IDCases 39 (2025) e02157

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Case report

Severe symptomatic hypocalcemia due to *Cyclospora cayetanensis* infestation: A rare case

Ali Ajmal [a,*], Camelia Chirculescu [b], Tariq Alyamani [b], Gregory J. Hiett [b], Dhan Bahadur Shrestha [c]

[a] Division of Endocrinology, Department of Medicine, Joan C. Edwards School of Medicine-Marshall Univeersity, Huntington, West Virginia 25701, USA
[b] Department of Internal Medicine, Johnston Memorial Hospital, Abingdon, VA 24211-7664, USA
[c] Division of Cardiology, Department of Internal Medicine, Bassett Medical Center, Cooperstown, NY 13326, USA

ARTICLE INFO

Keywords:
Hypocalcemia
Trousseau sign
Chvostek sign
Cyclospora cayetanensis

ABSTRACT

Introduction: Severe hypocalcemia can affect multiple systems, causing a wide variety of symptoms ranging from muscle weakness to twitching. In severe cases, it can lead to heart rhythm disturbances and seizures. A rare cause of hypocalcemia is due to malabsorption associated with prolonged gastroenteritis.
Case presentation: We present a 35-year-old female with persistent watery diarrhea of eight weeks presented with neuromuscular symptoms. Trousseau sign and Chvostek sign were positive bilaterally. Laboratory test results revealed severe hypokalemia, hypocalcemia, and anemia, with prolonged QT interval in electrocardiogram (EKG). Her stool polymerase chain reaction (PCR) revealed *Cyclospora cayetanensis*. Her electrolytes were appropriately replaced during her hospital stay. The patient was successfully treated with trimethoprim-sulfamethoxazole, calcium, and oral iron supplementation.
Conclusion: This case demonstrates a unique presentation of a healthy young female with symptomatic hypocalcemia resulting from malabsorption due to *Cycolospora cayetanensis*. This case emphasizes the importance of early diagnosis using newer techniques, such as polymerase chain reaction (PCR) for parasite DNA, which can result in appropriate diagnosis and timely treatment.

Introduction

The electrolytes are present in both intracellular and extracellular environments, and their presence within a precise range is important for the normal functioning of all the cells of the body, such as the maintenance of electrical neutrality and generation and conduction of action potential in the muscles and nerves. We obtain most of them through food, and their absorption depends on the functioning of the gastrointestinal tract. Various disease processes, dietary deficiencies, and medications can result in either low (hypo) or high (hyper) levels. Any acute inflammatory process affecting the absorption at the small intestine can result in electrolyte imbalances, leading to cellular and molecular dysfunction, subsequently causing multiple symptoms based on affected organs. The symptoms of an electrolyte imbalance can include muscle weakness and twitching, and if severe, they can lead to heart rhythm disturbances and seizures. Hypocalcemia can cause exaggerated reflexes, muscle spasms, and heart problems, including rhythm changes and prolonged QT interval. Hypokalemia can cause muscle weakness, cramps, spasms, paralysis, and respiratory problems. Trousseau sign (the inflation of the cuff resulted in flexion of wrist and metacarpophalangeal joints, the extension of interphalangeal joints, and adduction of thumb) [1] and Chvostek sign (manual stimulation of facial nerve by tapping of the masseter muscle at the angle of the mandible caused facial muscle twitching demonstrating hyperexcitability of the facial nerve) [2] are the hallmark of severe hypocalcemia.

This report describes a patient in whom malabsorption due to *Cyclospora cayetanensis*, an uncommon food-borne pathogen, resulted in multiple electrolyte imbalances, including severe hypocalcemia, hypokalemia, hypomagnesemia and severe iron deficiency anemia.

Case report

A 35-year-old female presented with persistent watery diarrhea approximately 8–10 times per day for approximately eight weeks and also reported paresthesia in hands, feet, and face, more pronounced in hands associated with pain and difficulties in moving arms, especially

* Corresponding author.
E-mail address: aliajmalpak@yahoo.com (A. Ajmal).

https://doi.org/10.1016/j.idcr.2025.e02157
Received 30 April 2024; Received in revised form 8 January 2025; Accepted 13 January 2025
Available online 16 January 2025

the hands. On physical examination, the Trousseau sign was positive bilaterally, and the inflation of the cuff resulted in flexion of the wrist and metacarpophalangeal joints, extension of interphalangeal joints, and adduction of the thumb.

Chvostek sign was positive; manual stimulation of the facial nerve (tapping of the masseter muscle at the angle of the mandible) caused facial muscle twitching, demonstrating hyperexcitability of the facial nerve (Video 1.).

Supplementary material related to this article can be found online at doi:10.1016/j.idcr.2025.e02157.

Laboratory values revealed severe hypokalemia, with potassium of 2.5 mmol/L (3.5–5.1 mmol/L), calcium level of 7.7 mg/dL (8.6–10.0 mg/dL), albumin adjusted serum calcium of 7.5 mg/dL (8.6–10.0 mg/dL), ionized calcium of 1.10 mmol/L (1.12–1.32 mmol/L), parathyroid hormone (PTH) level was 84.6 ng/mL (12.0–88.0 pg/mL), 25-hydroxy vitamin D was 31 pg/mL (30.0–100.0 ng/mL) (Table 1). In addition, the magnesium level was 1.3 mmol/L (1.6–2.4 mg/dL). The PTH level was appropriately near the upper limit, and Vitamin D levels were at the borderline, likely due to malabsorption. An electrocardiogram at admission showed a prolonged QT interval (462 msec). She was administered intravenous (IV) potassium chloride with oral potassium chloride, IV magnesium sulfate, and IV calcium gluconate (3 g); the subsequent calcium levels were 7.2 mg/dL, potassium 2.8 mmol/L, magnesium 1.7 mmol/L, she was started on oral calcium carbonate-vitamin D 500–5 mg-mcg twice a day and potassium chloride 40 mEq three times daily. The next day, she reported improvement in her muscle spasms and hand movements; however, minimal improvements in bilateral hand/arm and facial paresthesia. With continuous oral calcium and potassium supplementation, the potassium levels improved to 3.4 mmol/L and calcium levels to 8.7 mg/dL, further improving symptoms. Repeat electrocardiogram showed improvement in QT interval (454 msec).

The stool studies showed elevated calprotectin 74 μg/g, positive lactoferrin test, normal fecal fat, and gastro-intestinal panel by polymerase chain reaction (PCR) revealed *Cyclospora cayetanensis*. The patient was started on trimethoprim-sulfamethoxazole 800–160 mg twice daily.

Further review of blood tests showed that the patient has microcytic anemia, with a hemoglobin level of 8.7 g/dL (12.4–15.2 g/dL), and mean corpuscular volume (MCV) 63.8 fL (80.0–100.0 fL). Further workup was remarkable for iron deficiency anemia, with a total iron of 15.0 μg/dL (50.0–170.0 μg/dL), saturation 3 % (20–55 %), iron binding capacity (IBC) 449 (240−450) and ferritin less than 2.0 ng/mL (11.0–307.0 ng/mL). Folate 12.5 ng/mL (6.6–20.0 ng/mL and vitamin B12 379.0 pg/mL (211–911 pg/mL) levels were within normal limits. Based on low hemoglobin, hematocrit, low iron saturation, and ferritin levels, the patient met the criteria for IV iron supplementation and was administered IV iron during the hospital stay. It was recommended that oral iron supplementation be continued at discharge.

The patient was discharged from the hospital in stable condition with prescriptions for trimethoprim-sulfamethoxazole twice daily for complete 7 days, calcium, and oral iron supplementation.

Table 1
Relevant significant laboratory parameters.

Laboratory parameters	Lab values at admission	The following day	At the time of discharge	Reference range
Sodium	144	143	139	136–145 mmol/L
Potassium	**2.5**	**2.8**	**3.7**	3.5–5.1 mmol/L
Chloride	101	104	108	98–107 mmol/L
CO2	30	32	29	22–32 mmol/L
AG	13	7	2	5–15 mmol/L
BUN	9	10	6	6–20 mg/dL
Cr	0.83	0.62	0.63	0.60–1.10 mg/dL
Glucose	86	113	122	70–99 mg/dL
Magnesium	**1.3**	**1.7**	**2.0**	mg/dL
Calcium	**7.7**	**7.6**	**8.7**	8.6–10.0 mg/dL
Ca, corrected for Albumin	7.5			8.6–10.0 mg/dL
Albumin	4.2			3.5–5.2 g/dL
Total Protein	7.0			6.4–8.3 g/dL
Ionized Calcium		1.10		1.12–1.32 mmol/L
PTH intact	84.6			12.0–88.0 pg/mL
25 OH Vitamin D	31			30.0–100.0 ng/mL

Discussion

Cyclospora cayetanensis is a protozoan, and the first cases of infection were reported in the 1970s; however, it was fully recognized as a human intestinal parasite in the early 1990s [3]. *Cyclospora* has been established as a food-borne pathogen, and multiple outbreaks have been reported in different parts of the world and as endemic infection in tropical and subtropical areas from April through August [4,5]. This coincides with our patient as she presented in mid-August in the hospital, and her symptoms started 8 weeks before presentation coinciding with onset in May. The outbreaks in non-endemic areas are associated with fresh produce (cilantro, basil, raspberries) [6–8]. In the United States, the majority of cases are reported during the spring and summer months. Outbreaks have been identified nearly every year since the mid-1990s. A large outbreak in North America in 1996 was linked to the raspberries imported from Guatemala [9]. No animals have been identified as reservoirs of infection for *Cyclospora* isolates that infect humans. The transmission mode is considered fecal-oral or via ingestion of contaminated water [5].

Cyclospora oocysts do not multiply outside the host. The cysts are morphologically similar to cysts of *Cryptosporidium parvum* [10]. The difference is in size; oocysts are 8–10 μm in diameter, approximately twice the size of *Cryptosporidium parvum* oocysts (4–6 μm). The unsporulated oocysts are not infective when passed in the stool [3,11]. *Cyclospora* has an incubation period that ranges from 2 to 11 days and a median incubation period of one week [12]. After ingesting contaminated food and water, the sporulated oocysts travel to the small intestine's lumen and excystation release of sporozoites [13].

The sporozoites invade the enterocytes, causing dilation of vessels, villous capillary congestion, diffuse mucosal edema, and inflammatory cell infiltrate, causing shortening and widening of intestinal villi (villous atrophy) [14]. Symptoms usually include nausea, voluminous watery diarrhea, abdominal pain, flatulence, and bloating, resulting in fatigue and weight loss [15].

If untreated, the symptoms can last for six weeks to three months (even longer in immunocompromised patients, particularly those with acquired immunodeficiency syndrome) [7,9,15]. Histopathological appearance is usually similar to celiac disease, viral enteritis, and giardiasis (all causing villous atrophy) [3]. Clinical history (onset and duration, sick family members/relatives) can help diagnose. Stool examination can detect *Cyclospora cayetanensis*. Stool specimens sent to laboratories for ova and parasites are usually not examined for *Cyclospora spp* [8]. The severe iron deficiency further supported villous atrophy-induced malabsorption (characteristic of *Cyclospora*) as a possible etiology in the present case [16].

Cyclosporiasis is diagnosed by examining stool specimens. Diagnosis may be difficult because even symptomatic individuals can shed oocysts at low levels that are not readily detected by laboratory examination. Multiple specimens, collected on different days, may be needed [17]. The sediment can be examined microscopically with different techniques including wet mounts, and stained smears (both modified acid-fast stains and modified safranin staining will stain *Cyclospora* cysts from a pink to brilliant red). Molecular Diagnosis using real-time PCR protocols has been developed to specifically detect *Cyclospora cayetanensis* in stool [18].

It is important to differentiate from *Cryptosporidium* as treatment is

largely different and supportive in the case of *Cryptosporidium* and with antibiotics in the case of *Cyclospora*. The treatment of choice is trimethoprim-sulfamethoxazole [19]. Ciprofloxacin can be an alternative treatment but is less effective than trimethoprim-sulfamethoxazole [20].

Conclusion

This case emphasizes the gastrointestinal physiology in electrolyte absorption, especially calcium homeostasis, and highlights the electrolyte disturbances as a complication of malabsorption in the setting of *Cyclospora cayetanensis*. It also signifies that early diagnosis and appropriate management of persistent diarrhea using newer technology and prompt diagnosis and treatment with antibiotics are important to establish a complete cure.

Ethics approval

This is a case report; therefore, it did not require ethical approval from the ethical review committee.

Consent

Written consent was obtained from the patient for academic purposes when publishing the case.

Registration of research studies

NA.

Funding

The study did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors

CRediT authorship contribution statement

Camelia Chirculescu: Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Ali Ajmal:** Writing – review & editing, Writing – original draft, Validation, Software, Data curation, Conceptualization. **Dhan Bahadur Shrestha:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Gregory J. Hiett:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Tariq Alyamani:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Acknowledgments

We acknowledge the patient for consenting to report the case and the entire team involved in the patient care.

Data Availability

All data related to the study presented in the study and supplementary files

References

[1] Rehman HU, Wunder S. Trousseau sign in hypocalcemia. E498–E498 CMAJ 2011; 183. https://doi.org/10.1503/CMAJ.100613.
[2] Hujoel IA. The association between serum calcium levels and Chvostek sign. Neurol: Clin Pract 2016;6:321–8. https://doi.org/10.1212/CPJ.0000000000000270.
[3] Ortega YR, Sanchez R. Update on Cyclospora cayetanensis, a food-borne and waterborne parasite. Clin Microbiol Rev 2010;23:218–34. https://doi.org/10.1128/CMR.00026-09.
[4] Ortega YR, Sterling CR, Gilman RH. Cyclospora cayetanensis. Adv Parasitol 1998; 40:399–418. https://doi.org/10.1016/S0065-308X(08)60128-1.
[5] Almeria S, Cinar HN, Dubey JP. Cyclospora cayetanensis and cyclosporiasis: an update. Microorganisms 2019;7. https://doi.org/10.3390/MICROORGANISMS7090317.
[6] Connor BA, Shlim DR. Foodborne transmission of cyclospora. Lancet 1995;346: 1634. https://doi.org/10.1016/S0140-6736(95)91972-4.
[7] Milord F, Lampron-Goulet E, St-Amour M, Levac E, Ramsay D. Cyclospora cayetanensis: a description of clinical aspects of an outbreak in Quebec, Canada. Epidemiol Infect 2012;140:626–32. https://doi.org/10.1017/S095026881100121X.
[8] Mansfield LS, Gajadhar AA. Cyclospora cayetanensis, a food- and waterborne coccidian parasite. Vet Parasitol 2004;126:73–90. https://doi.org/10.1016/J.VETPAR.2004.09.011.
[9] Herwaldt BL, Ackers ML. Cyclospora Working Group. An Outbreak in 1996 of Cyclosporiasis Associated with Imported Raspberries. NEJM 1997;336:1548–56. https://doi.org/10.1056/NEJM199705293362202.
[10] Sun T, Ilardi CF, Asnis D, Bresciani AR, Goldenberg S, Roberts B, et al. Light and electron microscopic identification of cyclospora species in the small intestine: evidence of the presence of asexual life cycle in human host. Am J Clin Pathol 1996;105:216–20. https://doi.org/10.1093/AJCP/105.2.216.
[11] Plutzer J, Karanis P. Neglected waterborne parasitic protozoa and their detection in water. Water Res 2016;101:318–32. https://doi.org/10.1016/J.WATRES.2016.05.085.
[12] Li J, Cui Z, Qi M, Zhang L. Advances in cyclosporiasis diagnosis and therapeutic intervention. Front Cell Infect Microbiol 2020;10:516184. https://doi.org/10.3389/FCIMB.2020.00043.
[13] Ahmed M, Ahmed M. Intestinal parasitic infections in 2023. Gastroenterol Res 2023;16:127–40. https://doi.org/10.14740/gr.v16i3.1622.
[14] Ortega YR, Nagle R, Gilman RH, Watanabe J, Miyagui J, Quispe H, et al. Pathologic and clinical findings in patients with cyclosporiasis and a description of intracellular parasite life-cycle stages. J Infect Dis 1997;176:1584–9. https://doi.org/10.1086/514158.
[15] Giangaspero A, Gasser RB. Human cyclosporiasis. Lancet Infect Dis 2019;19: e226–36. https://doi.org/10.1016/S1473-3099(18)30789-8.
[16] Zehra Saboor M, Qamar A, Moinuddin K. Disorders associated with malabsorption of iron: a critical review. Pak J Med Sci 2015;31:1549–53. https://doi.org/10.12669/PJMS.316.8125.
[17] Ortega YR, Sterling CR, Gilman RH, Cama VA, Diaz F. Cyclospora species – a new protozoan pathogen of humans. NEJM 1993;328:1308–12. https://doi.org/10.1056/NEJM199305063281804.
[18] Relman DA, Schmidt TM, Gajadhar A, Sogin M, Cross J, Yoder K, et al. Molecular phylogenetic analysis of cyclospora, the human intestinal pathogen, S, gests that it is closely related to eimeria species. J Infect Dis 1996;173:440–5. https://doi.org/10.1093/INFDIS/173.2.440.
[19] Hoge CW, Gaudio P, Echeverria P, Shlim DR, Rabold JG, Pandey P, et al. Placebo-controlled trial co-trimoxazole for cyclospora infections among travellers and foreign residents in Nepal. Lancet 1995;345:691–3. https://doi.org/10.1016/S0140-6736(95)90868-4.
[20] Verdier RI, Fitzgerald DW, Johnson WD, Pape JW. Trimethoprim-sulfamethoxazole compared with ciprofloxacin for treatment and prophylaxis of Isospora belli and Cyclospora cayetanensis infection in HIV-infected patients. A randomized, controlled trial. Ann Intern Med 2000;132:885–8. https://doi.org/10.7326/0003-4819-132-11-200006060-00006.