Fatal Human Rabies Caused by European Bat Lyssavirus Type 2a Infection in Scotland


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We wish to report the first recorded case of indigenous human rabies caused by a bat bite in the United Kingdom in 100 years. This instructive case report highlights a number of key lessons: first, bites from insectivorous bats indigenous to the United Kingdom can cause rabies in humans; second, rabies immunization is essential for bat-handlers, and postexposure treatment for rabies is essential for patients bitten by bats; third, patients able to give a history who present with acute flaccid paralysis and/or presumptive viral encephalitis should be asked if they have been bitten by bats, irrespective of travel history, or this history should be obtained from family or friends; fourth, antemortem diagnosis of bat rabies (EBLV type 2a infection) in humans is possible using RT-PCR.

The United Kingdom is considered free from terrestrial rabies, with the most recent human death from indigenous rabies recorded in 1902. However, 2 cases of rabies have been confirmed in the United Kingdom in Daubenton’s bats (Myotis daubentonii), the first in 1996 at Newhaven and the second in September 2002 in Lancashire; both cases were caused by European bat lyssavirus (EBLV) type 2a [1, 2]. In Europe, 3 human deaths from rabies caused by EBLV have been reported [3–5]. The United Kingdom’s Departments of Health have long recommended vaccination of licensed bat-handlers [6]. We report a case of rabies acquired in the United Kingdom in an unvaccinated volunteer bat-handler and bat-rescuer, confirmed by antemortem testing to be caused by EBLV 2a infection.

Case report. A 55-year-old man presented to our hospital with an acute hematemesis attributed to nonsteroidal anti-inflammatory drugs prescribed by his general practitioner for left-shoulder pain and left upper-limb paresthesia and tightness which commenced 5 days before referral. On the day of admission to hospital, he was hemodynamically stable with no evidence of active gastrointestinal bleeding. He was an artist but had worked voluntarily as a bat-handler and bat-rescuer for many years. He last travelled abroad (to Papua, New Guinea) 7 years prior to the onset of illness. He had been bitten by bats in Angus, Scotland, while not wearing gloves. The most recent occasion was ~19 weeks before presentation, when he was bitten on the ring finger of the left hand by what he believed to be a Daubenton’s bat.

On examination, the patient’s temperature was 38.5°C, but there was no meningism. He was lucid and complained of increasing left-arm pain, paresthesiae in both upper limbs, and subjective difficulty in swallowing. His behavior was inappropriately familiar, and he was mildly dysarthric with gaze-evoked nystagmus. His upper limbs were areflexic with brisk reflexes in the lower limbs. Truncal, upper limb, and gait ataxia was present. Sensation was altered to touch over the left upper limb (dysesthesia), but there was no motor weakness. The patient was treated with high-dose flucloxacillin, high-dose acyclovir, and ciprofloxacin.

An urgent CT scan of the head and subsequent MRI of the brain were performed on the day of admission. The findings of the CT scan were reported as normal except for a suggestion of increased density in the left cerebellum. The MRI of the brain without gadolinium enhancement was performed as an emergency procedure and findings were entirely normal. MRI of the patient’s cervical spine revealed a focal central-cord linear high-density signal from C5 to T1 which did not enhance. This was a possible syrinx but was not thought to be of clinical relevance. Samples of CSF obtained from the patient on day 2 of hospitalization had a mildly raised protein level of 582 mg/L, and the cell count was normal. Intravenous immunoglobulin therapy was administered at a dosage of 400 mg/kg per day for 5 days to treat presumptive Guillain-Barré syndrome.

On day 5 of hospitalization, the patient became acutely confused, aggressive, and agitated, and he required sedation. The patient’s score on the Glasgow Coma Scale (GCS) was 6 prior to sedation. A second CT scan (without contrast) was per-
formed, and findings were normal. The patient’s CSF protein level on this occasion was 1091 mg/L with 20 lymphocytes per high-powered field on microscopy. On day 6 of hospitalization, the patient deteriorated acutely with collapse of the right lung, ventilatory failure, decreased consciousness (GCS score, 3), and transient hypersalivation. Aerophobia or hydrophobia were not present. He was transferred to the intensive care unit for mechanical ventilation. His mental state deteriorated quickly, and all of his limbs were completely flaccid. The plantar responses were intermittently extensor. An electroencephalogram showed a nonspecific “encephalitic pattern” with no evidence of seizure activity. Nerve conduction studies were complicated by peripheral edema of hands and feet. The left upper limb was not examined. Right ulnar, right tibial, left tibial, both peroneal motor, and the right sural sensory nerves were tested. Electromyography (EMG) of the right tibialis anterior and the small muscles of the right hand was also performed. The small and absent motor responses and evidence on EMG of acute partial denervation in the small muscles of the hand tibialis anterior confirmed the presence of peripheral axonal loss. This condition appeared to be generalized. The relative preservation of the sural sensory response pointed towards a predominantly motor axonal polyneuropathy.

In light of the patient’s rapidly progressive, unexplained neurological illness and ensuing encephalitis with coma, associated with a history of bat bites, the diagnosis of infection with EBLV leading to a rabies-like encephalitis was thought likely. Confirmation of the diagnosis was sought from samples of saliva and blood and from skin biopsy samples obtained from the nape of neck and the presumed site of the bite (although the bite had healed and the precise site was unclear).

Saliva samples obtained on day 7 of hospitalization had negative results when subjected to initial first-round PCR tests. Subsequently, tests of a saliva specimen obtained on day 9 of hospitalization verified the presence of low levels of Lyssavirus RNA in a first-round PCR reaction. Results of heminested RT-PCR [7] for both these saliva samples were positive for Lyssavirus RNA. A 300-bp region of the nucleoprotein gene was sequenced for confirmation and showed 98% homology to the 2 previous EBLV type 2a isolates obtained from bats in the United Kingdom [1, 2]. Although the sequence data confirms that this virus was an EBLV type-2a strain, it is genetically distinct from the 2 previous EBLV type-2 viruses isolated from bats from the United Kingdom in 1996 and 2002, respectively (data not shown). The PCR products were sequenced within 36 h of sample receipt and, in the absence of postmortem samples, provided the only confirmation that this was a Lyssavirus infection.

As a result of the relative toxicity of the saliva samples to human neuroblastoma cells, both in culture and in mice, conventional rabies diagnostic methods, including the rabies tissue culture inoculation test (RTCIT) and mouse inoculation test (MIT), failed to isolate virus from CSF samples or from skin biopsy samples [8]. Antibody to EBLV was not detected in CSF or blood samples (even in samples obtained from the patient on the day of death).

The patient died on day 14 of hospitalization, 19 days after his first prodromal symptom appeared. The antemortem diagnosis was confirmed by immunofluorescence, RTCIT, MIT, and RT-PCR tests performed on brain samples obtained postmortem. Smears of brain samples obtained from infected mice 13–17 days postinfection had positive results by fluorescent antibody test, and a viable virus was isolated [8].

Discussion. This patient presented with rabies that had mixed components of furious and paralytic rabies, which is strikingly similar to the only other reported case of human rabies due to EBLV type 2 [3, 4]. Guillain-Barré syndrome, vasculitis, and other causes of encephalitis were considered as possible diagnoses early in this patient’s clinical illness. The clinical diagnosis of rabies was made possible by the clear history of bat bites, and was made despite an absence of travel outside the United Kingdom within the past 7 years. This case demonstrates that EBLV infection must now be a part of the differential diagnosis of Guillain-Barré syndrome and viral encephalitis throughout Europe, including the United Kingdom. A history of exposure to bats must now be sought in all such cases, but the absence of such a history does not necessarily exclude the diagnosis of rabies contracted from a bat bite.

The last human death from a case of indigenous classical rabies in the United Kingdom occurred in 1902. There have been 25 human cases of imported rabies reported since 1946 [9, 10, 11, 12]. This is the first case of human EBLV infection to be confirmed antemortem, viral RNA being detectable by RT-PCR in 4 of the 5 saliva samples obtained. Antibody testing was not useful because no neutralizing antibody was detectable, even on the day of death; this phenomenon has been reported before [4].

This tragic outcome might have been prevented by a greater appreciation of the need for prior vaccination followed by a short course (2 doses) of postexposure vaccination, as recommended by the Centers for Disease Control and Prevention (Atlanta, GA) [6]. The United Kingdom’s Departments of Health currently advise that all bat-handlers should be vaccinated routinely against rabies whether they are licensed or not [13]. The need for adequate training of handlers and use of protective equipment cannot be overemphasized.

Previously unvaccinated people are not infrequently bitten by bats in the course of their occupations or their recreations (such as roofing and fly fishing). When people are bitten, they should urgently commence postexposure treatment for rabies [6]. Bat bites are very small and easily missed, so a history of close exposure to bats should give clinicians a low threshold
for provision of postexposure treatment [14]. To minimize their chance of getting bitten, the public should not approach any bat, especially one that appears ill (for recommendations, see http://www.snh.org.uk or http://www.defra.gsi.gov.uk).

Several hundred people in The Netherlands and 2 people in the United Kingdom have been vaccinated with rabies vaccine after being bitten by an EBLV infected bat, and no EBLV infection has been confirmed to date in any of these people [15]. Since 1977, 630 cases of EBLV infection have been identified in European bats [16]. The surveillance of bat bites around Europe is inadequate and must be strengthened. There is evidence of cross-immunity between classical rabies virus of genotype 1 and Lysaviruses of genotypes 5 and 6 (EBLV types 1 and 2); however, definitive proof of cross-protection is lacking [17].

Prevalence of EBLV in UK bats is uncertain; only 2 of 3213 bats tested to date have been infected (Veterinary Laboratories Agency, unpublished data) [1, 2]. Both the infected bats were Daubenton’s bats (figure 1), the second-most-common species in the United Kingdom, with a population estimated at 150,000, but representing only 56 of those bats tested to date. Bats tested are those submitted to the Veterinary Laboratories Agency (Wyebridge, United Kingdom) and are not representative of the bat population in the United Kingdom, geographically or taxonomically. More exacting studies of the prevalence of EBLV in Daubenton’s bats are planned in the United Kingdom. Cases of EBLV infection in animals other than bats (and rare cases of EBLV infection in humans) are rarely reported [18], but surveillance could be strengthened.

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References


