case report

Cryptosporidiosis in a renal transplant patient treated with paromomycin

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Cryptosporidium is an intracellular protozoan parasite and one of the most commonly reported enteric pathogens in both immunocompetent and immunocompromized hosts worldwide. It causes an infection resulting in diarrhea and biliary tract disease[1] and is now recognized as a major cause of diarrhea in both immunosuppressed and immunocompetent hosts. The risk of severe and or prolonged disease is high in immunocompromized patients including solid organ transplantation recipients. It is more commonly seen in countries with increasing population and poor sanitary conditions. Prevalence is much higher in human immunodeficiency virus (HIV)-infected patients.[2] The treatment of cryptosporidiosis in immunosuppressed patients is still not clearly defined and response to proposed therapies is suboptimal.

CASE

A 60-year-old woman who received a living-related renal transplant 4 months earlier, presented with a 5-day history of colicky abdominal pain and watery diarrhea 6-7 times per day. There was no vomiting, fever, or other constitutional symptoms. Her immunosuppressant regimen included tacrolimus 2 mg twice daily, prednisolone 10 mg once daily, and co-trimoxazole DS once daily. Other medications included mycostastin Suspension and omeprazole.

On examination she was fully oriented and afebrile with a blood pressure of 70/40 mm Hg. Her abdomen was soft and lax, with mild tenderness in the epigastrium, left flank and sluggish bowl sounds. The remainder of her physical examination was unremarkable. She was started on intravenous fluid resuscitation with a normal saline bolus.

Lab results showed a normal complete blood count, urea 22 mmol/L, creatinine 351 umol/L, potassium 4.1 mEq/L, and sodium 132 mEq/L. Blood and stool cultures were negative. Stool for *Clostridium difficile* toxin was negative. Colonoscopy with multiple biopsies from transverse, descending and rectosigmoidal colon were taken, and all showed the heavy presence of cryptosporidium on PAS stain (Figure 1). Esophageogastroduodenoscopy was normal. Biopsies taken from the esophagus, stomach and duodenum showed no evidence of parasite, granuloma or inclusion bodies.

She was started on paromomycin 500 mg twice daily and loperamide. Her condition gradually improved, and her creatinine normalized with intravenous hydration. She was discharged after four days of admission on paromomycin 500 mg orally three times dailty for 1 month in addition to her previous anti-rejection regimen. On follow-up visits, her diarrhea had completely stopped. One month after discontinuing paromomycin she had her regular bowel movement while her immunosuppressant was the same as before her hospitalization. Her serum creatinine was 73 µmol/L and her trough tacrolimus level was 6.6 µmol/L.

DISCUSSION

Cryptosporidiosis is a protozoal infection, which has been increasingly recognized as a cause of diarrheal illness in both immunocompetent and immunocompromised hosts. The risk of severe and prolonged disease is more in patients with cellular and humoral immune deficiencies including HIV-infected population, organ transplant recipients, patients on immunosuppressant drugs, patients with IgA deficiency or hypogammaglobunemia.[3]The frequency of isolating *Cryptosporidium* from stool of renal transplant patients was significantly higher than that found in two control groups, one consisting of patients with end-stage renal disease on hemodialysis and the other consisting of patients with hypertension without renal abnormalities.[15] Infection is more common in countries with poor sani-

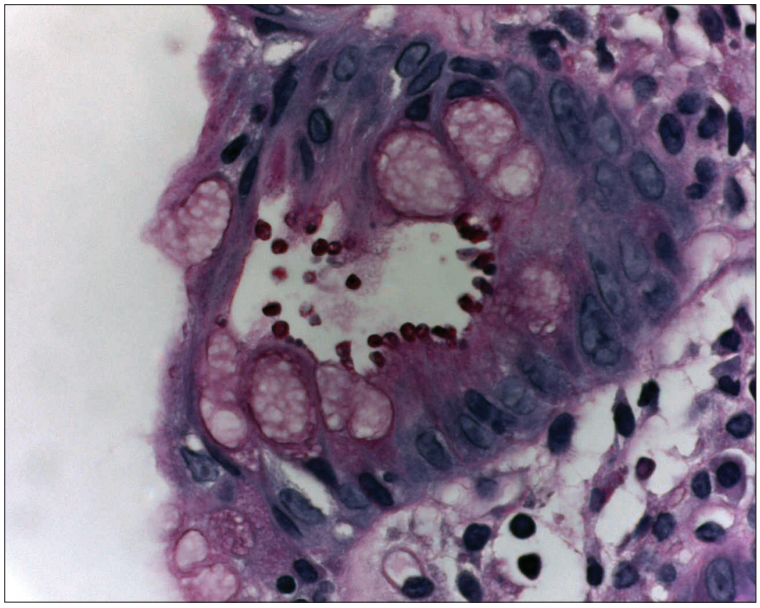

Figure 1. PAS stained section of colon biopsy showing positive organisms in the glandular lumen (100X, PAS Stain).

tary conditions and increased crowding. Although more frequent in children less than 2 years of age, outbreaks occur worldwide in all age groups.[4,5] Since early 1980s, massive outbreaks have been linked to municipal drinking water supplied in different parts of the world, especially Europe and North America.[6]

Twenty-four species of *Cryptosporidium* have been identified. *Cryptosporidium parvum* is the only species responsible for clinical disease in humans, but it is not host specific, since it also infects other mammals.[7] Its transmission is via spreading from infected person or animal or fecally contaminated environmental source, such as food or water.[8] Pathogenesis is not well understood, and no toxin has been identified. It causes secretary diarrhea, and the intracellular nature of the infection interferes with absorption of gut secretions. The organism can spread via intestinal lumen to involve biliary system where they can cause strictures and cholangitis.

Diagnosis is usually established by identification of the organism in stool, duodenal aspirate or biopsy specimen. Since cryptosporidia spores are not detected by routine examination of the stool for ova and cyst, special stains are used such as Modified Acid Fast Stain. Fluorescent assays have been used to increase the sensitivity compared to light microscopy.[9,10] Enzyme immunoassay (EIA) kits are also available. Acid fast stain has a sensitivity of 94% and a specificity of 76% and EIA has a sensitivity and specificity of 100% compared to direct immunofluorescence.[11] Serological detection using indirect fluorescent-antibody (IFA) assay or ELISA is also available. In our case, stool examination for parasite was negative but biopsies from the colon were positive.

There is no reliable therapy for cryptosporidiosis. Recovery usually depends on immune status of the host. Non-specific therapies are often given to immunodeficient patients including anti-diarrheal and supportive care with enteral or parenteral nutrition. A number of specific therapies have been tried. The largest experience is with paromomycin in acquired immune deficiency syndrome (AIDS) patients, where it was not found to be more effective than placebo.[12] In AIDS patients, the best treatment is improvement of the immune status with Highly Active Antiretroviral Therapy, which can help resolve cryptosporidium infection.

In renal transplant patients, no data are available on the best modality to treat this infection. Reduction of immunosuppressive therapy alone was reported to be associated with cure of *Cryptosporidium*-induced sclerosing cholangitis.[13] Our patient responded well to paromomycin combined with an anti-motility agent. Establishing a definite role for paromomycin in treating cryptosporidium infections in renal transplant patients needs a well-designed clinical trial. This is the first case report of the use of paromomycin in the treatment of *Cryptosporidium* in a renal transplant patient.

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