Annals of Parasitology 2022, 68(2), 399–403
doi: 10.17420/ap6802.446
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Case report

Intractable diarrhoea due to co-infection with *Cystoisospora belli* and *Trichuris trichiura* unraveling a severely compromised host immune status

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ABSTRACT. *Cystoisospora belli* is an obligate intracellular coccidian parasite known to cause chronic persistent diarrhoea in immunocompromised individuals such as human immunodeficiency virus (HIV) infection, long term corticosteroid therapy, cancer chemotherapy and solid organ transplant recipients. *Trichuris trichiura* is a soil transmitted helminth, which predominantly causes asymptomatic or mild infections but heavy worm load can sometimes lead to chronic diarrhoea, tenesmus or rectal prolapse. We report a case of co-infection with *Cystoisospora belli* and *Trichuris trichiura* in an adult patient causing intractable diarrhea, which led to the unraveling of a severely compromised immune status in the patient enabling an appropriate therapeutic approach and further management.

Keywords: *Cystoisospora belli*, *Trichuris trichiura*, coccidia, diarrhoea

Introduction

Cystoisospora belli (formerly *Isospora belli)*, is an obligate intracellular coccidian parasite known to cause chronic persistent diarrhoea in immuno-compromised individuals such as human immunodeficiency virus (HIV) infection, long term corticosteroid therapy, cancer chemotherapy and solid organ transplant recipients [1–3]. *Trichuris trichiura* (whip worm) is a soil transmitted helminth, which predominantly causes asymptomatic or mild infections but heavy worm load can sometimes lead to chronic diarrhoea, tenesmus or rectal prolapse [4,5]. We report a case of intractable diarrhea due to co-infection with *C. belli* and *T. trichiura* in an adult patient, following which diligently conducted investigations led to the unraveling of a severely compromised immune status in the patient, enabling an appropriate therapeutic approach and further management. The case is being reported to re-emphasize the importance of thoroughly investigating for any underlying immune-compromised disease in case of finding any coccidian parasite in clinical samples.

Case presentation

A 41-year-old man, goldsmith by occupation and a frequent traveler, presented with large volume, foul-smelling, painless, watery diarrhea (with a stool frequency of 10–12/day), associated with excessive flatulence and vomiting for the past two days. Further history revealed that he was having persistent painless, watery and foul smelling loose stools for the past 4 months (with a stool frequency of 4–6/day) associated with nausea and occasional non-bilious vomiting. He had a significant weight loss of approximately 12 kg in last 3 months. Patient was a known diabetic on medication since the past 5 years and chronic alcoholic for past 10 years (with an approximate intake of 60 ml/day). He had no history of any gastrointestinal bleed, fever, pain

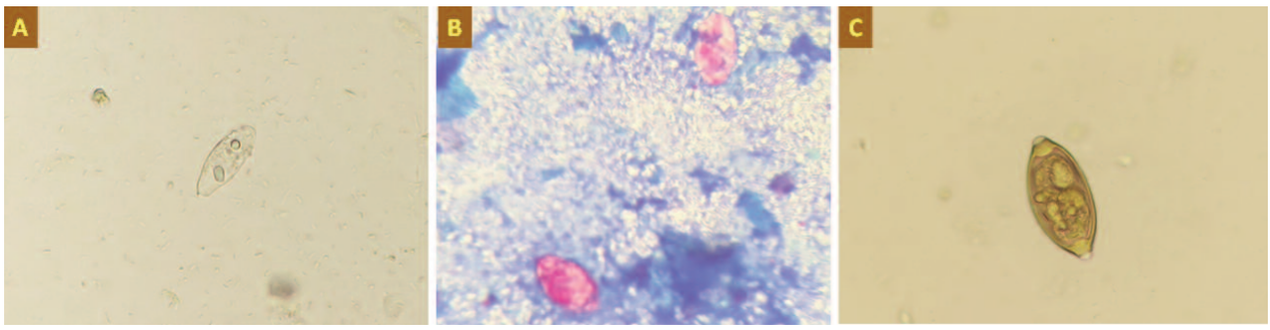

Figure 1. A. Stool sample showing oocysts of *C. belli* in wet-mount, 400×; B. oocysts of *C. belli* in modified acid-fast stain, 1000×; C. bile-stained ova of *Trichuris trichiura*, 400×

abdomen, joint pain cough or shortness of breath.On examination, the patient was alert and oriented with a blood pressure of 100/68 mmHg, a pulse rate of 122/min and a temperature of 37°C. Laboratory investigations revealed a slightly low total leucocyte count of 3.6×10^9/l (N_{76} $L_{11}E_8M_5$), low total red blood cell count (2.48×10^{12}/l), low platelet count 99×10^9/l, a low hemoglobin level of 73 g/l and low hematocrit of 23.8%. He had an extremely low serum iron level of 28 µg/dl, low total iron binding capacity of 161 µg/dl and a high serum ferritin level of 617 ng/ml. Investigations also revealed elevated levels of serum enzyme parameters (amylase 215 U/l, lipase 176 U/l, alkaline phosphatase 1076 U/l, alanine aminotransferase 71U/l, aspartate aminotransferase 69 U/l and gamma-glutamyl transferase 446 U/l) and raised erythrocyte sedimentation rate of 125 mm/hr. Serum electrolytes, random blood sugar level, glycosylated haemoglobin level, and lipid profile were within normal limits. An ultrasonogram of the abdomen revealed a 5×5 cm, well-defined, hypoechoic, thick-walled collection without any internal vascularity in segment 7 of the liver possibly indicating a resolving hepatic abscess.

Stool sample submitted for microscopic examination revealed many oocysts of *Cystoisospora belli* (4–6/high power field) both in saline wet-mount and modified acid-fast stain preparation (Fig. 1A and 1B) as well as few barrel-shaped, bile-stained ova of *Trichuris trichiura* (2–3/coverslip) (Fig. 1C). Subsequently, the patient tested reactive for anti-HIV-1 antibodies and hepatitis B surface antigen indicating an underlying severely compromised immune status. He had a high hepatitis Be antigen (HBeAg) level of 1490.33 signal-to-cut off ratio and high hepatitis B virus deoxyribonucleic acid (HBV DNA) level of $>10^7$ IU/ml indicating active virus replication and high infectivity. He was treated with high-dose trimethoprim-sulphamethoxazole (TMP-SMZ) oral therapy (160/800 mg) four times a day for two weeks followed by twice daily for three weeks and oral albendazole (400 mg twice a day for 3 days) for his diarrheal symptoms due to *Cystoisospora* and *Trichuris* infections respectively. He was also counseled and for HIV-HBV co-infection, he was started on highly active antiretroviral therapy, which included tenofovir. Supportive therapy was provided to improve his hydration and iron status. Symptoms improved within one week of therapy with decrease in diarrheal episodes to 2–3/day along with decrease in vomiting. The patient was advised for regular follow-up on discharge and to repeat stool microscopic examination at periodic intervals (at least once every two months). He was also counseled to continue regular therapy for HIV and HBV infection with continuous monitoring of his immune status.

Discussion

Cystoisospora belli is a major health concern among HIV-infected patients as well as in patients with other immunosuppressive conditions, such as prolonged use of steroids and other immuno-suppressive therapy for primary autoimmune disorders, solid organ transplant recipients and those treated for tumours [1–3,6]. It is responsible for causing chronic diarrhoea in 8% to 23.81% of acquired immunodeficiency syndrome (AIDS) patients and in 0.7% to 8% in patients with other types of compromised immune status [7–10]. The infection is common in many tropical and subtropical regions of the world including the Caribbean, Central and South America, Africa, and South-East Asia, and is acquired through the ingestion of a sporulated oocyst either through contaminated food or water. Since humans are the only known natural hosts of the disease, transmission appears to be confined to a

direct faecal-oral anthroponotic cycle [6]. Although generally a self-limiting infection in immunocompetent patients, cystoisosporiosis in the immunocompromised status can result in the development of chronic life-threatening diarrhoea and dehydration. It is also considered an AIDS-defining illness.

Worldwide, *Cryptosporidium* species has generally been reported to be the most common coccidian parasitic infection in the immunocompromised host, followed by *Isospora* and *Cyclospora*, including studies reported from India [1,8–11]. In a meta-analysis, the pooled prevalence of *Cryptosporidium* infection in HIV-infected people was found to be 14.0% (3283/43,218; 95%CI: 13.0–15.0%) while that for *Isospora* was found to be 2.5% (788/105,922; 95%CI: 2.1–2.9%) [1]. However, several recent studies, both from India and outside, have noted the emergence of *C. belli* as the most common enteric pathogen in HIV-infected individuals [12–16]. Infection with the parasite usually leads to chronic persistent diarrhoea. Severe diarrhoea has been reported on instances such as renal transplant patient on immunosuppressive drugs [17], infection with human T-lymphotropic virus type I (HTLV-1) [18,19], Good syndrome [20], complication in ulcerative colitis during treatment with azathioprine and infliximab [21], rheumatoid arthritis treated by corticosteroids and methotrexate immunosuppressive therapy [22], thymoma [23], non-Hodgkin's lymphoma [24], and in HIV-infected patients [25]. Similar to the present case, a patient with severe large volume diarrhoea, with 10–20 bowel movements per day and a history of intermittent diarrhoea, nausea, vomiting, severe loss of appetite, and a 100-pound weight loss in the preceding nine months was diagnosed with underlying HTLV-1 infection [19]. In another case, a patient presenting with severe and extremely watery diarrhea was discovered to have stage IV non-Hodgkin's lymphoma during examinations for his chronic diarrhoea persisting since one month [24]. Isosporiosis usually responds well to treatment with a 7–10-day course of oral TMP-SMZ therapy which provides rapid clinical and parasitological cure [18,19,24]. Other treatment regimens include pyrimethamine-sulfadoxine and nitazoxanide. As diarrhoea frequently recurs in AIDS patients; hence, secondary prophylaxis is recommended, using either TMP-SMZ three times weekly or sulfadoxine-pyrimethamine weekly [19]. Repeated stool microscopy at monthly intervals may be done to ensure eradication of infection.

As regards the other parasite found in the patient, *Trichuris trichiura* or whipworm is a soil transmitted helminth infecting about 600–800 million individuals worldwide [26]. Thus even though trichurosis is one of the commonest soil-transmitted helminthoses worldwide, most people affected are usually asymptomatic or have mild infections and harbor only small numbers of worms. Dysentery-like syndrome consisting of abdominal pain, tenesmus and bloody diarrhea with mucus and even rectal prolapse can occur with *T. trichiura* infection, but usually with massive and heavy worm load burden [4,5,27–30]. In the present case, even a low number of *Trichuris* infection in conjunction with *Cystoisopora* was able to facilitate a severe disease pathogenesis probably aided by the immune-compromised milieu of the patient. The patient may have acquired the infections due to contaminated food and water as he was a frequent traveler. *Trichuris* infection usually responds promptly to oral albendazole treatment.

In conclusion, a vigorous and aggressive search for an underlying immune disorder should always be done in a person testing positive for *Cystoisospora belli* infection. Co-infections with mildly pathogenic organisms, may contribute to severe disease pathogenesis in such cases. Immunocompromised individuals should be treated with a prolonged course of TMP-SMZ and routine prophylaxis should be considered as well. Periodic stool examinations should be done for *C. belli* as well as for other intestinal parasites in patients with recurrent or protracted episodes of diarrhoea with immunosuppressive disease.

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Received 24 January 2022
Accepted 04 April 2022