

# Clinical Manifestation and Diagnosis of Cryptosporidiosis In Adult Infected with HIV

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## ABSTRACT

*Cryptosporidiosis is a rare infection caused by a coccidian parasite, Cryptosporidium, which could cause diarrhea in humans, especially those who are immunocompromised. Cryptosporidiosis could cause self-limited diarrhea infection in immunocompetent hosts, but in immunocompromised hosts, especially those with AIDS, the diarrhea can be chronic and severe. To date, no known effective therapeutic agents have been identified. The following is one case report of cryptosporidiosis of a 27 year-old male admitted with chronic diarrhea since 2 months. Endoscopy of the ileum and colon showed hyperemia, erosion and edema, and biopsy was performed. Histopathological examination of ileum showed an atrophic villous and atypical degeneration. There was a number of circular cryptosporidium lining up along the surface of epithelium. There was inflammatory cell infiltration, consisting of lymphocytes, eosinophils and a few neutrophils in the lamina propria. Serological examination revealed an HIV-positive result.*

**Keywords:** *Cryptosporidiosis, HIV, diarrhea*

## INTRODUCTION

Cryptosporidiosis is a disease of the digestive system cause by an intracellular protozoan parasite called *Cryptosporidium parvum*, which could cause diarrhea in humans. Occasionally, the parasite may also be found in the pancreatic duct<sup>1</sup>; hepatobiliary or respiratory system<sup>1-3</sup>.

First recognized by Clarke and Tyzzer over 80 years ago, *Cryptosporidium* was reported as a human pathogen in 1976 by Nime. The outbreak in Carrollton, Georgia in 1987 involved 13.000 suspected cases. The largest and most publicized water-borne disease outbreak in U.S. history occurred in the spring of 1993 in Milwaukee, Wisconsin, which affected an estimated number of over 403.000 people and caused 4,400 to be hospitalized<sup>4,5</sup>. A study in the region of Ljubljana 1998-1999 found 360 cases with positive stool samples for *Cryptosporidium* spp<sup>6</sup>. In developed countries, the

prevalence of infection ranged from < 1% to 4.5 % of individuals surveyed by stool examination. The prevalence is significantly higher in developing regions of the world. Cryptosporidiosis can infect normal hosts and immunosuppressed patients. Cryptosporidiosis is among the most common causes of persistent diarrhea in patients with AIDS in the United State.<sup>7</sup> Cryptosporidiosis has been increasingly recognized as a cause of severity in AIDS.<sup>2-4</sup> Children under two years of age, animal handlers, travelers to endemic areas, men who have sex with men, and people who came in close contact of infected individuals are those most likely to be infected.<sup>7</sup>

The symptoms of cryptosporidiosis were watery, non-bloody to severe diarrhea, stomach cramps, nausea, vomiting, anorexia, fever, and weight loss. Symptoms can occur 2-12 days after exposure to infected feces<sup>7</sup>. The infection is usually self-limiting and symptoms last for up to two weeks. However, in

individuals with weakened immune systems, such as cancer patients, those on steroid therapy, organ transplant recipients, and HIV-infected persons, cryptosporidiosis can be long-lasting and in some cases fatal<sup>2,3,8,9</sup>. We report one case of cryptosporidiosis which has been identified at the Department of Anatomical Pathology, Faculty of Medicine, University of Indonesia, which is the first known case in our Department.

The purpose of this report is to draw attention to this case because it may cause endemic and epidemic diarrhea and there is still no effective therapeutic means to treat it. It can be cause of mortality in patients with weakened immune systems, particularly those with AIDS.

### CASE REPORT

A 27 year-old male was admitted to Dr. Cipto Mangunkusumo National General Hospital with chronic diarrhea and weakness in his legs since two months prior to admission. The patient had already been treated at the hospital for the diarrhea twice.

Physical examination showed general weakness. Other results of the physical examination were within normal limits.

The routine blood examination revealed a hematocryte of 36% (normal 40-48%), SGOT 78  $\mu$ /l (normal 10-36  $\mu$ /l), and SGPT 63  $\mu$ /l (normal 10-45  $\mu$ /l). Chemical blood examination found a sodium level of 134 mEq/L (normal 135-145 mEq/L), a potassium level of 2.1 mEq/L (normal 3.5-5.5 mEq/L), and a chloride level of 111 mEq/L (normal 100-106 mEq/L).

Endoscopic examination of the ileum and colon showed hyperemia, erosion and edema. Hence, the patient was diagnosed with ileitis and colitis (Figure 1, 2).

### PATHOLOGICAL REPORT OF THE BIOPSY

#### Gross examination

The biopsy specimen measured 0.2 cm in diameter.

#### Microscopic findings

The specimen from the ileum showed villous atrophy and atypical degeneration at the gland. The lamina propria was massively infiltrated with lymphocytes, eosinophils and neutrophils. There were *Cryptosporidium* that appeared as tiny spherical bodies lining up along the epithelium surface. It was concluded as an ileitis cryptosporidiosis (Figure 3, 4, 5).

The specimen from the colon showed similar appearance. The surface epithelium was intact, the crypt structure was normal, and the lamina propria was infiltrated with lymphocytes and a few neutrophils. It was concluded as a chronic in-destructive colitis.

The stool examination was found to contain gram-negative bacteria and pseudohypha. The serological examination for HIV presented a positive result.

### DISCUSSION

The pathophysiology of the diarrhea that accompanies cryptosporidiosis has been suggested to be a cholera-like enterotoxin,<sup>2</sup> but this issue remains controversial. Infection localized in the small intestine results in villous atrophy and fusion, with leukocyte infiltration into the intestinal mucosal. Although morbidity is high, mortality is low and recovery is spontaneous. T-lymphocyte-mediated immune response has been implicated in the recovery from cryptosporidiosis.<sup>10</sup> Since this immune response is

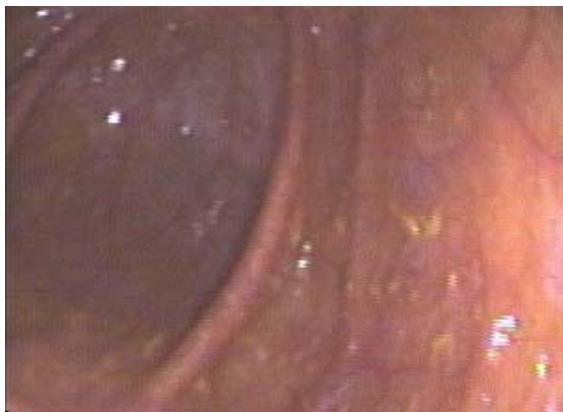


Figure 1 & 2: Endoscopy of ileum and colon showing hyperemia, erosion, and edema

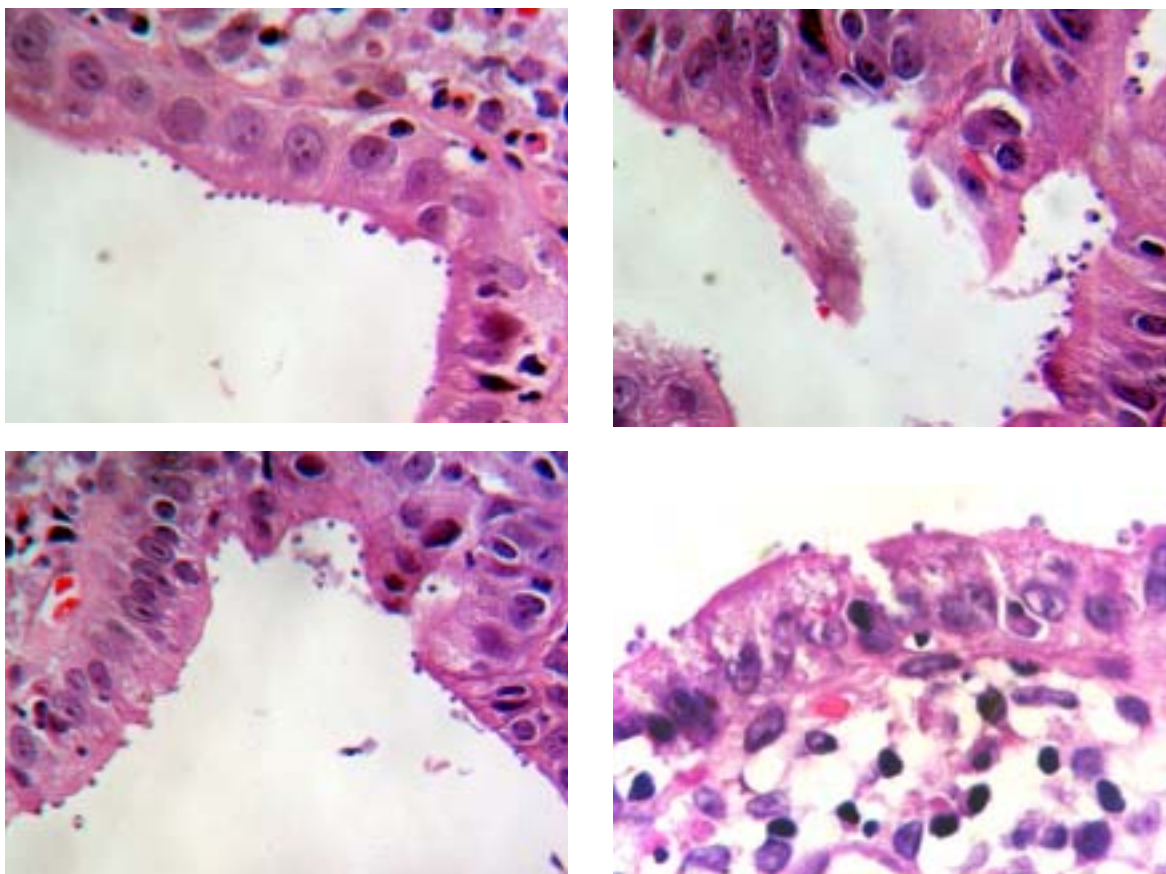


Figure 3, 4, 5, 6. Cryptosporidium appearing as tiny spherical bodies lining up along the epithelial surface (H&E, 400x, 1000x)

decreased in immunodeficient hosts, in such patients the infection can be long lasting and can be a cause of mortality.

In this case, the patient suffered from AIDS that weakened his immune system, so that he was not able to recover from chronic intestinal infection.

The diagnosis of Cryptosporidium in patients with diarrhea was based on stool examination.<sup>7</sup> The characteristic finding was the presence of acid-fast staining oocysts. The oocysts are small, spherical, measuring 4 to 5  $\mu\text{m}$  in diameter.<sup>1,2,11</sup> They may be concentrated by the formalin – ether technique, but must be identified by staining methods. The recommended method is the modified Ziehl-Neelsen technique. An alternative is the safranin-methylene blue technique<sup>11</sup> and modified acid-fast technique. Serologic tests are available for detection of fecal cryptosporidial antigen.<sup>7</sup> Enzyme immunoassays (EIA) can be used to measure serum antibodies to Cryptosporidium<sup>12</sup>. Microscopy using direct fluorescent antibody (DFA) assay offers the highest combination of sensitivity and specificity, and is

considered the gold standard by many laboratories.<sup>4,13</sup> Polymerase chain reaction (PCR) provides a new method that may help detect Cryptosporidium in water supplies or asymptomatic carriers.<sup>4</sup> Upper and/or lower endoscopy with biopsy may establish a diagnosis of microsporidial infection of the small intestine in over half the patients.<sup>7</sup> Organisms may be seen adhering to the brush border of intestinal epithelium.<sup>2</sup>

In this case, the diagnosis had been made by endoscopy with biopsy that showed Cryptosporidium appear as tiny spherical bodies along the epithelium. They are 4-5  $\mu\text{m}$  in diameter. Unfortunately, Cryptosporidium oocysts could not be found in the stool examination. This was because the stool examination that was done with wet stain and was not stained used the Ziehl-Neelsen technique, causing oocysts to appear similar to yeast. They only found gram-negative bacteria and pseudohypha that may be a cause a chronic colitis in this patient.

The differential diagnosis of Cryptosporidium is *Isospora belli*. This can be differentiated from

Cryptosporidium in stool examination by virtue of differences in size, shape, and number of sporocysts. Isospora oocysts are large, oval, slightly elongated, measure about 32 x 16 µm and contain a central individual mass of protoplasm.<sup>11</sup>

To date, no known specific therapy effective against Cryptosporidium has been identified. The treatment is supportive, and is directed toward preventing dehydration and electrolyte imbalance. Anti-diarrhea medications may be prescribed.<sup>2</sup>

Although treatment is very limited, new approaches that may reduce secretion or enhance repair of the damaged intestinal mucosa are under study. Paramomycin (500 to 750 mg qU) is one of few agents that have shown modest benefit in controlled studies. This agent does not eradicate the parasite in immunocompromised patients, but it slightly reduces parasite number (from 314 x 10<sup>6</sup> to 109 x 10<sup>6</sup> oocysts shed per day) and decreases stool frequency.<sup>4</sup> In some HIV-infected patients, the symptom of cryptosporidiosis abated when they began zidovudine (AZT) or somatostatin therapy.<sup>3</sup>

In this case, the patient had antimicrobial, antifungal, symptomatic drug and intravenous fluid therapy with NaCl and KCl. Antimicrobial and antifungal agents were administered for this patient due to the finding of gram-negative bacteria and pseudohypha in the stool examination. Intravenous fluid therapy was to treat electrolyte imbalance.

The most important thing is to prevent spreading of Cryptosporium oocysts. The oocysts are quite hardy and resist killing by routine chlorination. It is also difficult to filter.<sup>2,4,13</sup> Ozone is probably the most effective chemical means of inactivating Cryptosporidium oocysts. New approaches to the eradication of infectious oocysts from water supplies are needed, possibly using reverse osmosis, membrane filtration, or electronic or radiation methods, instead of the ineffective chemical or difficult filtration techniques currently used.<sup>4</sup>

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