

Rabies in Transplant Recipients

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Today I'm talking with Dr. Richard Franka about rabies in transplanted organs. He's a scientist with CDC.

Welcome, Dr. Franka.

[Richard Franka] Thank you for having me.

[Sarah Gregory] Dr. Franka, other diseases, such as West Nile virus and HIV, have been found in transplant recipients. But rabies is a new one, isn't it? Tell us what happened in China.

[Richard Franka] It's true that donor-derived disease transmission following organ transplantation has been reported for many different pathogens, essentially since the beginning of wider use of organ and tissue transplantation. However, it is also true that only a fraction of 1 percent of all transplant procedures in the United States result in donor-derived disease in the recipient. When transmission occurs, significant morbidity and mortality may result. On the other hand, more than 100,000 patients are currently on organ transplant waiting lists in the U.S., but only approximately 28,000 solid organ transplantations are performed annually. As a result of long waiting periods, on average, 22 people die each day while waiting for a transplant. One organ donor can save as many as eight lives.

To answer your question, organ transplant transmission of rabies is not an entirely new occurrence. This case in China is the 5th reported cluster of rabies transmission by solid organ transplant in the past 13 years. The first documented cases occurred in Germany in 2003, the second and third in the U.S. in 2004 and 2013, and the 4th in Kuwait and Saudi Arabia in 2014. In addition, since 1978, there have been 8 documented cases of rabies transmission following corneal transplant, which is not an organ, but technically also human tissue, in the United States, France, Thailand, India, and Iran.

The most recent organ transplant rabies transmission was detected in Beijing, China, in July 2015, when rabies was diagnosed in two patients who both received a kidney from same organ donor approximately 6 weeks earlier.

[Sarah Gregory] How did this happen?

[Richard Franka] As discovered in a public health investigation conducted by the authors, on May 13, a 6-year-old boy from Guangxi Province developed fever, loss of appetite, and insomnia. He was hospitalized, and his symptoms worsened and progressed towards irritability, slurred speech, dysphagia and hyper salivation. Viral encephalitis, complicated with pulmonary infection, was suspected as a potential diagnosis. The boy was treated symptomatically, as well as with ribavirin for possible viral infection, but his status deteriorated, progressing to coma and he died on May 26. Tests for HIV, hepatitis B and syphilis, as required according to organ donation law in China,

were performed with negative results; and so 2 kidneys and 2 corneas were transplanted to 4 recipients on May 27th and June 1st. Within 6-7 weeks, both kidney recipients (55 and 43 years old) developed symptoms, including incoherent speech, anxiety, altered mental status, and hydrophobia. Rabies was suspected clinically and confirmed in a laboratory. Both kidney recipient patients died 11 weeks after receiving the transplant.

Both cornea recipients received post-exposure prophylaxis immediately after it was confirmed that the cornea they received was from a donor suspected of dying from rabies. And both are currently reporting good health.

[Sarah Gregory] Are there ways to prevent this happening again?

[Richard Franka] Common among the majority of transplant-associated infectious diseases are initial organ donor misdiagnosis or omission of particular infectious diseases from differential diagnosis, inadequate donor screening, and the inability to rapidly test donors for potential infectious diseases, given the short time between organ removal and transplantation. Clinicians only have a few hours to make a risk assessment and decide if organs from a donor can be transplanted. Decision is made with the knowledge that a patient on the waiting list may not live long enough to wait for another donor.

We can certainly decrease the frequency of transplant-associated diseases transmission and the associated morbidity and mortality through preventive approaches and rapidly implemented therapeutic ones.

In many of the clusters of rabies transmission through organ transplants, identification of the cause was complicated by delayed diagnosis or misdiagnosis due to the rarity of the disease, geographic distance separating transplant recipients, and lack of prompt recognition and reporting systems. These are critical issues to overcome.

Education of physicians to include rabies in their differential diagnoses for encephalitis patients, enhancement of donor screening, including questionnaires for next to kin regarding the donor's possible exposures to rabid animals, as well as development and implementation of a rapid laboratory diagnostic using modern molecular methods for detection of encephalitis causing pathogens, are a few ways in which the risk for transplant transmission of rabies could be mitigated. Although test results may not be always available prior to transplantation, which is usually done within 24 hours, prompt notification to transplant centers of the donor's postmortem test results would allow for the rapid delivery of post-exposure prophylaxis, appropriate treatment, and management of recipients.

[Sarah Gregory] Would it make sense to give rabies prophylaxis to all transplant recipients, just in case?

[Richard Franka] Not to all transplant recipients, but rabies prophylaxis should certainly be considered for recipients receiving organs from donors with neurological symptoms who died from

unknown acute progressive encephalitis, especially if the donor lived in or traveled to rabies endemic areas.

[Sarah Gregory] So what actions were taken?

[Richard Franka] Immediately following the diagnoses of rabies in the kidney recipients, an epidemiologic investigation was initiated. Medical records and histories for the donor, as well as the recipients, were reviewed and family interviews were conducted. Immediately, post-exposure prophylaxis was initiated for the 2 cornea recipients. A risk assessment was conducted to identify any other potentially exposed individuals and determine if there was any need for vaccination among immediate contacts of the donor or either kidney recipient. Of 290 identified contacts, 233 received vaccine.

[Sarah Gregory] It seems the child had no obvious exposure to rabies virus. Did they ever discover how the child got it?

[Richard Franka] You are correct that no rabies exposure in the donor was reported. The boy lived with his grandmother, and as many kids do, he also frequently played with dogs in the area where rabies is unfortunately still endemic. The grandmother was not aware of any dog bites, but one cannot exclude potential small bites or tooth scratches, which the grandmother may not have known about. His clinical symptoms were typical of rabies. The kidney recipients, on the other hand, had not had any history of travel or exposure to animals. With both recipients developing symptoms of rabies within 6 weeks after receiving a kidney from the same donor, transmission of rabies virus from the organ transplant is the best explanation in this particular case. Unfortunately, direct genetic comparison of rabies virus ribonucleic acids between donor and recipients was not possible, since there were no suitable samples remaining from the donor.

[Sarah Gregory] In this age of world globalization, do you foresee a time when people should be vaccinated for rabies routinely?

[Richard Franka] Approximately 60,000 people die annually from rabies worldwide. In 2015, World Health Organization, World Organization for Animal Health, and Food and Agriculture Organization of the United Nations set up a target of eliminating human rabies of canine origin globally by 2030. Besides mass dog vaccination campaigns and stray dog population management, which are critical for elimination of rabies in dogs, rabies pre- and post-exposure vaccination of humans constitutes an important part of the tools we have on hand to achieve that goal. Currently, pre-exposure prophylaxis is recommended for professionals working with potentially rabid animals, as well as for travelers visiting canine rabies endemic areas. It may not be cost-effective to routinely vaccinate everyone for rabies, but it would certainly be beneficial to vaccinate the most vulnerable population – children – especially those living in the areas where canine rabies is endemic. Discussions about effectiveness and feasibility of inclusion of rabies vaccination in the World Health Organization Expanded Program for Immunizations are currently under way.

In addition, proper risk assessment of potential exposures to rabid animals supported by decentralized laboratory diagnostics will ensure that rabies cases are recognized quickly and that

vaccines are used most effectively and given as post-exposure prophylaxis to those who truly need them.

Once human rabies of canine origin is eliminated, transmission of canine rabies through organ transplantation will also be eliminated. Until then, we need to ensure that donors with encephalitis are adequately screened and excluded from transplantation if rabies is detected. Or that proper post-exposure prophylaxis or organ removal is initiated once diagnosis is obtained post-transplantation.

If your loved one is receiving an organ transplant from a donor who died from unknown encephalitis, please ask the physicians if rabies was ruled out or if rabies immunization should be given as a preventive measure. If you have any rabies related questions or concerns, please call the Centers for Disease Control and Prevention rabies phone line 404-639-1050 during working hours or the CDC Emergency Operation Center at 770-488-7100 after hours.

[Sarah Gregory] Thank you, Dr. Franka, for talking with me. Listeners can read the entire August 2016 article, Probable Rabies Virus Transmission through Organ Transplantation, China, 2015, online at cdc.gov/eid.

I'm Sarah Gregory for Emerging Infectious Diseases.

[Announcer] For the most accurate health information, visit www.cdc.gov or call 1-800-CDC-INFO