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Structural Changes of the Urinary Organs in Case of Triple Phosphate Urolithiasis in Cats

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Abstract

The purpose of the study is to study the pathomorphological picture of the urinary system in cats with triple phosphate urolithiasis. The study was carried out by using cadaveric materials from 18 cats diagnosed with triple phosphate urolithiasis on the basis of clinical signs (pollakiuria, hematuria, ischuria), and laboratory diagnostic methods (clinical studies of urine and blood, biochemical blood analysis). Macropreparations were studied visually by evaluating the linear size of the kidneys, condition of the capsule, surface appearance on the section, density, and the presence of inhomogeneous inclusions. The authors studied wall thickness of the bladder and urinary tract (urethra and ureters), their configuration, and condition of the mucous membrane on the section. Hematoxylin and eosin staining were used for histostructural diagnostics, as well as picrofuxin staining by Van Gison. During the study, it has been found that urolithiasis leads to structural changes in the urinary organs, while characteristics of organ and tissue damage vary depending on the duration of urolithiasis. The macroscopic study allows registering acute or chronic urocystitis, interstitial nephritis, sometimes with the deposition of concrements in the renal pelvis. The most significant microscopic changes are recorded in the renal tissues. Thus, renal changes are presented by conditions from acute interstitial nephritis to necrosis of renal tubules and nephrosclerosis. In the urinary tract (urethra and ureters) there are inflammatory changes with deposition of urolithes. These processes have seriously affect the general condition of animals and require quality control and the optimal selection of medicines during treatment.

Keywords: cats, histostructural diagnostics, macroscopic picture, pathomorphology, triple phosphate urolithiasis, urinary system.

INTRODUCTION

Triple phosphate urolithiasis refers to chronic diseases of the urinary system, which does not have pathognomonic signs accompanied by violation of general hemodynamics leading to serious complications and recurrence rate reaching 50% [1-5]. This problem is a fairly common pathology with severe consequences. In addition, it has a high mortality rate [6]. In order to establish an adjusted approach to treatment, it is necessary to identify the pathology that causes the formation of uroliths, and such factors as the presence of bacterial infection and urinary obstruction [7]. However, it should be immediately noted that the role of microflora in the pathogenesis of urolithiasis in cats has rather a controversial position today. Some authors give it an important place in this pathology, while others dispute its significance [8, 9]. At the same time, diagnosis of this disease is carried out in a comprehensive way and includes laboratory studies in the form of clinical and biochemical blood and urine tests, and such visual diagnostic methods as ultrasonography and radiological test [8, 10-12]. However, the pathological study followed by the study of a macroscopic and microscopic picture of the urinary organs have the greatest value in terms of information for the clinician. It minimizes the subjectivity typical of other research methods [13, 14].

Purpose of the study is to study the pathomorphological picture of the urinary system in cats with triple phosphate urolithiasis.

MATERIALS AND METHODS

The study was carried out by using cadaveric materials from 18 cats diagnosed with triple phosphate urolithiasis on the basis of clinical signs (pollakiuria, hematuria, ischuria, etc.), and laboratory diagnostic methods (clinical studies of urine and blood, biochemical blood analysis). Macropreparations were studied visually by evaluating the linear size of the kidneys, condition of the capsule, surface appearance on the section, density, and the presence of inhomogeneous inclusions. We studied wall thickness of the bladder and urinary tract (urethra and ureters), their configuration, and condition of the mucous membrane on the section. For normal histological structure diagnostics [13-15] we used universal histological staining of the sections with hematoxylin and eosin. Dyeing properties of hematoxylin are realized in slightly alkaline medium, while basophilic structures (cell nuclei, deposits of lime salts and bacteria colonies) are stained with this dye in blue or dark blue. Weak basophilia can be produced by some types of mucus. In acidic medium eosin stains oxyphilic components (cytoplasm of cells, fibers, RBCs, protein masses and most types of mucus) in rosy red or red color [14, 15]. In addition, picrofuxin staining by Van Gieson was used for identification and study of connective tissue. Collagen fibers of connective tissue were stained in red color, cell protoplasm and RBCs in yellow; nuclei in lilac or brown. Van Gyzon method makes it possible to detect even a small amount of connective tissue indiscernible when staining with hematoxylin and eosin [15].

RESULTS AND DISCUSSION

During our studies of the fallen/euthanized cats with triple phosphate urolithiasis during pathoanatomical autopsy, we detected significant changes in the urinary tract. Urinary tracts (ureters and urethra) had a number of macroscopic changes, as the edema and wall thickening from moderate to severe degree have been recorded most often in deceased animals with urolithiasis. It could be interpreted as a result of the inflammatory process due to the constant excretion of concrements of the different diameters and repeated obstruction of the urogenital tract. In addition, hyperemia of the mucous layer was noted on the section, as well as the presence of fine, dusty sand.

When studying the bladder, it has been found that the picture varies significantly depending on the duration of the pathological process. Thus, during the autopsy of euthanized animals, we noted both acute and chronic urocystitis. On macroscopic examination of the bladder with an acute course of urolithiasis, edema, hyperemia of the mucosa, the surface was covered with exudate from mucous-hemorrhagic to purulent color, deposition of fibrin. These changes can be interpreted as a consequence of the inflammatory process, i.e. complex morphochemical process. Its main elements include histamine, serotonin, cytokines, etc. Due to these elements, we can note vasodilation and an increase in the permeability of the vessel wall, pain and impaired function of the organ. On the surface, there are petechial hemorrhages and ulcers (Fig. 1a, 1b). Also, there were deposits of calculi having the diameter from a grain to several millimeters/centimeters.

With the development of chronic urocystitis, the mucous membrane of the bladder is thickened due to the proliferation of fibrous connective tissue, and there also may be polyposic

growths. At the same time, an urine has a turbid appearance with a sharp odor, flakes and an admixture of sand [13].

In view of the similarity of the histological structure of the urinary bladder and urinary tract, we noted a disturbance in histological architectonics of the organ similar to those found in the ureters and urethra, i.e. there was edema, inflammatory hyperemia of the wall, dystrophic changes in the mucous layer, as well as deposition of microliths in the lumen of the organ. When analyzing a histological picture of the urinary tract, we registered significant mucosal and hydropic dystrophy of the epithelial lining with necrobiosis of cells and their desquamation into the lumen of the urethra, swelling of the submucosal layer with blood overflow, i.e. inflammatory hyperemia. In the lumen of the urethra, there is an accumulation of urolithes of various diameters (Fig. 2a, 2b).

However, as it has been mentioned earlier, the most serious and vivid changes were noted in kidneys (Fig. 3a, 3b). At the same time, it should be noted that pathological changes significantly vary depending on the duration of the course of urolithiasis, its recurrence, and also localization of the pathological process [16-18]. Thus, depending on the main focus, we can mention glomerulonephritis, interstitial nephritis and pyelonephritis, and depending on the nature of exudates, there is serous, fibrinous, purulent and hemorrhagic nephritis.

In the course of this study, most often we noted an acute interstitial nephritis. During the development of interstitial nephritis, the stroma of the organ is involved in the process, i.e. interstitium. Kidneys affected by interstitial nephritis are enlarged in volume, gray in color. In focal interstitial nephritis, kidneys have a larger size, gray in color. White cone-shaped spots represented by an overgrown granulation tissue transilluminate from the surface under the capsule. With the development of pyelonephritis, the interstitial system and pelvic system are involved in the process. Kidneys are enlarged in volume, under the capsule there are grayish foci of various sizes and shapes with irregular contours, the capsule is easily removed. On the section, the loci are softened, filled with purulent contents. Suppuration is also found on the mucous membrane of the pelvis.

Fig. 1. Macroscopic picture of the cat's bladder in the development of urolithiasis. There is significant variability from acute (a) to chronic (b) urocystitis. Ruler - centimeters.

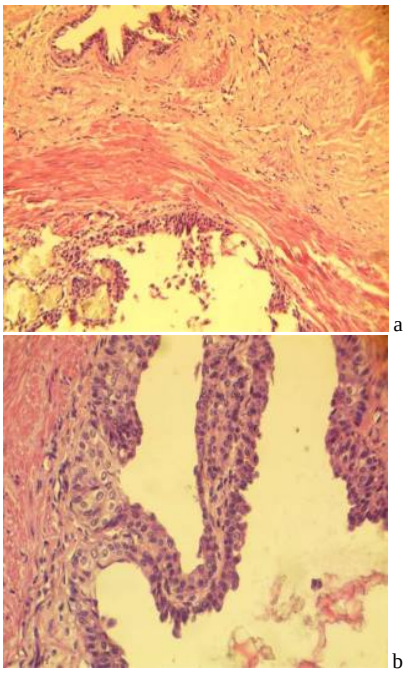


Fig. 2. Histological picture of ureter (a) and urethra (b). There are inflammatory hyperemia, desquamation and degeneration of the epithelium, accumulation of microlithes in the lumen. Magnification x400. Stained with hematoxylin-eosin.

Fig. 3. Kidney with acute interstitial nephritis. The organ is enlarged in volume, swollen, vascular pattern is significantly strengthened (a). On the section there is significantly reduced corticomedullary differentiation, puffiness of the tissue (b). Ruler - centimeters.

According to the literature, violation of the adequate renal perfusion and renal/systemic hypertension are among the main components in pathogenesis and thus in pathological changes in kidneys in small domestic animals. They result in hypoxia of the organ followed by an atrophy of the functional tissue of the organ. In addition, the formation of antigen-antibody complexes, i.e. autoimmune reactions due to various infectious agents, plays an important role in the pathogenesis of renal diseases in cats. In the case of urolithiasis, we have a complex cascade of morphofunctional transformations, including the above-noted changes [14, 16, 17, 19-24].

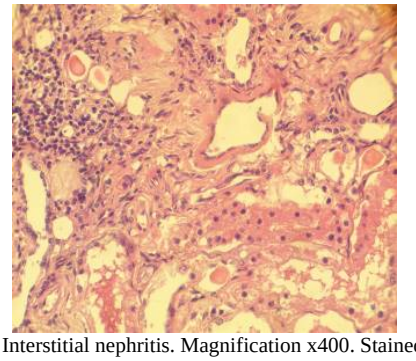


Fig. 4. Interstitial nephritis. Magnification x400. Stained with hematoxylin-eosin.

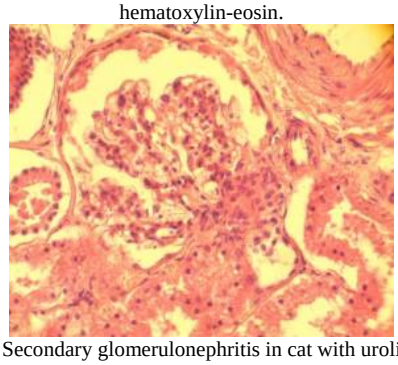
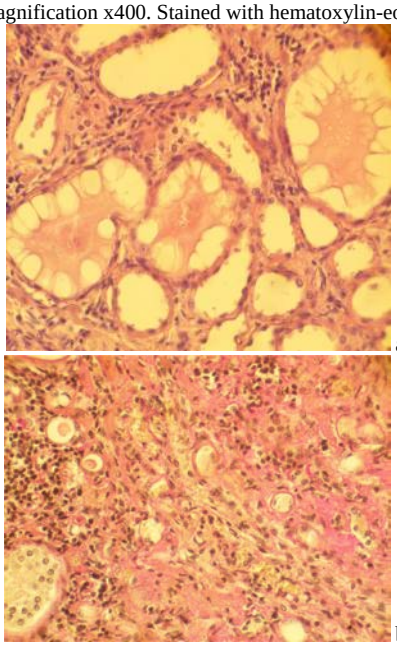


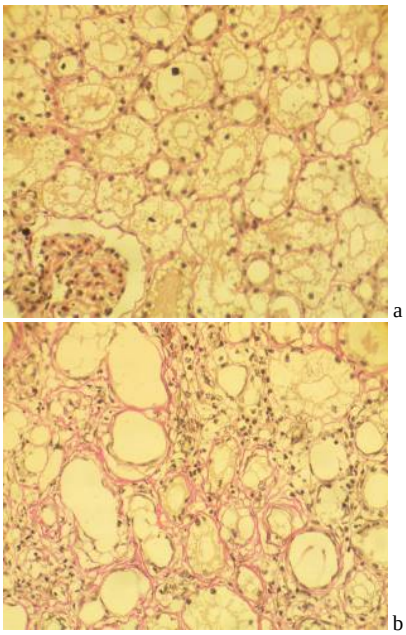
Fig. 5. Secondary glomerulonephritis in cat with urolithiasis. Magnification x400. Stained with hematoxylin-eosin.



a b

Fig. 6. Dystrophic changes in renal tissue during the development of interstitial nephritis: a – magnification x400, b - magnification x100. Stained with hematoxylin-eosin.

In the renal tissues, there are marked signs of degenerative-inflammatory changes. In this case, inflammation has diffuse, lymphocytic-plasmacytic nature. In the epithelium of the renal tubules, there are signs of dystrophic changes and a tendency toward cyst formation in renal tissue. Cysts have different calibers and lined with a flattened renal epithelium (Fig. 4). Renal glomeruli have a tapered form, which is a sign of secondary glomerulonephritis (Fig. 5). In case of urolithiasis in cats, the latter may indicate an occurrence of a complex of autoimmune processes. This leads to considerable violations of organ histoarchitectonics. However, this theory requires an additional study.



a b

Fig. 7. Kidney of a cat. Necrosis of the renal tubules (a) and nephrosclerosis (b). Magnification x400. Stained by Van Gieson.

In case of a longer course of the pathological process, chronic interstitial nephritis develops. Herewith an organ macroscopically decreases in size, secondary cyst formation is observed, and corticomedullary differentiation is poorly traced. Histological examination in renal tissue helps to reveal significant proliferation in form of abundant cell clusters around the vessels and renal tubules. These clusters consist of lymphoid cells, histiocytes and fibroblasts with moving of functional elements of the renal tissue aside from each other and their atrophy. Cells of the epithelium of the renal tubules are in a state of severe vacuolar dystrophy (formation of “cylinders”) (Fig. 6a). The interstitial tissue of the kidney has the signs of fibrosis, which is well traced when staining by Van Gieson (Fig. 6b). Blood vessels have signs of mild hyperemia. Renal glomeruli have a regular structure, there is a congestion of serous exudate in the lumen of the glomerular capsule, and a tendency towards cyst formation.

With the development of the chronic pathological process, frequent relapses and inadequate correction, we have recorded severe and irreversible changes in organ histoarchitectonics in kidneys of the cats. These were represented by tubular necrosis and nephrosclerosis. In the first case, the tubular epithelium is in the state of dystrophy, areas of atrophy were revealed. Cellular cytoplasm is optically empty or colored unevenly. Renal glomeruli have altered morphological properties. Bowman's space is dilated. However, these changes have a secondary character. The interstitial tissue has signs of secondary edema (Fig. 7a). These changes can be interpreted as a borderline condition with nephrosclerosis.

During the development of nephrosclerosis, the tubular epithelium is in the state of necrosis, interstitial tissue has signs of secondary fibrosis and diffuse inflammatory infiltration. The competent tissue of the kidney is replaced by a connective tissue of fine-fibrous structure. Renal glomeruli in the state of degenerative changes, glomeruli are reduced in size, Bowman’s space is widened. The latter indicates terminal changes in the organ (Fig. 7b).

CONCLUSIONS

Thus, we have established that pathological and histological examination of the urinary organs is forced, but the most informative method of the study. It allows obtaining the most complete picture of changes resulting from urolithiasis. Clinical studies found that urolithiasis in the absence of timely correction leads to serious morphological changes in the urinary organs. The macroscopic study allows to register acute or chronic urocystitis, interstitial nephritis, sometimes with the deposition of concrements in the renal pelvis [8, 9]. The most significant microscopic changes are recorded in the renal tissues. At the same time, the nature of lesions varies depending on the duration of urolithiasis. Thus, renal changes are presented by conditions from acute interstitial nephritis to necrosis of renal tubules and nephrosclerosis. In the urinary tract (urethra and ureters) there are inflammatory changes with deposition of urolithes. Noted structural changes in the urinary tract have a severe impact on the general condition of the animals and require quality control and optimal selection of medicinal products [18, 19, 24, 25] during treatment of cats.

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