response (a few inflammatory cells), and secondary dilatation of lymphatics, to granulomatous reactions with variable degrees of worm disintegration. Ultimately, scarring (and fibrosis) occurs with an absence of identifiable adult worms. This last stage, scarring with absence of worms may not resolve over time.⁹

Clinically, this case reminds us of the natural history of LF that was well documented in U.S. military troops in the South Pacific Islands during World War II.¹⁰ The incubation period (between landing in an endemic area and the onset of symptoms) was reported to be as early as 1 month in U.S. soldiers. The clinical manifestations of the infection can be variable (from asymptomatic to severe local reactions)⁷ with the majority of infected individuals in endemic areas being clinically asymptomatic. Nevertheless, a high prevalence of disease (23%) has been reported in autopsy studies several decades ago.^{9,11}

In travelers, military personnel, and other expatriates who acquire *W. bancrofti* infection, the presence of microfilaremia in the blood is rare. We did not screen for microfilaremia in the blood before surgery because the diagnosis was not clear at the time. However, based on the size and reproductive status of the worm, and length of incubation, it is likely that the worms had not fully matured (and the female was not gravid) making microfilaremia unlikely. Eosinophilia may be present in only half of the patients with *W. bancrofti* and its absence does not exclude the infection¹⁰; we note that the Bm14-based IgG4 immunoassay (ELISA) was negative 3 months after onset of symptoms, whereas 1 year after the onset of symptoms both antifilarial IgG and IgG4 were positive. These serologic differences reflect the prolonged time from infection to the development of an antifilarial IgG4 response

FIGURE 2. Natural course of the infection in relation to symptoms and serological tests in this patient.

and the lower sensitivity of a single recombinant antigen than crude worm extract in diagnostic screening¹; the lack of personal protective measures such as insect repellent and bed net use may have increased the likelihood of exposure to infected mosquitoes in this individual.

Based on the morphology of the adult parasite in histopathological tissues, it would have been difficult to differentiate with certainty between zoonotic *Brugia* and *Wuchereria*. The molecular identification of *W. bancrofti* was crucial in arriving at a final diagnosis.

In conclusion, despite being uncommon in travelers, this presentation of *W. bancrofti* highlights the possibility of acquiring *W. bancrofti* during short-term trips to highly endemic regions of the world (i.e., Haiti). Given the rarity of this infection in short-term travelers, this case should encourage clinicians to be aggressive in their pursuit of biopsy material even in a returned traveler from a filarial-endemic region of the world.

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Authors' addresses: Luis A. Marcos, Infectious Diseases, Hattiesburg Clinic, Hattiesburg, MS, E-mail: marcoslrz@yahoo.com. Nathan P. Shapley, Urology Clinic, Wesley Medical Center, Hattiesburg, MS, E-mail: nps@megagate.com. Mark Eberhard and LeAnne M. Fox, Division of Parasitic Diseases and Malaria, CDC, Atlanta, GA, E-mails: mle1@cdc.gov, meberhard@cdc.gov, and lff4@cdc.gov. Jonathan I. Epstein, Pathology Department, Johns Hopkins University, Baltimore, MD, E-mail: jepstein@jhmi.edu. Alan Magill, Malaria, Global Health Program, Bill and Melinda Gates Foundation, Seattle, WA, E-mail: Alan.Magill@gatesfoundation.org. Thomas B. Nutman, Laboratory of Parasitic Diseases, National Institutes of Health, Bethesda, MD, E-mail: tnutman@niaid.nih.gov.

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