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**Case Report**  
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# *Clostridioides difficile* Infection after Antibiotics Treatments for Acute Appendicitis in a 2-year-old Girl: A Case Report

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## Summary

*Clostridioides difficile* infection (CDI) is an intestinal infection caused by intestinal dysbiosis due to exposure to antibiotics. We describe the case of a 2-year-old girl who developed CDI after antibiotic treatment for acute appendicitis. She presented to our hospital with fever, abdominal pain, and frequent diarrhea. She was diagnosed with acute appendicitis following abdominal contrast-enhanced computed tomography and was treated with cefmetazole for 5 days. Eight days after discontinuation of cefmetazole treatment, she experienced abdominal pain, associated with the passage of loose stools. Abdominal ultrasonography revealed no swelling of the appendix. Both the *Clostridium difficile* antigen and toxin tests were positive. She was diagnosed with CDI due to her recent antibiotic treatment for acute appendicitis. Intravenous metronidazole (30 mg/kg/day) and probiotics were administered for 10 days. Her abdominal pain improved gradually and did not recur after discontinuation of metronidazole. The increasing global prevalence of CDI in low-risk populations and children necessitates its consideration in both pediatric patients, and even children without preceding underlying disease. There have been no reports on the development of CDI in patients receiving antibiotic treatment for appendicitis. If gastrointestinal symptoms relapse after an antibiotics treatment for acute appendicitis, CDI should be considered while investigating for possible relapse of appendicitis.

**Key Words:** antibiotics, appendicitis, cefmetazole, *Clostridioides difficile* infection, diarrhea

## Introduction

*Clostridioides difficile* infection (CDI) is an intestinal infection caused by intestinal dysbiosis due to exposure to antibiotics, especially broad-spectrum antibiotics. Older adults and individuals with certain underlying diseases are predisposed to CDI and its serious complications, including pseudomembranous colitis and toxic megacolon. The incidence of community-associated

CDI in low-risk populations<sup>1)</sup> and children<sup>2)</sup> has increased. We herein describe a 2-year-old girl who developed a CDI after an antibiotic treatment for acute appendicitis.

## Case Presentation

A 2-year-old girl, presenting with fever, abdominal pain, and frequent diarrhea, was admitted to our hospital. She had no specific medical and family history. On

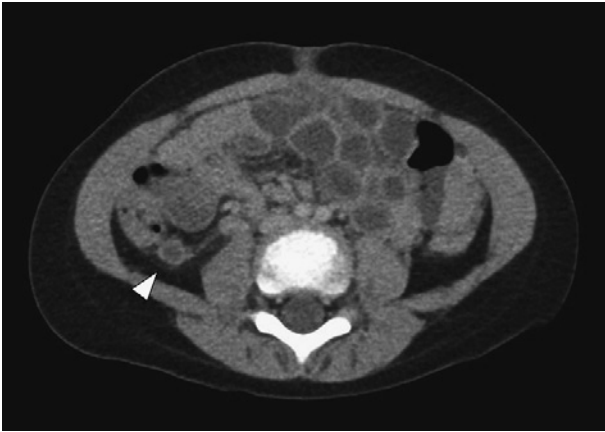
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**Figure 1** Abdominal contrast-enhanced computed tomography scan.

Abdominal contrast-enhanced computed tomography scan reveal swelling of the appendix, suggesting acute appendicitis.

physical examination, the patient appeared well without abdominal tenderness and other abnormal findings. Blood examination revealed the following: white blood cells (WBCs), 17,100/ $\mu\text{L}$  (neutrophils, 58.5%; lymphocytes, 32.5%); hemoglobin, 12.5 g/dL; platelets, 529,000/ $\mu\text{L}$ ; albumin, 3.4 g/dL; C-reactive protein (CRP), 10.98 mg/dL; and procalcitonin, 0.63 ng/mL. Urine analysis revealed no pyuria and bacteriuria. The fecal rapid antigen test results were negative for rotavirus, norovirus, and adenovirus. Fecal bacterial culture (both aerobic and anaerobic) revealed no pathogenic bacteria, and the fecal *Clostridioides difficile* antigen and toxin tests were negative as well. An abdominal contrast-enhanced computed tomography scan revealed acute appendicitis (Fig. 1). She was treated with cefmetazole for 5 days. Thereafter, she was discharged due to improvement in her symptoms and laboratory findings.

Eight days after the discontinuation of cefmetazole treatment, the patient experienced abdominal pain, associated with the passage of loose stools. Thus, she visited our hospital again. On physical examination, she appeared well without abnormal findings; furthermore, abdominal ultrasonography showed no swelling of the appendix. However, both the *Clostridioides difficile* antigen and toxin tests were positive. Whether CDI is caused by short-term antibacterial drug administration in children without preceding underlying disease is unclear; hence, we followed up the patient without treatment since her general condition was good. However, 3

days later, she was hospitalized for fever and worsening abdominal pain. Blood examination revealed the following: WBCs 17,000/ $\mu\text{L}$  (neutrophils, 53.7%; lymphocytes, 36.6%); albumin, 3.8 g/dL; and CRP, 7.08 mg/dL. Fecal bacterial culture (both aerobic and anaerobic) revealed no pathogenic bacteria, including *Clostridioides difficile*. However, both the *Clostridioides difficile* antigen and toxin tests were positive again. Thus, she was diagnosed with CDI secondary to her recent antibiotic treatment for acute appendicitis. Intravenous metronidazole (30 mg/kg/day) and oral probiotics were administered for 10 days. The abdominal pain improved gradually and did not recur after the discontinuation of metronidazole.

### Discussion

Based on the clinical practice guidelines for CDI established by the Infectious Diseases Society of America, routine *Clostridioides difficile* testing is not recommended in children aged < 2 years old who present with infantile diarrhea<sup>3</sup>. However, the patient in the present case was a 2-year-old girl with a recent history of antibiotic treatment and no findings suggestive of recurrent appendicitis. Therefore, CDI testing was performed. The *Clostridioides difficile* antigen often indicates just a carrier status; if the test for *Clostridioides difficile* toxin is also positive, it is said to indicate CDI<sup>4</sup>. In our patient, the test for *Clostridioides difficile* toxin was positive twice, indicating that our patient had true CDI. In a previously reported case, *Clostridioides difficile* was identified as the causative agent of appendicitis<sup>5</sup>. While the causative bacteria for appendicitis in our case remained unclear, bacterial culture (aerobic and anaerobic) revealed no presence of *Clostridioides difficile*, and the *Clostridioides difficile* antigen and toxin tests were negative when she had appendicitis. Furthermore, *Clostridioides difficile* is generally not susceptible to cefmetazole. Therefore, we believe that *Clostridioides difficile* may not have been the causative agent of appendicitis in our case.

The increasing prevalence of CDI worldwide necessitates its consideration among pediatric patients (even among those without preceding underlying diseases) who present with gastrointestinal symptoms and a recent history of antibiotic treatment. There have been no previous reports on the development of CDI among

patients receiving an antibiotic treatment for appendicitis. If gastrointestinal symptoms relapse after the use of antibiotics for acute appendicitis, it is necessary to consider the possibility of CDI while investigating relapse. Further studies on CDI in healthy children are required.

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#### Author Contributions

YF collected and analyzed the data and drafted and revised the initial manuscript. TY, NY, and SY interpreted all the data and critically revised the manuscript for important intellectual content. All authors approved the final manuscript and agreed to be accountable for all aspects of the work.

#### Patient consent for publication statement

Written informed consent for publication was obtained from the patient's guardian.

#### Access to data

The data that support the findings of this study are available from the corresponding author, YF, upon reasonable request.

#### Conflict of interest

The authors declare no conflicts of interest. No specific funding was received from any bodies in the public, commercial, or not-for-profit sectors to carry out the work described in this article.

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