An Unusual Case of Human Rabies Thought to be of Chiropteran Origin*

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SUMMARY

On 21 February 1970 a White male patient died in the H. F. Verwoerd Hospital, Pretoria after a 5-day illness diagnosed clinically as rabies. The source of exposure to the disease was reported to be a bat bite sustained approximately 5 weeks earlier. Fluorescent antibody (FA) tests using standard conjugate on the deceased's brain were negative but Negri bodies were found histologically in the Purkinje cells of the cerebellum. A strain of rabies virus not demonstrable with standard FA conjugate was isolated from brain tissue. Specific FA conjugate prepared from this virus revealed the presence of typical rabies fluorescent inclusions in the brain of the deceased.

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Rabies has occurred in Southern Africa since the earliest White settlement and probably before that time. Bantu folklore describes what is probably rabies in ascribing poisonous properties to the saliva of genets (Genetta species).[1] Several outbreaks of rabies due to the introduction of dogs from overseas[2,3] are recorded in veterinary history but it is unlikely that they were responsible for the establishment of the enzootic infection that persists today among the members of the subfamily Viverridae and other feral carnivores over large portions of southern Africa. In 1950 and again in 1961 canine rabies, i.e. direct dog-to-dog transmission without wild life involvement, invaded the Republic of South Africa in the Northern Transvaal and Northern Natal respectively, the source in 1950 being the then Bechuanaland Protectorate and in 1961, Moçambique. Strict control measures and dog immunization programmes have virtually suppressed these outbreaks (Fig. 1).

The transmission of rabies by bats to domestic stock and man was first observed in Brazil[4] in 1908 and in Trinidad[5] in 1924. The bats involved were mostly of the vampire variety but some non-haematophagous bats were found to be infected in the Trinidad outbreak.[6] In 1953 the first case of rabies in an insectivorous bat was described in Florida, USA,[7] and since that time many species of insectivorous bats have been found to be infected in the USA and Canada.[8] Unconfirmed reports of bat-borne rabies have also emanated from Germany,[9] Yugoslavia[10] and Turkey[11] within the last few years.

A number of workers have sought rabies virus among the vast bat population of Africa but although a number of new viruses have been recovered, some apparently closely related to rabies,[12] there is as yet no confirmed case of rabies virus isolation from African bats.

Fig. 1 indicates the present (1970) rabies position and shows the enzootic and epizootic regions at their estimated maximum limits.

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CASE HISTORY

On 20 February 1970 a General Practitioner in the Warmbaths area was called to the farm Tooyskraal some 100 km north and east of Pretoria. The patient, a White adult male aged 31 years was in a highly agitated state, sweating profusely and continuously and exhibited signs of involuntary muscle spasm of neck and back. Examination showed a temperature of 38·3°C, pulse 120/minute and marked exaggeration of all reflexes. More detailed physical examination was impossible as the slightest touch provoked generalized convulsive spasms particularly of face, arms and torso. During these attacks the patient became wild and aggressive in manner.

The patient's illness had commenced about 3 days earlier with headache, vertigo and muscular aches in neck and back. Later continuous sweating developed and involuntary spasms of facial, arm and leg muscles. He also complained of increasing confusion, irritability and aggressiveness. He had difficulty in sleeping and suffered nightmares. He was concerned over a progressive interference in swallowing and felt that this illness was somehow connected with the fact that a bat had bitten him on the lip while he was sleeping about a month earlier.

An attempt to drink caused, as soon as water was taken, a tremendous spasm of mouth and throat muscles preventing swallowing and causing dyspnoea. The spasm subsided after 20 to 30 seconds but was repeated whenever the cup was raised to the mouth.

Valium (2 ml intravenously and 2 ml intramuscularly) was administered and the patient became calmer. He was referred to hospital with a diagnosis of rabies. The same afternoon the patient was admitted to the casualty section of H. F. Verwoerd Hospital in Pretoria. At the time he was tense, anxious and sweating profusely. In addition he was slightly confused and very restless. When coaxed to drink water he cried out in pain and underwent intense spasms of the pharyngeal muscles as well as the upper part of the body and arms. A period of hyperpnoea accompanied by cyanosis was recorded by the Casualty Officer.

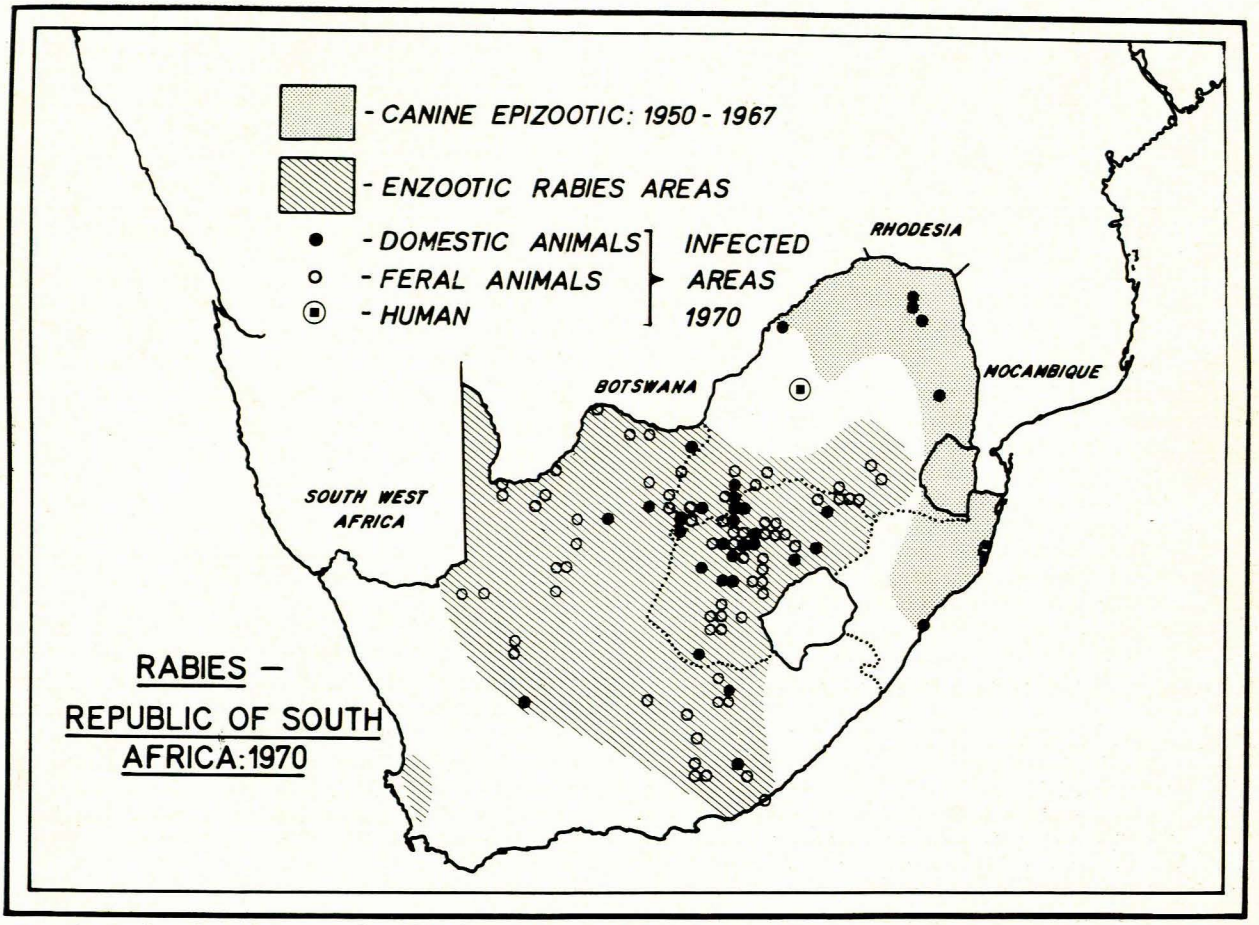

Fig. 1. Confirmed rabies cases for 1970 in relation to infected areas. The human case shown is that referred to in the text.

A barium swallow and chest X-rays showed no abnormality but the patient refused permission for a lumbar puncture.

During the night the patient became increasingly violent and difficult to control. A variety of drugs (Valium, Phenergan, Largactil, paraldehyde and sodium gardenal) was administered with little, and then only temporary, effect. By morning he was 'completely beserk' and frothing at the mouth. He pulled down the Vacoliter bottle and dashed it against the wall and also kicked at his attendants.

Forcible restraint was necessary to administer a sodium pentothal drip to achieve sedation. At this stage a drop of water on the lips provoked intense spasms with respiratory arrest and cyanosis. Spontaneous uncontrollable paroxysms supervened and recurred at ever-decreasing intervals until death occurred from respiratory arrest during a seizure less than 24 hours after admission.

Necropsy Findings

The postmortem examination was carried out on 24 February 1970. The deceased was of normal build, well nourished and, apart from a somewhat shrunken right leg possibly a sequel of poliomyelitis, showed no exterior abnormality.

The brain was slightly congested: the spinal cord appeared macroscopically normal. Trachea and main bronchi contained a little blood-stained foam while the lungs were severely congested and moderately oedematous. Slight atheromatous changes were observed in the coronary vessels and abdominal aorta.

The stomach was empty except for a little mucus, the intestines and mesentery normal. Kidneys, spleen and adrenals exhibited moderate congestion. The bladder was distended with a large quantity of urine.

Histopathologic studies were carried out on the following portions of the central nervous system—ganglion of the fifth cranial nerve, right frontal lobe, right parietal lobe, right occipital lobe, pons, medulla, vermis cerebelli, cerebellum, nucleus dentatus, hippocampus, substantia nigra, basal ganglia, thalamus and corpora mamalaria. Sections were also prepared from various levels of the cervical thoracic, lumbar and sacral spinal cord and cervical dorsal root ganglia.

Histologic abnormalities found consisted of the following:

1. Cerebellum: Small, intracytoplasmic inclusion bodies were observed in numerous Purkinje cells, the number varying from 1 to 3 per cell, and with special staining for inclusion bodies of the central nervous system these were clearly visible and morphologically indistinguishable from Negri bodies. No other abnormality other than congestion was present.

2. Hippocampus: Occasional intracytoplasmic inclusion bodies as described above were also found in the large neurons.

3. Substantia nigra: In sections of the substantia nigra occasional inclusion bodies were also present intracytoplasmically but these were not as convincing as those seen in cerebellum and hippocampus. Congestion and some slight perivascular lymphocytic infiltration were present.

4. The medulla showed lymphocytic perivascular infiltration and occasional small microglial nodules.

5. The thalamic region similarly showed congestion, cellular infiltration and microglial nodules.

6. Sections of the upper and lower cervical spinal cord showed lymphocytic perivascular infiltration, the other descending sections were negative.

7. Cervical dorsal root ganglion sections showed only slight perivascular cellular infiltration.

Virological Examination

Brain tissue from the deceased was brought to the Rabies Diagnostic Unit of the Central Veterinary Investigation Centre and subjected to the fluorescent antibody (FA), histopathological and biological (mouse) tests for rabies. The FA test proved negative. When the positive results of the histopathological examination became known, the FA test was repeated several times with special emphasis on the cerebellar region but all these tests remained negative.

On the tenth day after intracranial inoculation one mouse of the biological test was found dead and others showed signs of ascending paralysis culminating in death on the eleventh (1 mouse) and thirteenth (3 mice) days. From these mice which were also negative to the FA test, but showed occasional Negri bodies on histopathological examination, a virus, assumed to be a hitherto unknown strain of rabies, was isolated. Details of the characteristics of this virus will be published later.

Guinea pig hyperimmune serum prepared by using a beta-propriolactone inactivated antigen and labelled with fluorescein-isothiocyanate has proved entirely specific for this strain of rabies virus for which the name Duvenhage is proposed. Using this conjugate typical rabies-like aggregations are demonstrable in the brain tissue of the deceased thus confirming the initial diagnosis.

DISCUSSION

Despite the large rabies virus reservoir in South Africa rabies in man is infrequent due, to a large extent, to rapid diagnostic techniques in case of human exposure and prompt therapeutic measures. It is very unusual for human cases to occur outside of the recognized enzootic and epizootic areas, and the fact that the subject of this report was resident outside of these areas, and had been for a considerable time, was in itself sufficient to attract attention. Furthermore, careful questioning of the deceased's wife and other intimates revealed no known exposure other than the bat incident described earlier.

As near as can be ascertained the incubation period in this case, assuming the bat bite to have been the source of infection, was a little over 4 weeks and while this is relatively long for an infection site in such close proximity to the brain it is in keeping both with the characteristics of this virus, which shows longer incubation periods than other street strains, and strains of rabies isolated from bats in the USA.

This circumstantial evidence, plus other characteristics of the virus, namely its antigenic and pathogenic peculiarities (to be published), strongly favours a host source not as yet incriminated in rabies transmission in Africa and one in which this virus has been able to develop and adapt free from observation and interference. The known ability of Chiropteran species to produce modified rabies virus strains and their mode of life which keeps them largely isolated from man make them a target for suspicion. Bites from bats are not common in man and most bats are small and have difficulty in inflicting penetrating wounds. It would require a particular set of unusual circumstances such as an infected bat, a penetrating bite wound in a thin, nerve-rich mucous membrane and a failure to seek prompt advice and treatment for chiropteran rabies to manifest itself. It is probable that this case history represents such a manifestation.

CONCLUSIONS

Further investigation into the role of bats in rabies dissemination in Africa is urgently needed. Confirmation of the existence of antigenically different strains of rabies in feral animals could have important influence on the public health aspects of rabies prophylaxis and therapy.

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