



## A Case Series of Lung Transplant Recipients Who Developed Life Threatening Diarrhea from *Cryptosporidium* Contaminated Water Supply

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### Abstract

**Background:** *Cryptosporidium* is a protozoan known to cause acute gastroenteritis. Solid organ transplant recipients are at increased risk of infection but reports of infection in lung transplant recipients are limited. In September 2023, the Baltimore City Department discovered low levels of *Cryptosporidium* within the Druid Lake Reservoir. We present three cases of cryptosporidiosis in lung transplant recipients at our institution and report their disease course, response to treatment, and potential affiliation with the reservoir contamination.

**Methods/Results:** Chart reviews were conducted on the three cases of cryptosporidiosis in lung transplant recipients at our institution between 2023 to 2024. *Case 1:* 47-year-old female from near Baltimore with a bilateral lung transplant (BLTx) for bronchiectasis presented with severe sepsis from *Cryptosporidium* diarrhea and *C. difficile* colitis. She was started on nitazoxanide and oral vancomycin and discharged on hospital day 7. *Case 2:* 60-year-old male from Baltimore with a redo BLTx presented with septic shock due to *Cryptosporidium* diarrhea and was upgraded to the ICU. He started on norepinephrine drip, steroids, broad-spectrum antibiotics, and nitazoxanide. He was discharged home on hospital day 19. *Case 3:* 35-year-old male with a BLTx for cystic fibrosis presented with severe sepsis, renal failure and electrolyte derangement due to *Cryptosporidium* diarrhea and was upgraded to the ICU. He was started on nitazoxanide and discharged on hospital day 4.

**Conclusion:** To our knowledge, this represents the largest case series of *Cryptosporidium* in lung transplant recipients. It is important to include cryptosporidiosis on the differential for these patients.

**Keywords:** Lung transplant recipients; *Cryptosporidium*; Immunocompromised; Opportunistic infections.

### Introduction

*Cryptosporidium* is a widespread protozoan that is known to cause acute gastroenteritis in humans. Clinical symptoms of cryptosporidiosis include abdominal pain and watery diarrhea that can range in severity from mild symptoms to life-threatening illness. Transmission occurs via the fecal-oral route, due to contaminated food and water sources or contact with infected animals [1,2,3]. The infection is prevalent in approximately 70 countries with the greatest levels of disease burden found in Mexico, Bangladesh, Nigeria, and the Republic of Korea [4]. Outbreaks of cryptosporidiosis have been rising in the United States at a rate of approximately 13% per year [5]. Immunocompetent patients are typically asymptomatic or have

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mild gastrointestinal (GI) symptoms, such as self-limited diarrhea. More severe manifestations of the infection are seen in certain populations, including children, advanced ages, and those with immuno-compromising conditions. These patients are known to suffer severe diarrhea that can be life-threatening [6]. The first-line treatment and only FDA approved medication for patients with moderate-to-severe symptoms is the anti-parasitic medication nitazoxanide [7, 8]. Solid organ transplant recipients are typically on multiple immunosuppressive medications to prevent allograft rejection. This places them at increased risk for infection from many opportunistic pathogens, including *Cryptosporidium*. Most *Cryptosporidium* infections reported in transplant patients have been in renal transplant recipients [9, 10]. Reports of infection in other solid organ transplant patients, especially lung transplant recipients, are limited [11]. On September 28, 2023, the Baltimore City Department of Public Works discovered low levels of *Cryptosporidium* within the Druid Lake Reservoir during routine testing. The reservoir serves as the drinking water source for Maryland including the regions of Baltimore City, Baltimore County, and Howard County, Maryland [12]. The Baltimore City Health Department sent out an advisory reassuring that the general population did not have to take any additional measures due to the low levels of detection. However, the immunocompromised population were advised to consume bottled water, boil water for one minute prior to consumption, or utilize specialized filtered tap water [13, 14]. Here, we present three cases of cryptosporidiosis in lung transplant recipients at our institution and report on their disease course, response to treatment, and potential affiliation with the contamination of Druid Lake Reservoir.

## Methods

We obtained records of nitazoxanide prescriptions at Inova Fairfax Medical Center Pharmacy from January 1st,

2023 to May 28th, 2024. 57 nitazoxanide prescriptions were identified, 3 of whom were identified to be lung transplant recipients. A detailed chart review was conducted on each patient to confirm that diagnosis of *Cryptosporidium*, and to analyze their vitals throughout their hospitalization, physical exam findings, laboratory results and subjective findings on nursing and physician notes (Table 1).

## Results

### Case 1

A 47-year-old female with a history of bilateral lung transplant for bronchiectasis presented to the emergency department (ED) of an outside hospital (OSH) in late August 2023 with 2 days of lightheadedness, nausea, and multiple episodes of diarrhea. She had a history of chronic intermittent diarrhea that was initially thought to be related to her immunosuppressive medications. She presented with continuous, severe watery bowel movements associated with bowel incontinence.

Three weeks prior, she had traveled to the West Coast but denied any sick contact. She reported swimming in a saltwater pool in Arizona and drinking tap water out of repurposed wine bottles at a restaurant in California. She was admitted a week before for COVID infection without pneumonia and was treated with a 3-day course of remdesivir and a higher dose of prednisone. Her symptoms presented a month prior to the discovery of the Druid Lake Reservoir contamination. At the time, she resided in Maryland county adjacent to the affected regions.

The patient received a bilateral lung transplant for familial bronchiectasis with airway destruction and emphysema five years prior. She also has common variable immunodeficiency disorder (CVID) managed with weekly subcutaneous immunoglobulin therapy. At the time of the current presentation, her immunosuppressive regimen consisted

**Table 1:** Three Cases of *Cryptosporidium* Infections in Lung Transplant Recipients at INOVA Fairfax Medical Campus.

Patient	Age (years)	Time since lung transplant	Medical Comorbidities	Cryptosporidium exposures	Immunosuppression at presentation	Immunosuppression changes	Clinical summary	Treatment Regimen	Total Hospital Days
1	47	5 years (bilateral)	CVID	County resident adjacent to Druid Lake	Prednisone 10 mg, Tacrolimus 0.5 mg twice daily, Sirolimus 1 mg	Prednisone decreased to 7.5 mg daily, Tacrolimus stopped, Sirolimus increased to 1.5 mg daily	Severe sepsis from <i>Cryptosporidium</i> and <i>C. difficile</i> colitis	Nitazoxanide (14 days) Oral vancomycin (10 days)	7
2	60	15 years (single R) 3 years (bilateral)	ESRD on HD	Baltimore resident, local takeout food	Prednisone 5 mg, Tacrolimus 3 mg in AM and 2 mg in PM	Tacrolimus decreased to 2 mg twice daily	Septic shock from <i>Cryptosporidium</i> diarrhea	Nitazoxanide (14 days)	19
3	35	4 years (bilateral)	Cystic Fibrosis related Diabetes	Salads, raspberries	Prednisone 10 mg, Tacrolimus 5 mg twice daily, Sirolimus 1 mg	No changes made	Severe sepsis from <i>Cryptosporidium</i> diarrhea	Nitazoxanide (14 days)	4

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of prednisone 10 mg daily (with an ongoing taper from her recent COVID infection) and tacrolimus 0.5 mg twice daily. She previously was on mycophenolic acid, but this had been held due to recent COVID.

In the ED, she was febrile up to 37.8°C, tachycardic, and relatively hypotensive. Her lab work showed a white blood cell (WBC) count of 18,000 cells/microliter and lactic acid level of 3.1 mmol/liter. She was resuscitated with normal saline and her blood pressure (BP) normalized. Repeat COVID test was negative. A dose of meropenem was given due to her history of extended spectrum beta-lactamase (ESBL) producing *E. coli* infection during a prior hospitalization. Stool studies and respiratory pathogen panel were sent.

She was admitted to an OSH, and over the next 24 hours, the WBC count decreased to 16,000 cells/microliter, the lactic acid level normalized and the fever resolved. She was later transferred to our transplant center for further care. Repeat chest X-ray showed no evidence of consolidations or effusions. Her original stool studies tested positive for *Cryptosporidium* antigen and *Clostridioides difficile* toxin B. She started on 14 days of nitazoxanide and 10 days of oral vancomycin.

She continued to have voluminous diarrhea, which was managed with supportive care via intravenous (IV) fluids and simethicone as needed for abdominal cramping. Her prednisone dose was reduced to 7.5 mg given recurrent infections. On the day of discharge (hospital day 7), her oral intake had improved, and the diarrhea was resolving with more formed bowel movements. Her WBC and vital signs were within normal limits. At follow up outpatient a few days later, she endorsed mild diarrhea with occasional watery bowel movements that were much improved from her initial presentation.

## Case 2

A 60-year-old male with a history of a redo lung transplant three years prior presented to the ED in late September 2023 complaining of three weeks of watery diarrhea. His vitals were stable, abdominal CT showed fluid in the colon suggestive of diarrhea and no evidence of diverticulitis. He had asymptomatic pyuria on urinalysis. Stool studies for bacterial, parasitic, and fungal sources were sent. He was discharged from the ED with antibiotics for a possible urinary tract infection. The next day, stool studies were positive for *Cryptosporidium* antigen, and he was prescribed a 14-day course of nitazoxanide. He was unable to fill the medication at his pharmacy and returned to the ED four days later with persistent diarrhea, now up to 10 episodes a day, associated with progressive fatigue. His symptoms presented during the same week of the Druid Lake Reservoir contamination discovery, and he resided in Baltimore at the time. He stated that his girlfriend had brought him food from several local takeout restaurants in the preceding weeks.

He had a right single lung transplant in 2008 for nonspecific interstitial pneumonia secondary to rheumatoid arthritis and then a redo bilateral lung transplant in 2020 for chronic lung allograft dysfunction. He subsequently developed end stage renal disease necessitating hemodialysis three days a week. His second transplant course was complicated by bacterial pneumonias as well as pulmonary aspergillosis as well as rhino-orbital and pulmonary mucormycosis, managed on long-term isavuconazole. His immunosuppressive medications at time of the current presentation included tacrolimus 3 mg in the morning and 2 mg in the evening, and prednisone 5 mg daily. The patient had been off mycophenolate due to his history of persistent fungal infections and EBV viremia.

He was admitted to the medical floor, but he developed hypotension and lactic acidosis leading to transfer to the intensive care unit for management of mixed hypovolemic and septic shock. He started on norepinephrine drip, stress dose steroids, and empiric piperacillin-tazobactam and vancomycin. Nitazoxanide was started and post-transplant prophylactic medications (isavuconazole and trimethoprim-sulfamethoxazole) were continued. Prophylactic valganciclovir was held for leukopenia which improved with G-CSF treatment. His blood cultures showed no growth and chest X-ray showed no evidence of an acute pulmonary process. Antibiotics were later discontinued.

He continued nitazoxanide but had ongoing high stool output requiring a rectal tube. Stool output was over 1-3 L every 24 hours for the next 4 days. He was able to maintain appropriate oral intake and was discharged home on day 19. At clinic follow up two weeks later, the diarrhea had fully resolved, and he was consuming three meals a day.

## Case 3

A 35-year-old male with a history of bilateral lung transplant for cystic fibrosis was brought in by ambulance to the ED in February 2024 with complaints of one day of headache followed by abdominal pain, nausea, vomiting, and multiple episodes of watery diarrhea. At presentation, he was four years post-transplant. His postoperative course was complicated by three admissions within the first year for gastrointestinal related illnesses, twice for *Clostridioides difficile* colitis and once for enteritis. His immunosuppressive medication regimen at the time of the current presentation included tacrolimus 4 mg twice daily, sirolimus 1 mg daily and prednisone 10 mg daily. He had been off mycophenolate prior to the current presentation due to his history of recurrent infections and EBV viremia.

At presentation, he reported over 20 episodes of non-bloody, watery diarrhea that night with intermittent epigastric pain. He denied fevers, chills, or sick contacts. Upon arrival, he was found to be tachycardic to the 120s, relatively hypotensive with systolic BP in the 100s, and afebrile. Lab

work from the ED revealed a leukocytosis of 28,000 and a lactate of 3.7. He was also found to have acute on chronic kidney injury and to be hyperkalemic at 7.1 with no evidence of ECG changes. Calcium gluconate, potassium shifting agents, and 3L of normal saline boluses were given in the ED. He was admitted to the ICU for management of septic shock, renal failure and electrolyte derangement. He was a resident of Northern Virginia but often consumed take out salads and raspberries which may have exposed him to contaminated water.

Noncontract CT abdomen and pelvis revealed mildly distended and moderately thickened small bowel concerning for enteritis versus ischemic bowel. His abdominal pain and lactic acidosis improved with fluid resuscitation. The patient was pan-cultured, and stool studies were sent. Oral and IV vancomycin and piperacillin-tazobactam were ordered.

Tacrolimus, sirolimus and prednisone were discontinued due to inability to tolerate medications orally. He started on an equivalent dose of tacrolimus sublingual and methylprednisolone IV. On hospital day 2, he was clinically improving with less abdominal pain and no additional episodes of diarrhea or vomiting. His stool tested positive for the *Cryptosporidium* antigen and treatment with nitazoxanide was started. All other antibiotics were discontinued.

Over the next two days, he had one to two loose bowel movements but began to tolerate a diet and was transitioned back to his prior oral immunosuppressive regimen. He was deemed stable for discharge by the fourth day of his hospitalization. On the day of discharge, he was having formed stool and denied abdominal pain, nausea, vomiting, or diarrhea. His white count had completely normalized, lactic acidosis resolved, and all remaining electrolytes were within normal limits with his creatinine returning to his baseline. He completed a 14-day course of nitazoxanide 500 mg twice a day and was seen in transplant clinic a month after discharge. He had no additional gastrointestinal complaints at the time and felt like he had returned completely to his normal routine and diet.

## Discussion

*Cryptosporidium* is an opportunistic parasite known to cause severe gastrointestinal illness in immunocompromised patients, especially solid organ transplant recipients. Solid organ transplant recipients are susceptible to numerous opportunistic infections in the setting of their immunocompromised state. In this series, we present three cases of *Cryptosporidium* diarrhea, which were potentially related to contamination of water in Druid Lake Reservoir in Baltimore, Maryland. To our knowledge, this series represents the largest case series of *Cryptosporidium* in lung transplant recipients.

Each patient case presented in this case series manifested a severe disease course requiring hospitalization, but each had a favorable response to treatment. All three patient cases initially presented to the hospital with severe episodes of watery, non-bloody diarrhea. Case 2 and 3 are notable for admission to the intensive care unit for septic and hypovolemic shock, which illustrates that lung transplant recipients can develop severe life-threatening diseases from cryptosporidiosis. All three patients had lactic acidosis that improved with appropriate fluid resuscitation and initiation of nitazoxanide. Each patient completed a 14-day course of nitazoxanide with an eventual resolution of their symptoms and returned to baseline.

In solid organ transplant recipients that present with nonspecific symptoms such as diarrhea, it is important to include cryptosporidiosis on the differential. A high index of suspicion and a thorough social history and exposure history is essential to making the diagnosis. *Cryptosporidium* is not often tested in routine stool pathogen testing, and it is important to consider adding antigen testing in workup for these patients. The prior literature on cryptosporidiosis in transplant patients is limited largely to renal transplant recipients and thus this case series provides an understanding of how this infection may present in lung transplant recipients. This case series also highlights the importance of transplant programs being vigilant for outbreaks or contaminations and providing timely warnings and precautionary guidance to their vulnerable populations.

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