CLINICAL VIGNETTE

Treatment of Refractory Norovirus Enteritis in a Pediatric Hematopoietic Stem Cell Transplant Recipient

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Introduction

Norovirus can cause a prolonged refractory diarrheal illness in immunocompromised patients. Treatment remains supportive. Oral immunoglobulin has been used in immunocompromised patients with norovirus and rotavirus-induced enteritis with demonstrated success,[1-6] however, data remains limited. We report a child post allogeneic hematopoietic stem cell transplant (HSCT) with severe refractory diarrhea due to norovirus infection successfully treated with oral immunoglobulins.

Case

A 2-year-old male with Wiskott-Aldrich Syndrome 217 days status-post unrelated umbilical cord HSCT was admitted for fever and diarrhea and found to be positive for norovirus (genotype 2). He was continued on his home immunosuppression including Tacrolimus 1.1 mg twice daily and oral prednisone 1.5 mg daily. There was initial concern for graft versus host disease (GVHD) so his immunosuppression was increased to intravenous methylprednisone 8 mg three times daily. However, his lower endoscopy did not identify any findings of acute GVHD and instead showed bowel wall edema consistent with norovirus enterocolitis.

Despite aggressive weaning of steroid immunosuppression and treatment with intravenous 0.5 g/kg immunoglobulin every two weeks, and a 14-day course of 100 mg twice daily nitazoxanide, his stool output over 24 hours continued to remain >20cc/kg/day. His symptoms began to improve 7 weeks into his hospital stay after he was started on oral loperamide (1mg three times daily) followed by oral immunoglobulins (25 mg/kg every 6 hours for a total of 8 doses) started two days later. There was a significant reduction in stool output from an average of 25-30 cc/kg/day to 5-8 cc/kg/day despite dietary advancement.

Discussion

This case demonstrates potential therapeutic efficacy of oral immunoglobulins in the treatment of norovirus in patients who have a history of HSCT, intercurrent immunosuppression at substantial risk of severe and prolonged norovirus symptomatic infection. Although our patient was previously treated with multiple doses of intravenous immunoglobulin, there was no significant improvement in stool output which suggests that oral immunoglobulin may be able to reach higher intestinal concentration.[7]

Some small case series of immunocompromised patients support the efficacy of oral immunoglobulins for the symptoms of viral gastroenteritis[1-6] though several report no difference.[7,8] There is no clear consensus on dosage, treatment length or time to respond to treatment (Figure 1).[1,2,4,6,8]

Case Number Type of study (# of patients)	Author (year)	Type of viral gastroenteritis	History of transplant	Time to respond to treatment
1. Case Series (19)	Alexander (2020)	Rotavirus/norovirus	Undisclosed	3.1 days
2. Case Series (2)	Kanfer (1994)	Rotavirus	Hematopoietic stem cell transplant	N/A
3. Case Series (9)	Nussbaum (2020)	Norovirus	Solid organ transplant	4.1 days
4. Case Series (12)	Florescu (2011)	Norovirus	Small bowel transplant/immunocompromised	7 days
5. Case Series (3)	Losonsky (1985)	Rotavirus	Primary immunodeficiency	N/A
6. Case Series (4)	Williams (2015)	Rotavirus	Hematopoietic stem cell transplant	3 days
7. Case series (36)	Flerlage (2018)	Rotavirus	Hematopoietic stem cell transplant	N/A
8. Case Series (12)	Gairard-Dory (2014)	Norovirus	Solid organ transplant	2 days

Figure 1: Treatment with oral immunoglobulins for norovirus and/or rotavirus enterocolitis in immunocompromised patients

Loperamide also likely contributed to the improvement in stool output, however, the improvement persisted even after loperamide was tapered. It is possible that the combination of loperamide and oral immunoglobulins had a synergistic impact. Notably, oral immunoglobulins were well-tolerated without evidence of toxicity.

Conclusion

Oral immunoglobulin is a safe and potentially effective option to help reduce stool output in HSCT patients with norovirus. Additional studies are needed to further elucidate the efficacy of oral immunoglobulins in HSCT patients.

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