

Case Report: Evidence of Rise in Rabies Cases in Southern Malawi – Better Preventative Measures Are Urgently Required

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Abstract

We describe five children who died of clinical rabies in a three month period (September to November 2011) in the Queen Elizabeth Central Hospital. From previous experience and hospital records, this number of cases is higher than expected. We are concerned that difficulty in accessing post-exposure prophylaxis (PEP) rabies vaccine may be partly responsible for this rise. We advocate:

(a) prompt course of active immunisation for all patients with significant exposure to proven or suspected rabid animals. (b) the use of an intradermal immunisation regime that requires a smaller quantity of the vaccine than the intramuscular regime and gives a better antibody response. (c) improved dog rabies control measures

Introduction

Rabies virus is one of the lyssaviruses and causes an acute viral encephalomyelitis that is invariably fatal. Worldwide, there are estimated to be over 10 million human exposures to rabies with approximately 55,000 rabies deaths a year, almost half of which occur in Africa. These pose a significant public health burden with an estimated annual cost of \$583.5 million and deaths from rabies being responsible for an estimated 1.74 million disability-adjusted life years lost each year.¹ Transmission is through the saliva of an infected animal introduced usually via a bite penetrating the skin. Dogs are the most common source, accounting for 96% of human rabies cases.² The virus may also be transmitted by wild animals such as bats, foxes and wolves. The incubation period in humans is generally between 3-8 weeks but is highly variable and has been described from a few days up to several years in rare cases. In contrast, signs of rabies in animals usually develop within 4-7 days.³

There are two main clinical presentations in humans: furious and paralytic rabies. Furious rabies accounts for nearly two-thirds of cases. It is characterised by fever, pain or parasthesia at the site of the bite, fear and apprehension, agitation, aero and hydrophobia involving spasms of the muscles involved in swallowing and late signs of delirium, reduced conscious level and occasionally seizures. Paralytic rabies causes paralysis of the limbs and respiratory muscles. Consciousness is not depressed although aero and hydrophobia can be seen. Death is usually secondary to respiratory and cardiac failure⁴. The hydrophobia can be especially distressing as the patient becomes progressively thirsty and therefore we advocate the use of intravenous fluids in the palliation of these patients.

Case Reports

The following patients presented to Queen Elizabeth Central Hospital, Blantyre between September and November 2011 with clinical rabies encephalopathy:

Case 1: A 9 year old boy, previously fit and well, presented with a two day history of shoulder/neck and abdominal pain and a one day history of difficulty in swallowing. There was a history of a dog-bite 6 months previously on the right

hand. On admission we were told that he had received a full course of post-exposure rabies vaccine but it later transpired that although his mother had taken him to the local health centre for treatment, there was no vaccine available. Although he demonstrated laryngeal spasms on drinking water i.e. hydrophobia, there was no aerophobia and he was not agitated. There was no further deterioration during the two-day admission and so following discussion with his family he was discharged home with instructions to return if he became more unwell. He returned after seven days with obvious signs of rabies encephalitis including agitation, drooling, hydrophobia and aerophobia. He was started on a diazepam infusion and intravenous fluids and died less than 24 hours after this second admission.

Case 2: A 9 year old boy with a history of cerebral palsy following meningitis at six months of age presented with new onset lower limb flaccid paralysis for one day and signs of acute confusion, hydrophobia and aerophobia. There was history of a dog bite 6 months previously. He was seen by the palliative care team and started on a diazepam infusion and intravenous fluids. He became increasingly more agitated and confused and died on day 5 of admission.

Case 3: A 14 year old girl, previously fit and well, presented with a two day history of painful right arm followed by a one day history of acute agitation and a painful throat. She had been bitten on her right arm by a dog 4 months previously. The dog had been killed at the time of the bite. She had presented to her local hospital but as there were inadequate ampoules of rabies vaccine, this was shared out between a total of three patients and she only received 3 intramuscular injections. On initial examination she was mildly agitated but could be settled. She became increasingly confused with signs of hydrophobia and excessive salivation. She was started on a diazepam infusion and intravenous fluids and died 8 hours following admission.

Case 4: A 3 year old boy presented with a two day history of fever and one day history of agitation. On examination he had frank signs of rabies encephalitis i.e. obvious hydrophobia and aerophobia. There was no history of dog-bite and on examination no dog-bite scar. He deteriorated rapidly and died 3 hours after admission. Despite lack of history of exposure, his clinical presentation was agreed by more than two experienced health professionals to be consistent with rabies infection. It was postulated that he may have been licked in the mouth and nose by a rabid dog as at his young age we would expect a mother to know if he had been bitten.

Case 5: A 6 year old boy presented with a 12 hour history of priapism. A sickle cell solubility test was negative. He was started on analgesia, antibiotics and intravenous fluids. He was reviewed by the surgeons but his priapism had started to resolve and a surgical intervention was not required. On day 3 of admission, the patient developed confusion, hydrophobia and aerophobia. His mother reported a history of a dog bite a month ago. He had not received anti-rabies vaccine. He was started on a diazepam infusion and died the next day.

Discussion

The estimated normal incidence of rabies seen in the paediatric department at Queen Elizabeth Central Hospital is approximately five cases/year. In the last year we have recorded a total of 12 clinical cases of rabies in children, 9 of whom have presented since July 2011 i.e. in a 5 month period. The cases we have seen are likely to represent a much larger overall number of rabies cases in Southern Malawi as it has been demonstrated that current reporting systems in Africa significantly under-estimate true incidence⁵. Active surveillance in Tanzania found up to a 100-fold increase of rabies deaths when compared to official reported cases⁶. Similar rates have been estimated throughout Africa.¹ We also know that some patients with rabies infection in Malawi are misdiagnosed as other infections such as cerebral malaria⁷. Diagnosing paralytic rabies clinically may be particularly difficult. The paediatric population is most at risk with 40% of PEP (Post Exposure Prophylaxis) vaccine being given to children aged 5-14 years⁹. Also children tend to be bitten more frequently on the head, face and neck which carries the greatest risk of rabies transmission.^{1,6,10}

The most effective and cost-effective strategy of reducing rabies incidence is the control of dog populations and mass rabies vaccination of dogs^{2,6}. This needs consistent advocacy in countries such as Malawi where rabies is endemic. Evidence shows that mass vaccination of domestic dogs within Africa is feasible and cost-effective in preventing human rabies cases¹¹. The rise in cases suggests that dog control measures are inadequate.

All clinical cases of human rabies represent either a failure to recognise the exposure to a rabid dog and/or absent or inadequate PEP which if administered correctly is highly effective at preventing rabies infection¹². From experience within our own institution and reports from local health centres, rabies vaccine is often not available, or very difficult to access, when patients present with a history of dog bite. One of our cases failed to obtain vaccine despite visiting the local health centre, and another child received an incomplete course of vaccine. It is unacceptable that children are succumbing to a devastating and fatal disease when the risk has been identified but an effective preventative treatment has failed to be administered.

Post-Exposure Prophylaxis

All patients with significant exposure to suspected rabies should start rabies PEP as soon as possible. Exposure includes a bite breaking the skin but also saliva in contact with mucous membranes or a previous skin lesion where the skin barrier has been disrupted (Table 1). Unprovoked bites from an agitated animal (most commonly a dog) are obviously a high risk but the animal may also be paralysed or, in the case of wild animals, be unusually tame. If in doubt, treatment should be started immediately and discontinued if the animal is still healthy after 10 days. While it may be necessary to provide a vet's certificate confirming clinical rabies infection of the animal in order to continue the full course of post-exposure vaccination, this should not delay initiation of treatment. If the animal cannot be identified, the full course must be given. Current post-exposure treatment includes immediate good irrigation of the wound with soap and water and the application of iodine. The wound should not be sutured if possible. Bacterial infection should be treated with antibiotics and tetanus immunisation given if

appropriate. Rabies immunoglobulin is recommended if the bite is high risk but is currently unavailable in Malawi and most of the developing world. Active immunisation with rabies vaccine should be started as soon as possible after the exposure. There are a number of PEP schedules approved by WHO using concentrated and purified cell culture (CCV) or embryonated egg based (EBV) vaccines. Nerve tissue vaccines are no longer recommended.⁸ The most commonly used regime is the Essen 5 intramuscular (IM) injections of one ampoule (0.5ml or 1ml depending on type of vaccine) given into the deltoid muscle or anterolateral thigh on days 0,3,7,14 and 28.³ However there is good evidence to support the use of intradermal (ID) regimes which use sixty percent less vaccine per course compared to IM regimes as each ID injection uses only 0.1ml of vaccine^{13,14}. If ID injections are given, vials can be shared between patients although once reconstituted the vaccine must be used within 6-8 hours. Even taking into account potential vaccine wastage for health centres with few patients requiring PEP, ID regimes are estimated to cost two-thirds less than IM regimes.² ID regimes have also been shown to have as much, if not more, effective immunogenicity as IM regimens and have been used successfully in countries such as Thailand and Sri Lanka as the primary PEP regime.² The ID regime currently recommended by WHO is the 2-site regimen¹⁵ (updated Thai Red Cross regimen) which involves giving two 0.1ml intradermal injections at two sites (deltoid and thigh) on days 0,3,7 and 28. The additional dose given on day 90 was dropped following evidence of efficacy without this additional booster¹⁶. More recently, a 4-site ID regimen has been shown to be as immunogenic as current ID regimens¹³ (4 injections on day 0, 2 injections on day 7 and 28 and an optional booster dose on day 90), and a further 1-week regimen (4 ID injections on days 0,3 and 7) has also been developed. Both these latter regimens are advantageous in reducing the number of clinic attendances and thereby improving compliance and reducing vaccine waste but are not yet approved by WHO. Completing the full course of any rabies vaccine schedule is essential in ensuring full protection against the infection and patients and guardians should be counselled regarding this; almost ten per cent of human rabies cases in India had received incomplete PEP vaccination¹⁸, while a study conducted in the Ivory Coast found 47% of patients started on PEP failed to complete the course of injections¹⁹.

Our current recommendations for rabies PEP is summarised in Figure 1. Intradermal injections should be given with an insulin or Mantoux needle and the injection should raise a papule in the skin. If the vaccine is given subcutaneously by mistake, the dose should be repeated.

Conclusion

We have seen an increased incidence of human rabies infection in children presenting to the QECH with over double the number of cases we would normally expect to see in a one-year period. This is likely to significantly under-represent the overall incidence of rabies cases in Southern Malawi and so is of significant concern. The most likely causes of this rise are inadequate supply of anti-rabies vaccine and inadequate dog-control measures. Intradermal vaccine regimens are as efficacious as intramuscular regimens and will lead to substantial cost savings and use of less vaccine. This is particularly pertinent in the current setting where rabies vaccine is in short supply worldwide and we would strongly advocate the use of ID regimens. This,

together with the recognition of patients at risk of rabies infection, good wound care and stressing the importance of completing the vaccine course requires ongoing education and support within the medical community. In addition, we call on the responsible government agencies in Malawi to introduce mass dog vaccination campaigns. Taking these steps, combined with ongoing public awareness of the problem should result in the prevention of this devastating illness.

Risk	Definition	Treatment
Category 1 (no exposure)	Touching/feeding of animal: licks on intact skin	None if history is reliable
Category 2 (moderate exposure)	Nibbling uncovered skin Minor scratches or abrasion without bleeding	Administer vaccine immediately Stop PEP if animal healthy throughout observation (10 days). If dog cannot be observed then complete vaccination course
Category 3 (severe exposure)	Single/multiple transdermal bites/scratches Contamination of mucus membranes with saliva (licks); licks on broken skin	Rabies immunoglobulin if available is injected around the bite Administer rabies vaccine immediately Stop PEP if animal healthy throughout observation (10 days). If dog cannot be observed then complete vaccination course.

Table 1: Adapted from WHO guide to Rabies Post-Exposure Prophylaxis⁷

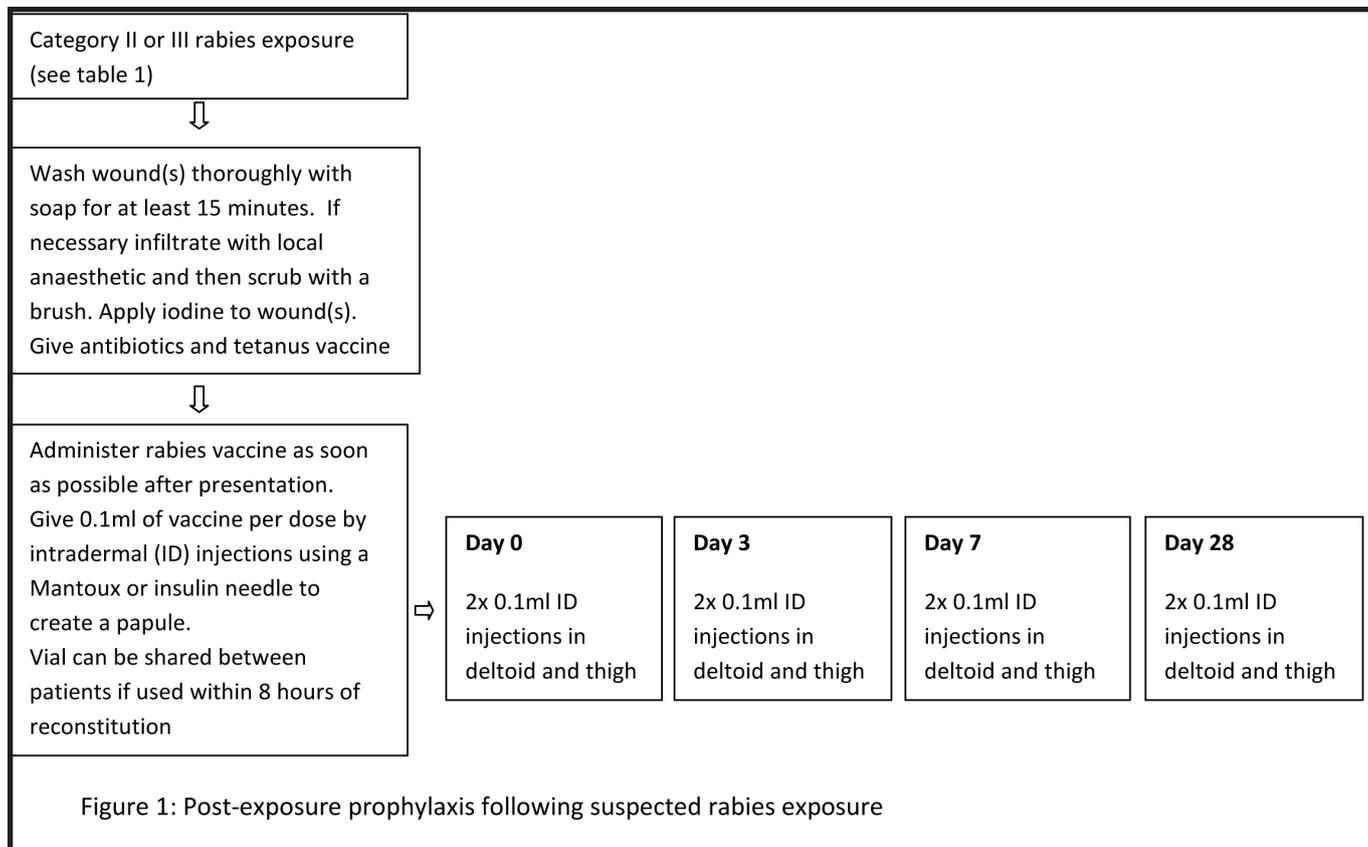


Figure 1: Post-exposure prophylaxis following suspected rabies exposure

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