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A Case of Rabies in a Child

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Human rabies is an acute viral encephalomyelitis which is ordinarily transmitted to man by the bite of a rabid dog, occasionally by a rabid cat or a wild animal. Characteristic features of the disease are excitation and severe painful spasm of the muscles of the pharynx and larynx. These spasms are stimulated by attempts at swallowing and later even the sight of food or liquids may elicit them, and it is this feature which accounts for the name hydrophobia.

Rabies is a rare disease in Rhodesia, but sporadic cases have always occurred from time to time. Routine anti-rabies immunisation of domestic dogs has greatly reduced this reservoir of infection, but recently this vaccination campaign has not been as successful in the rural areas as before, so that an increase in the number of cases may be expected.

CASE REPORT

The patient, a four-year-old European girl, became ill on 6th June, 1965, when she appeared unusually tired, refused her food and vomited in the evening. When seen by the family doctor in the evening she had a temperature of 102° F. and had signs of mild pharyngitis. She had difficulty in swallowing almost from the onset of her illness and her doctor noted that her respirations tended to be sighing. The difficulty in swallowing was interpreted at first as being due to a sore throat. The following morning she was still feverish and drowsy, and on 9th June she was admitted to the Rusape hospital for her state of drowsiness and inability to drink. She was afebrile on admission and seemed to be suffering from mild diarrhoea. In hospital she became excessively excitable and talkative. She required sedation, but combinations of Largactil and Paraldehyde by injection, together with Phenobarbitone given by stomach tube, did not prove very effective. Attempts to drink fluids were accompanied by excessive frothy salivation

and attempts at swallowing were interrupted by shuddering and frequent stoppages for breathing. On 11th June she was transferred to Salisbury.

Examination revealed an ill child who was hallucinated and delirious. She showed bursts of excessive motor activity accompanied by slight tremor of the hands. Every now and then bubbly froth appeared at the mouth, and this was particularly noticeable when she attempted to drink fluids. No signs of external injury and no foetor hepaticus were found. The pupils were dilated and did not react to light. The tendon reflexes were present, the plantars were flexor and the abdominal muscle reflexes were present. There was no trismus, no guarding of the abdominal muscles, and there was also no palatal paralysis. The rest of the examination was negative.

There was no story of ingestion of poisonous plants or drugs and the parents at first denied the history of a dog bite. On subsequent questioning, however, they recalled that she had been bowled over by a running stray dog one month previously. They had noticed a superficial tooth mark on her face which had not drawn any blood and which was in the nature of a superficial abrasion. In view of the minor nature of the injury the parents had not thought it necessary to obtain advice on the need for immunising the child, though neighbours had remarked on the possibility of the dog being rabid. Unfortunately the animal was not captured and observed.

Special investigations showed the following results: Haemoglobin 15.4 g.—96 per cent., P.C.V. 42 per cent., M.C.H.C. 35 per cent. The white blood count was 17,000, with neutrophils 74 per cent., lymphocytes 19 per cent., monocytes 6 per cent. and eosinophils 1 per cent. The blood glucose level was 140 mg. per cent. and the serum glutamic pyruvic transaminase 18 Frankel units. A blood culture taken on admission proved negative after 10 days' incubation. The cerebrospinal fluid was clear, colourless, with no clot and contained six leucocytes per cm.

The protein was 20 mg. per cent. with Pandy's test for globulin negative, and the culture was sterile.

In hospital her temperature ranged between 98 and 105° F. Her condition deteriorated further and the frothing at the mouth became more noticeable, and several hours later she started vomiting altered blood. Her mental state varied between periods when she was lucid for a short while and periods of delirium and hyper-excitability. Attempts at passing a nasal tube were unsuccessful, the tube being held up by spasm at the level of the posterior nares. Despite the administration of oxygen, intravenous infusions, including hydrocortisone given by this route and antibiotics, her condition progressively deteriorated, and after a period of Cheyne-Stokes breathing she died the following morning, having been comatose over the preceding 12 hours.

The brain was removed at autopsy and sections were examined microscopically. Typical Negri inclusion bodies were seen in areas of the hippocampus (Fig. 1).

PATHOLOGY AND PATHOGENESIS

The virus present in the rabid animal's saliva is introduced into the inflicted wound. Whether or not the patient contracts the disease depends on several factors. The virus is present in the saliva of only 50 per cent. of rabid dogs (Dekaban, 1959). The presence of clothing may prevent the entry of virus into the wound. Early cleansing of the wound may prove effective in removing the infected saliva. The risk of acquiring rabies after being bitten by a rabid animal

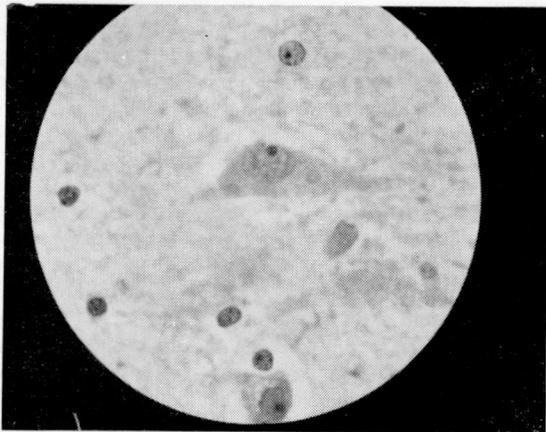


Fig. 1—Photomicrograph showing two Negri bodies in a pyramidal cell. The darker staining nucleus shows degenerative changes.

varies between 8 and 50 per cent (Krugman and Ward, 1964). The disease is more likely to follow bites of the head and neck than those of the lower part of the body.

The incidence of the disease is higher in children than in adults, probably because of increased chances of exposure resulting from their friendliness towards animals and their inability to defend themselves against attack (Krugman and Ward, 1964). However, the risk of contracting fatal rabies following similar bites is higher in children than in adults (Dekaban, 1959). In this case the great risk of an injury in a completely exposed part in a child is well demonstrated. Human to human spread is possible, but only after actual bites (Krugman and Ward, 1964).

Rabies virus has great affinity for nervous tissue. It is said to propagate along the peripheral nerves, spinal cord and brain. The basic lesion consists of damage and degeneration of neurones in the basal ganglia, medulla, pons and mid-brain and in the hippocampal area of the cerebral cortex. Inflammatory reaction consists of perivascular accumulation of mononuclear cells and the presence of glial nodules. The diagnosis is established by the finding of large intracytoplasmic inclusions called Negri bodies in the brain. These are most commonly found in the Purkinje cells and in the large neurones of the hippocampus (Dekaban, 1959). Similar changes may be found in the sympathetic ganglia and dorsal root ganglia of the spinal cord. The salivary glands may show degenerative changes of the acinar cells and neurones; Negri bodies may be found in the latter (Krugman and Ward, 1964).

CLINICAL MANIFESTATIONS

The incubation period is usually between one and two months, but ranges from ten days to a year have been observed. Shorter periods are said to follow lacerations of the head and neck, apparently because of the greater laceration and the larger amount of virus thus introduced rather than on account of the closer proximity to the central nervous system (Nelson, 1959).

The illness may present as in other forms of encephalitis with fever, malaise, drowsiness and behaviour changes. Disturbances of sensation, taking the form of hyperaesthesia, paraesthesia or anaesthesia in the area of the bite or along the course of the involved peripheral nerve may be noted. The disease rapidly progresses to the stage of hyper-excitability, twitching movements and convulsions, delirium and maniacal behaviour

alternating with periods of lethargy. A characteristic feature is the occurrence of violent spasmodic contractions of the muscles of deglutition. These are especially set off by attempting to swallow, but other stimuli like light and touch may provoke them too. Drooling of saliva is another characteristic feature caused by the patient's inability to swallow. Difficulty in swallowing was the first definite sign in this patient, and this was accompanied soon by excessive frothy salivation. Pharyngeal muscle spasm was so marked as to prevent passage of a nasal tube by the fifth day of her illness.

Rabies is invariably a fatal disease, death usually occurring within a week. Periods of responsiveness become less frequent and muscular spasms may give place to paralysis in the later stages of the disease.

Occasionally the clinical picture is that of ascending myelitis with paralysis from the early stages, resembling cases of infective polyneuritis. In other patients the symptoms may be so bizarre as to suggest hysteria; such a case is described by Ridley (1965).

The cerebrospinal fluid is usually normal. The white cell count may show polymorphonucleocytosis, but laboratory investigations are not helpful in establishing a diagnosis.

DIAGNOSIS

In the differential diagnosis tetanus will be considered, and while laryngeal and pharyngeal spasm occur in both diseases, trismus is not seen in rabies. Various other forms of encephalitis and encephalopathy may show behaviour disorders with fluctuations from wild delirium to lucidness, but the spasm of the muscles of deglutition and drooling are not usually seen to such a degree. It was this feature, coupled with the obvious severity of the illness, which excluded a diagnosis of stramonium poisoning or phenothiazine intoxication in this patient. History of an animal bite gives an immediate clue to the diagnosis, but as in this case the information may not be volunteered.

TREATMENT

Treatment can only hope to alleviate suffering and consists mainly of adequate sedation.

Though the risk of acquiring the disease from a patient is very slight, the attending staff should wear gloves and carefully avoid being bitten or getting saliva into abrasions.

The most important aspect is, of course, prevention. Fortunately the virus is present in the

saliva in only about 50 per cent. of rabid dogs, so that the bites from such animals do not invariably result in the disease. The rabid animal secretes the virus for three to five days before the onset of the illness and during the course of the disease, so that observation of the biting animal for a short while will show whether he is rabid or not. If the animal becomes ill or dies, the diagnosis must be confirmed by looking for Negri bodies in the animal's brain. Unfortunately microscopic examination can be negative in 12 per cent. of rabid dogs (Habel, 1957). Therefore complete laboratory investigation includes intracerebral inoculation of emulsions of brain and salivary gland into mice. The mice are sacrificed on the sixth day and their brains examined for Negri bodies. A veterinary diagnosis made on clinical grounds will thus have to be accepted, even though histology is negative. Though 50 per cent. of rabid dogs do not have the virus present in the salivary glands, most people would treat the victim of an animal in whom the presence of Negri bodies or virus was shown in the brain alone. If the animal cannot be captured or shot it may on occasion have to be assumed as rabid, especially in endemic areas.

MANAGEMENT OF THE EXPOSED SUSCEPTIBLE SUBJECT

The management of the patient who has been in contact with a stray or wild animal, or bitten, raises difficult problems. It may be particularly difficult to decide whether or not to start rabies immunisation. There is no doubt that many people have been unnecessarily subjected to this potentially hazardous procedure.

A doctor treating a patient for an animal bite should employ one or more of the following preventative measures: (1) local treatment; (2) rabies vaccine; and (3) rabies hyperimmune serum.

LOCAL TREATMENT

As it has been shown experimentally (Habel, 1957) that rabies virus may be present at the injured site for at least four days, local treatment should be instituted for bites in which there has been a delay before treatment is sought, as well as in those patients seen immediately after exposure. The object is the elimination of residual virus, though this can only be achieved to a limited extent. The wound should be thoroughly washed with soapy water, and the addition of solutions like 1 per cent. Zephiran chloride is useful. Cauterisation with fuming nitric acid is reserved for deep, inaccessible puncture wounds.

Delayed closure of the wound and encouragement of free bleeding is recommended. When rabies hyperimmune serum is available this may be infiltrated into the tissues beneath the wound.

The risk of tetanus and bacterial infection must not be overlooked and appropriate measures must be taken to prevent these complications.

RABIES VACCINE

The dangers of postvaccinal encephalitis have largely been overcome since the Semple vaccine derived from rabbit brain suspension was re-

placed by the use of duck embryo vaccine. With the latter vaccine there is the theoretical risk of reactions occurring in egg-sensitive individuals. One ml. is given subcutaneously once a day for 14 or 21 days, dependent upon the severity of the exposure. Vaccine is administered in an effort to produce immunity before the disease sets in. It can thus only prove effective when the incubation period is not of the very short variety and when it is given soon after exposure.

HYPERIMMUNE RABIES SERUM

This substance is a concentrated horse-serum product which confers passive immunity rapidly.

RECOMMENDATIONS FOR SPECIFIC ANTIRABIES PROPHYLAXIS*

* Modified from Report of the WHO Expert Committee on Rabies.

Exposure	Condition of Animal		Recommended Measures
	At Exposure	During Ten Days' Observation	
I. No lesions on contact II. Licks— (A) Unabraded skin (B) Abraded skin or mucosa III. Bites— (A) Simple exposure (B) Severe exposure (multiple; or face, head or neck bites)	Rabid		None
	Rabid		None
	(a) Healthy	Healthy	None
	(b) Healthy	Clinical signs of rabies	Start vaccine at first signs in animal.
	(c) Clinical signs	Healthy	Start vaccine immediately. Stop if animal is normal on fifth day after exposure.
	(d) Rabid, escaped, killed or unknown		Start vaccine immediately.
	(a) Healthy	Healthy	None
	(b) Healthy	Clinical signs of rabies or proved rabid	Start vaccine at first signs of rabies in animal.
	(c) Signs suggestive of rabies	Healthy	Start vaccine immediately. Stop treatment if animal is normal on fifth day after exposure.*
	(d) Rabid, escaped, killed or unknown; or any bite by wolf, jackal, fox, bat or other wild animal		Start vaccine immediately.
	(a) Healthy	Healthy	Hyperimmune serum immediately. No vaccine as long as animal remains normal.
	(b) Healthy	Clinical signs of rabies or proved rabid	Hyperimmune serum immediately, but start vaccine at first signs of rabies.†
	(c) Signs suggestive of rabies	Healthy	Hyperimmune serum immediately, followed by vaccine. Vaccine may be stopped if animal is normal on fifth day after exposure.
	(d) Rabid, escaped, killed or unknown. Any bite by wild animal		Hyperimmune serum immediately, followed by vaccine.†

* Alternative treatment would be to give hyperimmune serum and not start vaccine as long as animal remained normal.

† Course of vaccine to be followed by booster doses of avian vaccine at 10 and 20 days after last usual dose.

It is of particular value in bites around the head and neck where a short incubation period might be expected. It is given as a single injection, 0.5 ml./kg., and followed by a full course of vaccine. The risk of reactions to horse serum, viz., serum sickness and anaphylaxis, exist.

FACTORS AFFECTING THE MANAGEMENT OF A PERSON BITTEN BY AN ANIMAL

The physician carries a heavy responsibility when deciding whether or not immunisation should be started, and his decision is influenced by several factors.

Geographical Area.—Where the incidence of rabies is known to be high in the area, immunisation will more readily be started than in other parts.

The Biting Animal.—In cases where the animal cannot be captured for observation or destroyed for examination, a knowledge of the likelihood of animals of that species being rabid will influence a decision.

Type of Exposure.—The rabies virus does not invade intact skin, so that simple contact with the animal does not result in the disease. Even a lick on unabraded skin should not constitute a risk.

Site of Exposure.—Bites around the face are more likely to be followed by the disease than bites elsewhere. Similarly, an area unprotected by clothing is more likely to allow entry of the virus.

Age of the Patient.—Children under the age of five appear to be more susceptible than older children and adults, and one would tend to start treatment more readily in such patients.

Re-exposure.—If an individual has been immunised within a previous three-month period he does not require further prophylactic treatment unless the injuries are severe and extensive. If re-exposure occurs within three to six months after previous treatment, two booster doses of vaccine one week apart are recommended. After six months a full course of treatment is required. Expert committees have published guides to post-exposure prophylactic treatment, and Table I is a reproduction of the American Academy of Pediatrics' recommendations (American Academy of Pediatrics, 1957).

It has recently been suggested that routine pre-exposure prophylactic immunisation might

prove feasible in "high-risk" individuals, e.g., veterinary surgeons and people living in areas where rabies is endemic. Two injections of 1 ml. duck-embryo vaccine one month apart, followed by a third injection seven months later, will result in rabies-neutralising antibodies in 80 per cent. of individuals (Veterinary Public Health Notes, 1965). Permanent immunity might be achieved by yearly booster doses. As the antibody response is not 100 per cent., the antibody titre should be determined in people managed in this way. If mild exposure subsequently occurs in individuals in whom rabies antibody has been determined, a single 1 ml. booster dose of vaccine may be given. If exposure is severe the usual post-exposure regime should be followed.

SUMMARY

A case of rabies in a four-year-old child following a superficial bite by a dog is described.

The high risk of facial injuries and the susceptibility of young children to the disease are confirmed.

The importance of direct questioning about animal bites in unusual acute neurological syndromes is stressed.

Specific prophylactic measures and their indications are discussed.

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