BRIEF REPORT

Rabies in Turkey: Three Human Cases Illustrating the Importance of Suspecting Exposure

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Rabies, a fatal encephalitis of viral origin, is still a major health problem in the developing world. It begins, after exposure, with centripetal spread of the virus through peripheral nerves to the central nervous system. The virus proliferates there and spreads to the tissues via peripheral nerves. The diagnosis is not difficult when a nonimmunized patient presents with hydrophobia after a bite by a known rabid animal. Failure to identify an exposure and administer postexposure prophylaxis, however, can lead to a fatal outcome. We report 3 fatal cases of rabies in which the risk of developing rabies had not been seriously considered. Two had apparent dog bites, but 1 had a minor abrasion. Because rabies is uniformly fatal, possible exposure should be seriously considered in patients with mammalian bites or scratches.

Key words: rabies, encephalitis, prophylaxis

Introduction

Rabies is a fatal encephalitis of viral origin in humans and some other mammals. It is still a major health problem in the developing world and has medical and economic implications: nearly 4 million people receive postexposure prophylaxis annually.¹ It begins, after exposure, with centripetal spread of the virus through peripheral nerves to the central nervous system. The virus proliferates within the central nervous system and then spreads to the tissues via peripheral nerves.² The diagnosis of rabies is not challenging when a nonimmunized patient presents with hydrophobia after exposure to a known rabid animal. However, failing to take an adequate history or underestimating the exposure with resulting failure to administer postexposure prophylaxis can lead to a fatal outcome. We report 3 cases of rabies in patients who were not given appropriate immunization due to failure to seriously consider the risks.

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Case presentations

PATIENT 1

A 24-year-old man was admitted with fasciculations in his upper extremities. He reported a dog bite to his left wrist 17 days previously. He was given a single dose of rabies vaccine just after the bite during care of his wound. The remaining doses were not applied. On admission he was conscious but seemed uncomfortable. There was a single bite mark 0.4×0.5 cm and a 2-cm abrasion on the ulnar side of his left wrist. Spontaneous fasciculations were apparent in both upper extremities. His blood pressure was 170/80 mm Hg, pulse 106/min, and temperature 37.7°C. He was given tetanus immune globulin and tetanus vaccine, penicillin, mannitol, and diazepam. The following day he was transferred to another center because his condition had deteriorated and it was suspected that he might need intensive care. He developed refractory seizures and subsequent cardiopulmonary arrest from which he could not be resuscitated. On autopsy, his lungs were edematous and hemorrhagic. Sections of his brain revealed neuronal degenerations, microglial proliferations, and perivascular and intraparenchymal neutrophilic and mononuclear in-

Figure 1. Intracytoplasmic inclusions (Negri bodies) (arrows) in neurons (HE $\times 100$).

flammation. Some neurons were found to contain pink, intracytoplasmic inclusions (Negri bodies) (Figure 1).

PATIENT 2

A 44-year-old man was admitted with left shoulder pain and dysphagia on drinking for 4 days. He was a worker in a dockyard and reported that 2 months previously a local dog that had given birth to puppies had died at the worksite. He cared for the puppies closely, but a few days later they also died. The veterinary surgeon of the dockyard did not consider this event as suspicious. The patient reported small scratches due to bites of the puppies on his finger tips. On admission, he was conscious. His cervical muscles were tense. There was a 1-mm lesion on the pulp of his left thumb. The same day, he developed agitation and was given tetanus vaccine and tetanus immune globulin for presumptive diagnosis of tetanus. Metronidazole was also started. His mental status began to fluctuate after admission. On the second day, his agitation progressed and he experienced tonic, clonic, generalized epi-

leptic seizures 3 times. His vital functions deteriorated, and he died within 2 days of admission. On autopsy, mild to moderate, perivascular mononuclear infiltration was noted in cerebral tissues. Cerebral tissue had scanty microglial cellular aggregations, and cortical and periventricular areas had basophilic amorphous inclusions. Oval or round, eosinophilic inclusions (Negri bodies) were apparent in the cytoplasm of large neurons, especially in the cerebellar Purkinje cells.

PATIENT 3

A 64-year-old man had a history of dog bite 70 days previously that occurred after provocation, and he did not consider it to be serious. During local care by a physician, he was not given prophylaxis. Forty days later, he described drowsiness, and 45 and 55 days after the bite, he fell when walking. At that time, his physical examination, blood pressure, and blood glucose levels were found to be normal, and he was placed on bed rest. He could not walk without aid, but this was ascribed to

Figure 2. Suspected bites and deaths from rabies in Turkey (1973–2002).

his injuries. Ten days later, he developed fever, nausea, cough, and somnolence, and he was hospitalized. His temperature was 38.3°C. On examination, he had ecchymotic lesions on the dorsal sides of both hands and a 5-cm abrasion on his right anterior superior iliac crest. There were fine crackles heard at his left lung base. He was given intravenous ceftriaxone 1 g daily. His temperature returned to normal within 2 days; however, generalized muscle spasms were noted. His general condition deteriorated, and he developed epileptic convulsions and died. On autopsy, there were findings of early pneumonia and neuronal degeneration with intracytoplasmic inclusions (Negri bodies) in the cerebellar Purkinje cells. Chemical studies for alcohol, carboxyhemoglobin, and other toxic substances were all negative.

Discussion

Rabies is currently distributed all over the world, except Antarctica and some island nations. Its epidemiology in humans follows that of local animal rabies.³ In developing countries where dog rabies is common, most human cases result from dog bites.

Rabies is uniformly fatal. Human rabies can manifest in either encephalitic (furious) or paralytic (dumb) forms. In its classic furious form with hydrophobia or aerophobia, human rabies encephalitis is unmistakable. However, clinical descriptions over the centuries have shown the protean manifestations of the disease.⁴ Local paraesthesias at the site of the bite may be the single prodromal symptom. Paralytic forms of rabies and rare presentations with subtle seizures or with psychiatric disturbances are especially likely to be misdiagnosed.⁴

As in our cases, rabies cases can sometimes be misdi-

agnosed as tetanus. Tetanus resembles rabies only in the presence of reflex spasms. In tetanus, the sensorium is clear. On the other hand, rabies patients do not have persistent rigidity or sustained contractions of axial musculature, such as the jaw, neck, back, and abdomen. Spasms in rabies predominantly affect accessory respiratory muscles and the diaphragm, whereas in tetanus, spasms occur in axial muscles. Opisthotonos is extremely rare in rabies.⁵ Given the history of previous exposure, neurological signs and symptoms, and autopsy findings, our 3 cases were ultimately confirmed to be rabies.

Given the uniformly fatal outcome of clinical rabies, prevention is essential. Prompt postexposure treatments for people who may have been exposed is the only means of preventing human infection,⁶ highlighting the importance of obtaining a careful history. Our second patient had a single, small abrasion, but the unexpected death of the dogs should have raised suspicion. In one series, physicians considered rabies in only 3 cases out of 21 patients on their initial visit, despite a history of exposure in many of them.⁷ No rabies deaths have been reported in anyone who has had pre-exposure treatment followed by a booster dose after exposure.⁴ On the other hand, postexposure prophylaxis is often given unnecessarily, and the costs of these measures increase.⁸ Dog bites are common and account for up to 1% of all emergency department visits in the United States, and it has been estimated that up to 20% of all children in the United States will be bitten by a dog at some time in their lives.⁹

In Turkey, rabies still remains a health problem. Although the number of people subjected to suspicious bite exposure has increased, deaths have decreased (Figure 2).¹⁰ This decrease is most probably due to increased use of postexposure prophylaxis. Since 1990, annual re-

ported deaths due to rabies in Turkey have been less than 10. Dog rabies prevails in Turkey, and it is the only European country in which dog rabies is prevalent.¹¹ Between the years 1988 and 1997, 76% of all registered rabies cases were in dogs and only 1% of cases were diagnosed in wildlife.

Given the social, psychological, and economic impact of animal bites, efforts should be made to reduce the number that occur by educating adults and children regarding bite prevention. Efforts are being made to decrease or prevent exposures by controlling dogs. Street dogs are captured, surgically neutered, and vaccinated against rabies. Some municipalities have established pet housing facilities that do not release dogs into the streets. Of equal importance is the need to stress the value of obtaining an adequate history of possible animal exposure and the education of practitioners regarding the judicious use of postexposure prophylaxis. In some areas of the world, it may be helpful to refer patients with suspicious exposures to specialized centers to decrease unnecessary costs and prevent delay in treating vulnerable patients.

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