

Occurrence of Human Rabies in Peninsular Malaysia

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Summary

The occurrence of a case of human rabies in Peninsular Malaysia is reported. Despite the various control measures taken, sporadic cases of rabies have continued to occur in Peninsular Malaysia, especially in the northern states. Clinical awareness of the occurrence of rabies is therefore important and effective post-exposure prophylaxis should be instituted as soon as possible to prevent the possible occurrence of this dreaded disease.

Key words: Rabies, Peninsular Malaysia, diagnosis, prophylaxis.

Introduction

Rabies is an acute infectious disease of the central nervous system which is caused by the rabies virus. This zoonotic disease is communicable to man through the bites of infected animals or through contact with secretions, and is almost invariably fatal.

In Malaysia rabies is a public health problem, mainly along the Malaysian-Thailand border where the disease has been periodically introduced through infected dogs crossing over from Thailand. Dogs appear to be the primary reservoir of rabies in Malaysia and there does not appear to be a significant reservoir of rabies infection in wildlife^{2,3}.

Rabies control in Malaysia is based upon the regulation of importation of dogs from other countries and upon the maintenance of a canine rabies 'immune belt', of 50 to 80 km width, along the Thai border, to prevent the extension of the disease from the north⁴. Dog movement between the immune belt and the rest of Malaysia is strictly regulated. Continual surveillance is maintained throughout Malaysia and prompt measures are taken to suppress any outbreaks of rabies.

Although rabies has been known to occur in Malaysia since 1884⁵, it was only since 1924 that records of human cases have been kept³. Most of these cases occurred in Malaysian states bordering Thailand, which is highly endemic for rabies. A major outbreak of rabies in Province Wellesly and Perak in 1945, and subsequently in Selangor in 1952, prompted a National Rabies Control Programme of compulsory vaccination of all dogs and a rigorous programme of destruction of stray dogs. The success of this control programme resulted in Malaysia being declared rabies-free in April, 1954^{6,7}. Besides Singapore, Malaysia was the only other ASEAN country to be free of rabies. However, soon afterwards small outbreaks and sporadic cases of animal and human rabies once again commenced, and these have continued to occur in the northern states of Perlis, Kedah and Kelantan and also in Selangor.

In this paper, the postmortem laboratory findings from a human case of rabies in the Alor Setar Hospital in Kedah are reported and the currently available preventive measures and diagnostic methods for rabies are discussed.

Clinical Findings and Laboratory Methods

A 7 year old Indian boy was admitted to the Alor Setar General Hospital on 22nd January, 1990. One month prior to admission, he was said to have been bitten on the buttock by a stray 'mad dog' for which he had received toilet and suturing of the wound at the Outpatients Department of the same hospital. The dog that had bitten this patient had not been found. On admission he had fits, twitching of facial muscles, hydrophobia and ascending flaccid paralysis. Consciousness deteriorated into coma and the patient died on 1st February, 1990. A postmortem was performed at the Alor Setar Hospital 4 hours after death and the brain was removed. The right hemisphere was placed in glycerol saline for virological examination. These specimens were sent in ice to the Institute of Medical Research in Kuala Lumpur (IMR). At the Virology Laboratory of the IMR, impression smears were made from the hippocampus, cerebrum, cerebellum and temporal lobe of the left hemisphere of the brain. These smears were examined for specific rabies antigen by the Fluorescent Rabies Antibody Technique. Virus isolation studies in suckling mice were also carried out. The right hemisphere of the brain was examined histologically. Sections were also stained by the Seller's method for Negri bodies.

Results

Virological examination

The impression smears made from the hippocampus, cerebrum, cerebellum and temporal lobe of the human brain were positive for specific rabies antigen by the Fluorescent Rabies Antibody Technique (Fig 1). Virus isolation studies, however, failed to reveal live virus through its multiplication in the suckling mice brain. This was probably the result of the 4 day delay for the brain specimen to reach the virology laboratory and its resultant partial autolysis.

Histological findings

On gross examination, the right hemisphere of the brain showed no abnormality other than slight congestion. Sections were taken from the hippocampus, cerebrum, cerebellum and the temporal lobe.

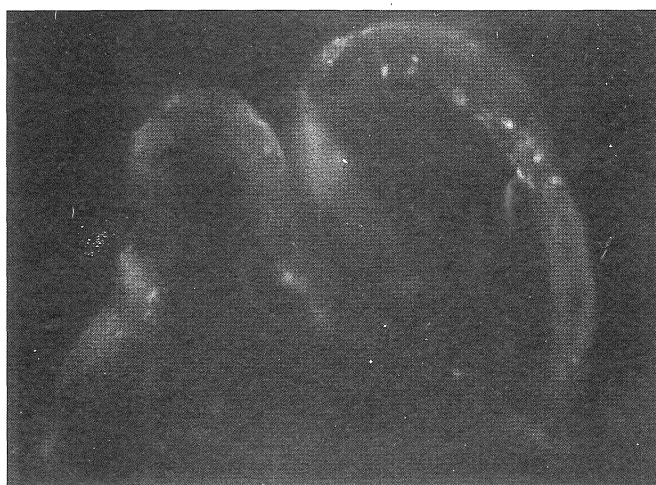


Fig 1: Demonstration of rabies antigen by the Fluorescent Rabies Antibody Technique in an impression smear from the hippocampus.

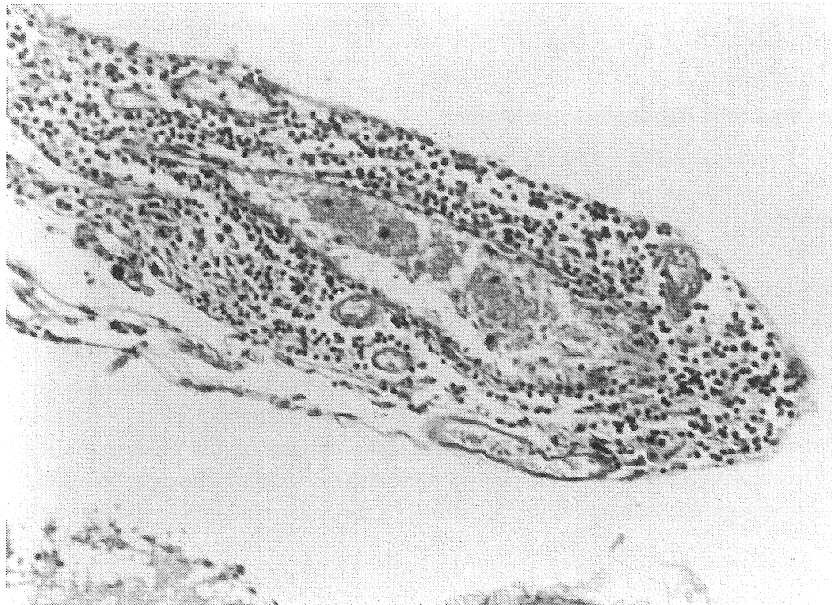


Fig 2: Section of the brain showing leptomeningeal infiltration by chronic inflammatory cells.

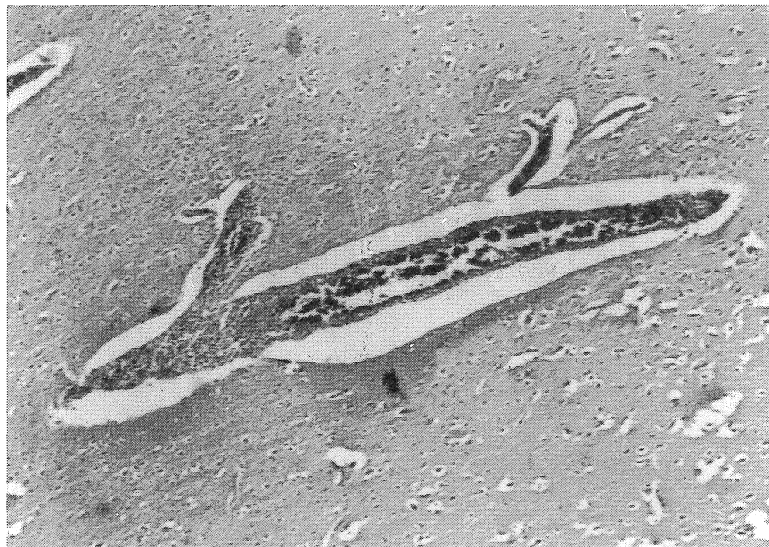


Fig 3: Section of the brain showing perivascular infiltrate of primarily round cells.

Histologically, the sections showed vascular congestion of the meninges with infiltration by lymphocytes, plasma cells and occasional polymorphs (Fig 2). Foci of neuronophagia could also be seen. The sections, especially those from the hippocampus, when stained by the Seller's method, showed largely oval intracytoplasmic acidophilic inclusion bodies containing, within their magenta-red structure, small basophilic inner bodies (Innerkörperchen) staining dark-blue to black. These inclusion bodies were identified as Negri bodies (Fig 4). The histological features are therefore consistent with those of a meningoencephalitis due to rabies.

Discussion

In rabies the incubation period following a bite by a rabid dog is usually 1 to 3 months, but may vary from 9 days to over 8 months⁸. The onset is marked by 2 to 4 days of prodromal symptoms such as moderate fever, headache, malaise, anorexia and sore throat. The earliest specific symptom is an abnormal sensation about the site of the bite wound. Difficulty in swallowing may then occur and this may be followed by painful spasmodic contractions of the throat muscles and general convulsive seizures. Early symptoms of excitation, nervousness, anxiety and apprehension are interspersed with quiet periods when the mental state appears normal. Objective signs include increased reflexes, muscle twitching and a general increase in muscle tone.

Besides the classical encephalitic form, human rabies can also present as the paralytic (Guillain-Barre'-like) variety and 30% of human rabies in Thailand is said to be of this variety⁹. This clinical presentation can be difficult to diagnose unless the attending physicians are aware that rabies can appear clinically as ascending paralysis. Bites inflicted by a single animal can cause both the paralytic and the encephalitic form of human rabies; this observation indicates that the viral strain involved is not the determinant of clinical expression¹⁰.

The diagnosis of human rabies in most centres is made by a clinician who carefully examines and monitors the patient, by a virologist who examines the brain biopsy or by a pathologist at autopsy. Inspiratory spasms are said to be the only reliable form of the disease¹⁰. Clinical laboratory findings have not been very helpful in

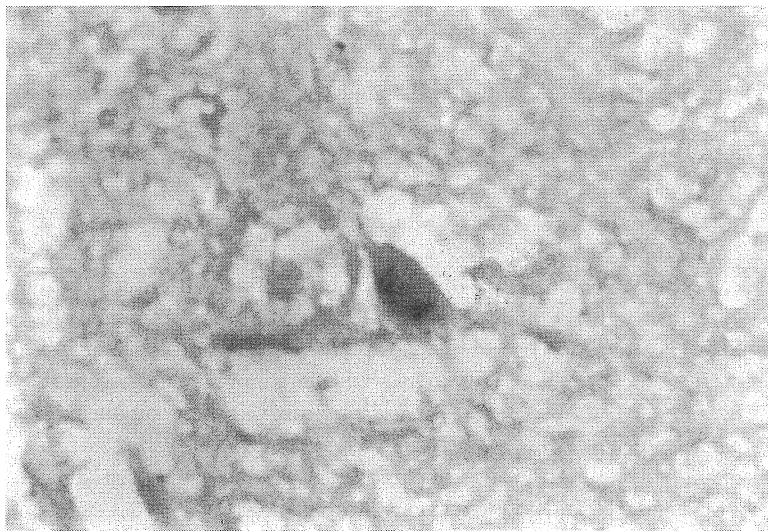


Fig 4: A Negri body shown in a section of the hippocampus stained by Seller's stain.

making an early diagnosis of human rabies. Corneal and salivary impression smears are usually negative on fluorescent antibody testing. Serum antibodies are detected in only a small percentage of cases and rabies antibodies are rarely detected in the cerebrospinal fluid⁹. Immunofluorescent identification of rabies antigen in skin biopsies from the nape of the neck has, however, been reported to be the most useful laboratory test for the diagnosis of rabies in humans and is said to give a positive result in most cases¹¹. Antemortem brain biopsies have also been carried out at some centres and the biopsied specimens may give positive results in a portion of the cases.

The diagnostic procedures taken after death are as carried out in this case. Impression smears of the brain, especially those from the hippocampus, should be examined by the Fluorescent Rabies Antibody Technique, using specific monoclonal antibody. Histological examination of the brain should be carried out and evidence of viral encephalitis and the presence of Negri bodies looked for. Mice inoculation studies should also be carried out and fluorescing rabies viral antigens in the inoculated mice brains can be detected after the third day or the antigens can be detected subsequently in the mice when they die. If a full postmortem examination is not carried out in human cases, bilateral transorbital Silverman needle brain biopsy examined for fluorescent rabies antibody-positive material has been found to be useful⁹. However, negative results in transorbital specimens do not exclude the possibility of rabies.

Recently, there have been reports of studies on the Polymerase Chain Reaction (PCR) technique as a rapid method of diagnosis for rabies, and this technique may be used in the future¹².

Rabies is one of the most terrible and hopeless of all human infections and prevention is the only answer to human infection. The Veterinary Department should continue to maintain strict control measures through their programme of destruction of stray dogs, mass vaccination, licensing of dogs and control of animal importation in addition to a nationwide awareness campaign. However, should rabies in dogs still occur sporadically, humans who are bitten by such dogs should be managed promptly and efficiently by the attending clinicians.

The essential components of rabies post-exposure prophylaxis are local wound treatment and the administration, in most instances, of both human rabies specific immunoglobulin and rabies vaccine¹³. Persons who have been bitten by animals suspected or proven rabid should begin treatment as soon as possible — preferably within 24 hours. Immediate and thorough washing of all bite wounds and scratches with soap and water is an important measure for preventing rabies. In studies of animals, simple local wound cleaning has been shown to markedly reduce the likelihood of rabies^{14,15}. Tetanus prophylaxis and measures to control bacterial infection should be given as indicated. Human rabies immunoglobulin (HRIG) 20 IU/kg body weight should be given; half the dose should be infiltrated around the wound(s) and the rest should be administered intramuscularly in the gluteal area. HRIG should not be administered in the same syringe or into the same anatomical site as the vaccine. Of the vaccines available, the one that has been most rigorously assessed is the human diploid cell vaccine (HDCV). A regimen of five 1 ml doses of HDCV should be given intramuscularly. The first dose of the 5 courses should be given as soon as possible after exposure. Additional doses should be given on days 3, 7, 14 and 28 after the first dose. For adults, the vaccine should be administered intramuscularly in the deltoid area. For children, the anterolateral aspect of the thigh is also acceptable. Studies conducted in the United States by CDC showed that a regimen of 1 dose of HRIG and 5 doses of HDCV over a 28 day period was safe and induced an excellent antibody response in all recipients¹⁶. Rabies immunoglobulin and rabies vaccine should therefore be readily available, at least in hospitals in the northern states of Malaysia. Unavailability may lead to delay in instituting treatment.

Those who have previously received complete vaccination requirements with a cell culture vaccine, or persons who have been vaccinated with other types of vaccines and have had documented rabies antibody titres, should

receive only vaccine, and 2 intramuscular doses (1.0 ml each) of vaccine should be given, one immediately and one 3 days later.

Pre-exposure vaccination should be offered to persons among high risk groups, e.g., certain laboratory workers and animal handlers. Three 1.0 ml intramuscular injections of HDCV should be given on days 0, 7 and 21 or 28. A booster dose of vaccine should be given at intervals (e.g., 2 years) to those at very high risk after testing a serum sample for rabies antibody titre.

A healthy domestic dog that bites a person should be confined and observed for 10 days. If signs suggestive of rabies develop, the animal should be killed and its brain examined for evidence of rabies. Treatment of the patient who was bitten can be discontinued if the dog remains healthy during the 10 day observation period.

Monoclonal antibodies to rabies virus have been developed and have appeared promising in animal experiment¹⁷. These monoclonal antibodies and interferona may prove to be tools in the future for post-exposure prophylaxis.

Should there be a failure of preventive measures and prophylactic treatment and should neurological signs develop in a case of rabies, the outcome appears to invariably be a fatal one. And at that terminal stage all that can be done, other than supportive intensive care, is symptomatic relief of fear, pain and suffering in these patients by suitable medication. This was also our observation in the present case, wherein the patient had neurological symptoms and signs at the time of admission and death was virtually inevitable.

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