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ORIGINAL ARTICLE

Epidemiologic Features of Animal Bite Cases Occurring in Rabies-Endemic Areas of Korea, 2005 to 2009

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Abstract
Objectives: Human rabies is a reemerging infectious disease in Korea. There was no human rabies case for 14 years until the disease had reoccurred in 1999. To prevent occurrence of human rabies, surveillance for animal bite patients in rabies endemic areas in Korea was conducted since 2005 as a part of a human rabies control program. The animal bite cases were analyzed to determine whether patients were treated according to the post-exposure prophylaxis (PEP) guideline of the Korea Centers for Disease Control and Prevention.
Methods: Information of animal bite cases that occurred from 2005 to 2009 in rabies high-risk regions were collected by cooperation with Regional Public Health Centers in 18 cities/districts of rabies endemic areas.
Results: A total of 2458 animal bite cases were reported. Dogs accounted for 86% of animal bites and 67% of the animals were not vaccinated against rabies virus. For PEP, among rabies-vaccinated animals, 92.7% were observed for clinical signs and 1.4% underwent necropsy. Among unvaccinated animals, 72.7% were observed for clinical signs and 4.1% underwent necropsy. The remaining animals were not available for examination. Of the animal bite patients, 32.5% received PEP and 51.6% were treated by first aid or by washing the wound.
Conclusions: Given that no human rabies cases were reported since 2005 and animal rabies was continuously reported in endemic areas of Korea, the human rabies control program implemented in 2005 appears to have a significant role in the prevention and control of human rabies.

1. Introduction

Rabies is a representative zoonosis and a reemerging disease in Korea. In Korea, the raccoon dog (*Nyctereutes procyonoides*) is a principal natural reservoir of rabies virus, but dogs are a predominant animal for transmission. There were no human cases of rabies from 1985 to 1998, but the disease reoccurred in 1999, following a new case of animal rabies in 1993 [1,2].

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Human rabies can be prevented by avoiding bite of rabid animals, pre-exposure vaccination or post-exposure prophylaxis (PEP). The guidelines for Human Rabies Prevention and Control (HRPC) by Korea Centers for Disease Control and Prevention (KCDC) recommends PEP based on the anatomical locations of the bite, animal species, wound status, and rabies vaccination history of the animal [3]. Patients who acquired bites that were applicable to World Health Organization (WHO) Categories II and III in high-risk regions should immediately receive PEP, and animals should be observed for clinical signs or be examined for rabies diagnosis [5]. According to the KCDC rabies guidelines, PEP should be completed by administering vaccine on Days 0, 3, 7, 14 and 28, with human rabies immune globulin (HRIG) on Day 0. Equine rabies immunoglobulin is not permitted to use for animal bite patients in Korea. If no clinical signs of rabies in an animal were observed within 10 days or if an animal was negative for rabies diagnosis by molecular and histopathological examinations, the remainder of PEP is not necessary. Alternatively, for animal bites that occur nationwide, including the suspect-risk regions, animals should be observed for clinical signs for 10 days. If animals are clinically normal, PEP is not necessary. However, if abnormal clinical signs are observed, PEP is required, and the animal should be considered for rabies diagnosis. If no animal is available for rabies examination or if the bite is caused by a wild animal regardless of geographical location, PEP should be administered to a patient immediately.

Due to expanding regions of animal rabies outbreaks and to increasing public health threats, the National Animal Bite Patient Surveillance (NABPS) program was implemented in 2005 by guidelines of the HRCP to prevent human rabies. The NABPS was performed in close cooperation with KCDC, the Regional Public Health Centers (RPHC), and two Provincial Veterinary Service Laboratories in the rabies endemic areas. High-risk and suspect-risk regions were designated by guidelines of the HRCP. Animal bite patients in the high-risk region report to RPHC and are received a proper measurement including PEP.

In this study, we analyzed animal bite cases from the high-risk region from 2005 to 2009 to determine the current status of animal bites and to determine whether patients were properly treated. We also discuss risk factors of rabies in the high-risk region and conclude that NABPS contributed to human rabies prevention since 2005, although animal rabies, including wildlife, has continuously been reported in the high-risk region.

2. Materials and Methods

The risk areas of rabies were divided into high-risk and suspect-risk regions according to the KCDC guideline of the HRCP (Figure 1) [4]. The cities/districts where human or animal rabies had occurred since 1993 are designated as high-risk regions. Cities/districts which are adjacent with the high-risk regions are assigned to suspect-risk regions. There are nineteen and 14 cities/districts in the high-risk region and in the suspect-risk region, respectively. Two cities/districts were switched to the high-risk region from suspect-risk region in 2005 due to the occurrence of rabies in

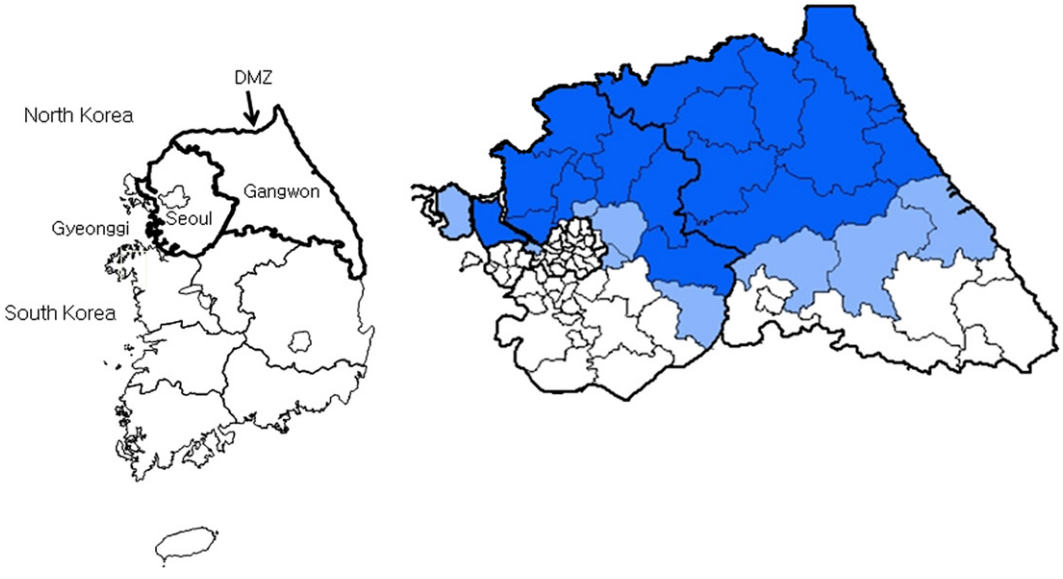

Figure 1. High-risk and suspect-risk regions of human rabies in Korea. The cities/districts where human or animal rabies had occurred since 1993 are designated as high-risk regions. The regions are located in the northern part of Gyeonggi and Gangwon provinces and are surrounded by the Han River, an expressway, the East Sea and the demilitarized zone. High-risk and suspect-risk regions are indicated in blue and light blue, respectively.

raccoon dogs and farm animals. The high-risk region in Gangwon province was 1.7 times wider than that in Gyeonggi province. The human population in the high-risk region was 3.5 times higher in Gyeonggi province than in Gangwon province.

Human rabies data from 1999 to 2009 were collected from case reports of written epidemiologic investigations in the KCDC. We also collected animal bite case data from high-risk regions from 2005 to 2009 and calculated animal bite incidences for the city/district and for different age groups. According to the guideline of the HRCP, animal bite patients should be reported to the RPHCs in the patient's residential region. The information from cases reported to the RPHCs was submitted quarterly to the KCDC for analysis. All RPHCs in 18 cities of two provinces in the high-risk region participated in the NABPS. Information was divided into patient information and animal information. Patient information included date and region where the animal bite occurred, sex, age, location of wounds, and types of PEP applied (complete or appropriate). Complete PEP means that both HRIG and vaccination were administered. Appropriate PEP means that vaccination was administered without HRIG. Animal data included animal species, rabies vaccination history and analysis of animal after biting including observation of clinical signs or necropsy. Animals were considered as vaccinated if vaccinated or boosted within 1 year of the biting incident. Clinical signs were observed by veterinarians employed in local governments and rabies diagnoses by animal necropsy were accomplished at the Provincial Veterinary Service Laboratories by histopathology, indirect immunofluorescent assay and reverse transcription-polymerase chain reaction (REF).

The study was approved by the KCDC in 2005 and complied with the guidelines of the KCDC. The data were submitted to KCDC by the RPHCs without information about individuals and clinical intervention. Information on human rabies cases did not include any personal information. All data were analyzed anonymously.

3. Results

3.1. Rabies cases

Since the reoccurrence of human rabies in 1999, six cases of human rabies were reported to KCDC to 2004 from the high-risk region located near the DMZ (Table 1) and there were no human rabies case since 2005. The estimated incubation periods of the patients varied from 3 to 11 weeks. Three patients with facial wounds had shorter incubation periods than two patients with wounds on their arms. Details of the first case of rabies were missed because of delayed reporting. Of the six cases, four were caused by dogs and two were caused by raccoon dogs. Rabies PEP was applied to two cases that had wounds around their eyes. One patient was administered rabies vaccine and an inaccurate dose of HRIG. Another patient was administered PEP after the onset of clinical symptoms.

3.2. Animal bite cases

A total of 2,458 animal-related potential rabies exposures in high-risk regions were reported to RPHCs from 2005 to 2009. The annual number of animal bite case was ranged from 359 to 658 (mean: 491.6). The lowest number of annual cases was reported in 2005 and the number increased thereafter. A mean bite rates in each city/district in the high-risk regions of Gangwon and Gyeonggi provinces were 61.4 $\pm$ 41.2 (mean $\pm$ SD) and 22.0 $\pm$ 21.0, respectively, and ranged from 0.3 to 113.7 per 100,000 individuals. An annual mean incidence rate of more than 50 was recorded in five cities/districts of Gangwon province and in one cities/districts of Gyeonggi province.

Most patients were bitten in the hand or leg (44.2% and 33.9%, respectively), followed by the arm (9.6%), foot (4.0%), face (2.5%), and hip (1.1%). Some patients (2.8%) were bitten on more than two body sites. Most bite patients had Category III exposure, as per the WHO classification and Category II exposure reported in less than 5% of the cases. The incidence was highest in adults in their 50s (18.0%), followed by 40s (17.6%), 60s (15.8%), and 30s (12.5%). Young children under 9 years of age accounted for 7.2% of all cases. The number of cases was higher in men (62.4%) than women (37.6%) and there was no significant difference of patient's sex between two provinces or among different ages. The cases of animal bite patients were higher in July and gradually increased from winter and spring to summer.

Dogs were the predominant biting animals and were responsible for 86.0% of animal bites. Unprovoked bites

Table 1. Human rabies cases from 1999 to 2004

Year	City/district	Site of wound	Rabid animal	Incubation period (wk)	PEP
1999	Paju-si	Unknown	Dog	Unknown	Unknown
2001	Hwacheon-gun	Arm	Raccoon dog	11	No
2002	Yeoncheon-gun	Face	Dog	5	Yes
2003	Pocheon-si	Face	Dog	3	Yes
2003	Pocheon-si	Face	Raccoon dog	8	No
2004	Goyang-si	Arm	Dog	11	No

PEP = post-exposure prophylaxis.

by stray dogs accounted for 3.2% of animal bites (Figure 2). Cats, including strays, were responsible for 6.2% of animal bites. Wildlife accounted for 3.7% of animal bites. Raccoon dogs (1.4%) were the common wildlife species. Four cases were from cattle in high-risk regions. Wild rats, badgers, otters, wild boars, squirrels, weasels, and bats were also involved in producing wounds in humans. Exposure to bat bites was reported in only one case in 2006. The species of biting animal was not identified for 96 cases, of which were 75 cases from one city in 2005.

Of the 2,273 animal bite cases, 67.4% of the animals were not vaccinated against rabies or were vaccinated more than one year before the incident. The ratio of animals vaccinated against rabies within 1 year before biting decreased each year (46.7%, 36.0%, 33.8%, 27.7%, and 27.2% in 2005, 2006, 2007, 2008, and 2009, respectively). Of 95 cats, only two were vaccinated against rabies. A total of 77 animals were examined by necropsy for the rabies and 22 were rabid. These included 16 dogs, three raccoon dogs, and three cattle.

Animals were divided into two groups depending on rabies vaccination history to analyze whether measurements were appropriately applied. Measurements to vaccinated and unvaccinated animals were to observe clinical signs of rabies for 92.7% and 72.7%, respectively, of the cases and to perform necropsy for 1.4% and 4.1%, respectively (Table 2). No animals showed clinical signs during the observation period. For 1.6% and 16.6% of the vaccinated and unvaccinated animals, respectively, no measurements were available due escape of the animals (including wildlife) or improper disposal. Complete or appropriate PEP was administered more in patients bitten by unvaccinated animals (40.6%) than in patients bitten by vaccinated animals (13.2%). Of animal bite patients, 21.8% had complete PEP and 10.7% were treated with appropriate PEP. Of the patients bitten by vaccinated animals, 12.8% (±3.4) (from 7.4% to 16.9%) received complete or appropriate PEP. Among patients that were bitten by unvaccinated animals (including wildlife), 31.7% received PEP in 2005, and gradually increased to 37.0%, 42.2%, and 47.7% in 2006, 2007, and 2008, respectively. In 2009, 39.8% of patients received PEP. Of 430 patients that were bitten by unavailable animals, 272 cases (63.3%) received PEP. Complete PEP was administered in all patients bitten by confirmed rabid animals.

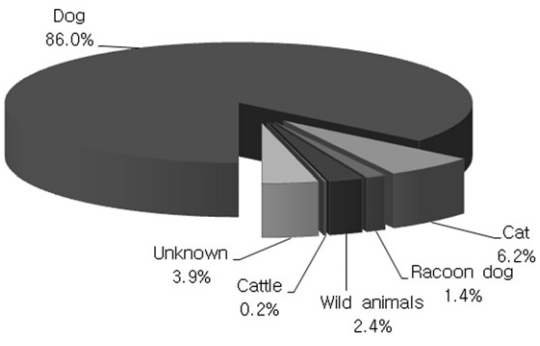

Figure 2. Animal species causing bites from 2005 to 2009. Other animals include badger, wild boar, chipmunk, otter, rats, hamster, monkey, and weasel. Dogs and cats also include stray animals. Dogs (86.0%) were the primary animals causing bites, followed by cats.

4. Discussion

Due to outbreaks of animal rabies in limited areas, HRCP focused mainly on management of animal bite patients and on public education in the endemic areas. Unexpectedly high number of animal bite cases was reported in the first year of HRCP, although PEP data were only passively collected by the reporting of patients to RPHCs that were provided PEP. This may be because the PEP service was free. The total number of reported cases gradually increased, although this was affected by many factors. This finding may reflect increased knowledge about rabies among the residents in the high-risk region rather than due to more bite cases.

HRCP plays a key role in preventing human rabies in Korea. However, several risk factors should be considered to keep a free of human rabies. A high incidence of rabies was reported in dogs, cattle, and raccoon dogs. More than 70% of the domestic animals causing bites were unvaccinated or had been vaccinated more than one year after the booster. To encourage animal vaccination in high-risk regions, cattle, dogs, and cats have been vaccinated free of cost by public health veterinarians in local governments since 1993. In spite of the strengthened animal vaccination program, the number of unvaccinated biting animals remains high. Raccoon dog rabies remains high and has resulted in of transmission of the virus to cattle and dogs in the endemic areas [1,6]. These data suggest that mass vaccination programs should be strengthened in the high-risk regions to prevent rabies outbreaks [2].

After the recurrence of animal rabies in 1993, the virus gradually spread southward and eastward in the two endemic provinces. The endemic areas of rabies are surrounded by a river and an expressway on the southern side, shoreline on eastern and western sides and the demilitarized zone (DMZ) on the northern side. If the rabies virus crosses the southern barrier, it can rapidly spread nationwide. Other factors include possible introduction of the virus from endemic countries [7−11] and misdiagnosis and delayed PEP due to a lack of experience among health care providers and the general community outside of the risk areas [12]. Therefore, it is necessary to expand the animal bite monitoring areas to cities/districts adjacent to endemic areas and to strength

Table 2. Animal management and patient treatment after animal bites, 2005 to 2009

Animal vaccination to rabies	Animal management	Treatment of animal bite case (%)[a]			
		Wound treatment	Incomplete PEP	Appropriate PEP	Complete PEP
Vaccination	Observation	20.1	4.4	1.0	2.1
	Necropsy	0.1	0	0	0.3
	None	1.0	0.1	0.2	0.4
Nonvaccinated	Observation	26.3	9.3	5.1	10.4
	Necropsy	0.5	0.2	0.4	1.8
	None	3.6	1.8	4.0	6.8

[a]*Complete post-exposure prophylaxis (PEP) means that both human rabies immune globulin (HRIG) and vaccination were administered. Appropriate PEP means that vaccination was administered without HRIG.*

PEP = post-exposure prophylaxis.

information, education, campaign and communication programs in the suspect-risk areas.

The KCDC guidelines recommend that both HRIC and rabies vaccine are administered to patients in the high-risk region who had WHO Category III exposure or wild animal bites as soon as possible, regardless of the observations of biting animals. However, in almost one-half of the animal bite cases, the animals were managed by observation of clinical signs or by laboratory examination. According to WHO guidelines, several factors should be considered in deciding whether or not to start PEP [5]. Based on WHO and KCDC guidelines, 6% of animal bites did not comply with regulations. This suggests a high risk factor for a rabies outbreak although biting animals were not managed because of unavailability of the animals.

Human rabies can be prevented by multiple control strategies, including vaccination of pets against rabies, bait vaccine supply for wildlife, and a well-working reporting system for PEP. The network for HRCP by KCDC was successfully established and contributed to the prevention of human rabies. There were no human rabies cases after the implementation of HRCP, although rabies in animals has been continuously reported in the high-risk region. In conclusion, HRCP played a principal role in preventing human rabies in Korea.

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