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Case Report

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Fatal cases in pediatric patients after post-exposure prophylaxis for rabies: A report of two cases

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ABSTRACT

Rationale: Rabies is a zoonotic disease with a high mortality, primarily transmitted through the bite of infected mammals, particularly dogs and cats. Despite being a well-known disease since ancient times, it continues to cause a significant number of human deaths worldwide, with approximately 65 000 fatalities reported annually.

Patient concerns: We present two fatal cases of rabies in a 12-year-old immigrant boy and a 7-year-old boy. The first case was subject to a 24-hour delay in receiving appropriate medical attention and rabies preventive measures due to the lack of awareness among emergency hospital staff, leading to the administration of wound dressing only. The second case received timely rabies immunoglobulin administration; however, there was a 4-day delay in administering the fourth dose of the rabies vaccine, despite presenting evident symptoms of rabies.

Diagnosis: Postmortem examination of brain samples from both patients confirmed the presence of rabies virus.

Interventions: Post-exposure prophylaxis for rabies.

Outcomes: Both patients were admitted to the hospital after the manifestation of rabies-related symptoms, with the 12-year-old child seeking medical care 47 days after the animal bite and the 7-year-old child seeking medical care 58 days after the exposure. Finally, the first patient died after 27 days and the second patient died after 40 days of hospitalization.

Lessons: There is an urgent need for heightened awareness and education among both healthcare professionals and the public regarding the urgency of seeking immediate medical attention after potential rabies exposure. Timely recognition and initiation of post-

exposure prophylaxis are pivotal in preventing the progression of the disease. Strengthening surveillance and reporting systems, coupled with continuous training for healthcare professionals, can contribute to early detection and management of rabies cases.

KEYWORDS: Rabies; Encephalitis; Pediatric patients; Rabies prophylaxis; Public health awareness.

1. Introduction

Rabies, caused by the rabies virus, a member of the *Lyssavirus* genus within the Rhabdoviridae family, manifests as a nearly universally fatal encephalitis in infected individuals. Without adequate pre-exposure or post-exposure prophylaxis, clinical rabies invariably ensues, entailing a swift, lethal course that typically culminates in death within 5-7 days from the onset of symptoms,

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unless specialized supportive care is promptly administered[1]. However, even with the provision of supportive treatment in intensive care settings, survival rate beyond three weeks remains low[1].

Rabies, an acute viral encephalitis transmitted between animals and humans, continues to pose a public health challenge in Iran, particularly in the southeastern region. This zoonotic infection is notorious for its almost universal fatality, both in humans and other mammals[2]. Recent reports of survival from rabies, although rare, may indicate an enhanced awareness of the disease and greater access to specialized care centers in endemic regions[3]. However, after COVID-19 pandemic, disrupted healthcare systems may potentially lead to delays and disruptions in the management of various diseases including rabies[1,4]. As a result, the pressing need for preventive strategies to alleviate the burden of this dread-inducing disease in endemic areas cannot be overstated[4].

In this report, we presented two fatal cases of children with rabies in Iran to stress the pressing need for preventive strategies to alleviate the burden of this disease.

2. Cases presentation

Case 1: A 12-year-old boy was unexpectedly attacked by a roaming dog in their neighborhood. In the act of protection, the boy sustained an injury and experienced bleeding between his right-hand fingers. However, it should be noted that the incident occurred on a Friday, which is a public holiday in Iran. At the hospital, the wound was solely disinfected using Povidone-iodine and then covered with a bandage. The nurse instructed them to visit the health center the next day. They were unaware that the anti-rabies treatment facilities operate 24/7 nationwide, and they should have been referred to the facility on the same day. Additionally, it was crucial to clean the wound promptly with soap and water and they should have also been advised against re-dressing the wound.

On the second day following the incident, they visited the anti-rabies treatment center to receive post-exposure prophylaxis services. The affected areas were meticulously cleaned, and the boy received rabies immunoglobulin (CSL Behring 300 IU/2 mL, Marburg, Germany Serums and Vaccines Ltd. Ambernath) at a dose of 20 IU/kg, totaling approximately 100 IU. Additionally, a rabies vaccine (Verorab 0.5 mL) was administered intramuscularly in the deltoid region. The parents were not instructed against reapplying a dressing after the wound was reopened. Consequently, the parents inadvertently redressed the boy's wound at home, whereas suturing the wound or dressing the wound not be recommended. The boy received the second dose of the vaccine on day 3 and the third dose on day 7. Additionally, he received a fourth dose of the vaccine on the 14th day post-exposure.

Following the transfer to a hospital in the provincial center and

admission, the patient received an initial diagnosis of probable rabies and encephalopathy in the Pediatric Neurointensive Care Unit. The clinical manifestations and progression of symptoms were as follows: Before Admission, the patient experienced fever, headache, loss of appetite, pain, and swelling of lymph nodes under the armpit, along with a sore throat. On admission, similar symptoms persisted, including fever, headache, loss of appetite, pain, and swelling of lymph nodes under the armpit, along with a sore throat. Throughout the hospitalization period, the patient's condition evolved, manifesting confusion, unawareness of time and place, inability to speak, vomiting, and eventual progression to a state of coma. Despite rigorous medical intervention, the patient's condition deteriorated rapidly. Regrettably, after 27 days of hospitalization, the patient succumbed to the disease.

In terms of laboratory investigations and sample collection, on the first day of hospitalization for Patient 1, a series of medical diagnostic tests were administered, revealing generally normal brain function. Subsequently, on day 3, a saliva sample was obtained; however, the report yielded inconclusive results. Similarly, on day 5, a second saliva sample was collected, again producing inconclusive results. Regrettably, on day 32, a brain autopsy was conducted, ultimately confirming a positive diagnosis for rabies.

Case 2: The second case occurred four months following the first human rabies case in the same city of Iran. A 7-year-old child was attacked by a stray dog while he was playing in the neighborhood. The attack resulted in injuries to the right arm, left ear, and two head injuries. Swift action was taken, and within 30 minutes of washing the affected areas, rabies immunoglobulin (CSL Behring 300 IU/2 mL, Marburg, Germany Serums and Vaccines Ltd. Ambernath) at a dose of 20 IU/kg, totaling approximately 100 IU was administered. Additionally, a rabies vaccine (Verorab 0.5 mL) was administered intramuscularly in the deltoid region. It is noteworthy that the immunoglobulin injected into the patient was residual, having previously been used for other animal bite victims and stored in the refrigerator. If the product had previously come to room temperature and then returned to the refrigerator, it was probably not stable and not active for use for administration.

With inadequate human rabies immunoglobulin (HRIG) administration both by dose and storage of product and vaccine doses given in the gluteus, the patient experienced rabies symptoms on day 15. Both the passive and active immunization of the post-exposure prophylaxis (PEP) protocol failed due to improper protocol and administration of the HRIG and vaccine. Following subsequent injections and on the fifteenth day after the bite, the patient experienced symptoms such as headache. On the sixteenth day, they were referred to Hospital, where they received further treatment before being discharged. However, on the seventeenth day after the bite, the patient returned with distressing symptoms, including ear buzzing, burning sensations in the palms and soles of the feet, needle-like sensations, and a pervasive feeling of being

stung by bees all over the body. Hallucinations, fear, and convulsions further compounded their suffering. Despite the emergence of these alarming symptoms, the fourth dose of rabies vaccine was administered. As the patient's condition rapidly deteriorated, they were admitted to the Pediatric Intensive Care Unit of the Children's Hospital on the eighteenth day after the bite.

Eventually, on December 28, 2022 (the twentieth day after the bite), the child fell into a coma and was transferred to a private hospital in the central region of another province. During the hospitalization period, the child exhibited a range of symptoms, including insomnia, delusions, confusion, hallucinations, a decreased level of consciousness, and eventually progressed to a state of coma.

In terms of laboratory investigations and sample collection, on the first day of hospitalization, gastric lavage and sample collection were conducted, revealing normal brain function. On day 2, both saliva and blood serum samples were obtained; however, the results were inconclusive. Subsequently, on day 27, a second saliva sample was collected, once again yielding inconclusive results. On day 38, a neck biopsy and a third saliva sample were obtained; however, the results remained inconclusive. Tragically, on day 42, the patient passed away, and a postmortem examination confirmed a positive diagnosis for rabies.

3. Discussion

Rabies, a viral encephalitis transmitted between animals and humans, remains a significant public health concern, particularly in endemic regions such as southeastern Iran[1]. The two fatal cases presented in this report underscored the continuing threat posed by rabies in Iran and emphasized the urgent need for preventive measures to avert further fatalities from this disease. Despite advancements in medical knowledge and easier access to specialized care centers, survival from rabies remains an exceptional outcome. While rare reports of survival may indicate increased awareness and improved healthcare access[3], it is crucial to emphasize the importance of timely preventive strategies in endemic areas, particularly in the aftermath of the COVID-19 pandemic, which has disrupted healthcare systems and posed greater challenges to disease management[4].

Both cases highlighted the critical role of PEP in mitigating the progression of rabies[5]. In the first case, the 12-year-old boy, despite receiving inappropriate PEP services, developed symptoms indicative of rabies on the 14th day post-exposure. Such delays in seeking treatment and deviation from recommended protocols have been previously reported and are associated with increased morbidity and mortality. Research findings indicate that delays in seeking medical care after an animal bite have been linked to an extended incubation period for the rabies virus, allowing for viral propagation within the central nervous system[6]. These delays and

deviations contribute to a higher mortality, as they allow the virus to progress unchecked, resulting in a more severe clinical course and poorer treatment outcomes. Deviations from recommended protocols, such as inadequate wound care and failure to administer rabies immunoglobulin or vaccine, can compromise the effectiveness of PEP and increase the risk of symptomatic rabies. Addressing these challenges requires prioritizing public education and healthcare provider training to raise awareness about the importance of immediate medical attention after an animal bite and ensure adherence to PEP protocols.

Moreover, the lack of clear instructions regarding wound care resulted in inadvertent reapplication of dressings, potentially compromising the efficacy of PEP. It is crucial to emphasize the significance of proper wound management to prevent rabies progression. However, proper dosage and infiltration of HRIG, full vaccine course, and education on wound care and timely treatment are more critical factors to address. Training initiatives should stress refraining from dressing animal bite wounds to allow air exposure, thus limiting virus proliferation[5]. Patient education and continuous training of healthcare personnel in rabies control centers are crucial for reinforcing preventive measures, adherence to protocols, and staying updated on emerging researches, ultimately enhancing patient care and outcomes.

The second case highlights the complexities in managing rabies despite the prompt initiation of PEP. Despite receiving appropriate immunoglobulin and vaccine, the 7-year-old patient ultimately succumbed to the disease. This outcome aligns with previous studies noting variable treatment responses and limited effectiveness of supportive care in rabies cases[7]. The patient's distressing symptoms, including hallucinations, convulsions, and sensory abnormalities, exemplify the diverse clinical manifestations of rabies. Early laboratory confirmation is crucial for effective patient management and implementing infection control measures. Factors such as the administration of improperly stored immunoglobulin and the continuation of vaccine doses despite symptomatic disease require further investigation to comprehend their impact on the patient's condition and treatment outcomes[6].

These cases have significant implications not only for the patients themselves but also for their families, particularly in the context of immigrant populations. Socioeconomic status and a lack of knowledge about preventive measures, such as wound washing can increase vulnerability to animal bites[8]. Limited awareness of rabies centers, vaccine availability, and timely vaccination may further hinder proper care. Besides, tailored educational programs are crucial to enhance population at risk understanding of rabies prevention, treatment options, and available resources for seeking appropriate care[8]. The long-term consequences of rabies, including moderate to severe neurological sequelae and functional impairments, significantly impact patients' quality of life, necessitating ongoing rehabilitation and support. Addressing the challenges faced by at-

risk populations such as immigrants, improving access to healthcare services, and advancing antiviral drugs and innovative therapies are essential to alleviate the burden of rabies and enhance long-term outcomes for patients and their families.

In conclusion, the tragic outcomes of these two cases highlighted the continuing threat of rabies in endemic regions and emphasized the importance of preventive measures. Enhanced awareness among the general public and healthcare providers regarding prompt management of animal bites, adherence to standardized PEP protocols, and the pursuit of innovative therapeutic approaches are crucial for mitigating the burden of this devastating disease. Efforts must be intensified to educate communities, improve access to specialized care, and foster research collaborations to unravel the complexities of rabies pathogenesis and develop effective interventions. In both cases, the outcomes could have been different with proper education of the health-care workers and facilities. Inappropriate storage, dosing, and administration of HRIG and vaccines was observed in both cases.

Conflict of interest statement

The authors declare that there is no conflict of interest.

Ethics approval and consent to participate

The case report's Research Ethics Committee Certificate has been approved by the Ethics Committee of Iranshahr University of Medical Sciences (IR.IRSHUMS.REC.1402.015). Written informed consent was obtained from the family patients for the publication of this manuscript and any accompanying images.

Availability of data and materials

This published article includes all the data that was generated or analyzed during the study.

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Authors' contributions

Design and drafting of the study: HKH, MJ, FH, HB, and VR. Revision of the article: VR, MR and RB. All authors have read and approved the manuscript.

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