

## Secondary transmission of cryptosporidiosis associated with well water consumption: two case studies

**Natania Carol Cavalcante Rezende<sup>[1]</sup>, Camila Loredana Pereira Alves Madeira Bezerra<sup>[1]</sup>,  
Jéssica Jacinto Salviano de Almeida<sup>[1]</sup>, Tatiane Uetti Gomes Fernandes<sup>[1]</sup>  
and Kleber Giovanni Luz<sup>[2]</sup>**

[1]. Centro de Ciências da Saúde, Universidade Federal do Rio Grande do Norte, Natal, Rio Grande do Norte, Brasil. [2]. Instituto de Medicina Tropical do Rio Grande do Norte, Natal, Rio Grande do Norte, Brasil.

### ABSTRACT

Cryptosporidiosis is a very prominent disease in the field of public health, and usually causes diarrhea. We describe two immunocompetent patients who presented with chronic diarrhea that was ultimately found to be caused by continuous exposure to well water contaminated with the microbial cysts (oocysts) of the *Cryptosporidium spp* parasite. We describe the patients' histories and possible explanations for their prolonged symptoms.

**Keywords:** *Cryptosporidium spp*. Well water. Diarrhea.

### INTRODUCTION

*Cryptosporidium spp* is responsible for approximately 6% of diarrhea cases that afflict immunocompetent individuals in developing countries<sup>(1)</sup>. Generally, these individuals experience mild and self-limited diarrhea, while chronic cases are more frequent in immunocompromised individuals<sup>(2)</sup>. Herein, we describe cryptosporidiosis cases caused by contaminated condominium well water in immunocompetent individuals who presented with chronic diarrhea due to recurrent infections. In these cases, the continuous exposure to contaminated water – in association with a depressive disorder and/or immunosenescence – led to the development and establishment of symptoms.

### CASE REPORT

**Case 1:** A 60-year old otherwise healthy woman who is a single real estate administrator, and is a native and resident of Natal (Northeast Brazil), presented with a complaint of diarrhea for the past six months. In November 2013, the clinical case was intermittent diarrhea with aqueous feces but no mucus, blood or fat; symptoms were sometimes accompanied by abdominal cramps in the lower abdomen. In the following month, she presented with a single episode of fecal incontinence. From then until March 2014, she reported alternations between liquid

feces and separate, hard lumps. From March 2014 onwards, the patient reported progressive worsening, with an increase in the volume of feces and number of evacuations (up to six per day), in addition to flatulence and abdominal cramps in the lower abdomen that were alleviated after evacuation. The symptoms were even more pronounced after the ingestion of fatty or dairy foods. The patient reported weight loss of four kilograms in a month, as well as abdominal distension and rigidity. Although the patient reported that she had ceased psychiatric treatment, she had been taking trazodone hydrochloride for six months.

A hemogram revealed the following: hemoglobin 13.6g/dL, leukocytes 5,100/mm<sup>3</sup>, segments 63%, eosinophils 4%, and platelets 250,000/mm<sup>3</sup>. Kidney function and urine samples were normal, and cluster of differentiation 4 (CD4+), cluster of differentiation 8 (CD8+), and immunoglobulin dosage were within normal levels. The patient tested negative for human immunodeficiency virus (HIV).

Given the persistence of the symptoms, a diagnostic-epidemiological investigation was performed. When searching for the presence of *Cryptosporidium spp* in the feces using the Ziehl-Neelsen staining method, oocysts of this parasite were identified. Analysis of the condominium well water (**Figure 1**) revealed the presence of the same oocysts. Therefore, the usage of contaminated water was immediately ceased, and psychiatric treatment was resumed. Currently, the patient follows medical recommendations and is asymptomatic.

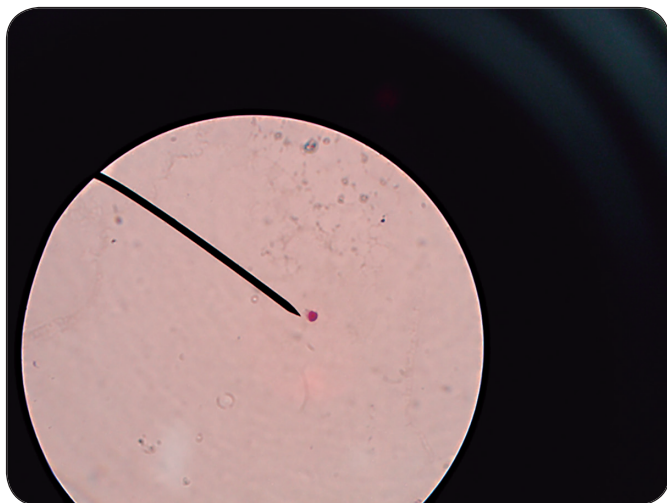
**Case 2:** An 87-year-old woman, a homemaker who is a native of and residing in the municipality of Natal, presented with diarrhea for the past six months. The patient had a background of endometrial malignant neoplasm diagnosed through biopsy after hysterectomy, and was treated with

**Corresponding author:** Natania Carol Cavalcante Rezende.

**e-mail:** carolcavalcante.r@gmail.com

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**FIGURE 1** - Analysis of the condominium well water, using modified cellulose membrane filtration and Ziehl-Neelsen methods, revealed oocysts of *Cryptosporidium spp* (Products and Environment Microscopic Center – LACEN/RN). Natal, State of Rio Grande do Norte, 2014.

radiotherapy and chemotherapy 17 years prior. Her symptoms began in January 2014 and involved intermittent diarrhea of yellow, aqueous feces with undigested food, and two-to-three evacuations per day. She presented with diffuse abdominal pain that improved after evacuations, flatulence, and cold sweats. She reported a weight loss of six kilograms over six months.

A diagnostic investigation was performed, and a hemogram revealed the following: hemoglobin 12g/dL, leukocytes 5,610mm<sup>3</sup>, segments 57.5%, and platelets 201 mil/mm<sup>3</sup>. CD4+, CD8+, and immunoglobulin were within normal levels, and the patient tested negative for HIV. A stool analysis test was ordered using modified acid-fast staining; two out of five stool samples revealed *Cryptosporidium spp* oocysts. The well water of the condominium was also analyzed and tested positive for the protozoan parasite. Azithromycin was prescribed to the patient and mineral water was used for cooking and bathing thereafter. The symptoms resolved after adopting these measures.

## DISCUSSION

*Cryptosporidium spp* is one of the most common intestinal parasites responsible for human gastroenteritis<sup>(3)</sup>. Symptoms of cryptosporidiosis depend on several factors, especially the immune competence of the individual, age, and existence of co-morbidities<sup>(1)</sup>. The intestinal form of this disease has been chiefly associated with immunosuppression. However, the cases presented herein are notable because both women were HIV-negative and immunocompetent, according to their CD4+ counts. In such cases, we postulate that the disease developed due to intense and regular exposure to *Cryptosporidium spp* in their condominium water supplies, and was associated with a drop in immunity because of a depressive disorder, an senescence, or chemotherapy, which made the patient more susceptible to infection.

The water wells in the residences of both patients contained *Cryptosporidium spp* oocysts, which is the infectious agent in cryptosporidiosis (**Figure 1**). Daily consumption of this water resulted in continuous exposure to the microorganism, which is very resistant to chlorination, disinfection, and several forms of filtration at the oocyte stage of its biological cycle. This allows the microorganism to survive in the environment for a long period of time.

Cryptosporidiosis transmission is increasingly found to be associated with the consumption of contaminated water, whether treated or not. In one study, untreated and treated water samples were analyzed for *Cryptosporidium* in 66 water treatment plants in 14 sites in the United States and one Canadian province; 97% of the samples from untreated water were positive for the parasite. In the treated water, parasites were detected in 22% of the samples<sup>(4)</sup>. Hence, water is an important vehicle for the transmission of this parasite.

Furthermore, a decrease in the immune function of patients may have hindered the development of efficient immune cell and humoral responses. This may have caused the prolongation of infection for approximately six months. In patients who can develop adequate immune responses, the disease is often self-limiting and resolves in approximately two weeks.

In Case 1, a depressive disorder was probably the main factor causing the immune system deficiency. Psychological stressors cause alterations that reverberate in the hormonal system and neurotransmission pathways, which directly influence the immune response. This change is mainly caused by the activation of the hypothalamic-pituitary-adrenal (HPA) axis and liberation of glucocorticoids during emotional stress, which can reduce the production of interleukin (IL)-1, IL-13, IL-5, IL-6, IL-8, tumor necrosis factor (TNF), and colony-stimulating factor. Additionally, migration and chemotaxis of neutrophils and eosinophils are also inhibited<sup>(5)</sup>.

All these alterations can contribute in turn to the development of leukocytosis, a decrease in the number and activity of natural Killer (NK) cells, an increase in the CD4+/CD8+ ratio, and a decrease in the activity of T cells. Furthermore, there are alterations in the T-helper 1/T-helper 2 (Th1/Th2) balance that favor Th2, following the inhibition of IL-12, TNF-alpha, and interferon-gamma production<sup>(6)</sup>.

In cases of cryptosporidiosis, which is caused by an intracellular parasite, it is important to develop an effective Th1 response to combat the parasite. However, as mentioned above, immune function changes can increase Th2 at the expense of Th1; the former is more effective against extracellular pathogens<sup>(1)</sup>. In sum, all these changes can contribute to an inefficient defense against the parasite.

Case 2 was similar to Case 1 in terms of emotional stress, as physical or neurogenic stress activates the HPA axis causing an increase in adrenocorticotrophic hormone secretion followed by the adrenocortical liberation of cortisol<sup>(6)</sup>. This may explain the development of an ineffective immune cell response to the protozoan parasite, allowing for the manifestation of the disease.

There are additional factors that may facilitate prolonged infection, including advanced age, previous history of cancer, and chemotherapy treatment and basal disease<sup>(1)</sup>.

It is known that the normal process of aging is accompanied by a reduction in mucus membranes that act as barriers against pathogens. Furthermore, there is a significant decrease in macrophage precursors in the bone marrow<sup>(7)</sup>, as well as a decrease in the production of nitric oxide and reactive species of oxygen that are essential for the activity of these cells<sup>(8)</sup>. Additionally, age-related thymic involution occurs with substitution of fatty tissue<sup>(9)</sup>, causing a decrease in CD4+ T-cells, which is reflected in the decrease in B cell activity, since these are stimulated by the former<sup>(10)</sup>. These immune system alterations in the elderly may predispose such individuals to a higher number of infections, including cryptosporidiosis.

In conclusion, neurogenic aspects such as depression and emotional stress, along with comorbidities and a history of malignant diseases, can possibly create a state of depressed immunity. Therefore, otherwise immunocompetent individuals are susceptible to the development of diarrhea, as was the case in the patients reported here who were persistently exposed to contaminated water.

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