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West Nile Virus Infections in Organ Transplant Recipients — New York and Pennsylvania, August–September, 2005

In September 2005, West Nile virus (WNV) infection was confirmed in three of four recipients of organs transplanted from a common donor. Two recipients subsequently had neuroinvasive disease, one recipient had asymptomatic WNV infection, and a fourth recipient apparently was not infected. This report summarizes the ongoing investigation. Clinicians should be aware of the potential for transplant-associated transmission of infectious disease.

Organ Donor

The organ donor, a New York City resident, was hospitalized on August 23 after a traumatic head injury and underwent emergency evacuation of an epidural hematoma, during which he received one unit of packed red blood cells (PRBCs). He was declared brain dead on August 26. Liver and associated vessels, one lung, and both kidneys were recovered. On August 28, the liver and kidneys were transplanted into three recipients at two transplant centers in New York City, the lung was transplanted into a recipient at a transplant center in Pittsburgh, and the vessels were discarded.

After unexplained neurologic illness occurred in two organ recipients, an investigation was initiated. Investigators determined that the donor had lived near an area where mosquitoes positive for WNV were collected on August 16, 2005. The donor's wife reported that he had spent time outdoors and felt febrile before sustaining the fatal head injury. Serum and plasma collected from the donor on August 27 were retrieved. The samples tested positive for WNV immunoglobulin M antibodies (IgM) and IgG by enzyme immunoassay but negative for WNV RNA by polymerase chain reaction (PCR). Immunohistochemical analyses of liver, gallbladder, kidney, and epidural hematoma were negative for WNV antigens. The PRBC unit received by the organ donor was donated on July 30 and was negative for WNV RNA by minipool nucleic acid-amplification test (mpNAT). A repeat donation on September 22 was WNV mpNAT and IgM negative.

Liver Recipient

The liver recipient had end-stage liver disease caused by hepatitis C virus infection. She initially did well after the transplantation. She required multiple transfusions of blood products, all of which were WNV RNA negative by mpNAT. On post-transplant day 13, she had a fever and altered mental status. On day 18, she experienced respiratory distress requiring endotracheal intubation. A lumbar puncture revealed mild lymphocytic pleocytosis (8 cells/mm^3) and elevated protein (81 mg/dL). She became comatose and developed acute flaccid paralysis consistent with WNV encephalitis.

Serum and cerebrospinal fluid (CSF) specimens collected on day 23 were positive for WNV IgM, and CSF contained WNV RNA. That day, the patient began treatment with four doses of intravenous Omr-IgG-am™ (Omrix Biopharmaceuticals, Tel Aviv, Israel, supplied by the National Institutes of Health [NIH]), an immune globulin with high antibody titers against WNV under an investigational new drug (IND) compassionate-use protocol; however, the patient had no subsequent clinical improvement and remains in a coma.

Lung Recipient

The lung recipient had end-stage lung disease caused by pulmonary fibrosis. The initial post-transplant course was uneventful aside from blood-product receipt. The patient went home on post-transplant day 16 but was readmitted the following day with fever and dyspnea requiring endotracheal intubation, followed by altered mental status, seizures, and acute flaccid paralysis consistent with WNV encephalitis. On day 23, a lumbar puncture revealed elevated CSF protein (149 mg/dL) but no white blood cells; a brain magnetic resonance image taken the same day was normal. Serum collected on day 19 was negative for WNV IgM, but, by day 23, serum was IgM and IgG positive. CSF from day 24 was negative for WNV IgM and WNV RNA, but CSF from day 27 was positive for WNV IgM and IgG. The patient completed experi-

mental treatment with four doses of Omr-IgG-am, without clinical improvement, and remains in a coma.

Kidney Recipient 1

The first kidney recipient had end-stage renal disease attributable to IgA nephropathy. She had no immediate post-transplant complications, received no blood products, and was discharged home on day 3. Serum collected on day 22 was negative for WNV IgM but positive for IgG (consistent with a previous flavivirus infection) and was positive for WNV RNA. The patient was readmitted to the hospital on day 27 for experimental Omr-IgG-am treatment and remains asymptomatic.

Kidney Recipient 2

The second kidney recipient had end-stage renal disease caused by Alport syndrome. He received blood products after the transplant and was discharged home on post-transplant day 7. Serum collected from the patient on day 16 was negative for WNV IgM, IgG, and RNA. As a precaution, the patient was rehospitalized on day 27 for experimental Omr-IgG-am treatment. He remains well.

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Editorial Note: This report describes the second report of WNV transmission associated with organ transplant (*1*). Several important differences exist between this and the previously reported occurrence. The first organ-donor–associated WNV transmission, reported in August 2002, occurred after the donor received a transfusion of WNV-positive blood 1 day before organ recovery. A serum sample collected immediately before organ recovery subsequently tested positive for WNV by PCR and culture but lacked WNV IgM antibodies. All four organ recipients were infected and became ill. In contrast, the current organ donor was likely infected via a mosquito bite rather than through blood transfusion, and a serum sample obtained 1 day before the organs were recovered had WNV IgM and IgG antibodies but was PCR negative. The lung and liver transplant recipients had severe WNV encephalitis and acute flaccid paralysis with respiratory failure, one kidney recipient had a positive PCR test result in serum 22 days after transplantation and remains asymptomatic, and the other kidney recipient had no evidence of WNV infection.

Serologic and clinical studies indicate that organ-transplant recipients have a risk approximately 40 times that of the general population for neuroinvasive disease after WNV infection (*2*). Infected organ-transplant recipients and other immunosuppressed persons typically have prolonged WNV incubation periods, during which asymptomatic viremia can be detected (*3*). The infected kidney recipient had asymptomatic viremia 22 days after transplant. All of the recipients were treated through a Food and Drug Administration (FDA)-approved IND compassionate-use protocol with Omr-IgG-am, an intravenous immunoglobulin product with high-titered neutralizing antibody to WNV. No proven effective treatment or prophylaxis for WNV infection exists; a randomized placebo-controlled, double-blind trial of Omr-IgG-am is under way (*5*).

Investigation of 30 recognized cases of WNV transmitted by blood transfusion documented to date indicated that the donors' viremias can be of low titer and that all resulted from IgM antibody-negative donations (*4*). Conversely, transfused viremic donations that were recognized only after retrospective testing did not transmit WNV infection if IgM antibody was present (*6*). Since 2003, the U.S. blood supply has been screened for WNV using NAT, which has reduced the risk for transfusion transmission (*4*). The organ-transplant–associated WNV transmission described in this report suggests that transmission through solid organ transplantation can occur from donors with IgM and IgG antibodies and without detectable nucleic acid by PCR in their serum. Experimental evidence in humans and animals suggests that WNV might persist in organs after clearance of viremia (*7*). Further testing of the donor serum using a highly sensitive NAT assay for blood-donor screening is pending.

Organ donors are screened to identify infectious risks on the basis of national organ-procurement standards (*8*). Screening of all organ donors with WNV NAT is not currently required or routinely performed because of 1) NAT availability only through IND applications for blood screening, 2) the length of turnaround time to obtain WNV NAT testing, and 3) the unproven test performance on donated organs. One analysis suggested that WNV NAT screening might result in a net loss of years of life among certain types of potential transplant recipients (*9*) by excluding healthy donors from an already limited donor pool. National guidelines for organ-donor screening are continuously reevaluated by the Health Resources and Services Administration in consultation with FDA, CDC, and organ-procurement organizations (*10*).

Clinicians should be aware that transplant-associated infectious disease transmission can occur and should be vigilant for unexpected outcomes in transplant recipients, particularly when they occur in clusters. Cases of suspected WNV infection through organ transplant should be reported promptly to local and state health departments and CDC.

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