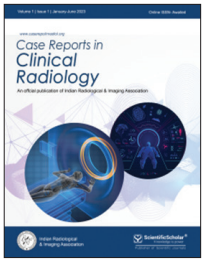
ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.caserepclinradiol.org

Case Reports in Clinical Radiology



Case Series

The catastrophe of rabies encephalitis: A case series

Satya Jha[1], Taruna Yadav[1], Amit Kumar Rohila[2], Sanjiv Kumar Sharma[3], Sarbesh Tiwari[1]

Departments of [1]Diagnostic and Interventional Radiology, [2]General Medicine, [3]Neurology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India.

***Corresponding author:**
Sarbesh Tiwari,
Department of Diagnostic and Interventional Radiology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India.

sarbesh1984@gmail.com

Received: 06 January 2023
Accepted: 21 June 2023
EPub Ahead of Print: 20 July 2023
Published: 26 July 2023

DOI
10.25259/CRCR_1_2023

Quick Response Code:

ABSTRACT

Rabies is one of humankind's oldest and most fatal zoonotic diseases. Few cases of survival post rabies infection have been documented so far. Due to its rapid course of progression, patients succumb before acquiring magnetic resonance imaging (MRI). However, in cases where MRI is feasible, the latter is a valuable source of information that aids in antemortem confirmation of diagnosis when backed by clinical data. We present two cases of rabies encephalitis, with classic imaging features on MRI. Symmetrical involvement of the basal ganglia, mesial temporal lobes, and dorsal portion of the brainstem should raise a suspicion of rabies encephalitis in the proper clinical situation.

Keywords: Encephalitis, Gray matter, Symmetrical, Negri bodies

INTRODUCTION

Rabies is a neurotropic viral illness that follows infection by a family of rhabdovirus. Human rabies, though rare in developed nation, continues to be a major problem in developing nations like ours. It is transmitted from an animal bite, usually following a dog bite, and travels to the central nervous system (CNS) trans-synaptically. Human rabies presents in encephalitis or paralytic form and is nearly always fatal. The literature on neuroimaging features in human rabies infection is scarce, due to its fulminant course. We present imaging features of two cases of rabies encephalitis who presented with an encephalitic form of rabies.

CASE 1

A 22-year-old female with a history of dog bite over the dorsal aspect of the right wrist 7 days back was brought to the emergency department with disorientation, altered sensorium, and irrelevant talks since the morning of that day. She had fever for the past 4 days and had difficulty swallowing water and breathing on the day of admission. On examination, Glasgow Coma Scale (GCS) was E3V2M5 on the day of admission, that is, a total score of 10, meaning she had a lack of spontaneous eye opening; however, eye-opening in response to the speech was present, the verbal response was found to be incomprehensible, inability to exhibit movements in response to a command was found; however, she was able to respond to focal painful stimulus and localize its site. The family provided an account of her receiving three doses of post-exposure prophylaxis injections after the bite, the details of which were not available, as family members did not have any medical documents or records for the same. A computed tomography (CT scan) of the head performed on the day of admission was normal. A cerebrospinal fluid (CSF) obtained from a lumbar puncture demonstrated significantly elevated proteins (506 mg/dL). CSF glucose was

within normal limits. Blood examination revealed elevated counts and inflammatory markers. No organism growth was found in the blood culture. Eventually, she developed progressive hydrophobia and photophobia.

Magnetic resonance imaging (MRI) of the brain [Figure 1] revealed symmetrical T2/fluid-attenuated inversion recovery (FLAIR) hyperintensities in bilateral basal ganglia, dorsal aspects of the midbrain, pons, medulla, and visualized cervical cord. Abnormal T2 hyperintensity was also noted in internal and external capsules, mimicking the lentiform fork sign. There was no noticeable post-contrast enhancement. Given the clinical history and physical examination findings, MRI features were consistent with rabies encephalitis. Biopsy samples obtained from the skin of the nape of the neck revealed perivascular lymphocytic inflammation. The patient was managed conservatively in the intensive care unit (ICU). Her condition rapidly deteriorated over the next 2 days with progressively increased oxygen requirement. She also developed acute kidney injury. There was a fulminant progression, and the patient succumbed to non-responsive metabolic acidosis.

CASE 2

A 15-year-old right-handed adolescent was brought to the emergency room with a history of altered sensorium for the past 3 days. He was intubated in the district hospital and shifted to our hospital. There was a history of a bite by a street dog with evidence of a level 4 bite over the right leg 15 days back. The patient's family provided a history of agitation and irritability, which started 8–9 days after the dog bite; however, they denied noticing hydrophobia-like symptoms. There was no antecedent history of fever, convulsion, or psychosis. The family was not able to trace the status of the dog. On examination, GCS was E2VtM5 (without sedation) and plantars were equivocal. Imaging revealed T2/FLAIR hyperintensity in the bilateral basal ganglia, posteromedial aspect of bilateral thalami dorsal aspect of the midbrain, pons, and medulla, cervical cord. The internal capsule, external capsule, corona radiata, and centrum semiovale also appeared hyperintense [Figure 2]. Clinical suspicion of rabies encephalitis was made and managed conservatively in the ICU isolation room. Family deferred lumbar puncture and nuchal skin biopsy. However, due to rapid clinical deterioration, the patient died after 4–5 days of admission. Family members denied brain autopsy.

DISCUSSION

The term "rabies" originates from the Latin word rabere, meaning rage, and is also derived from the Sanskrit word rabhas, meaning "the act of violence" to do violence.[1] Rabies, also known as hydrophobia or aquifuge, is a zoonotic disease caused by rabies virus, a type of ribonucleic acid virus of the rhabdovirus family.[2-4] Even though preventable by timely vaccination, it is nearly always fatal after the onset of symptoms. It spreads to humans through the infected saliva of wild and domestic animals, the most common culprit being non-vaccinated rabid dogs. Other unusual modes of infection are transmission through organ transplantation and aerosols.[5] Numerous deaths occur yearly due to rabies, predominantly in Asia and Africa. Most patients (40%) bitten by rabid animals are <15 years of age.[6]

The World Health Organization has classified exposure into three categories depending on the severity and risk of progression: Category I: Touching or feeding animals and animal licks on intact skin (no exposure); Category II: Nibbling of uncovered skin, minor scratches, or abrasions without bleeding (exposure); and Category III: Single or multiple transdermal bites or scratches, contamination of mucous membrane, or broken skin with saliva (severe exposure).[7]

Human rabies presents in encephalitic and paralytic forms, the former being more common.[8] Rabies encephalitis presents as an acute CNS infection. The brainstem and cerebrum are the most common parts of the brain affected; however, the cortex is relatively spared. The early localization of the virus in the limbic system correlated with these patients' emotional and early behavioral changes. Similarly, cortical sparing correlates with the fact that the affected person is alert and cognitively intact.[2,3]

Patients with rabies encephalitis present with hyperactivity that rapidly escalates into episodes of fluctuating consciousness. Hallmark features of rabies encephalitis are phobic spasms, aerophobia, and hydrophobia, triggered by puffs of air and sounds or even the mention of water.[8] Routine CSF examination shows elevated CSF protein levels. The medulla and spinal cord are primarily involved in paralytic rabies.[2]

Imaging features

Rabies encephalitis has a short incubation period with a fulminant course and dramatic progression, leaving very little time between the onset of symptoms and mortality, turning fatal before acquiring MRI. However, in cases where feasible, MRI plays a significant role in early detection and diagnosis.[9] Imaging may be normal in the early phase of the disease, followed by evidence of cerebral edema in CT and MRI of the brain.[4]

MRI in rabies shows almost exclusive gray matter involvement, including bilateral basal ganglia, thalami, hypothalami, and hippocampi, along with pontine and mid-brain nuclei and periaqueductal gray matter, dorsal medulla,

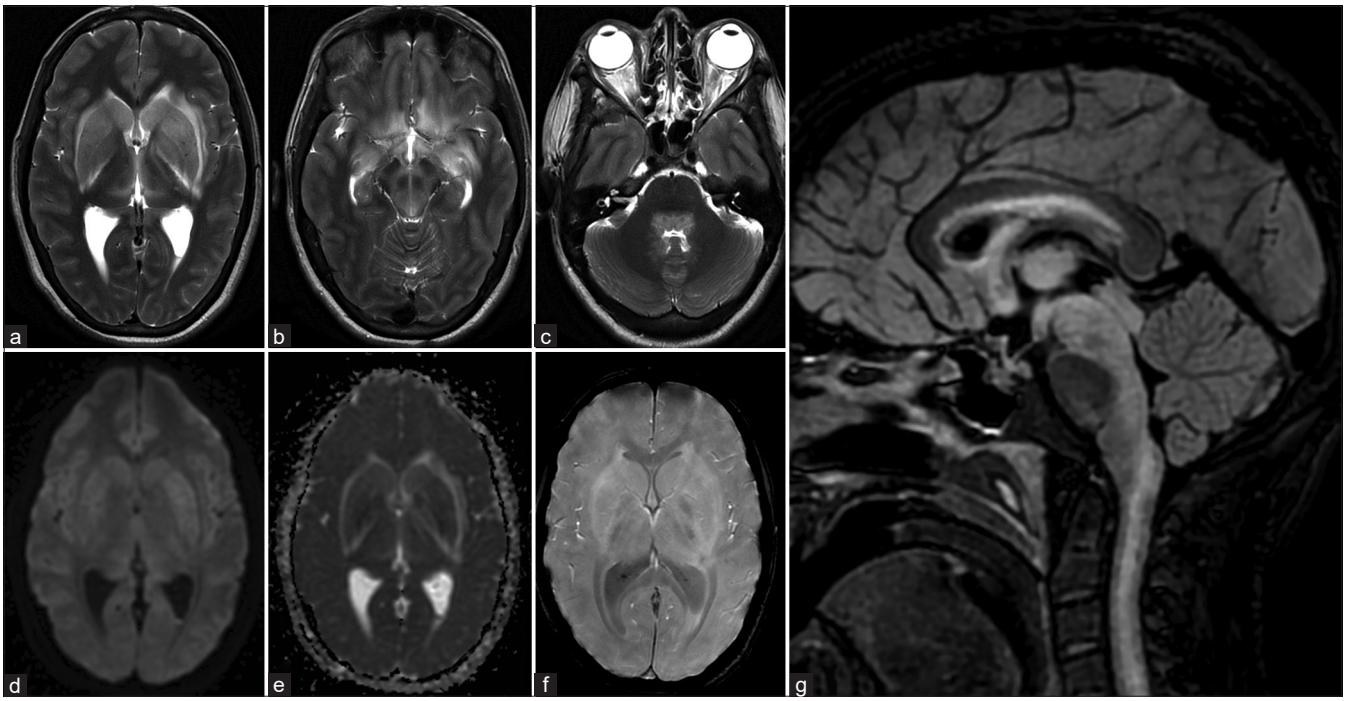


Figure 1: Case 1 – The axial T2 images (a-c) shows symmetrical hyperintensity in the basal ganglia, the dorsomedial thalami, bilateral mesial temporal region (uncus and amygdala), the basifrontal region, midbrain, the pontine tegmentum, medulla, and the cervical cord. Involvement of bilateral dentate hilus was also evident. The diffusion images (d and e) were negative for any restriction. (f) No abnormal blooming noted in the susceptibility-weighted images. The sagittal fluid-attenuated inversion recovery image (g) showed the diffuse brainstem and cervical cord involvement.

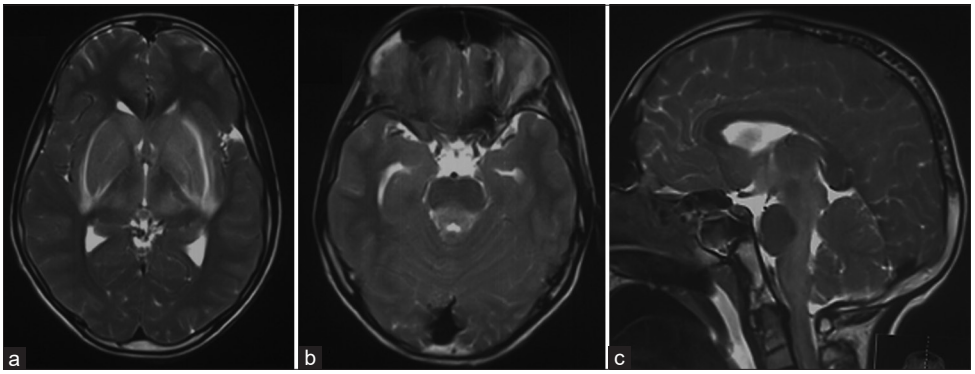


Figure 2: Case 2 – The axial T2 images (a and b) shows symmetrical hyperintensity in the basal ganglia, the dorsomedial thalami and the pontine. The sagittal T2 image (c) showed contiguous involvement of the medulla and adjacent cervicomedullary junction.

collicular plates, and cerebellar peduncles. Both of our cases showed symmetrical involvement of the basal ganglia with extensive signal changes in the brainstem, predominantly the dorsal aspect. The aforementioned areas have been found to contain maximal concentrations of Negri bodies and viral antigens in various studies.[2,4,9] There may also be involvement of gray matter, along with blurring of the cortex and white matter junction; however, not seen in all cases. Similar changes may be seen in the spinal cord, although this is more commonly seen in a paralytic form than an encephalitic form.[2] The involved areas appear hyperintense on T2/FLAIR and hypointense on T1, with mildly restricted diffusion on the apparent diffusion coefficient. The majority of these cases succumb within a few days of the onset of symptoms.

Subsequent imaging in survivors of full-blown rabies is extremely rare due to the nearly fatal nature of the disease. However, few studies have described cases of rabies

Table 1: Imaging features and differentials for Rabies Encephalitis.

S. No.	Disease	Distinguishing MRI features
1.	Rabies encephalitis	• T2/FLAIR hyperintense lesions involving the dorsal aspect of the medulla, pons, periaqueductal gray matter, collicular plate • Spinal cord involvement is seen in paralytic form • Hemorrhagic changes are uncommon
2.	Herpes simplex encephalitis	• Involvement of mesial temporal lobes and insular cortex is seen, with sparing of the basal ganglia, thalami and brainstem
3.	Japanese B encephalitis	• Bilateral thalamic involvement is classic, along with bilateral basal ganglia involvement. • Hemorrhagic areas may be seen. • Variable DWI restriction
4.	Acute demyelinating encephalomyelitis	• Can occur post Flu vaccination and after post-exposure immunoglobulin prophylaxis against rabies. • Bilateral asymmetrical Fluffy opacities involving cerebral subcortical white matter.
5.	Mitochondrial disease	• Deep gray matter involvement along with delayed myelination of white matter
6.	Guillian–Barre disease (Symptoms mimic paralytic rabies)	• Thickening and contrast enhancement along nerve roots of conus medullaris and cauda equina.

MRI: Magnetic resonance imaging, DWI: Diffusion-weighted imaging, FLAIR: Fluid-attenuated inversion recovery

survivors.[10-12] Goyal *et al*.[11] have described late imaging features in rabies patients at 4 months follow-up. These features are marked atrophy of the cerebrum, head of caudate nuclei, sclerotic and cystic changes in the bilateral putamen and thalamus, and periventricular white matter hyperintensities with gliotic changes.

Histopathology specimens show intracytoplasmic Negri bodies within the affected neurons, particularly in hippocampal pyramidal cells, cerebral cortex, and Purkinje cells. These cells are round to oval and sharply demarcated.[2] Antemortem samples are obtained from nuchal skin and saliva. Direct fluorescent antibody test to detect virus antigens in brain impressions is the gold standard diagnostic test.[13]

Imaging differentials include Japanese B encephalitis and other viral encephalitides, extrapontine myelinolysis, uremic encephalitis, acute demyelinating encephalomyelitis, and ischemic encephalitis. The preference of rabies for the gray matter areas, that is, brainstem, thalami, and limbic system, the absence of enhancement, the absence of hemorrhages, and minimal diffusion restriction make it distinct from these differentials [Table 1].

CONCLUSION

MRI, in the presence of appropriate clinical history, has the potential to diagnose rabies encephalitis due to unique imaging features. It can also distinguish rabies encephalitis from other close differentials.

TEACHING POINTS

1. Involvement of the dorsal aspect of the brainstem, along with bilaterally symmetrical involvement of the limbic system, basal, and thalami, with the absence of hemorrhagic changes, is a hallmark feature of rabies encephalitis.
2. Involvement of the spinal cord can be seen in encephalitis and paralytic forms; however, more common in the latter.

MCQs

1) Which of the following statements in relation to rabies infection is false?
   a) Almost exclusive grey matter involvement is characteristic
   b) Paralytic form is less common than the encephalitis form
   c) Spinal cord involvement is more common in encephalitis form
   d) Short incubation period with rapid progression of disease and the fatal outcome is seen

Answer: c

2) The pattern of grey matter involvement in rabies encephalitis
   a) Bilaterally symmetrical
   b) Bilateral but asymmetric
   c) Unilateral
   d) Random

Answer: a

3) All of the following aid in the diagnosis of rabies encephalitis except:
   a) Isolation of intracytoplasmic Negri bodies from a biopsy sample
   b) Elevated CSF proteins and normal CSF sugar
   c) Diffuse white matter involvement with restricted diffusion
   d) Patient symptoms such as aerophagia and dysphagia

Answer: c)

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Hatami H. History of rabies in traditional medicine's resources and Iranian research studies: On the occasion of the world rabies day (September 28, 2012). Int J Prev Med 2012;3:593-5.
2. Awasthi M, Parmar H, Patankar T, Castillo M. Imaging findings in rabies encephalitis. AJNR Am J Neuroradiol 2001;22:677-80.
3. Villamar MF, Smith VD, Smith JH, Wilson D, Nuovo GJ. Rabies encephalitis presenting with new-onset refractory status epilepticus-update. Neurol Clin Pract 2020;10:e1-4.
4. Gajurel BP, Gautam N, Shrestha A, Bogati N, Bista M, Ojha R, *et al*. Magnetic resonance imaging abnormalities in encephalomyelitis due to paralytic rabies: A case report. Clin Case Rep 2022;10:e05308.
5. Srinivasan A, Rupprecht C, Ksiazek TG, Guarner J, Hanlon CA, Niezgoda M, *et al*. Transmission of rabies virus from an organ donor to four transplant recipients. N Engl J Med 2005;352:1103-11.
6. Soler-Rangel S, Jiménez-Restrepo N, Nariño D, Rosselli D. Rabies encephalitis and extra-neural manifestations in a patient bitten by a domestic cat. Rev Inst Med Trop São Paulo 2020;62:e1.
7. Rabies. Available from: https://www.who.int/news-room/fact-sheets/detail/rabies [Last accessed on 2023 Jun 17].
8. Jassi P, Attri A, Dhawan R, Kakkar C, Saggar K. MR imaging in rabies encephalitis: A rare entity. Ann Indian Acad Neurol 2016;19:125-8.
9. Jain H, Deshpande A, Favaz AM, Rajagopal KV. MRI in rabies encephalitis. BMJ Case Rep 2013;2013:bcr2013201825.
10. Rao A, Pimpalwar Y, Mukherjee A, Yadu N. Serial brain MRI findings in a rare survivor of rabies encephalitis. Indian J Radiol Imaging 2017;27:286-9.
11. Goyal K, Bhagwat C, Suthar R, Saini A, Ravikumar N, Singh P, *et al*. Enigma of rabies: Prolonged survival in a boy with rabies brachial plexitis and encephalomyelitis. Neurol India 2020;68:673-6.
12. Mani RS, Damodar TS, Domala S, Gurung B, Jadhav V, Konanki R, *et al*. Case reports: Survival from rabies: Case series from India. Am J Trop Med Hyg 2019;100:165-9.
13. Fooks AR, Cliquet F, Finke S, Freuling C, Hemachudha T, Mani RS, *et al*. Rabies. Nat Rev Dis Primer 2017;3:17091.

How to cite this article: Jha S, Yadav T, Rohila AK, Sharma SK, Tiwari S. The catastrophe of rabies encephalitis: A case series. Case Rep Clin Radiol 2023;1:70-4.