

Case Report

Cyclosporiasis Cases in Six Immunocompetent Patients in a Turkish University Hospital and a Literature Review from Turkey

Mutalip Çiçek^{1*}, Fatih Çakır², Alican Bilden², Nida Özcan², Özcan Deveci³, and Kadri Gül²

¹Department of Medical Microbiology, Ahi Evran University Faculty of Medicine, Kırşehir/Turkey

²Department of Medical Microbiology, Dicle University Faculty of Medicine, Diyarbakır/Turkey

³Department of Clinical Microbiology and Infectious Diseases, Dicle University Faculty of Medicine, Diyarbakır/Turkey

*Corresponding author

Mutalip Çiçek, Department of Medical Microbiology, Ahi Evran University Faculty of Medicine, 40100 Kırşehir/Turkey, Tel: 90-386-2803900; Fax: 90-386-2803917; E-mail: mutalipcicek@hotmail.com

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Abstract

Cyclospora cayetanensis is a coccidian protozoan causing gastroenteritis and has become a major agent of diarrhea in recent years. Six patients were admitted with complaint of diarrhea and abdominal pain to the infectious diseases outpatient clinic of Dicle University's Research and Training Hospital. Stool specimens were examined with the wet mount and modified acid-fast staining methods. These patients were diagnosed as having cyclosporiasis. Of the *Cyclospora cayetanensis* positive patients, three subjects were females and the other three were males. Different parasite species other than *Cyclospora cayetanensis* was not detected in these patients. Laboratory examinations, whole blood counts, urine analyses, and hepatic and renal function were normal in patients. The patients had diarrhea, fatigue, fever, anorexia, and abdominal pain complaints. This research reports the clinical, diagnostic, and therapeutic features of six cyclosporiasis cases in Diyarbakir province of southeastern Turkey. Additionally, a review of the literature from Turkey on this protozoan is included.

INTRODUCTION

Cyclospora cayetanensis has become a major agent of diarrhea in recent years. While this agent gives rise to mild, self-limiting diarrhea in immune competent individuals, it generates serious intestinal damage and leads to severe intestinal symptoms and diarrhea of a longer duration in immune compromised individuals [1-3]. Its oocysts are 8-10 µm size and spherical. Unsporulated oocysts are passed with stool, and sporulation occurs within 7-13 days' outdoors. *Cyclospora cayetanensis* oocysts are infectious when ingested through contaminated water and food while direct person-to-person transmission has not been observed [4].

In recent years, Cyclosporiasis outbreaks have been reported to be associated with imported basil, lettuce, raspberry, mesclun, and pea consumption and with consumption of contaminated water worldwide [5,6]. Currently, 19 *Cyclospora* species have been reported to be potential disease agents in different animal species. The *Cyclospora cercopitheci*, *Cyclospora colobi*, *Cyclospora papionis* and *Cyclospora macacae* species were determined to be disease causative agents in monkeys. There are morphological and molecular similarities between these three species and along with *Cyclospora cayetanensis* [7-9].

Studies concerning the epidemiology of this parasite have been increasing in recent years. *Cyclospora cayetanensis* infections

have been noted in Turkey since they were first reported in 1998 [10-21]. *Cyclospora cayetanensis* was reported in 23 out of 4,986 stool specimens in a study conducted in Izmir [22], in 20 out of 1,876 stool specimens in a study carried out in Istanbul [23], in 13 out of 75 stool specimens in a study performed in Diyarbakir [2], in 129 out of 2,281 stool specimens in a study conducted in Malatya [19], in 3 out of 115 stool specimens from HIV-1-positive patients in a study carried out in Istanbul [21].

We were aimed with this case report to present the clinical, diagnostic and therapeutic features of six cyclosporiasis cases in a province located southeast Turkey and report literature review on this protozoan from Turkey.

CASE PRESENTATIONS

These cases were identified in Diyarbakir province of southeastern Turkey in July and August 2016. Six patients were admitted with complaint of diarrhea and abdominal pain to the infectious diseases outpatient clinic of Dicle University research and training hospital. Stool specimens were examined with the wet mount and modified acid-fast staining methods. *C. cayetanensis* was identified in these six patients by measure and staining characteristics. Formations measuring 8 to 10 µm which were thought to belong to *Cyclospora* in the wet mount method were examined with modified acid-fast staining and the structures detected as *Cyclospora cayetanensis* showed different

staining characteristics (dark red, pink, or colorless) [Figure 1,2]. At the same time, native preparations were examined under a fluorescence microscope with a 40X objective lens using 380 to 420 wavelength filters, and the formations generated auto fluorescence that they gave a yellow, greenish shadow with all body surfaces of oocysts. The informed consent form was obtained from the patient included in work.

Of the *Cyclospora cayetanensis*-positive patients, three subjects were females and the other three were males. All of the six patients were adults. One patient had a history of travelling abroad (Spain, Germany, and Greece). Four of the cyclosporiasis patients were couples (i.e., husband and wife). Different parasite species (pathogenic or nonpathogenic) other than this parasite was not detected in these patients. No pathological findings were identified in the systemic examinations of *Cyclospora cayetanensis*-positive patients. Laboratory examination, whole blood counts, urine analyses results, and hepatic and renal function test findings were found to be normal. Bacteria were not cultivated in stool cultures, and occult blood tests were negative. ELISA tests for HIV were negative.

None of the cases had immune deficiencies or chronic illnesses. In addition to this, immunoglobulin levels, viral hepatitis tests and autoimmune tests were negative. The similar symptoms in all patients were diarrhea, abdominal pain, loss of appetite, and fatigue. Nausea and fever were present in four patients, and vomiting was present in five patients. The diarrhea was aqueous, bloodless, and mucous. Defecation number of the patients ranged from 6 to 12. The fever was in moderate type increased 0.5-1 °C at the onset of the illness. It returned to normal when the disease became chronic. During patient anamnesis they told that they have experienced weight loss since the day disease first appeared.

The *Cyclospora cayetanensis*-positive patients took 160 mg of Trimethoprim and 240 mg of sulfamethoxazole orally twice a day for two weeks. The complaints were resolved on controls after the treatment, and oocysts were not detected in stool examinations.

DISCUSSION

Cyclospora cayetanensis infections can be transmitted in four different ways, including travel to an endemic region, contact with soil, water and food. In tropical and subtropical countries such as Nepal, Peru, and Haiti, the transmission and the infection rate is quite high among healthy people. Water and food-borne outbreaks are also seen in developed countries [5,24]. *Cyclospora cayetanensis* has been reported in numerous stool samples throughout Turkey by several researchers over the years [2,10-23]. The agent was reported in 0.46 % out of 4.986.

Stool specimens in a study performed in İzmir [22], in 1.06% out of 1.876 stool specimens in a study carried out in Istanbul [23], in 17.33% out of 75 stool specimens in a study conducted in Diyarbakır [2], in 5.65% out of 2281 stool specimens in a study performed in Malatya [19], in 2.60 % out of 115 stool specimens from HIV-1-positive patients in a study conducted in İstanbul [21]. This agent has been identified in both immune compromised and many immune competent individuals in researches conducted in different provinces of Turkey.

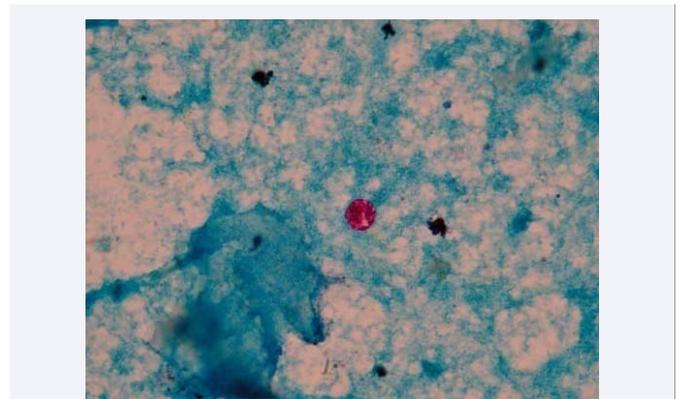


Figure 1 *Cyclospora* acid-fast staining oocysts X1000.

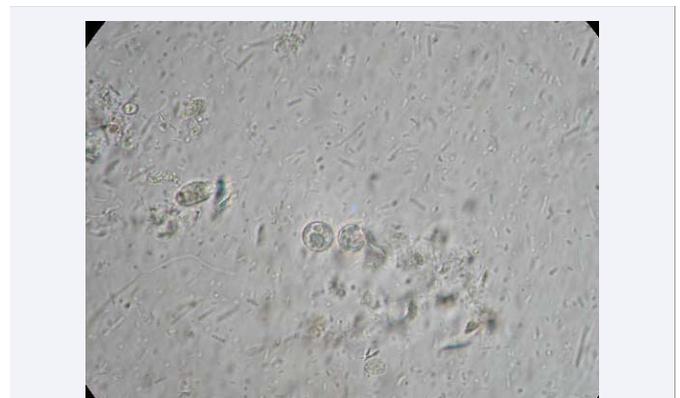


Figure 2 *Cyclospora* oocysts X1000 diagnosed in wet mount.

In a study conducted in Istanbul, *Cyclospora cayetanensis* was diagnosed in a seven-year-old male patient with acute myeloblastic leukemia who had suddenly developed acute diarrhea (11). The infection is also diagnosed in a 30-year-old immunocompetent woman who had diarrhea in İzmir (12), in immunocompetent woman patient aged 24 who had prolonged diarrhea in Ankara (13), in three immunocompetent female patients aged 27, 28 and 67 who had diarrhea, and two immunocompetent male patients aged 44 and 31 who had diarrhea in Ankara (14), in three immunocompetent female patients aged 18, 26 and 34 who had diarrhea in Kayseri (15), in a 28 year old pregnant woman with prolonged diarrhea in Eskişehir (16), in a 32 year old immunocompetent woman who had diarrhea in İzmir (17). Furthermore, in two immunocompetent woman patients aged 20 and 50 with diarrhea in Diyarbakır (17), in a 26 year old immunocompetent male patient who had diarrhea, in three immunocompetent male patients aged 26, 30 and 34 having diarrhea, in an immunocompetent pregnant woman patient aged 23 who had prolonged diarrhea, in two immunocompetent 16 and 48 year old female patients with diarrhea in Van (total of seven cases) (18), *Cyclospora cayetanensis* infections were detected. These case reports and studies from different provinces of Turkey define *Cyclospora cayetanensis* as a mesoendemic species in this country, indicating that the transmission of infection is not related to travel only.

The rainiest seasons have been reported to be the top

seasons of this protozoon in most countries. It has been defined that *Cyclospora cayetanensis* has been seen in rainy and warmer seasons more common in Guatemala, Honduras, Jordan, Nepal, Indonesia [25-29]. However, it has been reported that the agent has been detected in less rainy, drier and colder months of the year more frequently in Haiti and Peru [30,31]. Accordingly, the detection seasons of this protozoon also differ in Turkey [14,21-23]. Cyclosporiasis has been detected during the hot and dry seasons (July and August) in Istanbul, Izmir and Ankara [14,21-23], while the high prevalence of cyclosporiasis has been reported in spring (i.e., March, April, May) and summer seasons (i.e., June, July, August) in Malatya [19]. The city Diyarbakir where the cases were reported is a province with a tropical climate in southeastern Turkey. This region is rainless in summer, and July and August are the hottest months of the year. The cases presented in studies conducted by us [2,18] were seen in July and August. Our cases are different from the cyclosporiasis cases detected in other countries in terms of season. In addition, in our cases detection seasons are also different of those noted in Malatya (a province of Turkey) but are similar to those reported in Izmir, Ankara and Istanbul (provinces of Turkey) as they were seen in the dry and hot season. Due to the increased travel frequency and amount of imported food in the world, the agent has been detected in almost all seasons, in all climates and in many countries.

Cyclospora cayetanensis is a protozoan transmitted by soil, food and water. It is not transmitted directly from human to human. But family infections can likely occur due to consumption of the same food and water. In our study conducted among three different families, oocysts were detected in five out of eight members of one family, in two out of eight family members in the second, and in three out of six family members in the last family in the same region, in 2013. In this investigation, four of the cyclosporiasis patients were spouses (i.e., husband and wife). We have observed that the proximity of the family has not been investigated in the studies and case reports made in Turkey [14,19,20,22,23]. However, in an epidemiological study conducted in Guatemala; they had screened stool specimens from 182 family members belonging to 56 families of case-patients. Of these, 14 people from 11 families were reported to be positive for *Cyclospora cayetanensis* [25]. In our previous study conducted in 2013 [2] and in the present case report, oocysts were identified in members of the same family. *Cyclospora cayetanensis* may give rise to familial infections, hence it might be useful to examine all family members who have diarrhea, if *Cyclospora cayetanensis* is detected in one.

The first case of *Cyclospora cayetanensis* in our hospital was detected in two patients in 2012 [18]. Thereafter, 13 cases were reported in 2013 [2]. The six cases described in this article were applied to the hospital in 2016. These last cases are similar to those from the other two years in terms of the period when they occurred, familial transmission, and the clinical findings. The *Cyclospora cayetanensis* cases detected by us in recent years, indicate that the climate and environmental factors in our region provide optimum conditions for the transmission and development of oocysts. Our evidence suggests that the parasite might be mesoendemic in southeastern region of Turkey and this agent will continue to be seen in this region. Therefore, stool specimens with diarrhea are examined for this protozoon through modified acid-fast staining in our hospital parasitology

laboratory.

In recent years, there has been an increase in reports of this infection in Turkey. A reason for this is that the awareness of clinicians for this infection is increased compared to previous years, and many laboratories have begun to use acid-fast staining methods routinely for the diagnosis of the agents. In addition to this, this protozoan has been researched with real-time and conventional PCR methods. Studies reported in different provinces and our case reports explain the existence of cyclosporiasis as mesoendemic in Turkey. Investigations for *Cyclospora cayetanensis* should not be disregarded in patients with diarrhea, and studies should be conducted to investigate the source of the infection.

CONFLICT OF INTEREST

Dear Editor,

We are sending our manuscript to your journal after all the authors have seen and approved the final form of it. We declare that we have not published it anywhere else before nor is it being considered simultaneously in another journal. The authors have no financial conflicts of interest. We do look forward to hearing from you soon.

Best wishes,

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