A New and Highly Divergent Enterocytozoon bieneusi Genotype Isolated from a Renal Transplant Recipient

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CASE REPORT

A 49-year-old renal transplant recipient was admitted to our hospital due to abundant liquid diarrhea and dehydration. Parasitological investigations, including genotyping, led to the diagnosis of intestinal microsporidiosis due to a new and highly divergent internal transcribed spacer (ITS) genotype of Enterocytozoon bieneusi. The potential route of transmission through horse stools is discussed.

Microsporidia are a diverse group of obligate intracellular parasites currently classified as fungi (10). They infect a wide range of eukaryotic cells in numerous invertebrate and vertebrate hosts, including humans and domestic and wild animals (10). Enterocytozoon bieneusi and the Encephalitozoon spp. are the major species infecting humans, with E. bieneusi being the most prevalent (10, 14). Transmission occurs mainly through fecal-oral routes, with sources of infection including other infected humans and animals, contaminated water, and, as illustrated recently, food (1, 4). Microsporidia have emerged as an important cause of opportunistic
tems). Surprisingly, comparison of the nucleotide sequences of this isolate to the GenBank database using the BLAST algorithm (http://blast.ncbi.nlm.nih.gov/Blast.cgi) revealed only a weak similarity to previously reported E. bieneusi genotypes. The most similar genotypes (94% homology, 241 bp) were genotypes Horse 2 and KB-5 (GenBank accession numbers GQ406054 and JF681179, respectively), which have been recently described in horses and in captive baboons, respectively (9, 14).

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infection in patients with AIDS, being predominantly associated with wasting and diarrhea. However, recent studies have provided clear evidence that these infections are not restricted to AIDS and are also common in immunocompromised non–HIV-infected individuals, such as solid-organ transplant recipients (5, 7, 8). Moreover, Sak et al. have recently provided new insights into the understanding of microsporidiosis, highlighting a high prevalence of microsporidia in healthy subjects (11,12). These findings suggest that the real distribution of microsporidiosis in humans is probably underestimated (1).

*Enterocytozoon bieneusi* is probably the species in the genus with the most extensive genetic diversity (13). This genetic diversity of *E. bieneusi* relies on molecular methods, genetically distinct isolates having similar morphological characteristics (13). Presently, sequencing analysis of the ITS rRNA region is still considered the gold standard for genotyping and epidemiological studies of *E. bieneusi* (13, 15). Until now, more than 90 *E. bieneusi* genotypes have been reported, with new genotypes being regularly described (9, 13). It is now clear that both host-adapted *E. bieneusi* genotypes with narrow host ranges and potentially zoonotic genotypes with wide host specificity have been identified (13). Analysis of nucleotide sequences of ITS rRNA provides valuable information about the transmission and pathogenic potential of *E. bieneusi* because it allows determination of the genotype in human and animal isolates. The most striking finding of our report is the discovery of a new and highly divergent *E. bieneusi* genotype in a human host. Indeed, nearly all of the genotypes that have been shown to infect humans so far belong to group 1 (3). To the best of our knowledge, human infections by *E. bieneusi* isolates that cluster outside group 1 are exceptional and have been described in a single recent study performed in Central Africa (3). Taken together, *E. bieneusi* genotype MAY1 and the one recently reported by Breton et al. in Gabon and Cameroon (genotype CAF4) are the only descriptions of a highly divergent *E. bieneusi* genotype infecting a human host (3). Genetic similarity between our new genotype and the one described in an equid species, as well as the close contact with horse stools, suggest a zoonotic transmission from horses to our patient. Unfortunately, stools from horses were not available for analysis.

In the present case, *E. bieneusi* infection appeared 7 years after transplantation. This finding is in agreement with previous data.

**FIG 1** Phylogenetic relationships among *Enterocytozoon bieneusi* genotype group 1 and all other genotypes reported and available in GenBank as well as the nucleotide sequence identified in this study (MAY1), inferred by a neighbor-joining analysis of the ITS rRNA gene sequence, based on genetic distances calculated by the Kimura two-parameter model. ○, nucleotide sequence determined in this study (MAY1). Bootstrap values of less than 75% are not shown. The complete phylogenetic tree, including all *E. bieneusi* ITS genotypes published at the time this report was prepared, is available upon request.
from literature showing reported cases occurring from 19 days to up to 15 years after kidney transplantation (7). At the time of diagnosis, the patient was given immunosuppressive therapy that was maintained while nitazoxanide was introduced. Albendazole and fumagillin are the main drugs used to treat *E. bieneusi* infections (7). However, relapse is often observed after albendazole withdrawal and the efficacy of fumagillin is counterbalanced by its adverse effects, with fumagillin exhibiting bone marrow toxicity leading to thrombocytopenia and neutropenia (1, 7). Here, a complete recovery was obtained with nitazoxanide. This drug is not considered the first-line therapy but has been already used with success in an HIV-infected patient (2).

In conclusion, we report a new and highly divergent genotype of *E. bieneusi* that is also the first described *E. bieneusi* genotype with close proximity to one recently described in horses (14). Whereas the real prevalence of microsporidiosis in equid species has been poorly investigated so far, our data suggest that horses could act as potential sources of human microsporidial infections as suggested recently (14). These findings must be considered for the management of immunocompromised patients such as HIV-infected patients and solid-organ transplant recipients. In high-risk patients, giving advice such as avoiding close contact with animals and following prophylactic measures will probably reduce the burden of this neglected disease.

**Nucleotide sequence accession number.** ITS rRNA nucleotide sequences of our *E. bieneusi* isolate have been deposited in the GenBank database under accession number JN595887.

**REFERENCES**