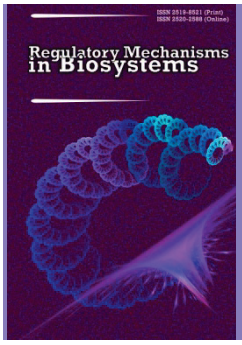

Regulatory Mechanisms in Biosystems

ISSN 2519-8521 (Print)
ISSN 2520-2588 (Online)
Regul. Mech. Biosyst.,
2023, 14(1), 3–9
doi: 10.15421/022301

Pathomorphology of the renal form of lymphoma in cats

K. Oriekhova, O. Shchebentovska

Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies, Lviv, Ukraine

Article info

Received 04.01.2023
Received in revised form 05.02.2023
Accepted 07.02.2023

Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies, Pekarska st., 50, Lviv, 79010, Ukraine.
Tel.:+38-067-701-81-46.
E-mail: schebentovskaolga@gmail.com

Oriekhova, K., & Shchebentovska, O. (2023). Pathomorphology of the renal form of lymphoma in cats. Regulatory Mechanisms in Biosystems, 14(1), 3–9. doi:10.15421/022301

Lymphoma is one of the most common neoplasias in cats, affecting various organs and tissues. Extranodal lymphoma is characterized by local damage to such organs as the nose, eyes, skin, central nervous system, and kidneys. Cats usually have bilateral kidney damage with possible metastatic damage to the liver and lungs. Statistically, the extranodal type of lymphoma, namely the renal form, is found in 7% to 30% of cases, mainly in cats older than five years. Clinical signs of renal lymphoma are non-specific and variable, typical for acute renal failure, and manifest themselves through general exhaustion, polyuria, polydipsia, and renomegaly. In most cases, the prognosis for lymphoma in cats is cautious. The article describes two clinical cases of outbred cats with a primary renal form of lymphoma. In both cases, the cats were clinically diagnosed with acute kidney injury and treated symptomatically. An ultrasound examination of the cats' kidneys revealed a sharp increase in their volume and increased echogenicity of the cortical layer with a fine-grained and nodular structure. The cytological picture in fine-needle aspirates from the kidneys was characterized by a massive monomorphic population of lymphoblasts, which exceeded erythrocytes by 2–3 times in diameter. The cytoplasm of the lymphoblastic cells was sparse with large round nuclei with dense chromatin. The cells were mostly uninucleate, with atypical mitoses and moderate cellular atypism. Epithelial cells, which were occasionally visualized between large lymphoblastic cells, had broad vacuolated cytoplasm and a large round nucleus. Express tests for feline leukemia virus showed negative results. Both cats died 7 and 10 days after initiation of treatment, respectively. During the autopsy, sharply enlarged and deformed kidneys were recorded, and the border between the cortical and medullary substances was difficult to differentiate. Irregularly shaped, white tumorous formations were visualized in the cortical layer. Diffuse infiltration of the kidneys' cortical layer with large monomorphic lymphoblastic elements with large hyperchromic nuclei and narrow cytoplasm was noted histologically. Lymphoblastic cells in a state of vacuolar and hydropic dystrophy were located between the proximal and distal tubules. The lumens were filled with protein mass and desquamated epithelium. The capsule of the kidney glomeruli was slightly thickened and the vessel walls were soaked with plasma proteins. Immunohistochemically, intensive expression of the CD79a marker and high expression of the Ki-67 marker were detected in the examined kidney samples, which indicates the development of diffuse B-cell lymphoma with an unfavourable prognosis.

Keywords: cats; lymphoblasts; kidneys; B-lymphocytes; CD79a marker; Ki-67 marker; proliferation.

Introduction

Lymphoma is one of the most common neoplasias in cats. Depending on the lesions' localization, lymphomas are divided into alimentary, mediastinal, multicentric, and extranodal (Brodey, 1970; Vail et al., 1998; Chan, 2001; Ettinger, 2003; Blackwood, 2013). Extranodal lymphoma is characterized by limited damage to the nose, eyes, larynx, skin, kidneys, and central nervous system (Taylor et al., 2009; Bound et al., 2011). According to the scientific literature on this matter, kidney lymphoma is found in 7% to 30% of lymphoma cases in cats. Most often, it is registered in older cats with acute kidney damage. Usually, kidney damage is secondary, mostly with a multicentric lymphoid neoplasm in the gastrointestinal tract, but sometimes primary damage is also found (Ettinger, 2003).

Renal lymphoma is the second most common form of extranodal lymphoma after a nasal one, which occurs in about a third of cases. Most researchers note there is no sexual predisposition to the renal form of lymphoma in cats (Blackwood, 2013; Graf et al., 2015). The average age of the animal was approximately 8–9 years when the disease was detected, although in 6% of cases the disease was registered from the first year. As a rule, adult animals were tested negative for FeLV and FIV, and the majority of diagnosed lymphomas were of B-cell immune phenotype (Holzworth, 1960; Dorn et al., 1967; Mahony et al., 1995; Chan, 2001; López-Guillermo et al., 2005). European Shorthairs are reported to be genetically predisposed to renal lymphoma development. However, cases of the disease in British Shorthair and Scottish Fold cats have been also described (Guimarães-Okamoto et al., 2016). Some authors believe that Siamese cats are genetically predisposed to mediastinal lymphoma development. At the same time, there have been no reports on other lymphoma types in this breed (Gospodarowicz & Sutcliffe, 1995). It is also known that cats infected with the feline leukemia virus (FeLV) have a high chance of developing a virus-induced lymphoma (Roca et al., 2005; Weiss et al., 2010; Meichner et al., 2012). FeLV has been suggested to have a direct oncogenic effect (Hartmann, 2012), while FIV may promote lymphoma development through virus-induced immunosuppression (Matsumoto et al., 1992; Weiss et al., 2010).

Clinical signs of lymphoma are non-specific and variable, so it is extremely difficult to diagnose the renal form in the early stages, since most sick cats are brought to clinics with signs of acute kidney injury with leukocyturia, proteinuria, and azotemia (Moore, 2013). In cases of kidney lymphoma described in the literature, the authors noted bilateral damage to the organ (Brodey, 1970; Chan, 2001; Guimarães-Okamoto et al., 2016). Cats were characterized by general exhaustion, polyuria and polydipsia, azotemia, and non-regenerative anemia (Dorn et al., 1967; Moore, 2013).

The prognosis for lymphoma in cats is mostly cautious. Veterinarians consider the stage, topographic location, histological grade, immunophenotype, and comorbidities of patients (Snyder et al., 1978; Vaden, 2005; Moore, 2013; Durham et al., 2014). Treatment in cats includes supportive care, as well as chemotherapy, radiation therapy, and surgery, depending

on the lymphoma classification. Chemotherapy is the treatment of choice in cats with renal lymphoma, because both kidneys are predominantly affected, making the organ's surgical removal impossible (Blackwood, 2013; Moore, 2013). Antitumour drugs such as cyclophosphamide, doxorubicin, vincristine, prednisolone, and L-asparginase can be used in lymphoma chemotherapy protocols, taking into account the stage and clinical condition of each patient (Court et al., 1997; Malik et al., 2001; Taylor et al., 2009; Moore, 2013; Limmer et al., 2016; Kopecny et al., 2020).

Despite the progress in the diagnostics of neoplasms in domestic animals, the morphological diagnostics of lymphoid tissue tumours remains one of the most difficult. The problems are related to the peculiarities of this group of neoplasms, namely: the diversity of nosological forms, the similarity of histological manifestations of certain lymphoma types, the cytological similarity of normal and tumour lymphocytes, and the morphological similarity of some reactive processes, especially in lymphoid organs (Jeraj et al., 1982; Raskin & Meyer, 2010; Bound et al., 2011; Oriekhova & Shchebentovska, 2022). The process of early diagnostics of renal lymphomas is facilitated by ultrasonography as well as fine needle aspiration (FNA), which is specific for lymphoma diagnostics (McAloney et al., 2018). It is necessary to conduct immunohistochemical studies to verify the morphological types of lymphoma.

Our work was aimed at the verification of lymphoma in cats through ultrasound, cytological, pathohistological, and immunohistochemical studies using markers CD79a, CD3, and proliferation marker Ki-67.

Materials and methods

In our studies we followed the international and national biotic positions on experiments on animals: the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (ETS No. 123, Strasbourg, 1986), Law of Ukraine "On Protection of Animals from Cruel Treatment" No. 3447-IV as of 21.06.2006 with amendments as of 04.08.2017.

The article describes two cases of kidney lymphoma in outbred male cats, aged 6.3 and 7.0 years, who received primary veterinary care during October–November 2022 at Vetpraktik clinic, located in Lviv, 5 P. Panch Str. Both cats were kept at home and had unlimited access to walking. They were admitted to the clinic with similar symptoms, namely, apathy, anorexia, polydipsia, and polyuria. The mucous membranes of the mouth and eyes were anemic, the abdomen was visually enlarged, and palpation of the kidneys revealed renomegaly. A general blood test revealed leukocytosis and an increased number of neutrophils in both cats. A biochemical study of blood serum demonstrated an increase in creatinine and urea level on the background of relatively physiological levels of alanine aminotransferase (ALT) and alkaline phosphatase (ALP). Kidney architecture assessment was carried out using ultrasound examination. Also, cytological samples were selected directly from neoplasms using a fine-needle aspiration biopsy. Ultrasound diagnostics was performed on an ESAOTE MyLab 40 device using a multi-frequency linear sensor at a frequency of 6.0–13.0 MHz. At least three cytological smears were prepared for the cytopathological examination, dried, fixed in methanol, stained according to the Romanowsky-Giemsa method, and examined under a Leica DM-2500 light microscope. The lymphoma diagnosis was based on generally accepted cytological criteria. The enzyme-linked immunosorbent assay for FeLV and FIV in both cats showed a negative result. X-ray examination of the chest cavity demonstrated no signs of metastasis. Despite the unfavourable prognosis, with the consent of the animals' owners, treatment was started according to the chemotherapy protocol, but the animals' condition worsened significantly in a few days.

From the moment of diagnosis, treatment and until their very death, the cats were kept in the clinic under supervision. After the animals' death, autopsy and pathohistological examination were performed in the laboratory of the Department of Normal and Pathological Morphology and Forensic Veterinary Medicine. The tissues were selected for histological and immunohistochemical research. Kidney fragments were fixed in a 10% aqueous solution of neutral formalin, washed, and dehydrated in an ascending series of alcohols, followed by embedding in paraffin according to the generally accepted method. Histosections with a 7 μm thickness were made from paraffin blocks on an MC-2 sledge microtome. For light microscopy, deparaffinized sections were stained with Mayer's hematoxylin and eosin (Kiceli, 1962). Lymphoma immunophenotyping was performed using CD3 (T-cells) and CD79a (B-cells) markers as well as Ki-67 proliferation marker. A kidney with no deviations from the norm from a clinically healthy cat that had died from a traumatic injury was used as a control specimen. Light microscopy and photo fixation of the obtained tissue preparations were carried out using Leica DM-2500 microscope and Leica DFC 450C camera.

Results

During the ultrasound examination of the abdominal cavity in cats, a sharp increase in the volume of both kidneys, a change in their shape, uneven contours, unevenly increased echogenicity of the kidneys' cortical layer, a fine-grained structure (Fig. 1a, 1b) and nodulation (Fig. 1c, 1d) were detected. Layer-by-layer differentiation and filling of the medullary layer are moderately preserved in one cat (Fig. 1a, 1b), and weakly differentiated in another cat (Fig. 1c, 1d). The trabecular sinuses are slightly expanded, and the pelvis is moderately dilated with signs of pyeloectasia (Fig. 1a, 1c, 1d). Cytologically, a significant number of large, rounded cells with a small basophilic cytoplasm, large round nuclei with dense chromatin, and, mostly, one or two nucleoli were found in smears stained according to Romanowsky-Giemsa. Anisocytosis and anisokaryosis were not expressed, and mitoses were atypical. Renal epithelial cells with bright, wide, and vacuolated cytoplasm, as well as large round nuclei with one nucleolus, were visualized between the lymphoblasts (Fig. 2).

Enlarged, deformed, unevenly coloured kidneys with whitish, bumpy, and tumorous protrusions were found in the cats during a pathological autopsy (Fig. 3a, 3c). On the very section, there were clearly contoured, white, fat-like growths, which occupied almost the entire part of the kidneys' cortical layer. The boundaries between the cortical and medullary layers were not differentiated in some parts of the kidneys and were difficult to see in others (Fig. 3b, 3d).

Massive diffuse infiltration of the interstitium (both cortical and medullary layers) with round-celled lymphoblastic elements was noted during the kidneys' pathohistological examination. These elements densely filled the lumen between the kidney's glomeruli and tubules (Fig. 4a). Multifocal aggregates of large round lymphoblastic cells also infiltrated the subcapsular surface of the kidneys. Cellular atypism was moderately pronounced. The cytoplasm of these cells was insignificant, oxyphilic, and moderately demarcated. The nuclei were round, mostly with one nucleolus (Fig. 4b). Mitotic figures were atypical, there were 3–5 pieces in the field of vision. Most structures of the kidney parenchyma (tubules and glomeruli) underwent dystrophic and necrobiotic changes. The epithelium of the proximal and distal tubules was in a state of vacuolar and hydropic dystrophy. The tubules' lumen was filled with a protein mass and desquamated epithelium (Fig. 4b, 4c, 4d). Epithelial cell nuclei were in a state of rhexis and lysis, focal necrosis of epithelial cells was observed in some places. Vascular glomeruli were also affected. The Shumlyansky-Bowman capsule was thickened and the vessel walls were impregnated with plasma proteins (Fig. 4d). In arterioles, endothelial cells were swollen and sometimes desquamated. Individual glomeruli underwent necrotic changes and were filled with eosinophilic protein masses (Fig. 4c).

The mechanism of acute renal failure development, which was clinically detected in the cats, was related to the formation of a lymphomatous interstitial infiltrate, which led to the compression of tubules and interstitial capillaries, intratubular obstruction, and an increase in postglomerular vascular resistance. Microscopic examination of the kidney tissue made it possible to detect specific cellular infiltration with lymphoblastic cells of the same type, which literally filled the interstitial space.

An immunohistochemical method with markers CD3, CD79a, and proliferation marker Ki-67 was used to verify the lymphoma type. The immunohistochemical study defined that approximately 85% of neoplastic cells in both the cortical and medullary layers of the kidneys had the intense cytoplasmic expression of the CD79a marker, which confirmed the B-cell lymphoma type (Fig. 5). However, among the large number of lymphoblastic cells in the kidneys' interstitium, scattered small T-lymphocytes were noted, which had a moderate expression of the CD3+ marker (Fig. 6).

One of the molecular parameters that characterize the biological properties of malignant neoplasms is the assessment of the tumour's proliferative activity by determining the expression degree of the non-histone protein Ki-67, which is synthesized in cell nuclei during the late G-phase, S, G2 and M phases of the cell cycle. Our immunohistochemical study of kidney fragments in cats showed sufficiently high proliferative activity of B-cell lymphoma, which indicates an unfavourable prognosis (Fig. 7).

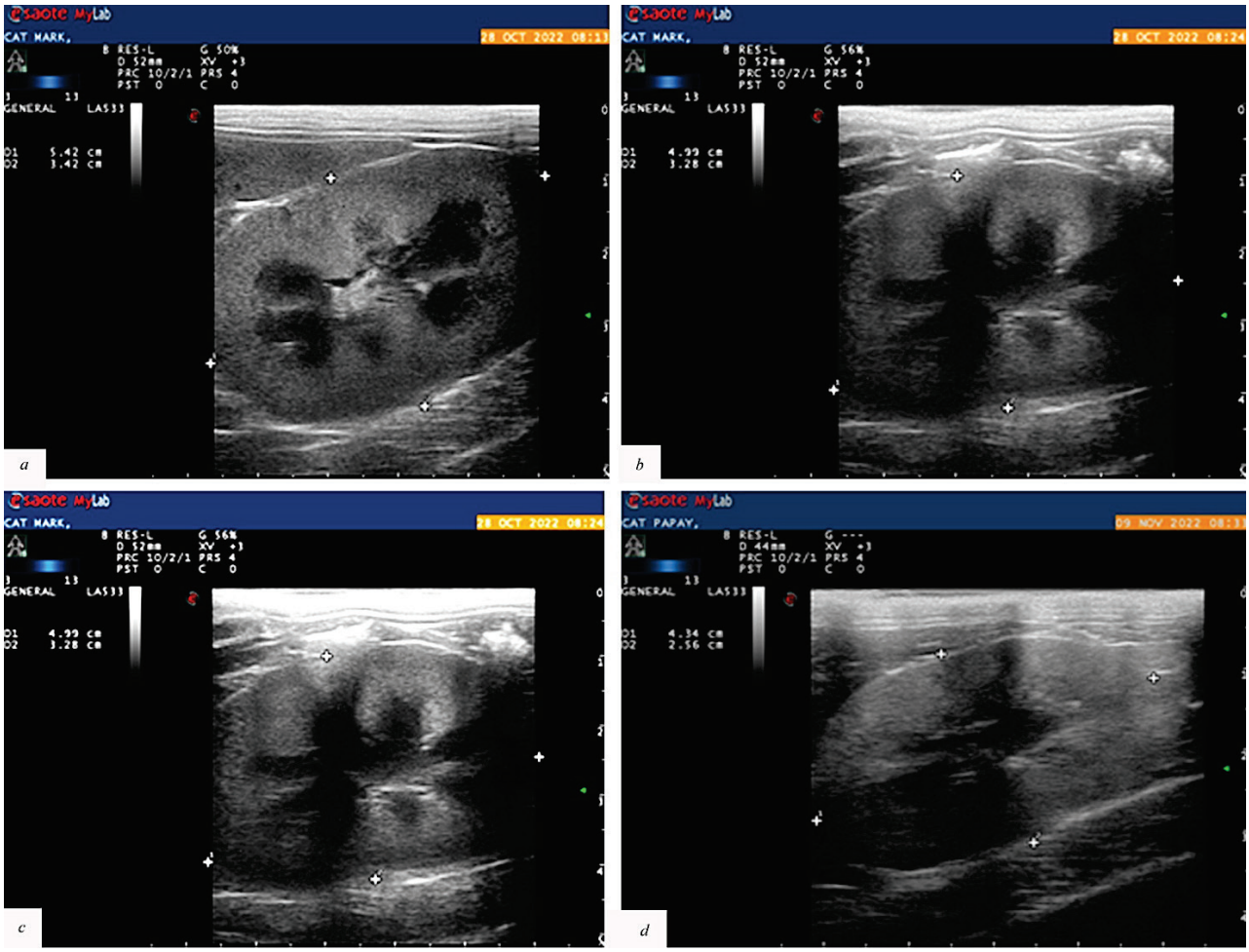

Fig. 1. Ultrasound image of the kidney in a cat with primary renal lymphoma: the kidney is enlarged, with a loss of corticomedullary clarity, irregular parenchyma, and areas of heterogeneous echogenicity

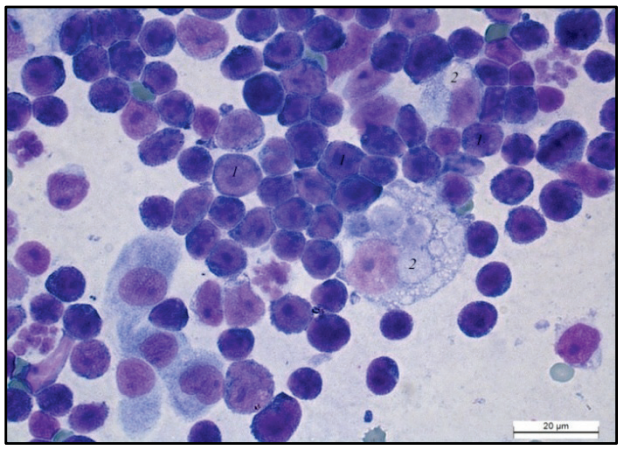

Fig. 2. Cytological sample of a kidney in a cat with renal lymphoma: the diffuse monomorphic population of large lymphoblasts (*1*) and epithelial cells with vacuolated cytoplasm (*2*); Romanowsky-Giemsa

Discussion

Although lymphoma is the most common neoplasm in cats, the primary renal form is not so often recorded, which is confirmed by the Williams' study, which analyzed 740 cases of lymphoma in cats, of which only 3.6% had a renal form (Brodey, 1970; Williams et al., 2021). According to the scientist (Gospodarowicz & Sutcliffe, 1995; Vaden, 2005; Williams et al., 2021), metastatic kidney tumours in cats are 7 times more common than primary tumours. Having explored 27 cases of feline renal lymphoma, he revealed that approximately 51% had multicentric damage. In addition, cases of renal lymphoma with dissemination to the central nervous system, lungs, and heart have also been described (Bound et al., 2011).

In his study of renal lymphoma in a domestic Siamese cat, Guimarães-Okamoto et al. (2016) noted significant weight loss, vomiting, anorexia, polydipsia, and polyuria. Clinical parameters, such as temperature, heart rate, breathing, pulse, and capillary refill time were within the physiological norm. The unsatisfactory condition of the animal was indicated by the mucous membranes'paleness and dehydration. Abdominal palpation revealed bilateral renomegaly and irregular contours of both kidneys. A general blood test and biochemical profile revealed anemia (hematocrit 17%) and severe azotemia (creatinine 8.5 mg/dL). Ultrasound diagnostics revealed bilateral asymmetric renomegaly, changes in kidney morphology, and absence of corticomedullary differentiation. Distortion of the kidney's intraparenchymal channel and intraparenchymal vascularization were recorded by colour doppler. The cat's clinical condition did not allow a kidney biopsy to be performed, so the doctors started symptomatic treatment after cytological diagnostics. Cardiopulmonary failure occurred on the second day of treatment and the animal died. The pathological autopsy confirmed that two kidneys were enlarged, and spherical

formations protruded from their surface. On the very section, the tumour was located in the cortical substance, infiltrating the pelvis, and consisted of a homogeneous solid tissue of white to yellow colour. Pathohistological examination of the kidneys showed large round cells with acidophilic cytoplasm, round nuclei with dense chromatin and one nucleolus, marked anisokaryosis and anisocytosis. An immunohistochemical evaluation of the neoplastic kidney tissue showed an expression of CD20 and a negative expression of CD3, which made it possible to establish a final diagnosis of primary diffuse large B-cell kidney lymphoma.

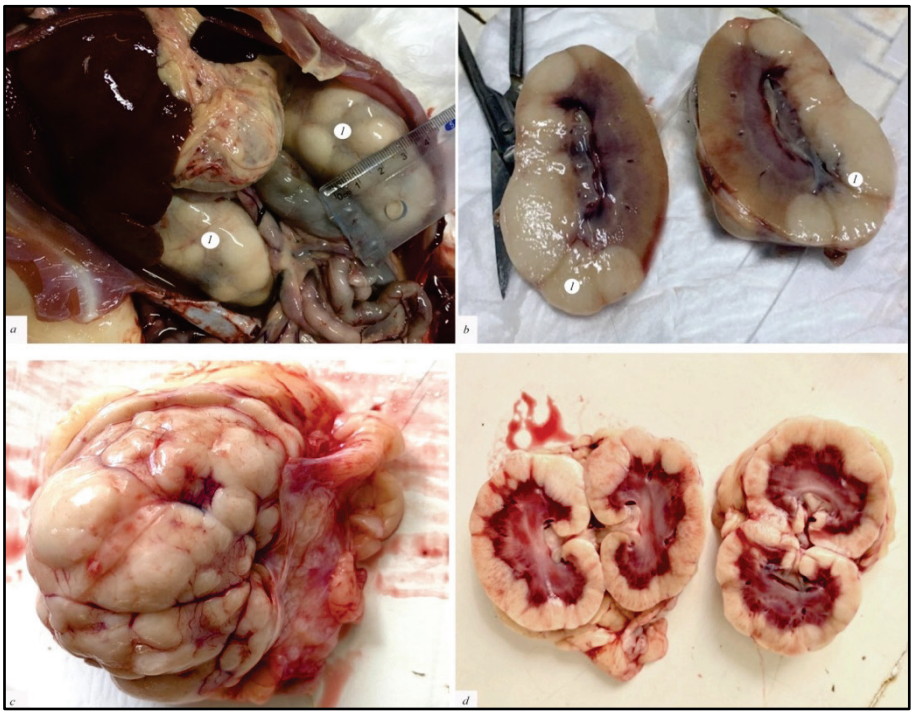

Fig. 3. Kidneys of cats with an extranodal form of lymphoma: *a*, *c* – tumorous bumpy protrusions in the kidney parenchyma; *b*, *d* – no differentiation between the cortical and medullary layers, massive fat-like growths in the cortical layer of both kidneys

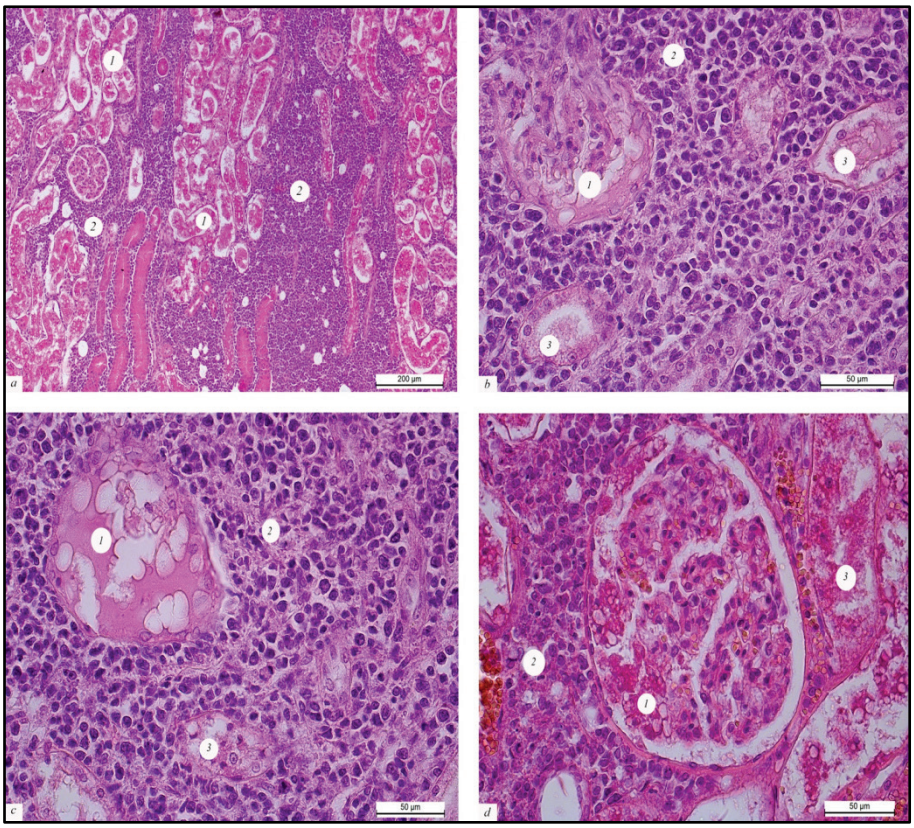

Fig. 4. Kidney lymphoma in cats: *a* – tubule lumens are filled with protein masses, nuclei are in a state of rhexis and lysis (*1*), massive diffuse lymphoblastic proliferation (*2*); *b* – protein masses are available in the glomerulus lumen (*1*), lymphoblastic cells with moderately pronounced cellular atypism (*2*), tubular dystrophy (*3*); *c* – glomerular necrosis (*1*), lymphoblastic proliferation (*2*), vacuolar dystrophy of the proximal tubule (*3*); *d* – protein masses in the glomerulus lumen (*1*), lymphoblastic proliferation (*2*), necrosis of renal tubules (*3*); hematoxylin and eosin

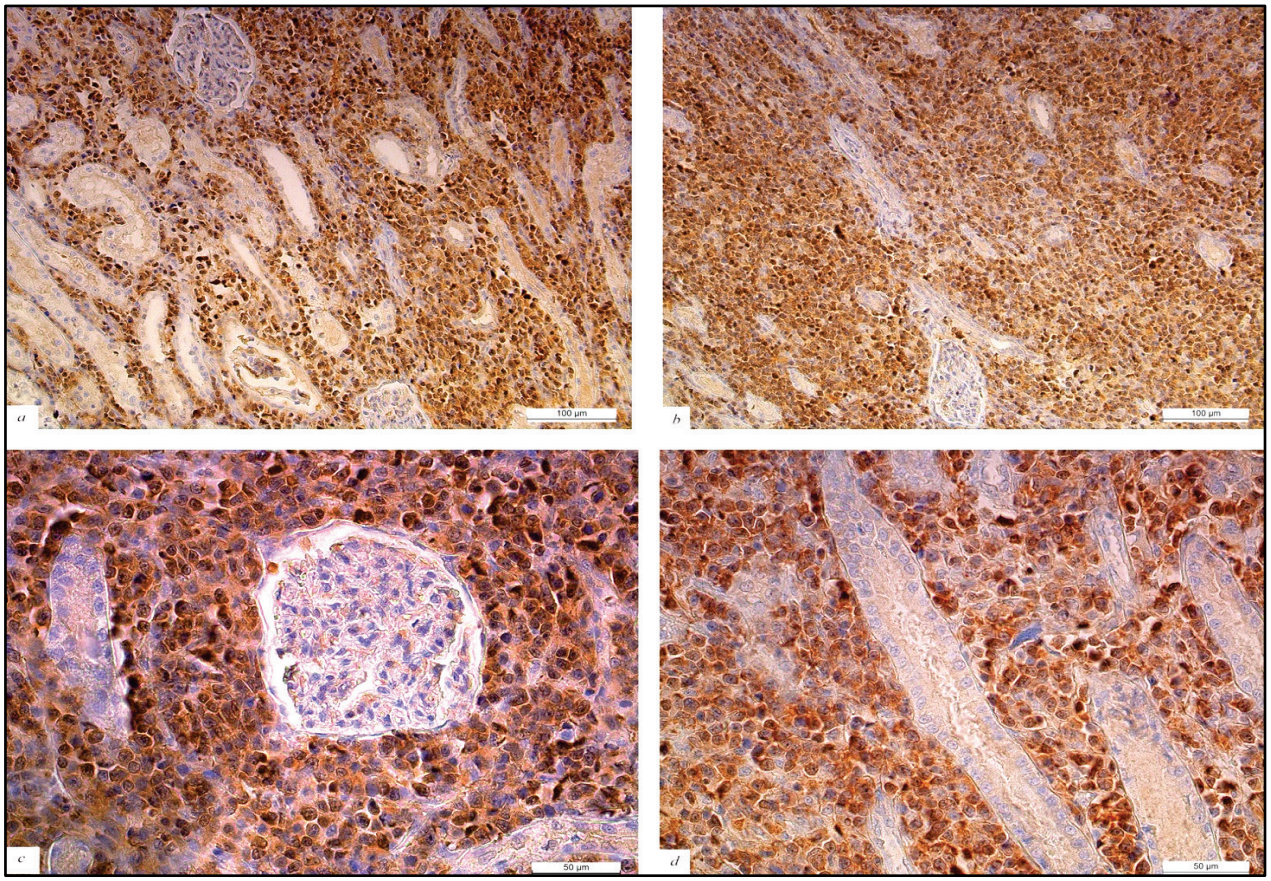

Fig. 5. Kidney lymphoma in cats: immunohistochemical typing by CD 79a marker: *a*, *b* – diffuse B-cell infiltration of the kidney parenchyma; *c* – cell nuclei are large, round with a single noticeable central nucleolus; *d* – a positive result of CD79a antibody labeling of neoplastic B-cells infiltrating kidney tubules; IHC

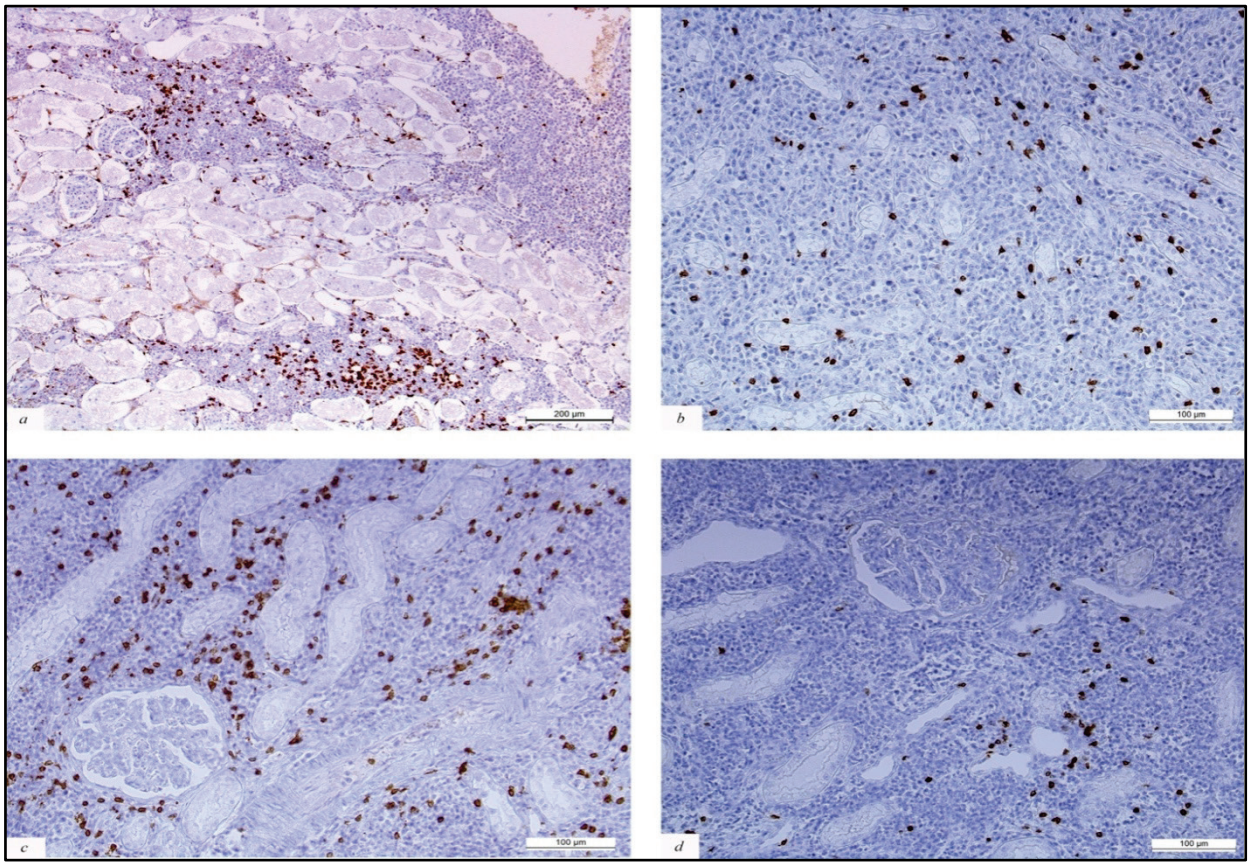

Fig. 6. Kidney lymphoma in cats: immunohistochemical typing by CD3 marker; *a*, *b*, *c*, *d* – single CD3+ T-lymphocytes are noted among the large number of lymphoblastic cells infiltrating the kidney parenchyma; IHC

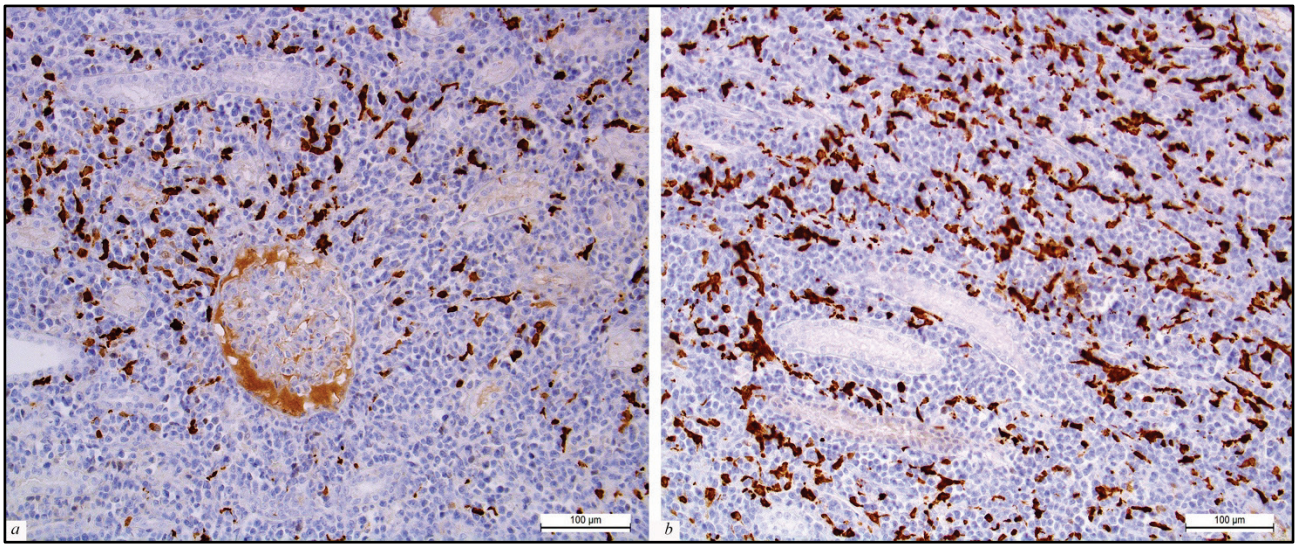

Fig. 7. Kidney lymphoma in cats: *a*, *b* – proliferative activity of Ki 67 marker; IHC

Some authors (Osborne et al., 1971; Mooney et al., 1987; Podell et al., 1992; Chan, 2001; López-Guillermo et al., 2005; Moore, 2013; Graf et al., 2015) claim that cats with renal lymphoma demonstrate signs of acute kidney injury, characterized by rapid weight loss, vomiting, dehydration, polyuria, and polydipsia that occurs on the background of renal tubules and glomeruli compression by lymphoblastic cells. Renal lymphoma frequently manifests itself as bilateral renomegaly with diffuse or nodular lesions of the renal parenchyma. According to some scientists, most renal lymphomas consist of large lymphocytes, which are easily identified by cytological examination (Hodson, 1998; Lees et al., 2011; Monaghan et al., 2012; Durham et al., 2014; Pinello et al., 2022). Such lymphoblasts have sufficiently large cytoplasm with massive nuclei, and one or two nucleoli. Renal epithelial cells have much larger cytoplasm, often vacuolated, and round nuclei with less pronounced nucleoli. Desquamated renal epitheliocytes on cytological preparations are usually placed in the form of small clusters. Small cell kidney lymphoma is quite difficult to diagnose cytologically due to the similarity of inflammatory lymphocytic infiltrates. In such cases, pathohistological diagnostics is necessary, which makes it possible to verify inflammatory and neoplastic processes.

In the cases of lymphoma in cats described in our study, bilateral kidney lesions were also detected during ultrasound examination and the cytological pattern of biopsies with a characteristic monomorphic population of large lymphoblasts correlated with the results of studies by other scientists. The immunoenzymatic test for FeLV and FIV was negative in both cases. As noted by various authors, the frequency of FeLV-positive animals among cats with renal lymphoma varies in different studies from 25% to 100% (Jackson et al., 1993; Roca et al., 2005; Stützer et al., 2011; Hartmann, 2012; Ludwig et al., 2022). Our results are similar to studies in which the FeLV test was negative for multicentric and renal lymphomas in cats (Moore, 2013). Nowadays, it should be taken into account that preventive measures (vaccinations) are being carried out among animals, so the correlation between FeLV and lymphoma development may be somewhat reduced (Jackson et al., 1996; Krick et al., 2011; Meichner et al., 2012). Some authors monitored the situation with lymphoma in cats in Brazil and noted that 56.6% of cats with lymphoma were FeLV-positive, thus indicating the need for prevention and control of factors associated with infection in this country (Court et al., 1997; Krunic et al., 2015).

In our research, we report on primary renal lymphoma in outbred cats, as lesions of other organs were not found during the post-mortem examination. From the moment of the final diagnosis and the start of treatment, both cats did not live long, since late diagnostics do not contribute to a quick recovery, even after appropriate chemotherapy. The cytological examination was a fast and good non-invasive method for diagnosing lymphoma, but it did not provide an opportunity to determine its stage. The lymphoblastic cells had a large hyperchromic nucleus with prominent nucleoli and small cytoplasm. According to clinicians, renal lymphoma should be considered a potential cause of severe azotemia. It should also be regarded as a primary differential diagnosis among feline renal neoplasms. Making the differential diagnostics, it is worth remembering about pyogranulomatous inflammation and infectious peritonitis in cats. Further classification of lymphoma was based on the results of immunophenotyping using CD3 and CD79a immunohistochemical markers. Lymphoblastic cells massively infiltrating the cortical and medullary layers of the kidney had an intense cytoplasmic expression of the CD79a marker, which confirmed the population of B-lymphoblasts.

It is known that the kidneys ensure the removal of cytolysis products and regulate the water-electrolyte balance, so the prognosis of the disease as a whole depends on their functioning. The use of chemotherapeutic agents, especially in the late stages of neoplasm detection and differentiation, even in therapeutic concentrations, has a nephrotoxic effect on the tubular necrosis development.

Lymphoma is a common diagnosis in cats, which has been associated with the leukemia virus in the past. However, most clinical cases show a negative result for this virus as the vaccination becomes increasingly popular.

Conclusion

A complex of clinical, cytological, pathomorphological, and immunohistochemical studies allowed us to verify the primary extranodal B-cell form of lymphoma in cats with high proliferative activity.

The authors declare that they have no potential conflict of interest concerning the authorship or publication of this article.

References

Blackwood, L. (2013). Cats with cancer: Where to start. Journal of Feline Medicine and Surgery, 15(5), 366–377.

Bound, N. J., Priestnall, S. L., & Cariou, M. P. (2011). Lingual and renal lymphoma in a cat. Journal of Feline Medicine and Surgery, 13(4), 272–275.

Brodey, R. S. (1970). Canine and feline neoplasia. Advances in Veterinary Science and Comparative Medicine, 14, 309–354.

Chan, J. K. (2001). The new World Health Organization classification of lymphomas: The past, the present and the future. Hematological Oncology, 19(4), 129–150.

Court, E. A., Watson, A. D., & Peaston, A. E. (1997). Retrospective study of 60 cases of feline lymphosarcoma. Australian Veterinary Journal, 75(6), 424–427.

Dorn, C. R., Taylor, D. O., & Hibbard, H. H. (1967). Epizootiologic characteristics of canine and feline leukemia and lymphoma. American Journal of Veterinary Research, 28(125), 993–1001.

Durham, A. C., Mariano, A. D., Holmes, E. S., & Aronson, L. (2014). Characterization of post transplantation lymphoma in feline renal transplant recipients. Journal of Comparative Pathology, 150, 162–168.

Ettinger, S. N. (2003). Principles of treatment for feline lymphoma. Clinical Techniques in Small Animal Practice, 18(2), 98–102.
Gospodarowicz, M. K., & Sutcliffe, S. B. (1995). The extranodal lymphomas. Seminars in Radiation Oncology, 5(4), 281–300.
Graf, R., Grüntzig, K., Hässig, M., Axhausen, K. W., Fabrikant, S., Welle, M., Meier, D., Guscetti, F., Folkers, G., Otto, V., & Pospischil, A. (2015). Swiss feline cancer registry: A retrospective study of the occurrence of tumours in cats in Switzerland from 1965 to 2008. Journal of Comparative Pathology, 153(4), 266–277.
Guimarães-Okamoto, P. T. C., da Silva, M. C. L., Sequeira, J. L., Hataka, A., Chacar, F. C., Geraldes, S. S., Ribeiro, J. F. A., & Melchert, A. (2016). Primary diffuse large B cell lymphoma in kidney with involvement of central nervous system and heart in a siamese cat. Acta Scientiae Veterinariae, 44(1), 4.
Hartmann, K. (2012). Clinical aspects of feline retroviruses: a review. Viruses, 4(11), 2684–2710.
Hodson, S. (1998). What is your diagnosis? Renal lymphoma in a cat. The Journal of Small Animal Practice, 39(4), 157–195.
Holzworth, J. (1960). Leukemia and related neoplasms in the cat. I. Lymphoid malignancies. Journal of the American Veterinary Medical Association, 136, 47–69.
Jackson, M. L., Haines, D. M., Meric, S. M., & Misra, V. (1993). Feline leukemia virus detection by immunohistochemistry and polymerase chain reaction in formalin-fixed, paraffin-embedded tumor tissue from cats with lymphosarcoma. Canadian Journal of Veterinary Research, 57(4), 269–276.
Jackson, M. L., Wood, S. L., Misra, V., & Haines, D. M. (1996). Immunohistochemical identification of B and T lymphocytes in formalin-fixed, paraffin-embedded feline lymphosarcomas: Relation to feline leukemia virus status, tumor site, and patient age. Canadian Journal of Veterinary Research, 60(3), 199–204.
Jeraj, K., Osborne, C. A., & Stevens, J. B. (1982). Evaluation of renal biopsy in 197 dogs and cats. Journal of the American Veterinary Medical Association, 181(4), 367–369.
Kiceli, D. (1962). Prakticheckaja mikrotehnika i gistohimija [Practical histotechnique and histochemistry]. Budapest (in Russian).
Kopecny, L., Palm, C. A., Skorupski, K. A., Delgado, M., & Rebhun, R. B. (2020). Risk factors associated with progressive increases in serum creatinine concentrations in cats with cancer receiving doxorubicin. Journal of Veterinary Internal Medicine, 34(5), 2048–2055.
Krick, E. L., Moore, R. H., Cohen, R. B., & Sorenmo, K. U. (2011). Prognostic significance of weight changes during treatment of feline lymphoma. Journal of Feline Medicine and Surgery, 13(12), 976–983.
Krunic, M., Ertl, R., Hagen, B., Sedlazeck, F. J., Hofmann-Lehmann, R., von Haeseler, A., & Klein, D. (2015). Decreased expression of endogenous feline leukemia virus in cat lymphomas: A case control study. BMC Veterinary Research, 11, 90.
Lees, G. E., Cianciolo, R. E., & Clubb Jr., F. J. (2011). Renal biopsy and pathologic evaluation of glomerular disease. Topics in Companion Animal Medicine, 26(3), 143–153.
Limmer, S., Eberle, N., Nerschbach, V., Nolte, I., & Betz, D. (2016). Treatment of feline lymphoma using a 12-week, maintenance-free combination chemotherapy protocol in 26 cats. Veterinary and Comparative Oncology, 14(Suppl. 1), 21–31.
López-Guillermo, A., Colomo, L., Jiménez, M., Bosch, F., Villamor, N., Arenillas, L., Muntañola, A., Montoto, S., Giné, E., Colomer, D., Beà, S., Campo, E., & Montserrat, E. (2005). Diffuse large B-cell lymphoma: Clinical and biological characterization and outcome according to the nodal or extranodal primary origin. Journal of Clinical Oncology, 23(12), 2797–2804.
Ludwig, L., Dobromylskyj, M., Wood, G. A., & van der Weyden, L. (2022). Feline oncogenomics: What do we know about the genetics of cancer in domestic cats? Veterinary Sciences, 9(10), 547.
Mahony, O. M., Moore, A. S., Cotter, S. M., Engler, S. J., Brown, D., & Penninck, D. G. (1995). Alimentary lymphoma in cats: 28 cases (1988–1993). Journal of the American Veterinary Medical Association, 207(12), 1593–1598.
Malik, R., Gabor, L. J., Foster, S. F., McCorkell, B. E., & Canfield, P. J. (2001). Therapy for Australian cats with lymphosarcoma. Australian Veterinary Journal, 79(12), 808–817.
Matsumoto, Y., Momoi, Y., Watari, T., Goitsuka, R., Tsujimoto, H., & Hasegawa, A. (1992). Detection of enhancer repeats in the long terminal repeats of feline leukemia viruses from cats with spontaneous neoplastic and nonneoplastic diseases. Virology, 189(2), 745–749.
McAloney, C. A., Sharkey, L. C., Feeney, D. A., & Seelig, D. M. (2018). Diagnostic utility of renal fine-needle aspirate cytology and ultrasound in the cat. Journal of Feline Medicine and Surgery, 20(6), 544–553.
Meichner, K., Kruse, D. B., Hirschberger, J., & Hartmann, K. (2012). Changes in prevalence of progressive feline leukaemia virus infection in cats with lymphoma in Germany. The Veterinary Record, 171(14), 348.
Monaghan, K., Nolan, B., & Labato, M. (2012). Feline acute kidney injury: 1. Pathophysiology, etiology and etiology-specific management considerations. Journal of Feline Medicine and Surgery, 14(11), 775–784.
Mooney, S. C., Hayes, A. A., Matus, R. E., & MacEwen, E. G. (1987). Renal lymphoma in cats: 28 cases (1977–1984). Journal of the American Veterinary Medical Association, 191(11), 1473–1477.
Moore, A. (2013). Extranodal lymphoma in the cat: Prognostic factors and treatment options. Journal of Feline Medicine and Surgery, 15(5), 379–390.
Oriekhova, K., & Shchebentovska, O. (2022). Pathohistological features of mediastinal lymphoma in domestic cats. Regulatory Mechanisms in Biosystems, 13(3), 317–323.
Osborne, C. A., Johnson, K. H., Kurtz, H. J., & Hanlon, G. F. (1971). Renal lymphoma in the dog and cat. Journal of the American Veterinary Medical Association, 158(12), 2058–2070.
Pinello, K., Pires, I., Castro, A. F., Carvalho, P. T., Santos, A., de Matos, A., Queiroga, F., Canadas-Sousa, A., Dias-Pereira, P., Catarino, J., Faísca, P., Branco, S., Lopes, C., Marcos, F., Peleteiro, M. C., Pissarra, H., Ruivo, P., Magalhães, R., Severo, M., & Niza-Ribeiro, J. (2022). Cross species analysis and comparison of tumors in dogs and cats, by age, sex, topography and main morphologies. Data from Vet-OncoNet. Veterinary Sciences, 9(4), 167.
Podell, M., DiBartola, S. P., & Rosol, T. J. (1992). Polycystic kidney disease and renal lymphoma in a cat. Journal of the American Veterinary Medical Association, 201(6), 906–909.
Raskin, R., & Meyer, D. J. (2010). Canine and feline cytology: A color atlas and interpretation guide. 2nd ed. Saunders Elsevier, St. Louis.
Roca, A. L., Nash, W. G., Menninger, J. C., Murphy, W. J., & O'Brien, S. J. (2005). Insertional polymorphisms of endogenous feline leukemia viruses. Journal of Virology, 79(7), 3979–3986.
Snyder Jr., H. W., Hardy Jr., W. D., Zuckerman, E. E., & Fleissner, E. (1978). Characterisation of a tumour-specific antigen on the surface of feline lymphosarcoma cells. Nature, 275(5681), 656–658.
Stützer, B., Simon, K., Lutz, H., Majzoub, M., Hermanns, W., Hirschberger, J., Sauter-Louis, C., & Hartmann, K. (2011). Incidence of persistent viraemia and latent feline leukaemia virus infection in cats with lymphoma. Journal of Feline Medicine and Surgery, 13(2), 81–87.
Taylor, S. S., Goodfellow, M. R., Browne, W. J., Walding, B., Murphy, S., Tzannes, S., Gerou-Ferriani, M., Schwartz, A., & Dobson, J. M. (2009). Feline extranodal lymphoma: Response to chemotherapy and survival in 110 cats. The Journal of Small Animal Practice, 50(11), 584–592.
Vaden, S. L. (2005). Renal biopsy of dogs and cats. Clinical Techniques in Small Animal Practice, 20(1), 11–22.
Vail, D. M., Moore, A. S., Ogilvie, G. K., & Volk, L. M. (1998). Feline lymphoma (145 cases): Proliferation indices, cluster of differentiation 3 immunoreactivity, and their association with prognosis in 90 cats. Journal of Veterinary Internal Medicine, 12(5), 349–354.
Vail, D., Thamm, D., Liptak, J. (Eds.). Withrow and MacEwen's small animal clinical oncology. 6th ed. Elsevier.
Weiss, A. T., Klopfleisch, R., & Gruber, A. D. (2010). Prevalence of feline leukaemia provirus DNA in feline lymphomas. Journal of Feline Medicine and Surgery, 12(12), 929–935.
Williams, A. G., Hohenhaus, A. E., & Lamb, K. E. (2021). Incidence and treatment of feline renal lymphoma: 27 cases. Journal of Feline Medicine and Surgery, 23(10), 936–944.