Successful Treatment of Pseudomembranous Colitis with Fecal Microbiota Transplantation – A Case Study on A Patient Rescued by Extracorporeal Cardiopulmonary Resuscitation After Cardiac Arrest

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Background: Pseudomembranous colitis (PMC) is an opportunistic, nosocomial infection caused by Clostridium difficile.

Case Report: Here we described a patient who developed PMC during her recovery from cardiac arrest. A 16-year-old female high school student experienced sudden cardiac arrest. Spontaneous circulation was not returned by standard cardiopulmonary resuscitation. After her admission to the emergency unit, her cardiac function and neurologic function were finally resumed by extracorporeal cardiopulmonary resuscitation (ECPR); however, after 14 days, her recovery was complicated with excessive diarrhea and shock. Colonoscopy confirmed the diagnosis of PMC. Metronidazole and vancomycin were immediately administered; however, the treatment did not result in any improvement. Fecal microbiota transplantation was then performed, and after 4 transplantations, her diarrhea was significantly ameliorated. After hospital stay for 135 days, the patient was finally discharged with grade II brain function. She later recovered self-care ability in follow-up.

Conclusions: The patient suffered from a long-term gastrointestinal ischemia-hypoxia resulting from cardiac arrest. The use of broad-spectrum antibiotics in the later treatment led to refractory PMC, which was successfully managed by multiple fecal microbiota transplantation.

MeSH Keywords: Case Reports • Death, Sudden, Cardiac • Enterocolitis, Pseudomembranous

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Background

Cardiac arrest represents a major cause of death in well-developed countries. In the United States and Canada, cardiac arrest causes more than 300,000 deaths, while in China, according to the epidemiological data of the World Health Organization, there are nearly a half million cases of cardiac arrest-related deaths.

The 2015 American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation indicates that extracorporeal cardiopulmonary resuscitation (ECPR) may be considered in patients who cannot recover spontaneous circulation or have repeated episodes of cardiac arrest after conventional cardiopulmonary resuscitation. Indeed, it has been reported that prompt ECPR would rescue ~36% of the hospitalized patients with cardiac arrest [1].

However, the recovery of resuscitated patients is always complicated with pseudomembnanous colitis (PMC). The administration of antibiotic agents in resuscitated patients can cause an imbalance of intestinal flora, leading to an uncontrolled propagation of Clostridium difficile, causing clinical manifestations such as intractable diarrhea, hematochezia, fever, electrolyte imbalance, hypoproteinemia, septic shock, and in some severe cases, death [2]. Recently, fecal microbiota transplantation has emerged as an effective treatment option for patients with recurrent and antibiotic-refractory PMC [3,4]. In this report, we described a successful treatment of PMC with the use of FMT in a 16-year-old female high school student who was rescued from cardiac arrest by ECPR.

Case Report

A 16-year-old female who weighted 60 kg suddenly lost consciousness when she was running in her physical education class (at ~11: 20 on April 16, 2018). CPR was immediately applied before the patient was admitted to the Emergency Department of our hospital around ~11: 40. CPR was continuously applied; however, spontaneous circulation was not returned. At noon, ECPR was performed using femoral cannula kit (Medtronics) combined with Stöckert centrifugal pump and D905 EOS membrane oxygenator. At 13: 00, extracorporeal membrane oxygenation (ECMO) was successfully established with a speed of 2650 rpm and a flow rate of 3.6 L/minute. Heparin was administered; at the same time, metronidazole, Bifidobacterium, Enterococcus, and Bacillus cereus were administered. After treatment, the body temperature decreased to 38°C, but there was no significant improvement in diarrhea.

On May 2, considering the possibility of PMC, the combined regimen of vancomycin (0.5 g, every 6 hours via nasogastric tube) and metronidazole (0.5 g, every 6 hours intravenous medical drip) was applied. Diarrhea was not mitigated, with a frequency of 20–40 times a day and a volume of 3000–4000 mL. On May 5, bedside colonoscopy suggested PMC (Figure 1). To this end, the original anti-infectives were changed to piperacillin/tazobactam.
Figure 1. Bedside colonoscopy confirmed the diagnosis of pseudomembranous colitis in our patient.

Figure 2. Coronary computed tomography angiography (CTA) was performed to delineate the underlying cause of cardiac arrest. The imaging finding suggests that the origin of the right coronary artery is at the top of the sinus. In the CTA, anomaly of origin of the right coronary artery was observed, in which the right coronary artery origin was above the intersinus ridge. The right coronary artery traveled between the aortic root and the right ventricular outflow tract. During strenuous exercise, the patient’s right ventricular outflow tract would thicken, compressing the right coronary artery origin, leading to myocardial ischemia and cardiac arrest.
was adjusted to protect the integrity of the intestinal mucosa, to modulate intestinal flora and to ensure water-electrolyte balance. Disappointedly, these approaches did not ameliorate diarrhea in a significant manner.

On May 15, dark red diarrhea was observed. Hematochezia and poisoning symptoms became more severe. In view of this, the first fecal microbiota transplantation (5 U) using the microbiota from the Chinese FMT Bank was performed. Thereafter, diarrhea was slightly improved, with the volume reduced to about 1500–2000 mL. Two additional FMTs were done on May 20 and May 22. The patient’s diarrhea was further mitigated, and the stool color changed from red to yellow. On May 23, nasogastric feeding of lactose-free formula milk started, and since then, the number of diarrehas was reduced to 10 times a day with a volume of 1000 mL. The fourth FMT was done on June 2. After this transplantation, diarrhea was further significantly improved to 2–4 times a day with a volume of 300–600 mL. Gradual transition to total enteral nutrition started on June 3.

On June 5, the tracheotomy was closed. On June 18, the patient was significantly improved and coronary computed tomography angiography (CTA) was performed to determine the cause of cardiac arrest. CTA suggested that the origin of the right coronary artery was at the top of the sinus in this patient (Figure 2). Due to functional impairment of the left lower limb, starting from June 21, the patient received rehabilitation therapy. On August 29, the patient was finally discharged with grade II brain function. After 6 months of follow-up, the patient restored her self-care ability.

Discussion

The right coronary artery originates normally in the middle of the adjacent aortic sinus. Abnormality in the origin of the coronary artery can be seen in 0.3% to 2% of the population, and among them, extremely rare cases show that the right coronary artery originates from the top of the sinus [5,6]. Most patients with an anomalous coronary origin have no obvious clinical symptoms with good prognosis, but some can be inflicted with heart failure, myocardial infarction, arrhythmia, and sudden cardiac death [7–9]. This study presented a case of sudden cardiac death that was attributed to the rare coronary origin at the top of the sinus. Fortunately, prompt CPR was applied, allowing the patient to be further rescued using ECMO.

ECMO-supported CPR is commonly named as ECPR. It has been indicated that the success rate of ECPR for hospitalized patients is 34% to 36%, and the success rate of out-of-hospital cardiac arrest patients ranges 4% to 36% [1]. For CPR, for every 1-minute increase in the duration, the probability of spontaneous recovery and survival of the patient is reduced by 1% and 4%, respectively. Stub et al. concluded from his findings from multiple centers that the survival rate of patients with cardiac arrest would drop to zero if the duration elapsed before ECMO establishment was longer than 60 minutes [10]. In this case, despite the time-to-ECMO of nearly 100 minutes, the patient was successfully discharged from hospital after treatment with different complications. Similar cases, to our best knowledge, are rarely seen in ECPR reports.

Unfortunately, although our patient resumed a good neurological outcome after ECPR, she suffered from excessive diarrhea and shock, which are the clinical presentation of PMC. The underlying cause of PMC was attributed to the imbalance of the intestinal flora that resulted from the administration of antibacterial agents. The uncontrolled propagation of Clostridium difficile can lead to notorious accumulation of toxins, causing clinical manifestations such as intractable diarrhea, hematochezia, fever, electrolyte imbalance, hypoproteinaemia, septic shock, and in some severe cases, death [2]. The typical findings of colonscopy include hyperemic edema, mucosal leukoplakia, pseudomembrane formation, and non-specific small ulcers or erosions. In the reported case, the time that elapsed from cardiac arrest to ECMO establishment was about 100 minutes. The intestinal hypoxia-ischemia was therefore relatively long. In the process of intestinal function recovery, the occurrence of clinical manifestations such as refractory diarrhea, hypoproteinaemia, and septic stock after the application of broad-spectrum antibiotics (i.e., meropenem) confirmed the diagnosis of PMC. To manage PMC, we ceased antibiotics, supplemented probiotics, maintained intestinal stability, strengthened supportive treatment, and at the same time administered first-line anti-Clostridium difficile drugs metronidazole and vancomycin as suggested by the Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children (2017) published by Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) [2,11]. Treatment with vancomycin and metronidazole, however, did not result in substantial improvement in clinical outcome of the patient. Indeed, relevant clinical studies have suggested that the use of certain antibiotics, e.g., vancomycin, would neither restore the intestinal microflora nor reduce the risk of recurrent Clostridium difficile infection and more importantly, would elevate the risk of other complications [12]. In view of this stringent recurrent Clostridium difficile infection, we decided to perform fecal microbiota transplantation as suggested by the Guidelines for Diagnosis, Treatment, And Prevention Of Clostridium difficile infections published by IDSA, SHEA, and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). After 4 transplantsations, the patient showed significant improvement.

Comparing to the brain and heart, the digestive organs can tolerate a longer duration of ischemia and hypoxia. However, if digestive organs were widely distributed anatomically, the full
recovery from dysfunctions would be a slow process. This would substantially affect the prognosis of patients after cardiac arrest. In ECPR, in addition to early cardiopulmonary and cerebral resuscitation, the functional recovery of the digestive system is a key determinant of patient’s survival. Broad-spectrum antibiotics are often administered as a prophylactic approach for infection; however, its excessive use has been identified as a risk factor for PMC.

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**Conclusions**

In this report we presented a patient who suffered from prolonged gastrointestinal ischemia-hypoxia due to cardiac arrest. The use of broad-spectrum antibiotics in subsequent treatment led to refractory PMC, which was successfully managed by multiple rounds of fecal microbiota transplantation.