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(Research Article)

The wave front spread rate of Chinese ferret-badger rabies in eastern Taiwan

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Abstract

This study used epidemiological data of Chinese ferret-badger (CFB) rabies in eastern Taiwan, the Hualien County, from July 2013 to December 2020 to estimate its wave front spread rate. The first case of the CFB rabies virus in eastern Taiwan was detected in Zhuoxi Township in Hualien County on July 31, 2013. Our technique regressed TIME (months elapsed from the first case in Zhuoxi and the first case in each infected township invaded by the first case of CFB rabies) on DISTANCE (kilometers between locations of the first case in Zhuoxi and centroids of each infected township invaded by the first case of CFB rabies), using simple linear regression. The mean rate of wave front spread was 10.698 kilometers/year. The correlation between TIME and DISTANCE was R = 0.9273 at p = 0.0001. As CFB rabies has only occurred in China and Taiwan, studies on its epidemiology are extremely rare. This paper is the first study to estimate the wave front spread rate of CFB rabies in the world.

Keywords: Rabies; Chinese ferret badger (*Melogale moschata*); Epidemiology; Taiwan

1. Introduction

Rabies virus (RABV) is the prototype virus of the genus *Lyssavirus* in the family Rhabdoviridae and is the causative agent of classic rabies in all mammals. Once the infection is established and has reached the brain, RABV will cause fatal encephalomyelitis. Rabies infection in terrestrial animals is maintained in two epidemiological cycles: one is urban and the other is sylvatic. In the urban rabies cycle, dogs are the main reservoir host in the world. In the sylvatic rabies cycle, reservoirs comprise foxes, skunks, raccoons, mongooses, coyotes, raccoon dogs, Chinese ferret-badgers (CFBs), etc. [1, 2]. On July 17, 2013, Taiwan confirmed RABV in wild CFBs [1], marking the first appearance of rabies in Taiwan since WHO declared Taiwan rabies-free in 1961 [3-5]. During the epidemic period, many CFBs were found dead on the road, and people were occasionally bitten or potentially exposed by rabid CFBs [6, 7]. To date, CFB rabies has only been reported in China and Taiwan [8]. The CFB is an omnivorous wildlife mustelid. The general color of its upper parts is chocolate brown, and the hairs of the dorsum are pale basally. White facial markings are variable, generally covering the sides of the face below the eyes and in front of the ears, and continuous with the yellowish-white of the lips, chin, throat, and venter; there is a squarish white spot between the eyes in the median line and a narrow, whitish stripe runs medially from the occiput, extending up to but rarely beyond the shoulders [9]. Important food sources are earthworms and insects [10]. The mean body mass for adults is less than 2 kilograms [9, 11]. CFBs have a poor visual perception, small teeth, and weak biting force and are weaker than a dog, and not as commonly found in urbanized areas as raccoons [12-14].

Since 1999, rabies was elevated from Second-Category into First-Category under the National Notifiable Diseases of Taiwan, and the Communicable Disease Control Act of Taiwan was amended simultaneously. As required by law, the

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Taiwan government has instituted elevated rabies control policies since 1999, when Bureau of Animal and Plant Health Inspection and Quarantine (BAPHIQ) implemented a surveillance program for the detection of animal rabies. Furthermore, in 2008 BAPHIQ instituted several surveillance programs for the detection of rabies in bats and in 2013 additional programs for the detection of zoonotic diseases in wild mesocarnivores [3]. Data indicated that up to December 31, 2020, a total of 845 rabid CFBs had been confirmed and that CFB was the sole recognized rabies reservoir species in Taiwan.

There were 12 cases of rabies spillover from the CFB rabies to non-reservoir hosts, including 1 Asian house shrew (*Suncus murinus*), 1 six-week-old puppy, 1 Yellow-throated marten (*Martes flavigula*), and 9 Masked palm civets (*Paguma larvata*) [3, 6, 15]. A retrospective survey found that the CFB rabies occurred in Midwestern Taiwan (Nantou County and Chiayi County) prior to 2010 [16]. The temporal dynamics of rabid CFBs in Midwestern Taiwan (Taichung City, Nantou County, Yunlin County, and Chiayi County), Southern Taiwan (Tainan City, Kaohsiung City, and Pingtung County), and Southeastern Taiwan (Taitung County) appeared to have subsided to enzootic levels as of December 2019. Instead, the epidemic in Eastern Taiwan (Hualien County) exhibited a typical epidemic curve similar to when the rabies virus has entered into a new region of the previously naïve population [7, 17]. It has been postulated that the Central Mountain Range has blocked the extension of the endemic from Midwestern Taiwan to Eastern Taiwan ever since 2010 [7]. This study aimed to investigate the wave front spread rate in Eastern Taiwan, using data of CFB rabies from July 2013 to December 2020, which was kindly provided by the Bureau of Animals and Plants Health and Quarantine (BAPHIQ).

2. Material and methods

2.1. Rabies diagnosis

Rabies tests were performed on brain tissue from all submitted animals, including road-kills and those found dead. Animals submitted for testing were collected by County/City Veterinary Departments with assistance from local law enforcement officers, animal wardens, and the general public. The National Animal Health Research Institute (AHRI) performed the rabies diagnostic test, using the method of the direct fluorescent antibody test (DFA) in Chapter 3.1.17 of the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2021 [15]. For the DFA test, two subsamples for each submitted animal brain were conducted concurrently. In cases of inconclusive results from the DFA test, samples were further inoculated into an MNA (Murine Neuroblastoma) cell line to detect replication of the virus [7]. In this study, when the first case was detected in a township, that township was considered as “infected”.

2.2. Distance between two coordinates and identification of the centroid of a township

Coordinates with decimal degrees of collected animals were searched from Google Earth Help, using the addresses of samples. The distance between two coordinates with decimal degrees was calculated using the method provided by the National Oceanic and Atmospheric Administration [18], U.S. Department of Commerce, a governmental website of the United States. The centroid of each township was the average coordinate with decimal degrees for four points of the northmost, southmost, eastmost, and westmost of each township on the Google map.

2.3. Modeling of simple linear regression

The first case of the CFB rabies virus epidemic of Eastern Taiwan was detected in Zhuoxi Township, Hualien County on July 31, 2013. In the subsequent 78 months, at least one case of CFB rabies was detected in 10 of 13 townships of Eastern Taiwan. In this study, we restricted our analysis to cases observed in the 78 months following the first case in Zhuoxi. We let M_i denote the number of months elapsed from the first case in Zhuoxi and the first observed case in i^{th} township. We let D_i denote the distance in kilometers between the first case in Zhuoxi and the centroid of i^{th} township [19]. A simple linear regression was developed using GraphPad Prism version 9.2.0 for Windows, GraphPad Software, San Diego, California U.S.A. We regressed M_i (months) on D_i (kilometers) to the first case in Zhuoxi.

3. Results

3.1. Epidemic curve of CFB rabies cases in Eastern Taiwan and other endemic areas

Red bars in Figure 1 show the annual numbers of all 131 confirmed cases of CFB rabies in Eastern Taiwan, from July 2013 to December 2020. The number of confirmed cases were 3, 15, 16, 4, 17, 53, 19, and 4 separately. The blue curve in Figure 1 shows the annual numbers of all 714 confirmed cases of CFB rabies in endemic areas other than Eastern Taiwan, comprising Midwestern, Southern, and Southeastern areas of Taiwan, from July 2013 to December 2020. The number of cases were 273, 132, 72, 38, 53, 57, 53, and 36 separately. In Eastern Taiwan when the first case occurred on July 31, 2013, the epidemic trend started to elevate, in the mode of a propagated outbreak, peaking at 53 positive cases of CFB rabies in 2018. It then subsided to enzootic levels as of December 2020, or similar to an epidemic trend when the rabies virus has entered into a new region of a previously naïve population [17]. Similar situations also happened when raccoon rabies initially occurred in Virginia and Connecticut [20, 21]. Instead, when the first case of CFB rabies was confirmed in Midwestern Taiwan (Gukeng, Yunlin County) on July 17, 2013 and OIE was notified through immediate notification [1], the epidemic curve of the endemic areas other than Eastern Taiwan had been at the peak at 273 positive cases of CFB rabies simultaneously, as shown by the blue curve in Figure 1. Afterwards, the blue curve sharply subsides to enzootic levels as of December 2020. However, the epidemic areas other than Eastern Taiwan missed the opportunity to be surveyed in the early stage of the CFB rabies epidemic.

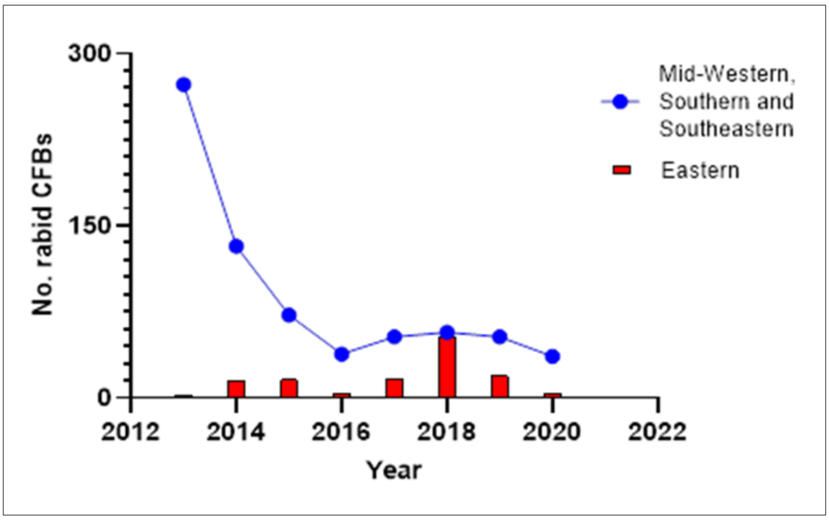

Figure 1 Red bars show the epidemic of 131 cases of rabid CFBs in Eastern Taiwan. The blue curve shows the epidemic of 714 cases of rabid CFBs in Midwestern, Southern, and Southeastern areas of Taiwan, 2013 to 2020

3.2. The coordinates of the first case in Eastern Taiwan and centroids of infected townships

There were ten infected townships in Eastern Taiwan from July 2013 to December 2020. The first case of the CFB rabies in Eastern Taiwan was detected on July 31, 2013 in Zhuoxi, Hualien County. Table 1 presents the coordinates with decimal degrees of the first case in Zhuoxi and the centroids of other 9 infected townships, distances from the first case to the centroids of every infected township, and the number of months elapsed between the first case in Zhuoxi and the first case in every infected township.

Table 1 Coordinates with decimal degrees of the first case in Zhuoxi of Eastern Taiwan and the centroids of every infected township of the CFB rabies from July 2013 to December 2020

Ser. no.	Year	Sampling date	Township	Latitude (N)	Longitude (E)	Distance (km)*	Month**
1	2013	31-July	Zhuoxi	23.276161	121.241501	0	0
2	2013	26-Aug	Yuli	23.382275	121.352611	16	1
3	2014	18-Feb	Fuli	23.204495	121.298451	10	7
4	2016	18-Sep	Fengbin	23.594776	121.498045	44	38
5	2018	08-Jan	Juisui	23.512556	121.384036	30	54
6	2018	18-Feb	Guangfu	23.644102	121.443101	46	55
7	2018	09-Jul	Wanrung	23.806201	121.285844	59	60
8	2018	05-Aug	Shoufeng	23.825429	121.456494	65	61
9	2018	02-Oct	Fonglin	23.739093	121.470748	56	63
10	2020	09-Jan	Hualien City	23.750418	121.610837	65	78

* Distance in kilometers from the location of the first case in Zhuoxi to the centroids of every infected township; ** Months elapsed between the first case in Zhuoxi and the first case of each infected township.

3.3. Modeling of a simple linear regression

A simple linear regression was developed as shown in Figure 2. Figure 2 presents the data in Table 1 of months (Y-axis) regressed on the distances (X-axis) from the first case in Zhuoxi to the centroids of every infected township in kilometer. The regression equation is:

$$\text{Months} = 1.122 \times \text{Distance (km)} - 2.161$$

Since the observations were recorded by month, and distance was measured in kilometers, 1/slope (1/1.122 = 0.8915) represents the rate of spread in kilometers per month. By linear regression, the wave front spread rate was 0.8915 kilometers/month, or 10.698 kilometers/year. The simple correlation was R = 0.9273 (p = 0.0001), which indicates a high degree of correlation. The R square was 0.86, which indicates how much of the total variation in the number of Months (Y-axis) was able to be explained by the number of Distance (X-axis). In this case, 86% was able to be explained, which is very large. The statistical significance of the regression model was $p = 0.0001$, which was less than 0.05, and indicated that overall the regression model statistically significantly predicted the outcome variable. Consequently, it was a good fit for the data.

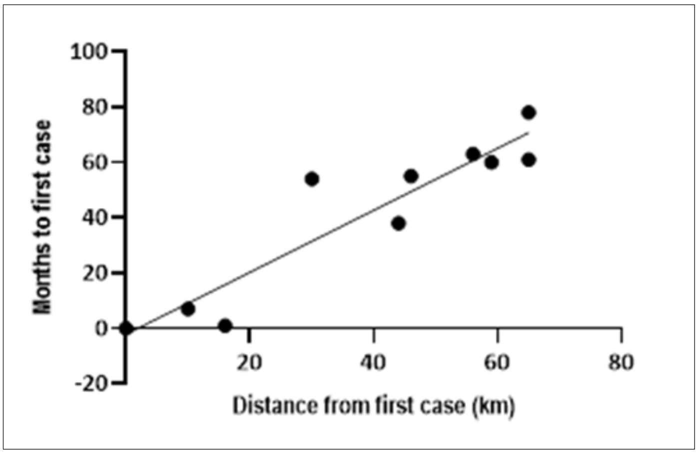

Figure 2 A simple linear regression to model the months elapsed from the first case in Zhuoxi to infected townships and the corresponding distance between the first case to the centroids of infected townships

4. Discussion

Spatial heterogeneity, distributions of habitats of reservoirs, and long-distance translocation (LDT) play important roles in the spatiotemporal dynamics of the sylvatic rabies cycle of rabies infections [19, 22, 23]. When the front of the rabies epidemic is advancing, it will be inhibited due to terrain factors such as high mountains, large rivers, heavily forested areas, or due to low reservoir population density in the neighboring townships of the epidemic area. Therefore, the time of the progression of the epidemic does not necessarily have a positive correlation with the distance of the progression of the epidemic. This phenomenon is called "Boundary conditions" [19]. Another rare phenomenon for the dispersal of sylvatic rabies is LDT, which is a kind of atypical dispersal mode that implies leaping across bad habitats or barriers to invade farther areas [19]. Table 1 indicates that the dispersal mode of LDT did not appear in Eastern Taiwan (Hualien County).

A common method used to estimate the rate of progression in the wild is based on the linear regression of TIME (months elapsed from the first case of the epidemic and the first case in other infected townships) on DISTANCE (kilometers between locations of the first case of the epidemic to the centroid of every township invaded by the pathogen of the first case) [19, 24]. Data in Figure 2 showed a high degree of correlation between TIME and DISTANCE in the epidemic of CFB rabies in Eastern Taiwan (R = 0.9273, p = 0.0001).

The first case of the CFB rabies virus epidemic of Eastern Taiwan was in the township of Zhuoxi. Case number 2 in Table 1 indicates that the distance between the first case in Zhuoxi and the centroid of the township of Yuli is 16 km. The time elapsed from Zhuoxi to Yuli was 1 month. However, case number 3 in Table 1 indicates that the distance between the first case in Zhuoxi and the centroid of the township of Fuli is 10 km, bringing the time elapsed from Zhuoxi to Fuli in 7 months. The period appears to be longer than case number 2. One probable reason is that the Siouguluan River, which is located between Fuli and Zhuoxi, impeded and hindered the progression of the epidemic. Similarly, case number 5 in

Table 1 also shows that the epidemic progressed very slowly in the township of Juisui. One may also consider that this was very slow, because in the middle part of Juisui the epidemic was impeded by the Fuyuan River and Hongye River, in the south side the epidemic was impeded by the broad Siouguluan River, in the western side the epidemic was impeded by the Central Mountain Range, and in the eastern side the epidemic was impeded by the Coastal Mountain Range. Similarly, case number 9 in Table 1 also shows that in the township of Fonglin the northern, central, and southern parts were impeded by Shoufeng River, Wanli River, and Ma'an River, respectively, while the west side was impeded by the Central Mountain Range. Thus, the spread of the epidemic was slow. The above phenomenon illustrates the influence of spatial heterogeneity on the progression of the epidemic.

CFB rabies in the world have presently only occurred in China and Taiwan, and studies on the epidemiology of CFB rabies are extremely rare. As stated, the spread of rabies was related to the population density of reservoirs, size of animals, and habitat distribution of reservoirs [19, 22, 23]. The CFB is a *small* carnivorous mustelid mammal, and because of its short stature, CFB's survival competitiveness is far less than that of general mesocarnivores such as dogs, raccoons, foxes, and skunks. Therefore, it would be very difficult to survive in urban areas where humans and stray dogs are dominant in the region [25].

Hanlon and Childs [17] indicated that when a rabies epidemic invades a naïve population of reservoirs, there will be an extremely large number of deaths. When a large number of reservoirs in the habitat die, the epidemic will temporarily decrease to zero. At this time, because the population of reservoirs in the habitat decreases and there is no food competition, the population of reservoirs will gradually increase. When the population of reservoirs increases to a threshold, a small-scale epidemic will occur again. Such small-scale epidemics will continue to repeat in the mode of an intermittent source. The large-scale death epidemic in the early stage of the epidemic will no longer occur. This phenomenon is consistent with the epidemic curve in Figure 1. Tu et al. [7] also reached similar conclusions.

5. Conclusion

In conclusion, the wave front spread rate of rabies should be estimated using the record of a virus entering into a new region of a previously naïve reservoir population. This study used the epidemiological data of the CFB rabies in Eastern Taiwan from July 2013 to December 2020 for the estimation. Judging from the epidemic curve of CFB rabies in Eastern Taiwan in Figure 1, the CFB rabies did not occur until July 2013, which was different from the record in endemic areas other than Eastern Taiwan. Consequently, it is fortunate that the Central Mountain Range blocked the epidemic of CFB rabies in Midwestern Taiwan from entering Eastern Taiwan, allowing Eastern Taiwan to reserve a full epidemic record of CFB rabies and leaving extremely precious data to study in the future.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

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