Issues in Chemotherapy

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Pediatrics in Review 2011;32;86
DOI: 10.1542/pir.32-2-86

In Brief

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Author Disclosure

Drs Van Dyne and Serwint have disclosed no financial relationships relevant to this In Brief. This commentary does contain a discussion of an unapproved/investigative use of a commercial product/device.

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Children who have cancer may be severely immunocompromised by the oncologic process and the immunosuppression that results from chemotherapy. Their increased susceptibility to infection directs the scheduling of vaccine administration and the urgent treatment of the febrile child.

Live (attenuated) vaccines should not be given to patients undergoing immunosuppressive therapy, specifically chemotherapy and radiation treatment. Live vaccines include those manufactured to protect against *Salmonella typhi*; influenza (live intranasal vaccine); measles, mumps, rubella (MMR); varicella; rotavirus; polio (oral vaccine); yellow fever; and smallpox. The recommendation is to wait *at least* 3 months after completion of the last immunosuppressive treatment before administering live vaccines, and many oncologists wait 6 to 12 months. Because the time to immune reconstitution depends on the type of chemotherapy given, the dosage, and the patient's degree of responsiveness to treatment, the recommendations must be tailored to the individual patient and his or her circumstances. Vaccination with inactivated vaccines can be completed without increased risk of infectious complications, but the timing is important because the immune response may be inadequate in immunocompromised patients. An adequate response is usually achieved from 3 months to 1 year following the discontinuation of the radiation or chemotherapy. Inactivated influenza vaccine is recommended before each influenza season for patients 6 months of age and older. If possible, influenza vaccination should be postponed until no sooner than 3 to 4 weeks after a chemotherapy course is completed and when the granulocyte and lymphocyte counts are greater than 1,000 cells/μL.

Varicella infection can be severe in immunocompromised children, resulting in encephalitis, hepatitis, pneumonia, and, in some cases, death. An extended period of vesicular eruptions may occur. Immunocompromised patients who have well-documented exposure to varicella and no history of varicella infection or serologic titers should receive varicella-zoster immune globulin (under the brand name VariZIG™). (Note: VariVIG is distributed in the United States by FFF Enterprises, Temecula, CA, and can be requested at any time by calling 800-843-7477.) Varicella virus replicates rapidly, ceasing replication within 24 hours of the onset of rash, at which time treatment with immunoglobulins is less effective. It is crucial to treat the infection as soon as possible, at the latest by 96 hours after exposure, and not base treatment on presentation of the rash. Some experts recommend treatment with VariZIG whether or not there is a past history of varicella infection because immunologic responses are low and serologic tests can be unreliable in immunocompromised children. VariZIG is a new investigational drug and somewhat difficult to obtain but preferable to immune globulin intravenous because it contains concentrated immunoglobulin specific to varicella. If VariZIG is unavailable, one dose of immune globulin intravenous can be administered instead. If neither is available or 96 hours has passed, chemoprophylaxis with acyclovir should be initiated specifically at 7 to 10 days postexposure to attenuate or prevent infection.

Another major concern for the immunocompromised child who has cancer is fever in the setting of neutropenia. Patients must present emergently for rapid triage, evaluation, and prompt administration of antibiotics. Increased

risk of morbidity and mortality due to infection correlates with the severity and duration of neutropenia. Bone marrow suppression, impaired immunologic responses, the presence of a vascular access device, and the breakdown of mucocutaneous barriers from chemotherapy all contribute to the risks for the immunocompromised child.

A thorough physical examination must be performed on the child who has neutropenia, assessing vital signs; evaluating potential sites of infection; and paying special attention to all areas of the skin, mucous membranes, gastrointestinal tract (eg, mouth, rectum), and vascular access devices. A patient who has neutropenia may not mount an inflammatory response, resulting in minimal erythema, exudate, or pain at infected sites. A complete blood count with differential count and blood cultures from all lumens of vascular access devices are recommended. Patients who have an absolute neutrophil count less than 500 cells/mm^3 or who appear ill are at greatest risk. Although a microbiologic diagnosis is made in 10% to 30% of pediatric patients who have neutropenia, most do not have an obvious source of fever or clear infection. Further evaluation with chest radiography, urinalysis, urine cultures, or additional cultures is warranted, based on the patient's symptoms.

Aggressive intravenous hydration and urgent antibiotic administration is imperative for the febrile neutropenic patient because infection can progress rapidly. Frequent monitoring of vital signs and surveillance of urine output is essential because tachycardia and decreased urine output may be the initial signs of compensated shock. After drawing cultures, immediate antibiotic coverage for gram-positive and -negative organisms (including *Pseudomonas*) should be administered. Individuals who appear toxic should receive dual gram-negative coverage. Consideration must also be given to fungal, viral, and other opportunistic infections and appropriate therapy tailored to the patient. Oral antibiotics are not appropriate in pediatric patients who have fever and neutropenia.

The child undergoing treatment for cancer presents the additional concern for life-threatening infections. Practitioners must be aware of established guidelines and consultative resources to provide the highest quality of care.

Comment: This In Brief reviews important concepts for all who provide medical care to children who have cancer. Provision of care requires collaboration and consultation among the patient's primary care clinician, emergency department staff, the patient's oncologist, and an infectious disease specialist, along with the patient and family. The immunization of household contacts and siblings is imperative to minimize disease transmission to the patient. Family members and household contacts should *not* be given smallpox or oral polio vaccines because of potential transmission to the patient but should receive MMR, varicella, and rotavirus vaccines, which have a very low risk of transmission to the patient. If a household member develops a rash following the varicella vaccine, the child who has cancer should avoid contact with that person, but no other precautions are currently warranted. Inactivated influenza vaccine should be given to household contacts 6 months of age and older, and age-appropriate inactivated vaccines are important to administer. The universal administration of varicella vaccine hopefully has decreased the risk exposure for patients who have cancer. For those who have neutropenia and fever, urgent evaluation and administration of antibiotics is imperative. Specific antibiotic and antifungal choices must be guided by individual risk factors and local microbiologic profiles and tailored to the individual patient. Hence, the coordinated care of the cancer patient with oncology and infectious disease consultation is important to provide individualized care and demonstrates the importance of true medical home principles.

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