CORRESPONDENCE

Transmission of Rabies from an Organ Donor

TO THE EDITOR: Srinivasan and colleagues (March 17 issue)[1] report the transmission of rabies virus from an organ donor to four recipients. Three recipients had neurologic deterioration and encephalitis and died about five weeks after transplantation; one died of intraoperative complications. The authors investigated the medical records of the donor and the recipients and performed serologic and histopathological tests on the recipients' blood, fluids, and tissues with a variety of assays. Although the results of these tests suggest that rabies is the etiologic pathogen that was transmitted from the donor to the recipients, these tests do not provide conclusive information about the original source of the virus. The origin of the pathogen could be identified by means of molecular typing techniques, such as a heteroduplex-mobility assay, gene sequencing, or phylogenetic analysis.[2-4] The conclusion of the study would be different if the genotypes of the viruses isolated from the donor and the recipients were distinctly different. The conclusion that these organ recipients died from rabies infection transmitted by the donor would be more convincing if a high degree of homology among the viral genotypes were demonstrated.

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TO THE EDITOR: Srinivasan et al. report the death of four patients who had received transplanted solid organs and a vascular graft from a donor with rabies. The donor presented with fever, altered mental status, difficulty swallowing, and autonomic dysfunction, which are clinical features of rabies,[1] and apparently he had no ictus suggestive of aneurysmal subarachnoid hemorrhage. An important issue is whether the donor had two coexisting, fatal neurologic diseases (rabies and severe subarachnoid hemorrhage) or whether he had rabies and either an unrelated, minor subarachnoid hemorrhage that would not explain his neurologic presentation and subsequent deterioration or a pseudosubarachnoid hemorrhage, which may be associated with diffuse cerebral edema and other conditions.[2,3] There is extensive information available about the neuropathology of rabies,[4] but there is no support for the speculation that rabies virus might infect and cause pathologic changes in the blood vessels, leading to subarachnoid hemorrhage. Hence, it would have been very informative if the authors had provided the computed tomographic images of the donor's brain showing the subarachnoid hemorrhage.

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TO THE EDITOR: In France, to limit the transmission of infectious diseases in allogeneic tissue or cells, a quarantine period of at least two months is mandatory when tissue or cell storage is compatible with subsequent clinical use.[1] When such a biologic product is collected from a live donor (e.g., in the case of cord blood or amniotic membranes), repeated testing for infectious markers is performed on completion of the quarantine period. When the biologic product is collected from an organ donor (as in the case of arteries, bones, or cardiac valves), testing for infectious markers is performed two months after transplantation in all the recipients of organs collected from the same donor. Furthermore, any clinically significant event occurring among the organ recipients during the quarantine period is recorded by the Etablissement Français des Greffes and transferred to the relevant biobank. Implementation of such a policy would prevent the transmission of rabies virus in an arterial graft, as in the case described by Srinivasan et al. Indeed, the arterial graft would have been cryopreserved, stored, and subsequently discarded, in view of the encephalitis that occurred in one or more of the recipients who had received an organ from that donor.

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1. Law No. 94-654 of 29 July 1994 on the donation and use of elements and products of the human body, medically assisted procreation, and prenatal diagnosis. (Journal officiel de la Republique francaise, Lois et Decrets, 30 July 1994, No. 175, p. 11060-11068). Int Dig Health Legis 1994;45:473-82.

THE AUTHORS REPLY: With respect to Dr. Jenwitheesuk's point about the source of the infections, we believe that the epidemiologic evidence does point overwhelmingly to the organ donor as the source. In addition, sequencing data confirm that the rabies virus in all the recipients was identical.

The subarachnoid hemorrhage in the organ donor was severe and was associated with herniation. We agree with Dr. Jackson's assertion that there is no evidence that the subarachnoid hemorrhage in the organ donor was related to the rabies infection. As we mention in the article, subarachnoid hemorrhage has not been described in previous reports of neurologic imaging in patients with rabies.[1-3] The cause of the subarachnoid hemorrhage in this case remains unknown. One possibility is hypertension in the setting of a positive toxicologic screen for cocaine.

We appreciate learning from Drs. Lapierre and Tiberghien about practices in France with respect to the mandatory quarantine of allogeneic tissues and the central reporting of any adverse events that occur among organ recipients. The required quarantine period they describe, which necessitates cryopreservation of arterial conduits, would indeed have prevented the case of rabies in the recipient of the arterial conduit described in our report. However, some transplantation surgeons prefer fresh arterial conduits to cryopreserved ones, and the successful use of fresh arterial conduits has been reported both in primary transplantation procedures and in the management of vascular complications after transplantation. Whether fresh conduits lead to better outcomes and justify a slightly increased risk of disease transmission remains unknown. Certainly, the ability to track and account for these vascular conduits is essential for the rapid identification of patients who might be at risk for infections from transplants. Improving nationwide detection and central reporting of unexpected or serious outcomes in organ recipients, as described by Drs. Lapierre and Tiberghien, might indeed facilitate the discovery of transplant-related transmission of pathogens by allowing connections to common donors to be made. This concept remains a topic of discussion between the Department of Health and Human Services, including the Centers for Disease Control and Prevention, and members of the organ and tissue transplantation community.

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