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Successful Treatment with Nitazoxanide of *Enterocytozoon bieneusi* Microsporidiosis in a Patient with AIDS

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A patient with AIDS and chronic diarrhea caused by *Enterocytozoon bieneusi* was successfully treated with nitazoxanide, producing a complete clinical and parasitological response, while off of antiviral therapy. This suggests that nitazoxanide may be effective in treating microsporidiosis caused by *E. bieneusi*, a disease for which there is no established treatment.

Microsporidiosis can be responsible for a severe diarrheal syndrome in AIDS patients, the severity of which is related to the degree of immunosuppression of the patient. Clinical trials have shown partial effectiveness of albendazole in treating microsporidiosis caused by *Encephalitozoon intestinalis* (8), but there is no established treatment for infection caused by *Enterocytozoon bieneusi*, the most prevalent microsporidian pathogen. We report a case of *E. bieneusi* diarrheal syndrome associated with AIDS and successfully treated with nitazoxanide.

Nitazoxanide is a new broad-spectrum antiparasitic drug effective against a broad range of protozoa, nematodes, cestodes, and trematodes (10, 12). It has been used for the treatment of cryptosporidiosis in AIDS patients (4, 11).

A 37-year-old formerly intravenous-drug-addicted male, infected with both human immunodeficiency virus (HIV) and hepatitis C, presented in early April 1997 in the day care HIV clinic of the Purpan Hospital in Toulouse with mild diarrhea consisting of four pasty stools per day without weight loss. Examinations of three pretreatment fecal samples over approximately 90 days by the Weber trichrome stain technique and with a fluorescence assay (Uvitex 2B, Ciba-Geigy, Basel, Switzerland), later confirmed by PCR (9), showed that this patient was infected by *E. bieneusi*, his first opportunistic infection. The number of spores observed in fecal samples by Weber trichrome stain and fluorescence assay increased significantly between the time of the initial diagnosis in April and later examinations in June and just before treatment in July. A full workup did not reveal any other protozoal or bacterial pathogens (7). The source of microsporidial infection could not be identified. His travel in the previous 12 months had been limited to southern Europe and North America. He had been HIV positive since 1986, and at the time of consultation, his CD4 count was 126/mm^3 (14%), with a viral load of 5.2 log (156,000) copies/ml. He had previously received several antiviral combination therapies, beginning in October 1989 with zidovudine alone, and he was currently taking stavudine, lamivudine, and indinavir. Approximately 1 month after the initial diagnosis of *E. bieneusi* infection, the patient was hospitalized with mixed hepatitis consistent with his hepatitis C, probably worsened by his antiretroviral therapy (1, 5, 6) (alkaline phosphatase, 498 IU/liter [normal, <280 IU/liter]; γ-glutamyltransferase, 141 IU/liter [normal, <25 IU/liter]; serum glutamic oxaloacetic transaminase, 340 IU/liter [normal, <34 IU/liter]; serum glutamic pyruvic transaminase, 185 IU/liter [normal, <37 IU/liter]; total bilirubin, 213 μM/liter [normal, <17 μM/liter]). Triple therapy was discontinued, and his hepatitis symptoms improved, but the diarrhea worsened, with 5 to 10 episodes of liquid stool per day and with night awakening. An attempt was made to treat the condition with albendazole at a dose of 1,200 mg/day for a total of 15 days (30 April to 14 May 1997). The patient did not respond. This is not surprising, because albendazole is known to be weakly effective against *E. bieneusi* (2). While he was in the hospital in May 1997, he experienced pain at the profound palpation of the right hypochondrium. His weight remained stable at approximately 70 kg, and he was still negative for other protozoal or bacterial pathogens.

Nitazoxanide therapy was initiated on 1 July 1997 at a dose of 1,000 mg twice a day for 60 consecutive days. Informed consent was obtained from the patient prior to initiation of treatment. The drug was supplied by Romark Laboratories, Tampa, Fla., for compassionate use in France. At the time of treatment, the patient was not receiving any antiretroviral therapy. When treatment with nitazoxanide was initiated, his CD4 count was 85/mm^3 (13%), and his viral load was 5.5 log (330,000) copies/ml. The diarrhea resolved during treatment, with pasty stools on day 10 of treatment and normal bowel movements by the end of the 60 days of treatment with nitazoxanide. Fecal examination by the techniques described above showed a few spores on day 7 of therapy and negative stools on days 11, 19, and 60 of treatment. Clinical and biological tolerance were good. Liver function tests conducted during and after treatment showed no significant changes compared to baseline values. Three posttreatment fecal examinations, including PCR, conducted over 2 months following the end of the treatment with nitazoxanide did not reveal any microsporidial spores, and the patient continued normal bowel movements.

After it was evident that the patient's microsporidial diarrhea had resolved in August 1997, antiviral therapy was reinitiated with dianosine and lamivudine. At the end of the treatment with nitazoxanide, his CD4 count was 53/mm^3 (10%), and his viral load was 5.2 log (170,000) copies/ml. The patient remained without any symptoms of microsporidiosis until he died in December 1997 due to chronic cirrhosis of the liver secondary to hepatitis C.

Nitazoxanide has been reported to be effective in cell culture against *E. intestinalis* and *Vittaforma corneae* (3). This case study suggests that nitazoxanide is effective clinically and that pro-

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spective trials should be performed to evaluate its possible role in treating microsporidiosis in patients with AIDS.

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