



BRIEF COMMUNICATION

Successful Immunization of an Allogeneic Bone Marrow Transplant Recipient with Live, Attenuated Yellow Fever Vaccine

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Vaccination against yellow fever is effective, but available live virus vaccines are not recommended for use in immunocompromised or elderly patients. We report the successful and uneventful immunization of a 62-year-old man with a history of allogeneic bone marrow transplant and discuss evidence for this recommendation.

Vaccination against yellow fever is a simple and effective method to protect travelers to or residents of endemic regions. The 17D yellow fever vaccine (YF-VAX, Aventis Pasteur, Swiftwater, PA, USA) available in the United States is composed of live attenuated virus; consequently, it is usually contraindicated in immunocompromised or elderly patients.¹ We report the successful and uneventful immunization of a 62-year-old man with a history of allogeneic bone marrow transplant for chronic myelogenous leukemia (CML) 9 years earlier. This is the second case report of safe vaccination with this vaccine in a bone marrow transplant recipient and the first report in one above 60 years of age.

Case Report

The patient is a 62-year-old gentleman who was diagnosed with CML in October 1996. He was admitted later that month for tumor lysis syndrome and was treated with hydroxyurea, intravenous hydration, and allopurinol. Bone marrow biopsy confirmed CML, chronic phase, and cytogenetics confirmed the presence of the Philadelphia chromosome. He received a 6/6 human leukocyte antigen-matched unrelated donor

transplant on March 20, 1997 and engrafted on day 16. His post-transplant course was complicated by *Streptococcus sanguis* bacteremia and cellulitis of the right foot that resolved completely on intravenous antibiotic therapy.

Bone marrow biopsy performed 1 year after transplantation showed a complete cytogenetic remission with marrow cellularity of 20% and no evidence of leukemia. Standard post-transplant immunosuppression was discontinued on September 15, 1997. During the years that followed, he experienced several episodes of bronchitis and developed xerophthalmia due to chronic graft-versus-host disease (GVHD); however, no immunosuppression was necessary. He received immunizations with inactivated influenza virus vaccine beginning in 1998 and polyvalent pneumococcal capsular vaccine in 1999. In spite of the latter, he developed invasive pneumococcal pneumonia in 2001. He received hepatitis A and B and diphtheria–tetanus vaccinations in 2005 without incident.

In August 2005, he was referred to the University of Michigan Overseas Travel Clinic to prepare for a 2-week birdwatching trip in the rainforests of Eastern Ecuador, an area endemic for yellow fever. At the time of this evaluation, his only symptoms were those of mild asthma; xerophthalmia had resolved 6 months previously. Clinically, he had no evidence of GVHD or recurrent malignancy (ie, quantitative real-time polymerase chain reaction for BCR-ABL was negative).

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His medications at the time of presentation included glucosamine and inhaled fluticasone.

After an extensive discussion about the possible risks of yellow fever vaccination following bone marrow transplantation, the patient remained convinced that the benefits outweighed the risks given his planned travel to Ecuador. As a crude evaluation of his capacity to respond to new immunogens, we confirmed that he had successfully developed antibodies to hepatitis A virus after having received the vaccine 1 month previously. We then administered yellow fever vaccine (17D-204 strain, YF-VAX, Aventis Pasteur, Swiftwater, PA, USA) to him on May 16, 2006. No evidence of local or systemic adverse effects was noted or reported during his clinic visit or by telephone follow-up 7 days post-vaccination. Plaque-reduction neutralization testing performed at the Centers for Disease Control and Prevention (CDC) 6 weeks later yielded a neutralizing antibody titer of 1:1280. A titer of 1:20 is considered protective at CDC. The patient subsequently traveled to the Ecuadorian rainforest without any consequence to his health. He remains well 14 months post-YF vaccination.

Discussion

Guidelines from the United States, Canada, and Europe advise that live vaccines are contraindicated in solid organ transplant patients for the first 2 years following transplant or in those on continuing immunosuppressive therapy.²⁻⁴ In bone marrow or hematopoietic stem cell transplant patients, the same interdictions apply; however, live vaccines are also contraindicated in patients with acute GVHD and those with recurrent malignancy.⁵ Most travel medicine authorities advise immunosuppressed patients to avoid yellow fever endemic regions altogether or provide letters of exception when there is an entry requirement but little or no actual risk of exposure.⁶ There is only one previous case report of successful YF vaccination in an allogeneic bone marrow transplant in a 50-year-old male patient with multiple myeloma.⁷ This patient tolerated the vaccine well 3 years after an allogeneic bone marrow transplant and 2 years after discontinuing immunosuppressive therapy. He had a positive yellow fever serology at 2 and 9 months after vaccination. Case reports suggest that vaccine can be given safely to patients with human immunodeficiency virus (HIV) without significant immunosuppression;⁸ however, a fatal reaction was reported in a previously undiagnosed HIV patient with high viral load, found to have a CD4 count of 108 cells/mm³.⁹

Older adults who contract wild-type yellow fever virus have the highest risk of morbidity and mortality.¹⁰ Vaccination in elderly persons also has risks, as advanced age and immune senescence seem to be associated with yellow fever vaccine-associated neurotropic disease (YEL-AND) and yellow fever vaccine-associated viscerotropic disease (YEL-AVD).¹⁰⁻¹² For this reason,

it has been suggested that yellow fever vaccine should be contraindicated in patients above 60 years of age; however, this remains an area of controversy.^{13,14}

Our patient was 10 years post-bone marrow transplant without recurrent malignancy, GVHD, or ongoing immunosuppressive therapy. He was adamant about traveling to the Napo region of Ecuador, which is endemic for YF. We discussed with him the limited data available and uncertainty to fully understand the risk of YF vaccination in post-transplant patients. However, available data do suggest the risk of illness and death from YF in a healthy, non-immunized person taking a 2-week trip to an YF endemic area in South America is approximately 5 per 100,000 and 1 per 100,000, respectively.¹ Additionally, the risk for YEL-AND is approximately 0.4 per 100,000 doses of vaccine distributed and the risk of YEL-AVD is approximately 0.3–0.5 cases per 100,000 doses of vaccine distributed.^{1,15} Although lower than the risk for illness and death from natural YF infection, these risks of serious vaccine-related adverse effects increase in travelers over the age of 60 and have been reported at 4 per 100,000 doses in patients aged 60–69 and 7.5 per 100,000 doses for people over 70 years of age.¹⁵ When presented with this data, our patient felt comfortable that his relative benefits outweighed his potential risks and he opted for YF vaccination. He was immunized at 62 years of age.

Our patient had two potential contraindications to YF vaccination. Based on his favorable transplant outcome, his documented responsiveness to a killed vaccine, his general good health, and his unshakable desire to visit an endemic region, we concluded that the potential benefits of YF vaccination outweighed the possible risks. Decisions to vaccinate with yellow fever vaccine in the post-transplant setting should be individualized, taking into account the risk of potential adverse events based on the patient's immune status and potential exposure to wild-type YF.

Acknowledgment

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Declaration of Interests

The authors state they have no conflicts of interest.

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