Isospora belli in a Patient with Liver Transplantation

Karaciğer Transplantasyonlu Bir Hastada *Isospora belli*

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ABSTRACT

Isospora belli is an opportunistic protozoon which should be monitored in patients with gastrointestinal complaints such as abdominal pain, nausea and diarrhoea, in both immune-compromised and immune-competent patients. Our case was a 35 year-old male patient who had received a liver transplant because of cirrhosis and hepatic fibrosis. A diarrhoeic stool sample of the patient was sent to the laboratory for microbiological and parasitological analyses. Faecal occult blood was positive and bacteriological analysis was negative. *Isospora belli* infection was diagnosed by detection of the oocysts in stool samples. Per oral trimethoprim-sulphamethoxazole treatment was given in 500 mg bid dose for 10 days. At the end of the treatment, no oocyst of *Isospora belli* was seen but non-pathogenic cysts of *Entamoeba coli* and vacuolar forms of *Blastocystis hominis* were observed. Two months later the patient had abdominal pain, fatigue and diarrhoea again and parasitological re-evaluation showed oocysts of *Isospora belli*. *(Turkiye Parazitol Derg 2012; 36: 247-50)*

Key Words: *Isospora belli*, post-transplant infections, liver transplantation

Received: 11.06.2012 **Accepted:** 03.10.2012

ÖZET

Isospora belli, immün yetmezlikli ve/ veya immun sistemi baskılanmış olgularda, karın ağrısı, ishal gibi gastrointestinal şikayetlerle başvuran hastalarda akla getirilmesi gereken fırsatçı bir protozoondur. Olgumuz; 2008 yılında Hepatit B'ye bağlı karaciğer sirozu ve fibroz tanısıyla karaciğer transplantasyonu uygulanmış 35 yaşında erkek hastadır. Hasta parazitolojik inceleme için başvurduğundan bu yana immmun-supresif tedavi almaya devam etmektedir. Karın ağrısı, halsizlik, ishal yakınmaları nedeniyle dışkının mikrobiyolojik ve parazitolojik açıdan değerlendirilmesi istenmiştir. Hastanın yapılan dışkı incelemesinde gizli kan pozitif, bakteriyolojik inceleme negatif olarak saptanmıştır. Parazitolojik incelemede nativ-lugol, parakon dışkı konsantrasyon tüpü ile çöktürme yöntemi ve modifiye asit-fast boyama yöntemleri ile Isospora belli ookistleri görülmüştür. Hastaya 500 mg bid dozda 10 günlük 2x1 trimethoprim-sulfamethoxazole tedavisi uygulanmıştır. Tedavi sonrası dışkı incelemesinde I. belli ookistleri görülmemiş, ancak apatojen amip olan *Entamoeba coli (E. coli)* kistleri görülmüştür. Hastanın 4 ay sonra yine karın ağrısı, halsizlik, ishal yakınmaları nedeniyle parazitolojik incelemeler yapılmıştır. Dışkı örneği incelendiğinde *I. belli* ookistleri yeniden görülmüş ve tedavi önerilmiştir. Sonuç olarak; klinisyen hekimlerin, özellikle immün yetmezlikli ve/veya immun sistemi baskılanmış olgularda karın ağrısı ve ishal gibi gastrointestinal şikayetleri olan hastalarda parazitolojik inceleme yaptırmaları faydalı olacağı kanaatindeyiz. *(Turkiye Parazitol Derg 2012; 36: 247-50)*

Anahtar Sözcükler: *Isospora belli*, transplantasyon sonrası infeksiyonlar, karaciğer transplantasyonu

Geliş Tarihi: 11.06.2012 **Kabul Tarihi:** 03.10.2012

This study is presented in 34th National Congress on Turk Microbiology which was held in Girne/Cyprus (7-10 November 2010).

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doi:10.5152/tpd.2012.58

Turkiye Parazitol Derg
2012; 36: 247-50

INTRODUCTION

Isospora belli (*I. belli*) is a coccidian parasite found in epithelium of the intestines, only causing infection in humans (1-3). Although widely seen all over the world, isosporiasis, which is caused by *I. belli*, is more frequent, especially in tropical and subtropical regions (2, 4-6). In developing countries, the incidence is particularly high in patients with chronic diarrhoea and those affected with-AIDS (1, 2, 7). It accounts for 10-20% of chronic diarrhoea cases of AIDS patients in Haiti and Africa (2).

Infected oocysts of *I. belli* measured about 22-33x12-15 µm in size, with round granular centres (2, 7, 8). In the oocyst wall, each one of the two sporoblasts develops into a sporocyst, which contains four sporozoites that are released from the cysts. Oocysts can survive for months in normal environmental conditions (2, 7). Fluidic and bloodless diarrhoea develops one week after the intake of water and foods contaminated with mature sporule oocysts via digestion. Colic, anorexia, weight loss and abdominal cramps may accompany diarrhoea problems, which sometimes last for 2 or 3 weeks. Fever is generally not common or rarely seen. Oocyst excretion may last for a few weeks after recovery. Cases with extra-intestinal isosporiasis where liver, spleen and lymphatic nodules were affected have also been reported (2, 5, 9).

Isosporiasis leads to acute and self-limiting diarrhoea in people with healthy immune systems, whereas it causes life-threatening persistent enteritis in immune-deficient individuals, particularly in those with AIDS (4, 6, 7, 10, 11).

Isospora oocysts are diagnosed by microscopic detection in stool by an ethyl alcohol-formaldehyde concentration technique, once with and once without iodine for staining; this can reveal suspicious oocyst-like features, so modified acid-fast stains are performed on a fresh smear.

CASE REPORT

This study was approved by the Ethics Committee of Dokuz Eylul University. A 35 year-old male patient who had been living in Balikesir underwent a liver transplantation 4 years ago due to liver cirrhosis and fibrosis. Since the right hepatectomy transplanted from his brother was rejected, he was operated on for a second time (a cadaveric transplantation). A Takrolimus, Mikofenolik asit Prednisolone and immunosuppressive treatment was conducted, and continued. The patient had colic and debilitating diarrhoea when he came to our clinic. Microbiological and parasitological analyses of the stool were performed. The results showed that the occult blood test was positive, and the bacteriological analysis was negative. *I. belli* oocysts were seen in the parasitological analysis conducted with native, lugol and modified acid-fast dye techniques (Figure 1). The biochemical results are as follows: creatinine: 1.30 mg/dL), Uric acid: 7.7 mg/dL, AST: 48 U/L, ALT: 67 U/L, ALP: 269 U/L, GGT: 188 U/L, Total protein: 9.1 g/dL, K: 5.2 mmol/L, Cl: 111 mmol/L. Other parameters were normal. The patient received a 10-day Trimethoprim/sulphamethoxazole (TMP-SMX) bid treatment. No *I. belli* oocysts were found in the stools in the post-treatment analyses. However, there were *Entamoeba coli* (*E. coli*) cysts, which are apathogenic amoebae, and *Blastocystis hominis* (*B. hominis*) vacuolar forms (less than 5 of each in X40 microscopic area). *I. belli* oocysts were found again in the stools examined 2 months later when the patient had recurrent diarrhoea.

DISCUSSION

Isosporiasis is a parasitic infection which can be seen worldwide and can cause long-lasting and persistent diarrhoea in people whose immune system has been suppressed. In our country, it is seen in patients who have undergone organ transplantations, those affected with AIDS, cancer patients, patients with tuberculosis, those with malignant haematological diseases, in cases with other haematological diseases and in people whose immune systems are healthy (2-4, 7, 12-15). Our case was a patient whose immune system had been suppressed due to liver transplantation. In a study by Yazar et al. (7), *I. belli* oocysts were found in a kidney-transplant patient with abdominal colic, fatigue, nausea, vomiting, and bloodless, fluidic, temporarily-recovering and recurrent diarrhoea for 15 days. He was seen after a one-week TMP-SMX 60/240 mg, BID treatment; following this the clinical symptoms disappeared and microscopic analyses revealed that there were no *I. belli* oocysts. Koru et al. (3) reported *Entamoeba histolytica* in the stool analysis of a 32 year-old male, kidney-transplanted patient who had been complaining about abdominal cramps, fluidic, bloodless and mucousless diarrhoea, mild fever and nausea. Metronidasole treatment was given. In the stool analysis, *Salmonella typhi* C was found and native-lugol and acid-fast dye techniques showed that there were also *I. belli* oocysts. A ciprofloxacin treatment was prescribed. Analysis after 1 week demonstrated that oocysts were still there and, thus, a 10-day TMP-SMX treatment was started. Aksoy et al. (12) examined 554 diarrhoea patients' stools using Kinyoun acid-fast dye technique and sporulated and unsporulated *I. belli* oocysts were found in two patients, one of whom was HIV-positive and the other who had undergone a liver transplantation. In Büyükbaba-Boral's study, a 33 year-old female patient from Elazig suffering from acute diarrhoea, nausea, vomiting, fatigue and sweating accompanied with significant weight loss was diagnosed with AIDS, and lamivudine + zidovudine + nevirapin treatment was started. She was reported to have no complaints other than bloodless, mucousless and yellow diarrhoea 8-10 times a day. The stool samples were diagnosed by microscopic detection three times and no pathogenic bacteria or parasites were found. A fourth analysis revealed many *I. belli* oocysts. The TMP-SMX treatment was given 4x1 for the first 16 days and then 2x1 for the following 16 days, after which the diarrhoea ceased (2). Balcioglu et al. (4) investigated the incidence of parasitic infections in village children and the case of a 12 year-old boy diagnosed with isosporiasis. Although the patient had no complaints at first, the detailed history revealed that he had been having recurrent colic and diarrhoea with nausea, vomiting, and joint pain for some time and had lost 3 kg during the last month. After diagnosis, all immunoglobulin, IgG subgroups, complement levels and CD4+/CD8+ levels of the patient were normal. He was given 5-25 mg/kg TMP-SMX four times a day during the first ten days and TMP-SMX 5-25 mg/kg twice a day for the following three weeks. Three different stool samples were analysed 30, 60 and 90 days after the treatment

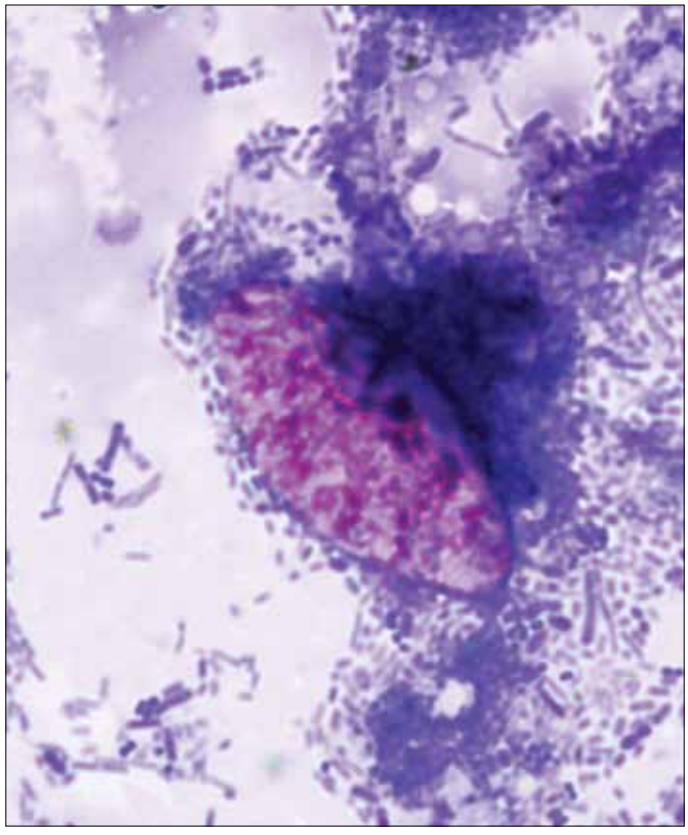

Figure 1. *I. belli* unsporulated oocyst in modified acid-fast stain technique

was completed to test the efficiency of the treatment; no parasites were found in the analyses. Atambay et al. (11) found many oocysts in a stool analysis of a female patient (aged 25) who had been receiving immunosuppressive treatment for 8 months after having a liver transplant and had colic, nausea and diarrhoea. TMP-SMX was given twice daily for ten days. Her diarrhoea disappeared on the second day of the antibiotic treatment and no oocysts were found in the subsequent stool analyses.

In our report, a male patient who had received a liver transplant four years ago and who had been suffering from colic, fatigue, and diarrhoea came to our clinic. Parasitological analysis of the stools using native, lugol and acid-fast dye techniques showed *I. belli* oocysts. In our case, after TMP-SMX 60/240 mg, BID, P.O. treatment, no *I. belli* oocysts were found in the stool analysis, but there were less than five *E. coli* cysts and there were *B. hominis* vacuolar forms. The stool was analysed 2 months later due to the recurrent diarrhoea and *I. belli* oocysts were found.

Bialek et al. (16) reported chronic bilier isosporiasis in a 60 year-old male patient whose immune system was healthy. Oral cotrimoxazole, oral nitazoxanide and 5-nitrothiazole benzamide treatment was given; however, due to the patient's malabsorption problem, the treatment did not produce a good result. Thus, a 5-day intravenous cotrimoxazole treatment was given which eradicated the oocysts in the stool sample. It was noted that extra-intestinal isosporiasis was seen not only in cases with immune suppression, but also in those with a healthy immune system. In the study by Mudholkar et al. (8), which investigated a 35 year-old HIV-affected male patient suffering from weight loss, vomiting, bloody and mucous diarrhoea continuing for two years and fever for eight days, *I. belli* oocysts were found and TMP-SMX treatment was given. However, the patient died one week after the treatment. Gruz et al. (10) reported a 23 year-old male patient with short bowel syndrome and found inflammation in biopsy following the transplantation, although there was no rejection or clinical problems after the operation. Diarrhoea occurred three months later and *I. belli* oocysts were found in the stool analysis. TMP-SMX treatment was started as a four times a day regime for ten days, then decreased to 2 times a day for three weeks and further decreased to prophylactic treatment once a day for one month, and led to complete recovery. *I. belli* oocysts were found in duodenum and colon biopsy in the study by Meamar et al. (6) which investigated a male patient (aged 43) who had intermittent fever, severe dehydration, vomiting, colic, diarrhoea at times over 8 months, weight loss, debility, gastrointestinal problems apart from coughs, phlegm and chest pain. It was reported in this study that there was a large number of *I. belli* oocysts in the patient's stools. Diarrhoea ceased two days after oral TMP-SMX treatment started. Thymectomy was performed, but it was found that the patient had diarrhoea three times following discharge from hospital due to isosporiasis. Prophylactic treatment continued after the antibiotic treatment which lasted for three weeks. No recurrent diarrhoea was reported in the subsequent examinations for 6 months.

CONCLUSION

We believe that coccidian parasites should always be taken into account when investigating the aetiologies of long-term and intermittent diarrhoea which appears in cases where the immune system has been suppressed. Equally important is the application of an effective treatment.

Conflict of Interest

No conflict of interest was declared by the authors.

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