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Case Report

Suspected case of rabies in a patient immunized with anti-rabies vaccine

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ABSTRACT

Rabies remains a major public health threat, especially in developing countries like India, where stray dogs account for 99% of human cases. The disease is almost always fatal once symptoms appear, with death occurring within days. Despite highly effective pre- and post-exposure prophylaxis (PEP) with WHO-recommended vaccines, challenges like occasional vaccine failure persist. In India, rabies causes approximately 20,000 deaths annually. This case highlights a suspected rabies infection that developed despite receiving PEP, exploring potential reasons for the failure. This case emphasizes the necessity for a deeper understanding of factors that may lead to vaccine ineffectiveness. It also underscores the critical role of administering rabies immunoglobulin (RIG), proper wound care and following established guidelines.

Keywords: Post exposure prophylaxis failure, Rabies, Rabies vaccine

INTRODUCTION

Despite significant public health advancements, rabies remains a major threat, especially in developing countries, where stray dogs are the primary transmitters.[1] In India, rabies is endemic, causing around 20,000 human deaths annually, with dogs responsible for 99% of cases.[2] Rabies, a fatal viral encephalitis, is spread through the saliva of infected animals, and once clinical symptoms appear, death usually follows within 5.7 days in furious rabies and 11 days in paralytic rabies.[3]

Although rabies is almost always fatal after symptoms develop, it can be prevented with either pre-exposure or post-exposure prophylaxis (PEP). The WHO recommends the use of purified cell culture and embryonated egg-based rabies vaccines, which can be administered intramuscularly or intradermally.[4] Existing vaccine regimens for rabies PEP are close to 100% effective and WHO-prequalified vaccines are highly effective.[5]

While we have the knowledge and tools to control rabies, challenges remain, including occasional failures in PEP. Here we present a case of suspected rabies that developed disease despite having taken PEP. This case will also discuss plausible reasons for vaccine failure.

CASE REPORT

A 30-year-old woman presented at the hospital with worsening difficulty in breathing while at rest over the past day and reported having involuntary urination and defecation once. For the last 3 days, she also experienced fever, headache, difficulty swallowing, and problems in walking. Additionally, she had a tingling sensation at the site of the bite that progressed to loss of muscle tone over the past 10 days. Past history of the patient is positive for a dog bite 43 days back on her right arm (category III bite wound), for which she received sutures, one dose of tetanus toxoid vaccine, and four doses of cell culture rabies vaccine as PEP (intramuscular regimen) on days 0, 3, 10, and 24, with day 0 being the date of the bite.

She visited a local hospital where a cerebrospinal fluid (CSF) FilmArray meningitis/encephalitis panel was conducted and returned negative. A magnetic resonance

imaging (MRI) of her cervical spine indicated acute transverse myelitis, and she was treated with six doses of 1 g Methylprednisolone and discharged home. After 4 days she came to our hospital as there was no improvement in symptoms.

Upon admission at our hospital, her vital signs were as follows: temperature—normal, pulse—112 beats per minute, blood pressure—112/70 mmHg, SpO_2—90% on room air, and respiratory rate—26 breaths per minute. On CNS examination, she was conscious, oriented, and responsive to verbal commands. Due to respiratory distress, urgent intubation was performed.

An MRI of the brain, cervical spine, and dorsal spine with contrast revealed several findings: there was abnormal hyper-intensity in the anterior part of the right lentiform nucleus, the head of the right caudate nucleus, and the anterior limb of the right internal capsule. Additionally, from the cervicomedullary junction to the C7 vertebral level, a long segment of intra-medullary hyper-intensity was noted, suggesting probable transverse myelitis. The results indicated a potential diagnosis of acute disseminated encephalomyelitis, a demyelinating condition.

Table 1 shows the patient's blood investigation results (with normal range) during her hospital stay.[6] CSF analysis revealed a glucose level of 100 mg/dl (normal range: 40-70) and a protein level of 88.3 mg/dl (normal range: 8-32). A sufficient amount of rabies antibodies was detected in the CSF sample. Cultures and sensitivity tests from the endotracheal tube, blood, CSF, and urine samples showed no growth. Tests for autoimmune disorders, including serum myelin oligodendrocyte glycoprotein (MOG), neuromyelitis optica antibody (NMO), antinuclear antibody (ANA), and CSF oligoclonal immunoglobulin G bands (OCBs), all returned negative results. With all other causes of encephalitis excluded, rabies was suspected as the likely diagnosis.

During the patient's hospital stay, supportive treatment was administered, including broad-spectrum antibiotics (inj. Meropenem and inj. Clindamycin), anticonvulsants (syrup Levetiracetam), antipyretics, proton-pump inhibitors, anticoagulation (inj. LMWH), and nebulized bronchodilators (Ipratropium bromide).

Table 1: Blood investigations during course of hospitalization.

Day of admission	0	3	7	10	16	Normal range
Hb (g/dl)	11.2	10	8.5	8.3	10.2	12-15
WBC (10^3/ul)	20.7	18.21	11.36	6.69	3.54	4-10
Platelet count (10^3/ul)	207	204	150	241	306	150-410
Urea (mg/dl)	46.5	29.5	23.5	27.3	20.7	19.3-49.2
Creatinine (mg/dl)	0.74	0.51	0.5	0.4	0.3	0.5-1.1

Hb – Hemoglobin, WBC – white blood count

Initially clinician suspected it to be side effect of rabies vaccine that caused neurological symptoms. On follow up, probable diagnosis was shifted to paralytic rabies. The patient did not show any response to the treatment and passed away.

DISCUSSION

The incubation period for rabies typically ranges from 20 to 90 days, though in rare cases, it can be as short as a few days or extend beyond a year. Initial symptoms of rabies are often nonspecific and include fever, malaise, headache, nausea, and vomiting. Rabies presents in two forms: encephalitic (furious) in 80% of cases and paralytic in 20%. Rabies encephalitis is distinguished by early involvement of the brainstem, leading to characteristic symptoms such as hydrophobia and aerophobia.[7] The patient in this case did not exhibit the typical symptoms of rabies and had already received four doses of the rabies vaccine. Additionally, a sufficient level of rabies antibodies was detected in the CSF sample. As a result, rabies was not the presenting diagnosis.

The patient's CSF tested negative for all common CNS pathogens. MRI revealed transverse myelitis (TM). A systematic review identified 37 cases of TM associated with vaccines, including those for hepatitis B, measles–mumps–rubella, and diphtheria–tetanus–pertussis with most occurring within a month of vaccination. Four cases were associated with rabies vaccination.[8] Thus, at first, the patient was thought to have vaccine-induced TM. As the disease progressed, the signs and symptoms began to resemble those of rabies, leading to a shift in the diagnosis to rabies.

Rabies-related deaths are often due to poor adherence to PEP, despite its availability. Compliance with PEP varies based on factors like location (rural versus urban), administration method, and vaccination schedule. Adherence to rabies immunoglobulin (RIG) is even lower, with many patients not receiving it due to unavailability or reluctance. Proper administration of RIG—by infiltrating it around all bite sites—can also be difficult, particularly in children or patients with multiple wounds.[4] Despite recommendations, the patient chose not to receive RIG for her category III bite wound.

Adherence to PEP vaccination and immunoglobulin in India is notably low, with only 20.9% for vaccination and 1.3% for immunoglobulin, mainly due to high cost and

limited availability of RIG.[2] The price of PEP for a category III bite in India for a patient weighing 60 kg, includes 5 doses of the anti-rabies vaccine, costing Rs. 1,750. Additionally, 4 vials of human RIG (20 IU/kg) costing Rs. 21,144, which are expensive for the general population of India, which might be an additional reason for our patient's refusal to take RIG.[9]

However, recent data from Cambodia and Tanzania suggest that when category III bite victims receive prompt wound washing and immediate rabies vaccination, 99% survive, even without RIG.[4] But this was not applicable in our case.

Bite wounds should not be stitched, except in cases involving major arteries as stitching can increase the spread of the rabies virus. The virus is sensitive to light, oxygen, and disinfectants like soap, iodine, or alcohol, making proper wound care crucial. Animal studies show that early and effective wound cleaning with soap, water, or antiseptics can reduce the risk of rabies.[10] For our patient, suturing of the wound was done on the same day.

Reported failures of PEP are typically not due to vaccine ineffectiveness but rather due to lapses in following WHO-recommended guidelines such as omitting or incorrectly administering RIG, inadequate wound care, insufficient vaccine doses, or improper vaccination sites. True PEP failure is more likely in cases where the bite occurs in highly sensitive areas, such as the face, neck, hands, or fingers, or when multiple bites are involved. The virus's direct entry into nerves shortens the incubation period, reducing the effectiveness of both active and passive immunization.[4]

The Essen regimen (1-1-1-1-1) is a five-dose intramuscular vaccination schedule for PEP, with doses given on days 0, 3, 7, 14, and 28, starting on day 0. The deltoid region is the preferred site for injection, while the gluteal region is not recommended due to slower antigen absorption. For infants and young children, the antero-lateral thigh is used.[7] Only four doses were given to our patient, and they were not given in accordance with the national guidelines schedule, the third and fourth doses were delayed, and the vaccine was given in the thigh, which may have reduced the immune response.

CONCLUSION

Rabies vaccine failure despite adequate PEP is a rare but critical concern. This case highlights the importance of RIG administration, adequate wound treatment, and adherence to established guidelines. Further research is necessary to understand factors contributing to vaccine failure and improve rabies prevention strategies.

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