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Transmission of SARS-CoV-2 from humans to a 16-year-old domestic cat with comorbidities in Pennsylvania, USA

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Abstract

Background and Objectives: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), besides causing human infection, has been shown to naturally infect several susceptible animal species including large cats (tigers, lions, pumas, spotted leopards), dogs, cats, ferrets, gorillas and minks. Cats and minks are continuing to be the most reported species with SARS-CoV-2 infections among animals but it needs to be investigated further.

Methods and Results: We report the detection of SARS-CoV-2 from a domestic cat that exhibited respiratory disease after being exposed to SARS-CoV-2 virus from humans in the same household. SARS-CoV-2 RNA was detected in two oropharyngeal swabs collected at two time points, 11 days apart; the first, when the cat was reported to be sick and the second, before euthanasia due to poor prognosis. The viral nucleic acid detected at two time points showed no genomic variation and resembled the clade GH circulating in humans in the United States. Clinical and pathological findings noted in this 16-year-old cat were consistent with respiratory and cardiac insufficiency.

Conclusions: SARS-CoV-2 viral infection was likely an incidental clinical finding, as the virus was not detected in fixed lungs, heart, or kidney tissues. Only fresh lung tissue collected at necropsy showed the presence of viral nucleic acid, albeit at a very low level. Further research is needed to clarify the clinical course of SARS-CoV-2 in companion animals of advanced age and underlying cardiac disease.

KEYWORDS
cat, histopathology, infection, lungs, rRT-PCR, SARS-CoV-2, transmission

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) belongs to the species SARS-related coronavirus of the *Coronaviridae* family (Abdelrahman et al., 2020; Haake et al., 2020; Li et al., 2020). The receptor-binding domain of the spike protein of SARS-CoV-2 binds to the angiotensin converting enzyme-2 (ACE2) receptor. The ability to bind to ACE-2 receptors is one of the key determinants of

the susceptibility of a given host species to infection by SARS-CoV-2. Based on the receptor homology, even though SARS-CoV-2 has caused primarily human infection, interspecies transmission of SARS-CoV-2 was predictable (Chiocchetti et al., 2020; Luan et al., 2020; Shi et al., 2020). Subsequently, several reports of SARS-CoV-2 infection of feline and canine species have been recorded worldwide (Barrs et al., 2020; Garigliany et al., 2020; Gaudreault et al., 2020; Musso et al., 2020; Sailleau et al., 2020; Segalés et al., 2020; Sit et al., 2020). Cats and minks have been the most reported species with SARS-CoV-2 infection; but animals so far have not been shown to be responsible for disease transmission to humans, except for one report of human transmission from minks in Europe (Molenaar et al., 2020; Newman et al., 2020; Oude Munnink et al., 2021). In this study, we report transmission of SARS-CoV-2 to a domestic cat (*Felis catus*) in the U.S. state of Pennsylvania, from infected humans living in the same household. The cat exhibited clinical signs consistent with respiratory disease and cardiac insufficiency. The study highlights the pathological and viral observations in the cat where SARS-CoV-2 infection was considered an incidental finding.

2 | MATERIALS AND METHODS

2.1 | Case history

A 16-year-old, domestic long-haired neutered male cat weighing 7.5 lb with prior history of hypertrophic cardiomyopathy and no other history of underlying conditions was examined at a veterinary clinic on October 2, 2020, for evaluation of signs of respiratory disease including coughing and dyspnea. The cat was living in a household with multiple family members who had been diagnosed with SARS-CoV-2 infection. The earliest confirmed case in the household was reported on September 12, 2020. Additional three family members were confirmed SARS-CoV-2 positive on or by September 18, 2020. SARS-CoV-2-positive family members had maintained close contact with the cat while they were sick. Nasal, oropharyngeal and rectal swabs were collected from the cat 11 days apart; the first, when the cat was reported to be sick, and the second, before euthanasia due to poor prognosis. No additional animals were living in this household.

2.2 | Histopathology

Whole lung, heart and liver were placed in 10% neutral buffered formalin at room temperature for at least 3 days. Tissues were subsequently processed for histopathology using a routine paraffin embedding and haematoxylin and eosin (H&E) staining procedure using Tissue-Tek Automated slide-stainer (Sakura Finetek, USA).

2.3 | SARS-CoV-2 rRT-PCR

Oral, nasopharyngeal and rectal swabs in brain heart infusion broth, and fresh tissues collected post-mortem (lung, heart and kidney), were evaluated for the presence of SARS-CoV-2 RNA by real-time reverse transcription PCR (rRT-PCR) (Corman et al., 2020; Lu et al., 2020). All specimens were screened with four separate rRT-PCRs targeting the SARS-CoV-2 RNA-dependent RNA polymerase (RdRP), Envelope (E) and Nucleocapsid (N1 and N2) genes. RNA was extracted using the EZ1 Virus Mini Kit version 2.0 (Qiagen, Germantown, MD). Briefly, minced tissue was added to 1 mL of brain heart infusion broth, and specimens were vortexed prior to centrifuging at 1500 × *g* for 5 min. A total of 200 μL of ATL buffer was mixed with 200 μL of the tissue homogenate or swab fluid. RNA was extracted from 400 μL of the liquid on an automated nucleic acid purification workstation (BioRobot EZ1 workstation, Qiagen) following the manufacturer's recommendations. rRT-PCR primers and probe for the RdRP-gene and E-gene assays were obtained from TIB MOLBIOL, Berlin, Germany (LightMix® Modular Wuhan CoV RdRP-gene assay and LightMix® Modular SARS and Wuhan CoV E-gene assay) and were described previously (Corman et al., 2020). rRT-PCR primers and probe for the CDC N1 assay and N2 assay were obtained from Integrated DNA Technologies, Inc. (IDT, Coralville, IA) and were described in the CDC 2019-Novel Coronavirus (2019-nCoV) rRT-PCR Diagnostic Panel (Lu et al., 2020). The rRT-PCR reaction mixes consisted of RT-PCR buffer, RT-PCR enzyme mix (AgPath-ID™ One-Step RT-PCR Reagents, ThermoFisher Scientific), primers/probe sets (RdRP, E, N1 or N2 primer probe mix), and 5 μL of extracted nucleic acid. Primer/probe concentrations were used as recommended in Corman et al. (2020) and by a CDC recommended protocol (Corman et al., 2020; Lu et al., 2020). rRT-PCR was performed using thermal cycling condition consisting of 1 cycle at 50°C for 10 min, 1 cycle at 95°C for 10 min followed by 45 cycles of 95°C for 15 s, 55°C for 45 s (ABI 7500 Fast, ThermoFisher Scientific, Waltham, MA). All specimens were submitted to the USDA National Veterinary Services Laboratories for confirmatory rRT-PCR testing after the initial SARS-CoV-2 detection. In addition, formalin fixed tissues were subjected to rRT-PCR at the CDC as described previously (Martines et al., 2020).

2.4 | Viral sequencing

A library of SARS-CoV-2 viral nucleic acid recovered from the cat oropharyngeal swab was generated using the Ion AmpliSeq Kit for Chef DL8 and Ion AmpliSeq SARS-CoV-2 Research Panel (Thermo Scientific) for the whole genome sequencing. Specimens that were positive for the virus or nucleic acids material were, however, not available from humans in the same household who had been confirmed positive. The library was sequenced using an Ion 520 chip on the Ion S5 system using the Ion 510™ & Ion 520™ & Ion 530™ Kit. Sequences were assembled using IRMA version 0.6.7 and visually verified using DNAStar SeqMan NGen version 14. MAFFT was used to align FASTA files using a maximum number of iterative refinement number of 1000 (Katoh et al., 2002; Shepard et al., 2016). The alignment was used to output a phylogenetic tree using RAxML with GTRCAT model.

The data sets of 1343 SARS-CoV-2 genomes deposited in GISAID from North America (sampled between December 2019 and

December 2020) were used for phylogenetic analysis using the standard protocol from Nextstrain/Nextclade (https://nextstrain.org/sars-cov-2/). MAFFT version 7.471 was used for the alignment and implemented the rapid phylodynamic alignment pipeline for clade assignment leveraging the maximum likelihood as described (Hadfield et al., 2018). Assemblies were also uploaded to GISAID-CoVSurver (https://www.gisaid.org/epifluapplications/covsurver-mutations-app/) to determine the mutations relative to SARS-CoV-2 assemblies available on the GISAID database.

Fourteen complete genomes of SARS-CoV-2 isolates from feline and canine species in the United States were downloaded from NCBI GenBank. MAFFT alignment was performed along with the case cat sequence assembly and pursued Neighbor-Joining phylogenetic tree with Tamura-Nei (genetic distance model) using Geneious Tree Builder (v. 2021.0.3).

3 | RESULTS

3.1 | Case clinical observations and testing

On initial presentation at the veterinary clinic on October 2, 2020, the cat exhibited signs of respiratory distress, including congestion and dyspnoea, with a respiratory rate of 45 breaths per minute, a body temperature of 99.8F and a heart rate of 220 beats/min. The cat's hair coat, skin, eyes, ears, nose, throat and mouth appeared normal. The cat had normal mentation, and no urogenital or gastrointestinal issues were appreciated. Diagnostics performed included radiographs of the thorax and abdomen with ventro-dorsal and lateral views and swabs of the cat's upper respiratory tract were collected to test for common respiratory pathogens including feline calicivirus, H1N1 influenza, *Bordetella bronchiseptica*, *Chlamydophia felis*, feline herpesvirus-1 and *Mycoplasma felis*, as well as SARS-CoV-2. Swab submitted to Antech was negative for all the common respiratory pathogens and were positive for SARS CoV-2 (Ct 28.2) with N gene rRT-PCR testing. This initiated additional follow-up as the cat was presented for examination due to deteriorating condition (Supporting information Figure S1).

Radiographic examination was conducted at the initial visit to the veterinary clinic. Lateral and ventro-dorsal views of the thorax showed progressive cardiomegaly when compared to radiographs taken 1 year ago, which was interpreted as probable feline cardiomyopathy. The suspected pulmonary venous enlargement and the pulmonary interstitial to alveolar patterns observed were consistent with left-sided heart failure. The radiographs revealed poorly defined patches of interstitial to alveolar patterns in the caudal lung field that were less marked cranioventrally (Figure 1a). There was also a triangular soft tissue opacity to the right of the cardiac silhouette on the ventro-dorsal view and mild pleural effusion. No mediastinal mass or lymphadenopathy was identified. The oesophagus and the trachea were within normal limits. The gastrointestinal tract was generally unremarkable with mild hepatomegaly and incidental age-related changes.

The cat returned to the veterinary clinic on October 13, 2020 due to progression of clinical signs including severe respiratory distress, abdominal paradoxical breathing, severe exercise intolerance, pale mucous membranes and a body condition score of 1/5. Due to poor prognosis and to avoid further suffering, the cat was euthanized. The cat was necropsied at the veterinary clinic and formalin-fixed whole lung, heart and liver and fresh heart, kidney and lung were submitted for examination. For histologic examination, lung, heart and liver tissues were fixed in 10% neutral-buffered formalin, embedded in paraffin, sectioned at 5 μm, and stained with H&E for examination by light microscopy.

3.1.1 | Pathological finding

The gross and histological findings in the heart were consistent with myocardial hypertrophy most likely due to hypertrophic cardiomyopathy. Grossly, the heart weighed >0.36% of body weight with nearly diffuse mineralization throughout the ventricular walls and increased left ventricular wall thickness consistent with left ventricular myocardial hypertrophy. There was dark discoloration of the cranial aspect of the left caudal lung lobe, sections of which sank in formalin. The liver had a diffuse faint reticular pattern.

Microscopically, the heart had moderate multifocal cardiomyocyte hypertrophy and disarray with degeneration, necrosis and severe mineralization and fibrosis (Figure 1b). The lungs had mild to moderate multifocal alveolar histiocytosis and interstitial fibrosis with oedema, congestion,and haemorrhage. Both right and left caudal, cranial, middle and accessory lung lobes showed fibrosis, increased numbers of macrophages and lymphocytes, minimal to mild oedema, fibrin and minimal type II pneumocyte hyperplasia, and mild to moderate multifocal congestion including alveolar involvement. In a small sub-pleural focus on the left caudal lung lobe, there was increased alveolar septal thickness and moderate alveolar haemorrhage; multifocally bronchi and bronchioles contained few to moderate numbers of macrophages, rare neutrophils, few necrotic mononuclear cells admixed with fibrillar eosinophilic material and a small to moderate amount of blood and mucus (Figure 1c and d). Also, there was moderate multifocal peribronchovascular oedema; bronchial glands were occasionally dilated, lined by attenuated epithelium, and filled with eosinophilic secretion; accompanied with multifocal calcification of bronchial cartilage. The liver had moderate diffuse centrilobular congestion with hepatocellular atrophy and perivenous and perisinusoidal fibrosis, and mild to severe multifocal lymphocytic cholangitis. There was severe chronic lymphocytic cholecystitis with adenomatous hyperplasia in the gallbladder.

3.1.2 | Viral detection and phylogeny

SARS-CoV-2 was initially detected by rRT-PCR in oropharyngeal swab collected October 2, 2020 with the N gene testing only (Ct 28.4) at Antech Diagnostics (Fountain Valley, CA). The oropharyngeal swab collected post-mortem on October 13, 2020 showed the following *Ct* values for the genes N1: 30.1; N2: 30.1, E: 31.3 and RdRP: 37.0.

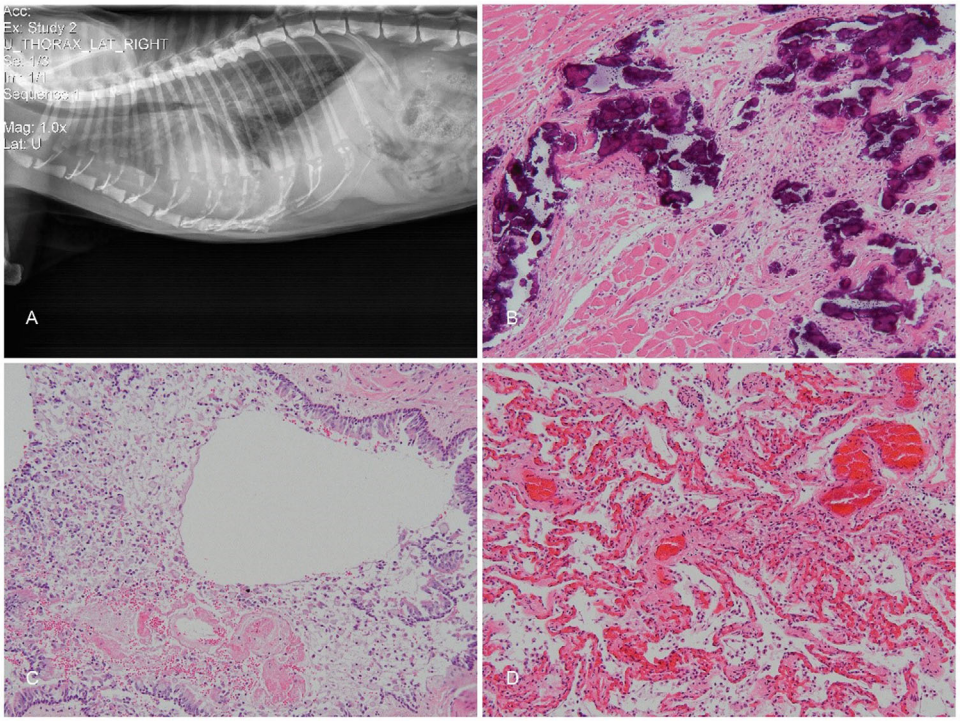


FIGURE 1 (a) Radiograph of thorax (lateral right) view showing cardiomyopathy and pulmonary interstitial to alveolar patterns in the lung of a SARS-CoV-2 infected cat. (b) Heart showing histologically cardiomyocyte hypertrophy and degeneration, mineralization and fibrosis (hematoxylin and eosin stain 10×). (C) Left caudal lung histologically showing macrophages, mononuclear cells with fibrillar material in bronchi and bronchioles (hematoxylin and eosin stain 10×). (D) Right caudal lobe histologically showing alveolar histiocytosis and interstitial fibrosis with edema, congestion, and hemorrhage (hematoxylin and eosin stain 10×)

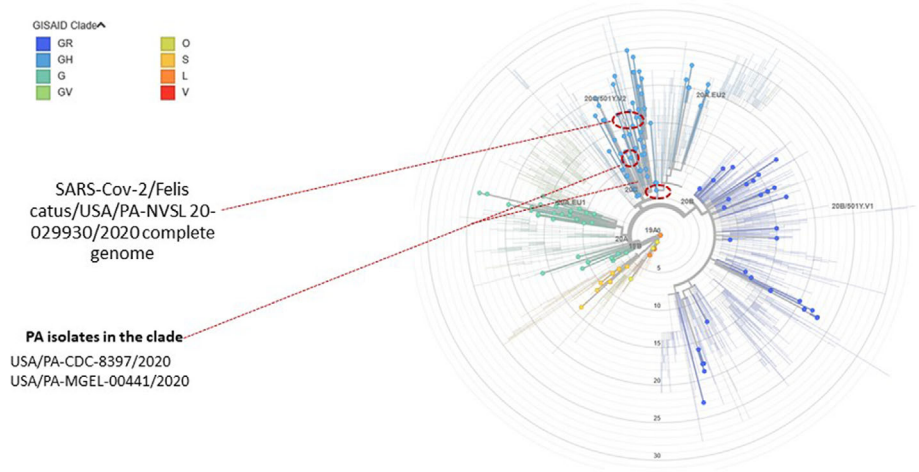
Additionally, rectal and nasal swabs collected post-mortem from external nares did not show presence of the virus with rRT-PCR. Lung tissue was rRT-PCR positive with N1 *Ct* value 36.8 and N2 *Ct* value 36.9, while heart and kidney tissues were negative for SARS-CoV-2 but negative with formalin-fixed, paraffin-embedded (FFPE) tissue-rRT-PCR targeting the N gene specifically examining the cranial-cranial, caudal and cranial lung lobes for SARS-CoV-2. Sequencing directly from the positive PCR specimen yielded 29,834 bp viral sequence, which has been uploaded in FASTA format (GISAID accession ID EPI_ISL_3128551) as SARS-Cov-2/Felis catus/USA/PA-NVSL 20–029930/2020.Phylogenetic analysis and gene assembly showed ten amino acid mutations compared to the Wuhan-Hu-1 sequence (GenBank accession number NC_045512) as per the mutant calling analysis performed using GISAID-CoVSurv (Table 1). The NextClade analysis (Bosco-Lauth et al., 2020; Shi et al., 2020; Oude Munnink et al., 2021) performed confirmed the clade as GH defined by D614G and Q57H mutations (Pereson et al., 2021). The cat sequence and two other sequences from human clinical specimens from the state of Pennsylvania clustered in the clade node of GH/20C (Figure 2).

Geneious Tree Builder (Genious Prime) was utilized to build Neighbor-Joining phylogenetic tree with Tamura-Nei (genetic distance model) to understand the level of relatedness among the feline and canine sequences from the cases reported in the United States. The sequences clustered well within the defined specific clades. The Pennsylvania cat SARS-CoV-2 sequence was observed to have minimal pairwise distance from the Texas cat sequence (TAMU) which also belongs to clade GH, and greater diversity from the lion sequences which belong to clade V (Supplementary Figure 2).

TABLE 1 Genome-wide mutations for SARS-Cov-2/Felis catus/USA/PA-NVSL 20–029930/2020 nucleic acid recovered from cat in Pennsylvania, USA

Location	Mutaion	Count
S	N_S183Y	1
Q	NS3_Q57H	1
Q	NSP3_Q168K	1
T	NSP2_T85I	1
T	NSP3_T749I	1
T	NSP3_T1348I	1
D	Spike_D614G	1
I	NSP13_I570V	1
P	NSP12_P323L	1
R	NSP2_R27C	1

SARS-Cov-2/Felis catus/USA/PA-NVSL 20–029930/2020 complete genome was used to perform the genome-wide mutation and the clade analysis. Compared to the Wuhan-Hu-1 sequence (GenBank accession number NC_045512), the cat sequence contained 10 amino acid variations. NextClade analysis performed confirmed the clade as GH defined by D614G and Q57H mutations.



PA Cat SARS-CoV-2 isolate clustered closely with SARS-CoV-2/human/PA isolates (in GSAID database)

FIGURE 2 Whole genome phylogeny of the SARS-CoV-2 nucleic acid sequence obtained from clinical specimen from infected cat. The 87 consensus reference genomes deposited from United States are available in GISAID database. The cat sequence and two other sequences from human clinical specimens from the state of Pennsylvania clustered in the same clade node. The NextClade analysis performed confirmed the clade as GH defined by D614G and Q57H mutations

4 | DISCUSSION

The virus that causes COVID-19 originated in an animal reservoir, likely a bat, but is now primarily spreading person to person (Abdelrahman et al., 2020; Li et al., 2020). Several instances of SARS-CoV-2 animal infections have been reported worldwide, primarily in Felidae (cats, lions tigers), non-human primates, dogs and minks (Barrs et al., 2020; USDA, 2021; Garigliany et al., 2020; Gaudreault et al., 2020; Li et al., 2020; Molenaar et al., 2020; Musso et al., 2020; Sailleau et al., 2020; Segalés et al., 2020; Sit et al., 2020; Zhang et al., 2020). Similar to animal infections reported worldwide, animals with exposure to human COVID-19 cases in the United States have been found to be permissive for SARS-CoV-2 infection and viral replication in some situations, after close contact with humans. SARS-CoV-2 so far has been shown to replicate poorly in these animal species, with the exception of mink (Bosco-Lauth et al., 2020; Shi et al., 2020; Oude Munnink et al., 2021). Natural SARS-CoV-2 infection of birds, horses, cattle and camelids has not been recorded (USDA, 2021). Viral transmission has been documented to occur from human to domestic animals, and animal to animal transmission in companion animals has only been shown to occur in experimental settings and naturally among minks (Hamer et al., 2020; Oude Munnink et al., 2021). Guidance for veterinarians and pet owners with concerns about COVID-19 is available from CDC (CDC, 2021).

The SARS-CoV-2 virus has already caused more than 2 million human deaths worldwide and more than 500,000 deaths in the United States as of March 12, 2021 https://coronavirus.jhu.edu. Viral detection primarily relies on rRT-PCR testing for one or more of the following gene targets: Open reading frame (ORF1ab), N1, N2, E and RdRP (Corman et al., 2020; Lu et al., 2020). In this study, we described exposure and infection of a cat with SARS-CoV-2 and described radiographic and pathological changes in the lungs to investigate if such changes were caused by or were exacerbated by viral presence.

The cat was euthanized because of poor prognosis and severe disease providing a unique opportunity to combine radiographic, pathologic and virological findings for studying the disease pathogenesis in this host. One other recent study from Spain reported SARS-CoV-2 infection in a 4-year-old cat with hypertrophic cardiomyopathy, oedema and thrombosis in the lungs (Segalés et al., 2020). The pathological findings reported in our study were consistent with this previous report; and in addition, we provide details of lung pathology and cardiomyopathy observed during the examination. The virus was readily detected in the upper respiratory tract by all virus gene targets used for detection of SARS-CoV-2. Even though RdRP rRT-PCR showed detection, higher *Ct* value was observed consistently in our hands. This gene target is used in combination with E gene for SARS-CoV-2 infection confirmation (Corman et al., 2020). Both N1 and N2 showed weak reactivity upon testing of fresh lung tissue with rRT-PCR, while E and RdRP genes were not detected. The SARS-CoV-2 nucleic acid was also not detected in the lungs, including major bronchial areas, with rRT-PCR performed on formalin-fixed tissue. Weak viral detection in the lung (only for N1 and N2) could be due to the presence of mucus and necrotic debris in larger airways containing viral nucleic acid fragments but is probably not caused by virus replication as ascertained by FFPE rRT-PCR. This was further supported with histopathologic observations within the bronchi and bronchioles showing small to moderate amount of blood and mucus as likely source of weak detection in the fresh tissue. Weak or no detection of virus in the lungs was in contrast to reports of extensive virus replication in the lungs of humans infected with SARS-CoV-2. However, the finding of higher

virus detection in the upper respiratory tract in the cat was similar to humans, where the virus has been shown to replicate preferentially (Wölfel et al., 2020).

Pathological observations in humans have shown diffuse alveolar disease, oedema, with cellular fibromyxoid exudates, desquamation of pneumocytes and hyaline membrane formation, indicating acute respiratory distress syndrome. Interstitial lymphocytic infiltrates and syncytial cells showing viral cytopathic-like changes have been reported (Geramizadeh and Marzban, 2020; Xu et al., 2020). Another human study reported congestion, oedema and moderate infiltration by monocytes and lymphocytes of the blood vessels of alveolar septae as well as exfoliation of bronchial epithelial cells along with pulmonary interstitial fibrosis (Tian et al., 2020; Yao et al., 2020). In the cat's lungs from the present study, the predominant finding was mild to moderate multifocal alveolar histiocytosis and interstitial fibrosis with edema, congestion and haemorrhage. There was fibrosis, increased numbers of macrophages and lymphocytes, minimal to mild edema, fibrin, minimal type II pneumocyte hyperplasia and mild to moderate multifocal congestion including alveolar involvement. Changes in the lungs were referable to the advanced cardiomyopathy with extensive mineralization rather than a primary viral aetiology.

Presence of co-morbidities can strongly influence disease progression and disease outcomes in humans and animals infected with the SARS-CoV-2 virus (Fang et al., 2020). Serious disease outcomes have been documented when advanced age and or co-morbidities are contributing factors in humans with SARS-CoV-2 infection. The SARS-CoV-2 infected cat described in this study suffered from both age-related changes and hypertrophic cardiomyopathy along with other co-morbidities as also reported previously in this and other cats (Carpenter et al., 2021). SARS-CoV-2 infection was not associated with virus-mediated tissue damage in this cat and was not the primary cause of morbidity, however, further research is needed to understand SARS-CoV-2 presentation and contribution in animals with severe underlying disease. Dysregulated proinflammatory cytokine response often referred to as a cytokine storm has been attributed to the severe disease pathogenesis in SARS-CoV-2 infected humans (Ruscitti et al., 2020). Interestingly, the cat lung in this study did show presence of increased lymphocytes. For species in which SARS-COV-2 seems to cause serious disease, further study to characterize the types of cells involved and the up- or down-regulation of cytokines or other cell markers could further elucidate the disease pathogenesis in this and other susceptible species.

Importantly, the viral nucleic acid recovered from specimens collected at two different time points, with the encounters 11 days apart, showed no mutation from human virus circulating in the United States, implying that recovered virus did not develop any changes while undergoing limited replication (data not shown). At this time, there is no evidence that animals play a significant role in spreading the virus that causes COVID-19. Based on the limited information available to date, the risk of animals spreading COVID-19 to people is considered to be low. The virus is still evolving with several mutations in coding and non-coding regions with a few being ascribed to severe outcome (e.g., G614) (Korber et al., 2020). Mutations in feline enteric coronavirus have been shown to result in more serious outcomes for cats. For example, mutations in the spike protein of feline infectious peritonitis virus were ported to cause serous effusions in cats (Paltrinieri et al., 2020). As with other animals, it is possible that SARS-CoV-2 could mutate and become adapted to cause severe disease or increase transmission among cats. Increased exposure of cats to SARS-CoV-2 could result in the virus becoming a multi-species zoonosis. Therefore, a comprehensive One Health approach is urgently needed to control the COVID-19 pandemic including continued efforts directed at minimizing the exposure of susceptible animals to COVID-19 positive humans (CDC, 2021).

STATEMENT

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services or CDC.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

ETHICAL STATEMENT

The authors confirm that the ethical policies of the journal have been adhered to. No additional ethical approval was required. The disease investigation was approved by state regulatory officials.

AUTHOR CONTRIBUTIONS

Deepanker Tewari: Conceptualization; Investigation; Project administration; Supervision; Writing–original draft; Writing–review & editing. Lore Boger: Data curation; Investigation; Methodology; Resources; Supervision; Visualization; Writing–review & editing. Steven Brady: Investigation; Methodology; Resources. Julia Livengood: Investigation; Methodology; Validation; Writing–original draft. Mary Lea Killian: Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing–original draft; Writing– review & editing. Meera Surendran Nair: Data curation; Formal analysis; Investigation; Methodology; Resources; Software; Writing–original draft. Nagaraja Thirumalapura: Investigation; Methodology; Resources; Supervision; Validation; Writing–original draft; Writing–review & editing. Corey Zellers: Data curation; Investigation; Methodology; Software. Ann Carpenter: Formal analysis; Investigation; Methodology; Writing–original draft; Writing–review & editing. Amber Kunkel: Investigation; Methodology; Writing–review & editing. Kevin Brightbill: Funding acquisition; Project administration; Resources; Supervision

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