Case Report: Chronic Microsporidial Enteritis in a Missionary from Mozambique

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Abstract. Microsporidiosis often occurs in immunocompromised persons but may also occur in those who are immunocompetent. Infection by Microsporidia involves a variety of organs and systems, most notably, intestine, lung, kidney, brain, sinuses, muscle, and eyes. Enterocytozoon bieneusi and Encephalitozoon intestinalis are associated with gastroenteritis, and Enterocytozoon hellem and Encephalitozoon cuniculi are associated with keratoconjunctivitis. We report a case of chronic microsporidiosis in a 28-year-old woman missionary from Mozambique who came to our diagnostic laboratory with nausea, lower abdominal pain, and frequent bowel movements. Over two years, the patient was clinically assessed and treated for malaria and giardiasis without laboratory diagnosis while in Mozambique. Identification of the causative agent of her condition was not attempted during the course of her illness in Mozambique. Furthermore, adverse effects of malaria and giardiasis medications may have exacerbated the chronic illness in this patient and mimicked chronic microsporidiosis.

Microsporidia is a phylum of spore-producing unicellular parasites. Once considered to be protests, they are now classified as a phylum under the Kingdom Fungi.¹ To date, more than 1,200 species belonging to 143 genera that have been described as parasites of a wide range of vertebrate and invertebrate hosts. There are at least 14 microsporidian species identified as human pathogens. However, only a few genera are of medical importance, including Enterocytozoon and Encephalitozoon.

Microsporidiosis more often occurs in persons who are immunocompromised, although the disease may occur in persons who are immunocompetent.² The disease involves a variety of organs and systems, most notably, intestine, lung, kidney, brain, sinuses, muscle, and eyes. Enterocytozoon bieneusi and Encephalitozoon intestinalis are associated with gastroenteritis, and Encephalitozoon hellem and Encephalitozoon cuniculi are associated with keratoconjunctivitis.³⁴ We report a case of chronic microsporidiosis from Mozambique.

On February 10, 2010, a 28-year-old woman missionary from Mozambique came to our diagnostic laboratory with nausea, lower abdominal pain, and frequent bowel movements that were up to 10 per day. The patient had visited Pemba, Mozambique many times since December 2008. The patient reported severe diarrhea and nausea that lasted more than a week after her return to the United States in December 2008. Symptoms recurred periodically over the following year, especially on an empty stomach. During September and October of 2009 the patient experienced severe diarrhea and vomiting.

At this time, the patient visited a local clinic in Mozambique, was clinically assessed without laboratory diagnosis, and subsequently treated for malaria with 20 mg of artemether and 120 mg of lumefantrine (Coartem®), which lessened the severity of her symptoms. Periodic nausea, stomach cramps, and diarrhea recurred over the following year. The patient was then treated with metronidazole for giardiasis at the same clinic, again without laboratory diagnosis. Her symptoms subsequently improved but did not completely resolve. The patient also reported keratoconjunctivitis 5–6 times throughout the course of her illness while in Mozambique. During December 2009–January 2010, the patient reported increased stomach pain and up to 10 bowel movements per day.

Upon the patient’s return to the United States in January 2010, she visited a gynecologist to be evaluated for a potential gynecologic source of her abdominal discomfort. A diagnosis of a urinary tract infection was made and she was prescribed sulfamethoxazole, trimethoprim, and metronidazole. The gynecologist also recommended consulting a gastroenterologist because of her travel history to Africa.

On February 10, 2010, a fecal sample was submitted to our diagnostic laboratory for evaluation. This was the first time since the beginning of the patient’s illness that a fecal sample was examined. The fecal sample was small, soft, and pasty. The sample had an especially foul and objectionable odor. Direct microscopic examination of the fecal sample initially showed a normal appearance with no fatty droplets, occult blood, ova, or parasites. After concentration and multiple examinations by using phase contrast microscopy, no parasites or ova were found. The fecal mass was then preserved in 10% formalin and a portion was diluted in saline and reexamined by using phase-contrast microscopy. Many ovoid spore-like structures were observed in multiple samples. Initially, the spores were incorrectly identified as Cystoisospora spp. on the basis of shape, but not size.

The patient provided this diagnosis to her gastroenterologist. The gastroenterologist noted that the patient’s immune system was not compromised and thus was not convinced of the diagnosis of cystoisosporiasis, but prescribed 25 mg of pyrimethamine (Daraprim®) and leucovorin for 10 days. The patient completed a 10-day course of pyrimethamine but did not take the leucovorin and experienced only partial relief of her symptoms. The next day, fecal samples were reexamined in our laboratory, and the size of the spores accurately measured and found to be 4.0 µm in length and 2.5 µm in width. On the basis of the reexamination, the size, shape, and appearance of the spores were consistent with Microsporidia. Treatment with 400 mg of albendazol was recommended. The patient took two courses of albendazol one week apart, had complete recovery, and has been free of symptoms as of May 26, 2010.

Microsporidiosis has emerged as an opportunistic disease in Africa that is associated with immunocompromised persons.

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or those with acquired immunodeficiency syndrome.\textsuperscript{3} \textit{Enterocytozoon bieneusi} and \textit{Encephalitozoon intestinalis} are two of the most common microsporidian parasites that infect humans and cause diarrhea and systemic disease.\textsuperscript{4} Spores of microsporidia have been reported in drinking water, soil, and domestic and wild animals in Africa, which suggests waterborne, foodborne, zoonotic, or anthropogenic transmission and may explain how the patient acquired the infection during her stay in Mozambique.\textsuperscript{14–16}

There are several factors that contributed to the chronic nature of this patient’s illness. As a missionary, the patient was exposed to primitive conditions in rural areas of Mozambique, with questionable food and water sources, for extended periods of time. The patient’s initial symptoms that occurred while she was in Mozambique were indicative of gastrointestinal illness. Although the patient promptly visited the local clinic, a definitive diagnosis was not made and her illness was assumed to be malaria because this disease is endemic to Mozambique.\textsuperscript{9–12}

The incorrect diagnosis of malaria was apparently made solely on the basis of the patient’s symptoms of nausea and vomiting and explains why Coartem\textsuperscript{\textregistered} did not relieve the patient’s symptoms. Ironically, some of the adverse effects of Coartem\textsuperscript{\textregistered} are diarrhea, and abdominal pain.\textsuperscript{13}

An apparent tentative diagnosis of giardiasis was made by the same clinic in Mozambique on the basis of her upset stomach, nausea, and diarrhea. This diagnosis was also apparently made without a definitive diagnosis, which explains why metronidazole did not completely relieve the patient’s symptoms. The patient’s visit to the United States and to a gynecologist resulted in her treatment for a urinary tract infection even though her original symptoms were gastrointestinal. Her gastrointestinal and genitourinary symptoms may be explained by the adverse effects of metronidazole, which include nausea, stomach pain, diarrhea, vomiting, and vaginal irritation.\textsuperscript{14}

Alternatively, the patient may also have had a concurrent underlying urinary tract infection.

Because the patient’s symptoms were mainly gastrointestinal, her keratoconjunctivitis was overlooked during the course of her illness and may not have been related to the microsporidal infection. However, keratoconjunctivitis is associated with microsporidiosis, especially with infections by \textit{Encephalitozoon hellem} and \textit{Encephalitozoon cuniculi}.

Microsporidial infections are not life-threatening in the immunocompetent patient but are one of the most frequent life-threatening opportunistic infections in the immunocompromised patient.\textsuperscript{15,16} Microsporidia became prominent as a common cause of diarrhea in patients with acquired immunodeficiency syndrome and is now emerging as a pathogen responsible for severe diarrhea in solid organ transplant patients.\textsuperscript{17} Thus, the inability to perform a laboratory diagnosis and identify the source of the patient’s illness may have resulted in unnecessary treatment for malaria and giardiasis. Her gastroenteritis in Mozambique may not have been caused by infection with Microsporidia. Treatments for malaria and giardiasis may have exacerbated her gastroenteritis. Alternatively, while in Mozambique, she may have had undiagnosed chronic microsporidiosis. There is no solid evidence of the source of this patient’s gastroenteritis while in Mozambique.

According to the Centers for Diseases Control and Prevention, laboratory diagnosis of microsporidiosis is made by using light microscopic examination, special stains, transmission electron microscopy (which is not feasible for routine diagnosis), an immunofluorescent assay with monoclonal and or polyclonal antibodies, and molecular methods that use the polymerase chain reaction. However, many of these procedures are not routinely available in developing countries.

Our findings emphasize the need to obtain a definitive diagnosis by identification of the causative agent prior to treatment in cases of infectious diseases, particular in developing countries. The incorrect diagnosis of malaria and giardiasis in this patient was made on the basis of symptoms alone. These symptoms overlapped those of microsporidiosis and led to a delay in proper treatment of her condition and administration of unnecessary medications. Furthermore, the adverse effects of those medications may have compounded her original symptoms and contributed to the chronicity and severity of her disease.

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