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Major article

Control of norovirus outbreak on a pediatric oncology unit

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Background: Patients undergoing treatment for cancer with chemotherapy and hematopoietic stem cell recipients are at risk for severe morbidity caused by norovirus (NV).

Methods: We describe a NV outbreak on the Memorial Sloan Kettering Cancer Center's pediatric oncology unit. Stool testing for diagnosis of NV was performed by real-time polymerase chain reaction (PCR).

Results: Twelve NV cases occurred; 7 were hospital acquired. Twenty-five health care workers reported NV compatible illness. Patient-to-patient transmission occurred once. The practices of the Centers for Disease Control and Prevention were supplemented with electronic surveillance, surrogate screening for NV, and heightened cleaning. Two additional cases occurred after implementation of interventions. Long-term shedding was detected in 2 patients.

Conclusion: We describe interventions for controlling NV on a pediatric oncology unit. High-risk chronic shedders pose ongoing transmission risks. PCR is a valuable diagnostic tool but may be overly sensitive. Surrogate markers to assess NV burden in stool and studies on NV screening are needed to develop guidelines for high-risk chronic shedders.

Norovirus (NV) is the most common cause of gastroenteritis in the United States.[1] Three NV genogroups are known to cause disease in humans; among these, genogroup 2 genotype 4 is associated with a high rate of hospitalization and occasional mortality.[2] For all genogroups, the incubation period is short (15-50 hours), and time to symptoms appears to correlate with the viral inoculum. In otherwise healthy individuals, illness is sudden with short, self-limiting symptoms of gastroenteritis, including nausea, vomiting, diarrhea, and abdominal pain.[3] NV has been identified as a cause of prolonged and severe gastroenteritis in immunocompromised hosts, especially solid organ and hematopoietic stem cell transplant (HSCT) recipients.[4,5]

The infectious dose (50%) of NV is low (approximately 1,320 genomic equivalents) with transmission occurring via the fecal-oral route, contact with secretions during vomiting, contaminated food with improper handling, and fomites.[6] The virus can survive in the environment for up to 12 days on certain surfaces but is generally susceptible to sodium hypochlorite (concentration $\geq$ 1000 ppm).[7,8]

NV cannot be isolated using traditional cell culture. Antigen tests have limited sensitivity and negative predictive value and therefore are not ideal for clinical diagnostics.[9] The current gold standard for diagnosis of NV is genetic detection by reverse transcriptase real-time polymerase chain reaction (PCR).[10] Hospital outbreaks caused by NV are usually associated with >50% attack rate and often require ward closures.[11]

We describe an outbreak of NV infection on the pediatric oncology unit at Memorial Sloan Kettering Cancer Center (MSKCC) in January-February 2014. We discuss the infection control interventions and novel surveillance strategies that helped

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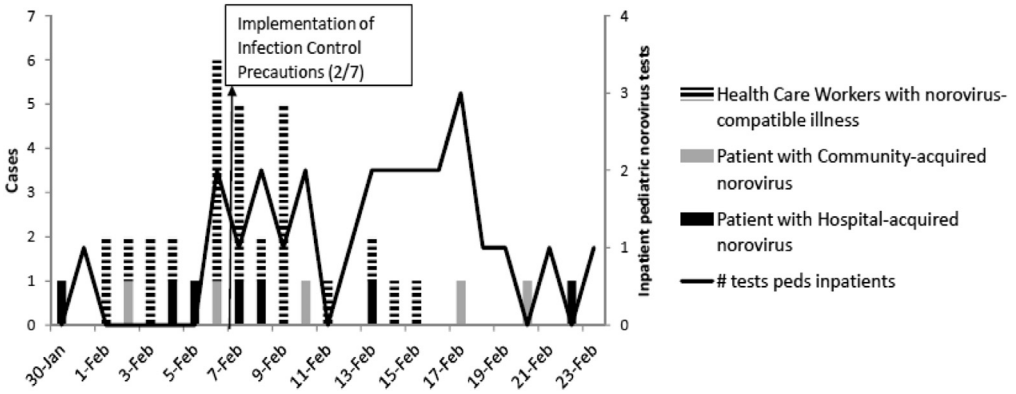

Fig 1. Timeline of onset of the norovirus cases among 25 health care workers (clinical) and 12 patients (laboratory confirmed). *peds*, pediatric.

successfully contain the outbreak. We also discuss unresolved infection control issues surrounding the isolation and management of NV cases in the outbreak and nonoutbreak oncology-transplant setting, especially in the context of highly sensitive and rapid newer nucleic acid amplification–based detection methods that are now the most widely used tests for routine diagnosis of NV.[12]

MATERIALS AND METHODS

MSKCC is a 470-bed tertiary care hospital in New York City with a 33-bed inpatient pediatric unit. Each year there are approximately 1,500 pediatric admissions and 11,000 pediatric patient days. The average length of stay for pediatric patients is 7.4 days. The pediatric day hospital is a 36-bed facility for outpatient chemotherapy administration and outpatient evaluation and management with 110-150 visits per day. The pediatric day hospital is located adjacent to the inpatient pediatric unit and incorporates a 9-bed pediatric urgent care center.

A case was defined as a patient with symptoms and a positive PCR test. For staff, a case was defined as sudden onset gastrointestinal illness (nausea, vomiting, or diarrhea) that resolved in <72 hours. Hospital-acquired cases were defined by onset of illness 24 hours after hospital admission. For the purpose of this article, special contact precautions refer to use of gowns, gloves, hand hygiene (alcohol based gel or handwashing with soap and water) before entry into patient room, and handwashing after patient encounter. All special contact isolation rooms are cleaned daily with bleach.

Stool specimens were tested for NV by a reference laboratory (ViraCor-IBT Laboratories, Lee's Summit, MO) using qualitative real-time reverse transcription PCR assay detection and differentiation of NV genogroups I and II.[10] Additional testing (surveillance) was performed in-house on a limited number of specimens using the Luminex xTAG Gastrointestinal Pathogen Panel Assay (Luminex, Austin, TX).[10] The xTAG Gastrointestinal Pathogen Panel (GPP; Luminex, Austin, TX) is a multiplexed nucleic acid test which was developed and received clearance from the United States Food and Drug Administration in 2013. The current version of the GPP assay detects the following targets: *Salmonella* spp, *Shigella* spp, *Campylobacter* spp, *Clostridium difficile* (toxins A and B), shiga toxin–producing *Escherichia coli*, enterotoxigenic *E coli*, vibrio cholera, NVs (group GI and GII), rotavirus, adenovirus (40/41), *Entamoeba histolytica*, *Giardia lambia*, and *Cryptosporidium* spp. Detection of pathogens by the GPP assay is accomplished using 4 steps: nucleic acids extraction from stool samples, amplification of targets DNA-RNA by PCR or real-time PCR, hybridization of amplified DNA to Luminex beads, and detection of the beads by the Luminex 200 platform. All steps are performed in a single reaction with a turnaround time of 5-6 hours. The rapid turnaround time of the GPP (within 24 hours) and its inclusion of NV allows for almost real-time detection of NV outbreak because the number of stool samples positive for NV can be monitored and tracked daily, and any increase over baseline can readily be identified.

The MSKCC Institutional Review Board granted a Health Insurance Portability and Accountability Act waiver of authorization to conduct the study.

Table 1
Demographic and clinical characteristics of patients with community-onset and hospital-acquired norovirus infection

Characteristic	Value
Sex	
Male	6 (50)
Female	6 (50)
Mean age (y)	5.5
Underlying disease	
Acute lymphoblastic leukemia	3 (25)
Chronic granulomatous disease	1 (8)
Ewing sarcoma	1 (8)
Neuroblastoma	4 (33)
Non-Hodgkin lymphoma	1 (8)
Severe combined immunodeficiency	2 (17)
Hematopoietic stem cell transplant recipient	3 (25)
Hospital day of onset (mean)	29
Origin of infection	
Hospital acquired	7 (58)
Community acquired	5 (42)

NOTE. Values are n (%) or as otherwise indicated.

RESULTS

Outbreak

The timeline of cases, including patients and health care workers (HCWs), is shown in Figure 1. Fourteen cases of NV were identified at MSKCC between January 31, 2014, and February 22, 2014. Twelve occurred in pediatric patients, and 2 occurred among adult patients admitted on separate floors. Their demographic and clinical profile is shown in Table 1. Seven cases were hospital acquired, occurring on days 2, 2, 5, 12, 19, 45, and 115 of hospitalization. The index case (case 1) was diagnosed on a specimen sent January 30, 2014. The patient was a 21-month-old boy with severe combined immunodeficiency who had undergone allogenic HSCT complicated by gastrointestinal graft versus host disease. Only 2 cases shared a room and appeared linked epidemiologically; these