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Morphological changes in the small intestine mesentery of cats with infectious peritonitis

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Abstract. The research relevance is determined by an insufficient study of morphological changes in the mesentery of cats with infectious peritonitis, even though their understanding is necessary to explain the mechanism of development of the main symptom of the disease – the effusion of fluid into the abdominal cavity. The research aims to establish gross and microscopic changes in the mesentery of the small intestine of cats with infectious peritonitis. The research employs gross and histological examination of the mesentery of the small intestine of cats at the infectious peritonitis.

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Slides of the mesentery were stained with haematoxylin and eosin. At dry and mixed forms of infectious peritonitis, gross and microscopic changes in the mesentery of the small intestine of cats are similar. In the mesentery grossly, small white spots were found, which protruded above the general surface and had a homogeneous appearance on the section. Microscopic changes in the mesentery of the small intestine of cats with dry and mixed forms of infectious peritonitis were also similar. When conducting histological studies, it was established that the mesothelium on the surface of the mesentery was necrotized or absent. The submesothelial layer of collagen fibres was necrotized or contained partially lysed and fragmented fibres. The loose fibrous connective tissue of the mesentery was swollen, necrotized in places, and infiltrated by lymphocytes, monocytes, and macrophages. Eosinophilic inclusion bodies were detected in the cytoplasm of some monocytes and macrophages. Foci of adipose tissue in the mesentery of the small intestine were infiltrated by lymphocytes and monocytes. Necrosis and destruction of their walls were found in blood vessels and destruction of endothelial cells in lymphatic vessels. Perivascular lymphoid nodules were markedly enlarged due to their swelling and an increase in the number of cells in them. In perivascular lymphoid nodules, expansion of lymphatic vessels and destruction of part of their endothelium cells were also established. Some of the lymphatic vessels of the mesentery were expanded and filled with lymph, which contained a significant number of lymphocytes, monocytes, and single neutrophils. The materials presented in the article are of practical value for anatomists, histologists and pathomorphologists, as well as for scientists who study the pathogenesis of infectious peritonitis in cats

Keywords: feline coronaviruses; perivascular lymphoid nodules; eosinophilic inclusion bodies; gross changes; microscopic changes

Introduction

Feline infectious peritonitis (FIP) is diagnosed worldwide. Some cat breeds (e.g., Bengals) and certain lines within breeds are more often affected. At the same time, infectious peritonitis is rarely reported in stray and feral cats (Thayer *et al*., 2022). The causative agent is a virus that belongs to the feline coronavirus group, which also includes feline enteric coronavirus (Haake *et al*., 2020). Feline enteric coronavirus is dominant in cat populations. It is low virulent. Infection of animals with this virus occurs through the faecal-oral route and the pathogen primarily enters the intestines. In this case, the disease does not occur at all or manifests itself only in the form of mild enteritis. However, in 4-5% of adult cats and 5-10% of kittens, due to mutations of the enteric coronavirus in the body of a particular infected animal, the pathogen of infectious peritonitis is formed, and this disease occurs. This usually occurs without horizontal transmission of the pathogen. In general, the incidence of infectious peritonitis in cats in their populations is low and rarely exceeds 5% of all cats infected with coronavirus. Kittens are protected from feline coronaviruses by maternal antibodies until 5-6 weeks of age, but after weaning, 90% of kittens exposed to coronaviruses become infected. Approximately 5-12% of these cats develop classic clinical symptoms of FIV (Khalaniia, 2020; Zappulli, 2020).

Feline infectious peritonitis is widespread among different cat populations worldwide. It's in vivo diagnosis is quite complex and is based on a combination of many clinical and laboratory

findings, including the detection of the FIV virus. At the same time, clinical symptoms (anorexia, lethargy, weight loss, pyrexia, ocular and neurological manifestations such as gait abnormalities, etc.) as well as laboratory test results are nonspecific (Felten & Hartmann, 2019). This disease is more commonly reported in animals under the age of one year. The postulated breed predisposition of cats to infectious peritonitis has been identified, as animals genetically related to certain family lines are more likely to be affected. However, in shelters, the disease also occurs in genetically unrelated cats. Factors in the cat's body that contribute to the occurrence of infectious peritonitis include the characteristics of the major histocompatibility complex, the quality of cytokine responses, and some others.

According to M.A. Kennedy (2020), histological examination and immunohistochemistry remain the best tests for the diagnosis of UC. However, intravital biopsy is difficult or impossible in some cases. Therefore, the conclusion about the death of cats from infectious peritonitis is made posthumously in some cases. When diagnosing IPC, it is necessary to keep in mind that tissues that do not replicate this virus contain only small amounts or no pathogen at all. Among the organs with the highest content of the causative agent of UTI are the omentum, mesenteric lymph nodes and spleen. Therefore, these tissues are the most useful for diagnosis. On the contrary, the kidneys, liver, lungs, myocardium, and popliteal lymph nodes contain little or no pathogen. Diagnostics based on the detection of antibodies also do not give a stable and reliable result. For example, the detection of antibodies to feline coronavirus in the CSF of animals with neurological infectious peritonitis was initially considered necessary for diagnosis. However, studies by S. Felten & K. Hartmann (2019) showed that the detection of antibodies in CSF, serum and effusion is not suitable for a definitive in vivo diagnosis. The sensitivity and specificity of antibody detection were compared with histological and immunohistochemical findings as a reference standard, and control groups included cats with only any type of neurological disease or both neurological and non-neurological disorders. A recent study included cats with neurological symptoms that were likely caused by infectious peritonitis, although the diagnosis was not confirmed by histopathological examination. In this study, cerebrospinal fluid from a large number of animals was analysed and the sensitivity of feline coronavirus antibodies for the diagnosis of infectious peritonitis was found to be low. However, it was hypothesised that the detection of feline coronavirus ribonucleic acid in the cerebrospinal fluid could confirm the diagnosis of infectious peritonitis, as it was found in all cats with a cerebrospinal fluid antibody titer of 1:640 or higher. Based on these results, it is concluded that a cerebrospinal fluid antibody titer of 1:640 or higher can be used to diagnose this infectious disease. However, these results are of limited value because control cats were not included in the study and the diagnosis of infectious peritonitis was not confirmed.

The international literature describes macroscopic and microscopic changes in spontaneous IPC and its experimental reproduction (Lisova & Kotliarov, 2022). All identified changes are summarised in several review studies (Thayer *et al.*, 2022). However, morphological changes in the intestinal mucosa of cats with infectious peritonitis have not been studied before. Currently, in human medicine, the mesentery is considered a separate organ that maintains the systemic continuity of all abdominal and pelvic organs. According to the currently accepted mesenteric model of abdominal anatomy, all abdominal and pelvic organs are organised into 2 domains: mesenteric and non-mesenteric. This model explains the

positional anatomy of all abdominal and pelvic organs and the associated vascular system. The microscopic structure of the mesentery is not fully understood. It has been established that this organ in humans and animals of some species is a mesothelium-covered lattice of loose fibrous connective tissue, with adipocyte populations in the cells. The loose fibrous connective tissue of the mesentery is made up of bundles of collagen elastic fibres and fibroblasts. The mesentery also contains blood vessels, lymphatic vessels, nerves, and perivascular lymph nodes (Coffey *et al.*, 2020). In modern human anatomy, the mesentery is divided into upper, middle, and lower sections (D'Souza *et al.*, 2020). Based on the abovementioned, the research aims to investigate morphological changes in the mesentery of cats that died from dry and mixed forms of infectious peritonitis.

Materials and Methods

The research was carried out at the Kasyanenko Department of Anatomy, Histology and Pathomorphology of Animals, Faculty of Veterinary Medicine, National University of Life and Environmental Sciences of Ukraine in 2019-2022. Histological examinations of the small intestine mesentery of 27 cats of different breeds and ages that died from the mixed form of the disease and 7 cats of different breeds and ages that died from the dry form of the disease were performed. During the studies, access to the abdominal organs was obtained by cutting the abdominal wall along the midline of the abdomen. The small intestine was removed along with the mesentery. The mesentery of the small intestine of each cat was examined and pieces of mesentery measuring 2 × 2 cm were cut out with scissors at an equal distance from the small intestine and mesenteric lymph nodes: in the duodenum – 1 piece (from the middle part of this intestine), in the jejunum – 3 pieces (from the middle part of the cranial, middle and caudal thirds), in the ileum – 1 piece (from the middle part of this intestine).

All selected pieces of the small intestinal mesentery were fixed in formalin for 5 days, then rinsed under running tap water for 24 hours, dehydrated in 60°, 70°, 80°, 96° and 100° ethanol, kept in each of them for 24 hours, and then embedded in paraffin. When embedded in paraffin, the pieces of small intestinal mesentery were first transferred from 100º ethanol to a mixture of 100º ethanol and chloroform 1:3 for 4 hours, then to a mixture of 100º ethanol and chloroform 1:1 for 4 hours, and then to chemically pure chloroform for 12 hours at room temperature. After that, the pieces of the mesentery of the small intestine were transferred to a mixture of chemically pure chloroform and paraffin 1:1 at 37°C for 12 hours in a thermostat TSO-80 (Ukraine), and later to molten paraffin at 56°C for 6 hours in a thermostat TSO-80 (Ukraine). After that, they were poured into a new portion of molten paraffin and cooled at +8°C until the paraffin completely solidified. Sections of the mesentery of the small intestine (9±2 µm thick) were obtained in cross-section on a sledge microtome MS-2 (Ukraine), after which they were stained with haematoxylin and eosin (Goralskij *et al.*, 2011). Histological sections were photographed under an MC 100 LED microscope (Austria) using a Canon EOS 550D camera (China). All experimental studies were conducted in accordance with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (European convention..., 1986).

Results and Discussion

In both dry and mixed forms of UC, small white spots were found in the thickness of the small intestinal mesentery, which protruded above the general surface of the mesentery, had a homogeneous appearance in the section and were located far from the mesenteric lymph nodes (Figs. 1, 2). Considering the presence of

these spots, a histological examination of the areas of the mesentery of the small intestine located far from the mesenteric lymph nodes was performed. According to the histological studies, it was found that the mesentery of cats is covered with a serous membrane represented by a layer of mesotheliocytes. Currently, as noted by J.C. Coffey & and D.P. O'Leary (2017), mesotheliocytes are an almost unexplored pool of stem cells.

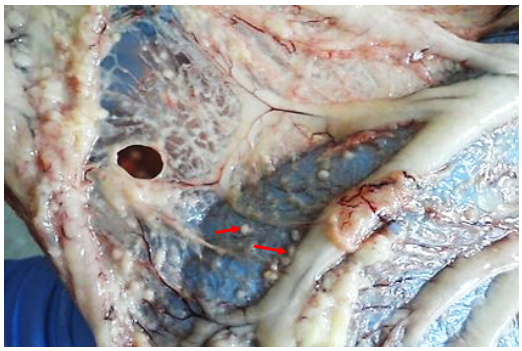

Figure 1. White spots in the mucosa of the cat's small intestine in the dry form of infectious peritonitis (arrows)

***Source**: developed by the author*

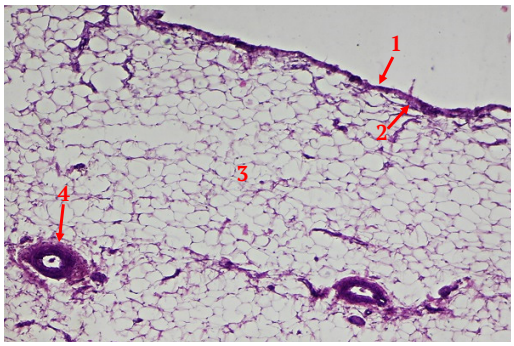

Figure 2. Mesentery of the small intestine of a control cat

***Note:** 1 – mesothelium; 2 – submesothelial layer of collagen fibre bundles; 3 – loose fibrous connective tissue; 4 – artery. Karatsi haematoxylin and eosin, ×100*

***Source**: developed by the author*

The study revealed that the mesothelium covering the mesentery of the small intestine, similar to that covering other internal organs of the abdominal and thoracic cavities, is represented by a single row of highly flattened, elongated cells with a rather large volume of cytoplasm, in the central, slightly thickened part of which there is a nucleus elongated along the long axis of the cell, containing distinctly basophilic condensed chromatin (heterochromatin) and 1-2 nucleoli. The long axis of mesothelial cells on the surface of the mesentery of the small intestine is oriented parallel to the outer surface of this mesentery. This orientation is also characteristic of mesothelial cells covering all abdominal organs (Fig. 3).

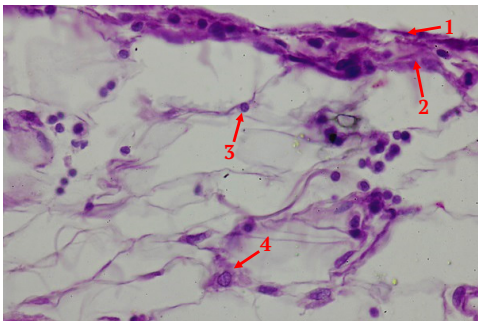

Figure 3. Loose fibrous connective tissue of the mesentery of the small intestine of a control cat
Note: *1 – mesothelium; 2 – submesothelial layer of collagen fibre bundles; 3 – fibrocyte with heterochromatin nucleus; 4 – fibrocyte with euchromatin nucleus. Karatsi haematoxylin and eosin, ×400*
Source*: developed by the author*

Beneath the mesothelium is a thin layer of rather thick and densely packed collagen fibre bundles (Figs. 2, 3). These bundles have a specific packaging. The vast majority of them are thick, densely packed bundles of fibres oriented parallel or almost parallel to the outer surface of the mesentery. These bundles are interconnected by a large number of slightly less densely packed and thinner collagen fibre bundles. It can be assumed that such a microscopic structure of the layer of collagen fibre bundles ensures the integrity and strength of the small intestine mesentery and enables this mesentery to maintain its integrity under various changes in position in the lumen of the abdominal cavity and under physical exertion due to peristaltic movements of the intestine.

Under the layer of collagen fibres, there is a loose fibrous connective tissue, which makes up the bulk of the mesentery tissue (Figs. 2, 3). This tissue is represented by a large number of fibrocytes located quite distantly from each other. These fibrocytes are connected by thin bundles of collagen fibres. Thus, fibrocytes together with collagen fibre bundles form a mesh-like structure with a fairly large mesh. Fibrocytes of the loose fibrous tissue of the mesentery of the small intestine have a typical microscopic structure for these cells. They are cells with a relatively large volume of oxyphilic cytoplasm and many processes of different lengths and thicknesses. In the central part of these cells are round or slightly oval nuclei, which contain mainly basophilic condensed chromatin (heterochromatin) and 1-2 nucleoli. Only in some fibrocytes do the nuclei contain uncondensed chromatin (euchromatin) (Figs. 3, 4).

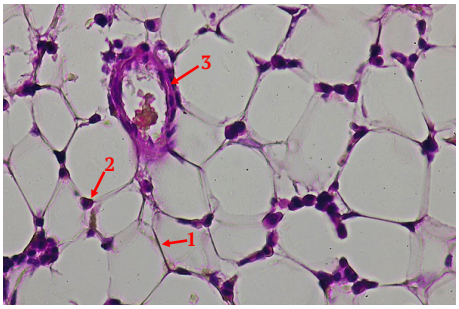

Figure 4. Adipose tissue of the mesentery of the small intestine of a control cat
Note: *1 – lipocyte cytoplasm; 2 – lipocyte nucleus with condensed chromatin; 3 – arterioles. Karatzi's haematoxylin and eosin, ×400*
Source*: developed by the author*

Focal accumulations of adipose tissue are scattered in the loose fibrous connective tissue of the mesentery of the small intestine without any noticeable pattern. This tissue is represented by densely packed fat cells (lipocytes) of rather large size (Fig. 4). They were characterised by a very narrow band of cytoplasm at the cell periphery. This band of cytoplasm was slightly widened in the area of nuclei. Lipocyte nuclei were small in size and, like the nuclei of mesotheliocytes and fibrocytes, contained distinctly basophilic, condensed chromatin (heterochromatin). The large size of mesenteric adipose tissue lipocytes was due to the presence

of a large fat droplet in each of them, which occupied almost the entire cell area in the plane of the histological section. Each accumulation of adipose tissue is separated from the surrounding loose fibrous connective tissue of the mesentery by a thin layer of collagen fibre bundles, among which there were few fibrocytes. These collagen fibre bundles are oriented parallel to the outer surface of each adipose tissue focus. The peculiarities of the microscopic structure of the mesentery of the small intestine of cats allow us to conclude that loose fibrous tissue together with foci of adipose tissue provides both the elasticity of the mesentery and the ability to easily stretch, and the ability to easily change its shape during the movements of the animal's body and the movements of its intestines and other abdominal organs. This microscopic structure of the mesentery of the small intestine of cats is assumed to provide the necessary mobility of the small intestinal loops of these animals. The microscopic structure of the mesentery of the small intestine of cats coincides with its structure described in the literature in other mammals, including humans (Sorenson & Brelje, 2014).

In addition, it was found that regardless of the form of infectious peritonitis, microscopic changes in the small intestinal mesentery of all cats studied were similar and concerned all types of tissues that make up this mesentery. These changes varied in different parts of the small intestinal mesentery, but there was no pattern or correlation between the nature and location of these changes. Mesothelium on the surface of the mesentery of the small intestine of cats killed by infectious peritonitis was necrotic, destroyed and underwent metaplasia in some areas, turning into cubic cells (Fig. 5). In other areas of the mesentery of this intestine, mesothelium was not detected at all (Fig. 6). This is likely caused by the fact that mesotheliocytes in these areas were destroyed in vivo before the cats died and their small intestinal mesentery was sampled for histological examination.

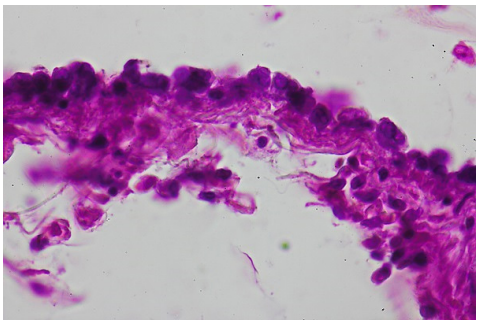

Figure 5. Cat's small intestine mesentery (a mixed form of infectious peritonitis)

Note: *1 – necrosis of mesothelium; 2 – destruction of mesothelium; 3 – cubic mesothelium; 4 – mesenteric edema Hematoxylin and eosin, ×400*

Source*: developed by the author*

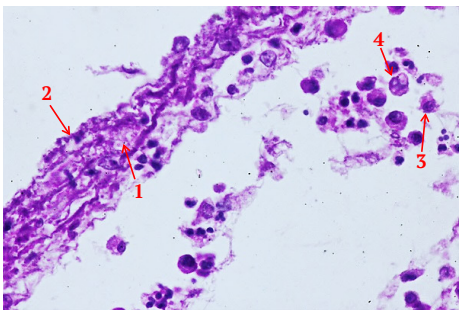

Figure 6. Cat's small intestine mesentery (dry form of infectious peritonitis)

Note: *1 – fragmentation and partial lysis of submesothelial collagen fibre bundles; 2 – absence of mesothelium on the outer surface of the mesentery; 3 – destruction of the monocyte; 4 – eosinophilic inclusion body in the vacuolated cytoplasm of the monocyte; Karatzi's haematoxylin and eosin, ×400*

Source*: developed by the author*

The layer of thick collagen fibre bundles located under the serosa was necrotic in some areas of the small intestinal mesentery, as well as the mesothelium, while in other areas these collagen fibre bundles were unevenly swollen,

partially lysed and fragmented (Fig. 6). The loose fibrous connective tissue underlying the layer of thick collagen fibre bundles was markedly swollen. Some of the cellular and fibrous components of this tissue were necrotic (Fig. 7). At the same time, unevenly granular oxyphilic substance or rather uniform oxyphilic substance with a small number of vacuoles in it was found in place of fibrocytes, and collagen fibre bundles turned into a structureless, heterogeneously stained mass. In many areas, the collagen fibre bundles were broken. The unevenly granular oxyphilic substance in the place of necrotic fibrocytes without any noticeable boundary turned into necrotic collagen fibre bundles, which made it impossible to differentiate the boundaries of the cellular and fibrous components of the loose fibrous tissue of the mesentery of the small intestine in most cases. Only in single necrotic fibrocytes the cell boundaries were visualised. In some places, foci of destruction of loose fibrous connective tissue were detected (Fig. 7). In such areas of the small intestinal mesentery, only small fragments of eosinophilic substance without any specific structure were detected, which were not structurally interconnected. This indicates that individual areas of loose fibrous connective tissue, which had previously undergone necrosis, were destroyed.

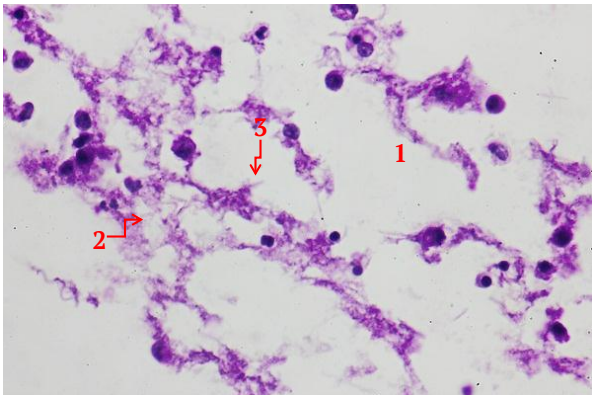

Figure 7. Cat's small intestine mesentery (dry form of infectious peritonitis)
Note: *1 – swelling of loose fibrous connective tissue; 2 – necrosis and destruction of collagen fibre bundles of loose fibrous connective tissue; 3 – necrosis of fibrocyte. Karatsi haematoxylin and eosin, ×400*

The loose fibrous connective tissue of the mesentery of the small intestine of cats that died as a result of infectious peritonitis was also unevenly infiltrated with lymphocytes and monocytes. These cells in the loose fibrous connective tissue were located both singly and in the form of clusters containing a different number of cells (Fig. 8). In this case, especially large clusters of these cells were located near the blood and lymphatic vessels of the mesentery. It should be emphasised that monocytes predominated in the cellular infiltrate in the loose fibrous tissue of the mesentery of the small intestine. Some monocytes were transformed into macrophages (Fig. 9). Since other researchers have found that such transformation occurs under the influence of various antigenic stimuli (Italiani & Boraschi, 2014; Yang *et al.*, 2014; Mysore *et al.*, 2022), the monocytes in the mesentery were in contact with the IPC virus or received appropriate signals from lymphocytes.

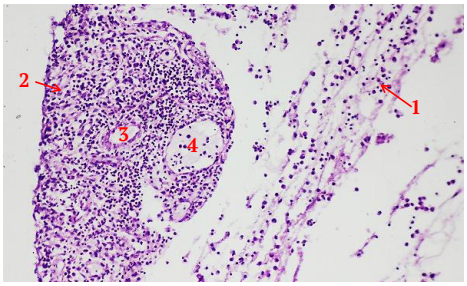

Figure 8. Cat's small intestine mesentery (dry form of infectious peritonitis)
***Notes**: 1 – infiltration of loose fibrous connective tissue with lymphocytes and monocytes; 2 – perivascular lymphoid nodule; 3 – venule; 4 – dilated lymphatic vessel. Karatsi haematoxylin and eosin, ×100*
***Source**: developed by the author*

A small number of small lymphocytes were detected between monocytes and macrophages infiltrating the loose fibrous connective tissue of the small intestinal mesentery (Fig. 9). At the same time, in addition to monocytes, macrophages and lymphocytes, neutrophils were also present in small numbers in the cellular infiltrate near the blood and lymphatic vessels of the small intestine mesentery. According to the results of microscopic studies, in the mesentery of the small intestine of cats killed by infectious peritonitis, vacuolation of the cytoplasm of some monocytes and macrophages infiltrating the loose fibrous connective tissue was also recorded (Fig. 9). According to S. Ohkuma & B. Poole (1981), such cytoplasmic vacuolation may indicate the activation of lysosomes of these cells as a result of their response to an antigenic stimulus or as noted by K. Miyata & K. Takaya (1983), about the accumulation of phagocytosed substances in the cytoplasm of monocytes and macrophages of the small intestine mesentery. The latter was primarily confirmed by the fact that according to the results of this work, phagocytosed basophilic material was found in the cytoplasm of some monocytes and macrophages (Fig. 10). The nature of this material could not be determined, as this requires electron microscopic examination. However, it can be assumed that these phagocytes phagocytosed fragments of destroyed cells and fibrous components (primarily collagen fibres) of the small intestinal mesentery tissues.

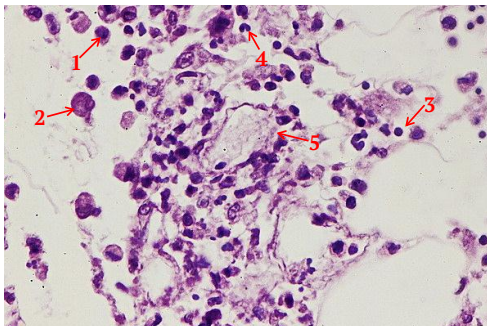

Figure 9. Accumulation of cells in the loose fibrous tissue of the mesentery of the cat's small intestine (a mixed form of infectious peritonitis)
***Note**: 1 – monocyte; 2 – macrophage; 3 – lymphocyte; 4 – segmented neutrophil; 5 – destruction of the lymphatic vessel wall. Karatsi haematoxylin and eosin, ×400*
***Source**: developed by the author*

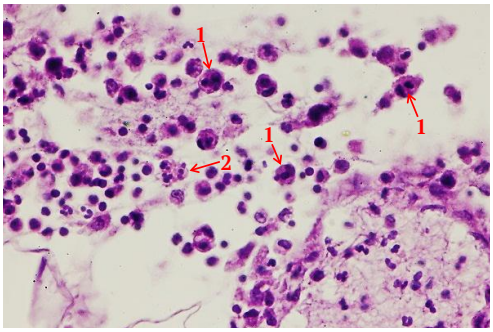

Figure 10. Accumulation of cells in the loose fibrous tissue of the mesentery of the cat's small intestine (dry form of infectious peritonitis)
***Note:** 1 – macrophages with phagocytosed basophilic material in the cytoplasm; 2 – apoptotic cells. Karatsi haematoxylin and eosin, ×400*
***Source**: developed by the author*

Some monocytes and macrophages were destroyed, resulting in the formation of apoptotic cells in their place (Fig. 10). The destruction of these cells is due to their direct damage by the infectious peritonitis virus. K. Shirato *et al*. (2018) found that this coronavirus is capable of infecting monocytes and macrophages, multiplying in these cells, and it is likely that the S gene mutations of the feline coronavirus occurred in these cells. Specific mutations of the S gene were identified during the full sequencing of the feline coronavirus genome. At the same time, other authors (Lewis *et al*., 2015) found that most feline coronaviruses of the pathotype that causes infectious peritonitis to have a mutation in a nucleotide position associated with a change in amino acids in the S protein putative fusion peptide and a substitution that leads to a change in the amino acid in the heptad repeat 1 (HR1) region. This can lead to a change in the fusogenic activity of protein S and, thus, to a change in cellular tropism.

According to the study, eosinophilic inclusion bodies were found in the cytoplasm of some monocytes and macrophages (Fig. 6). At present, domestic researchers consider such inclusion bodies to be microscopic changes specific to feline infectious peritonitis (Khalaniia, 2020), although it has not been confirmed that such inclusion bodies contain viral antigens or the feline infectious peritonitis virus itself. Other authors have found that viral inclusion bodies (also called viral non-proliferative complex or viral replication factories) are specialised structures that are built from viral and some cellular proteins and are a platform for viral replication (Zhang *et al*., 2017; Dolnik *et al*., 2021). Given these data, the presence of eosinophilic inclusion bodies in the cytoplasm of some monocytes and macrophages may indicate the replication of the causative agent of feline infectious peritonitis in these cells, although this is not direct evidence of replication of this particular virus, such as immunological methods of research.

At the same time, according to the available literature, eosinophilic inclusion bodies in the cytoplasm of cells in infectious peritonitis have not been studied. However, according to the world literature, in the case of the severe acute respiratory syndrome coronavirus (SARS-CoV), protein N was isolated from inclusion bodies (Li *et al*., 2021). As established by C. Chang *et al*. (2014), this protein is a nucleocapsid phosphoprotein that packages the viral genome into a helical ribonucleocapsid (RNP) and plays a fundamental role in virus self-assembly. The structures of this ribonucleoprotein (RNP) inside the virions of the causative agent of severe acute respiratory syndrome were also visualised.

The accumulation of adipose tissue in the mesentery of the small intestine in all cats that died as a result of infectious peritonitis was also unevenly infiltrated with lymphocytes and monocytes (Fig. 11). However, in contrast to the loose fibrous connective tissue of the mesentery, the transformation of monocytes into macrophages was not detected in this tissue. At the same time, the largest number of lymphocytes and monocytes in the foci of adipose tissue of the mesentery of the small intestine was localised in its peripheral parts, while the middle and peripheral areas of these foci were infiltrated with a significantly smaller number of lymphocytes and monocytes. From this, it can be concluded that lymphocytes and monocytes penetrated the foci of adipose tissue of the mesentery of the small intestine of patients with UC from the surrounding loose fibrous connective tissue.

In the blood vessels (arteries and veins) of the mesentery, necrosis, and destruction of their walls, as well as destruction of lymphatic endothelial cells were detected in all the studied cases (Fig. 12). A. Kipar & M. Meli *et al*. (2004)

found that coronavirus infection in cats leads to monocyte-associated viremia and the formation of circulating immune complexes. Foreign researchers have also found that circulating immune complexes can be deposited in the subendothelial region and damage endothelial cells, causing autoimmune vasculitis (Wang & Law, 2019), and endothelial cell damage occurs as a result of the interaction of immune complexes with Fcgamma receptors (FcγR) expressed on inflammatory cells. At the same time, nitric oxide (NO) induced by immune complexes is one of the main mediators of inflammation that contributes to vascular inflammation and endothelial cell death in immune complex vasculitis (Mula *et al.*, 2016). However, according to other authors (Xu *et al.*, 2022), endothelial cell damage is associated not only with the deposition of immune complexes, but also with complement activation, inflammatory factors and chemokines, oxidative stress, haemodynamic, and coagulation factors.

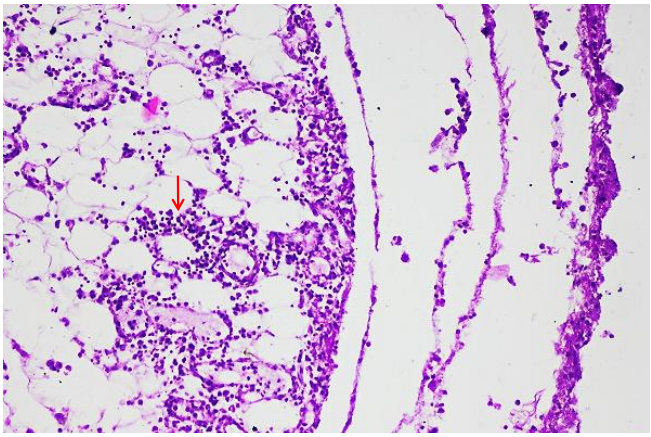

Figure 11. Cat's small intestine mesentery (dry form of infectious peritonitis)
Note: *infiltration of mesenteric adipose tissue by lymphocytes and monocytes (arrow). Hematoxylin and eosin, ×50*
Source*: developed by the author*

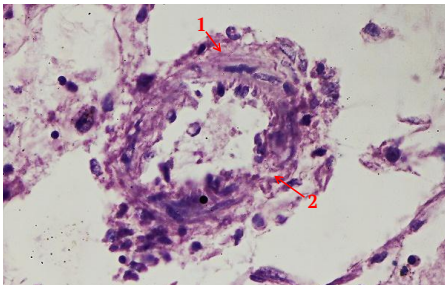

Figure 12. Cat's small intestine mesentery (dry form of infectious peritonitis)
Note: *1 – necrosis of the artery wall; 2 – destruction of the artery wall. Karatsi haematoxylin and eosin, ×400*
Source*: developed by the author*

In addition to other tissues, perivascular lymphoid nodules were found in the mesentery of cats outside the mesenteric lymph nodes (Fig. 8). These nodules in the mesentery of the small intestine of cats are localised around venules and postcapillaries and consist mainly of lymphocytes and a much smaller number of monocytes. Such microscopic structure of perivascular lymphoid nodules in the mesentery of the small intestine of cats corresponds to the microscopic picture of similar nodules in the mesentery and other mammalian organs previously described by researchers (Sorenson & Brelje, 2014; Evtushenko *et al.*, 2019).

In cats that died from infectious peritonitis, a distinct increase in perivascular lymphoid nodules of the small intestine was found. This increase is due to both swelling of these nodules and an increase in the number of cells in them. In the perivascular lymph nodes, lymphatic vessels were also found to be dilated and some of the endothelial cells of blood and lymphatic vessels were destroyed. Some of the lymphatic vessels of the small intestine mesentery, which ran both in the loose fibrous connective tissue and in the peripheral parts of adipose tissue foci and around which there were no perivascular lymph nodes, were distinctly dilated and filled with lymph, which contained a significant number of lymphocytes, monocytes, and single neutrophils (Fig. 13). Hypertrophic perivascular nodules together with distinctly dilated and lymphatic vessels filled with lymph formed the above-described macroscopically visible white spots on the intestinal mucosa of cats that died from infectious peritonitis.

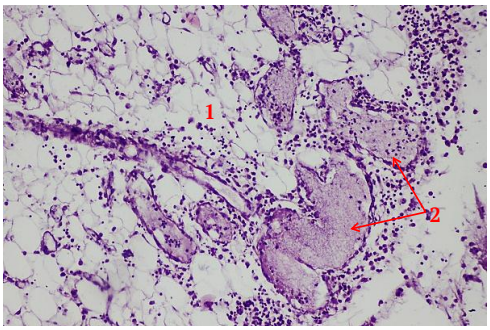

Figure 13. Cat's small intestine mesentery (a mixed form of infectious peritonitis)

Note: *1 – adipose tissue infiltrated with inflammatory cells; 2 – distinctly dilated lymphatic vessels. Karatsi haematoxylin and eosin, ×100*

Source*: developed by the author*

The changes in the small intestine mucosa of cats with infectious peritonitis established by this study significantly complement the previously described results on pathomorphological changes in cats with this disease, published in different chronological periods: from 1960 to 1979 (Wolfe & Griesemer, 1966; Ward & Pederson, 1969; Hayashi *et al*., 1977), at the beginning of 80s (Hayashi *et al*., 1980; Weiss *et al*., 1981; Weiss & Scott, 1981), from end of 80s to end of 90s (Boudreaux *et al*., 1989; Pedersen, 1995) and in different years of the XXI century (Pedersen, 2009; Kipar & Meli, 2014). The data obtained in this study are the basis for a deeper understanding of the processes that occur in the abdominal cavity of cats with UTI and lead to the accumulation of fluid in it.

Conclusions

For the first time, the peculiarities of the microscopic structure of the mesentery of the small intestine of cats were clarified and morphological changes in this mesentery were described in animals that died from dry and mixed forms of infectious peritonitis. Mesentery of the small intestine of cats was found to be covered with mesothelium of typical microscopic structure. The mesothelium layer was supported by a layer of thick collagen fibre bundles, which ensured the strength of the small intestinal mesentery. Under the layer of thick collagen fibre bundles was a loose fibrous connective tissue, which constituted the bulk of all tissues of the small intestine mesentery. This tissue contained nests of adipose tissue and perivascular lymphoid nodules. These nodules were formed around venules and postcapillaries and consisted of lymphocytes and monocytes. In dry and mixed forms of infectious peritonitis, necrosis and destruction of mesothelial cells and the layer of thick collagen fibre bundles located under them were microscopically detected in the mesentery of the small intestine of cats. The loose fibrous connective tissue of the small intestine mesentery was distinctly swollen and infiltrated with lymphocytes and monocytes.

Some monocytes transformed macrophages. Eosinophilic inclusion bodies were detected in the cytoplasm of some monocytes and macrophages, indicating replication of the virus in the cells. The adipose tissue of the mesentery of the small intestine was also unevenly infiltrated with lymphocytes and monocytes. The largest number of these cells was localised in the peripheral parts of the adipose tissue nests. There was no transformation of monocytes into macrophages in adipose tissue. Some lymphatic vessels of the mesentery, around which there were no perivascular lymphoid nodules, were distinctly dilated and filled with lymph, which contained a significant number of lymphocytes, monocytes, and single neutrophils. The perivascular lymphoid nodules were markedly enlarged due to their significant swelling and an increase in the number of lymphocytes and monocytes. Such enlarged perivascular nodules, together with severely dilated lymphatic vessels, looked like mesenteric granulomas at pathological autopsy.

In the future, it is necessary to establish macroscopic and microscopic changes in the colonic mucosa of cats with infectious peritonitis.

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None.

Conflict of Interest

None.

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Морфологічні зміни в брижі тонкої кишки котів за інфекційного перитоніту

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Анотація. Актуальність дослідження зумовлена тим, що морфологічні зміни в брижі котів за інфекційного перитоніту до цього часу не вивчені, але їх розуміння необхідне для пояснення механізму розвитку основного симптому хвороби – випоту рідини в черевну порожнину. Мета роботи – встановити макроскопічні і мікроскопічні зміни в брижі тонкої кишки котів за інфекційного перитоніту. Методами роботи є макроскопічне вивчення та гістологічні дослідження брижі тонкої кишки котів за інфекційного перитоніту. Зрізи брижі фарбували гематоксиліном та еозином. З'ясовано, що за сухої і змішаної форм інфекційного перитоніту котів макроскопічні та мікроскопічні зміни в брижі тонкої кишки подібні. У брижі макроскопічно виявлялися невеликі білі плями, які випинали над загальною поверхнею і мали однорідний вигляд на розрізі. Мікроскопічні зміни в брижі тонкої кишки котів за сухої і змішаної форм інфекційного перитоніту не відрізнялися. Під час гістологічних досліджень відмічали, що мезотелій на поверхні брижі некротизований чи відсутній. Субмезотеліальний шар колагенових волокон некротизований або містив частково лізовані чи фрагментовані волокна. Пухка волокниста сполучна тканина брижі була набрякла, місцями некротизована та інфільтрована лімфоцитами, моноцитами і макрофагами. В цитоплазмі частини моноцитів і макрофагів виявляли еозинофільні тільця-включення. Скупчення жирової тканини в брижі тонкої кишки виглядали інфільтрованими лімфоцитами й моноцитами. У кровоносних судинах виявляли некроз і руйнування їх стінок, а в лімфатичних судинах – руйнування клітин

ендотелію. Периваскулярні лімфоїдні вузлики також відзначалися збільшенням розмірів внаслідок їх набряку і збільшення в них кількості клітин. У периваскулярних лімфоїдних утвореннях встановлено розширення лімфатичних судин і руйнування частини клітин їх ендотелію. Частина лімфатичних судин брижі виразно розширена й переповнені лімфою, яка містила значну кількість лімфоцитів, моноцитів та поодинокі нейтрофіли. Представлені результати становлять практичну цінність для анатомів, гістологів і патоморфологів, а також для науковців, які вивчають патогенез інфекційного перитоніту котів

Ключові слова: коронавіруси котів; периваскулярні лімфоїдні вузлики; еозинофільні тільця-включення; макроскопічні зміни; мікроскопічні зміни