Cryptosporidium muris, a Rodent Pathogen, Recovered from a Human in Perú

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Cryptosporidium muris, predominantly a rodent species of Cryptosporidium, is not normally considered a human pathogen. Recently, isolated human infections have been reported from Indonesia, Thailand, France, and Kenya. We report the first case of Cryptosporidium muris in a human in the Western Hemisphere. This species may be an emerging zoonotic pathogen capable of infecting humans.

Cryptosporidiosis can be a debilitating diarrheal disease. While infections are normally acute and self-limiting in immunocompetent persons, cryptosporidiosis can be life threatening in those with compromised immune systems. In humans, cryptosporidiosis is caused predominantly by Cryptosporidium parvum or C. hominis (the latter was previously known as the C. parvum human genotype), and major outbreaks of the disease have been clearly associated with contaminated drinking water (1).

Recently, another species of Cryptosporidium, C. muris, has been suggested to be of concern to human health. C. muris is a parasite first identified in the gastric glands of mice (2). Experimental transmission studies have shown that the parasite readily infects multiple nonrodent hosts including dogs, rabbits, lambs, and cats (3). C. muris—like organisms have also been reported as opportunistic infectious agents in immunocompromised nonhuman primates (4). In the past 2 years, five cases of infections with C. muris or C. muris—like parasites have been reported from HIV-positive and healthy persons in Kenya (5), France (6), Thailand (7), and Indonesia (8). In this paper, we report on the first documented case of C. muris in a human in the Western Hemisphere. The parasite was recovered during the summer of 2002 in stools of an HIV-positive Peruvian woman with severe diarrhea. This finding was confirmed by light microscopy, polymerase chain reaction (PCR)–restriction fragment length polymorphism (RFLP), and DNA sequencing.

The Study

In 2002, we conducted a year-long collaborative study on the epidemiology of Cyclospora cayetanensis infections in Perú. As part of that study, we collected approximately 100 stool samples in 2.5% potassium dichromate solution from persons in Lima and Iquitos with Cyclospora infection. Fecal samples were initially identified as Cyclospora-positive in Lima, and then transported to the United States for additional confirmation using wet mount and Nomarski interference contrast microscopy.

Two stool samples, which were taken on two sequential days from an HIV-positive woman who was 31 years of age, contained oocysts that appeared, based on morphology, to be Cryptosporidium muris. Low numbers of Cyclospora cayetanensis and Blastocystis hominis oocysts were also identified in the stool samples. The Cryptosporidium muris infection was initially identified by using wet mount microscopy with oocysts (n=25) averaging 6.1 (± 0.3) x 8.4 (± 0.3) µM (range 5.6–6.4 x 8.0–9.0) and a shape index (length/width) 1.38 (1.25–1.61) (Figure 1). Numbers of oocysts were determined semiquantitatively in each sample by hemacytometer, with an estimated 737,000 and 510,000 oocysts/g recovered from the submitted samples on day 1 and day 2, respectively. The diagnosis of C. muris was later confirmed through DNA analysis.

HIV was first diagnosed in the patient in November 2000 by using enzyme-linked immunosorbent assay and Western blot (immunoblot). She arrived at the hospital clinic in June 2002 with fever and reported that she had been experiencing diarrhea for >3 months. The patient reported that she had lost approximately 25 lbs. in the past 7 months, consistent with HIV-wasting syndrome. Her chest x-ray was abnormal, but four direct sputum examinations for acid-fast bacteria using Ziehl-Neelsen staining were negative, as were efforts at culturing Mycobacterium tuberculosis.

Other laboratory values for this patient at the time of stool sample collection were as follows: CD4 cell count 66/µL; hematocrit 36%; leukocytes 4,100/µL with 4% bands, 55% neutrophils, 27% lymphocytes, and 0% eosinophils; urine examination normal; creatine 0.8 mg/dL; urea 21 mg/dL; glucose 105 mg/dL; serum glutamic oxalacetic transaminase 30 IU/L; serum glutamic pyruvic transaminase 46 IU/L; and bilirubin 0.9 mg/dL.

The diagnosis of Cryptosporidium in the patient’s samples was confirmed by a small subunit rRNA-based nested
Indonesian girls, but the diagnosis was not confirmed by Andersoni–like oocysts were found in two healthy microscopy and molecular analysis (5,7). In Thailand and in an HIV-positive adult in Kenya using infection was identified in an HIV-positive child in muris infection in humans. Previously, one case of Conclusions treatment. Molecular analysis of a stool sample collected became afebrile and had gained 5 kg as of 2 months’ posttreatment. She with no further evidence of muris in her stool sample is an unexpected finding. A major difference between C. parvum or C. hominis and C. muris, is that C. parvum and C. hominis normally colonize the intestine, whereas C. muris is a gastric pathogen in cattle. Anderson (12) and Esteban and Anderson (13) reported that another gastric species, C. andersoni, infects only the glands of the cattle stomach (abomasum), where it retards acid production. These researchers postulated that this process may affect protein digestion in the abomasum and account for the fact that milk production in cows that are chronically infected with C. muris appears to be reduced by approximately 13%. Thus, an infection by C. muris may perhaps cause similar protein digestion problems in human infections, particularly in HIV-positive persons.

Even though only a few cases of C. muris infections have been identified so far in humans, gastric cryptosporidiosis occurs much more often than believed, especially in HIV-positive persons. Up to 40 % of cryptosporidiosis in HIV-infected persons includes gastric involvement (14). Although most gastric Cryptosporidium infections in HIV-positive persons are likely caused by C. parvum or C. hominis because of immunosuppression, the contribution of C. muris probably has been underestimated. Thus, molecular characterizations of stomach tissues from patients with gastric cryptosporidiosis may help us to understand the pathogenesis of human Cryptosporidium infection.

Conclusions

This report represents the third confirmed case of C. muris infection in humans. Previously, one case of C. muris infection was identified in an HIV-positive child in Thailand and in an HIV-positive adult in Kenya using microscopy and molecular analysis (5,7). C. muris and C. andersoni–like oocysts were found in two healthy Indonesian girls, but the diagnosis was not confirmed by molecular tools (8). One putative C. muris infection was reported in an immunocompromised patient in France based on sequence analysis of a small fragment of the SSU rRNA (6). However, the sequence presented was more similar to that of C. andersoni (2-bp differences in a 242-bp region) than to C. muris (8-bp differences in the region).

Although determining whether or not the C. muris contributed medical problems in this patient is not possible, detecting C. muris in her stool sample is an unexpected finding. A major difference between C. parvum or C. hominis and C. muris, is that C. parvum and C. hominis normally colonize the intestine, whereas C. muris is a gastric pathogen in cattle. Anderson (12) and Esteban and Anderson (13) reported that another gastric species, C. andersoni, infects only the glands of the cattle stomach (abomasum), where it retards acid production. These researchers postulated that this process may affect protein digestion in the abomasum and account for the fact that milk production in cows that are chronically infected with C. muris appears to be reduced by approximately 13%. Thus, an infection by C. muris may perhaps cause similar protein digestion problems in human infections, particularly in HIV-positive persons.

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Our report expands the geographic range of suspect *C. muris* infections in humans and suggests that this species may be a global emerging zoonotic pathogen. This pathogen may be of particular importance to persons living in regions where rodents live in close proximity to humans and sanitation may be minimal. *C. muris* may also be more prevalent than currently recognized. The organism is nearly twice as large as *C. parvum* and closer in size to *Cyclospora cayetanensis*. Although *Cyclospora* autofluoresces while *Cryptosporidium* does not (15), *C. muris* could still be easily misdiagnosed, since few laboratory workers would be familiar with *C. muris* or its morphology.

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**References**


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