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ACTA PÆDIATRICA NURTURING THE CHILD WILEY

BRIEF REPORT

Faecal transplantation in a two-year-old child with therapy-resistant *Clostridiodes difficile*infection

*Clostridioides difficile*infection (CDI) is a bacterial infection presenting with symptoms ranging from mild diarrhoea to life-threatening colitis and is often preceded by multiple antibiotic treatment.[1] Typically, CDI is less frequent in children than in adults, but it has recently been recognised as a more common cause of hospital and community-acquired diarrhoea in children.[1,2]

Clostridioides difficile(CD) is a toxin-producing anaerobe and an early coloniser of the infant microbiota, which rarely initiates symptomatic disease before the age of 1 year. Juvenile lack of toxin receptor, as well as breastfeeding, has been suggested to be protective.[2,3] In a hospital setting study, nosocomial diarrhoea was found in 32% of children ($n = 99$) with a median age of three.[3] Community-acquired (CA) CDI lacks the typical risk factors such as disruptive antibiotic treatment or healthcare contact, according to Borali and De Giacomo.[1]

The composition of the intestinal microbiota in children is under development and less-stable, compared to adults. A microbial ecosystem characterised by low diversity seems to be associated with CDI.[4] Chronic underlying disease, hospitalisation, viral and bacterial diarrhoea also appear to be risk factors.

We present the case of a female child with Williams's syndrome, a rare genetic disorder involving cardiovascular disease including hypertension. Oral sensitivity and difficulty in sucking and swallowing are often present, as is cognitive impairment. Gastro-oesophageal reflux disease (GERD) has also been observed.

This child was born with her healthy twin brother at week 38. She had intrauterine-diagnosed heart failure (coarctation aorta), which was operated on 2 days after birth. Her birthweight was 2195 g, −3.15 SD, (Z-score) She received a short course of ranitidine postoperatively and propranolol for high blood pressure. She was partly breast and tube-fed, during the first months of life, with regular vomiting accompanied by constipation and stomach pain. The vomiting and coughing worsened and gastroesophageal reflux was obvious and resulted in treatment with esomeprazole. Vomiting was the leading symptom at 6 months, with occasional diarrhoea; 1 month later, she received a percutaneous endoscopic gastrostomy (PEG) and perioperative cefuroxime, which worsened both the vomiting and the diarrhoea. Because of the patient's stomach pain, vomiting and coughing (possibly indicating aspiration), an X-ray of oesophagus and ventricle was performed at 9 months of age to confirm GERD but was inconclusive; why, the patient was subsequently reinvestigated with 24-h pH monitoring, gastric emptying scintigraphy and X-ray of oesophagus and ventricle, which confirmed GERD. Fundoplication was performed, as recommended by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)/the North American Society for Paediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN).[5] Because of postoperative diarrhoea, culture of CD and isolate tested for toxin production was performed and was positive for the first time. Despite two courses of metronidazole, recurrent diarrhoea and stomach pain continued, after each PEG tube-administered meal. A third therapeutic course of vancomycin was given, followed by several attempts to taper the dose, as well as the proton pump inhibitor (PPI), resulting in diarrhoea accompanied by positive toxin test and, hence, vancomycin and PPI treatment continued. Intermittent nausea, fatigue, stomach pain, flatulence and persistent erosive diarrhoea, led to rectal ulcers. Reduced oral intake of food and different formulas were tried to control the diarrhoea but without success. Therefore, faecal microbiota transplantation (FMT) was chosen, to treat this therapy-resistant CDI. One tablespoon of fresh stool from the twin brother was mixed with 200 ml NaCl and administered as a rectal enema after slight sedation. The twin brother was tested negative for hepatitis A, B and C, human immunodeficiency virus (HIV), *Yersinia pestis* and cytomegalovirus (CMV), and the stool for parasites and CD.

In the female patient, vancomycin treatment was continued until 24 h before faecal transplantation. On day 3, after the FMT, her diarrhoea had improved.

After 1 month, the procedure was repeated, due to relapse of diarrhoea after X-ray using laxatives. This time the patient was treated with FMT only, without previous vancomycin. After the FMT, she started to eat more orally and the culture of CD and isolate tested for toxin production was negative. She had less diarrhoea and stomach pain. Over time, the patient's development improved and she started to walk. She gained weight from −3 SD at 2 years of age to −2 SD at age 3, still without vancomycin treatment. Her stool habits remained mostly normal despite esomeprazole and antibiotics for upper respiratory tract infection. The following year the patient started attending a

Abbreviations: CD, *Clostridioides Difficile*; CDI, *Clostridioides Difficile* infection; CMV, cytomegalvirus; ESPGHAN, European Society for Paediatric Gastroenterology; FMT, faecal microbiota transplantation; GERD, Gastro-oesophagal reflux disease; HIV, human immunodeficency virus; NASPGHAN, North American Society for Paediatric Gastroenterology; PEG, percutaneous endoscopic gastrostomy; PPI, proton pump inhibitor.

day care centre. She suffered from repeated gastroenteritis and occasionally constipation or diarrhoea but remained negative for CD.

Currently, at age 7, her weight is +1 SD and her height is somewhat short (−1 SD), owing to Williams syndrome. She still has recurrent gastrointestinal problems, sometimes with bloody diarrhoea. Vomiting is rare but she is still on esomeprazole treatment. The patient's oral food intake is low and most of her nutrition is formula administered via the tube due to her depressed oral motor skills. She can chew but does not swallow.

The patient continues to have frequent hospital visits related to the cardiovascular disorder, recurrent upper respiratory tract infections and swallowing problems. Although these medical problems remain, the family highly appreciate the prolonged absence of CDI infection. Despite her many risk factors for CD infections, the patient has been free from CDI for 5 years after two faecal transplantations. When she had not yet fully recovered from her gastrointestinal problems, colonic biopsies were taken some time after the FMTs, which supported an inflammatory picture resembling post-CDI; no other diagnosis was established.

1 | LESSONS TO LEARN

Children can suffer from CDI, even one-year-olds.[1]

A young child can present with multiple CDI recurrences, which may only be cured permanently by FMT and the donor faeces should preferably be age-matched.[5]

Antibiotics are still the most important risk factor for CDI in children along with reported risk factors for CDI: chronic disease with repeated hospitalisation, drugs and medical procedures, gastric acid suppression, enteral diet and gastrostomy.[1]

The ESPGHAN/NASPGHAN has published a report on FMT since this procedure is increasingly being considered as a treatment option for various gastrointestinal disorders.[5]

CONFLICT OF INTEREST

We declare no conflict of interest, financial or otherwise, that could have biased this work.

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