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Clinical Transplant Kidney Function Loss Due to Small Intestinal Bacterial Overgrowth

Abstract

Small intestinal bacterial overgrowth (SIBO) is a clinical syndrome involving gastrointestinal symptoms caused by the presence of excessive bacteria in the small intestine. SIBO often leads to diarrhea and poses diagnostic and treatment challenges. Here, we report about a renal transplant recipient who experienced diarrhea-induced hypovolemic shock due to SIBO, necessitating the reintroduction of dialysis, and aim to provide insights to aid health-care providers in diagnosing and managing severe diarrhea in this specific patient group. A 14-year-old boy, who had undergone renal transplantation at the age of 2 years, experienced severe, recurring diarrhea leading to hypovolemic shock. The patient underwent volume loading and continuous hemodiafiltration. Upper gastrointestinal endoscopy findings suggested Whipple's disease. Antibiotics were initiated; however, the diarrhea did not improve. Examinations for infectious enteritis and food allergies yielded negative results. The diarrhea improved with rifaximin (RFX), but recurred repeatedly after its discontinuation. Antibiotic rotation, wherein RFX, amoxicillin hydrate and potassium clavulanate, ciprofloxacin, and RFX were administered in this order for 4 weeks each, improved the diarrhea. A lactulose breath test performed immediately before the second RFX course yielded negative results. The patient's condition was diagnosed as SIBO based on the clinical course, although the diagnostic criteria were not met. SIBO should be considered in cases of gastrointestinal symptoms in patients with transplanted kidneys. Antibiotic rotation should be considered for SIBO treatment in immunosuppressed patients.

Keywords: *Antibiotic rotation, post-kidney transplant patient, severe diarrhea, small intestinal bacterial overgrowth, immunosuppression*

Introduction

Diarrhea is the most common gastrointestinal symptom in kidney transplant patients and is often caused by infections or drugs.[1] Small intestinal bacterial overgrowth (SIBO) is a clinical syndrome characterized by gastrointestinal symptoms due to excessive bacterial population within the small intestine.[2] Herein, we report about a renal transplant recipient who experienced diarrhea-induced hypovolemic shock due to SIBO, necessitating dialysis reintroduction.

Case Report

A 14-year-old boy was admitted to our intensive care unit with hypovolemic shock secondary to diarrhea. He underwent renal transplantation at 2 years of age owing to bilateral hypoplastic/dysplastic kidneys. He had chronic diarrhea and anorexia for 2 years before admission. Upper and lower gastrointestinal endoscopy revealed no abnormalities. He was prescribed loperamide and esomeprazole based on his symptoms. After the onset of chronic diarrhea, his weight decreased from 38 to 30 kg over 2 years. Regarding chronic rejection, his transplanted kidney function, indicated by the estimated glomerular filtration rate, was 40 mL/min/1.73 m^2. The immunosuppressants administered include methylprednisolone 4 mg every alternate day, cyclosporine 120 mg/day, and mycophenolate mofetil 750 mg/day.

On admission, the patient's vital statistics included weight, 25.8 kg; height, 152 cm; body temperature, 36.5°C; blood pressure, 98/60 mmHg; heart rate, 62 beats/min; and oxyhemoglobin saturation, 88%. Clinical findings revealed drowsiness, inability to walk, sunken eyes, clear breath sounds, absence of heart murmurs, flat abdomen with increased bowel sounds, and cold limbs. Laboratory data indicated renal dysfunction, hypokalemia, metabolic acidosis, and anemia.

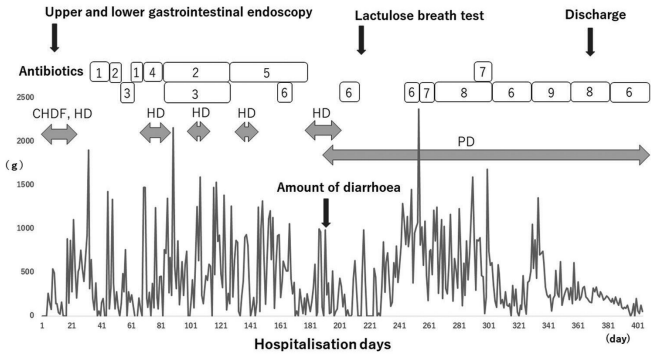

Figure 1: Progress after hospitalization. Numbers in the antibiotics column: 1. ceftriaxone, 2. doxycycline, 3. hydroxychloroquine, 4. meropenem, 5. ampicillin, 6. rifaximin, 7. metronidazole, 8. ciprofloxacin, 9. amoxicillin hydrate and potassium clavulanate. CHDF = continuous hemodiafiltration, HD = hemodialysis, PD = peritoneal dialysis

The patient underwent volume loading and continuous hemodiafiltration in the intensive care unit. Whipple's disease was suspected based on duodenal findings from upper gastrointestinal endoscopy, and intravenous ceftriaxone (CTRX) was initiated [Figure 1]. His diarrhea was initially ameliorated, but subsequently worsened. Transitioning from CTRX to doxycycline (DOXY) led to no improvement. Hydroxychloroquine (HCQ), CTRX, meropenem, DOXY + HCQ, and ampicillin were administered in that order, yet the diarrhea persisted. The patient could not eat and received total parenteral nutrition. In addition, he was sleep deprived because of nighttime episodes of diarrhea. Examinations for infectious enteritis and food allergies yielded negative results. Hemodialysis was then switched to peritoneal dialysis.

As pediatric nephrologists with 20 years of experience, we consulted a pediatric gastroenterologist regarding the patient's diagnosis and treatment. A 10-day regimen of rifaximin (RFX) was initiated for SIBO treatment; loperamide and esomeprazole were discontinued. Diarrhea improved 10 days after RFX initiation. Since diarrhea recurred after RFX discontinuation, three RFX courses were administered. A lactulose breath test performed immediately before the second RFX course yielded negative results. Ten days after initiating the third RFX treatment, diarrhea worsened, rendering the patient unable to consume food. RFX was replaced with metronidazole (MTR), but diarrhea worsened. Subsequently, MTR was substituted with ciprofloxacin (CPFX). Approximately 1 week after switching to CPFX, the diarrhea subsided, allowing the patient to resume eating. Following 4 weeks of CPFX treatment, CPFX and MTR were administered for 2 weeks. Owing to worsening diarrhea, CPFX and MTR were substituted with a fourth RFX course. Approximately 2 weeks after RFX initiation, the diarrhea decreased. RFX was administered for 4 weeks, followed by amoxicillin hydrate and potassium clavulanate for 4 weeks and CPFX for 4 weeks. The patient was discharged on hospitalization day 362. After CPFX, the fifth course of RFX was administered for 4 weeks and then discontinued. After discharge, the patient experienced solid and stable stools, occurring three to four times daily. Six months after discharge, the patient's weight improved to 40 kg. Even after the diarrhea subsided, the renal function did not improve, and peritoneal dialysis was continued. All immunosuppressants were discontinued after discharge.

Discussion

In SIBO treatment, antibiotic rotation and elimination of exacerbating factors help improve diarrhea. Several antibiotics are used, with an administration period of 5–28 days and an efficacy rate of 30%–100%.[2] RFX is the most widely studied antibiotic for SIBO.[3] Despite its effectiveness, relapse is common, with 44% of patients experiencing relapse within 9 months of the initial treatment.[3] Our patient had initial RFX efficacy, with repeated relapses, prompting antibiotic rotation every 4 weeks to prevent recurrence. The antibiotic rotation reported by Tauber *et al*.[4] did not include RFX and had a 57% efficacy rate. Antibiotic rotation should be considered in SIBO treatment for immunosuppressed patients.

SIBO risk factors include hypochlorhydria, pancreaticobiliary disease, motility disorders, anatomic disorders, and immune disorders.[5] In addition, chronic renal dysfunction worsens the intestinal flora.[6] In our patient, the use of immunosuppressants, proton pump inhibitors, and antidiarrheal agents worsened the intestinal flora and caused SIBO.

In our patient, although the diagnostic criteria were not met, SIBO was diagnosed based on clinical findings. SIBO is diagnosed using a small intestinal aspirate culture or lactulose or glucose breath test.[2] However, intestinal culture is invasive, and breath tests have a sensitivity of only 31%–68% for lactulose and 20%–93% for glucose when compared to cultures of the small bowel.[2] Improved SIBO diagnostic methods are needed. Nevertheless, SIBO should be considered in cases of gastrointestinal symptoms in kidney transplant patients.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Conflicts of interest

There are no conflicts of interest.

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Rituximab Induced Rare Cystic Lesion in Lungs in a Nephrotic Child: A Case Report

Abstract

Rituximab has been extensively used for managing B-cell lymphomas due to its anti-CD20 monoclonal antibody activity. Over the last decade, its application has been extended to manage frequent relapsing or steroid-dependent nephrotic syndrome. Its use has been comparatively safe, but few cases of adverse effects on the lung have been reported in the adult population. These lung injury presentations are rarely reported in a pediatric group with only four cases in the literature. Below is a rare case of rituximab-induced lung injury in a 9-year-old boy with frequent relapse of nephrotic syndrome, which developed after four days of rituximab infusion. Suspecting infection and sepsis, several antibiotics were started, but with no improvement in respiratory complaints, even antifungal and antituberculosis treatments were initiated. Finally, setting up a casual relation with the time of infusion to the development of complaints, association with rituximab was suspected. The patient responded to steroid therapy with complete resolution of respiratory complaints. To our knowledge, this is the first reported case of rituximab-induced cystic lesion in lungs from India.

Keywords: *Cystic lesion, nephrotic syndrome, rituximab children, ALI*

Introduction

Nephrotic syndrome (NS) has an average worldwide incidence of 2–16.9/100,000 children and is more prominent in Asians (incidence of 16 cases/100,000 children/year).[1,2] For idiopathic NS (INS), corticosteroids are the treatment of choice, and the majority of them respond well (complete resolution of proteinuria), labeled as steroid-sensitive NS (SSNS).[3] But around half of these cases may develop multiple relapses (steroid-dependent NS [SDNS]), having at least two consecutive relapses during tapering or within 14 days of cessation of steroids. Few may have frequent relapses; four relapses/year or two relapses within six months of the initial development of symptoms, termed frequent relapsing NS (FRNS). The standard management for children with FRNS/SDNS includes immunosuppressive like cyclosporine (CyA), tacrolimus, mycophenolate mofetil (MMF), and cyclophosphamide. But around 10–20% of children of FRNS on CyA have frequent relapses, while few cases report a lack of efficacy or side effects on long-term usage.[4,5] In cases with resistance or dependence on steroids, it poses the need to discover a novel drug for the treatment of FRNS/SDNS to prevent permanent renal damage.

Rituximab, a chimeric anti-CD20 IgG1 monoclonal antibody, has been effective in the treatment of several autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and lymphomas.[6-8] Rituximab has also shown satisfactory results in pediatric cases of FRNS or SDNS. It is comparatively safe in most adult cases, but in pediatric group, it is associated with several adverse effects such as pulmonary fibrosis,[9] pneumocystis pneumonia,[10] fulminant myocarditis,[11] and ulcerative colitis.[12] Post-rituximab pulmonary toxicities are rare and majorly seen in the elderly patient group. Here, we present a pediatric case of FRNS not responding to other immunosuppressive therapy, for which rituximab was infused. The patient developed symptoms of acute lung injury induced by rituximab, which resolved with prednisolone therapy.

Case Report

A 9-year-old male child, a known case of FRNS, was admitted for the first dose of rituximab therapy following remission on a daily dose of prednisolone and tacrolimus. He was diagnosed with NS at the age of 2.5 years and has had multiple episodes of relapse since then. Initially, he was on oral cyclosporine. But due to frequent relapses despite