Case Report

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Chronic Diarrhea Secondary to Human Sapovirus in a Renal Transplant Recipient

Andrew Dargan, Christina Tofani, Raja K Dhanekula and Daniel Quirk

Department of Gastroenterology, Thomas Jefferson University Hospital, Philadelphia, PA, USA

Corresponding author: Andrew Dargan, Department of Gastroenterology, Thomas Jefferson University Hospital, Philadelphia, PA, USA, Tel/Fax: 2159558900; E-mail: andrew.dargan@jefferson.edu

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Introduction

Diarrhea is common in renal transplant recipients. Although often a result of immunosuppressant medications, infection must be ruled out in patients who present with chronic diarrhea. This includes not only bacterial and parasitic infections, but also less common viral infections including sapovirus and norovirus.

Case

A 30 year old African American woman with a history of systemic lupus erythematosis (SLE) complicated by SLE nephritis, status post deceased donor renal transplant in 2005, on chronic immunosuppression with tacrolimus and mycophenolate mofetil (MMF), presented with two months of diarrhea. She described having four to seven watery bowel movements per day, accompanied by abdominal pain. She also reported a fifteen-pound unintentional weight loss, but denied any nausea, vomiting, melena, or hematochezia. She had two prior admissions for dehydration and diarrhea. During the first admission, she was diagnosed with viral gastroenteritis. During the second admission, it was suspected her immunosuppressants, Tacrolimus 10 mg total daily and MMF 750 mg per day were the cause of her diarrhea. During the subsequent admission, her mycophenolate mofetil was changed to mycophenolic acid. It was then discontinued as an outpatient for a period of time without improvement in symptoms. She presented to Thomas Jefferson University Hospital with persistent diarrhea. Significant labs during this admission included a positive fecal lactoferrin, a negative quantitative CMV PCR, a normal TSH, fecal fat, and anti-tissue transglutaminase antibody and total IgA, and a negative Clostridium difficile stool toxin. Hepatic function was normal, and a basic metabolic panel showed an elevated creatinine of 1.6 mg/dL, which was above the patient's baseline Cr of 1.1 mg/dL. A stool infectious panel was positive for sapovirus. Supportive care, with intravenous fluids and antidiarrheal agents, was provided. We also suggested the patient's mycophenolate mofetil dose be reduced or discontinued altogether.

Discussion

Diarrhea is frequently a side effect of immunosuppressants, such as mycophenolate mofetil. Up to 45% of patients experience gastrointestinal side effects of MMF, including nausea, vomiting, abdominal pain, and diarrhea [1]. Sapovirus, a member of the Caliciviridae family, affects both human and porcine populations. Norovirus, a fellow genus in the same family, is most commonly seen as a cause of acute gastroenteritis in immunocompetent individuals. It is the most common cause of viral gastroenteritis in adults, and the second most common cause in children [2-4]. Norovirus accounts for 90% of gastroenteritis outbreaks worldwide [5]. Neither virus has been very well-studied in immunosuppressed populations. However, multiple small cohort studies have shown that these viral infections may cause chronic diarrhea in both solid organ and bone marrow transplant patients [6,7]. Although less frequently observed causes of diarrhea in solid organ transplantation than bacterial causes, both sapovirus and norovirus should be considered in patients who develop chronic diarrhea following transplantation. Of the up to 45% of post-kidney transplant recipients who report chronic diarrhea, norovirus has been found to be the cause of 17-26% of these cases [8,9]. Chronic infection with sapovirus has only been reported in one retrospective cohort study, though the presentation and effects are very similar to those of norovirus [9]. As opposed to bacterial and parasitic infections, Roos-Weil et al. found patients with sapovirus and norovirus infections did not have elevated inflammatory markers, such as C-reactive peptide (6.6 as compared with 41.0, p=0.07), had more dramatic weight loss (8.5 pounds compared with 3.2, p=0.001) and longer duration of symptoms (262.2 days compared with 28.7 days, p<0.0001) [9]. Norovirus/sapovirus infection was also found to cause acute renal failure, along with irreversible renal graft impairment, confirmed by biopsy. The primary mechanism for renal graft failure and injury is thought to multifaceted, caused by dehydration from chronic malabsorption, which can have direct injury via renal hypoperfusion, but also increase concentrations of nephrotoxic agents such as tacrolimus [10]. In addition there is the added effect of increased enteric hyperoxaluria, which can have devastating effects on renal grafts through oxalate nephropathy [11]. Biopsies of failed grafts also showed antibody- and cellular-mediated rejection, acute tubular necrosis and calcineurin inhibitor-related nephrotoxicity [9].

Management of sapovirus-infected patients mainly includes supportive care, rehydration to prevent graft failure, and decreasing the dose of or even discontinuing MMF in 56% of patients. This may be due to mycophenolate-induced digestive tract toxicity and worsening diarrhea. Colonoscopy is often nondiagnostic in these patients, thus norovirus/sapovirus screening should be performed prior to endoscopic evaluation in patients with chronic diarrhea, after bacterial and parasitic infections have been ruled out [9]. Recently, screening methods for norovirus using PCR have been developed, and diagnostic PCR techniques have shown to be superior to previous culture methods to screen for bacteria, parasites, and also viruses including norovirus [8,12]. These PCR studies, however, are not readily available. Further improvement in availability of viral screening would ensure hasty diagnosis and treatment of chronic diarrhea in transplant patients. A vaccine has also been developed recently which prevents norovirus infections using viral-like particles [13], though it has not been used in post-transplant patients. Prospective studies using this vaccine in renal transplant patients should be performed, with hopes that the chronic diarrhea seen in this patient population may be able to be significantly decreased. Additionally, development of a vaccine against sapovirus may prove benefit in the same regard. Treatment of chronic norovirus infections has also been attempted with medications such as ribavirin, nitazoxanide, and oral immunoglobins, but the data on the efficacy of these treatments is lacking and further studies should be performed [14-16].

Conclusion

At present, infection with less common viruses, including norovirus and sapovirus remain significant causes of chronic diarrhea in solid organ transplant patients, namely renal transplant patients in the post-transplant period. The above-mentioned interventions remain possibilities that show promise and warrant further investigation; however at this time the most effective treatment for chronic diarrhea in norovirus/sapovirus infections remains immunosuppressant reduction. The lack of data and studies in other treatment modalities serves as proof that further investigation is needed for detection and treatment of these viral infections, in order to and to ensure more accurate diagnosis and management to prevent irreversible damage to the transplanted kidney.

References

1. Calmut F, Yarur A, Pukazhendhi J (2015) Endoscopic and histological features of mycophenolate mofetil colitis in patients after solid organ transplantation. Ann Gastroenterol 28: 366-373.
2. Phillips G, Tam C, Rodrigues L (2010) Prevalence and characteristics of asymptomatic norovirus infection in the community in England. Epidemiol Infect 138: 1454-1458.
3. Ajami N, Koo H, Darkoh C (2010) Characterization of norovirus-associated traveler's diarrhea. Clin Infect Dis 51: 123.
4. Moreno-Espinosa S, Farkas T, Jiang X (2004) Human caliciviruses and pediatric gastroenteritis. Semin Pediatr Infect Dis 15: 237.
5. Glass RI, Parashar UD, Estes MK (2009) Norovirus gastroenteritis. N Engl J Med 361: 1776.
6. Roddie C, Paul JP, Benjamin R (2009) Allogeneic hematopoietic stem cell transplantation and norovirus gastroenteritis: A previously unrecognized cause of morbidity. Clin Infect Dis 49: 1061.
7. Schorn R, Hohne M, Meerbach A (2010) Chronic norovirus infection after kidney transplantation: Molecular evidence for immune-driven viral evolution. Clin Infect Dis 51: 307.
8. Coste J, Vuiblet V, Moustapha B (2013) Microbiological diagnosis of severe diarrhea in kidney transplant recipients by use of multiplex PCR assays. J Clin Microbiol 51: 1841.
9. Roos-Weil D, Ambert- Balay K, Lanternier F (2011) Impact of norovirus/sapovirus-related diarrhea in renal transplant recipients hospitalized for diarrhea.http://www.ncbi.nlm.nih.gov/pubmed/?term=sapovirus+diarrhea+renalTransplantation 92: 61-69.
10. Lemahieu W, Maes B, Verbeke K (2005) Cytochrome P450 3A4 and P-glycoprotein activity and assimilation of tacrolimus in transplant patients with persistent diarrhea. Am J Transplant 5: 1383.
11. Rankin A, Walsh S, Summers S (2003) Acute oxalate nephropathy causing late renal transplant dysfunction due to enteric hyperoxaluria. Am J Transplant 2008; 8: 1755.
12. Kaufman S, Chatterjee N, Fuschino M, Magid MS, Gordon RE, et al. (2003) Calicivirus enteritis in an intestinal transplant recipient. Am J Transplant 3: 764.
13. Atmar R, Bernstein D, Harro C (2011) Norovirus vaccine against experimental human Norwalk Virus illness. N Engl J Med 365: 2178.
14. Chang K, George D (2007) Interferons and ribavirin effectively inhibit Norwalk virus replication in replicon-bearing cells. J Virol 81: 12111.
15. Rossignol J, El-Gohary Y (2006) Nitazoxanide in the treatment of viral gastroenteritis: a randomized double-blind placebo-controlled clinical trial. Aliment Pharmacol Ther 24: 1423.
16. Florescu D, Hill L, McCartan M (2008) Two cases of Norwalk virus enteritis following small bowel transplantation treated with oral human serum immunoglobulin. Pediatr Transplant 12: 372.