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Spontaneous Rabies in a Stray Bitch after Parturition Induced Immunosuppression

—Investigating an Impending Outbreak of Rabies with One Health Approach

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Abstract

Background: Rabies is endemic in India and every half an hour a person dies of this dreaded disease. Stray roaming dogs, mostly unvaccinated, are most dangerous host in spread of rabies in India and in our state of Himachal Pradesh. Timely prophylaxis is the only method to save animal bite victims, including that of rabid dog bite patients. **Objectives:** Objective of this study was to investigate an impending outbreak of rabies in Shimla town in the absence of life saving rabies immunoglobulins (RIGs) in the market, and to know the source of infection by using one health approach and using epidemiological tools. **Methods:** On April 7, 2015, there was a sudden surge in cases of suspected rabid dog bites. Impending rabies outbreak was suspected as there were no RIGs available in the market. A rapid Response Team (RRT) consisting of the author, veterinary doctor, dog squad of Municipal Corporation (MC) Shimla along with the vehicles to impound rabid dogs was constituted to investigate the terror spread by two rabid dogs on biting spree in the Shimla Municipality. **Results:** A total of 18 people were bitten by suspected rabid dogs within three days period. A black bitch and a brown dog, on the identity of affected people, were captured by the dog squad of Municipality next day on April 8, 2015 and taken to Dog Sterilization Centre, Animal Birth Control (ABC) programme, MC Shimla for observation. The most furious Black bitch died of clinically confirmed symptoms of furious rabies after three days. The second rabid dog, brown in color, died after a month of observation due to paralytic dumb rabies. The brain of the brown dog was extracted for Fluorescent Antibody Testing (FAT) at central research Institute (CRI)

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Kasauli and was found to be positive for FAT. Follow up of patients was 100% by house to house visit and over telephone and no casualty was reported. Conclusion: While we were working on hypothesis of rabid dogs getting the infection from nearby forest about 8 - 10 KM away but on follow up of the patients, they reported that both the dog and bitch used to stay in the compound of their colony since the bitch was pregnant and there was no history of the bitch moving for away to forests neither any outside dog which was seen near them in the compound. This led us to think of other causes of what must had happened to the bitch that caused her to be rabid as for the past 9 years we had observed bitches becoming rabid after litter birth (Whelping) and making their pups rabid due to licking. Since the carrier state for rabies virus in bitches/dogs is known and a state of immunosuppression after whelping/parturition is also known, therefore there is a possibility of latent rabies virus getting activated due to immunosuppression after litter birth and it is thought to be as one of the probable causes of black bitch getting rabid and inflicting the infection to accompanying brown dog. We need to do further studies to ascertain this phenomenon before coming to a definite conclusion and suspect such a possibility in case a dam suddenly becomes rabid among a pack of stray dogs in rabies endemic countries like ours.

Keywords

Human Rabies, Dog Rabies, Rabies Outbreak, Local Rabies Immunoglobulins, Anti Rabies Vaccination, Immunosuppression, FAT Testing, ONE Health

1. Introduction

Rabies is a dreaded disease and an estimated 55,000 people die of rabies every year and out of that 31,000 deaths are reported from the Asian continent. About 20,000 deaths are reported from India, *i.e.* one death every half an hour. Animal bite incidence rate is 17.4 million bites every year. Annual medicinal (vaccines + other drugs) cost for animal bite treatment is \$4 Million (2003) [1]. Stray roaming dogs, mostly unvaccinated, are most dangerous host in spread of rabies in India and in our state of Himachal Pradesh. Timely prophylaxis is the only method to save an animal bite victim including that of rabid dog bites.

2. Background

The state of Himachal Pradesh in India is in the North bordering China and is predominantly rural and hilly. Villages and towns are near forests, where wild reservoirs of rabies exist. Shimla is the capital of Himachal Pradesh and an international tourist destination with a population of 0.168 Million. Shimla municipality has ever increasing incident of dog and monkey bites. While in 2013, the number of patients reported at our Anti Rabies Clinic and Research Centre (ARC & RC) at DDU Hospital for post exposure prophylaxis (PEP) were 1168, in 2014 the number of patients reported were 2042. The population of dogs has increased to five folds in last 15 years since no culling is done now. For the last more than 15 years, no outbreak like situation was reported in the Municipality although some incidents of suspected rabid dog bites were reported by the patients but could not be investigated due to lack of co-ordination between Health and Veterinary departments. Last year an effort was made to have this much needed co-ordination by the corresponding author who was then posted as Corporation Health Officer MC Shimla.

2.1. Objectives

Objective of this study was to investigate an impending outbreak of rabies in Shimla town in the absence of RIGs in the market using one health approach and to know the source of infection using epidemiological tools.

2.2. Methods

On April 7, 2015, suddenly there was a surge in cases of suspected rabid dog bites, 15 cases reported for treatment from two adjoining localities bitten by two different dogs in the same ward of Shimla Municipality. An

outbreak of impending rabies was suspected in the absence of life saving RIGs in the market. A rapid Response Team (RRT) consisting of the author, Veterinary Doctor, Dog squad of MC Shimla along with the vehicles was constituted to investigate the terror spread by two rabid dogs in the municipality.

In order to determine the existence of an outbreak we collected data related to suspected dog bite cases from ARC & RC for previous years. We also collected information related to similar episodes in the past from the residents. The patients identified the color of the biting dogs and we confirmed the diagnosis of rabid dogs from the history by patients bitten by these dogs, their behaviour, expert opinion of Municipality veterinary doctor who observed them after capture and lastly by sending the brain sample of one of the dogs for lab confirmation to CRI Kasauli.

We defined a case as any person with history of suspected rabid dog bite in and around Kasumpti locality from April 6, 2015 to April 8, 2015. We searched the cases in other hospitals and the locality so that no one is left without PEP. A patient that was bitten by suspected rabid dog and went for treatment to a private hospital came for RIGs on day 3 to our ARC & RC. We also enquired of any change in surveillance or any population moment especially that of dogs in the locality.

We hypothesised that the outbreak could be due to two rabid dogs in Kasumpti locality in the city. We tested the hypothesis by trawling questionnaire on exposures including asking the affected patients if they have seen such dogs before. We could draw conclusions that both the black bitch and brown dog were residing in Kasumpti area and were stray kept as pets in the locality. Black bitch, that suddenly became furious, was having four pups of two and a half month old and ate all of them alive and attacked the household child nearby and then furiously attacked the passersby. The brown dog involved was probably bitten by black bitch on the nape of the neck as described by the residents. The history of movement of these rabid dogs was also reported by the patients from one area to another after they became rabid. The black bitch moved in and around Kasumpti locality area but the brown dog moved from Kasumpti area to Vikasnagar and then to Devnagar which are located at a distance of about 2 Km.

3. Results

We searched the records of the ARC & RC for the previous year and found that dogbite cases were in access this year than last year. Also none of the cases of dog bite last year had history of suspected rabid dog bite [2] while within three days 18 people were bitten by suspected rabid dogs 15 of them on same day in same locality on April 7, 2015, clearly showing a situation of outbreak.

A total of 18 patients were bitten by suspected rabid dogs. The incidence of suspected rabid dogbite is depicted in **Table 1**.

All the patients, except one, reported for treatment at ARC & RC, DDU Hospital Shimla within 24 hrs and were given thorough wound wash with soap and water alongwith local Betadine. Written informed consent was taken from the patients regarding local infiltration of RIGs. One patient who had gone to a reputed private hospital came to our clinic on Day 3 for RIG. We gave them ID rabies vaccination as per Modified Thai Schedule of intra-dermal anti-rabies vaccination *i.e.* 2-2-2-0-2. Only local RIG were infiltrated in and around the wounds [3] sourced from CRI Kasauli, as RIG were not available in the market to follow the WHO recommendations of using RIG based on calculations depending on the weight of the patient [4].

A huge outcry was in the media as the dogs were on biting spree in a VIP locality of the city. The higher authorities pressed into service the dog squad of MC Shimla working for Animal Birth Control (ABC) and after great difficulty cornered the suspected rabid dogs, black and brown and captured them for observation at Animal Birth Control Centre (ABC) near Tutikandi on April 8, 2015. The black rabid bitch was furious and died due to clinical symptoms of furious rabies after 3 days of isolation as confirmed by the observing veterinarian. The brown dog was lethargic and was given anti-rabies injections till 28th day while it started showing paralytic symptom and had left feeding few days before it died. The brain of the brown dog was extracted and sent to CRI lab at Kasauli for confirmation of rabies as it was not appearing to be rabid. CRI Lab confirmed the dog to be Rabid (FAT Positive) as conveyed by their written report dated May 12, 2015.

All the patients bitten by both Black and Brown dogs were periodically followed for six months, which is more than the longest incubation period known in Himachal [5], by house to house visit and telephonically. Minimum dose of RIG given locally in the bite wound was 0.5 ml and maximum dose given was 6.5 ml and none of the dosage was more than that required based on body weight (**Table 1**). 13 out of 18 patients bitten

Table 1. Age and sex distribution of 18 exposed patients in Shimla Municipality bitten by confirmed rabid dogs given IDRV and local RIGs in the wound only.

S. No.	Age in yrs	Sex	Site of wound (s)	Wt in kg	RIGs required as per body wt as recommended by the WHO	Actual RIGs in ml given locally in the wound	Dog colour
1	9	M	Both legs	32		4.5 ml	Black
2	25	M	Rt leg	45		0.5 ml	Black
3	12	M	Lt. leg	29		2.5 ml	Black
4	25	F	Rt leg	35		4.0 ml	Black
5	50	M	Rt. Leg	75		2.0 ml	Brown
6	25	F	Rt. Thigh	50		1.0 ml	Brown
7	17	M	Rt. Foot/leg	48		2.0 ml	Black
8	41	M	Rt.leg	98		6.0 ml	Brown
9	16	F	Rt.leg	56		0.5 ml	Brown
10	27	M	Rt.leg	62		6.5 ml	Black
11	12	F	Rt. Thigh	23		3.0 ml	Brown
12	6	M	Lt. Back	16		2.5 ml	Brown
13	40	M	Lt. Hand	45		0.5 ml	Black
14	19	M	Rt. Hand fingers	52		0.5 ml	Black
15	50	M	Lt. leg	50		2.0 ml	Black
16	40	M	Lt. leg	50		2.5 ml	Black
17	33	M	Lt. thigh	80		0.5 ml	Brown
18	57	F	Rt. Foot	55		0.5 ml	Black
Total				901 Kg	120 ml = 24 vials of RIGs	41.5 ml = 8.3 vials of RIGs	

were males. More than half of the patients were bitten on legs. As reported by Susilawathi NM *et al.* in Bali outbreak of Human Rabies [6] the estimated time from dog bite to the onset of signs and symptoms was 110.4 days (range 12 - 720 days; SD 118.2) which is consistent with our findings of maximum period of 102 days [5]. Therefore all the patients bitten by confirmed rabid dogs (Clinically as well as by Lab) were followed for six months and till date, all are healthy. Follow up was 100% and no death has been reported.

3.1. Discussion

All the 18 patients had type III bites and were given RIGs only locally along with ID anti rabies vaccination. Four of the patients (23%) bitten by rabid dogs were children less than 15 yrs. As per a report by P. Khawplod *et al.* [7] 30% - 50% of the reported cases of rabies occur in children under 15 years of age, the main route of transmission is rabid dog bite which is consistent with studies in India [8]. Severely exposed patients could expect a mortality rate of 13% if left untreated. As reported [9] by Muyila D I *et al.*, there was 100% case-fatality rate in children not fully treated with vaccine and immunoglobulins after unimmunized dog bites in rabies endemic country Congo (2008-2009). We could have observed at least three mortalities in this outbreak if left untreated but there was none. Most rabies incubation periods in Thailand are notoriously short with 71% succumbing within 1 month of exposure and 87% dying within 3 months [10] this is consistent with what we in India have seen as the least incubation reported at IG Medical College Shimla is 14 days for a wound on lower lip stitched without RIG last year (2014), RIGs being not available in the market or in many hospitals since last year. Limited availability of RIGs has been reported to be one of the causes of rabies deaths in Bali [6] where not all of the vaccinated patients completed their ARV regimens before developing the clinical symptoms of rabies. This shows the importance of RIG that need to be administered simultaneously with anti rabies vaccine in cases of rabid dog bites. Many experts have suggested local infiltration [11] of RIGs as failure of post-exposure treatment of rabies with systemic IM use of RIGs has been reported [12] by H. Wilde *et al.* However in a recent study [3] on local infiltration of RIGs in and around the wound without systemic IM injection, we did not had any mortality after a follow up period of more than nine months and RFFIT titers were well above the required 0.5 IU/ml without any immune suppression due to RIGs.

3.2. Does Low Immunity of Stray Unimmunized Bitches after Whelping/Parturition Play a Role in Making Them Rabid

For the last 15 years no outbreak like situation has been reported in Shimla municipality. While investigating the source of rabies in the dogs in Shimla Municipality, we initially theorized that, may be nearest forest may be the reason of the black bitch becoming rabid and infecting the brown dog but later intensive interviews with the residents of Kasumpti area of the Shimla MC clarified that both the black bitch and brown dog were domesticated strays (Unvaccinated) and suddenly turned to be rabid. We are surprised with the similarity in the pattern of lactating bitches becoming rabid after 1 - 3 months of litter birth (Whelping) in the last 9 years. If we take a pattern of people becoming rabid after bite/scratch of rabid bitches/pups below three months, it clearly show that may be low immunity of bitches after litter birth activates the latent rabies virus in their brains as 22.8% of the healthy dogs/bitches brought for slaughter in Nigeria [13] are found to be carrying rabies virus. The prevalence of rabies antigen in the saliva and brains of apparently healthy dogs sold for human consumption in Nigeria, is also in agreement with that of earlier work [14] which established that apparently healthy dogs excrete rabies virus in their saliva for long period of time without showing clinical signs. The new rabies virus strain found in Israel, V7, can both serve as reservoir in Dogs and dogs can transmit rabies as well [15]. We tested the brains samples of six animals in Shimla municipality and to our surprise all stray dogs, a pup and some wild animals were found to be positive for rabies virus [16] though none of them appeared to have died due to rabies. This underlines the endemicity of rabies virus in domestic as well wildlife in and around Shimla Municipality. Apart from a carrier status in dogs, some studies [17] have reported that rabies is maintained in one district in the Serengeti region of Tanzania with apparently healthy dog density $> 5/\text{km}^2$ as ours is the similar case having dog density more than 5 dogs/ Km^2 in the Shimla Municipality.

In 2006, a domesticated stray bitch had litter and one of the pup brought home for rearing had a scratch on the hand of 56 yrs male in Sangrah area of Sirmaur district (200 KM) and the person died after three months of clinically confirmed rabies at local hospital. In 2011, we investigated [18] death due to rabies in a village in Solan district (70 Km) where the two patients who died were bitten by a month old pup born to a bitch that died soon after birth of the pups, pup died soon after. In 2012, a lady from village Punjgain (60 KM) was referred to IG Medical College and died after three days after a two month old healthy looking stray pup had bitten her on leg. In the year 2014, one young lady tourist in Manali (300 KM) was bitten by a healthy looking pup of 2 months old and died after a month in Delhi as she was given the vaccine but not the rabies immunoglobulins, RIGs. Again in 2014, a 11 years old male child of Sirmaur district (150 KM) was bitten by a pup of 2 and a half month and died after a month later due to rabies. In Shimla municipality we tested the brain sample of 2.5 month old pup that was reported dead near the forest and it was found to be positive for FAT.

All these happenings point to the fact that may be stray bitches, that are mostly unimmunised, are prone to becoming rabid as their latent rabies virus gets activated in circumstances of lowered immunity during pregnancy due to prolonged exposure to elevated progesterone concentrations [19], their malnourished status and they being usually carrying worm infestation and all these contribute to lowering the natural immunity. Field observations support the view that stress reduces resistance to infections. This seems to be logical in the presence of higher than normal adrenocortical activity. Physiological stress such as birth causes immunosuppression in fetus and dam (mother) after parturition which leads to periparturent rise in worm infestation [20]. Immunocompromised dogs (Having demodicosis worm infestation) can become rabid has been demonstrated in a study [21] by Deborah J. Briggs *et al.* Similar immunosuppression has been reported in other animals/mammals e.g. the pasteurilla organisms remain as commensals in the terminal broncheols and alveoli of cattle, buffalo etc. The organisms cannot invade the lung due to pulmonary defence mechanism (Gills *et al.*, 1974). But due to stress in animals the organisms assume the virulent role and thereby bring about changes in lung and lung is unable to clear the pathogens [22] (Thomson *et al.*, 1975). In a recent report communicated by ProMed Mail [23] a six month old dog suddenly got rabid in French Guiana in August 2015 and the origin of infection could not be traced out. More so, the habit of these bitches to lick the pups causes the pups to become rabid as well and lowered pup immunity as described above may also be contributing to their becoming rabid.

4. Conclusions

While we were working on hypothesis of rabid dogs getting the infection from nearby forest about 8 - 10 KM away but on the follow up of the patients, they reported that both the dog and bitch used to stay in the compound

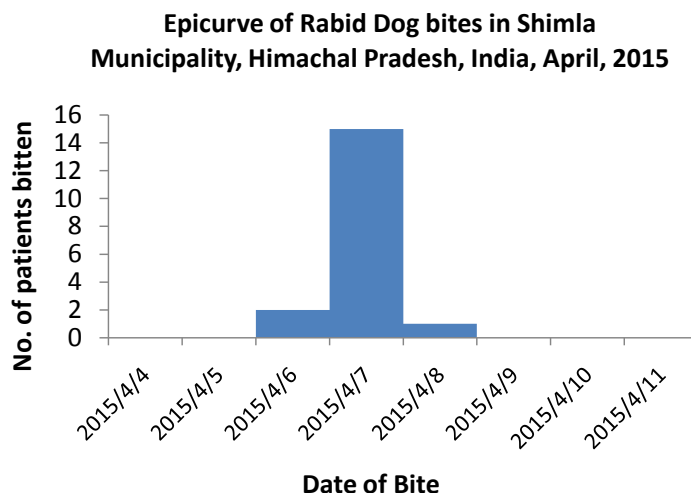


Figure 1. Epicurve/Time distribution of rabid dog bite patients in Shimla municipality bitten by confirmed rabid dogs, Himachal Pradesh, India, April, 2015. The rabid dogs were removed on 8th April, 2015 and there was no case of suspected rabid dog bite on 9th April, 2015.

of their colony since the bitch was pregnant and there was no history of the bitch moving far away to forests neither any outside dog which was seen near them as both of them were very furious. This led us to think of other reasons causing rabies in the bitch, as for the past 9 years we had observed bitches becoming rabid after litter birth that led pups becoming rabid thereafter. Since the carrier state for rabies virus in bitches/dogs is known and a state of immunosuppression after litter birth is also known, therefore there is a possibility of latent rabies virus in carrier bitches getting activated due to immunosuppression after litter birth and we hypothesize it as one of the probable causes. We need to do further studies to ascertain this phenomenon before coming to a definite conclusion and suspect such a possibility in case a dam suddenly becomes rabid among a pack of stray dogs in rabies endemic countries like India. Sahar Abd El Rahman *et al.* point out that confirmed diagnosis of rabies infection of buffaloes without a history of dog biting gives an announcement about other sources for rabies occurrence in animals [24].

An impending outbreak of rabies was managed jointly by using ONE Health approach by Health, Veterinary and Municipal authorities and by administration of RIGs locally in the wound as RIGs were not available in the market. The impending outbreak was over as soon as the identified rabid dogs were removed from the area on April 8, 2015 (Epicurve **Figure 1**).

5. Recommendations

A model to have a State Animal Bite Management Programme based on mutual coordination of Health, Veterinary and Forest departments was recommended to the government of Himachal Pradesh for implementation in the state so as to effectively control rabies through “ONE Health” approach and make the state rabies free by the year 2020 by knowing the causes of possible transmission of rabies among animals as well as human.

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RIGs shortage all over the market and for testing animal brains for FAT/BT free of cost. Lastly our thanks to Government of Himachal for all the help.

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