Letter to the Editor

An Investigation of the First Case of Human Rabies Caused by a Fox in China in May 2016

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This study assesses the causes and prevention measures of rabies through epidemiological investigation and analysis. A field epidemiological survey was conducted to investigate a case of rabies by fox bite. The onset of symptoms began 50 days after the bite. The patient did not receive standard treatment, rabies vaccination, or rabies immunoglobulin injection. The fox was killed on the spot. Saliva and pre-death blood samples were collected at different periods, and only blood RT-PCR tests yielded positive results. Wild fox bite is a major risk factor of rabies infection in Xinjiang Province, China.

Since the 1950s, several reports of locally acquired rabies in Xinjiang Province, China, have been published. The Yili Friendship Hospital received a suspected human rabies case on April 30, 2016. The patient presented with fever and back pain, and he reported having been bitten by a fox on March 6 in Nilka County. The patient had not been previously vaccinated against rabies. During hospitalization, the patient demonstrated rabies symptoms, including fear of water and wind, irritability, excitement, and paroxysmal pharyngeal muscle spasms, among others. The patient died on May 7, 2016, and his blood RT-PCR test results came out positive on July 11, 2016.

The patient was a Kazakh herdsman, aged 29 years, and married. While out grazing sheep near Bubulake (43°42’16” W, 83°18’7” E; altitude, 1,700 m) at around 15:00-16:00 on March 6, 2016, he saw a fox attacking a lamb. He shouted at the fox in an attempt to frighten it away, but he was attacked by the animal instead. The patient struck the fox on the head with a stone to kill it, but his hands (muscle of the hypothenar on the right hand and thumbnail on the left hand) were bitten during the attack. The wounds he sustained were not very deep, and the patient experienced minimal bleeding. At around 16:00-17:00 of the same day, the herdsman returned to his home to clean the wound with soap and disinfect it with alcohol. He and his brother-in-law then skinned the fox and buried the body. About a week later, the herdsman’s wounds appeared to heal, but he experienced numbness and itching. The patient was not vaccinated against rabies and did not receive an injection of any specific anti-rabies immunoglobulin. On April 25, the patient began to experience back pain, which increased in severity from April 26 onward. On April 28, he visited the village clinic because of abdominal pain and fever. During his hospitalization, he developed a fear of water, sound sensitivity, and irritability. On April 29, he was transferred to the Kunas County Hospital, where he vomited blood and his temperature was recorded as 38.5 °C. On April 30, the patient was transferred to a state hospital because of difficulty breathing, and he received a tracheotomy the next day. The patient died at 19:00 on May 7, 2016. On the same day, we found two fox heads that could be used for virus detection, one from the fox that had bitten the patient and another from a natural death nearby.

The two fox heads were sent to the laboratory for testing. One of the heads was recovered as a skull; this sample was considered to belong to a fox that had died of natural causes. The head of the fox presumed to have bitten the patient was crushed at the top of the skull and filled with maggots. After cleansing and treating the sample, no brain tissues were obtained, likely because these had been consumed by the maggots. As such, we were unable to obtain samples from the fox heads for testing. We were also unable to obtain any of the patient’s brain

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tissue, cerebrospinal fluid, and neck skin because of the family's religious beliefs. Thirteen samples obtained from the patient, including saliva and arterial blood, were tested by RT-PCR; the details of this process are described below. All tests were done by the Institute of Viral Diseases of the China Center for Disease Control and Prevention.

We used Trizol LS to extract total RNA from the specimen and obtained cDNA by RT-PCR. The complete sequence of the *N* gene was amplified with two pairs of primers: (Table 1) N127 and N8m primers were used for the first half segment with the locations of the primer sequences with respect to the full genome sequence of Pasteur virus (PV) strain (M13215); N577 and N829 primers for the latter half. During nested PCR amplification, the final amplification product was 256 bp long (Figure 1). After completion of the reaction, agarose gel electrophoresis was performed on the secondary PCR products. Two blood samples acquired from the patient before dying tested positive for specific nucleic acids found in the rabies virus; thus, the patient was confirmed as a rabies case by laboratory diagnosis. Because of the effects of long-distance transportation and suboptimal cold storage, the virus was heavily decayed and fragments of the *N* gene could not be obtained. As such, we were unable to build an evolutionary tree to understand the source of the virus.

To determine other cases of rabies in the area, we searched the records of four local hospitals (i.e., Nilka County Hospital, Kunas County Hospital, Xinhua Hospital, and Yili Friendship Hospital) from 2005 to the present. We focused on diagnoses of rabies and 15 other encephalitis-like diseases according to the hospital ICD-10 code and then filtered death cases within 10 days. We found a total of 642 encephalitis-like cases, 12 of which died. We were unable to gain access to the medical records of 2 of these 12 cases because they involved lawsuits; the remaining 9 cases were confirmed cases of other diseases without animal exposure and the last case was suspected of rabies. The suspected rabies case showed an obvious history of dog exposure without typical rabies manifestations and pathogen testing.

Rabies is a viral disease that causes acute inflammation of the brain in humans and other mammals; it is 100% fatal[1]. Rabies can occur at any time of the year in China but occurs most often in the summer and autumn (29.48% and 32.88%, respectively, of all cases recorded)[2]. Most rabies victims (61.60%) in the area are farmers. Students (18.37%) and children living in marginal areas (9.1%) are also at high risk of rabies infection[2]. These infection rates are reasonable because farmers and students tend to be widely exposed to dogs and wild animals. Contracting rabies during dog rabies epizootics is highly likely.

Table 1. Primers of the PCR Reaction

Primers	Sequence (5'-3')	Location
N127	ATGTAACACCTCTACAATGG	55-74
N8 m	CAGTCTCYTCNGCCATCT	1,570-1,587
N577	AAGATGTGYGCYAAYTGGAG	644-663
N829	GCCCTGGTTCGAACATTCT	881-899

Note. The location of primers was based on the Pasteur virus strain M13215.

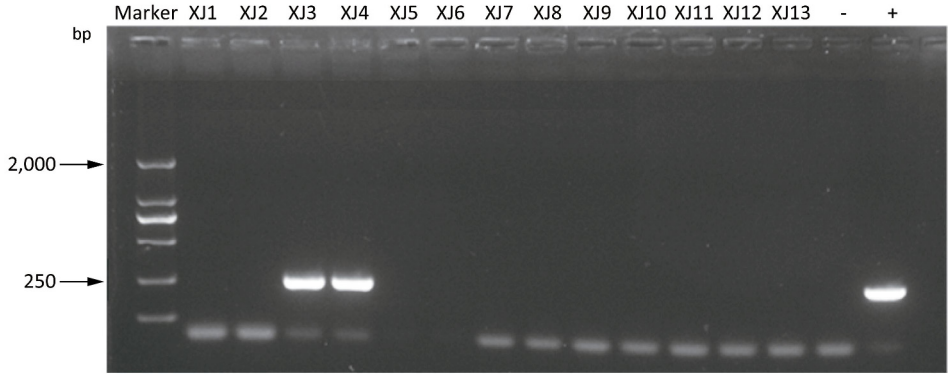

Figure 1. Electrophoresis of nested PCR. -, negative control; +, positive control.