Rabies encephalitis is one of the communicable diseases most feared by mankind and is invariably fatal. In its most common encephalitic form, the clinical presentation is classical and therefore neuroimaging is rarely performed. The less common paralytic form may be confused with other rapidly paralysing illnesses and recourse to investigations may be crucial for diagnosis. Antemortem laboratory diagnosis involves antigen or antibody estimation in various body tissues, the facility for which may not be readily available. Neuroimaging may prove to be a useful investigation in this situation. Here we report the findings of magnetic resonance imaging of the brain in a case of paralytic rabies that was proved by postmortem examination.

CASE REPORT

A 45 year old woman presented with a history of a moderate degree of fever and vomiting for six days. On the evening of the first day this had been followed by right upper limb weakness, dysarthria, dysphagia, and diplopia. The next day the weakness involved both lower limbs and the left upper limb. On the third day the quadriparesis worsened and she became stuporous. She was admitted to our hospital on day 6. There was no headache, seizures, hydrophobia, or aerophobia. Three weeks before the onset of symptoms a wild fox had attacked while she was in the forest collecting firewood. She had been bitten by the animal on her face and left forearm. The wound had been cleaned with soap and water. She was subsequently administered four doses of antirabies vaccine VeroRab (vero cell line culture vaccine) intramuscularly, but post-exposure antirabies immunoglobulin had not been given.

On admission the patient was unconscious, her pulse was 84 beats/min, regular, and blood pressure 118/80 mm Hg. Respiration was rapid and shallow, the cardiovascular system was normal, and there was no organomegaly. There were no bite marks. On neurological examination the patient was unconscious, the pupils were normal in size and reactive, doll’s eye movements were absent, and ocular fundi were normal. There was generalised hypotonia, quadriplegia, and areflexia. Myoedema was noted. The plantar responses were equivocal. No signs of meningeal irritation were noted. A diagnosis of paralytic rabies was considered. The less likely possibility was of acute disseminated encephalomyelitis after vaccination.

The haematological, renal, and hepatic parameters, electrolytes, and blood glucose were normal.

Abbreviations: ADEM, acute disseminated encephalomyelitis; FLAIR, fluid attenuation inversion recovery (image)
Chest radiography showed bilateral non-homogeneous opacities suggestive of bronchopneumonia and arterial blood gas estimation revealed hypoxia, suggestive of type 1 respiratory failure. Her respiratory effort weakened over the next 24 hours and she needed ventilatory assistance.

Magnetic resonance imaging of the brain done one day after admission and revealed bilaterally symmetrical hyperintensities in the thalamus, basal ganglia, midbrain, pons, and medulla on the T2 weighted and fluid attenuation inversion recovery (FLAIR) images (fig 1). These changes were restricted strictly to the grey matter. Corneal impression smears were negative. The patient was treated supportively, but deteriorated gradually, and succumbed on day 11 of illness. A postmortem of the brain was performed.

The brain appeared mildly swollen. The cut surface of the brainstem revealed few poorly defined grey-white punctuate areas; the basal ganglia and cerebellum appeared congested. Light microscopy of the brain tissue using haematoxylin and eosin stain showed typical acidophilic intracytoplasmic inclusions—that is, Negri bodies in some neurons in the hippocampi, basal ganglia, brainstem, and cerebellum. Immunocytochemistry with monoclonal antibodies revealed many more neurons loaded with viral antigen (fig 2).

DISCUSSION

Rabies is a zoonotic problem of considerable magnitude in India with an estimated annual human mortality of 30 000 in the Indian subcontinent.1 The more common presentation is the encephalitic form. It starts with malaise, fever, and paraesthesiae at the site of the bite followed by classical neurological symptoms of agitation, hydrophobia, aerophobia, hyperreflexia, and seizures. The clinical picture of fully fledged rabies encephalitis is unmistakable. Paralytic or dumb rabies resembles Guillain-Barré syndrome. The pathogenesis of paralytic rabies is poorly understood. Host immune factors may determine the clinical outcome.

Literature on neuroimaging in patients with rabies is available but necropsy of the brain in rabies shows scattered haemorrhages.1 Our patient showed hyperintensities in both thalami, basal ganglia, and pons on the T2 and FLAIR images (fig 1). These magnetic resonance imaging findings corresponded with the non-haemorrhagic lesions in the brain at necropsy. The lack of evidence of haemorrhagic lesions on magnetic resonance imaging or pathology may be due to the less fulminant immune response in patients with paralytic rabies. T2 and FLAIR hyperintensities of the basal ganglia may be seen in a variety of other conditions including hypoxic ischaemic encephalopathy, osmotic demyelination, hypoglycaemia, in the presence of toxins like cyanide and manganese, and in mitochondrial diseases. Desai et al suggest that selective involvement of the grey matter could be used to differentiate paralytic rabies from post-vaccinial acute disseminated encephalomyelitis (ADEM).1 In post-vaccinial ADEM there are discrete T2 weighted hyperintensities in the white matter of the brain and spinal cord.4 ADEM was conclusively ruled out after seeing the results of histopathology in our patient. Our patient also demonstrated selective involvement of grey matter on neuroimaging. Classical paralytic rabies has pathological lesions in the medulla and the spinal cord.5 The medullary involvement could be demonstrated on neuroimaging and on histopathology in our patient. Though our patient presented with the paralytic form, the brain imaging showed changes similar to those documented in encephalitic rabies.

Our patient developed rabies in spite of treatment with vero cell 3 line antirabies vaccine and adequate wound toilet. Currently available cell culture vaccines have equal efficacy with almost negligible neurological complications. In class III bites, in addition to active immunisation, passive immunisation with antirabies immunoglobulins is recommended.6 Lack of attribute the hyperintensity on the T1 image to extracellular methaemoglobin. Pathological findings in their patient are not available but necropsy of the brain in rabies shows scattered haemorrhages.1 Our patient showed hyperintensities in both thalami, basal ganglia, and pons on the T2 and FLAIR images (fig 1). These magnetic resonance imaging findings corresponded with the non-haemorrhagic lesions in the brain at necropsy. The lack of evidence of haemorrhagic lesions on magnetic resonance imaging or pathology may be due to the less fulminant immune response in patients with paralytic rabies. T2 and FLAIR hyperintensities of the basal ganglia may be seen in a variety of other conditions including hypoxic ischaemic encephalopathy, osmotic demyelination, hypoglycaemia, in the presence of toxins like cyanide and manganese, and in mitochondrial diseases. Desai et al suggest that selective involvement of the grey matter could be used to differentiate paralytic rabies from post-vaccinial acute disseminated encephalomyelitis (ADEM).1 In post-vaccinial ADEM there are discrete T2 weighted hyperintensities in the white matter of the brain and spinal cord.4 ADEM was conclusively ruled out after seeing the results of histopathology in our patient. Our patient also demonstrated selective involvement of grey matter on neuroimaging. Classical paralytic rabies has pathological lesions in the medulla and the spinal cord.5 The medullary involvement could be demonstrated on neuroimaging and on histopathology in our patient. Though our patient presented with the paralytic form, the brain imaging showed changes similar to those documented in encephalitic rabies.

Our patient developed rabies in spite of treatment with vero cell 3 line antirabies vaccine and adequate wound toilet. Currently available cell culture vaccines have equal efficacy with almost negligible neurological complications. In class III bites, in addition to active immunisation, passive immunisation with antirabies immunoglobulins is recommended.6 Lack of

Learning points

- About 20% of rabies occurs in its paralytic form. It lacks the classical symptoms of rabies and may be mistaken for acute disseminated encephalomyelitis (ADEM) or acute inflammatory demyelinating polyneuropathy.
- Magnetic resonance imaging of the brain in rabies shows exclusive involvement of the grey matter including the basal ganglia thalami pontine and midbrain nuclei. This is in contrast to the predominant white matter involvement in ADEM. Thus magnetic resonance imaging may be useful in the diagnosis of rabies.
- Use of an adequate rabies vaccine schedule and wound toilet may result in vaccine failure if concomitant rabies immunoglobulin administration is not done.

Figure 2 Histological section from the putamen. (A) Immunohistochemistry using monoclonal mouse antibodies to rabies virus nucleocapsid protein (1:20 dilution) and polyclonal antirabies ribonucleoprotein antibody (1:500 dilution). Section shows neurons loaded with rabies viral antigen (magnification × 400). (B) Haematoxylin and eosin staining showing intracytoplasmic Negri body (magnification × 400).
administration of rabies immunoglobulins may account for the failure of immunisation in our patient. Rabies deaths often relate to failure to comply with World Health Organisation guidelines for post-exposure therapy or to a significant delay in treatment.3 Non-availability of the antirabies immunoglobulin is a major handicap in post-exposure prophylaxis in developing countries.4 In these situations an alternative regimen of immunisation with the vaccine alone is recommended.10

Magnetic resonance imaging of the brain or spinal cord is not routinely performed in rabies. It may, however, prove useful in cases of paralytic rabies when the clinical picture is less obvious.

ACKNOWLEDGEMENT
The authors acknowledge Dr B Radotra from Post Graduate Institute, Chandigarh for the immunohistochemical studies.

Authors’ affiliations
J Mani, B C Reddy, R Borgohain, S Sitajayalakshmi, S Mohandas, Department of Neurology, Nizam’s Institute of Medical Sciences, Panjagutta, Hyderabad, India
Department of Pathology, C Sundaram

IMAGES IN MEDICINE
An unusual cause of acute upper oesophageal obstruction

A 85 year old man was admitted with acute dysphagia after eating steak. Apart from a history of hypertension he was otherwise fit and well. Further examination and a standard soft tissue neck radiograph were normal. Although the need for chest radiography was questioned, this actually revealed the cause of the problem: a large thoracic aortic aneurysm (see fig 1).

A water soluble contrast swallow was performed which showed a meat bolus in the upper oesophagus just above the level of the aortic aneurysm (see fig 2). This was subsequently removed with great care using rigid oesophagoscopy, while a consultant gastroenterologist provided flexible endoscopy cover. The patient was later referred for a cardiothoracic opinion.

This uncommon cause of acute upper oesophageal obstruction highlights the importance of obtaining a chest radiograph in every case.

C G L Hobbs
Laryngeal Research Group, University of Bristol, Churchill Building, Longford House, Bristol BS4 5DU, UK, chris.hobbs@doctors.org.uk

REFERENCES

www.postgradmedj.com
An unusual cause of acute upper oesophageal obstruction

C G L Hobbs

doi: 10.1136/pmj.79.932.354