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CASE REPORT

Infantile Clostridium Difficile Infection Presenting with Severe Metabolic Acidosis: a Case Initially Diagnosed as Norovirus

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SUMMARY

Background: **Clostridium difficile infection (CDI) is characterized by diarrheal illness with serious complications. Previous literature has not reported concurrent infections of Norovirus and *Clostridium difficile* (*C. difficile*) leading to severe acidosis.**
Methods: **Here, we report a case of *C. difficile* in a 55-day-old Chinese infant with severe acidosis.**
Results: **We present a unique case of a patient with an initial Norovirus-positive test who received appropriate treatment but showed a poor response. Five days later, the patient tested positive for *C. difficile* toxins A and B. Treatment with oral vancomycin resulted in an excellent response. The patient improved clinically and remained afebrile, with cessation of diarrhea and correction of acidosis.**
Conclusions: **This article reports a rare case of *C. difficile* infection in an infant presenting with persistent diarrhea and severe metabolic acidosis, which was initially diagnosed as Norovirus, despite the absence of obvious immune deficiency. This case emphasizes the importance of considering *C. difficile* infection in the differential diagnosis of unexplained diarrhea when routine tests are inconclusive.**
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KEYWORDS

clostridium difficile infection, metabolic acidosis, norovirus, children

INTRODUCTION

Clostridium difficile infection, characterized by watery diarrhea leading to serious complications, is a common pathology in clinical practice. It is caused by the opportunistic bacterial pathogen *Clostridium difficile*, which can produce a spectrum of diseases in humans, ranging from antibiotic-induced diarrhea to pseudomembranous colitis [1]. Human Noroviruses are the leading cause of acute gastroenteritis worldwide in all age groups and cause significant disease and economic burden globally [2]. Norovirus infection typically presents as a self-resolving illness, with gastrointestinal manifestations such

as diarrhea, vomiting, nausea, abdominal cramps, and low-grade fever, usually resolving within two to four days in healthy adults.

We present a unique case of a patient who initially tested positive for Norovirus and was treated accordingly, but with no clinical improvement. Five days later, the patient tested positive for *C. difficile*. After completing the prescribed treatment for *C. difficile*, the patient's clinical symptoms improved.

Coinfection with Norovirus and *C. difficile* is rarely reported. To our knowledge, this is the first reported case of such coinfection associated with severe metabolic acidosis in an immunocompetent individual. This case emphasizes the need to consider coinfection with Norovirus and *C. difficile* even in immunocompetent individuals.

CASE PRESENTATION

A 55-day-old female infant was admitted to our hospital with persistent diarrhea for one week, without vomiting, fever, or abdominal distension. Prior to the onset of symptoms, she had received a 14-day course of intravenous antibiotic therapy at a local hospital for pneumonia. The patient was born at term with a birth weight of 3,530 g. Her antenatal, perinatal, and family history were unremarkable, with no family history of gastrointestinal diseases. Despite treatment with probiotics, smectite powder, and lactose-free formula, the diarrhea persisted with worsening stool frequency. Additionally, the patient developed oliguria.

On admission, the patient weighted 4,000 g with a height of 54 cm. Her initial vital signs showed tachycardia (156 beats per minute), tachypnea (42 breaths/minute), oxygen saturation 91% on room air, blood pressure 70/45 mmHg, and temperature 36.9°C. The patient was conscious but physical examination revealed a sunken anterior fontanelle. Laboratory results indicated leukocytosis (WBC 21.4 x 10^9/L), elevated procalcitonin (PCT 1.54 ng/mL), and elevated C-reactive (CRP 15.3 mg/L). Routine laboratory tests, including renal function, transaminase, serum albumin, and bilirubin levels were within normal ranges (Table 1). Stool testing was negative for rotavirus and adenovirus but positive for Norovirus antigen, with 1+ leukocytes and 1+ erythrocytes. Blood gas analysis indicated severe metabolic acidosis: pH 7.21 (reference: 7.35 - 7.45), bicarbonate 5.2 mmol/L (reference: 18 - 23 mmol/L), and base excess (BE) -22.7 mmol/L (reference: -2 - 3 mmol/L). Electrolytes showed hyponatremia (128 mmol/L; reference: 136 - 145 mmol/L) and hypokalemia (2.4 mmol/L; reference: 3.4 - 4.5 mmol/L). Lactate was normal (1.4 mmol/L; reference: 0.5 - 2.2 mmol/L). Chest and abdominal radiographs were unremarkable.

Based on clinical presentation and laboratory findings, the patient was initially diagnosed with Norovirus infection. Antibiotics were discontinued, and alkaline fluids were administered to correct the acidosis and electrolyte imbalances. Smectite powder, *saccharomyces boulardii*, and oral rehydration salts III were continued. The patient had 9 - 12 daily stools with yellow, viscous (egg-yolk-soup-like) mucoid consistency and occasional blood streaks; stools were non-foul-smelling. Although electrolyte imbalances and dehydration were quickly corrected, metabolic acidosis persisted (pH 7.24, BE -23.1 mmol/L, HCO_3^- 4.3 mmol/L), and diarrhea remained refractory to therapy. Concurrently, CRP rose to 41.1 mg/L and PCT to 25.2 ng/mL. Somatostatin (3.5 µg/kg/hour) was added, and the formula was switched to an amino acid-base.

Given the history of prolonged antibiotics and the inability of Norovirus alone to explain severe metabolic acidosis and persistent diarrhea, *C. difficile* testing was performed. The positive result confirmed *clostridium difficile*-associated diarrhea. Oral vancomycin (15 mg/kg every 6 hours) was administered for 10 days. By hospital day 10, clinical improvement was observed: metabolic acidosis resolved (pH 7.46, HCO_3^- 24.2 mmol/L, BE +0.4 mmol/L, lactate 1.0 mmol/L; Figure 1) and serum electrolytes normalized (Na^+ 135 mmol/L, K^+ 4.0 mmol/L). Diarrhea significantly improved (2 - 3 formed stools/day). Subsequent stool analysis normalized, and Norovirus testing returned negative. No recurrence occurred during follow-up.

DISCUSSION

C. difficile, a Gram-positive, anaerobic, spore-forming, toxin-producing bacterium, exhibits broad antibiotic resistance due to spore formation, leading to high recurrence rates and treatment failure [3]. Colonization with *C. difficile* is typically benign as gut microbiota suppress. However, in predisposing conditions (e.g., antibiotic exposure or gastrointestinal surgery), *C. difficile* can transition to vegetative state, producing toxins that damage the intestinal epithelium. Early-stage CDI poses diagnosis challenges, as clinical presentation often overlaps with other enteric pathogens, potentially leading to missed diagnosis and delayed treatment. We present a case of CDI-induced severe metabolic acidosis successfully treated with orally vancomycin, providing evidence for clinical management.

In recent years, the incidence of pediatric CDI has increased. A systematic review in our country reported a 14% prevalence of toxigenic CDI among diarrhea patients [4]. *C. difficile* is the most common pathogen causing hospital-acquired and antibiotic-associated diarrhea [5]. The clinical spectrum of CDI varies significantly by age [6], ranging from asymptomatic carriage and mild self-limiting diarrhea to severe complications including pseudomembranous colitis, fulminant colitis, toxic megacolon, intestinal perforation, and multiorgan dysfunction syndrome [1]. Studies have indicated that *C. difficile* poses a potential pathogenic risk to pediatric inpatients and is considered a major complicating factor in high-risk populations such as pediatric oncology pa-

Table 1. Pertinent laboratory investigations.

Laboratory examination	Day 1	Day 3	Day 5 (oral vancomycin)	Day 7	Day 10	Reference range
WBC, 10^9/L	21.4	16.69	9.22	14.55	12.56	3.5 - 9.5
Neutrophils, %	61.2	48.5	61	41.3	42.1	40 - 75
Hemoglobin, g/L	147	123	109	116	118	97 - 183
Platelet, 10^9/L	360	274	390	329	465	125 - 350
CRP, mg/L	15.3	15.54	41.1	0.39	4.74	0 - 6
PCT, ng/mL	1.566	1.324	25.2	0.84	-	0 - 0.5
Total protein, g/L	68.9	-	67.5	55.3	-	65 - 85
Albumin, g/L	39.3	-	45.4	28.7	-	40 - 55

WBC White Blood Cell, CRP C-reactive protein, PCT Procalcitonin.

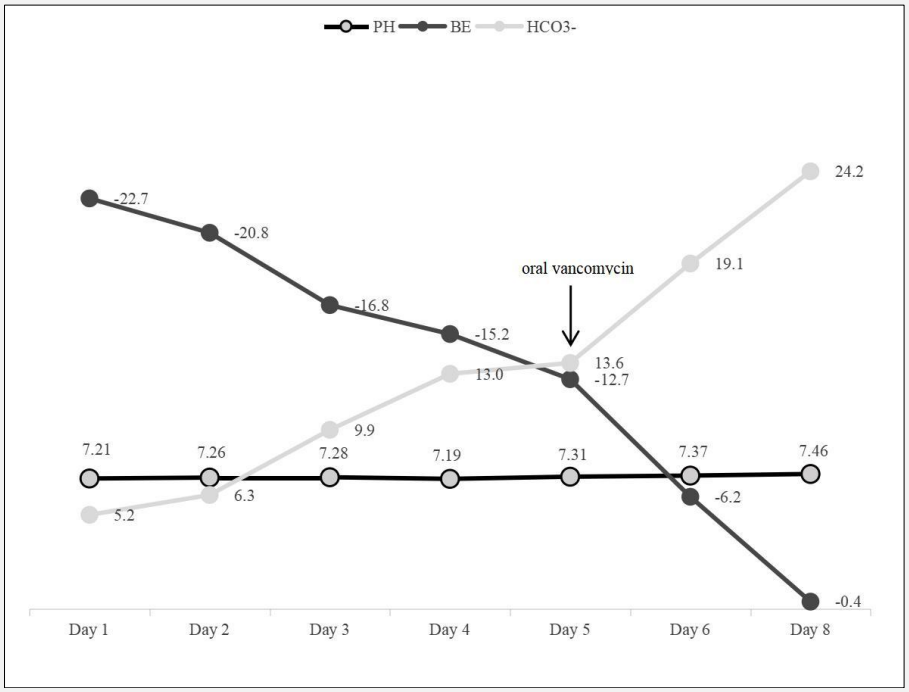

Figure 1. Timeline of blood gas parameters during the patient's hospital stay.

tients and children with gastrointestinal diseases [7].

Diarrhea is the most common clinical manifestation of CDI, often accompanied by abdominal pain, fever, and other infectious symptoms, with stools presenting as watery, mucoid, or bloody mucoid. The patient exhibited multiple CDI risk factors, including young age and antibiotic exposure [8]. However, early CDI was masked by concurrent Norovirus infection, leading to delayed diagnosis and prolonged hospitalization. Supportive therapy for Norovirus failed to alleviate symptoms; instead, classic CDI features emerged - high-volume diarrhea, fever, and elevated PCT levels. Following stool-confirmed CDI diagnosis, oral vancomycin was initiated alongside supportive care, resulting in gradual improvement and discharge. The disease mechanisms likely involved include: 1) Broad-spectrum antibiotic

overuse, 2) Immature immune function, 3) Post-Norovirus gastrointestinal dysmotility and functional disruption, collectively predisposing to secondary intestinal dysbiosis and CDI infection.

The primary therapeutic step in pediatric CDI management involves immediate discontinuation of high-risk antimicrobial agents [9]. Notably, antibiotics were discontinued early in our case. Research indicates that vancomycin and metronidazole are recommended first-line therapies [10]. For pediatric recurrent CDI, fecal microbiota transplantation (FMT) represents a promising therapeutic alternative [11].

This case highlights that in diarrheal illnesses refractory to initial therapy and complicated by metabolic acidosis, CDI should be considered. Perform stool pathogen testing early to enable timely, targeted treatment. For patients with poor oral medication response, FMT therapy can be considered.

Declaration of Interest:

The authors declare that they have no conflict of interest.

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