

Human Rabies — Missouri, 2014

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On September 18, 2014, the Missouri Department of Health and Senior Services (MDHSS) was notified of a suspected rabies case in a Missouri resident. The patient, a man aged 52 years, lived in a rural, deeply wooded area, and bat sightings in and around his home were anecdotally reported. Exposure to bats poses a risk for rabies. After two emergency department visits for severe neck pain, paresthesia in the left arm, upper body tremors, and anxiety, he was hospitalized on September 13 for encephalitis of unknown etiology. On September 24, he received a diagnosis of rabies and on September 26, he died. Genetic sequencing tests confirmed infection with a rabies virus variant associated with tricolored bats. Health care providers need to maintain a high index of clinical suspicion for rabies in patients who have unexplained, rapidly progressive encephalitis, and adhere to recommended infection control practices when examining and treating patients with suspected infectious diseases.

Case Report

On the morning of September 12, 2014, a Missouri resident, a man aged 52 years, visited hospital A's emergency department for evaluation of acute onset of severe neck pain that radiated down his left arm to his hand. After a cervical spine radiograph, a diagnosis of cervical muscle strain and radiculopathy was made, for which the patient received injections of orphenadrine (a muscle relaxant) and ketolorac (a nonsteroidal anti-inflammatory drug). He was instructed to take ibuprofen and cyclobenzaprine (a muscle relaxant) for pain relief and to return if symptoms worsened. The next day, he awoke with numbness and tingling in his left arm, severe bilateral upper body tremors, and sweating, as well as continued neck pain. He returned to hospital A's emergency department, where he received a diagnosis of a herniated disc and was discharged with instructions to take oral prednisone

and oxycodone HCl/acetaminophen. That same evening, while the patient was at home, his symptoms progressed, and he became anxious and fearful; family members transported him back to the emergency department, during which time he began experiencing visual hallucinations. He was admitted to hospital A with a diagnosis of suspected serotonin syndrome secondary to the cyclobenzaprine.

On September 13, the patient was treated with oral ibuprofen and cyproheptadine and with parenteral lorazepam, diazepam, diphenhydramine, and haloperidol. On September 14, losartan and hydrochlorothiazide were prescribed to be taken orally for hypertension, but the patient was unable to swallow these medications. His condition progressively worsened, with the development of considerable rigidity and action tremors in his upper extremities. That same day, he was transferred to hospital B, a tertiary care referral hospital, for neurologic

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evaluation. Upon admission, he was febrile (104.9°F [40.5°C]), tachycardic, tachypneic, and hypertensive with bilateral upper extremity tremors and whole body myoclonic jerks. On September 15, he required intubation and mechanical ventilation for airway protection. Before intubation, the patient orally communicated an aversion to water.

During the next 11 days the patient underwent an extensive laboratory evaluation to determine the cause of his encephalopathy, including a urine drug screen, tricyclic antidepressant levels, an arbovirus panel, and testing for antibodies to Rocky Mountain spotted fever, ehrlichiosis, syphilis, and herpes simplex virus; all test results were negative. The peripheral white blood cell count and liver enzymes were both slightly elevated. On September 19, a traumatic lumbar puncture yielded hemorrhagic cerebrospinal fluid (CSF) with elevated glucose, protein, and white blood cells. Electroencephalogram studies indicated generalized slowing of brain activity, minimal reactivity to noxious stimulation, and absent posterior dominant rhythm, consistent with encephalopathy. The patient required dopamine and norepinephrine for cardiovascular support, continuous mechanical ventilation for acute hypoxemic respiratory failure, and hemodialysis for acute kidney injury. Initial treatment included broad-spectrum antibiotics for presumed sepsis and acyclovir for suspected herpes encephalitis.

Family members initially reported that the patient lived in a trailer on 97 densely wooded acres, but his exposure to wildlife was not known at that time. Because of the acute and rapidly progressive clinical course of his illness and the elimination

of the most common etiologies of encephalitis from the differential diagnoses, the possibility of rabies was considered, public health officials notified, and confirmatory laboratory testing initiated on September 18. Serum, CSF, nuchal skin biopsy, and saliva specimens collected on September 19 were submitted to CDC on September 22 for rabies testing.

On September 24, rabies was confirmed by the presence of rabies virus antigen in the skin biopsy, and the detection of rabies virus in saliva and skin by reverse transcription polymerase chain reaction. Genomic sequencing found the variant to be associated with the tricolored bat (*Perimyotis subflavus* [formerly *Pipistrellus subflavus*]). Neither antirabies antibodies (immunoglobulin G or immunoglobulin M) nor rabies virus neutralizing antibodies were detected by indirect fluorescent antibody or rapid fluorescent focus inhibition tests in the serum and CSF specimens collected on September 19. However, both antirabies antibodies and rabies virus neutralizing antibodies were subsequently detected in a serum specimen collected on September 25. Because of the advanced stage of illness and worsening prognosis, the Milwaukee protocol (1) was not initiated. On September 26, the family elected to withdraw life support, and the patient died shortly thereafter.

Public Health Investigation

On September 18, an infectious disease specialist at hospital B notified MDHSS of the suspected human rabies case. After confirmation of the diagnosis, MDHSS, local public

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health agency officials, and infection prevention specialists at hospitals A and B interviewed family members, friends, and hospital personnel in an effort to determine the patient's exposure and travel history and to identify any high-risk exposures that would require rabies postexposure prophylaxis (PEP) (2). Two questionnaires developed by CDC were used to evaluate health care workers and family and community members for possible exposure to the patient.

The variant identified from genetic sequencing of rabies virus from the patient was from *Perimyotis subflavus* (tricolored bat), one of the smallest bats in eastern North America. The rabies variant associated with this bat species occasionally infects other bats (e.g., *Tadarida brasiliensis* [big brown bat]) as well as cats, foxes, and other species. Any of these animal sources could have accounted for the patient's exposure.

Although the exact exposure date is unknown, the patient had reported seeing a bat in his home in late August or early September 2014. He also worked in a warehouse in which coworkers reported that bats are occasionally seen, but no bat sightings in the several weeks before the patient's illness onset were reported. Public health investigators who visited the patient's trailer home noted several places where a small animal, such as a bat, could have entered. A family member reported having observed bats roosting on a utility pole near the trailer in the past. This information, combined with documentation of previous bat-variant rabies cases with undocumented or unidentified exposures (3), makes a bat the most likely source of rabies infection in this patient. Symptom onset was estimated to be September 6, based on a family member's recollection that the patient complained of fatigue and neck pain during that weekend. Rabies infection from a bat exposure during late August or early September would suggest a shorter incubation period than the typical 3–8 weeks (2). Thus an earlier, undetected bat exposure might be more likely.

Nine family members and friends were identified as having potential high-risk exposures to the saliva from the patient through mucous membranes or small, open hand wounds; all received rabies PEP. Among the 73 health care workers who provided care to the patient at hospitals A and B, seven met Advisory Committee on Immunization Practices criteria for rabies PEP (2). Health care-associated exposures primarily occurred through prolonged contact with the patient's face, saliva, or tears with ungloved hands and nonintact skin.

Discussion

This case illustrates the importance of educating the public about potential rabies reservoirs and exposure sources in the United States and of promptly seeking medical attention after any potential rabies exposure. Rabies is preventable after an

Summary

What is already known about this topic?

Human rabies in the United States is rare (one to three cases are reported annually). However, because the virus is endemic in the U.S. wildlife population, susceptible domestic animals and humans exposed to rabid animals are at risk for developing rabies infection.

What is added by this report?

Early diagnosis of human rabies infection might be hampered by delayed recognition, given the rarity of the disease, nonspecific initial symptoms, and difficulty in obtaining animal exposure history once the patient is in the later stages of illness.

What are the implications for public health practice?

To prevent rabies 1) continue to educate the public and health care providers about the risk for exposure to rabies virus from bats and other mammalian species and the importance of prompt medical evaluation and initiation of postexposure prophylaxis and 2) promote consistent adherence to standard precautions among health care providers in the treatment of all potentially infectious patients.

exposure through timely PEP, which includes wound washing and administration of rabies immune globulin and rabies vaccine (2). Bat exposures are high-risk exposures for rabies virus infection, particularly because the wounds inflicted by bats are often minor and easily overlooked. No evidence-based treatment approach for clinical rabies exists. An experimental approach, the Milwaukee protocol, which was first used in 2004 in a Wisconsin patient who survived rabies infection (4), has been implemented with varying outcomes (1).

This case is the second case of human rabies in Missouri in 6 years; during this time, specimens from six humans were referred from the Missouri State Public Health Laboratory to CDC for antemortem rabies testing. In 2008, a male aged 55 years died of rabies in Missouri after being bitten on the ear by a bat (5); before this, the last Missouri rabies case was reported in 1959. During 2008–2011, a total of 11 human rabies cases were reported in the United States and Puerto Rico, including five cases with infections acquired overseas (6). Among the six domestically acquired cases, five were associated with bat variant rabies viruses; in three cases, a confirmed bat bite was reported. In Missouri, bats and skunks are principal reservoirs of rabies (7). Given that wild animals might not display obvious signs of rabies illness, it is important that, whenever possible, all bats and wild terrestrial carnivores implicated in a potential rabies exposure be euthanized and tested for rabies. This testing can ensure that PEP is appropriately administered to prevent rabies in persons with exposures to confirmed rabid animals, and might avoid misadministration of PEP to nonexposed persons.

A review of human rabies cases in the United States during 1960–2010 found that a median of 39 contacts per case (range = 1–180) received PEP (8). Sixteen persons with possible exposure to the 2014 Missouri patient were identified (seven health care workers and nine community members). According to the indications for rabies PEP (2), human-to-human transmission of rabies virus can occur through exposure to virus in saliva through mucous membranes or fresh, open cuts in the skin. Consistent adherence to standard precautions should minimize the need for rabies PEP in health care settings (9).

Public education campaigns aimed at raising rabies awareness should address misconceptions about risk associated with bat encounters (e.g., lack of knowledge that bats can transmit rabies through small, undetected bites) that can lead to a delay in the timely response to potential rabies virus exposures. These campaigns should also emphasize the importance of completing the full rabies PEP series once initiated, unless the exposure source is determined not to be rabid through laboratory testing or successful (i.e., remains healthy) completion of a 10-day observation period for a dog, cat, or ferret (2). In addition to the importance of public education, health care workers should consider rabies in the differential diagnosis of any patient with acute, unexplained encephalitis, and use appropriate infection control practices when examining and treating patients with a suspected infectious disease.

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