TRANSFUSION MEDICINE UPDATE

Institute for Transfusion Medicine Issue #2 2006

Transfusion-transmitted West Nile Virus Infection Update

Ram Kakaiya, MD, Medical Director, LifeSource Blood Center

Epidemiology:
West Nile virus (WNV) is an RNA virus from the family *Flaviviridae* that is transmitted to humans by infected mosquitoes. Birds are the primary hosts for the virus. WNV infection epidemics had previously been reported outside the USA in the Middle East and in Europe. The first small epidemic occurred in the U.S. in 1999 in New York City. Since then, each year, a number of human infections have been reported. In 2002, a multi-state epidemic was observed in the U.S. and as many as 4,156 human cases were reported to the Centers for Disease Control (CDC). The epidemic peaked at 9,862 cases in 2003. The number of cases declined in 2004 and 2005 to 2,539 and 1,607 respectively.

WNV infection causes mild symptoms in 20% of the infected patients, severe symptoms in less than 1%, and no symptoms in the remaining 79%. Mild symptoms consist of those that are customarily seen in other mild febrile viral illness. In severe cases, patients show signs and symptoms of meningoencephalitis or polio-type illness. Since approximately 80% of infections are asymptomatic, asymptomatic infected donors may unknowingly donate blood and transmit infection to blood recipients. In fact, during the 1999 outbreak in Queens, New York, it was estimated that the risk of viremic donors might be as high as 2-3 per 10,000. In association with the marked increase in infection in the general population, several well-documented cases of infection from blood transfusion were discovered.

Characteristics of transfusion transmission:
The largest reported series of transfusion-transmitted WNV infection cases included 23 transfusion recipients.[1] This report showed for the very first time that WNV transmission can occur via blood transfusion. Past epidemics in Europe and the Middle East were not associated with transfusion-related WNV infection. The transfusion-related cases occurred in different geographic regions that were experiencing the epidemic in 2002. The infection in these patients was acquired through transfused leukocyte-reduced and non-leukocyte-reduced blood components. Transmission of WNV from donor to recipient was demonstrated from transfusion of infected red blood cells, platelets, and fresh frozen plasma.

Almost half of the recipients in the above series of cases were immunosuppressed. About one third were at least 70 years of age. Eight of the 23 recipients (35%) were asymptomatic, although they showed the presence of IgM antibodies against WNV in convalescent sera. Thirteen of the 15 symptomatic patients had meningoencephalitis and two patients had febrile illness. Median time to onset of symptoms was 10 days (range: 2-21 days). Mortality in these cases was 30% (7 of 23 cases).

Blood products donated by 16 viremic donors in the above series of cases were responsible for infection. It should be noted that one donor can transmit infection to more than one recipient because multiple blood components are generally prepared from one donation of a whole blood unit. Only 9 of the 16 (56%) donors had any WNV symptoms before or after the donation.

Transfusion transmission was diagnosed by confirming viremia in the blood donor and by demonstration of WNV infection in the recipient of a component from a donor with viremia. Laboratory testing was performed on blood samples obtained from archived retention segments of the transfused units. WNV RNA was identified by polymerase chain reaction (PCR) testing to show that the donors were

viremic at the time of donation. As noted above, in asymptomatic recipients, convalescent sera showed the presence of IgM antibodies directed against WNV.

Prevention of Transfusion-transmitted WNV Infection:

The following factors resulted in great concern for the safety of the blood supply: (a) most WNV infections are asymptomatic, thus viremic donors could not be identified prior to donation, (b) the estimated risk in epidemic areas could be as high as 2-3 cases per 10,000 donors; and (c) a high incidence of mortality was seen in transfusion recipients. These concerns led to a series of meetings between the US Public Health Service, CDC, FDA, AABB, American Red Cross, America's Blood Centers, and the companies that would develop a test for WNV in order to come up with strategies for prevention. These deliberations resulted in implementation of more refined donor selection criteria, as well as the development and implementation of a test for WNV RNA to screen the blood supply. With unprecedented speed, research test kits were designed and made available.

Routine donor screening using the test kits was implemented in July 2003. The numbers of viremic donors detected were 818 in 2003, 224 in 2004, and 417 in 2005. These numbers clearly demonstrate that a number of viremic donations were removed from blood supply, resulting in increased safety for transfusion recipients. Some of the viremic donors were also positive for IgM antibodies. However, the viral load in the IgM positive donors was quite low and probably insufficient to cause infection in the recipients.

Routine donor testing involves preparing a pool of donor blood samples. The pooled samples are then tested for WNV RNA by PCR. The pooled sample testing is necessary because individual donor sample testing would require a much higher level of laboratory automation than is currently available. Pooling does reduce the sensitivity of the test because each individual sample in the pool becomes diluted. Therefore, WNV infection from transfusion of WNV-tested blood can occur. In fact, the CDC has described six confirmed cases of WNV infection from blood transfusion during the 2003 season.[2] Nonetheless, current testing has reduced the risk of WNV significantly, and the prevention efforts undertaken have demonstrated a successful collaboration of the entities described above. Improvement in the sensitivity of the test by pooled sample testing has also been introduced to further reduce the risk.

Conclusion:

WNV transmission by blood transfusion serves as a reminder to all of us that new infectious agents can spread via the blood supply with great speed. Clinicians caring for the patients should continue to be vigilant that transfusion-transmitted WNV infection, although much less frequent than in 2002, can still occur. WNV transmission should be in the differential diagnosis in febrile transfused patients who have clinical manifestations of meningoencephalitis, especially among immunosuppressed patients. Appropriate laboratory studies for the diagnosis of WNV infection include WNV RNA testing of blood or cerebrospinal fluid and/or testing of convalescent sera for the IgM anti-WNV antibody.

References:

1. Pealer LN, Marfin AA, Peterson LR et al. Transmission of West Nile virus through blood transfusion in the United States in 2002. New Engl J Med 2003; 349:1236-45.
2. Anonymous. Update: West Nile virus screening of blood donations and transfusion-associated transmission – United States, 2003. MMWR 2004; 53:281-84.

Editor: Donald L. Kelley, MD, MBA: dkelley@itxm.org
For questions regarding this TMU, please contact Ram Kakaiya, MD at: (847) 803-7825.
Copies of the *Transfusion Medicine Update* can be found on the ITxM web page at www.itxm.org