zoonotic diseases

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Case Report

Rabies Exposure from Infected Horse Bite in an Urban Setting: A Case Study from Mongolia

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Simple Summary: In Mongolia, where nomadic pastoralism is still commonly practiced, a majority of reported human rabies exposure is attributed to dogs, with this case study highlighting an atypical exposure via horse bite occurring in an urban setting. The infected horse had been attacked by stray dogs prior to biting a 6 year old, which likely was the source of the rabies infection. This report highlights a successful response by the National Center for Zoonotic Diseases in conducting a thorough rabies investigation following a suspected exposure event and PEP initiation. Also discussed are common challenges in managing rabies in Mongolia, including limited access to vaccinations for domestic animals and wildlife due to financial constraints. Prompt and indiscriminate PEP initiation in rabies-endemic regions will need to be readily available across Mongolia, not just within proximity to Ulaanbaatar. Furthermore, integrated rabies management in Mongolia will need to be paired with community outreach and require coordination between veterinarians, health professionals, and policymakers to ensure proper access to care following exposure events from atypical sources such as livestock and horses.

Abstract: Rabies is a highly fatal zoonotic disease that causes an estimated 60,000 human deaths each year, many of which occur in Africa and Asia where the disease is likely underreported. Uncontrolled transmission of rabies presents a major threat to public health in countries such as Mongolia, where 26% of the population lives a pastoralist lifestyle characterized by increased interaction with livestock animals. Here, we report a case of rabies exposure in a six-year-old male after being bitten by a horse in both the head region and the leg. At the suspicion of rabies, post-exposure prophylaxis (PEP) was initiated, with the patient receiving four doses of PEP vaccine as well as a single treatment of rabies immunoglobulin. The horse was later confirmed to be rabies-positive through rapid antigen testing and RT-PCR. Human rabies exposure from horses is unusual within Mongolia, given that historically over 70% of human rabies cases within the country are attributed to dogs, wolves, or foxes. This case further emphasizes the need for more routine vaccination of domestic animals within Mongolia. Additionally, animal bites, even from animals not frequently associated with rabies, should be treated as possible rabies exposure events.

Keywords: rabies; animal bite; post-exposure prophylaxis

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1. Introduction

Rabies is a highly fatal zoonotic disease characterized by acute encephalomyelitis and caused by the neurotropic rabies lyssavirus [1,2]. An estimated 60,000 human deaths occur each year due to rabies, many of which occur in Africa and Asia where it is likely under-reported [2]. Transmission occurs primarily through bites by infected animals, with dogs representing the most common vector of rabies within Africa, Asia, and South America [3–5].

The uncontrolled transmission of zoonotic diseases with high case fatality rates represents a major public health threat in countries such as Mongolia, where livestock production is a major employment sector for the general population and around 26% of the population maintains a pastoralist lifestyle characterized by increased interactions with livestock [6,7]. Within Mongolia, over 70% of human rabies cases reported between 1970–2005 were attributed to dogs, wolves, or foxes [6]. These animals, in addition to the corsac fox, are considered the primary mammals responsible for maintaining rabies within Mongolia [6]. Both equine rabies and equine-sourced human rabies cases are uncommon, with only two reports of equine-sourced human rabies cases found in the literature [5,8]. Within Mongolia, over 600 cases of equine rabies were reported between 1970–2005, while 61 cases were reported between 2012–2018, averaging 10–20 cases per year [6,9]. Here, we report an unusual case study of a Mongolian child bitten by a horse that was later determined to be positive for rabies. This report highlights the need for healthcare providers to indiscriminately suspect rabies exposure in animal bite patients, even in instances in which the offending animal is not a typical rabies source for humans, in order to ensure the timely initiation of effective PEP.

2. Case Presentation

On the 28th of July 2018, a six-year-old male living in a "ger district" within Ulaanbaatar, Mongolia presented with a severe horse bite on the back of the head and on the left leg. The patient's wounds were initially washed according to World Health Organization (WHO) protocols for animal bites. At this point, the patient also began receiving PEP vaccine and immunoglobulin treatments for rabies, due to suspicion of the disease within the offending animal. PEP was initiated 48 h (about 2 days) after the bite occurred, with the patient receiving both the first dose of the rabies vaccine PEP series (Rabipur, serial number 2017/07224) as well as a single 5.3 mL treatment with rabies immunoglobulin (sourced from the Russian Anti-Plague Research Institute "Microbe", serial number 165, registration number PN002639/01). This immunoglobulin treatment consisted of the gamma globulin fraction of horse blood serum, which was obtained using the rivanol-alcohol method. The patient received the immunoglobulin treatment and first vaccine PEP dose on July 28th, the second dose August 3rd, the third dose August 10th, and the fourth dose August 29th. The bite victim is the only person who received PEP.

The horse that had bitten the patient had previously been attacked by stray dogs. Community members began to notice that the horse was behaving aggressively. After the horse bit the child, the owners contacted veterinary officials, who requested that the horse be tied to a post in isolation over the weekend until a veterinary official could visit that following Monday (Figure 1). The horse succumbed to disease that Sunday night and was sampled by veterinarian officials the following Monday morning. Besides the aggressive behavior, the owners did not report any additional symptoms to veterinary officials prior to the horse's death.

The horse was found to be positive for rabies at the State Central Veterinary Laboratory (SCVL) using the Antigen Rapid Rabies Ag Test Kit (BioNote). These results were confirmed through RT-PCR and sequencing that targeted the rabies virus N gene, as described previously [8]. Briefly, the P1 and 304 primers (see Boldbaatar et al., 2010) were first used to amplify the full-length N gene, with a PCR product size of ~1500 [10]. The primer walking technique was conducted using the P1 and B3, JW12 and B1c, and 113 and 304 primer pairs [8]. The final N gene sequence (1365 bp) was submitted to GenBank (GenBank Accession #OQ791973). The N gene sequence was aligned with reference sequences obtained from the BLAST program (http://www.ncbi.nlm.nih.go (accessed on 23 March 2023)) and using the MAFFT alignment protocol within Geneious Prime (Biomatters, Auckland, NZ, version 11.0.14.1+1). The gene alignments were used to produce a maximum likelihood tree within MEGA11 (MEGA, version 11.0.13) using the Tamura-Nei model and 1000 bootstrap iterations. Phylogenetic analysis demonstrated that the viral isolate obtained from the horse clustered with virus isolates that were obtained from both domestic animals and wildlife within Mongolia and neighboring regions of China (Figure 2).

Figure 1. Picture of offending horse after the bite event.

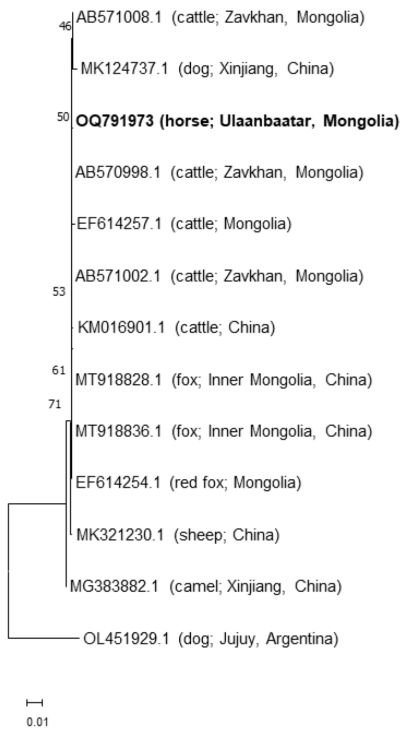

Figure 2. Maximum-likelihood phylogenetic tree showing rabies N gene sequence relatedness to other published sequences. The tree was generated using reference sequences obtained from the NCBI GenBank database through a BLAST analysis of obtained sequence. Sequences are labeled with accession numbers, animal source of viral isolate, and country of origin. The sequence obtained in this study is shown in bold.

Given that the offending horse was previously attacked by stray dogs living within the community, further surveillance was conducted in attempts to better characterize local rabies transmission within this dog population. The brains of over 300 local stray dogs were analyzed at The National Center for Zoonotic Diseases (NCZD) laboratories for evidence of rabies. No evidence of rabies infection was detected in the 300 specimens tested using the rapid antigen test.

3. Discussion

Cases of rabies in domestic animals such as horses often go undetected by owners until the initiation of symptoms, which is quickly followed by death within 3–5 days [10–14]. Reports have even demonstrated the occurrence of rabies in rabies-vaccinated horses [11]. Rabid horses are known to bite other animals and their handlers, and studies have demonstrated the presence of rabies virus in salivary glands from infected horses, which suggests that horses can be a source of rabies infections [8,13]. However, evidence of equine-sourced human rabies cases in the literature is limited, with only two reports of cases occurring in Ethiopia and Brazil [5,8]. Within Mongolia, while 74% of reported historical human cases are attributable to canids (dogs, wolves, foxes), the source for the remaining cases was not reported [6].

Our group recently assessed animal rabies cases reported by the General Authority for Veterinary Services and Center for Zoonotic Diseases within Mongolia, finding 61 rabies cases reported in horses across 13 aimags, with only 2 occurring within Ulaanbaatar between 2012 and 2018 [9]. In terms of carnivores testing positive within Ulaanbaatar, only three cases in dogs, one case in red foxes, and one case in wolves were reported within the same timeframe [9]. Despite the offending horse having been previously attacked by stray dogs, we were unable to detect rabies within any of the samples of the stray dog population. While this population may have excluded instances of rabies in stray dogs, these findings highlight the role dogs play in urban rabies transmission within Ulaanbaatar, necessitating further surveys and stray dog control efforts. The viral isolate described in this study was found to be closely related to isolates reported from China, suggesting transboundary viral exchange of rabies strains between Mongolia and neighboring provinces of China. Of note, a previous study characterizing the genetic epidemiology of rabies from Mongolia reported that these isolates clustered closely with viruses isolated from Russia [10]. These results may indicate that the disease ecology of rabies within Mongolia is complex, with virus exchange occurring between Mongolia and both China and Russia.

The patient in this case study was described as living in a ger district, which is a settlement of gers (traditional, portable tent-like structures) and brick-wood houses within the outskirts of Ulaanbaatar. These types of common living settlements represent over 50% of the city's population, where ger districts tend to be overcrowded and primarily inhabited by lower-income households, lacking basic infrastructure such as paved roads, which may complicate access to healthcare [15,16]. Of note, a previous study demonstrated that residents of ger districts utilized outpatient healthcare services less frequently than residents living outside of ger districts [17]. These qualities may predispose such residents to a disproportionate amount of morbidity and mortality from health challenges that require prompt healthcare, such as potential rabies exposures following animal bites.

The case patient was a 6-year-old boy who received bites in both the head region and on their leg. Between 1970–2005, 10 out of 34 human rabies cases reported within Mongolia occurred in children under the age of eight years, with over 80% of these children cases being male [6]. The epidemiological profile of the current case study suggests that the potential for rabies exposure was very high, given these known tendencies for rabies exposure. The location of the bite in the head region was of particular concern, as the duration of the incubation period to symptom appearance tends to be shorter for bites on the head [5]. Within Ethiopia, 43% of children under 10 years of age who died of rabies had reported bites on the head from the aggressor animal [5,18]. Previous studies have demonstrated that children experience equine injuries more frequently in the upper body region, particularly in the wrist/hand and head/neck, due to their shorter statures [5,18,19]. Given these circumstances, children may face an increased risk of rapidly progressing rabies disease when in the presence of rabid equine species.

According to WHO protocols, rabies PEP consists of wound washing, administration of the rabies vaccine and, in more severe exposure instances, administration of rabies immunoglobulin [20]. While PEP decreases the probability of rabies disease development to virtually 0%, various barriers are reported for obtaining rabies PEP [4,20]. These include the availability and cost of rabies vaccines and rabies immunoglobulin, both of which can interrupt prompt treatment initiation and thus impact the efficacy of rabies PEP [20]. Availability and access barriers are likely experienced by community members within the ger district of the current case study. Typically, the decision to begin PEP for rabies exposure is contingent on the availability of offending animals for laboratory examination or behavioral observation and on consideration of known rabies presence within the area [8]. Laboratory confirmation of rabies in horses is complicated however, as groups have previously shown reduced sensitivity for rabies confirmation tests in horse samples [21,22]. Bites from horses should raise concern in healthcare providers, as one study reported that bites only represented 3–4.5% of equine-related injuries, emphasizing the uncommon nature of horse bites [13].

Despite the limited knowledge concerning the transmission dynamics of rabies within Mongolia, there are still measures in place to mitigate the spread of rabies. Limitations concerning animal hunting periods and hunting quota are disregarded if the animals are being hunted to minimize infectious disease foci [6]. Prevention measures in the past have also included annual culling campaigns of the stray dog population [6]. Although there has been some progress towards the provision of vaccines within the country, it is difficult to implement a large-scale vaccination campaign for all livestock [6]. Additionally, rabies vaccine uptake within domestic animals has been low, as demonstrated by the reported vaccination rate of 17.8% in pet and guard dogs of Ulaanbaatar in 2007 [6]. The live veterinary vaccine, which is locally produced in Mongolia by a state-owned company, is comprised of ERA strain and piglet kidney primary cell culture. In response to positive diagnosis, all infected animals are euthanized, with remaining animals from the same herd or household vaccinated with the live vaccines, according to the manufacturer’s instructions. Pastoralists are never charged vaccination fees, since the government allocates funding for one million veterinary vaccine dosages. In regard to human rabies vaccines, there are set amounts of human rabies serum and equine rabies serum imported into Mongolia each year, with the PEP amounts typically ranging around 3500–5600 PEP.

Ongoing efforts are in place to improve community engagement and education, as demonstrated in Mongolia’s participation in World Rabies Day, which involves the ministry of health providing rabies-related training for both healthcare providers and veterinarians. As part of this, the veterinary sector began a vaccination campaign for dogs and conducted a culling of stray street dogs [23]. Education campaigns were also deployed in a multimedia format to improve community awareness of rabies and inform the general population about prevention strategies that are available [23]. At the World Rabies Day in 2013, the NCZD showcased the achievements of their dog population management strategy, which was approved by the government as another strategy to begin minimizing rabies transmission within the country [24]. Other agencies such as the Asia Pacific Strategy for Emerging Diseases (APSED) have made efforts towards minimizing rabies transmission through a proposed One Health approach towards tackling zoonoses in Mongolia, including rabies. APSED has been fundamental towards the development of strategic partnerships between national and regional sectors and international foundations, allowing for improvements to surveillance of zoonotic diseases, disease prevention strategies, and emergency preparedness [25]. An improved characterization of rabies transmission within Mongolia will serve to improve the mitigation strategies that are already in place within the country, while also allowing for the design of new, targeted preventative strategies.

4. Conclusions

This report highlights the need for healthcare workers within rabies-endemic countries to indiscriminately respond to animal bite cases as possible rabies exposure events, even in cases in which the offending animal is not a typical source of rabies. This is especially the case within countries such as Mongolia where routine vaccination of domestic animals and wildlife against rabies is lacking, often due to financial and infrastructure constraints. Prompt initiation of rabies PEP for animal bite victims regardless of the offending animal will avoid delaying treatment while diagnostic tests are being run, thus reducing the chances of the patient contracting the disease. The absence of data concerning the disease ecology of rabies within Mongolia emphasizes the need for enhanced surveillance systems for both reporting rabies cases and evaluating exposure sources in order to better characterize and manage risk factors associated with the incidence of rabies within both domestic animals and wildlife. This information can be used to inform the Mongolian government about the true burden of rabies within the country and help design effective mitigation policies that reduce the exposure risk for vulnerable communities such as rural pastoralists.

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