Natural History of Intestinal Microsporidiosis among Patients Infected with Human Immunodeficiency Virus

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A chart review of 73 human immunodeficiency virus (HIV)-infected patients with enteric microsporidiosis was conducted to define the natural history of microsporidiosis. A substantial proportion of patients remained symptomatic after 6 months (54.8% with persistent diarrhea and 51.2% with weight loss). Predictors for persistent diarrhea included high HIV RNA viral load and no initiation of protease inhibitor therapy.

Two microsporidia (Enterocytozoon bieneusi and Encephalitozoon intestinalis) have been identified as possible causes of diarrheal illness in human immunodeficiency virus (HIV)-infected patients. However, despite numerous clinical descriptions of patients with symptomatic gastrointestinal disease attributed to enteric microsporidiosis, studies have concluded that enteric microsporidia have limited pathogenicity (2, 6, 7). To better describe the presentation and clinical course of patients with enteric microsporidiosis, a retrospective chart review of patients with enteric microsporidiosis was conducted through a nationwide survey of the National Institutes of Health-sponsored AIDS Clinical Trials Group sites.

HIV-infected patients with a stool specimen positive for microsporidia between 29 January 1993 and 8 August 1997 at the Medical Center of Louisiana at New Orleans (MCLNO) (n = 47), San Francisco General Hospital (San Francisco, California) (n = 15), Cook County General Hospital (Chicago, Illinois) (n = 8), or State University of New York (Buffalo, New York) (n = 3) were eligible for this study. Stool specimens were examined for microsporidia at the clinical laboratory of each hospital, using a modified trichrome (chromotrope 2R) stain. Routine ova and parasite examinations to evaluate for other parasitic infections and screening for enteric infections caused by bacteria such as Aeromonas, Plesiomonas, Campylobacter, Yersinia, Salmonella, and Shigella were performed at all sites. In addition, bloody stools were tested for Escherichia coli O157H7 at the MCLNO and San Francisco sites. Specimens submitted to MCLNO were transported to the Tulane Regional Primate Research Center for secondary identification of microsporidia, using a fluorescent stain (Calcofluor 2MR white) to screen for microsporidia, followed by a modified trichrome stain for corroboration (3). Species identification was unavailable for all specimens.

Medical records of eligible patients were retrospectively abstracted 6 weeks after the first positive stool specimen (baseline data) and 6 months after the index stool specimen until death or study termination. Persistent diarrhea was defined as continued or worsening diarrhea within 6 months after initial diagnosis, as per the provider’s progress notes. Weight loss was defined as a loss of ≥10% of baseline body weight within 6 months of primary diagnosis. Statistical testing for categorical variables included Fisher’s exact test and chi-square analysis. Nonparametric median testing and analysis of variance were utilized for continuous variables.

The cohort was predominantly male (89.1%), between the ages of 30 and 40 years (57.1%), and of Caucasian or African American origin (42.5 and 46.5%, respectively). Most (57.4%) had a CD4 cell count at diagnosis of less than 50 cells/ml and a viral load of greater than 10,000 copies/ml (79.1%). Nine patients had stool specimens positive for other pathogens during follow-up. These pathogens included Cryptosporidium spp., Giardia lambia, Campylobacter, Entamoeba histolytica or Entamoeba dispar, and Blastocystis hominis. Testing to distinguish between E. histolytica and E. dispar was not performed. Three patients had microsporidia identified from additional specimens (conjunctival swab, sinus aspirate, or clean-catch urine specimen). These patients also had positive stool specimens. Forty-three (58.9%) of the 73 patients had 6 months of follow-up. There were no significant baseline demographic or clinical differences between the patients with 6 months of fol-

<table>
<thead>
<tr>
<th>Clinical characteristic</th>
<th>Persistent diarrhea after 6 mo (n = 23)</th>
<th>No diarrhea after 6 mo (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean no. of stools/day at diagnosis (SE)</td>
<td>5.6 (±1.0)</td>
<td>3.6 (±0.6)</td>
</tr>
<tr>
<td>Mean no. of stool specimens submitted after diagnosis (SE)</td>
<td>2.4 (±0.3)</td>
<td>1.2 (±0.5)</td>
</tr>
<tr>
<td>CD4 cell count of ≥50 cells/ml</td>
<td>60.0%</td>
<td>60.0%</td>
</tr>
<tr>
<td>Median viral load (no. of copies/ml)</td>
<td>63,863</td>
<td>9,360†</td>
</tr>
<tr>
<td>History of opportunistic process</td>
<td>60.9%</td>
<td>66.7%</td>
</tr>
<tr>
<td>ARV use at diagnosis</td>
<td>52.2%</td>
<td>63.2%</td>
</tr>
<tr>
<td>ARV use after diagnosis</td>
<td>73.9%</td>
<td>84.2%</td>
</tr>
<tr>
<td>PP use after diagnosis</td>
<td>21.7%</td>
<td>52.6%/‡</td>
</tr>
<tr>
<td>Albenza use at diagnosis</td>
<td>8.7%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Antidiarrheal use at diagnosis</td>
<td>78.3%</td>
<td>47.4%</td>
</tr>
<tr>
<td>Morphine use at diagnosis</td>
<td>8.7%</td>
<td>15.8%</td>
</tr>
<tr>
<td>Narcotic use at diagnosis</td>
<td>17.4%</td>
<td>26.3%</td>
</tr>
</tbody>
</table>

ARV, antiretroviral therapy (includes protease inhibitor and non-protease inhibitor regimens).

PI, protease inhibitor therapy.

¶ Not inclusive of morphine or antidiarrheal agents described in the text.

Statistically significantly different from the values for persistent diarrhea (P < 0.05 by Fisher’s exact test or by the nonparametric median test).

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Narcotic use at diagnosis
Antidiarrheal use at diagnosis 80.0% 60.6%
Albendazole use at diagnosis 10.5% 9.1%

(23.3%) of these patients experienced weight loss of 10% of body weight among patients with microsporidiosis

Mean no. of stool specimens submitted after diagnosis (SE)
Diarrhea after 6 mo of follow-up
CD4 cell count of 50 cells/dl
Median viral load
History of opportunistic process
ARV+ use at diagnosis
ARV use after diagnosis
PI+ use at diagnosis
Albendazole use at diagnosis
Antidiarrheal use at diagnosis
Narcotic use at diagnosis (probable use, diarrhea)
Narcotic use at diagnosis (probable use, pain)

Protease inhibitor therapy use was significantly associated with no persistent diarrhea (Table 1). In other prior studies, most patients with chronic enteric microsporidiosis who were initiated on potent antiretroviral therapy reported no further diarrhea (1, 4, 5). It is probable that administration of potent therapy may be effective in controlling HIV viremia, allowing immune restoration and resolution of intestinal infection. With the lack of an effective treatment against Enterocytozoon bieneusi, clinicians should be strongly encouraged to optimize antiretroviral therapy to avoid a poor outcome.

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REFERENCES