

Unprotected People #78

Rabies

Florida Man Dies from Rabies Eight Months After Receiving Dog Bite in Haiti

The following case report recounts the experience of a man hospitalized for four days before dying from undiagnosed rabies. The man's wife reported he had been bitten on the finger by a dog on a visit to Haiti eight months prior to hospitalization. Postmortem laboratory tests conducted by CDC determined the cause of death was a canine variant of the rabies virus present in Haiti.

Titled "Human Rabies—Florida, 2004," the case report first appeared in MMWR on August 12, 2005. It is reprinted below in its entirety with the exception of footnotes and acknowledgements.

Human Rabies—Florida, 2004

Rabies is a viral infection of the central nervous system, usually contracted from the bite of an infected animal, and nearly always fatal without postexposure prophylaxis. In February 2004, a man aged 41 years died after a 4-day hospitalization in Broward County, Florida. A diagnosis of rabies was considered on the day before the patient's death; however, no antemortem samples were obtained for testing. In March 2004, postmortem samples of fixed brain material were sent to CDC, where laboratory testing confirmed a diagnosis of rabies, the 47th case of human rabies reported in the United States since 1990 (CDC, unpublished data, 2005). This report summarizes results of the subsequent investigation led by the Broward County Health Department and laboratory testing at CDC, which determined that the rabies virus was a canine variant present in Haiti, where the man had traveled and reportedly been bitten by a dog. Rabies should be considered in persons after a dog bite, especially if the bite occurs in a country where canine rabies is enzootic.

The man arrived at the hospital emergency department with a 2-day history of dysphagia accompanied by hyperventilation and agitation when he attempted to swallow liquids. The problem had worsened by the time of admission; he was noted as "almost phobic" to liquids.

The patient reported having a brief period of mild fever. He was able to swallow soft, solid food and did not complain of throat pain or discomfort. Upon physical examination of his mouth and throat, the patient became agitated and experienced hyperventilation. He was admitted for further observation and diagnostic evaluation. On the day of admission, a neurology consultant concluded that the dysphagia etiology was unknown and recommended infectious disease, gastrointestinal, and pulmonary consultations. Examination results by a gastrointestinal consultant on the same day were unremarkable, except for dysphagia and phobia to liquids.

The patient reported a history of malaria and ureteral stricture and surgery. Magnetic resonance imaging study results were unremarkable. Results of examinations of the patient's ear, nose, and throat, including a swallow test (i.e., cervical esophagram), and radiographs of neck and soft tissue were normal. Because examination elicited substantial agitation and hyperventilation in the patient, anti-anxiety medical management was instituted, and the patient was referred for psychiatric evaluation.

On his third day of hospitalization, the patient had a consistent fever of 103 degrees F (39.4 degrees C) and an elevated white blood cell count of 14.5/microliter (normal: 3.6-11.0/microliter). An infectious disease consultant recommended a

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lumbar puncture and testing for viral illness, especially rabies. The patient's wife reported that her husband had been bitten on the fingertip by a dog 8 months earlier while he was visiting Haiti. The wife reported that the dog was still alive; however, that could not be confirmed by investigators. She said her husband had not traveled back to Haiti during the interim. Anti-malarial treatment of the patient also was empirically initiated pending the results of malaria testing.

On the fourth day of hospitalization, the patient experienced diplopia and was decreasingly responsive. He went into cardiopulmonary arrest and died. Antemortem rabies testing was under consideration, but the patient died before samples were collected. On histopathologic examination of the cerebral cortex, pons, hippocampus, and spinal cord, the medical examiner described cytoplasmic inclusions consistent with Negri bodies. Unstained slides of formalin-fixed samples of brain material were sent to CDC for diagnosis and typing. Rabies virus antigen was detected by a modification of the direct fluorescent antibody test. A reverse transcription-polymerase chain reaction assay produced an amplicon sequence that was compatible with a canine rabies-virus variant present in Haiti. This variant has not been documented among domestic or wild animal reservoirs in the United States. One close family member underwent postexposure prophylaxis for exposure to the patient's secretions.

Editorial Note

Of the 47 cases of human rabies reported in the United States since 1990, four occurred in organ transplant recipients and were associated with an undetected case of rabies in a single organ donor; the remainder apparently were acquired from contact with animals with rabies virus infections. Thirty-eight (81%) of the infections were acquired in the United States. Among the nine infections acquired elsewhere, two were acquired in Haiti (the 2004 case described in this report and a 1994 case), two in Mexico (1993 and 1994), and one each in India (1992), Southeast Asia (1996), Ghana (2000), the Philippines (2001), and El Salvador (2004).

The greatest risk for naturally acquired rabies in the United States is from encounters with and bites from insectivorous bats. In particular, a rabies-virus variant associated with two small-bodied bats, the eastern pipistrelle bat (*Pipistrellus subflavus*) and silver-haired bat (*Lasiurus noctivagans*) was identified in 20 (69%) of 29 persons with samples tested.

Human rabies is preventable if the exposure is recognized and the patient receives appropriate wound care and postexposure prophylaxis before clinical signs of rabies are evident. Postexposure prophylaxis consists of rabies immune globulin infiltrated at the site of the exposure and 1 dose of rabies vaccine administered in the deltoid (or anterolateral thigh of infants and small children) on days 0, 3, 7, 14, and 28. When applied appropriately, this combination has been effective in preventing death after an exposure. However, the continued availability of rabies vaccine currently relies upon only one licensed manufacturer in the United States; a second manufacturer suspended and has not resumed production after a voluntary recall of its rabies vaccine in March 2004.

In the United States, mandatory vaccination and stray-dog control programs have virtually eliminated circulation of any canine rabies-virus variant among dogs. In comparison, occurrence of rabies in dogs remains a problem in Haiti and other developing countries. Because of the risk for rabies exposure in these countries, travelers are advised to avoid contact with dogs and other animals, and rabies pre-exposure prophylaxis (consisting of 3 intramuscular doses of rabies vaccine on days 0, 7, and 21 or 28) is recommended for persons planning to stay 30 or more days in remote areas without access to medical facilities. The patient described in this investigation reportedly was bitten by a dog in Haiti 8 months before clinical signs of rabies became evident. This was the longest incubation period among 12 U.S. rabies cases with exposure history reported since 1997 (median: 39 days; range: 21–240 days); however, longer incubation periods of 11

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months to 6 years were suggested by findings in three cases previously described.

Although human rabies is rare in the United States, it should be considered in the postmortem differential diagnosis of fatal viral encephalitis cases with short morbidity periods if no cause of disease has been established. Hospitalized patients with encephalitis of unknown etiology should be on contact precautions, and rabies should be part of antemortem differential diagnosis in these patients. Both antemortem and postmortem testing for rabies are available at CDC and can be arranged through state health departments. Antemortem diagnostic samples consist of a full thickness skin biopsy (4–6 mm in diameter) from the nape of the neck, fresh saliva, serum, and cerebrospinal fluid. Although postmortem rabies diagnosis can be performed on formalin-fixed brain material, fresh brain material

provides the optimal sample for maximum sensitivity, specificity, and time efficiency.

With the recent report from Wisconsin of a survivor of clinical rabies, rapid diagnosis of rabies is even more critical to managing a patient's clinical course, despite a poor prognosis. In addition to enabling consideration of novel interventions, advantages of early diagnosis include prompt implementation of appropriate infection-control measures, thereby limiting the number of persons exposed or potentially exposed who require postexposure prophylaxis. Retrospective detection of four transplant-associated rabies cases and retrospective identification of an additional case in California in an immigrant from El Salvador, brought the total number of 2004 cases in the United States to eight, the highest number of human rabies cases reported since 1956, when 10 cases were reported.