

# An Acute, Progressive Encephalopathy

Ernesto Brauer, MD; John C. O'Horo, MD

## ABSTRACT

Rabies holds the distinction of having the highest case-fatality ratio of any infectious disease. Aggressive public health campaigns have reduced the incidence of this disease in the United States to a record low. We report a case of this increasingly rare disease in a 70-year-old man in Wisconsin.

## CASE PRESENTATION

A 70-year-old man with a past medical history significant for alcoholism (>7 drinks/day) was admitted to a community hospital for altered mental status of 2 days' duration. His confused state had been worsening, and his continuing deterioration led his wife to bring him to the emergency department. While there, the patient became increasingly agitated. Lorazepam and haloperidol were administered, but the patient became more irritable and began to have muscle spasms. He was admitted and evaluated by neurology; initial CT was negative for acute abnormality and the patient was treated for severe alcohol withdrawal. The patient's muscle spasms worsened overnight, and he was found to have rhabdomyolysis with a creatinine kinase over 26,000. By midnight, he was running a fever of 102.8°F. A diagnosis of neuroleptic malignant syndrome was entertained. Amantadine and bromocriptine were administered, and the patient was given diazepam for his myoclonus. Aggressive fluid resuscitation was initiated with normal saline.

Over the next day, the patient developed respiratory distress requiring intubation and mechanical support. The patient became oligouric, and creatinine had increased from 1.04 mg/dL to 6.63 mg/dL. The decision was made to start renal replacement therapy, and the patient was transferred to a tertiary referral hospital for continuous veno-veno hemodialysis. Upon arrival, patient had increasing oxygen requirements.

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**Author Affiliations:** Aurora St Luke's Medical Center, Milwaukee, Wis (Brauer); Aurora Health Care, Milwaukee, Wis (O'Horo).

**Corresponding Author:** Ernesto Brauer, MD; Intensivist, Aurora St. Luke's Medical Center, 2900 W Oklahoma Ave, Milwaukee, WI, 53215; e-mail ernesto.brauer@aurora.org.

Rhabdomyolysis was continuing in spite of not receiving any further neuroleptics; a wider range of causes for rhabdomyolysis was obtained including tetanus and stiff person syndrome. Tetanus and rabies studies were ordered. Negative titers for glutamic acid decarboxylase made stiff

person syndrome less likely. Aggressive supportive measures were continued for next 7 days.

Ultimately, punch biopsy of the neck returned a confirming diagnosis of rabies. The prognosis was discussed with the patient's family, and the decision was made to pursue a palliative course. The patient died several hours later.

Further testing identified the strain of rabies as being carried by *Lasionycteris noctivagans*, the silver-haired bat. Discussion with the family about this likely source elicited a history of bats living on the patient's property.<sup>1</sup>

## DISCUSSION

The differential diagnosis for a patient with acute hyperthermia, muscle rigidity, and rhabdomyolysis is constituted by a number of unusual entities, such as strychnine poisoning, neuroleptic malignant syndrome (NMS), malignant hyperthermia, *Clostridium tetani* or, as in this case, rabies.<sup>2</sup> This patient's case would be atypical for NMS or any of the drug- or toxin-induced syndromes, since his decline continued unabated in spite of not receiving any toxic agents once hospitalized. This progressive decline was the feature that prompted the evaluation for rabies in this patient.

Despite aggressive animal vaccination and prophylaxis campaigns, rabies still claims nearly 55,000 lives annually worldwide. In the United States, 31 cases were identified between 2000 and 2009, with 45% being diagnosed postmortem.<sup>3</sup> Mortality for clinically apparent disease approaches 100%, with a half-dozen survivors,<sup>4</sup> only one of whom had not received post-exposure prophylaxis.<sup>5</sup>

Rabies is caused by the *Rhabdoviridae Lyssavirus*, and transmitted primarily through infected saliva in animal bites. Rare cases transmitted through tissue transplantation have been reported, and laboratory research has demonstrated the theo-

retical possibility of aerosol transmission, but these modes remain of little clinical significance.<sup>3</sup>

The infection has a variable incubation period followed by a prodrome of nonspecific symptoms including fever, headache, and malaise. This progresses to the acute neurologic phase where the patient may present as encephalitic and irritable (80% of cases) or paralyzed (20% of cases). Progression into coma occurs within days of onset of the acute neurologic phase. Death is invariably heralded by multiple organ dysfunction and eventual circulatory collapse.<sup>4</sup>

Diagnosis of rabies is by serum, saliva, cerebrospinal fluid, and nuchal skin biopsy samples. Despite the lack of convincing human-to-human transmission, the exceptionally high fatality rate of the disease merits biosafety level (BSL) 2 precautions, and BSL-3 in select areas such as laboratories and autopsy, where concentrations of the virus may be higher.<sup>6</sup>

Treatment in patients who have progressed into the acute neurologic phase remains contentious, with mixed results from application of the Milwaukee protocol.<sup>4</sup> In the single reported survived case, a combination of antivirals and sedative medications were used to induce coma; with aggressive supportive care, the patient cleared the virus and survived, albeit with neurologic impairment.<sup>5</sup>

## CONCLUSION

Rabies is a rare, largely preventable cause of progressive encephalopathy in the United States. Despite the reported survival of a single case of confirmed rabies, this case is more typical, with rapid decline and death from multiple organ dysfunction.

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