Cryptosporidial enteritis in a homosexual male with an acquired immunodeficiency syndrome

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Enteritis associated with *Cryptosporidium sp* is described in a homosexual male with an acquired immunodeficiency syndrome.

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Infection in man by *Cryptosporidium sp* is an extremely unusual form of zoonosis.[1] The organism has been identified in approximately 12 different host animals[2] and has recently been implicated as an important cause of diarrhea in both animals[1, 3-6] and man.[1, 7-17] Of the 24 human cases reported, 16 occurred in previously healthy adults and were usually related to sporadic outbreaks of cryptosporidial enteritis in calves. Eight cases occurred in immunodeficient patients[2] who had been treated with chemotherapeutic agents.

To increase awareness of this unusual zoonosis as a cause of diarrhea, we present a case of cryptosporidial enteritis in a homosexual male with an acquired immunodeficiency syndrome.

Case report

A 38-year-old white male homosexual was well until 15 months before admission when proctitis and a perirectal abscess developed secondary to infection with *Entamoeba histolytica*. Soon after successful treatment with metronidazole, he complained of fatigue, intermittent colds with fever, chills, night sweats, and a cough. Nine months later, profuse, watery, nonbloody diarrhea developed, with up to 15 stools per day associated with a 40-pound weight loss. His physical examination was unremarkable. Diarrhea averaged 1110 cc/day in volume (normal, ≤200 cc) with 9.7 g/day fat (normal, ≤7.0 g). Stool was negative for phenolphthalein and was nonosmolar (stool sodium, 122 mEq/L; potassium, 17 mEq/L; and osmolality, 346 mOsm). Multiple stool cultures were negative for *Shigella sp*, *Yersinia sp*, *Salmonella sp*, and *Clostridium difficile*. Stool volumes decreased markedly on fasting. Serum gastrin was 154 pg/ml. Sweat chloride test results were within normal limits.

Results of other studies included a cytomegalovirus serum titer of 1:128, positive serology for hepatitis-B surface antigen, white blood cell count (WBC) of 3000 cells/mm^3 with 60% polysegmented neutrophils, 20% bands, and 10% lymphocytes. Hemoglobin was 8.8 g/dl, and the platelet count, 140,000/mm^3. Serum IgG and IgM levels were within normal limits whereas serum IgA was slightly increased at 505 mg/dl (normal, up to 490 mg/dl). He manifested cutaneous anergy to a skin test panel consisting of purified protein derivative, *Monilia*, *Trichophyton*, Varidase and mumps. Lymphocyte transformations with the use of phytohemagglutinin, pokeweed mitogen, and concanavalin A performed twice, 16 days apart, were markedly reduced (*Table*). The following were either within normal limits or negative: antinuclear antibody, rheumatoid factor, upper gastrointestinal tract endoscopy, colonoscopy, abdominal and head CT scans, chest radiograph, bone marrow differential, and stool specimen for ova and parasites.

Table. Results of lymphocyte transformation tests

Mitogen	Counts per minute		
	Original test	Repeat test	Lower limit of normal
Phytohemagglutinin	11,508	18,617	56,280
Pokeweed mitogen	3,379	2,241	11,245
Concanavalin A	1,496	3,262	35,109

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Cryptosporidium organisms were found on the biopsy specimen. Cytomegalovirus was subsequently identified in the urine. Routine blood cultures were negative. The patient was placed on successive trials of metronidazole and quinacrine. The diarrhea subsided only to return accompanied by a productive cough, fever, and dyspnea. Oral candidiasis was present and a chest radiograph revealed a new left lower lobe infiltrate. An open lung biopsy specimen demonstrated *Pneumocystis* pneumonitis. Culture obtained from the lung grew cytomegalovirus. The patient was treated with ketoconazol, sulfamethoxyzole (Bactrim), vancomycin, tobramycin, erythromycin, 6 alpha-methylprednisolone (Solu-Medrol), and later carbenicillin. Despite therapy, his pulmonary status continued to deteriorate and he died after two months of hospitalization.

At autopsy a severe, bilateral pneumonitis secondary to cytomegalovirus, *Pneumocystis*, and *Pseudomonas aeruginosa* was found. In addition, cytomegalovirus was cultured from the liver, gallbladder, and lungs. Cytomegalovirus inclusions were identified histologically in the lungs, gallbladder, and throughout the gastrointestinal tract. *Cryptosporidium* organisms, however, were not identified on postmortem sections of the gastrointestinal tract.

Methods and materials

Small bowel biopsy specimen was obtained by Rubin tube. Specimens were fixed in both zinc-substituted Zenker's and buffered formalin. Routine paraffin-embedded sections of 4μ thickness were stained with hematoxylin and eosin. For electron microscopy, tissue was salvaged from the formalin-fixed paraffin blocks and processed as follows: deparaffinization in xylol, graded alcohols to 50%, postfixation in osmium tetroxide, graded alcohols to 100%, and embedment in Spurr epoxy. Thin sections cut at 600–900 Å were stained with uranyl acetate and lead citrate and examined with a Philips 400 electron microscope.

Results

Examination of the small bowel biopsy specimen by light microscopy revealed moderate villous

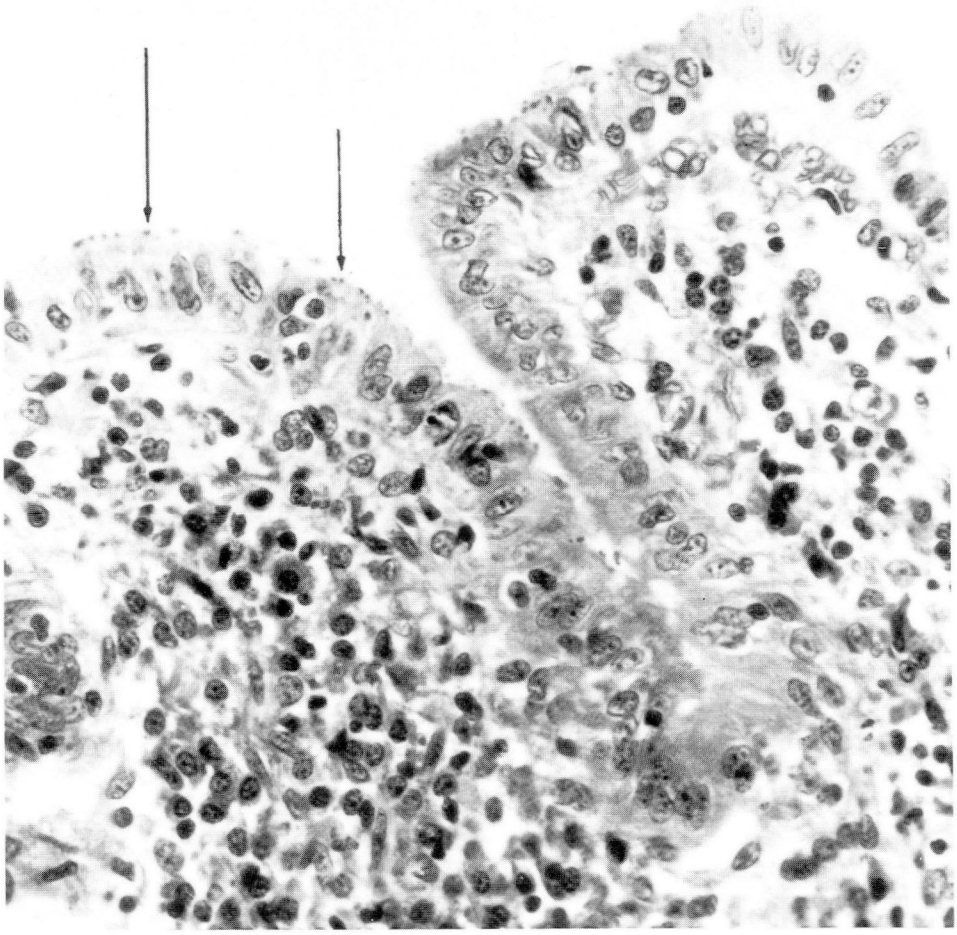

Figure 1. Small bowel biopsy specimen exhibiting shortened villi and increased inflammatory cell infiltrate throughout the mucosa. *Cryptosporidium* organisms appear as tiny dots (arrows) on the microvillous border (hematoxylin and eosin ×200).

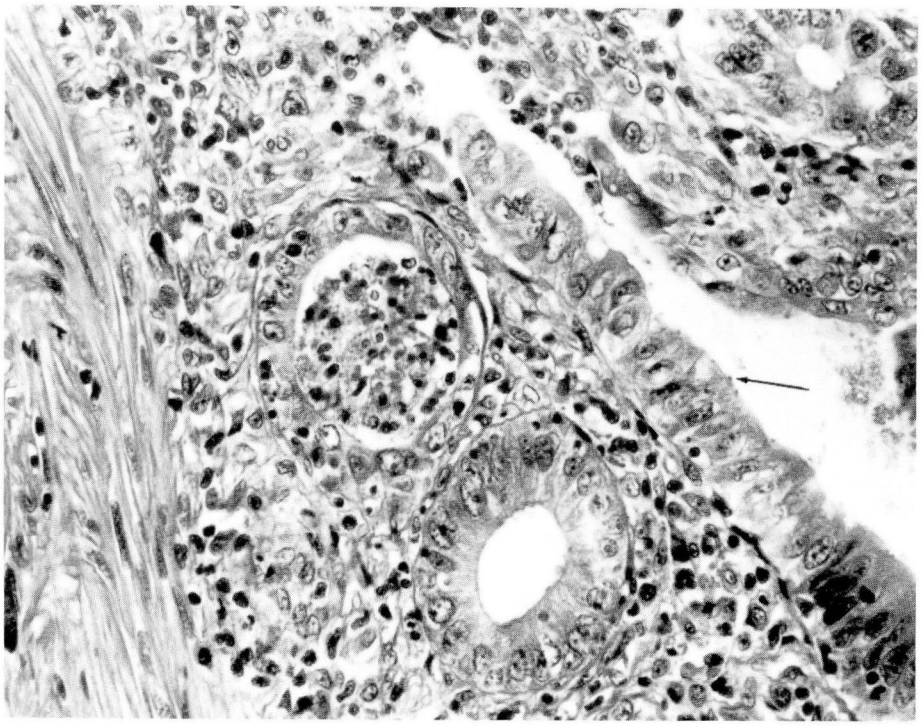

Figure 2. Small bowel biopsy specimen illustrating mixed inflammatory infiltrate and eosinophilic crypt abscess. Several *Cryptosporidium* organisms are also visible (arrow) (hematoxylin and eosin ×200).

shortening with lengthened, hyperplastic crypts. An increased inflammatory cell infiltrate in the epithelium and lamina propria was composed of lymphocytes, plasma cells, and a few eosinophils. A single eosinophilic crypt abscess was identified. On the luminal villous border, numerous basophilic-staining spherical organisms approximately 3μ in diameter were seen (*Figs. 1–3*). No intracellular organisms were identified. Electron microscopy demonstrated developing trophozoites and macrogametocytes of *Cryptosporidium sp.* These were located exclusively in the microvillous border, adhering by a specialized attachment organelle. Macrogametocytes could be distinguished by their intracytoplasmic clear "polysaccharide" granules and dense granules (*Fig. 4*).

Discussion

Male homosexuality and an acquired immunodeficiency syndrome have been associated with an aggressive form of Kaposi's sarcoma and with infections by a number of opportunistic organisms, including viruses (CMV, herpes simplex, hepatitis A and B), bacteria (*Mycobacterium tuberculosis*, *Mycobacterium avium-intracellulare*, *Klebsiella pneumoniae*, and other aerobic gram-negative bacilli), fungi (*Candida albicans* and *Cryptococcus neoformans*), and the following protozoans: *Pneumocystis carinii*, *Toxoplasma gondii*, and *Entamoeba histolytica.*[18–22]

To this list of opportunistic infections we now add a new case of enteritis secondary to the coccidian *Cryptosporidium.* Our patient exhibited all of the clinical and immunologic stigmata of an acquired immunodeficiency state.

Cryptosporidium sp are thought to be acquired by ingestion of contaminated food and water.[23,24] Although occasional human cases have been asymptomatic,[7] the vast majority of infections have been associated with diarrhea. In the previously healthy host the disease is self-limiting, running a course of approximately two weeks with ultimate complete recovery.[1,7] In the immunocompromised patient, however, the course tends to be protracted and refractory to drug therapy.[8–14] Moreover, the diarrhea is often voluminous, exceeding 1 L/day,[10] and many cases are fatal. No particular treatment has been shown to be of proved value in human cryptosporidiosis although quinacrine, metronidazole, trisulfapyrimidine, amphotericin, and chloroquine have all been tried.

The diagnosis of cryptosporidiosis depends upon demonstration of either the organism in biopsy ma-

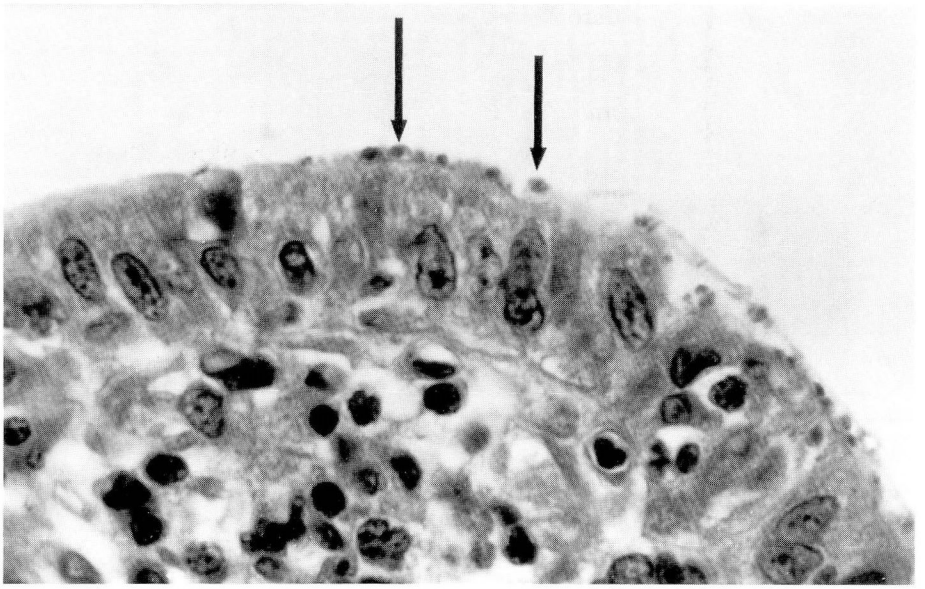

Figure 3. High magnification view of luminal surface of the small intestine. *Cryptosporidium* organisms appear as basophilic spherical bodies measuring approximately 3μ in diameter seen exclusively on the microvillous border (arrows) (hematoxylin and eosin ×1000).

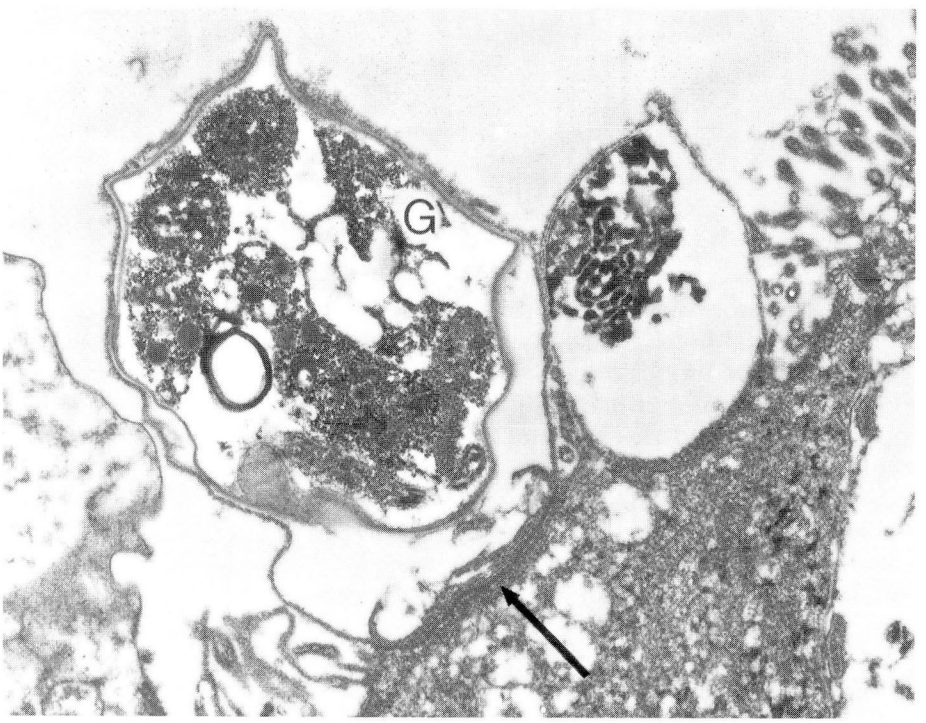

Figure 4. Electron photomicrograph illustrating developmental forms of *Cryptosporidium* organisms. Macrogametocyte (left) is distinguished from trophozoite (right) by presence of intracytoplasmic "polysaccharide" granules (*G*). Note the attachment organelle (arrow) (lead citrate and uranyl acetate ×24,000).

terial or the infective oocyst in fecal or duodenal aspirate specimens. Coverslip flotation with the use of Sheather's sugar solution with phase-contrast microscopy has been successfully employed to demonstrate the infective oocyst in stool in most veterinary and in some clinical cases.[1,7] However, the majority of clinical cases have been documented by either small bowel biopsy or rectal biopsy specimens with subsequent demonstration of the organism by both conventional light and electron microscopy.

Cryptosporidium organisms must be differentiated from the flagellate *Giardia lamblia* and other coccidia. *Giardia lamblia* is much larger and has a characteristically different morphology.[25] *Cryptosporidium sp* is distinguished from other coccidia in that it inhabits exclusively the striated or microvillous border of the intestinal epithelium and adheres to it by a highly specialized attachment organelle.[23, 24]

Recognition of this unusual cause of diarrhea requires a high index of suspicion on the part of both clinician and pathologist. Although coverslip flotation techniques with phase-contrast microscopy have been useful in the hands of some experienced investigators, the majority of cases have been diagnosed on the basis of characteristic light and electron microscopic findings in biopsy material. Only when additional cases are recognized will the various chemotherapeutic agents used for controlling this infection be adequately evaluated.

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