Cross-species transmission of feline herpesvirus 1 (FHV-1) to chinchillas

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Abstract
Background: Herpesviruses are a class of double-stranded DNA viruses found in both vertebrates and invertebrates. They are usually highly host-specific and do not easily spread across species. Chinchillas have gradually entered the Chinese pet market in recent years, but references to viral infections in chinchillas are extremely scarce, and only two reports about the herpesvirus in chinchillas are available at present.

Objectives: The aim of this study was to present the first report of FHV-1 infection in chinchillas.

Methods: A total of 130 nasopharyngeal swab samples of chinchillas and three nasopharyngeal swabs of domestic cats collected from a chinchillas farm were investigated by nested PCR for FHV-1.

Results: Four chinchillas were infected with FHV-1, the positive rate was 3.08% (4/130), and two domestic cats were FHV-1 positive (2/3). The 253 bp fragments of FHV-1 gD gene from four chinchillas and two domestic cats were 100% identical, respectively, and the homology between chinchillas and domestic cat was 99.21%, but they all shared nearly 98.81% homology with the reference strain sequences. Phylogenetic tree analysis showed that these four chinchillas strains were clustered together with FHV-1.

Conclusions: This is the first time that FHV-1 was detected in chinchillas and suggested chinchillas are susceptible to FHV-1 and may play a role as a temporary reservoir for FHV-1.

KEYWORDS
chinchillas, cross-species transmission, FHV-1, nested RCR
1 | INTRODUCTION

Herpesviridae is a big family, and the members of which could naturally infect humans and many different kinds of animals (Gatherer et al., 2021). According to the differences in genome sequence and their pathogenic characteristics, Herpesviridae is divided into three subfamilies: alpha-, beta- and gammaherpesvirinae (Leroy et al., 2016). Feline herpesvirus 1 (FHV-1) belongs to Herpesviridae, Alphaherpesvirinae and Varicellovirus. FHV-1 is one of the most common pathogens causing upper respiratory tract infection and can lead to infectious rhinotracheitis disease in felines, which is mainly transmitted via direct contact, contaminants and droplets. Studies on domestic cats have shown that 97% of cats have been exposed to the virus, 80% continue to be infected after exposure and 45% continue to transmit the pathogen intermittently (Gaskell et al., 2007; Lewin et al., 2020). FHV-1 naturally infects many different species of felines, such as Acinonyx jubatus, Leopardus tigrinus and Panthera leo beside domestic cats with high positive rates regardless of immunity (Table 1). Most infections are asymptomatic despite some manifesting respiratory symptoms. Chinchillas are usually kept as pet animals in Europe and North America and have gradually entered the Chinese pet market in recent years; however, reports on viral infections in chinchillas are extremely scarce. Although natural infection with herpes-like agent in a Chinchilla has been shown in 1970, and herpes-like viral particles have been demonstrated (Goudas & Giltoy, 1970). The other case of a spontaneous and severe human herpesvirus 1 (HHV1; human herpesvirus type 1) infection in a chinchilla with a probable ocular viral entry has been documented in 2002 (Wohlsein et al., 2002). Up to now, only these two studies are about herpes virus infection in Chinchillas. Here, we present the first report of FHV-1 infection in chinchillas without clinical signs and symptoms by nested PCR.

2 | MATERIALS AND METHODS

2.1 | Sample collection

A total of 130 nasopharyngeal swab samples of chinchillas and three nasopharyngeal swabs of domestic cats were collected in a chinchillas farm from Harbin, Heilongjiang, China. This project was carried out in three phases, from September to December 2021. And the age of these chinchillas ranged from 3 months to 6 years old, among which 121 were juveniles, and 9 were adults (the maturity period of Chinchillas was 6–8 months), 83 were male and 47 were female. The three domestic cats, aged about two, are kept loose in the farm as pets. They have no chance to contact chinchillas directly, but they often play on the new mat grass and fodder which will be used for chinchillas.

| TABLE 1 | Common Tree of species infected FHV-1 except for Felis catus and more detailed information of infected hosts |
| Species | Life style | Clinical signs | Infected cases | Infection route | References |
| Chinchilla lanigera | C | N | 4 | N.I | (Evermann et al., 1982; Kramer et al., 1991) |
| Canis lupus familiaris | D | Y,N | 13 | N.I; E.I | (Harrison et al., 2004) |
| Crocota crocota | F | N | 1 | N.I | (Ikeda et al., 1999) |
| Prionailurus bengalensis | C | N | 1 | N.I | (Marino et al., 2021; Thalwitzer et al., 2010; Witte et al., 2017) |
| Acinonyx jubatus | C,F | Y | En | N.I; V.I | (Biek et al., 2002) |
| Lynx canadensis | F | N | 1 | N.I | (Roelke et al., 2008) |
| Lynx pardinus | F | N | L.E | N.I | (Filioni et al., 2006; Ruthner Batista et al., 2005) |
| Puma concolor | C,F | N | En | N.I | (Filioni et al., 2006; Ruthner Batista et al., 2005) |
| Puma yagouaroundi | C | N | L.E | N.I | (Ruthner Batista et al., 2005) |
| Leopardus wiedii | C | N | En | N.I | (Ruthner Batista et al., 2005) |
| Leopardus pardalis | C,F | N | L.E | N.I | (Filioni et al., 2006; Ruthner Batista et al., 2005) |
| Leopardus tigrinus | C | N | En | N.I | (Furtado et al., 2017; Ruthner Batista et al., 2005) |
| Panthera leo | F | N | En | N.I | (Chaber et al., 2017; Ramsauer et al., 2007) |
| Panthera onca | C,F | N | En | N.I | (Furtado et al., 2017; Ruthner Batista et al., 2005) |
| Panthera unca | F | N | 2 | N.I | (Johansson et al., 2020) |
| Panthera tigris altaica | C | Y | 2 | N.I | (Xiao et al., 2013) |
| Panthera tigris tigris | F | N | En | N.I | (McCauley et al., 2021) |
| Panthera tigris amoyensis | C | Y | 5 | N.I | (Chen & Li, 2013; Sun et al., 2014; Xiao et al., 2013) |

Note: The number in Infected cases represents the number of infected hosts. C, captive; D, domestic; F, free-ranging; N, no clinical signs or anatomic lesions; Y, mild or significant clinical signs; En, endemic; L.E, low-level existence; N.I, naturally infect; E.I, experimentally infect; V.I, vaccine infect.
2.2 Nucleic acid extraction and PCR

Nucleic acid was extracted using the Baypure™ universal Magnetic bead Viral DNA/RNA Rapid Extraction Kit (Baybio, Guangzhou, China). FHV-1 detection was performed on all the samples by nested PCR (Linxiang et al., 2015). The first-round primers are gD OF, 5'-ACTTCAAGCCTTTACGACCCGCC-3'; gD OR, 5'-GGGGGC CATATACTCAACC-3'; and the second-round primers are gD IF, 5' -CAAGCCGAGATCGTCCGA-3'; gD IR, 5' -GAAGGCCGACCGTAAAAGCA-3'. The target fragment was 253 bp of the FHV-1 glycoprotein D (gD) gene.

2.3 Sequence and phylogenetic analysis

Sequence analysis of the 253 bp target fragment was performed using BLAST (http://www.ncbi.nlm.nih.gov/BLAST). Evolutionary analysis was conducted in MEGA7 and we selected reference sequences for phylogenetic analysis from the NCBI GenBank database (https://www.ncbi.nlm.nih.gov/nucleotide/). The DNAman software was used for sequence alignment.

3 RESULTS

The result showed that all four positive samples were from juveniles and the positive rate of female chinchillas (6.83%) was higher than that of males (1.2%). Overall, the molecular prevalence of FHV-1 in this study was 3.08% (4/130). And two domestic cats (one male, one female) were FHV-1 positive (2/3). The 253 bp fragments of FHV-1 gD gene from four chinchillas and two domestic cats were 100% identical, respectively, and the homology between chinchillas and domestic cat were 99.21%, but they all shared nearly 98.81% homology with the reference strain sequences. Phylogenetic tree analysis showed that these four chinchillas strains clustered together with FHV-1, showing closely genetic relationship (Figure 1). In parallel, there are three bases mutated in this fragment of chinchillas and domestic cats respectively (Figure 2).

4 DISCUSSION

In our study, the 253 bp fragments from chinchillas and cats all shared 98.81% homology with the other FHV-1 strains. We found that three bases mutated in gD gene of chinchillas and domestic cats respectively, but there was only one mutation site was different (Figure 2). This fragment in all FHV-1 reference strains was 100% homologous because it is located in a highly conserved region of the gD gene of FHV-1 and this is in line with the previous studies that there is considerable homogeneity in FHV-1 genomes (Herrmann et al., 1984; Vaz et al., 2016). At the same time, the gD gene plays an essential role in the selection process of virus adsorption to host cells (Gaskell et al., 2007). These chinchillas have been in the farm since birth and never come into contact with other animals except humans and domestic cats. Two of three domestic cats in the chinchillas farm are FHV-1 positive, and this may be the contagious source, considering they have no chance to contact with chinchillas directly, but they often play on the new mat grass and fodder, which will be used for chinchillas. Studies have shown that FHV-1 is horizontally transmitted through close contact with the body fluids of infected animals, such as nasal, eye and oral secretions (Fernandez et al., 2017); contaminated cages and food can also cause indirect contact transmission (Gaskell & Povey, 1982). Hence, it is possible that FHV-1 can be transmitted from domestic cats to chinchillas by contaminated mat grass and fodder. It is known that lower temperature contributes to viruses surviving. Coincidentally, the
farms are located in Harbin, China, and the samples were collected in winter, which makes it easier for the virus to survive a long time even leaving its host.

In the previous studies, most of the cases of FHV-1 transmission were confined to felines, even if FHV-1 has also been reported to be isolated from dogs (Evermann et al., 1982; Kramer et al., 1991); they also belonged to Carnivora like felids, whereas chinchillas belong to Rodentia and are greatly distant relationships to domestic cats. The cross-species transmission of DNA viruses is rare compared with RNA viruses theoretically, but in effect, cross-species transmission of herpesviruses takes place much more frequently than previously approximated (Escalera-Zamudio et al., 2016). Several studies have illustrated the presence of repeated cross-species transmission of beta- and gammaherpesvirus during the evolutionary process, and many viruses of alphaherpesvirus have the potential to infect different host species by experiment infected (Murthy et al., 2013; Tischer & Osterrieder, 2010). Consequently, in spite of their narrow host range and specificity, it is possible that herpesviruses can transmit to other species, due to the change of encoded nucleic acid in particular conditions (Ehlers et al., 2008). Furthermore, herpesviruses have residual potential to cross species barriers and adapt to new hosts (Woźniakowski & Samorek-Salamonowicz, 2015). Recombination is widespread in various herpesviruses and interclade recombination has occurred in FHV-1 (Kolb et al., 2017; Lewin et al., 2018). In recent years, it has been demonstrated that the evolution of some herpesvirus has been driven by both cross-species transmissions and subsequent cospeciation within particular viral lineages (Escalera-Zamudio et al., 2016). As mentioned above, a spontaneous HHV1 infection in a chinchilla has been documented in 2002 (Wohlsein et al., 2002). These facts and our results all speak to the possibility of long-distance cross-species transmission of FHV-1 from domestic cats to chinchillas. However, further research is needed to determine whether this is a novel alphaherpesvirus after cross-species transmission of FHV-1 to chinchillas and coevolution with the new host, or just FHV-1 transmission to chinchillas.

Chinchillas have been gradually introduced to the public as pets these days, and the infection of HHV-1 and FHV-1 in chinchillas indicated that it is necessary to pay more attention to them as a potential public health risk. Cross-species transmission naturally occurs more frequently in closely related host species, but the transmission of pathogens can also be found in places where transmission barriers are inherently low or artificially lowered. Barriers of transmission can be reduced by keeping different species animals together, helping them come into close contact, hence leading to the virus transmission between unrelated species animals together.
potentially giving rise to a new threat to public health security (Samorek-Salomonowicz et al., 2003; Woźniakowski & Samorek-Salomonowicz, 2015). In this report, the irregular feeding practices of farmers lower the transmission barriers and were primarily responsible for the spread of FHV-1 to chinchillas. In consequence, breeders should keep different species of animals separate, including anything belonging to them, to avoid direct or indirect contact between them.

5 | CONCLUSION

In conclusion, the molecular prevalence of FHV-1 in this study was 3.08% (4/130) and two domestic cats (one male, one female) were FHV-1 positive (2/3). Phylogenetic tree analysis showed that these four chinchilla strains were clustered together with FHV-1. It attests that long-distance cross-species transmission of FHV-1 from domestic cats to chinchillas. To the best of our knowledge, this is the first time FHV-1 was detected in chinchillas, suggesting that chinchillas are susceptible to FHV-1 and may play a role as a temporary reservoir for FHV-1, with potential public health risks. Nevertheless, additional studies are needed to substantiate this.

AUTHOR CONTRIBUTIONS

Longyan Shi: writing—original draft; Shuping Huang: performing experiments; Yuxin Lu: investigation and visualisation; Lin Guo: data curation; Lijun Guo: the sample collection; Wei Xie: the sample collection; Xiang Li: writing—guidance; Yulong Wang: investigation; Siyuan Yang: methodology; Hongliang Chai: methodology and writing – review; Yajun Wang: conceptualisation, funding acquisition, project administration, writing—review and editing.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

Please contact the corresponding author for all reasonable data requests.

ETHICAL APPROVAL

The authors confirm that the ethical policies of the journal, as noted on the journal’s author guidelines page, have been adhered to and the appropriate ethical review committee approval has been received.

PEER REVIEW

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