Norovirus in Immunocompromised Patients

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While undergoing a routine mammogram, Mrs. B, age 76 years and in good health, was found to have right axillary adenopathy. A core biopsy confirmed the diagnosis of follicular lymphoma and she was referred to an oncologist who recommended treatment with six cycles of bendamustine, mitoxantrone, and rituximab. She tolerated the treatment fairly well except for mild lower abdominal discomfort for three to four days following infusion of chemotherapy. Prior to her fifth cycle of therapy, she reported chills, vomiting, and watery diarrhea without fever. Mrs. B volunteered one day per week at a nursing home and she noted that a stomach virus had circulated among the residents. Her symptoms resolved five days after her initial episode occurred and she proceeded with her fifth cycle of therapy.

Six days later, Mrs. B called the clinic to report a two-day history of severe abdominal cramping and watery diarrhea with as many as seven stools daily. She denied nausea or vomiting. She was seen in the clinic and was afebrile with normal complete blood count, electrolytes, blood urea nitrogen, and creatinine. Her abdomen was soft, slightly tender to palpation; she had positive bowel sounds in all four quadrants. A stool specimen was obtained for *Clostridium difficile* toxin and empiric therapy was initiated with metronidazole. Mrs. B was instructed to take antidiarrheals to control the diarrhea. The stool specimen was found to be negative for *C. difficile* and resolution of the abdominal cramping and watery stools occurred after one week. However, within a few days, the symptoms recurred.

Prior to her sixth cycle of therapy, Mrs. B reported a decrease in the amount of watery diarrhea and the intensity of abdominal cramping, nausea, and vomiting, and was able to eat a regular diet. She was able to maintain her weight of 201 pounds. Following this cycle of therapy, Mrs. B called the clinic with complaint of severe abdominal cramping and watery diarrhea. She denied blood or mucous in her stools. A stool sample was obtained for *C. difficile*, ova and parasites, and norovirus by reverse-transcription polymerase chain reaction (RT-PCR). Mrs. B was encouraged to increase her fluid intake and to take antidiarrheal medication to decrease her risk of dehydration. Several days later, the clinic was notified that the stool sample was positive for norovirus. Mrs. B was notified of the result and encouraged to continue with aggressive oral hydration and antidiarrheal medication.

Mrs. B completed chemotherapy two months after developing norovirus gastroenteritis. She continued to experience watery diarrhea and abdominal cramping for the next eight months, with resolution of her symptoms for several days followed by recurrence. Stool samples were repeated at three, five, and six months, and remained positive for norovirus. During the course of her illness, Mrs. B lost 54 pounds and was hospitalized twice for dehydration and failure to thrive. Empiric therapy with oral metronidazole, vancomycin, and IV immunoglobulin did not alleviate her symptoms. Ten months after the development of symptoms, the abdominal cramping and diarrhea resolved. A stool specimen obtained at 11 months was negative for norovirus.

Norovirus

First identified as the cause of a gastroenteritis outbreak in Norwalk, OH, in 1968, noroviruses are small, nonenveloped viruses with a single-stranded RNA genome that make up the genus *Norovirus* in the family *Caliciviridae*. The viruses are divided into five major genogroups, designated GI through GV. Genogroups I, II, and IV infect humans, whereas III and V infect pigs and cows (Hall et al., 2011). Norovirus cannot be grown in cell cultures and no small animal models exist, which presents a major challenge in norovirus research. Despite these challenges, the application of molecular techniques has led to a greater understanding of the clinical significance of noroviruses (Estes, Prasad, & Atmar, 2006).

Incidence and Transmission

Noroviruses are the leading cause of food-borne disease outbreaks worldwide (Koo, Ajami, Atmar, & DuPont, 2010). The viruses cause infection throughout the year, although the peak incidence occurs in the winter months (Atmar & Estes, 2006). In the United States, an estimated 21 million people suffer from norovirus-induced gastroenteritis annually, which constitutes 60% of the illness burden caused by known enteric pathogens (Scallan et al., 2011). Noroviruses are primarily transmitted through the fecal-oral route. Fecal contamination of food, water, and contaminated surfaces, as well as direct person-to-person spread, account for most outbreaks. Airborne transmission of norovirus also occurs in infectious aerosols generated by vomiting. Because no lasting immunity takes place, and because the virus can be transmitted by a number of routes, outbreaks can occur in a wide variety of institutional settings (Atmar & Estes, 2006). Healthcare facilities, including hospitals and nursing homes, are the most commonly reported settings of norovirus outbreak within the United States (Hall et al., 2011). Other risk groups include immunocompromised individuals, older adults, restaurant patrons, young children, military