Medical Hypotheses 142 (2020) 109831

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Do pets protect their owners in the COVID-19 era?

Introduction

The outbreak of COVID-19 – the global spread of the disease caused by SARS-CoV2 – took place at the end of 2019 in Wuhan, China [1]. After the infection of more than 120.000 people and the death of almost 5.000, the World Health Organization announced it as a *global controllable pandemic* [2]. In April of 2020, the number of cases exceeded 2 million and the infection was spread over more than 180 countries [3,4]. Human coronaviruses (HCoVs) were on the origin of not only the current pandemic, but also of the SARS and MERS epidemics, which infected and took the lives of thousands of people [5,6]. Virologic and genetical studies confirmed that bats have been transmission hosts for both of the viruses, which were further spread by civets and dromedaries [7–9]. Recent studies suggest that specific types of animals can be the source of different coronaviruses: bats for alpha- and beta-CoVs, avian for gamma- and delta-CoVs, and rodents for the ancestor of the beta-CoVs lineage A [10–12].

The infection is not exclusive to wild animals and there are many known strains that affect livestock and pets [13]. Symptoms caused by coronaviruses depend on the type of strain; they may include gastrointestinal ailments (diarrhoea, vomiting, anorexia), respiratory ailments (dyspnoea, coughing, wheezing) and others. The animal origin of the novel coronavirus led to a discussion about the possible transmission of the disease by contact with pets. A common fear that raised even more after the confirmation of the SARS-CoV2 in a tiger in the Bronx zoological garden [14]. The World Health Organization faced those concerns stating the lack of evidence on the spreading of the novel coronavirus from pet animals to people [15].

The empirical observations show that the presence of pets may have a positive impact on the course of COVID-19. Anecdotal evidence try to persuade that veterinary doctors are rarely affected with COVID-19. Doctor Sabina Olex-Condor, a Spanish physician in Madrid, suggested in an interview that the mild course is more frequent in patients owning pets (available at: www.vetnolimits.com; www.psy.pl; www.plus.gloswielkopolski.pl). The correlation between pet-ownership and the presence of a mild course of COVID-19 has not been found yet. In our study, we conducted a review of the literature, trying to establish a possible explanation to this observation. We suggest that the re-emerging contact with animal coronaviruses may lead to the stimulation of the immunological system, thus creating an effective response to SARS-CoV-2 infection.

The occurrence of the animal coronavirus in pets

The possible positive effect of pet-ownership can be considered if the presence of the animal coronaviruses is high across the pet population. Therefore, we studied the papers presenting the occurrence of the animal coronaviruses. In our analysis, we focus on dogs, due to two reasons: 1) they are the most common species taken as home pets [16], 2) canine coronaviruses can be transmitted easily to humans via droplets. Feline coronaviruses are also detected in cats, but their symptoms are mainly related to the gastrointestinal tract or are causative agent of uncommon and usually fatal, aberrant immune response to viral infection, but transmission animal-to-human is highly limited [17].

Table 1 shows the detection rate in dogs. According to studies, the detection of canine respiratory coronavirus (CrCoV) is settled from 7.5% to 54.7%. Studies with the most prominent sample (Priestnal et al. 2006 and More et al. 2020) showed detection: 54.7% for North America, 36.0% for the United Kingdom, and 53.0% for New Zealand.

Data show that the occurrence of CrCoV is high in dogs, which might suggest that humans who possess a pet can have more frequent contact with different types of canine coronaviruses. Since the infected pets may not have symptoms, the contact of owners with pathogens can be unnoticed [31].

Cross-reactivity and immune system mobilization

The human immunological system fights different viral infections by three pathways: 1) interferon-mediated, 2) cytotoxic cells-mediated, and 3) antibody-mediated [32]. On the first, interferons provide an effective immunological reaction by the activation of NK-cells and macrophages, repression of viral proteins production, and regulation of antigen presentation to T-cells. On the second path, cytotoxic cells can directly kill the host cells infected by the virus using specific receptors and enzymes, thus stopping further infection [33].

The antibody-mediated ceasing of infection can be executed through different mechanisms: agglutination, phagocytosis or complement system degradation, but all of these are stimulated by the antibody opsonisation [32]. The effectiveness of this process is related to the specificity of the antibody – the capability of the antibody to discriminate between similar and dissimilar antigens. However, due to *cross-reactivity*, antibodies can respond to other antigen due to the resemblance of its structures [34]. Response to a similar antigen can lead to effective immunological protection as it was executed against the primary target. The cross-reactivity is related to the degree of the resemblance of the primary antigen to the other, for example: neutralizing antibodies against "old" SARS-CoV have moderate binding force to novel coronavirus SARS-CoV-2.

The coronaviruses genome encodes for four structural and sixteen non-structural proteins, approximately [35,36]. The spike proteins (S-protein) are the structural proteins that recognize and attach to ACE2 located on the cell membrane of the airways epithelia and lung parenchyma. In their study, Tilocca and colleagues sequenced the SARS-CoV-2 aminoacidic sequence and compared it to the sequences derived from the other animal coronaviruses [37]. The analysis showed that the resemblance of the whole sequence between SARS-CoV-2 and Canine Respiratory Coronavirus (CrCoV) is 36.39% (comparing the protein GI QHR63290 to QAY30030). However, further investigation of the

https://doi.org/10.1016/j.mehy.2020.109831
Received 21 April 2020; Accepted 9 May 2020

Table 1
Summary of studies detecting coronaviruses rate in dogs.

Author	Number of samples (n)	Detection rate	Method	Region
Priestnal et al. (2006) [18]	1000	54.7%	Serology testing	North America
	824	36.0%		UK
More et al. (2020) [19]	1015	53.0%	Serology testing	New Zealand
Priestnal et al. (2007) [20]	490	23.3%	Serology testing	Italy
An et al. (2010) [21]	483	12.8%	Serology testing	Korea
Hielb et al. (2019) [22]	264	7.5%	Serology testing	Austria
Knesl et al. (2009) [23]	251	29.0%	Serology testing	New Zealand
Mitchell et al. (2017) [24]	247	47.0%	Serology testing	Europe
		7.7%	molecular testing	
Decarao et al. (2007) [25]	215	32.0%	Serology testing	Italy
Schulz et al. (2014) [26]	151	9.8%	Molecular testing	Germany
Erles et al. (2003) [27]	119	37.0%	Molecular testing	UK
Erles et Brownlie [28](2005)	113	38.9%	Serology testing	UK
Sowman et al. (2018) [29]	93	50.5%	Serology testing	New Zealand
Wille et al. (2020) [30]	88	14.7%	Molecular testing	Sweden

epitope sequence shows the high homology: 57.14%, 80.00%, 83.33%, and 100.00% in CrCoV epitopes: 789–799, 754–764, 424–437, and 1139–1152, respectively. Based on the data, we suggest that recurrent contact with animal coronaviruses may lead to immunization. This effect was confirmed by ~~the~~ experimental studies. The investigation conducted by Lu and colleagues, showed that the nucleocapsid protein derived from CrCoV and expressed in *E. coli* displayed antigenic cross-reactivity with antisera against human coronaviruses [38].

Furthermore, Zhao and colleagues propose one more explanation to the protective effect of the contact with zoonotic coronaviruses [39]. Cross-reactivity with T-cells can induce the immunological response. CD4+ memory T-cells on the epithelium of the airways can effectively produce interferon-gamma, which leads to activation of other cells and effective reaction.

Thus, patients owning pets could have a mild course of the SARS-CoV-2 infection, which was observed in Spain. The recurrent contact with pathogens may work as immune-mobilization against SARS-CoV-2 in many different paths.

Conclusions

1. Canine respiratory coronaviruses occur often among dogs.
2. Ownership of a pet can lead to the contact with dogs' coronaviruses.
3. Re-occurring contact with dogs' coronaviruses might stimulate the human immunological system, and provide an effective response to SARS-COV-2.
4. There is a need for further investigation on the correlation between pet ownership and the course of COVID-19. Such data, even obtain retrospectively, are worth to analyse.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Wu Y-C, Chen C-S, Chan Y-J. The outbreak of COVID-19: an overview. J Chin Med Assoc 2020;83:217–20.
[2] WHO Coronavirus disease 2019 (COVID-19) Situation Report – 52.
[3] COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU).
[4] Mallapaty S. What the cruise-ship outbreaks reveal about COVID-19. Nature 2020;580:18.
[5] Sorensen MD. Severe acute respiratory syndrome (SARS): development of diagnostics and antivirals. Ann N Y Acad Sci 2006;1067:500–5.
[6] http://www.emro.who.int/health-topics/mers-cov/mers-outbreaks.html.
[7] Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia: MERS, SARS and coronaviruses. Respirology 2018;23:130–7.
[8] Li W. Bats are natural reservoirs of SARS-like coronaviruses. Science 2005;310:676–9.
[9] Ithete NL, et al. Close relative of human middle east respiratory syndrome coronavirus in bat, South Africa. Emerg Infect Dis 2013;19:1697–9.
[10] Woo PCY, et al. Discovery of seven novel mammalian and avian coronaviruses in the genus deltacoronavirus supports bat coronaviruses as the gene source of alphacoronavirus and betacoronavirus and avian coronaviruses as the gene source of gammacoronavirus and deltacoronavirus. J Virol 2012;86:3995–4008.
[11] Woo PCY, et al. Molecular diversity of coronaviruses in bats. Virology 2006;351:180–7.
[12] Lau SKP, et al. Discovery of a novel coronavirus, china rattus coronavirus HKU24, from Norway rats supports the murine origin of betacoronavirus 1 and has implications for the ancestor of betacoronavirus lineage A. J Virol 2015;89:3076–92.
[13] Wang Q, Vlasova AN, Kenney SP, Saif LJ. Emerging and re-emerging coronaviruses in pigs. Curr Opin Virol 2019;34:39–49.
[14] https://www.bbc.com/news/world-us-canada-52177586.
[15] WHO Coronavirus disease (COVID-19) advice for the public: Myth busters.
[16] Applebaum JW, Peek CW, Zsembik BA. Examining U.S. pet ownership using the General Social Survey. Soc Sci J 2020;1–10. https://doi.org/10.1080/03623319.2020.1728507.
[17] Jaimes JA, Whittaker GR. Feline coronavirus: insights into viral pathogenesis based on the spike protein structure and function. Virology 2018;517:108–21.
[18] Priestnall S, Brownlie J, Dubovi E, Erles K. Serological prevalence of canine respiratory coronavirus. Vet Microbiol 2006;115:43–53.
[19] More G, Dunowska M, Acke E, Cave N. A serological survey of canine respiratory coronavirus in New Zealand. New Zealand Vet J 2020;68:54–9.
[20] Priestnall SL, Pratelli A, Brownlie J, Erles K. Serological prevalence of canine respiratory coronavirus in southern italy and epidemiological relationship with canine enteric coronavirus. J VET Diagn Invest 2007;19:176–80.
[21] An D-J, et al. A serological survey of canine respiratory coronavirus and canine influenza virus in Korean dogs. J Vet Med Sci 2010;72:1217–9.
[22] Hiebl A, et al. Detection of selected viral pathogens in dogs with canine infectious respiratory disease in Austria. J Small Anim Pract 2019;60:594–600.
[23] Knesl O, Allan F, Shields S. The seroprevalence of canine respiratory coronavirus and canine influenza virus in dogs in New Zealand. New Zealand Vet J 2009;57:295–8.
[24] Mitchell JA, et al. European surveillance of emerging pathogens associated with canine infectious respiratory disease. Vet Microbiol 2017;212:31–8.
[25] Decaro N, et al. Serological and molecular evidence that canine respiratory coronavirus is circulating in Italy. Vet Microbiol 2007;121:225–30.
[26] Schulz BS, Kurz S, Weber K, Balzer H-J, Hartmann K. Detection of respiratory viruses and Bordetella bronchiseptica in dogs with acute respiratory tract infections. Vet J 2014;201:365–9.
[27] Erles K, Toomey C, Brooks HW, Brownlie J. Detection of a group 2 coronavirus in dogs with canine infectious respiratory disease. Virology 2003;310:216–23.
[28] Erles K, Brownlie J. Investigation into the causes of canine infectious respiratory disease: antibody responses to canine respiratory coronavirus and canine herpesvirus in two kennelled dog populations. Arch Virol 2005;150:1493–504.
[29] Sowman H, Cave N, Dunowska M. A survey of canine respiratory pathogens in New Zealand dogs. New Zealand Vet J 2018;66:236–42.
[30] Wille M, et al. Evolutionary genetics of canine respiratory coronavirus and recent introduction into Swedish dogs. Infect Genet Evol 2020;82:104290.
[31] Buonavoglia C, et al. Canine coronavirus highly pathogenic for dogs. Emerg Infect Dis 2006;12:492–4.
[32] https://www.immunology.org/public-information/bitesized-immunology/pathogens-and-disease/immune-responses-bacteria.
[33] Rosendahl Huber S, van Beek J, de Jonge J, Luytjes W, van Baarle D. T cell responses to viral infections – opportunities for peptide vaccination. Front. Immunol. 2014;5.
[34] Frank SA. Immunology and evolution of infectious disease. Princeton University Press; 2002.
[35] Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication, and

pathogenesis. J Med Virol 2020;92:418–23.
[36] Donnelly CA, et al. Epidemiological and genetic analysis of severe acute respiratory syndrome. Lancet Infect Dis 2004;4:672–83.
[37] Tilocca B, et al. Molecular basis of COVID-19 relationships in different species: a one health perspective. Microbes Infect 2020. https://doi.org/10.1016/j.micinf.2020.03.002. S1286457920300484.
[38] Lu S, et al. Genetic and antigenic characterization of recombinant nucleocapsid proteins derived from canine coronavirus and canine respiratory coronavirus in China. Sci China Life Sci 2016;59:615–21.
[39] Zhao J, et al. Airway memory CD4 + T cells mediate protective immunity against emerging respiratory coronaviruses. Immunity 2016;44:1379–91.

Jan Jurgiel[a,b], Krzysztof J. Filipiak[c,*], Łukasz Szarpak[d], Miłosz Jaguszewski[e], Jacek Smereka[f], Tomasz Dzieciątkowski[g]
[a] *Wroclaw Medical University, Poland*
[b] *Erasmus + Exchange Student at Nova Medical University, Lisbon, Portugal*
[c] *First Chair and Department of Cardiology, Medical University of Warsaw, Poland*
[d] *Lazarski Univeristy, Warsaw, Poland, Polish Society of Disaster Medicine, Warsaw, Poland*
[e] *First Department of Cardiology, Medical University of Gdansk, Gdansk, Poland*
[f] *Department of Emergency Medical Service, Wroclaw Medical University, Wroclaw, Poland*
[g] *Chair and Department of Medical Microbiology, Medical University of Warsaw, Poland*
E-mail address: krzysztof.filipiak@wum.edu.pl (K.J. Filipiak).

* Corresponding author.