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Histology as a diagnostic tool for intestinal isosporiasis in immunocompromised patients

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ABSTRACT

Isoospora belli is an opportunistic protozoan causing wasting diarrhea especially in patients with an immunocompromised status. Diagnosis is usually established by demonstrating the oocyst of the organism on stool examination, which however can often be inconclusive. Serological tests for isosporiasis are currently not available. In such a scenario, biopsy often provides evidence for a confirmatory diagnosis. We describe two such cases, in which intestinal biopsy was the only diagnostic evidence of isosporiasis as the cause for chronic diarrhea.

1. Introduction

An increasing number of zoonotic infections in humans are found to be associated with a declining immunocompetent status of patients. Isosporiasis is a diarrheal illness seen in immunocompromised individuals in the tropics. It was first described by Virchow in 1860. The causative agent *Isoospora belli* (*I. belli*) is closely related to *Cryptosporidium* species. Transmission is by ingestion of oocyst contaminated food and person to person contact.

2. Case report

Case 1: A 41-year-old man presented with complaints of watery diarrhea for a duration of 8 months. Peripheral smear showed mild eosinophilia. Ultrasound abdomen, upper gastrointestinal endoscopy and colonoscopy were normal. Stool examination was negative for ova and cysts.

The patient was subsequently found to be retropositive. Duodenal biopsy was performed to ascertain the cause of diarrhea.

Case 2: A postrenal transplant, diabetic patient on immunosuppressive therapy, presented with diarrhea of 1 year duration. Stool examination was negative for any ova or cysts. On follow up, upper gastrointestinal endoscopy was normal. Colonoscopy showed an erythematous cecal patch. Biopsies were taken from multiple sites in the cecum, ileum, duodenum.

2.1. Histopathological findings and follow up

Light microscopic evaluation of haematoxylin and eosin stained sections of duodenum in the first case and the ileum in the second case, showed relatively normal small intestinal mucosa with focal villous flattening and crypt distortion. Some of the enterocytes on the villous surface epithelium, showed elongated, fusiform organisms suggestive of *Isoospora* merozoites in maturing schizonts (Figure 1). The lamina propria showed lymphoplasmacytic infiltrate and congested vessels. The duodenal and cecal biopsies of the second patient did not show any organism. The first patient responded well to trimethoprim–sulfamethoxazole therapy.

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On follow up, the second patient's diarrhea had subsided without any treatment. On enquiry, he was found to have been noncompliant with immunosuppressive therapy during that period, perhaps explaining his recovery. Subsequent intestinal biopsies did not reveal any parasite.

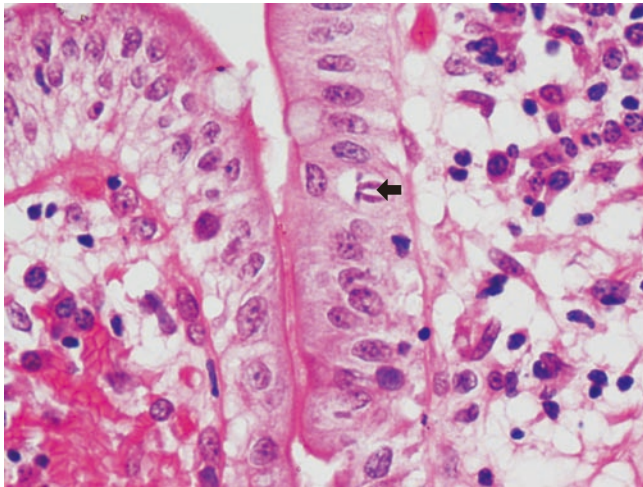


Figure 1. Microphotograph of *I. belli* organism in enterocyte (arrow). H & E X 400.

3. Discussion

I. belli is an obligate intracellular coccidian, spore forming parasite with a prevalence of 0.3%–0.5% in healthy individuals^[1]. Human Isosporiasis is caused by *I. belli*, though rarely, it can be caused by *Isospora natalensis*. It may cause acute, self limiting diarrhea in immunocompetent individuals or severe, chronic diarrhea in the immunocompromised^[2,3]. Stool examination may be unrewarding, as was noted in both cases. Diagnosis based on stool examination for oocysts is difficult, as these are scanty even in the presence of severe diarrhea. Incubation of the fecal specimen for 2 days with zinc flotation techniques often proves useful^[4].

I. belli, like cryptosporidium occurs in the small intestine. Cryptosporidium, however, appears to multiply only in the brush borders of the intestinal epithelial cells whereas *Isospora* invades them. Brandborg *et al*^[4] have elucidated, at length, the characteristic morphologic features of these organisms on light microscopy. Identification of any of the several sexual forms, gametocytes and merozoites in the subnuclear cytoplasm of the superficial epithelium and not in the crypts of the small intestine, is diagnostic of the disease. The organisms are rounded to banana shaped, pale staining^[1]. The sporozoite first colonizes the epithelial cell, and becomes a rounded trophozoite. These enlarge to mature into schizonts with numerous merozoites. Merozoites infest the adjoining epithelial cell and either become schizonts or sexual gametocyte. The macrogametocyte when fertilized, becomes the oocyst which is passed in the feces. It can also exist as unizuite tissue cysts with uninucleated zoites located in the centre with a vacuole around it^[4]. Non

diagnostic minimal histological alterations including mild shortening of villi, crypt hyperplasia, increased inflammatory cells especially eosinophils in the lamina propria of the infected intestinal mucosa may be observed. Hence, diligent search for these organisms under high power objective in an hematoxylin and eosin stained slide can prove to be rewarding. Special stains used to identify other organisms like *Giardia*, cryptosporidia and microsporidia may not be particularly useful in identifying *Isospora*. Besides the intestine, the organism has also been reported in lymph nodes and spleen in disseminated cases^[2]. The structure of the sporulated oocyst helps in deciding the species.

Sho Ogata and colleagues diagnosed an isolated case of intestinal cryptosporidiosis by endoscopic biopsy and have stressed the utility of histopathology in diagnosing such cases^[5]. No such reports however, have come to light of isosporiasis being diagnosed primarily on the basis of a biopsy. The diagnosis of isosporiasis is important, as patients respond promptly to treatment.

In conclusion, light microscopic examination of intestinal biopsy plays a crucial role in diagnosing intestinal parasitic infestation and can be instrumental in initiating prompt and specific treatment. Medical professionals treating immunosuppressed individuals should be aware of the role of biopsy in diagnosing this curable cause of diarrhea, especially in cases where fecal examination and endoscopy are inconclusive.

Conflict of interest statement

We declare that we have no conflict of interest.

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