Cryptosporidiosis: An Unrecognized Cause of Diarrhea in Elderly Hospitalized Patients

Marguerite A. Neill, Susan K. Rice,* Nadeem V. Ahmad,† and Timothy P. Flanigan

From the Department of Medicine, Division of Infectious Diseases, Brown University School of Medicine, Providence, Rhode Island

Human infection with Cryptosporidium species has been increasingly noted in the past decade. We conducted a broad-based longitudinal review in a community setting and found that a Cryptosporidium species was detected in one-third of the specimens screened over a 5-year period. Thirty-six patients were identified, comprising three distinct clinical groups: persons with human immunodeficiency virus (HIV) infection (18 patients); young, otherwise healthy persons (5 patients); and, surprisingly, chronically ill elderly persons (13 patients). In six (46%) of the 13 elderly patients, both Cryptosporidium and Clostridium difficile toxin was identified, suggesting that Cryptosporidium may be a copathogen in some instances of nosocomial diarrhea. Acquisition in an institutional setting was suspected for nine (69%) of the elderly and three (17%) of the HIV-infected patients. Elderly patients with chronic illnesses constitute a newly recognized category of persons at risk for cryptosporidial infection. In this group cryptosporidiosis may be far more common than previously recognized, may be acquired institutionally, and can mimic and occur with Clostridium difficile-associated diarrhea.

Enteric illness is the most common clinical feature of human cryptosporidial infection and ranges from self-limited diarrhea in immunocompetent children and adults to a severe prolonged enteritis refractory to treatment in immunocompromised persons [1]. Studies of the causative agents of diarrhea in both pediatric and adult populations suggest that this coccidian parasite is the most common parasitic cause of diarrhea worldwide, surpassing Giardia species [2]. The infective dose for healthy adults is \(10^2\) oocysts [3], and the high rates of secondary transmission in both sporadic [4–6] and outbreak [7] settings indicate the highly infective nature of cryptosporidial oocysts.

Anecdotal case reports, small series, and outbreak investigations have pointed to several patient groups with increased frequencies of cryptosporidial infection, such as day-care center attendees, travelers in and residents of less-developed countries, persons having contact with animals, hospitalized patients with hematologic malignancies, and (increasingly) patients with AIDS [2, 8–10]. The highest reported prevalence has been among children <2 years of age [2, 8], with overall infection rates being greater in the developing world than in industrialized nations.

Prior surveys of cryptosporidiosis (reviewed in [2] and [8]) have largely been conducted for periods of \(\leq 1\) year and have examined highly selected populations. Because a comprehensive survey over a several-year period had not previously been reported, we undertook a broad-based longitudinal review in which we sought to identify the clinical and epidemiological characteristics of patients with this infection seen in a community hospital setting.

Methods

A retrospective chart review was conducted at a 325-bed acute care community hospital in a university teaching program in Rhode Island. Microbiology records for the 5-year period from 1 January 1987 through 31 December 1991 were reviewed to identify persons whose stool smear was positive for Cryptosporidium oocysts. Data from the clinical records of these patients were collected on a standardized form.

Stool specimens were examined for cryptosporidial oocysts only if specifically ordered, as such testing was not included in coprodiagnostic studies for ova and parasites. Stools were concentrated by means of a formalin-ethyl-acetate suspension method. Fecal smears from the concentrate were made on glass slides and stained with DMSO modified acid-fast solution (Trend Scientific, St. Paul, MN). The stained slides were screened at 40× magnification for typical pink- or red-staining oocysts, which were then confirmed as Cryptosporidium species by examination under a 100× oil-immersion lens. Testing for fecal Clostridium difficile toxin was performed by cytotoxicity assay.
Table 1. Clinical characteristics of patients with cryptosporidiosis seen at a community hospital.

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Healthy (n = 5)</th>
<th>HIV-related* (n = 18)</th>
<th>Elderly (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>25 (16–35)</td>
<td>36 (27–65)</td>
<td>77 (63–93)</td>
</tr>
<tr>
<td>Male:female</td>
<td>4:1</td>
<td>18:0</td>
<td>4:9</td>
</tr>
<tr>
<td>No. (%) of patients with diarrhea necessitating hospitalization</td>
<td>0</td>
<td>5 (28)</td>
<td>7 (54)</td>
</tr>
<tr>
<td>Mean no. of days of diarrhea prior to diagnosis of cryptosporidiosis (range)</td>
<td>53 (21–92)</td>
<td>31 (2–120)</td>
<td>12 (1–90)</td>
</tr>
<tr>
<td>No. (%) of patients whose cryptosporidiosis possibly was nosocomial</td>
<td>0</td>
<td>3 (16.7)</td>
<td>9 (69.2)</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>0</td>
<td>8 (44)</td>
<td>6 (46)</td>
</tr>
<tr>
<td>No. (%) of deaths due to cryptosporidiosis</td>
<td>0</td>
<td>1 (12.5)</td>
<td>0</td>
</tr>
</tbody>
</table>

* Seventeen patients were seropositive for HIV, and one had risk factors for HIV infection.

Table 2. Characteristics of elderly patients with cryptosporidiosis.

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>No. (%) of patients (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical condition</td>
<td></td>
</tr>
<tr>
<td>Preexisting malignancy*</td>
<td>8 (62)</td>
</tr>
<tr>
<td>Chronic illness without malignancy*</td>
<td>5 (38)</td>
</tr>
<tr>
<td>Prior immunosuppressive medication</td>
<td></td>
</tr>
<tr>
<td>Cytotoxic chemotherapy</td>
<td>4 (31)</td>
</tr>
<tr>
<td>Corticosteroid therapy</td>
<td>3 (23)</td>
</tr>
<tr>
<td>Enteropathogen detected†</td>
<td></td>
</tr>
<tr>
<td>Salmonella, Shigella, or Campylobacter species</td>
<td>0</td>
</tr>
<tr>
<td>Clostridium difficile toxin</td>
<td>6 (46)</td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>1 (8)</td>
</tr>
</tbody>
</table>

* Includes lung cancer (2 patients), lymphoma (2 patients), colon cancer, prostate cancer, oral cancer, and metastatic adenocarcinoma with unknown primary source (1 each).

† Includes temporal arteritis, chronic obstructive pulmonary disease, coronary artery disease, hypertension, polycythemia vera, alcoholism, and dementia.

‡ All 13 patients were tested for each pathogen.

Results

During the 5-year study period, 36 patients with cryptosporidial infection were identified. The patients could be divided into three distinct clinical groups: (1) persons seropositive or with risk factors for HIV; (2) healthy adults without risk factors for HIV infection, and (3) elderly hospitalized persons. The clinical characteristics of these patients are presented in Table 1.

In none of the 17 patients with HIV infection was cryptosporidiosis a sentinel marker for undiagnosed HIV infection; 8 patients (47%) had previously diagnosed AIDS, and for 8 others cryptosporidiosis was an AIDS-defining criterion. Eight of the HIV-seropositive patients died, but only one patient’s death was directly attributable to unremitting cryptosporidiosis.

Clinical features of the elderly patients are shown in Table 2. All patients had diarrhea for an average of 11.9 days (range, 1–90 days) prior to the diagnosis of cryptosporidial infection, and all were hospitalized at the time of diagnosis. Two patients had colostomies, and in both cases cryptosporidial infection was associated with an increase in colostomy output, sufficient to require hospitalization. There were six deaths, none directly attributable to cryptosporidiosis. Nine elderly patients (69%) may have acquired cryptosporidial infection in an institutional setting, seven nosocomially and two during long-term nursing home residence. Nosocomial acquisition was suspected for four patients whose diarrhea developed >72 hours after hospital admission and for three patients who had diarrhea when readmitted within 10 days of a previous hospital discharge. Three nosocomially infected patients had overlapping hospital stays, but their rooms were on separate floors and different wings of the hospital, and the dates of onset of diarrhea did not suggest that the cases resulted from cross-infection.

An infectious disease specialist established the diagnosis of cryptosporidiosis for all 13 elderly patients. All were thought to have C. difficile-associated diarrhea and had been tested for fecal C. difficile toxin before stool smears were obtained for detecting Cryptosporidium. None of the six patients positive for C. difficile toxin responded to treatment with metronidazole and/or oral vancomycin. In the cases in which stools were tested, fecal leukocytes were more commonly present in those stools positive for C. difficile toxin than in those negative for C. difficile toxin (4/5 vs. 2/5 cases, respectively).

Discussion

In our longitudinal review of cryptosporidial infection at a community hospital, 36% of the patients identified were elderly, a finding not noted in previous reports [2, 8, 10–12]. Discussions of the age distribution of cases in earlier reviews have emphasized the high incidence in pediatric age groups, and patients older than 60 years were only rarely reported [2, 11]. A search of the medical literature found only one short note describing cryptosporidiosis in three patients aged 68, 70, and 78 years [13]. Our findings suggest that elderly patients, particularly those who are hospitalized, represent a group in
which cryptosporidial infection may occur more commonly than previously recognized.

All the elderly patients described herein were thought to have *C. difficile*-associated diarrhea, a highly plausible diagnosis when diarrhea develops in institutional settings. Coinfection with both *C. difficile* and *Cryptosporidium* species was found in six patients (46%). None responded to therapy for *C. difficile* infection, although fecal leukocytes were detected in four patients, a finding more consistent with *C. difficile* infection than cryptosporidial infection. From the remaining seven patients (54%), *Cryptosporidium* was the only (and unanticipated) pathogen recovered. Our interpretation of these findings is that even patients highly likely to have diarrhea due to *C. difficile* may not have it; moreover, patients who do have apparent *C. difficile*-associated diarrhea may be infected with other enteric agents as well. This latter observation offers a potential explanation for continued diarrhea in patients appropriately treated for enteric illness with *C. difficile*.

Nosocomial and institutional outbreaks among bone marrow transplant recipients [14], undernourished infants [15], and HIV-infected individuals [4, 16] have been reported. Our results suggest that elderly, chronically ill individuals may be an additional group at risk for institutional acquisition of cryptosporidial infection. Whether these patients acquired infection via person-to-person transmission or from another source (e.g., oocysts usually found in contaminated water, coupled with the susceptibility of this population to infection, make either mode of transmission plausible.

Morbidity associated with cryptosporidial infection (as assessed by hospitalization) was highest in the elderly, of whom more than one-half (54%) were hospitalized for diarrhea. There were no deaths directly attributable to cryptosporidial infection, despite the patients’ advanced age and the high frequency of comorbid conditions in this group. Of note, however, was the striking similarity of overall mortality among both the HIV-infected and elderly patients (44% and 46%, respectively).

Because many clinical laboratories do not include acid-fast staining for *Cryptosporidium* species in fecal tests for ova and parasites, this pathogen will remain undetected unless appropriate testing is ordered. Lack of detection due to lack of testing is common and can significantly delay both recognition of an outbreak and implementation of control measures, as illustrated in recent outbreaks [17, 18]. Although there is presently no accepted form of treatment, establishing the diagnosis of cryptosporidiosis can limit additional and potentially invasive testing as well as reinforce the need for strict enteric isolation of infected patients in the institutional setting.

In the United States, the proportion of the population that is >65 years of age and has malignancies or chronic medical conditions has been steadily increasing, and cryptosporidial infection in this group may be far more frequent than previously thought. Recent calls for public health surveillance for cryptosporidiosis [17, 18] should not overlook the potential utility of targeting the elderly as a sentinel population to assess the presence and extent of cryptosporidial infection in the community.

Acknowledgment

The authors thank Colette Meehen for her expert secretarial support.

References