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Case Report

Magnetic resonance imaging in rabies encephalitis, a case report, and review of the literature ☆,☆☆

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ABSTRACT

Rabies is an acute fatal disease of the central nervous system. Neuroimaging plays an important role, especially in establishing an early diagnosis and distinguishing it from other types of encephalitis. This case report aims to give a brief review of this condition and report the less common MRI findings of the disease. We herein report a case of a 61-year-old male bitten by a stray dog who presented with fever, vomiting, headache, sialorrhea, dysarthria, dysphagia, and upper limb weakness which progressed to lower limbs on the next day. T2W and FLAIR images demonstrated subtle bilateral hyperintense signal in the deep gray matter with more apparent increased signal intensity in the white matter of the frontal and parietal lobes which shows mild diffusion restriction but no postcontrast enhancement. The diagnosis of rabies encephalitis was made based on a typical history of exposure, a compatible clinical presentation, and MRI findings. Rabies diagnosis is essentially clinical. It is definitively confirmed by the isolation of the virus from biological samples such as saliva, CSF, hair, or detection of rabies antigens or antibodies. Magnetic resonance imaging (MRI) brain used as one of the modalities of investigation for distinguishing it from other encephalitis. Rabies per se does not have any characteristic features on the MRI brain.

Abbreviations: ADC, apparent diffusion coefficient; ADEM, acute disseminated encephalomyelitis; ARDS, acute respiratory distress syndrome; CHF, congestive heart failure; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; RNA, ribonucleic acid; T1W, T1-weighted; T2W, T2-weighted.

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Background

Rabies is considered one of the most fulminant neurotropic diseases and is caused by the rabies virus (single-stranded RNA virus) of the family of Rhabdoviridae which is transmitted to humans by contaminating saliva through bites, scratches, wounds, or even as the result of organ transplantation or laboratory accidents. In developing countries, rabid dogs are the main source of infection in humans, while in developed countries, most cases of infection are the result of rabid bat bites or inhalation when visiting bat caves [1,5,6,14,15]. Human-to-human transmission of the disease is rare [13]. Many cases of rabies in developing countries are not diagnosed with laboratory confirmation, and many cases are not even reported to health authorities [18].

The World Health Organization estimates that canine rabies kills about 35,000-55,000 people each year, which is most common in the rural population of developing countries, especially in Asia and Africa [2,16,17].

The incubation period of rabies varies from a few days to a year (usually 20-90 days), depending on the virus entering site and the viral load. Most of the time, the virus is present at the site of the bite/wound, and then the virus spreads along the peripheral nerves toward the CNS causing encephalitis. After the establishment of CNS encephalitis, the virus spreads along peripheral nerves to other organs, including salivary glands [2].

Rabies usually presents as atypical encephalitis with preservation of consciousness in the early stages, but after the onset of coma, the diagnosis of the disease becomes difficult and usually leads to death despite invasive supportive care. This disease progresses in 3 phases. 1) The prodromal phase: typically lasts 2-10 days and patients may experience paresthesia, pain, or itching at/near the site of exposure which suggests rabies. Other signs/symptoms including fever, headache, malaise, nausea, vomiting, irritability, and/or agitation may be present. 2) The acute neurologic phase: lasts for 2-10 days and patients present either with the classic encephalitic form (fever, anorexia, irritability, inspiratory spasms and cough, confusion, hallucinations, combativeness, seizures) accounting for 80% of cases or with the paralytic form (bilateral global motor weakness resulting in bilateral facial weakness and quadriparesis) accounting only for 20% of cases. Autonomic dysfunction (hypersalivation, gooseflesh, cardiac arrhythmia, priapism), early brainstem involvement (hydrophobia, aerophobia, and dysphagia), and even death can also be seen in this phase. 3) Coma and death: even with currently available intensive supportive treatment, recovery is very rare and the patient usually dies due to respiratory distress and apnea or cardiovascular collapse within 2 weeks [1,2,4–6].

Current diagnostic tools are not suitable for detecting rabies infection during the incubation period. Rabies should be considered in patients with acute atypical presentation of encephalitis or those with acute flaccid paralysis, including patients suspected of Guillain-Barré syndrome. Cerebrospinal fluid and most routine laboratory examinations are usually normal or non-specific. Serum-neutralizing antibodies against rabies virus and specific anti-rabies antibodies in the CSF may be positive [2,3].

Neuroimaging plays an important role, especially in establishing an early diagnosis and distinguishing rabies encephalitis from other types of encephalitis. Involvement of the deep grey matter including the thalami and brainstem is usually seen [4].

Case presentation

A 61-year-old man presented to our hospital with fever, vomiting, headache, sialorrhea, dysphagia, and upper limb weakness for 5 days. On physical examination, upper extremity deep tendon reflexes were absent but the strength and reflexes in the lower extremities were preserved. There were no seizures, hydrophobia, or aerophobia at the time of admission to the hospital. No positive meningeal signs were present. Cardiovascular and pulmonary examination findings were unremarkable. The values for routine laboratory tests, including routine blood examinations (hemoglobin, complete blood count) and blood biochemistry tests (blood glucose, electrolytes, liver, and renal function tests), were within normal limits.

On the next day, the upper limb weakness increased and now also involved both lower limbs. Psychomotor agitation and persecutory delirium were also seen. His condition worsened rapidly, the quadriparesis worsened, and became unconscious on the fourth day of hospitalization.

The recent history of the patient suggested no significant medical problem, except for a scar on his hands and right forearm. According to the patient's guardian, 4 weeks before the onset of symptoms, a stray dog had attacked him while he was coming home late at night. He had been bitten by the animal on his hands and right forearm.

His sons immediately took him to the nearby local primary health center, where the patient's wounds were cleaned with soap and water, and he was given some painkillers as well as oral antibiotics to prevent secondary infection of wounds. He was subsequently given 4 doses of the anti-rabies vaccine but did not receive postexposure anti-rabies immunoglobulin or monoclonal antibodies.

To rule out other causes of neurological deficits, Magnetic resonance imaging (MRI) of the brain with and without contrast was performed 2 days after the admission of the patient. Bilateral hyperintense signals in the basal ganglia and thalami are noted on T2-weighted (T2W) and fluid attenuation inversion recovery (FLAIR) images (Figs. 1A and D). These abnormal changes were not restricted strictly to the grey matter of the brain. More pronounced bilaterally symmetrical hyperintense signals are also seen in the white matter of the frontal and parietal lobes (Figs. 1A-F). The involved regions show no abnormal signal intensities on the T1-weighted (T1W) images (Figs. 2A and B). No evidence of contrast enhancement in postcontrast images is seen (Figs. 3A-C). The involved regions showed a mild increase in apparent diffusion coefficients (Figs. 4A-D). These imaging findings were in favor of encephalitis.

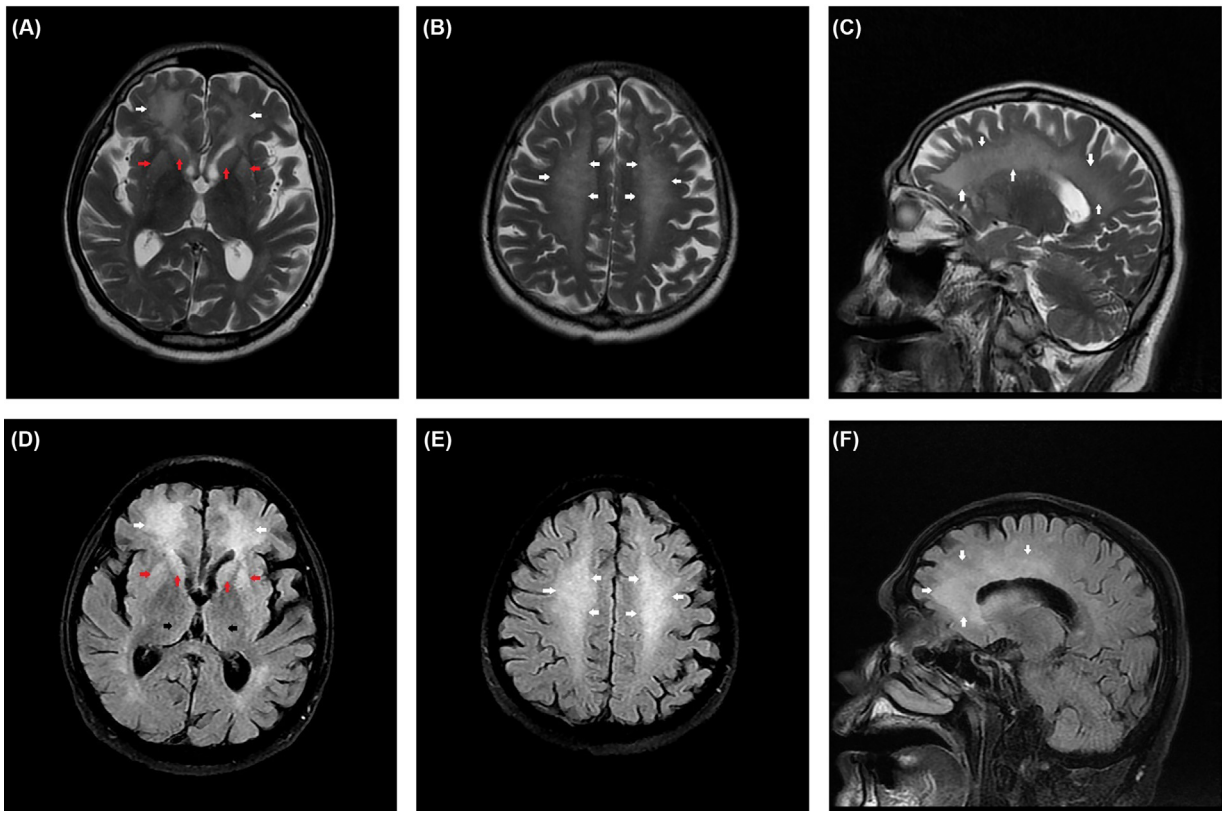

Fig. 1 – Axial (A and B) and sagittal (C) T2W images as well as axial (D and E) and sagittal (F) FLAIR images showing symmetrical bilateral hyperintense signal in the white matter of frontal and parietal lobes (white arrows). Similar bilaterally symmetrical hyperintense signals were also noted in the putamen and caudate on axial (A, D) T2W/FLAIR images (red arrows). Minimal increased signal intensity is also seen in the thalamus on axial (d) FLAIR image bilaterally (black arrows).

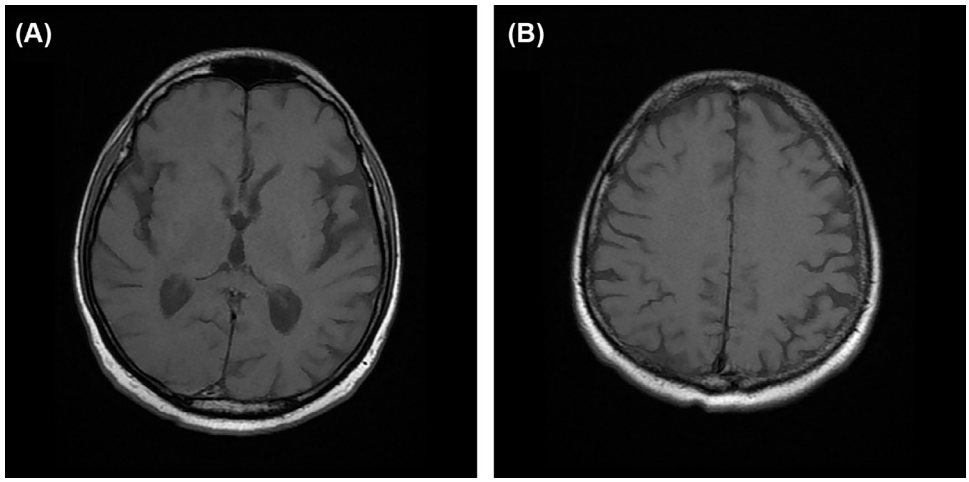

Fig. 2 – Axial (A and B) T1W images show no abnormal signal intensity in the affected gray matter structures as well as the white matter of the frontal and parietal lobes.

The diagnosis of rabies encephalitis in the present case was made based on a typical history of exposure, a compatible clinical presentation, and MRI findings. Laboratory confirmation of rabies was not performed due to the rapid progression of the illness to death and the lack of technical resources in the country.

Symptomatic treatment of the patient was done with phenobarbital, diazepam, acetaminophen, and supplementary fluid which unfortunately was not effective. The neurological status of the patient continued to deteriorate. Eventually, the patient died on the seventh day of hospitalization.

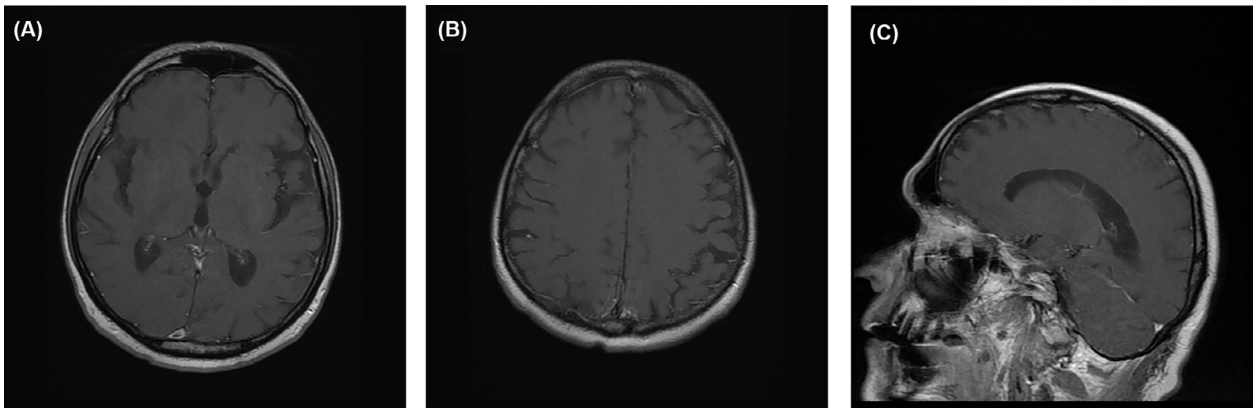

Fig. 3 – Axial (A and B) and sagittal (C) postgadolinium T1W images show no contrast enhancement in the basal ganglia, thalami, and frontoparietal region.

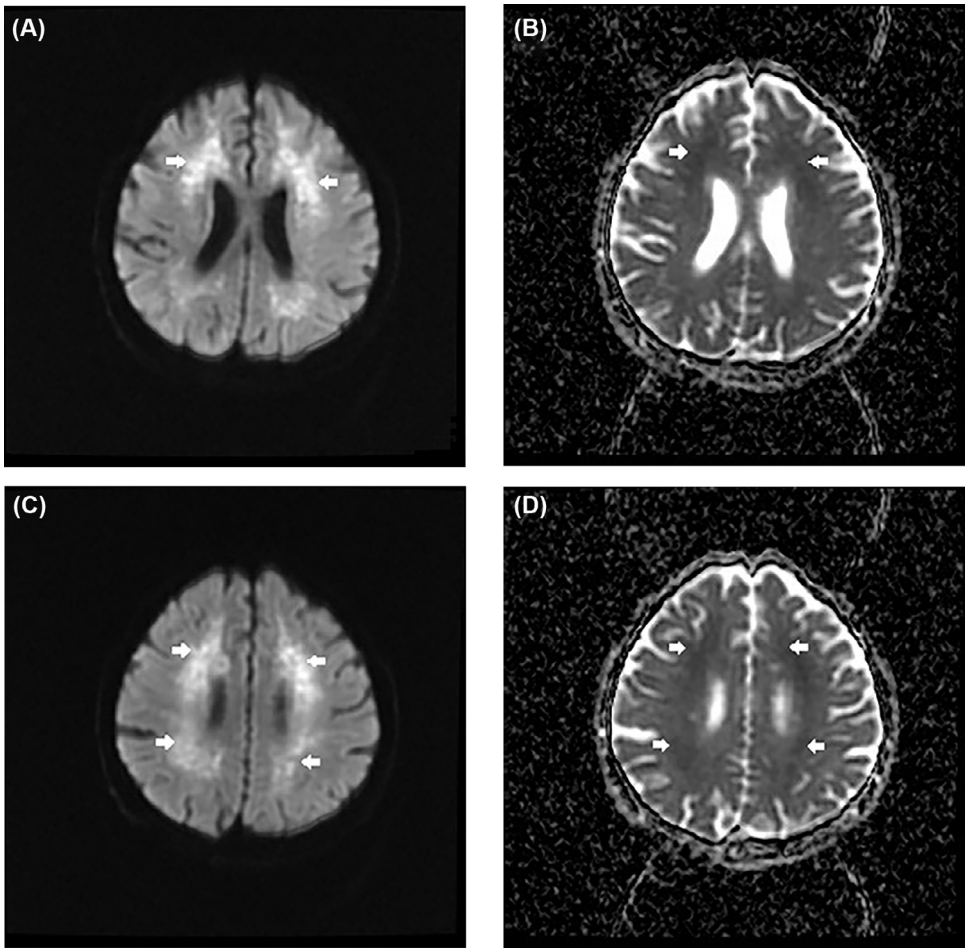

Fig. 4 – Axial diffusion-weighted images (A and C) and ADC maps (B and D) demonstrate corresponding diffusion restrictions in the bilateral frontoparietal regions (white arrows).

Discussion

The word rabies is derived from the old Indian root word rabh, which means "to make violent". This neurotropic zoonosis is also known as hydrophobia or aquifuga [7].

Diagnosis is usually made based on the typical clinical presentations. Brain and/or spinal cord imaging is not routinely performed in rabies [4]. There may be no abnormal CT/MRI findings in the early stages of the disease, but as the neurologic phase of the disease progresses, abnormal CT/MRI findings can be depicted. CT is usually normal. Occasionally, non-specific low-density cortical lesion (s) as well as hypoattenuation in the basal ganglia and periventricular white matter may be seen. Hemorrhagic changes can be seen in the later stages of the disease [5,6].

In classic rabies encephalitis, MRI may show increased T2/FLAIR signal intensity in the gray matter of the brain parenchyma; basal ganglia, thalami, hypothalami, brain stem, limbic system, and frontal and parietal lobes, indicating CNS infection. Moderate postcontrast enhancement may be seen in the thalami, brainstem, deep gray matter, and cranial nerves. In addition to the brain, spinal cord involvement can also be seen on postcontrast MRI, demonstrating non-specific low-level enhancement along the nerve plexus and nerve root ganglia in the early stages of the disease. In the paralytic form of rabies, involvement of the spinal cord and medulla is more pronounced, although there are no specific imaging features that allow differentiation from classic encephalitis [3–6,9,10].

Most routine laboratory examinations are normal or nonspecific but can help differentiate rabies encephalitis from other potentially treatable causes of encephalitis. Serum-neutralizing antibodies against rabies virus are diagnostic, but these antibodies may not be present until late stage of the disease course [2]. Cerebrospinal fluid (CSF) examination may be normal, although a slight increase in lymphocyte count and a moderate increase in the protein level are usually seen. Specific anti-rabies antibodies in the CSF may be positive, indicating rabies encephalitis. PCR can detect viral RNA in the saliva, CSF, urine, skin, and brain tissues. Direct fluorescent antibody testing of biopsy specimens for viral antigens has a high sensitivity and specificity [3,8].

Differential Diagnosis of rabies encephalitis from an imaging standpoint includes acute disseminated encephalomyelitis (ADEM), Japanese B and other viral encephalitis, ischemic encephalitis, mitochondrial diseases, rhombencephalitis, and Guillain-Barré syndrome [4,9].

ADEM is an important differential diagnosis of paralytic rabies but can be distinguished from the latter because of its involvement. MRI findings in rabies encephalitis are generally symmetrical, and predominantly involved deep grey matter structures. Bilaterally symmetrical involvement of white matter in frontoparietal regions can also be seen as described in the present case. In ADEM there are discrete and usually asymmetrical involvements of the white matter of the brain, brain stem, spinal cord, and optic nerves [4].

Gray matter involvement, the absence of hemorrhages, and the absence of enhancement during the acute phase of the disease help differentiate rabies encephalitis from Japanese B and other viral encephalitis like herpes simplex encephalitis which usually involve mesial temporal lobes and insular cortex [5,6,9,10].

Based on MRI findings, the differentiation of rabies encephalitis from ischemic encephalitis and mitochondrial diseases can be difficult. DW images may be useful as rabies encephalitis usually does not show obvious restriction as compared to these diseases which show intense diffusion restriction [4]. However, in some cases of rabies encephalitis, there may also be apparent diffusion restriction as shown in the present case.

It is difficult to differentiate the paralytic form of rabies encephalitis from Guillian-Barre syndrome and myelitis in which there is involvement of the spinal cord. A typical history of animal bites and rapid progression of illness are very helpful to differentiate them [5,9].

Despite the typical clinical features of rabies encephalitis, MRI is the imaging modality of choice for the early diagnosis of disease and it helps to differentiate rabies encephalitis from other types of encephalitis [9].

Unfortunately, there is still no definite curative treatment for rabies encephalitis, therefore, the management of these patients is usually palliative and supportive. Common therapeutic efforts that may help in some cases if started early include; human rabies immunoglobulin injected around the site of the bite, rabies vaccine, monoclonal antibodies, and antiviral drugs. Despite invasive care of the patient, the overall prognosis of the disease remains extremely poor and very few cases of survival have been reported [2,5,6,11,17].

The rabies is often fatal once the patient develops signs and symptoms [12,16,17]. The average interval from the onset of clinical disease to death was reported to be 5.7 days in furious rabies and 11 days in paralytic form of rabies [3].

Conclusion

Rabies encephalitis is one of the most fatal neurotropic diseases. Rabies should be considered in patients with acute atypical presentation of encephalitis or those with acute flaccid paralysis. The diagnosis is usually made based on the clinical presentations. It is definitively confirmed by the isolation of the virus from biological samples such as saliva, CSF, hair, or detection of rabies antigens or antibodies. Magnetic resonance imaging (MRI) brain used as one of the modalities of investigation for distinguishing it from other encephalitis. Rabies per se does not have any characteristic features on the MRI brain.

Patient consent

Written informed consent for publication has been obtained.

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