CASE REPORT

An unusual complication in ulcerative colitis during treatment with azathioprine and infliximab: *Isospora belli* as 'Casus belli'

Juergen Stein,¹ Egbert Tannich,² Franz Hartmann³

¹Department of Internal Medicine, Krankenhaus Sachsenhausen, Frankfurt/Main, Germany

²Department of Molecular Parasitology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany

³Crohn-Colitis Centre Rhein-Main, Frankfurt/Main, Germany

Correspondence to
Professor Juergen Stein,
j.stein@em.uni-frankfurt.de

SUMMARY

The treatment of ulcerative colitis is based on systemic corticosteroids, immunomodulators such as cyclosporine and azathioprine and TNF- α antagonists. Patients undergoing such immunosuppressive treatment are more susceptible for infectious pathogens. Here, we report the case of a patient with a 13-year history of ulcerative colitis, treated initially with systemic corticosteroids in combination with immunomodulators, and subsequently with infliximab. The patient presented with severe watery diarrhoea, abdominal cramps, weight loss and low-grade fever. Stool examinations for cytomegalovirus, bacteria and parasites were negative. Following detection of numerous oocytes of *Isospora belli* (IB) in direct smear preparations of the diarrhoeic stool samples, the patient was successfully treated with trimethoprim-sulfamethoxazole (co-trimoxazole).

BACKGROUND

Parasites and other infections are a significant problem for immunocompromised patients and represent a serious and underestimated source of complications especially in patients with inflammatory bowel disease (IBD) because of the similarity of their symptoms.

CASE PRESENTATION

A 61-year-old man was diagnosed with ulcerative colitis 13 years ago. Ten years after diagnosis, he was successfully treated with cyclosporine (4 mg/kg body weight (BW) as induction therapy)/azathioprine (2.5 mg/kg BW as maintenance therapy) because of chronically active steroid-dependent disease. He became unresponsive to this therapy 2 years later, leading to initiation of infliximab (5 mg/kg BW). One year later, despite being in stable remission on azathioprine and infliximab, the patient developed weight loss and watery diarrhoea. Cytomegalovirus (CMV)-colitis was diagnosed histologically, and he was successfully treated with ganciclovir (5 mg/kg BW) over 3 weeks. Six months later, after returning from a vacation in India, he was admitted to our centre with abdominal cramps, severe debilitating watery diarrhoea (8–10 bowel movements per day), marked weight loss and low-grade fever.

INVESTIGATIONS

CMV testing was negative. The results of conventional stool examinations for bacteria (incl *Clostridium difficile*) and parasites were also negative. Further parasite examination by means of an

ethyl alcohol/formaldehyde concentration technique revealed suspicious oocyst-like features. Using acid-fast stain on a fresh smear, these features were shown to be *Isospora belli* oocysts. No other intestinal parasites were detected at that time.

TREATMENT

Initial treatment with metronidazole and ciprofloxacin effected no improvement of his condition. After detection of *I belli* oocysts, the patient was treated with 160 mg trimethoprim and 800 mg sulfamethoxazole administered as a double-strength (DS) tablet twice daily (TMP-SMX-DS) for 14 days.

OUTCOME AND FOLLOW-UP

The patient responded clinically as well as microbiologically. Treatment success was measured by cessation of diarrhoea at day 3 and negative stool examinations at day 7. The patient remained disease-free for at least 9 months.

DISCUSSION

Isospora belli (IB), an opportunistic protozoon, is one of the most commonly recognised causes of diarrhoea in patients with AIDS. It has also been reported in other immunosuppressive diseases, such as lymphoblastic leukaemia, adult T-cell leukaemia and Hodgkin's disease. IB infection has also been described in patients taking immunosuppressive drugs following transplantation.^{1 2} Here, we describe for the first time, a case of immunosuppression-related IB infection in a patient with ulcerative colitis undergoing treatment with azathioprine in combination with infliximab. IB belongs to the coccidia subclass of the family *Eimeria*, is only known to infect humans and is transmitted mainly by ingestion of infective oocysts in faecally contaminated food or water.³ Infected individuals may be asymptomatic carriers, or may suffer from gastrointestinal disease ranging from mild to severe malabsorption syndrome characterised by loose, foul-smelling stools.

IB infection is diagnosed by examination of stool and/or duodenal biopsy specimens. However, diagnosis of IB infection is difficult, especially if the concentrated sediment is from polyvinyl alcohol-preserved stool, as the oocysts of the organism are difficult to differentiate from some other faecal matter. Acid-fast and/or iodine staining are used for detection of *I belli* oocysts. Fluorescence-microscopic analysis is also effective for *Isospora* detection, staining with the

To cite: Stein J, Tannich E, Hartmann F. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009837

Figure 1 *Isospora belli* oocysts in stool smear preparation: iodine staining (×400).

fluorescent dyes auramine and rhodamine.⁴ It should be noted that stool preparations must be examined with great care to avoid misinterpretation of oocysts among faecal compounds revealed by iodine staining. In oocysts of *I belli*, the inner germinal mass (sporoblast) stains an intense red (figure 1).

In summary, isosporiasis should be suspected along with viral infection in immunocompromised patients with ulcerative colitis suffering from chronic persistent diarrhoea, abdominal cramps and weight loss. However, symptoms are non-specific and stool samples must be investigated meticulously for possible existence of oocytes, especially for *I belli* oocysts. Also, TMP-SMX (co-trimoxazole) is the drug of choice in patients suffering from isosporiasis.⁵

Learning points

- ▶ Isosporiasis should be suspected along with viral infection in immunocompromised patients with inflammatory bowel disease suffering from chronic persistent diarrhoea, abdominal cramps and weight loss.
- ▶ If *Isospora belli* is suspected, acid-fast and/or iodine staining should be used for detection.
- ▶ TMP-SMX (co-trimoxazole) is the drug of choice in patients suffering from isosporiasis.

Contributors JS analysed and interpreted the data, drafted the article, revised the manuscript critically for important intellectual content and approved the final version to be published. ET carried out the microbiological and parasitological diagnostics, revised the manuscript critically for important intellectual content and approved the final version to be published. FH provided clinical data, revised the manuscript critically for important intellectual content and approved the final version to be published.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 DeHovitz JA, Pape JW, Boncy M, *et al.* Clinical manifestations and therapy of *Isospora belli* infection in patients with the acquired immunodeficiency syndrome. *N Engl J Med* 1986;315:87–90.
- 2 Atambay M, Bayraktar MR, Kayabas U, *et al.* A rare diarrheic parasite in a liver transplant patient: *Isospora belli*. *Transplant Proc* 2007;39:1693–5.
- 3 Lindsay DS, Dubey JP, Blagburn BL. Biology of *Isospora* spp. from humans, nonhuman primates, and domestic animals. *Clin Microbiol Rev* 1997;10:19–34.
- 4 Bialek R, Binder N, Dietz K, *et al.* Comparison of autofluorescence and iodine staining for detection of *Isospora belli* in feces. *Am J Trop Med Hyg* 2002;67:304–5.
- 5 Farthing MJ. Treatment options for the eradication of intestinal protozoa. *Nat Clin Pract Gastroenterol Hepatol* 2006;3:436–45.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow