Section: CCM

Case Series

BATTLING THE BITE: RABIES ENCEPHALITIS CASE SERIES

Anushapreethi S[1], Biswajit Nayak[2], Adya Kinkar Panda[3], Shakti Bedanta Mishra[4], Samir Samal[5]

[1]Senior Resident, Department of CCM, IMS & SUM Hospital, Bhubaneswar, Odisha, India.
[2]Associate Professor, Department of CCM, IMS & SUM Hospital, Bhubaneswar, Odisha, India.
[3]Professor, Department of Radiology, IMS & SUM Hospital, Bhubaneswar, Odisha, India.
[4]Professor & HOD, Department of CCM, IMS & SUM Hospital, Bhubaneswar, Odisha, India.
[5]Associate Professor, Department of Critical Care Medicine (CCM), IMS & SUM Hospital, Bhubaneswar, Odisha, India.

Received *: 29/03/2024*
Received in revised form *: 26/05/2024*
Accepted *: 13/06/2024*

Corresponding Author:
Dr. Samir Samal
Associate Professor, Department of Critical Care Medicine (CCM) , IMS & SUM Hospital, Bhubaneswar, Odisha, India.
Email: samirsamal@soa.ac.in

DOI: 10.5530/ijmedph.2024.2.123

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2024; 14 (2); 647-651

ABSTRACT

The zoonotic illness known as rabies is one of the oldest and deadliest diseases that has ever been discovered in the history. It is estimated that over 20,000 people in India pass away each year as a result of rabies infections brought on by Lyssavirus viruses. This accounts for roughly a third of the 61,000 fatalities that are attributed to rabies globally. Infection with rabies is a difficult clinical challenge that is defined by fast neurological degeneration and results in death in every single case. Fortunately, it has been shown that the administration of anti-rabies immunoglobulin, post-exposure rabies vaccine, and wound care in a timely manner may considerably reduce the likelihood of contracting rabies. Despite the fact that the recorded occurrences of real prophylaxis failures are exceedingly few in comparison to the millions of post-exposure prophylaxis that are administered yearly all over the globe, we are documenting two such rare case reports that were encountered at our hospital and ultimately resulted in the death.

Keywords: Bite, Rabies, Encephalitis.

INTRODUCTION

Rabies is one of the oldest and deadliest zoonotic diseases known in the history of mankind.
Approximately 20,000 persons in India die from rabies infections caused by Lyssavirus
viruses annually, which makes up nearly a third of the 61,000 rabies-related deaths
worldwide.[1,2] Rabies continues to be a chronic public health problem, especially in areas where there is insufficient access to healthcare and veterinary services.[3,4] It is most often transmitted from one animal to another by the bite or scratch of an animal that is infected with rabies. Dogs are the principal reservoir and vector of transmission in many regions of the globe. Other animals, such as bats, jackals, raccoons, foxes, skunks, cats, and so on, are also capable of transmitting the disease.[4]
Once the virus has gained entry into the body, it demonstrates a preference for the central nervous system, which ultimately results in a progressive and inevitably deadly encephalitis in both people and animals. Following exposure, the incubation period might range anywhere from three to eight weeks. When a person is infected with rabies, the site of the bite is an extremely important factor in the course of the illness. This is because the distance between the bite and the central nervous system (CNS) is a significant factor in determining how quickly the virus has the ability to reach the brain.[3] As a result, bites that are closer to the head or neck have a shorter incubation time and a more rapid start of symptoms, in contrast to bites that are on the extremities or distal areas of the body.
Rabies continues to take the lives of tens of thousands of people every year, mostly in low- and middle-income countries where resources for prevention and control are inadequate. This is the case despite the fact that there are very effective vaccinations and post-exposure prophylaxis available. We present two very rare instances in which post-exposure prophylaxis against rabies was unsuccessful and the patient ultimately died to rabies encephalitis. This highlights the critical need for

ongoing efforts to eradicate this potentially fatal threat and lessen the weight of suffering experienced by both humans and animals all over the globe.

CASE 1: A 27 years old male came to our emergency department with complains of fever, vomiting, altered sensorium and hydrophobia for two days. Relatives reported patient had a stray dog bite 16 days back and had received human rabies immunoglobulin (Rabishield) and 3 doses of ARV (Zoonovac-V, Essen regimen). On examination the patient had Glasgow Coma Scale (GCS) score of E1V1M2 with bite mark at the inner canthus of right eye. Patient was put on mechanical ventilation and started on intravenous paracetamol, ceftriaxone, acyclovir, midazolam and levetiracetam. Routine laboratory investigations yielded normal results for haemoglobin and total blood count, as well as blood chemistry tests for blood glucose, blood urea nitrogen, creatinine, electrolytes, and liver function with sterile blood culture. MRI brain revealed hyperintensity in upper cervical cord substance, medulla, inferior pons, in bilateral globus pallidus, caudate head, bilateral thalami and right anterior frontal subcortical white matter. The typical history along with clinical presentation was used to make the diagnosis of rabies encephalitis. Because of limited technical facilities, a laboratory confirmation of rabies could not be performed. Within the next eight days, the patient's condition further deteriorated and he succumbed to death. Following are the images of the MRI scan of the patient. (Fig no.1,2,3 and 4)

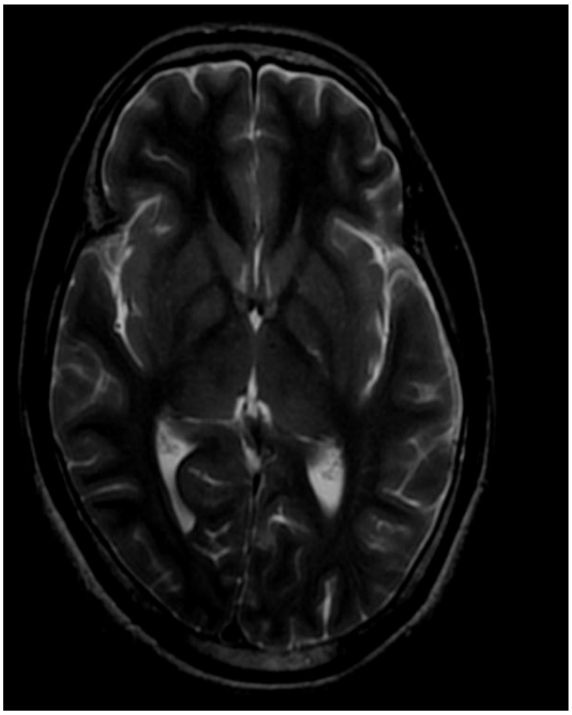

Figure 1: MRI scan case 1 (Bilateral symmetrical hyperintensity in Globus pallidus)

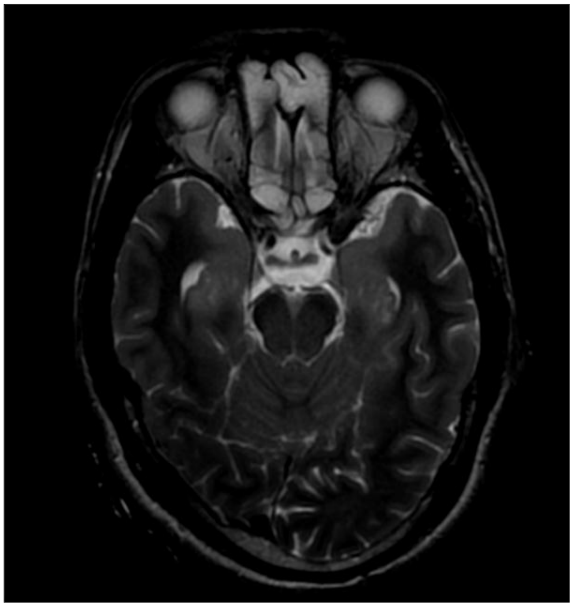

Figure 2: MRI scan case 1 (Bilateral medial temporal lobes and uncus hyperintensity)

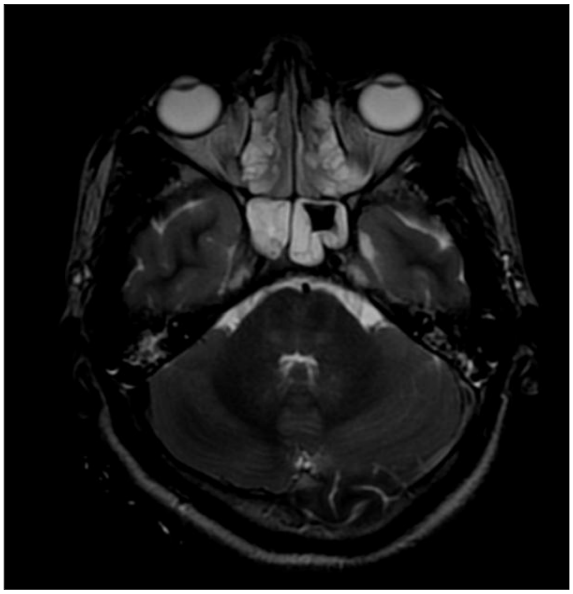

Figure 3: MRI scan case 1(Bilateral abnormal signal in inferior pons)

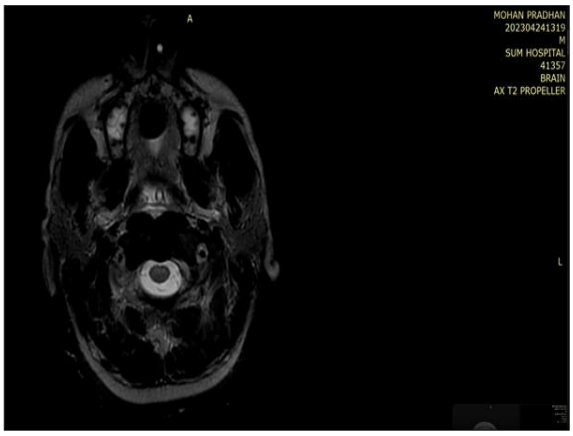

Figure 4: MRI scan case 1 (Abnormal signal in anterior part of cervical cord)

CASE 2: A 45year old male with alleged history of category 3 stray dog bite on left arm 20 days back, received human rabies immunoglobulin (Rabishield) and vaccination for Rabies (4 doses, Zoonovac-V ,Essen regimen), presented to our emergency with pain and burning sensation in the affected hand for last 5 days; fever with chills, slurred speech, tremors of limbs, inability to drink water and fear of water for 2days; 5-6 episodes of vomiting and 2 episodes of generalized tonic convulsions for one day. At arrival patient was having a GCS score of 5 with decreased tone in all limbs, no cranial nerve palsy or meningeal signs. The patient was admitted, put on mechanical ventilation and managed conservatively with intravenous ceftriaxone, acyclovir, paracetamol, midazolam, and levetiracetam. Routine blood investigations were normal, with no growth on blood culture. NCCT brain and EEG were normal. MRI brain revealed bilateral symmetrical abnormal hyperintense signal involving dorsal medulla, inferior cerebellar peduncle, dorsal pons, superior cerebellar peduncle, midbrain tegmentum, and tectal plate including peri-acqueductal grey matter suggestive of brainstem encephalitis. In this patient, laboratory confirmation of rabies was not possible due to inadequate technical facilities. The patient's neurological condition kept becoming worse. Ultimately, on the seventh day of the hospital stay, the patient passed away.

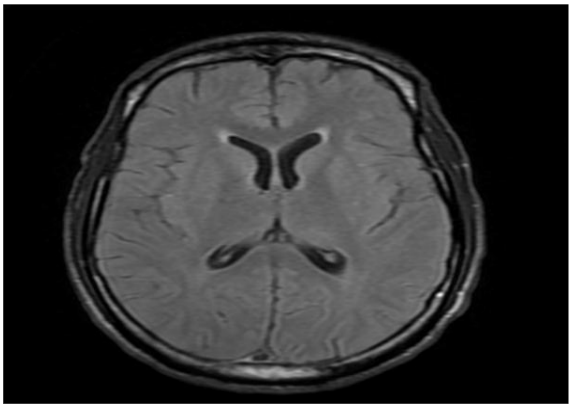

Figure 1: MRI scan case 2

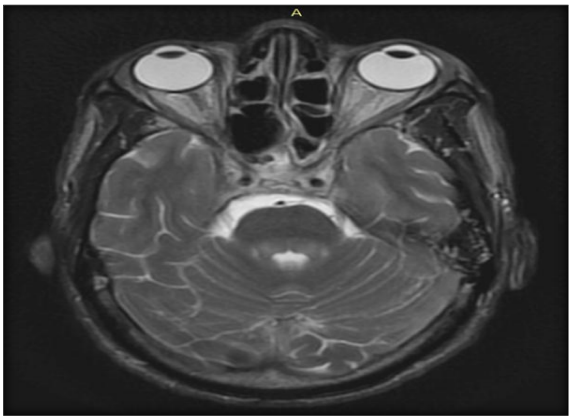

Figure 2: MRI scan case 2

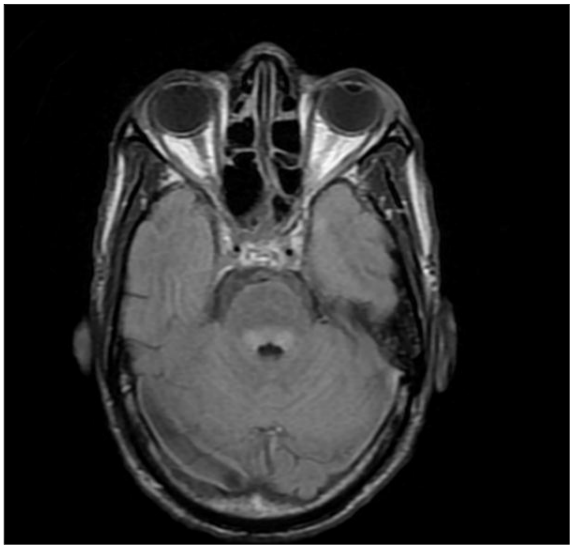

Figure 3: MRI scan case 2

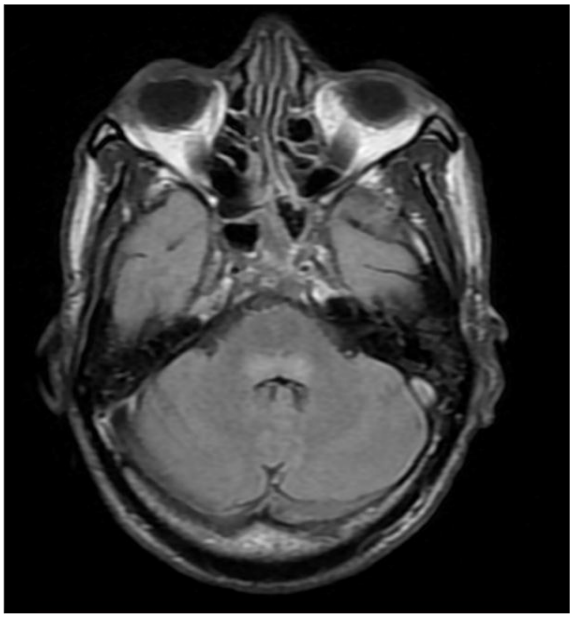

Figure 4: MRI scan case 2

DISCUSSION

Rabies, which is considered to be one of the most lethal infectious illnesses, has a case-fatality rate of one hundred percent after symptoms are discovered.[5] To the best of our knowledge, there have been around fourteen survivors of rabies who have been sufficiently recorded throughout the globe,[6] with five of them coming from India.

Rabies encephalitis is a severe and invariably fatal manifestation of rabies virus infection. It typically manifests with a constellation of neurological symptoms, which may include agitation, confusion, hallucinations, hydrophobia (fear of water), aerophobia (fear of drafts of air), paralysis, and coma.[7] Rabies encephalitis is a manifestation of rabies virus infection. The precise time period depends on the kind of rabies virus, the viral load, the location of the exposure site (the distance from

the brain), and any previous immunity that the individual may have had. These symptoms often manifest themselves anywhere from a few days to a few weeks after the rabies virus has been introduced. Rabies virus is capable of localised multiplication at the point of entrance (bite), which is generally in the muscular tissue of the host. From that point on, it makes its way to the central nervous system by way of the neurons in the periphery. The virus swiftly multiplies once it has entered the brain, and when it targets neurons, it causes inflammation and destruction of those neurons.[8]

The diagnosis of rabies encephalitis may be challenging, particularly in regions where diagnostic tools are readily available in limited quantities. It is necessary to have clinical suspicion based on the presence of neurological symptoms in the context of a history of exposure to a possibly rabid animal in order to initiate the appropriate diagnostic tests. When the illness is in its early stages, there is often no abnormality in the CT or MRI brain results that can be recorded. However, as the condition advances, an elevated T2/FLAIR signal intensity may be shown on magnetic resonance imaging (MRI) in the grey matter of the brain parenchyma, as well as in the brain stem, limbic system, frontal and parietal lobes, thalami, and hypothalami. This may indicate that there is an infection in the central nervous system.[9] Laboratory confirmation of rabies encephalitis often entails examining samples such as saliva, cerebrospinal fluid, or brain tissue for the presence of viral antigens or genetic material using methods such as polymerase chain reaction (PCR) or immunofluorescence tests.[10] These methods are used to determine whether or not the materials contain any genetic material produced by the virus.

As soon as clinical signs of rabies encephalitis arise, there are very few therapeutic options available, and the disease almost often results in death. Because there is no specific antiviral drug available for rabies, supportive therapy is often carried out in order to alleviate symptoms and maintain the patient's comfort. For the purpose of treating seizures, anticonvulsants may be administered, sedative may be administered to calm agitation, and care may be taken to prevent adverse effects such as respiratory failure.

The provision of postexposure prophylaxis (PEP), which normally consists of wound cleansing, rabies vaccination, and, in some instances, the injection of rabies immune globulin (RIG), is an essential component in the process of avoiding the start of rabies in those who have been possibly exposed to the virus.[11] In spite of the fact that PEP is successful in preventing rabies when it is delivered in a timely and suitable manner, there are situations in which it is not effective.[12] Despite receiving the appropriate vaccine, there are a number of hypotheses that have been proposed to explain the death rate in instances of rabies encephalitis. The delay in obtaining medical attention after a possible exposure to rabies is a critical factor that may considerably diminish the efficacy of the preventative and therapeutic intervention (PEP). It is essential to provide PEP as soon as possible after exposure in order to prevent the virus from establishing a foothold and developing into a clinical illness. Failure to comply to the approved protocol for the PEP, such as skipping doses of the vaccine or not finishing the whole course of therapy, might jeopardise the efficiency of the programme. In a similar vein, incorrect wound cleansing or the injection of RIG may decrease the effectiveness of PEP and raise the likelihood of suffering from rabies infection. When severe bites are delivered to highly innervated locations, such as the head, face, or neck, as well as mucosal membranes, there is a higher probability of rabies transmission to the central nervous system, which may result in rabies encephalitis. This is the case even when proper preventative measures are taken. It was mentioned in the two case reports that were quoted above that both of the patients got PEP on time; nevertheless, they were unable to complete the vaccine doses because they began exhibiting symptoms too quickly. The fact that the bite in the first instance was periocular and involved the conjunctiva may have been the cause of a shorter incubation period and a more rapid involvement of the central nervous system, which ultimately resulted in rabies encephalitis developing. Additionally, in both instances, the bites were transmitted by stray dogs that had not been vaccinated against rabies.

CONCLUSION

In spite of the availability of effective pre- and post-exposure prophylaxis with rabies vaccination, mortality in cases of rabies encephalitis remains high due to delayed presentation, inadequate immune response, the neurotropic nature of the virus, lack of specific treatment, and challenges in diagnosis. Continued efforts for mass vaccination campaigns targeting both human and animal populations, educating healthcare providers and the public about the importance of timely PEP, adherence to recommended protocols and access to medical care are essential for minimizing the risk of rabies transmission and preventing PEP failures thereby reducing the burden of rabies-related mortality and morbidity globally.

REFERENCES

1. World Health Organization, 2013. WHO Expert Consultation on Rabies: Second Report. World Health Organization Technical Report Series 982. Geneva, Switzerland: WHO.
2. Sudarshan MK, Madhusudana SN, Mahendra BJ, Rao NS, Ashwath Narayana DH, Abdul Rahman S, et al 2007. Assessing the burden of human rabies in India: results of a national multi-center epidemiological survey. Int J Infect Dis 11: 29–35
3. WHO. Rabies. https://www.who.int/news-room/fact-sheets/detail/rabies. Accessed 7 Aug 2020.
4. CDC. Rabies. https://www.cdc.gov/rabies/about.html. Accessed 7 Aug 2020

5. Mani RS, Willoughby RE, 2017. Human rabies in south Asia. Singh SK, ed. Neglected Tropical Diseases–South Asia. Neglected Tropical Diseases. Cham, Switzerland: Springer, 349–371.
6. Fooks AR et al., 2017. Rabies. Nat Rev Dis Primers 3: 17091.
7. Jackson AC. Update on rabies. Curr Opin Neurol. 2002 Jun;15(3):327-31.
8. Hemachudha, T., Laothamatas, J., & Rupprecht, C. E. (2002). Human rabies: a disease of complex neuropathogenetic mechanisms and diagnostic challenges. The Lancet Neurology, 1(2), 101-109.
9. Rupprecht CE, Hanlon CA, Hemachudha T. Rabies re-examined. Lancet Infect Dis. 2002 Jun;2(6):327-43.
10. Mahadevan A, Suja MS, Mani RS, Shankar SK. Perspectives in Diagnosis and Treatment of Rabies Viral Encephalitis: Insights from Pathogenesis. Neurotherapeutics. 2016 Jul;13(3):477-92.
11. Shantavasinkul P, Wilde H. Postexposure prophylaxis for rabies in resource-limited/poor countries. Adv Virus Res. 2011; 79:291-307.
12. Wilde H. Failures of post-exposure rabies prophylaxis. Vaccine. 2007 Nov 1;25(44):7605-9.