

Perirenal subcapsular hematomas in feline infectious peritonitis

Perirenale subcapsulaire hematomen bij feliene infectieuze peritonitis

¹L.E. de Jong, ²L. Vanden Buijs, ²S. Coppens, ²S. Theuns, ²H. Nauwynck, ¹K. Chiers, ¹B. De Jonge

¹Department of Veterinary Pathology, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, B-9820 Merelbeke, Belgium

²Laboratory of Virology, Department of Translational Physiology, Infectiology and Public Health, Faculty of Veterinary Medicine, Ghent University, B-9820 Merelbeke, Belgium

ledejong1011@gmail.com

ABSTRACT

In this article, the occurrence of perirenal subcapsular hematomas associated with feline infectious peritonitis (FIP) is described. The three cats included in the study showed signs of cachexia, anemia and icterus. Post mortem, typical lesions of FIP were found, as well as a subcapsular perirenal hematoma associated with renal pyogranuloma. Most likely, severe pyogranulomatous inflammation caused vascular rhexis eventually leading to this hematoma formation. Nanopore sequencing resulted in a genetic tree that showed that the sequences of the cats belonged to the same serotype, but were not related to each other. In this case series, it is demonstrated that perirenal hematomas can develop as a complication of FIP.

SAMENVATTING

In dit artikel wordt het voorkomen van perirenale subcapsulaire hematomen geassocieerd met feliene infectieuze peritonitis (FIP) beschreven. De drie katten in de studie vertoonden tekenen van cachexie, anemie en icterus. Post mortem werden typische letsels van FIP vastgesteld, evenals een subcapsulair perirenaal hematoom geassocieerd met renale pyogranulomen. Het meest aannemelijk is dat ernstige pyogranulomateuze inflammatie de oorzaak was van vasculaire rhexis, die uiteindelijk heeft geleid tot hematoom vorming. Nanopore sequencing resulteerde in een genetische boom waaruit bleek dat de sequenties van de drie katten tot hetzelfde serotype behoorden, maar niet gerelateerd waren. In deze casusreeks wordt aangetoond dat perirenale hematomen zich kunnen ontwikkelen als een complicatie van FIP.

INTRODUCTION

Feline infectious peritonitis, also known as FIP, is a severe systemic illness in cats. It is caused by a coronavirus, more specific the feline infectious peritonitis virus (FIPV). Based on gross lesions, two forms have been described: the wet or effusive form and the dry or non-effusive form (Hartmann, 2005; Pedersen, 2009; Drechsler et al., 2011). The wet form is characterized by fibrinous and pyogranulomatous polyserositis, in combination with protein rich serous effusion in the abdominal cavity. The dry form is known for typical pyogranulomatous formation in different or-

gans. A combination of the two forms, known as the transition form, frequently occurs. The kidneys are the most important target organ, but the virus also has a tropism for the brain and the eyes (Montali and Strandberg, 1972; Weiss and Scott, 1981b; Hartmann, 2005). Aside from these typical forms, a large variation in affected organs and body cavities can occur (Pedersen, 2009; Beatty and Barrs, 2010; Spencer et al., 2017; Green et al., 2023).

The feline coronavirus (FCoV) is part of group 1 alphacoronaviruses. It is an RNA virus with an envelope and a wide genome (Pedersen, 1976). The spike protein on the envelope consists of two domains: a

S1 receptor binding domain and the S2 fusion peptide domain (Bosch et al., 2003). These domains play a major role in the determination of cell tropism (Belouzard et al., 2012). The FIP virus replicates very efficiently in monocytes, resulting in a hematogenous spread and systemic illness (Weiss and Scott, 1981a). FIPV originates from the feline enteric coronavirus (FECV) being a cause for mostly subclinical enteritis in kittens (Pedersen et al., 1981). This is a mildly pathogenic virus which replicates in enterocytes. However, FECV can also infect monocytes and spread outside of the intestines via monocyte-associated viremia (Gunn-Moore et al., 1998; Kipar et al., 1999; Meli et al., 2004; Kipar et al., 2006). Chang et al. (2012) described a mutation in the spike protein to be responsible for the changing cell tropism between these coronaviruses. Another associated mutation is a deletion in the open reading frame (ORF) of the accessory 3c gene (Vennema et al., 1998).

Humoral immunity offers little to no protection against FIP because of a so-called antibody dependent enhancement (ADE) (Pedersen and Boyle, 1980). In vitro, the virus-antibody immune complexes that are formed due to the humoral immunity, will bind to the Fc-receptor of the macrophages, followed by endocytosis and infection of new monocytes/macrophages (Stoddart and Scott, 1989; Olsen et al., 1992). The S protein is shown to be responsible for this phenomenon (De Groot et al., 1989; Vennema et al., 1990; Corapi et al., 1992; Olsen et al., 1992).

Vasculitis, inflammation of blood vessels, is a histological hallmark of FIP infection (Hartmann, 2005). In particular, the small and medium sized veins of the renal cortex, the eyes and the leptomeninges can be affected (Montali and Strandberg, 1972; Kipar et al., 2005). The vasculitis has been described as granulomatous and necrotizing phlebitis and periphlebitis (Montali and Strandberg, 1972; Hayashi et al., 1977; Weiss et al., 1980; Kipar et al., 1998). This vasculitis is a consequence of virus-infected macrophages aggregating and infiltrating these blood vessel walls (Kipar et al., 2005). Although FIP is a well-described disease in cats, perirenal hematoma formation has not been reported in the current scientific literature.

The objective of this case series was to characterize three cases of FIP with perirenal hematoma formation. Therefore, gross immunohistological and histological findings are described, as well as the sequencing results.

MATERIAL AND METHODS

Animals and pathology

This article is based on three cases. Each cat was separately presented for autopsy at the Laboratory of Veterinary Pathology of Ghent University. They were in no way connected to each other. The first cat, from now on referred to as animal #1, was a male castrated

British shorthair of 8,5 months old. The post-mortem interval was three days. The second cat, from now on referred to as animal #2, was presented for autopsy with a post-mortem interval of one day. It was a British longhair, female spayed of six months old. A Ragdoll, from now on referred to as animal #3, was a male, castrated cat of eight months old. The post-mortem interval was three days. All three cats were necropsied in 2022.

A complete necropsy was performed on every cat. Animals #1 and #2 showed mild post-mortem autolysis, while animal #3 showed moderate autolysis. A random sample containing the complete cortex and medulla was taken from the kidneys with hematoma formation of each of the cats. Additional samples from the liver, lungs and spleen were collected in cases #2 and #3. The samples were fixated by immersion in 10%-buffered formalin. After fixation, sections of 5 µm thick were routinely stained using hematoxylin and eosin (H&E). From each animal, immunohistochemistry for FCoV was performed to identify the virus within the renal lesion and confirm the diagnosis of FIP.

Nanopore sequencing

The supernatant was obtained during tissue suspension and used for RNA extraction according to the protocol of the producer Indispin Pathogen Kit (Indical Bioscience). RT-qPCR was performed to detect the number of genome replications of Open Reading Frame 1b (ORF1b). The Precision OneStep RT-qPCR Mastermix was used in combination with Orf1bFW and Orf1bRV primers. Subsequently, whole genome sequencing was performed by PathoSense via nanopore sequencing (Oxford Nanopore Technologies, United Kingdom). This included cDNA generation and PCR amplification using in-house developed primers using an amplicon tiling approach. The library was prepared using the rapid library preparation (SQK-RBK110-96; ONT) protocol and sequenced on an R9.4.1 flow cell using a GridION device (ONT).

The raw reads were assembled into genomes using canu (v2.2; Koren et al., 2017) and polished with minimap2 (v0.2-r123; Li, 2018) and medaka (v1.7.3; ONT). Genomes were manually assessed and curated to ensure correct assembly.

Phylogenetic analysis

The assembled genome sequences were supplemented with the complete feline coronavirus sequences available from NCBI (15/10/2023). The sequences were aligned using MAFFT (v.7.453; Katoh et al., 2002). The tree was constructed using IQTREE (v1.6.12; Nguyen et al., 2015), IQTREE's built-in ModelFinder was used to select the best evolutionary model and visualized with iTOL (Interactive Tree Of Life (iTOL) v6: an online tool for phylogenetic tree display and annotation (<https://itol.embl.de/>)).

RESULTS

Anamnestic findings

Animal #1 was a British shorthair of 8.5 months old, male, castrated, weighing 2.86 kilograms. The animal showed signs of hyporexia, hypodipsia and hyperthermia. The cat was already on antimicrobials (amoxicilline with clavulanic acid) and meloxicam, which did not seem to alleviate his condition. The clinical signs progressed with icterus, anemia and weakness of the hindlimbs. On the abdominal ultrasound, bilateral renomegaly with an irregular cortex and cysts were observed. A large amount of fluid around the kidneys and in the abdominal cavity was seen. The cat was euthanized because of the bad clinical status and a high suspicion of FIP.

The British longhair of six months old, female, spayed, with a weight of 1.56 kilograms is referred to as animal #2. The cat showed the following clinical signs: icteric mucosae, dehydration and cachexia. She was hospitalized with fluids, antimicrobials and maropitant (Cerenia, Zoetis Belgium). The cat died before further diagnostics could be carried out.

The Ragdoll of eight months old, male, castrated is referred to as animal #3. His weight on autopsy was 1.88 kilograms. The cat showed signs of lethargy, icterus and had pale mucosae. There was a high suspicion of FIP, but despite the anti-viral treatment with GS-441524 and cortisone injection, his condition was still deteriorating with the development of anorexia and cachexia. Clinical examination showed bilateral renomegaly, severe dehydration and anisocoria. Blood examination showed severe regenerative normocytic normochromic anemia with a hematocrit of 13.4%, leukocytosis, mild thrombocytopenia, mild elevated urea and phosphor, mild hyperbilirubinemia and severe hypernatremia. Additionally, the abdominal ultrasound showed bilateral hyperechogenic kidneys with an irregular cortex and hydronephrosis of the left kidney (Figures 1 and 2). Free subcapsular fluid was observed. The mesenteric lymph nodes were mild to moderately enlarged. The final diagnosis was pyogranulomatous nephritis and lymphadenitis plus anisocoria, which was highly suspicious for FIPV. After the hospitalization with fluids, metoclopramide (Emepid, Ceva Belgium), maropitant (Cerenia, Zoetis Belgium) and a nasoesophageal feeding tube, the cat died. The total ill duration was seven days.

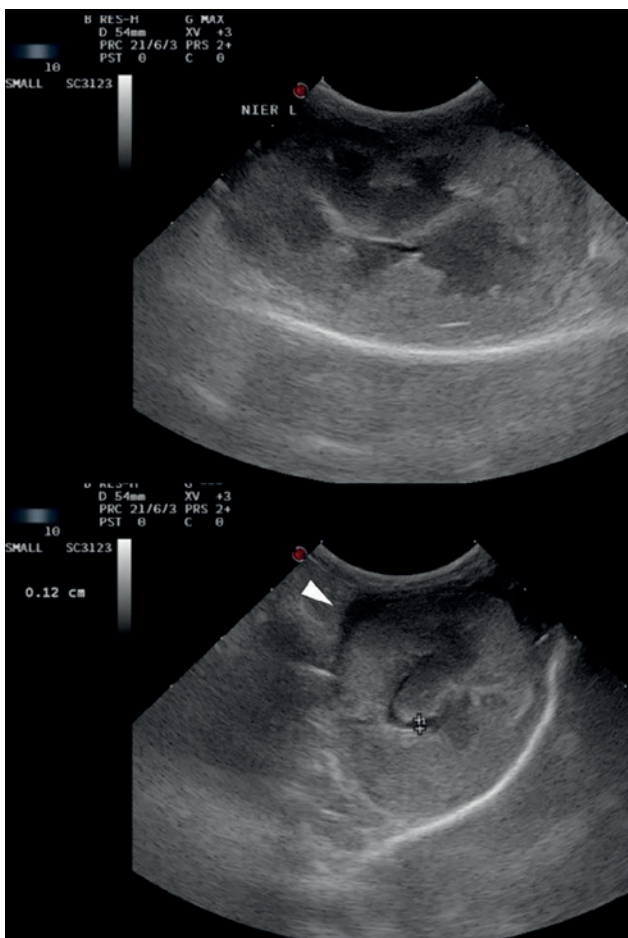


Figure 1. Longitudinal view (A) and transverse view (B) of the left kidney of animal #3. The longitudinal view shows an irregular renal cortex. Subcapsular free fluid is marked by a white arrowhead. Hydronephrosis is present on the transverse view.

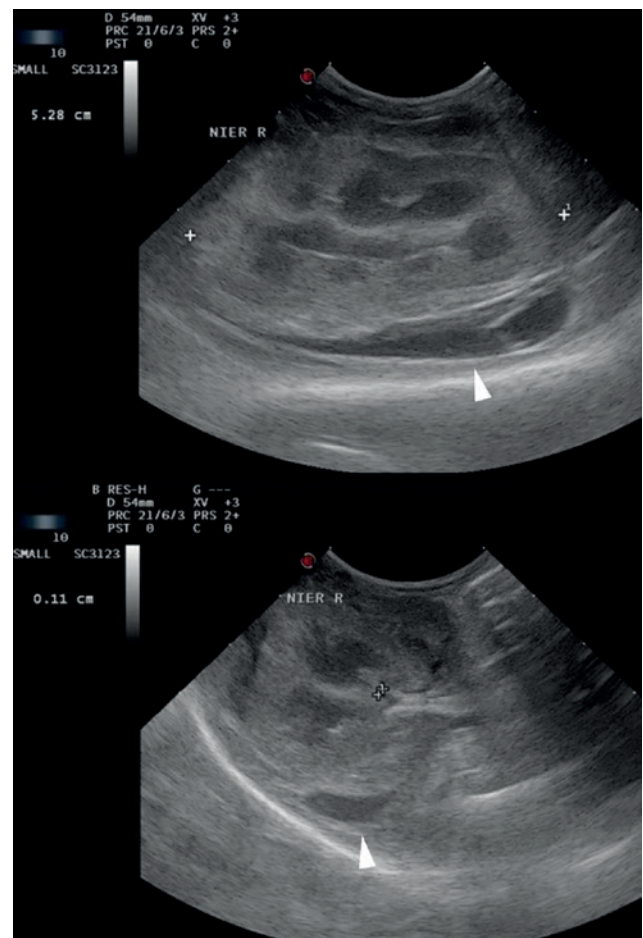


Figure 2. Longitudinal (A) view and transverse view (B) of the right kidney of animal #3. The longitudinal view shows an irregular renal cortex. Subcapsular free fluid is marked by a white arrowhead.

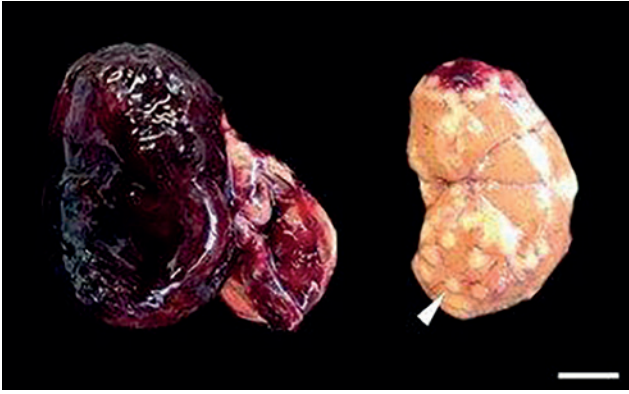


Figure 3. Kidneys of animal #2. Subcapsular hemorrhage (hematoma, left) is present with marked multifocal to coalescing cortical pyogranulomas (right) typical of FIP. Bar, 1cm.

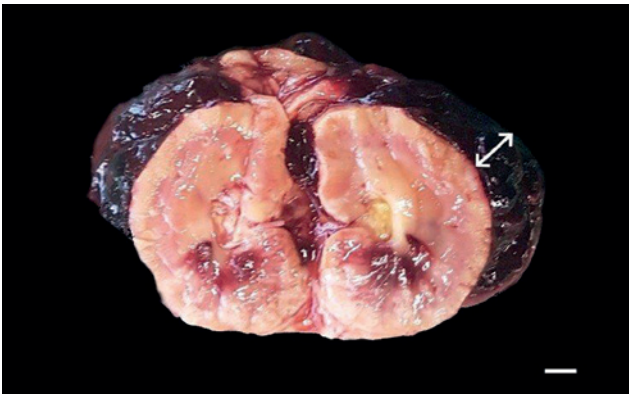


Figure 4. Longitudinal section of a kidney of the animal #1. It shows multiple medullary hemorrhagic infarcts with marked subcapsular hematoma formation (double arrow). Bar, 1cm.

Pathology

Gross pathology of the cats was typical of the wet form of FIP. However, remarkable in all three cases, was the diffuse accumulation of coagulated blood in between the renal cortical surface and the renal capsule, consistent with perirenal subcapsular hematomas (Figures 3 and 4).

Beside the findings in the kidneys, a mild to moderate amount of yellow viscous serohemorrhagic fluid with fibrine strands was present in the abdominal cavity (peritonitis). The same exudate was present in the pleural cavity (pleuritis) in animals #2 and #3 and in the pericardial cavity (pericarditis) of animal #3. Only animal #2 showed pleural pyogranulomas. There were multifocal to coalescing white/yellow nodules at the renal cortical surface, compatible with pyogranuloma formation. Animals #2 and #3 were mildly dehydrated. All cats showed signs of icterus. The mesenteric lymph nodes were mildly to moderately diffusely enlarged. The spleen and nervous system were grossly normal (Figures 3 and 4).

Histologically, at the renal cortical pyogranulomas,

the constitution of the inflammatory infiltrate varied with macrophages being most prevalent in cases #1 and #2, while in case #3, lymphoplasmacytic cells were most abundant. Neutrophils were present in mild to moderate numbers in cases #1 and #2. Necrosis at the renal lesions was severe in case #2 and mild in the other cases. In cases #2 and #3, concurring chronic interstitial nephritis was present with tubular atrophy, interstitial fibrosis and glomerular mucinous metaplasia. In all three cases, no vascular fibrinoid necrosis nor vasculitis was observed of any renal vein and artery or arteriole, as is described in FIP (Kipar et al., 2005) (Figure 5). Cytoplasmic immunolabeling of large numbers of macrophages in the renal pyogranulomas for FCoV confirmed intralésional presence of FIPV in all three cats (Figure 6).

Nanopore sequencing

The genetic tree shows that all three strains are part of serotype 1 FCoV. Although animal #1 and animal #2 cluster closely together, a large genetic distance is still present. Moreover, the strain from animal #3 also belongs to a different cluster (Figure 7).

DISCUSSION

The aim of this case series was to report the very first cases of FIP with secondary perirenal hematoma formation. Also, nanopore sequencing was done to identify the virus strains and establish a possible common genetic background.

Comparable to the cats presented in this case series, the clinical signs of FIP disease are variable and depend on the organs involved. They may include hyperoxia, dehydration, icterus and weight loss. Effusions e.g. in the peritoneal cavity and/or neurological signs in case of neurologic forms have been described. Young purebred cats are more susceptible to FIP (Rohrbach et al., 2001).

Perirenal hematoma can only occur because of vascular rhexis of a superficial renal blood vessel (vena capsularis). However, in this study, histological examination could not demonstrate any loss of vascular integrity in all three cats. Histologically, the kidney in case #1 showed mild renal parenchymal necrosis at superficially orientated pyogranulomas. Most likely, a capsular vein was affected and ruptured, explaining the hematoma formation. Kipar et al. (2005) showed that in case of FIP, renal vasculitis is characterized by intramural migration of inflammatory cells at the capsular veins, with occasionally inflammatory cells replacing the vascular wall. This was not evidenced in the three described cases in the current study. It should be pointed out that tissue samples were taken randomly, and only a very small portion of the entire kidney parenchyma could be visualized (<1%). If a subcapsular vein, which is most likely the source of hemorrhage, would have been severely affected by

vasculitis, there is a significant chance that it was not detected.

In the present study, coagulopathy due to severe thrombocytopenia could have been an underlying factor in the development of these hematomas. However, there was no information available about the presence of a coagulation disorder that could have caused these specific bleedings. It is known that FIPV infection can lead to a decrease in thrombocytes. In a study by Jordan et al. (1993), it has been shown that viral diseases are an important cause of thrombocytopenia in cats; this in contrast to dogs, where non-infectious causes are more common (Cockburn and Troy, 1986; Grindem et al., 1991). Furthermore, disseminated intravascular coagulation (DIC) can occur. Although, cats are more likely to develop microhemorrhages when in DIC, it could be a possible cause of hematoma formation (Pedersen, 2009). To

the authors' knowledge, hematoma formation in the kidneys or anywhere else due to FIP has not been reported in the current scientific literature.

According to the results of the nanopore sequencing, all strains belonged to serotype 1. This is in line with the expectations, because serotype 1 is much more common in Europe than serotype 2 (Benetka et al., 2004; Kummrow et al., 2005). FCoV genomes are known for their high level of genetic variations. This is due to a high error rate of the RNA polymerase (Herrewegh et al., 1998; Bank-Wolf et al., 2014; Paltrinieri et al., 2021). In this study, the virus sequences obtained from all three cats cluster together, but show large genetic distance. This indicates that the cats were affected by the different strains but.

Comparing the abdominal ultrasound findings and gross findings, free fluid indicating peritonitis, was detected on ultrasound. The irregular renal surface on

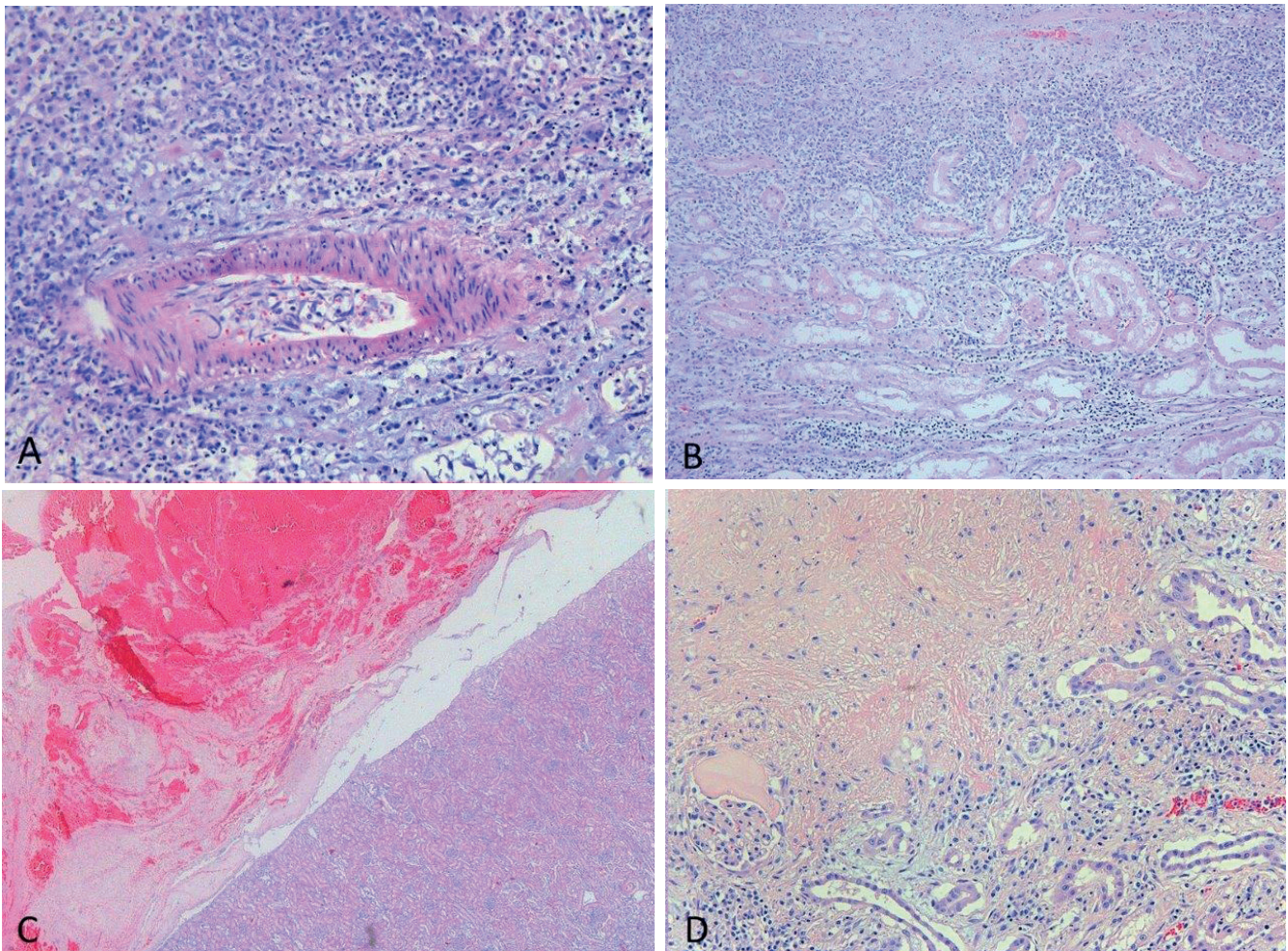


Figure 5. Four histological images with H&E staining of the renal cortex of the cats included in this study. Images A and B are from animal #1, 20x objective, respectively 10x objective. Images C and D are from animal #3, both 2,5x objective. (A) The cortical parenchyma is expanded and replaced by a dense mixed inflammatory infiltrate. Blood vessels do not show vasculitis here or anywhere else. (B) The cortical interstitium is severely expanded by an inflammatory infiltrate of both neutrophils, macrophages and lymphoplasmacytic cells. Normal tubuli and glomeruli are recognizable on the lowest part of the picture. On the upper part of the picture, there is loss of tissue architecture, consistent with necrosis. (C) The subcapsular space is extensively expanded by hemorrhage (hematoma). (D) There is an extensive area of necrosis, characterized by loss of tissue and cellular architecture and eosinophilia. On the right and lower part of the picture, normal tubuli and some glomeruli can be seen.

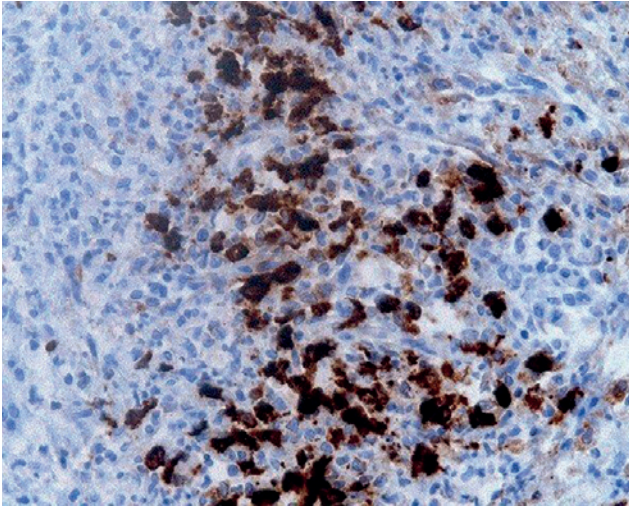


Figure 6. Immunohistochemistry with 20x magnification of a kidney of a cat with feline infectious peritonitis (FIP). There is extensive cytoplasmic immunolabeling in macrophages at the periphery of renal pyogranulomas.

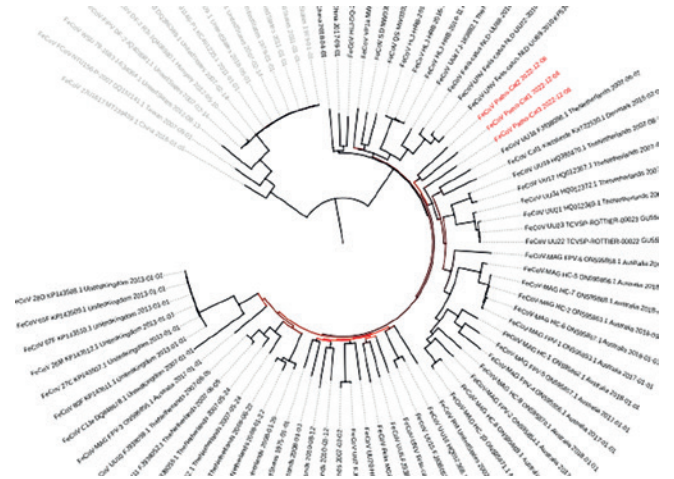


Figure 7. Genetic circular tree of the virus strains of FCoV obtained via nanopore sequencing. The strains of animal #1 (Patho-Cat1), animal #2 (Patho-Cat2) and animal #3 (Patho-Cat3) are indicated in red.

ultrasound correlated with the pyogranulomas found on autopsy. The hydronephrosis of cat #3 and cysts of cat #1 were not found during autopsy. Lewis and O’Brien (2010) described the presence of renal hypoechogenic subcapsular rim visible on ultrasound in five cats with FIP. It is unclear if this correlates with perirenal hematoma formation or with the more commonly seen edema in FIP.

In conclusion, in this case series, three cases of feline infectious peritonitis with not previously reported extensive perirenal subcapsular hematomas are described. The lesions were discovered during autopsy. Rhexis of capsular veins secondary to necrosis or vasculitis is the most likely cause of hematoma formation, although no vasculitis was observed. Whole genome sequencing of the kidney tissue showed that the virus sequences belonged to serotype 1 and were not related to each other.

ACKNOWLEDGEMENTS

The authors would like to thank PathoSense for providing access to the results of the nanopore sequencing used in this article. Without their cooperation, this part of the research would not have been possible.

REFERENCES

Bank-Wolf, B.R., Stallkamp, I., Wiese, S., Moritz, A., Tekes, G., Thiel, H.J., (2014). Mutations of 3c and spike protein genes correlate with the occurrence of feline infectious peritonitis. *Veterinary Microbiology* 173 (3), 177-188.

Beatty, J., Barrs, V., (2010). Pleural effusion in the cat: A practical approach to determining aetiology. *Journal of Feline Medicine and Surgery* 12 (9), 693-707.

Benetka, V., Kubber-Heiss, A., Kolodziejek, J., Nowotny, N., Hofmann-Parisot, M., Mostl, K., (2004). Prevalence of feline coronavirus types I and II in cats with histopathologically verified feline infectious peritonitis. *Veterinary Microbiology* 99 (1), 31-42.

Cockburn, C., Troy, G.C., (1986). A retrospective study of sixty-two cases of thrombocytopenia in the dog. *Southwestern Veterinarian* 37 (2), 133-141.

Corapi, W.V., Olsen C.W., Scott, F.W., (1992). Monoclonal antibody analysis of neutralization and antibody-dependent enhancement of feline infectious peritonitis virus. *Journal of Virology* 66 (11), 6695-6705.

De Groot, R.J., Van Leen, R.W., Dalderup, M.J.M., Venneema, H., Horzinek, M.C., Spaan, W.J.M., (1989). Stably expressed FIPV peplomer protein induces cell fusion and elicits neutralizing antibodies in mice. *Virology* 171 (2), 493-502.

Drechsler, Y., Alcaraz, A., Bossong, F.J., Collisson, E.W., Diniz, P.P.V.P., (2011). Feline coronavirus in multicat environments. *Veterinary Clinics of North America: Small Animal Practice* 41 (6): 1133-1169.

Green, J., Syme, H., Tayler, S., (2023). Thirty-two cats with effusive or non-effusive feline infectious peritonitis treated with a combination of remdesivir and GS-441524. *Journal of Veterinary Internal Medicine* 37 (5), 1784-1793.

Grindem, C.B., Breitschwerdt, E.B., Corbett, W.T., Jans, H.E., (1991). Epidemiologic survey of thrombocytopenic dogs: A report of 987 cases. *Veterinary Clinical Pathology* 20 (2), 38-43.

Gunn-Moore, D.A., Gruffydd-Jones, T.J., Harbour, D.A., (1998). Detection of feline coronaviruses by culture and reverse transcriptase-polymerase chain reaction of blood samples from healthy cats and cats with clinical feline infectious peritonitis. *Veterinary Microbiology* 62 (3), 193-205.

Hartmann, K., (2005). Feline infectious peritonitis. *Veterinary Clinics of North America: Small Animal Practice* 35 (1), 39-79.

Hayashi, T., Goto, N., Takahashi, R., Fujiwara, K., (1977). Systemic vascular lesions in feline infectious peritonitis. *The Japanese Journal of Veterinary Science* 39 (4), 365-377.

- Herrewegh, A.A., Smeenk, I., Horzinek, M.C., Rottier, P.J., de Groot, R.J., (1998). Feline coronavirus type II strains 79-1683 and 79-1146 originate from a double recombination between feline coronavirus type I and canine coronavirus. *Journal of Virology* 72 (5), 4508-4514.
- Jordan, H.L., Grindem, C.B., Breitschwerdt, E.B., (1993). Thrombocytopenia in cats: a retrospective study of 41 cases. *Journal of Veterinary Internal Medicine* 7 (5), 261-334.
- Katoh, K., Misawa, K., Kuma, K., Miyata, T., (2002). MAFFT : a novel method for rapid multiple sequence alignment based on fast Fourier transform. *Nucleic Acids Research* 30 (14), 3059-3066.
- Kipar, A., Baptiste, K., Barth, A., Reinacher, M., (2006). Natural FCoV infection: cats with FIP exhibit significantly higher viral loads than healthy infected cats. *Journal of Feline Medicine and Surgery* 8 (1), 69-72.
- Kipar, A., May, H., Menger, S., Weber, M., Leukert, W., Reinacher, M., (2005). Morphologic features and development of granulomatous vasculitis in feline infectious peritonitis. *Veterinary Pathology* 42 (3), 321-330.
- Kipar, A., Bellmann, S., Gunn-Moore, D.A., Leukert, W., Köhler, K., Menger, S., Reinacher, M., (1999). Histopathological alterations of lymphatic tissues in cats without feline infectious peritonitis after long-term exposure to FIP virus. *Veterinary Microbiology* 69 (1), 131-137.
- Kipar, A., Bellmann, S., Kremendahl, J., Kohler, K., Reinacher, M., (1998). Cellular composition, coronavirus antigen expression and production of specific antibodies in lesions in feline infectious peritonitis. *Veterinary Immunology and Immunopathology* 65 (2-4), 243-257.
- Koren, S., Walenz, B.P., Berlin, K., Miller, J.R., Bergman, N.H., Phillippy, A.M., (2017). Canu: scalable and accurate long-read assembly via adaptive *k*-mer weighting and repeat separation. *Genome Research* 27 (5), 722-736.
- Kummrow, M., Meli, M.L., Haessig, M., Gönczi, E., Poland, A., Pedersen, N.C., Hofmann-Lehmann, R., Lutz, H., (2005). Feline coronavirus serotypes 1 and 2: Seroprevalence and association with disease in Switzerland. *Clinical Diagnostic Laboratory Immunology* 12 (10), 1209-1215.
- Lewis, K.M., O'Brien, R.T., (2010). Abdominal ultrasonographic findings associated with feline infectious peritonitis: a retrospective review of 16 cases. *Journal of the American Animal Hospital Association* 46 (3), 152-160.
- Li, H., (2018). Minimap2: pairwise alignment for nucleotide sequences. *Bioinformatics* 34 (18), 3094-3100.
- Meli, M., Kipar, A., Müller, C., Jenal, K., Gönczi, E., Borel, N., Gunn-Moore, D., Chalmers, S., Lin, F., Reinacher, M., Lutz, H., (2004). High viral loads despite absence of clinical and pathological findings in cats experimentally infected with feline coronavirus (FCoV) type I and in naturally FCoV-infected cats. *Journal of Feline Medicine and Surgery* 6 (2), 69-81.
- Montali, R.J., Strandberg, J.D., (1972). Extraperitoneal lesions in feline infectious peritonitis. *Veterinary Pathology* 9 (2), 109-121.
- Nguyen, L., Schmidt, H.A., von Haeseler, A., Minh, B.Q., (2015). IQ-TREE: A fast and effective stochastic algorithm for estimating maximum-likelihood phylogenies. *Molecular Biology and Evolution* 31 (1), 268-274.
- Olsen, C.W., Corapi, W.V., Ngichabe, C.K., Baines, J.D., Scott, F.W., (1992). Monoclonal antibodies to the spike protein of feline infectious peritonitis virus mediate antibody-dependent enhancement of infection of feline macrophages. *Journal of Virology* 66 (2), 956-965.
- Paltrinieri, S., Giordano, A., Stranieri, A., Lauzi, S., (2021). Feline infectious peritonitis (FIP) and coronavirus disease 19 (COVID-19): Are they similar? *Transboundary and Emerging Diseases* 68 (4), 1786-1799.
- Pedersen, N.C., (1976). Morphologic and physical characteristics of feline infectious peritonitis virus and its growth in autochthonous peritoneal cell cultures. *American Journal of Veterinary Research* 37 (5), 567-572.
- Pedersen, N.C., Boyle, J.F., (1980). Immunologic phenomena in the effusive form of feline infectious peritonitis. *American Journal of Veterinary Research* 41 (6), 868-876.
- Pedersen, N.C., Boyle, J.F., Floyd, K., Fudge, A., Barker, J., (1981). An enteric coronavirus infection of cats and its relationship to feline infectious peritonitis. *American Journal of Veterinary Research* 42 (3), 368-377.
- Pedersen, N.C., (2009). A review of feline infectious peritonitis virus infection: 1963-2008. *Journal of Feline Medicine and Surgery* 11 (4), 225-258.
- Rohrbach, B.W., Legendre, A.M., Baldwin, C.A., Lein, D.A., Reed, W.M., Wilson, R.B., (2001). Epidemiology of feline infectious peritonitis among cats examined at veterinary medical teaching hospitals. *Journal of American Veterinary Medical Association* 218 (7), 1111-1115.
- Stoddart, C.A., Scott, F.W., (1989). Intrinsic resistance of feline macrophages to coronavirus infection correlates with in vivo virulence. *Journal of Virology* 63 (1), 436-440.
- Spencer, S.E., Knowles, T., Ramsey, I.K., Tasker, S., (2017). Pyrexia in cats: Retrospective analysis of signalment, clinical investigations, diagnosis and influence of prior treatment in 106 referred cases. *Journal of Feline Medicine and Surgery* 19 (11), 1123-1130.
- Vennema, H., De Groot, R.J., Harbour, D.A., Dalderup, M., Gruffydd-Jones, T., Horzinek, M.C., Spaan, W.J.M., (1990). Early death after feline infectious peritonitis virus challenge due to recombinant vaccinia virus immunization. *Journal of Virology* 64 (3), 1407-1409.
- Vennema, H., Poland, A., Foley, J., Pedersen, N.C., (1998). Feline infectious peritonitis viruses arise by mutation from endemic feline enteric coronaviruses. *Virology* 243 (1), 150-157.
- Weiss, R.C., Dodds, W.J., Scott, F.W., (1980). Disseminated intravascular coagulation in experimentally induced feline infectious peritonitis. *American Journal of Veterinary Research* 41 (5), 663-671.
- Weiss, R.C., Scott, F.W., (1981). Pathogenesis of feline infectious peritonitis: nature and development of viremia. *American Journal of Veterinary Research* 42 (3), 382-390.
- Weiss, R.C., Scott, F.W., (1981). Pathogenesis of feline infectious peritonitis: pathologic changes and immunofluorescence. *American Journal of Veterinary Research* 42 (12), 2036-2048.