Minimizing Hazards Associated With Live-Virus Immunotherapeutic Cancer Vaccines

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Therapeutic cancer vaccines that use attenuated vaccinia viruses as delivery vectors are undergoing clinical trials at dozens of sites internationally. Even in an attenuated form, these live viruses can cause severe illness if they are accidentally transmitted to immunocompromised people, pregnant women, or people with certain skin conditions. Oncology nurses should become familiar with how to manage patients’ vaccine injection sites to minimize these risks to patients’ close contacts and the community at large.

At a Glance

• Immunotherapeutic vaccines in clinical trials show promise in oncology treatments.
• Viral vector vaccines are generally safe for those working with them, and precautions needed are similar to those of other biohazardous materials, such as chemotherapy.
• Staff and patient education are important and necessary to minimize potential risks and hazards associated with the administration of immunotherapeutic vaccines.

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uring the past decade, a great deal of research interest has been focused on therapeutic cancer vaccines. These vaccines are designed to combat tumors by stimulating new responses and expanding existing responses from the patient’s own immune system (Wong, Li, Mooney, & Dranoff, 2016). As of this writing, only two such vaccines have been approved by the U.S. Food and Drug Administration (FDA): sipuleucel-T (Provenge®) for metastatic prostate cancer and talimogene laherparepvec (IMLYGIC®) for metastatic melanoma (National Cancer Institute, 2015). However, many more vaccines are being investigated. One class of investigational vaccines, which are now undergoing clinical trials at hundreds of sites internationally, use modified vaccinia viruses as vectors for delivering vaccine agents to tumor sites. In this class of vaccines, the vaccinia viruses are attenuated live viruses, which means that potential hazards are associated with the vaccines’ use, not unlike the hazards associated with common live-virus vaccines, such as the measles, mumps, and rubella vaccine. Oncology nurses should become familiar with how to recognize and minimize these potential hazards.

Although viral vector vaccines are generally safe for the patients who receive them, a potential risk exists to certain populations if the patient sheds live virus from the injection site (Gilbert, 2013; Rotz, Dotson, Damon, & Becher, 2001). Even in an attenuated form, vaccinia virus can cause severe illness in immunocompromised people and in people with certain skin conditions (Sepkowitz, 2003). If a pregnant woman is exposed, it can be hazardous to the fetus (Rotz et al., 2001). Therefore, precautions must be followed to ensure the safety of patients’ close contacts and the community at large.

The primary goal in the development of therapeutic cancer vaccines is to induce a response to tumor-specific antigens. Teaching immune cells to recognize malignant cells as foreign is the primary goal and major challenge in the development of effective cancer vaccines. In antigen-specific approaches, a tumor-associated antigen is directly targeted, either by loading antigen-presenting cells or by using protein, peptide, RNA, or DNA alone or via a vaccine vector (Geary & Salem, 2013). Some vaccines incorporate a live virus as part of the delivery system to allow the antigen to reach its intended target. Viral vectors are straightforward to engineer and can carry a large amount of genetic material. A great deal of experience exists with pox virus vectors, such as vaccinia virus, a double-stranded DNA virus related to cowpox virus, which has been used to vaccinate against smallpox for more than 100 years (Rotz et al., 2001). Pox viral vectors are ideal because they can infect human cells but cannot incorporate themselves into human DNA. They can contain a large amount of foreign DNA, can efficiently infect...
antigen-presenting cells, and are highly immunogenic.

Two prominent investigational therapeutic cancer vaccinations that use vaccinia vectors are PROSTVAC-V TRICOM and PROSTVAC-F TRICOM, which have been developed for use in prostate cancer (Gulley et al., 2014). Multiple clinical trials are currently in progress using these vaccines, including a global randomized, controlled phase III trial (NCT01322490) that is expected to report results in 2017. The PROSTVAC vaccine employs genetically altered poxvirus to deliver targeted information to immune cells and to generate an immune response. Administered subcutaneously, the poxvirus delivers the transgenes for the tumor-associated antigens to antigen-presenting cells through cellular infection. Once these poxviruses are within the cell cytoplasm, the transgenes are processed (Gulley et al., 2010). In a typical treatment schema being used in clinical trials, the vaccinia vaccine is the priming dose and is used only for the first treatment. All subsequent vaccine doses are considered to be boosters. The booster doses are manufactured differently, do not replicate in humans, and do not carry the same safety requirements (Singh, Pal, Alex, & Agarwal, 2015).

Staff Education

For oncology nurses, administering a live-virus vaccine presents a unique challenge—that of understanding the safety precautions when caring for and providing education to patients receiving live-virus vaccinia therapy. Vaccinia is classified as a biosafety level 2 hazard and is considered an infectious biologic substance (Centers for Disease Control and Prevention [CDC], 2009). CDC guidelines need to be followed in the administration of the vaccines to ensure staff safety and the safety of the patients’ close contacts.

Recommendations for working with live-virus vaccines are similar to those for working with other biohazardous materials, such as chemotherapy. Staff members administering these live-virus vaccines need to use standard personal protective equipment, such as gloves, gowns, and, depending on local requirements, goggles or masks. At the National Institutes of Health, the patient is placed in a private room, and contact isolation is used during administrations to protect other patients. Good hand washing is paramount in protecting against accidental spread. Proper disposal and handling of personal protective equipment and used syringes are required as per universal precautions.

Restrictions for working with the live-virus vaccine are for individuals who will actually be handling the study drug. Staff members who are pregnant or who intend to become pregnant and those who are immunocompromised or suffering from chronic skin disorders, such as atopic dermatitis, should not administer the vaccinia. All staff members must understand that the recombinant vaccine is not the causative agent of smallpox; smallpox is caused by the variola virus. The administration of the smallpox vaccine to staff members who are to administer the recombinant vaccine is not required but is recommended by the CDC (Rotz et al., 2001). Physicians and nurses whose contact with attenuated vaccinia viruses is limited to contaminated materials (e.g., dressings) and who adhere to appropriate infection control measures are at lower risk for inadvertent infection than laboratory workers. However, because a theoretical risk for infection exists, smallpox vaccination can be offered to physicians and nurses. At NIH, staff members who administer the vaccines are not routinely given the smallpox vaccination. In greater than 1,000 patients exposed to vaccinia vectors, no cases have been reported of contact vaccinia associated with the recombinant vaccine, neither from the patient nor from study personnel to anyone else (Kim et al., 2013). Subcutaneous administration of the vaccinia, as opposed to the scarification method, substantially reduces the risk of contact transmission.

Patient Teaching

Patient teaching should emphasize excellent hand washing to prevent accidental spread of the virus (e.g., touching the injection site area and then eyes). Soap and water are the preferred means to cleanse the site. The site should be covered after injection with gauze and a semipermeable dressing. The vaccination site should be protected by two barriers—an occlusive dressing and a layer of clothing (Talbot, Peters, Yan, Wright, & Edwards, 2006). The vaccine is typically given in the upper thigh area. The patient may shed live virus from the vaccination site until the site heals completely and could potentially spread the virus to others. Patients should be instructed to not pick or scratch at the site and not to apply salves or ointments to the area. Patients must not swim or bathe in a tub for two to three weeks after the injection. If the dressing becomes wet, the patient should be taught to remove it with gloves and put on a clean dressing; normal showering can continue. Contaminated bandages and the vaccination site scab, after it has fallen off, should be placed in sealed plastic bags with a small amount (roughly a capful) of bleach before disposal in the trash. Clothing or other cloth materials that have had contact with the site can be decontaminated with laundering in hot water with bleach (Rotz et al., 2001). Vaccinia virus is not transmitted by coughing or sneezing or by sharing food, cups, and dishes. No restriction is placed on normal errands or social activities.

Patients should be instructed not to touch the injection site and then touch their eyes, mouth, or any open skin breaks. If they have contact lenses, dentures, or colostomies, they should be particularly careful about hand hygiene. Intimate contact should be carefully limited. Potential risk exists to developing fetuses, so patients are instructed to use latex barriers with adequate contraception for at least four months after the vaccine injection. Patients are to be taught to avoid close contact (e.g., living in the same household) with certain categories of people for about two to three weeks after the vaccine injection. These include pregnant women, children aged three years or younger, and those who are immunosuppressed. Again, all of these restrictions apply only to the first treatment with the live-virus vaccinia. All subsequent injections are boosters and do not carry the same precautions.
Conclusion

As of this writing, no cases of accidental infection or transmission to health-care study personnel, caregivers, or relatives from patients exposed to vaccinia vectors have been reported. Although these vectors are being used only in clinical trials, FDA approval is possible in the near future, and these vaccines may soon be in widespread use for patients with metastatic prostate cancer and other conditions. With the proper education and knowledge, nurses can have confidence and feel comfortable in their ability to safely administer the live-virus vaccinia vaccine to patients.

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References


