Pup Vaccination Practices in India Leave People to the Risk of Rabies

—Lessons from Investigation of Rabies Deaths Due to Scratch/Bite by Pups in Remote Hilly Villages of Himachal Pradesh, India

Omesh Kumar Bharti[1*], Vidya Ramachandran[2], Sood Rajesh Kumar[3], Archana Phull[4]

[1]Municipal Corporation, Shimla, India; [2]National Institute of Epidemiology, Chennai, India; [3]Epidemiologist, Kangra at Dharamshala, India; [4]Daily Post, Shimla, India.
Email: [*]bhartiomesh@yahoo.com

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ABSTRACT

Rabies, a zoonotic disease, kills 55,000 persons every year globally and 20,000 persons in India. Two years back, we learnt of two deaths due to Rabies in remote village *Shiv Shankar Garh* of Arki block of District Solan and decided to investigate the deaths. Method: A rapid response team was constituted to investigate the deaths. We interviewed the villagers & family to conduct verbal autopsy. A line list of entire population of village and household contacts of the patients, who died, were made along with the line list of dogs and cattle. Results & Discussion: A-month-old stray pup brought home by the family and had caused an abrasion with its toes on the hands of both the deceased on June 2, 2011 while playing. The lady developed paralysis of the arm on July 3, 2011 and 3 days later developed symptoms of hydrophobia. She died on July 9, 2011. Her son had developed hydrophobia 10 days after that and died on July 19, 2011. Assumption that bite or abrasion by a small pup of one month cannot be fatal proved otherwise. Lack of awareness regarding the fatality of even a scratch and lack of knowledge regarding local treatment of the wound & vaccination of both human and pups, were the main reasons for the deaths. While such incidents keep on happening, and the veterinarians in India are refusing to vaccinate pups before three months of age, as pups may not develop immunity before that age, leaving unsuspecting people to the risk of rabies. Conclusions: Humans can be exposed to rabies even by pups below 3 months of age. Recommendation: Pup vaccination schedule in rabies endemic countries like India need revision. Veterinarians and public health experts need to strongly consider vaccinating pups at first contact with humans even if they are less than 3 months of age. A booster to the pup can be given at three months of age with subsequent yearly boosters.

KEYWORDS

Rabies; Pup Scratch; Pup Vaccination

1. Introduction

Rabies, a zoonotic disease, kills 55,000 persons every year globally and 20,000 persons in India [1]. Deaths due to rabies are responsible for 1.74 million DALYs lost each year. The annual estimated cost of rabies is USD 583.5 million [1].

In India, the animal bite incidence rate is 17.4 million bites every year. The frequency of animal bite is 1 every 2 seconds and that of death is 1 in 30 minutes. The annual medicinal cost (vaccines + other drugs) for treatment of animal bite is INR 2 billion (4.4 million USD) and annual man days lost due to animal bite is INR 38 million [2]. Two years back, we learnt of two deaths due to Rabies in remote village Shiv Shankar Garh of Arki block of District Solan and decided to investigate the deaths.

[*]Corresponding author.

2. Methods

A rapid response team was constituted to investigate the deaths. We interviewed the villagers of Shiv Shankar Garh & family members to conduct verbal autopsy and to understand the cause of death along with symptoms A line list of entire population of village and household contacts of the patients, who died, was made along with the line list of dogs and cattle.

We organised focus group discussion on rabies vaccination schedule with veterinarians and why the pups are not vaccinated before 3 months of age/at first contact with humans. A literature review was done to know/verify the facts. The diagnosis of rabies was made based on typical sign/symptoms of rabies in Humans like paresis/aerophobia/hydrophobia. Both the pups died after brief illness and the patients died after 4 - 6 weeks of either bitten by pups or having a scratch from them, we took 4 - 6 weeks incubation period as consistent with that of rabies.

3. Results

A month old stray pup had caused an abrasion with its toes on the hands of both the deceased on June 2, 2011 while feeding/playing with stray pup. The lady developed paralysis of the arm on July 3, 2011 and 3 days later developed symptoms of hydrophobia. She died on July 9, 2011. The boy developed hydrophobia 10 days after that and died on July 19, 2011.

Death of a woman aged 22 years on July 9, 2011 and that of 14 years old male patient in the same household on July 19, 2011 was confirmed clinically as due to rabies. 24 potential contacts were immunized with intra-dermal anti-rabies vaccine. Two dogs were vaccinated and villagers were requested to vaccinate all the 33 cattle heads listed in the village. Active case search for more cases among houses in the neighborhood that had pups was carried out but none had any history of scratch/bite by the deceased pups.

Last year (April 2012) a 62 years old woman of village Panjgaain in District Bilaspur was referred to medical college Shimla and investigated by the author for cause and symptoms of rabies. She was bitten by a two month old stray pup in her right leg, developed aerophobia and hydrophobia and died of rabies within a month of bite by the pup. Focus group discussion with veterinarians in Himachal, India, revealed the reasons for not vaccinating pups below 3 months of age as: Maternal antibodies interfere with the rabies vaccine given to pups before 3 months of age, the immune system of pups is not developed before 3 months of age for a good immune response and CDC guidelines for pup vaccination are being followed.

4. Literature Review and Discussion

Similar case of rabies by pup was reported by "Mail Online" [3] on November 2012, that Saranjit Ubhi, 58, died in UK from rabies after puppy bite in India, the first Brit. killed by the disease in 7 yrs in UK.

Though CDC guidelines say that "Vaccination of dogs, ferrets, and livestock can be started at no sooner than three months of age [4], yet at the same time emphasize that "Titers do not directly correlate with protection because other immunologic factors also play a role in preventing rabies, and the ability to measure and interpret those other factors are not well developed. Therefore, evidence of circulating rabies virus antibodies should not be used as a substitute for current vaccination in managing rabies exposures or determining the need for booster vaccinations in animals [4].

In another study it was found that low level of maternal antibodies in neonates may be insufficient to prevent a rabies infection, because only 26% of puppies had neutralizing (maternal) antibodies titers greater or equal to 0.5 IU/ml at day 0. One month after the first vaccination, puppies that showed titers >0.5 IU/ml at day 0, had a significantly higher neutralizing titers ($t = 2.68$, $df = 23$, $p = 0.011$) [5].

In a study conducted near Tunis during mass vaccination campaigns, 301 dogs, 16% of them below 3 months of age, were vaccinated with 1ml SQ at day 0 and again 1 year later. The study did not show any evidence of interference from maternally derived antibodies (MDA). Puppies with MDA actually had higher titer 1 month after 1st vaccination. Conclusions of Seghaier *et al*., 1999. "Despite the presence of maternal antibodies, puppies and young dogs responded to vaccination" [6]. No statistical difference was observed in the levels of antibodies to rabies in puppies at months 7, 12, and 13, regardless of the presence of maternal antibodies at day 0. Maternal antibodies did not hamper a rapid antibody response shortly after vaccination (1 month). This study confirmed that the vaccination of very young dogs (even before 3 months of age) can induce antibodies even when these dogs have maternal antibodies.

The serological response of puppies from Nigeria to live Flury low egg passage (LEP) rabies vaccine was determined. Two sets of puppies were used: one set from rabies-vaccinated bitches and another set from non-vaccinated bitches. Puppies were vaccinated intramuscularly with Flury LEP strain rabies vaccine and serially bled from the 4th week to the 30th week. Serum rabies virus neutralizing antibodies (VNA) were measured by a modified rapid fluorescent focus inhibition test (RFFIT). Puppies from non-vaccinated bitches responded well to vaccination after the 4th week and through to the 10th week of age, showing a progressive increase in VNA. In con-

trast, puppies from vaccinated bitches responded well to rabies vaccination only at 10 weeks of age, although detectable maternal rabies VNA and rabies anti-ribonucleoprotein (RNP) antibodies had decreased by 6 weeks *post partum* [7].

The WSAVA Vaccination Guidelines Group (VGG) has defined core vaccines which all dogs and cats, regardless of circumstances, should receive. In areas of the world where rabies virus infection is endemic, vaccination against this agent should be considered core for both species, even if there is no legal requirement for routine vaccination The VGG recognizes that maternally derived antibody (MDA) significantly interferes with the efficacy of most current core vaccines administered to pups and kittens in early life. As the level of MDA varies significantly among litters, the VGG recommends the administration of three vaccine doses to pups and kittens, with the final dose of these being delivered at 14 - 16 weeks of age or above [8]. The product manual of widely used vaccine in dogs in India [9] does not prohibit its use before three months of age, advising a booster in such cases at three months of age. "The Merck Veterinary Manual" (July 2011) advocates initial vaccination at 6 - 8 weeks followed by additional vaccination at 3-wk intervals until the animal is 4 - 5 months old. After this, most vaccines are given annually [10].

5. Conclusions

Popular assumption that bite or scratch from a small pup of one or two months cannot be fatal and cannot transmit rabies, proved otherwise. Lack of awareness regarding the fatality of even a scratch and lack of knowledge about local treatment of the wound & vaccination of human as well as puppies were the main reasons for the deaths. Humans can be exposed to rabies even by pups below 3 months of age. While such incidents keep on happening, and the veterinarians are refusing to vaccinate pups before three months of age because of the reasons described earlier.

Therefore, the traditional logic of veterinarians does not hold good as vaccine manufacturers and the scientific evidence support that pups can be vaccinated at 6 - 8 weeks and even at 2 wks, which is more relevant in rabies endemic countries like India where stray pups are picked up for rearing by the villagers, especially in remote villages.

6. Recommendations

We recommend that pup vaccination guidelines for rabies endemic countries like India be revised. Keeping in view the human rabies deaths caused by the pups in India, and serological evidence in the literature, we recommend that pups from stray bitches should be vaccinated against rabies as soon as they are brought home for rearing followed by booster at 3 months of age and yearly thereafter. Pups by the immunized bitches should also be given first shot of rabies vaccination at 6 - 8 weeks and then boosters at 3 months and yearly thereafter.

A strong IEC (Information, Education and Communication) campaign to educate people that even a scratch/bite by pup below three months of age can cause rabies, especially if pup is from a stray bitch, can help save lives. An IEC to educate veterinarians and public health experts in India to strongly consider vaccinating pups at first contact with humans can go a long way to contain rabies deaths. Later a booster to the pup can be given at three months of age with subsequent yearly boosters. Studies need to be done to make pup vaccination more potent to enable people vaccinate pups at birth or at first contact with humans.

We call for establishing effective rabies surveillance system as there is under-reporting of rabies cases in developing countries because lab confirmation is not feasible or easy, therefore clinical definition need to be adopted to track rabies cases as aerophobia/hydrophobia in humans are typical due to rabies. Some of these cases can be confirmed by lab later.

7. Limitations

We could not lab confirm the diagnosis of rabies in patients due to lack of facility nearby. In India, no data of rabies, specifically due to pup bite or scratch is available.

Authors Contribution

The corresponding author originally investigated the deaths and went to find out the reasons for that. The other authors helped in literature review and writing of the manuscript in perspective.

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