Imaging Findings in Rabies Encephalitis

Manasi Awasthi, Hemant Parmar, Tufail Patankar and Mauricio Castillo


http://www.ajnr.org/content/22/4/677

This information is current as of October 13, 2023.
Case Reports

Case 1
A 6-year-old boy presented with sudden onset of generalized seizures and altered consciousness 2 weeks after being bitten by a dog. On physical examination he showed increased tone in all four limbs, with hyperreflexia and extensor plantar responses. Plain and contrast-enhanced CT studies of brain showed nonenhancing, symmetrical hypodensities involving both basal ganglia (Fig 1A and B). No areas of altered attenuation were seen elsewhere in the brain (Fig 1C). In view of the clinical history, rabies encephalitis was considered a possible diagnosis, and was confirmed by detection of the viral antigens in corneal impression smears on immunohistochemistry. The viral antigens targeted by the fluorescein-labeled antibody appeared as apple-green fluorescent bodies under the fluorescent microscope using the fluorescein isothiocyanate filter (Fig 1D). The patient was managed conservatively and died within 4 days of admission. Postmortem examination was not performed.

Case 2
A 30-year-old man presented with acute onset of altered consciousness and drowsiness 3 weeks after being bitten by a dog. He had had prodromal symptoms of fever, headache, and lassitude for 4 days. On physical examination, the patient was unconscious, with flaccid paralysis in all four limbs. All reflexes were absent bilaterally. T1- and T2-weighted MR images of the brain revealed hyperintensity in the globus pallidus, putamen, and thalamus bilaterally (Fig 2A). Proton density-weighted axial images showed hyperintensity in the head of the caudate nucleus, globus pallidus, putamen, and pulvinar of the thalami bilaterally (right more than the left) (Fig 2B). No abnormal signal was detected from the brain stem (Fig 2C). Owing to the patient’s history, paralytic rabies encephalitis was diagnosed and subsequently established antemortem on the basis of findings on the corneal impression studies similar to the first case. The patient gradually deteriorated and died within 3 days of admission. Postmortem examination was not performed.

Discussion
The term rabies is derived from the old Indian root word rabh, meaning to make violent (1). The disease is also known as hydrophobia or aquifuga (1). Rabies encephalitis is an acute CNS infection caused by a type of RNA virus of the rhabdovirus family. Transmission to humans is mainly through bites of infected rabid dogs, cats, bats, and other wild animals. Other modes of transmission are through inhalation, by contact of infected saliva.

Address reprint requests to Dr. Hemant Parmar, Department of Radiology, King Edward VII Memorial Hospital, Parel, Mumbai 400 012, India.

© American Society of Neuroradiology
Fig 1. Case 1: 6-year-old boy with generalized seizures and altered consciousness.

A–C, Plain (A) and contrast-enhanced (B and C) CT scans show nonenhancing bilateral basal ganglia hypodensities. No other areas of altered CT attenuation were seen. There was no evidence of enhancement on administration of contrast material. No areas of altered attenuation are seen in the brain stem (C).

D, Photomicrograph with immunofluorescent staining of the corneal impression smear shows bright apple-green viral nucleocapsid antigen targeted by the virus-specific fluorescent-labeled antibodies and seen using fluorescein isothiocyanate filter.

Fig 2. Case 2: 30-year-old man with altered consciousness and drowsiness.

A, Axial spin-echo T1-weighted MR image (600/15 [TR/TE]) shows hyperintensity in the globus pallidus and putamen bilaterally. Minimal hyperintensities are also seen in the thalamus bilaterally.

B, Axial spin-echo proton density–weighted MR image (2600/22) shows hyperintensities in the heads of the caudate nuclei bilaterally. Hyperintensities are also seen in the globus pallidus and putamen bilaterally (right more than the left).

C, MR image at the level of the brain stem shows no abnormal signal.
with an open wound or mucus membrane, and via infected corneal transplants (2–4).

The incubation period of rabies is typically 2 to 8 weeks (6, 7), although it varies with the type of infecting strain, and is found to be inversely related both to the size of the inoculum and to the proximity of the site of the bite to the CNS. The viruses are usually introduced deep into the soft tissues by an animal bite and infect the muscle, possibly through an affinity for nicotinic cholinergic receptors. They replicate in the muscle before reaching the CNS, either through the neuromuscular spindles or the motor end plate (6). Alternatively, the virus may directly affect the sensory nerve endings of the superficial soft tissue. The passage of the virus to the CNS occurs axonally through retrograde axoplasmic flow of approximately 12 to 24 mm per day until the virus reaches the next neuronal cell body (8).

In the CNS there is an initial proclivity toward infection of the gray matter. Tirawatnpong et al (7) suggested involvement of the neuralgial cells along with the neurons. Once inside the CNS, rapid dissemination of the virus takes place and rapid progressive encephalitis ensues (8). In paralytic rabies, the medulla and the spinal cord are mainly involved by extensive neuronal damage and inflammation, whereas in the encephalitic form, it is the brain stem and the cerebrum, particularly the limbic system (9, 10). Involvement of the basal ganglia and the thalamus is usually seen late in the disease (6, 7). The early localization of the virus in the limbic system, with cortical sparing, correlates clinically with behavioral and emotional changes seen in an alert and cognitively intact patient (6). Rabies virus reaches the CNS early in the disease and returns to the periphery late in the process by intraneural transport (6). This centrifugal spread of the rabies virus is observed late in the disease. There is an unexplained tropism for the salivary glands and lacrimal glands, with infectious rabies particles appearing in the saliva, tears, and tracheobronchial secretions (6).

Clinical illness begins upon arrival of the virus into the CNS. Human rabies may present in one of two forms: encephalitic and paralytic (7). In encephalitic rabies, the initial symptoms are nonspecific, such as fever, malaise, anorexia, cough, and pain or paraesthesia at the bite site. Subsequently, patients develop hydrophobia, aerophobia, hyperirritability, hyperactivity, and priapism. Neurologic symptoms, such as seizures, agitation, and alternating mood swings, often occur. Paralytic rabies encephalitis causes more diagnostic problems, as the clinical symptoms of hydrophobia and aerophobia are present in only half these patients (7). Moreover, the initial presentation with flaccid paralysis resembles Guillian-Barré syndrome. The pathogenesis of paralytic rabies is poorly understood. Host immune response may be one of the factors deciding the clinical outcome (7). Paralytic rabies appears to correlate with absence

of significant immune response to the infection and diminished number of peripheral blood B lymphocytes. Both forms of the disease are invariably fatal and most patients die within 10 days of the onset of neurologic symptoms. Patients usually succumb to failure of basic central vegetative functions, although death may also be due to concomitant rabies myocarditis (6).

Because the disease has a rapidly fulminant course, imaging of these patients is uncommon and difficult. Hence, the imaging findings in naturally acquired rabies have received little attention in the literature. A CT scan may show focal or diffuse areas of decreased attenuation in the basal ganglia, periventricular white matter, hippocampus, and brain stem. Pontine hemorrhages have also been reported. Diffuse cerebral edema may be seen in advanced cases (11). Murthy (12) reported findings of multiple areas of white matter on MR images, including in the brain stem, cerebellar peduncles, and both cerebral hemispheres, in a case of vaccine-induced acute demyelinating encephalomyelitis. Sing and Soo (11) reported finding a narrowing in the supraclinoid internal carotid and terminal basilar arteries on a cerebral angiogram. This was postulated to be due to transient arterial spasm induced by the viral infection.

Both our patients had identical involvement of the basal ganglia bilaterally, seen as areas of hypodensity on CT scans and as areas of hyperintensity on T1- and T2-weighted MR images. In one of the patients, MR images also showed hyperintensities in the pulvinar of the thalamus bilaterally. The MR features suggested extracellular methemoglobin, perhaps due to the late presentation of the patients, when the disease was well established; however, we do not have pathologic proof of this. We do not believe that the hyperintensities were related to hydrated calcium because of the short duration of the disease in both patients. Similar imaging findings are seen in many conditions, such as infectious viral encephalitis, cholinergic poisoning, toxic encephalopathy (carbon monoxide, methanol, hydrogen sulphide, cyanide), severe hypoglycemia, extrapontine myelinsis, hypoxic/ischemic insults, and hemolytic-uremic syndrome; and in unusual conditions, such as Wilson disease and Leigh disease. Such a finding in patients with a history of an animal bite and clinical sequelae, as in our patients, is highly suggestive of rabies encephalitis. Both our patients had incurred a dog bite, and corneal impression smears obtained from both of them showed the presence of the viral antigens on fluorescent microscopy. The atypical sparing of the brain stem cannot be explained in either of the patients.

Gross pathologic specimens of the brain in rabies show scattered haemorrhages, necrosis, and surrounding edema in the cerebral gray matter, predominantly involving the basal ganglia and the brain stem. Histopathologically, the changes seen in the neuron are of necrosis. There can be asso-
is suspected, special management of the tissues obtained for the histopathologic study is necessary. Use of face masks, gowns, and gloves by all the personnel in contact with the patient and the tissue sample is necessary. Saliva, CSF, and tissues should be handled and disposed of with precautions. In addition, all known or suspected human contacts (premortem or postmortem) should receive postexposure prophylaxis (6).

Conclusion

The diagnosis of rabies is essentially clinical. Patients may present with a wide variety of symptoms, ranging from widespread CNS excitation to flaccid paralysis. Although a differential diagnosis based on imaging findings of basal ganglia involvement is remote, in the appropriate clinical context, encephalitis due to rabies needs to be considered. In diagnosed cases, managing of patients and handling of tissues require special precautions.

References


Fig 3. Histopathologic section of the brain from a different case shows the presence of intracytoplasmic Negri bodies (arrow) in the cortical neuron (hemotoxylin-eosin, original magnification ×400).