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Cystic Urogenital Anomalies in Ferrets (*Mustela putorius furo*)

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Abstract. Single or multiple semispherical to bilobulated fluid-filled cystic structures of variable size were observed on the dorsal aspects of the urinary bladder of four male and two female ferrets (*Mustela putorius furo*). All ferrets had been neutered. On physical examination, the cysts were palpated as caudal abdominal masses. Three of the six ferrets presented with dysuria, and two ferrets had signs compatible with endocrine dysfunction. Adrenal cortical hyperplasia or neoplasia were observed in all of the five ferrets examined. Sex hormones assayed in one of the six ferrets revealed elevated levels of serum estrodiol. The posterior aspect of the cysts was located on and/or attached to the trigone or neck of the bladder, with variable intraluminal communication with the bladder and/or the urethra. The anterior aspect of the cysts projected dorsally or dorsocranially into the caudal abdomen. The cysts were thin walled and contained urinelike fluid ($n = 5$) or viscous yellow fluid ($n = 1$). Histologically, the cyst walls were composed of three layers, epithelium, muscle, and serosa, with fibrovascular stroma between layers. The epithelium consisted of simple to stratified transitional, columnar, or squamous epithelial cells. The muscular layer consisted of intermittent bundles and/or single to double layers of continuous to discontinuous smooth muscle. The serosal layer consisted of loose fibrous stroma covered by flattened mesothelial cells. The cystic anomalies in these ferrets were most likely derived from the urogenital glands/ducts or other remnants.

Key words: Anomaly; bladder; cyst; ferret; urogenital tract.

Urinary and genital systems both derive from intermediate mesoderm in early fetal life and are closely associated embryologically and anatomically in avian and mammalian species.[5,17,21,24] Both systems are embryologically unique in that 1) some of their organs, such as pronephroi, appear early and then disappear late in fetal life without becoming functional in many species, 2) some organs, such as mesonephroi, function only for a short period of time in the early fetal life, 3) some organs, such as metanephroi, develop into permanent organs and function during the entire postnatal life, and 4) other organs, such as the paramesonephric (Mullerian) duct in males and the mesonephric (Wolffian) duct in females, regress and only certain portions may be salvaged by a new organ. During the conversion of the primordial urogenital system into a postnatally functional system, certain organs and/or ducts degenerate and are subsequently resorbed. They may be resorbed completely before or shortly after birth or may persist in vestigial forms into adulthood.[5,17,21,23,24,37,42] Incomplete resorption of these embryonic organs or ducts and/or postnatal regrowth of the vestigial remnants result in a heterogeneous group of urogenital anomalies.[1,3,6,10,11,14,15,23,27,31–33] Frequently, the vestigial remnants become fluid-filled cystic structures of variable size and shape along the urogenital tracts or in the retroperitoneal and/or pelvic cavities.[5,23,24,33] Furthermore, some of the primordial urogenital cells/organs, such as the urogenital sinus, differentiate postnatally into multiple organs.[5,24] Abnormal differentiation of the primordial cells/organs and/or aberrant growth of the postnatal organs may also give rise to the cystic or glandular anomalies.[5,15,24]

Various urogenital anomalies have been described in humans and other mammalian species.[5,15,17,21,23,24,37,42] Clinically, most of these anomalies are found incidentally, whereas others may present clinically as distinct pathologic entities. The diagnosis of these anomalies has been based principally on their anatomic location and/or histologic features. Some may display distinctive histologic features from which their embryonic origin can be inferred, whereas others display no clue as to their embryonic origin. Consequently, the anomalies may be misdiagnosed as neoplastic or other abnormalities.[10,14,33] In this report, we describe cystic urogenital anomalies on the dorsal aspect of the urinary bladder in six ferrets (*Mustela putorius furo*).

Material and Methods

Six ferrets (four males, two females) were referred to the Division of Comparative Medicine at the Massachusetts Institute of Technology between 1985 and 1993. The ferrets were 1–8 years of age ($\bar{x} = 5.3$ years). All of the animals were

Table 1. Clinical signs and lesions in six neutered ferrets with cystic urogenital anomalies.

Ferret No.	Age (years)	Sex	Cyst Shape, Size	Clinical Signs	Other Lesions
1	6	Male	Oval, bladderlike; 4 × 4 × 6 cm (trigone), 1.3 × 1.5 × 2 cm (urethra), 0.8 × 1 × 1.2 cm (urethra)	Alopecia, dysuria, anemia, splenomegaly, weight loss, depression	Hemolytic *E. coli* cystitis, bilateral adrenal cortical carcinoma, squamous metaplasia of ureter and urethra, multifocal prostatitis
2	8	Female	Semispherical; 2 × 2 × 1 cm	Marked vulvar swelling, severe diffuse alopecia, hypoglycemia depression	Adrenal cortical adenoma, multiloculated adrenal and renal cysts, islet cell adenoma, gall-bladder cystic hyperplasia
3	2	Female	Oval, bladderlike; 0.6 × 0.6 × 0.8 cm	None observed	Adrenal cortical hyperplasia, lymphocytic adrenalitis, left hydronephrosis/hydroureter (iatrogenic)
4	7	Male	Bilobulated; 4 × 5 × 5 cm	Tenesmus, hematuria, anorexia and weakness	Necrotizing cystitis (adrenal not examined)
5	5	Male	Multiloculated; 6.5 × 3 × 4 cm	Anorexia, weight loss	Adrenal cortical carcinoma
6	4	Male	Oval (three cysts); 1.5 cm diameter, 1.8 cm diameter, 2.1 cm diameter	Dysuria, severe alopecia	Necrotizing cystitis, adrenal cortical carcinoma, bilateral cataracts

neutered and presented with a variety of histories and clinical signs (Table 1).

A complete necropsy was performed on three ferrets (Nos. 1–3), and biopsies of affected tissues were collected from the remaining three ferrets (Nos. 4–6). The adrenal gland in ferret No. 4 was not examined. Tissue samples were fixed in neutral buffered 10% formalin, embedded in paraffin, cut at 5 μm, and stained with hematoxylin and eosin. Tissue samples from five ferrets (Nos. 1–5) were used for histopathology. The biopsy sample from ferret No. 6 was not processed promptly, and a histopathologic evaluation could not be performed. Trichrome and periodic acid–Schiff (PAS) stains were also applied to the tissue samples from the cystic structures and the associated urinary bladder.

Serum samples from two ferrets (Nos. 1, 2) were evaluated for steroid hormones by radioimmunoassay.[7,8,13,22] In ferret No. 1, a single sample taken at necropsy was assayed for estradiol. Samples from two sex- and age-matched ferrets were also assayed as controls. In ferret No. 2, steroid hormone assays were performed monthly for 5 months for cortisol, estradiol, estrone, testosterone, dihydroxytestosterone, and androstenedione.

Urinalysis and aerobic bacterial culture of the bladder and cyst fluid were performed for ferret Nos. 1 and 2, contrast cystography for ferret Nos. 1 and 4, and serum biochemistry for ferret No. 1.

Results

Clinical findings

Three of the six ferrets presented with dysuria and/or hematuria (Nos. 1, 4, 5). Three ferrets presented with alopecia (Nos. 1, 2, 5) and/or vulvar swelling (No. 2), which were compatible with an endocrinologic disorder. On palpation, the cysts were interpreted as a caudal abdominal mass, and in several cases were suspected to be a tumor of the urinary bladder. A cystogram performed on ferret No. 1 revealed that both the cyst and urinary bladder filled with contrast medium, but the cyst retained the medium after bladder voiding. The cystogram in ferret No. 4 yielded an image of a triple bladder, i.e., both the bilobulated cyst and urinary bladder filled with the contrast medium. Other clinical findings are summarized in Table 1.

Necropsy and biopsy findings

Macroscopically, all of the ferrets had single or multiple semispherical to bilobulated fluctuant cystic structures of various sizes located on the dorsal aspects of the urinary bladder (Table 1; Figs. 1, 2). The cysts were thin walled and smooth and contained clear to yellowish and odiferous urinelike fluid in five ferrets (Nos. 1, 2, 4–6) and whitish to yellow mucoid fluid in ferret No. 3. In three ferrets (Nos. 1, 4, 5), the fluid contained debris, degenerating cells, and/or bacteria. The posterior aspect of the cysts was adjacent and/or attached to the trigone or neck of the bladder. Serosal adhesions to adjacent pelvic soft tissues were observed in ferret Nos. 2 and 3. The anterior aspect of the cysts projected dorsally if small or empty (ferret No. 3) or dorsocranially if large or distended (ferret Nos. 1, 2,

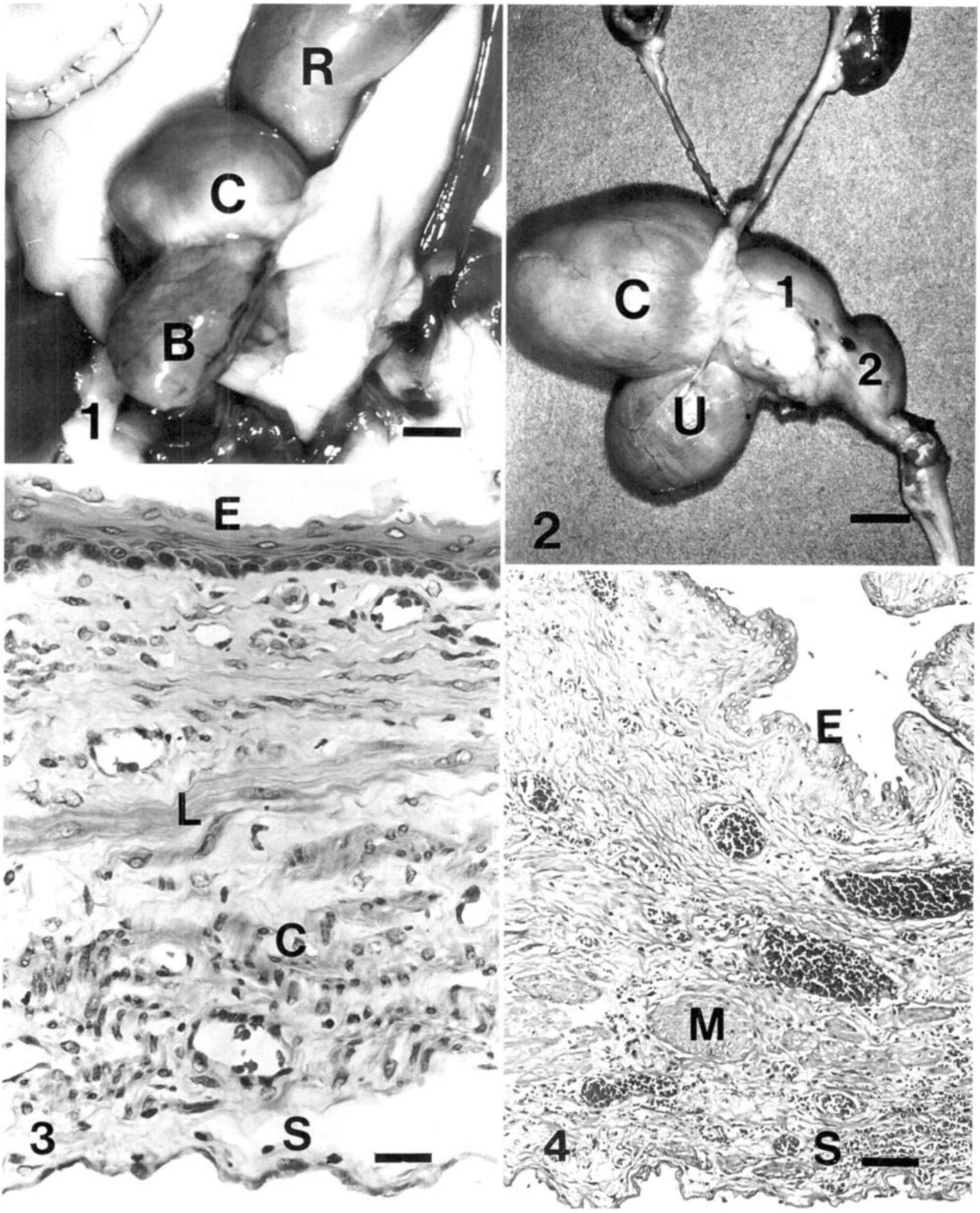

Fig. 1. Pelvis and caudal abdomen; ferret No. 2. A smooth semispherical cyst (C), 2 × 2 × 1 cm, is attached to the dorsal neck of the urinary bladder (B). Above the cyst is the colon or rectum (R). Bar = 11.7 mm.

Fig. 2. Urinary bladder and urethra; ferret No. 1. A thin-walled cyst (C) is on the dorsal aspect of the urinary bladder (U), and two thick-walled cysts (1, 2) are on the dorsal aspect of the proximal urethra. Bar = 6.7 mm.

Table 2. Histopathologic findings in the cystic anomalies in the ferrets. The cyst walls were composed of 3 layers, i.e. epithelium, muscle and serosa, with fibrovascular stroma between each layer and/or between the muscular bundles.

Ferrets	Cysts	Epithelial Layers	Muscle Layers	Serosal Layers
#1	Multiple oval cysts intercyst tubular glands	Simple to stratified squamous cells multifocal keratinization	Intermittent bundles or discontinuous layer	Mesothelial cells ducts in stroma
#2	Single oval cyst	Stratified squamous cells multifocal keratinization	Double continuous layers	Mesothelial cells ducts in stroma
#3	Single oval cyst	Simple flattened to cuboidal cells without keratinization	Double continuous layers	Mesothelial cells
#4	Single bilobulated cyst focal necrosis and ulcer	Transitional epithelial cells multifocal squamous metaplasia	Single to double discontinuous layers	Mesothelial cells duct in stroma
#5	Single multiloculated cyst septal tubular glands	Squamous to columnar cells multifocal keratinization	Intermittent bundles or discontinuous layer	Mesothelial cells
#6	Multiple cysts	Not examined histologically		

4–6) into the caudal abdominal cavity. Ferret Nos. 1 and 6 had multiple cysts, ferret Nos. 2 and 3 had single cysts, ferret No. 4 had a bilobulated cyst, and ferret No. 5 had a multiloculated cyst. A direct intraluminal connection between the cysts and urinary bladder or urethra was observed in five ferrets (Nos. 1, 3–6).

The cranial cyst in ferret No. 1 was about three times the size of the urinary bladder and extended dorsocranially 4 cm beyond the bladder apex (Fig. 2). The cyst was attached to the dorsal trigone of the bladder by bilaterally symmetric folds of fibrous tissue. The folds appeared to originate between the ureters and inserted along the lateral aspect of the cyst. A retrograde flush of air or fluid via the urethra revealed a communication between the cyst and the urinary tract in ferret No. 1. There were three tiny porelike openings grossly visible on the ventral aspect of the cyst lumen, but the points of communication with the bladder and/or urethra were not clearly discerned. Two additional cysts were located on the dorsal aspect of the pelvic urethra and projected into or from the dorsal prostatic parenchyma (Fig. 2). A direct intraluminal communication between the two cysts and the urethra was also noted. The cysts were filled with yellowish clear urinelike fluid mixed with some concentrically laminated debris. The cyst in ferret No. 2 was adherent to but did not appear to communicate with the bladder neck (Fig. 1). The cyst in ferret No. 3 was attached to the trigone and resembled the urinary bladder. The bilobulated cyst in ferret No. 4 was attached to the trigone, with intraluminal connection to the bladder. The oval cyst in ferret No. 5 was located on the trigone and/or around the dorsal junction between the bladder neck and the urethra, with the long axis perpendicular to that of the bladder neck. This cyst had three chambers separated by thick septa, with intraluminal connections between the chambers and between the central chamber and bladder neck. Ferret No. 6 had three cysts attached to the dorsal neck of the bladder; the largest cyst was located on the central-dorsal aspect of the bladder neck and the other two were on both of its sides.

Histopathologic findings

The cyst walls were composed of three distinctive layers, i.e., epithelium, muscle, and serosa, with fibrovascular stroma between the layers and/or between the muscular bundles (Table 2; Figs. 3, 4). The cysts in ferret Nos. 1 and 2 were lined with squamous epithelium with variable keratinization (Fig. 3), and the one in ferret No. 3 was lined with a single layer of flattened to cuboidal epithelium without keratinization. The cyst

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Fig. 3. Cyst on urinary bladder; ferret No. 2. The cyst wall is composed of stratified squamous epithelium (E), longitudinal (L) and cross (C) sections of smooth muscle, and loose serosa (S), with fibrovascular stroma between layers. Bar = 37 μm.

Fig. 4. Cyst on urinary bladder; ferret No. 4. The cyst wall is composed of transitional epithelium (E), irregularly scattered smooth muscle bundles (M), and loose serosa (S), with fibrovascular stroma between layers and between muscle bundles. Bar = 72 μm.

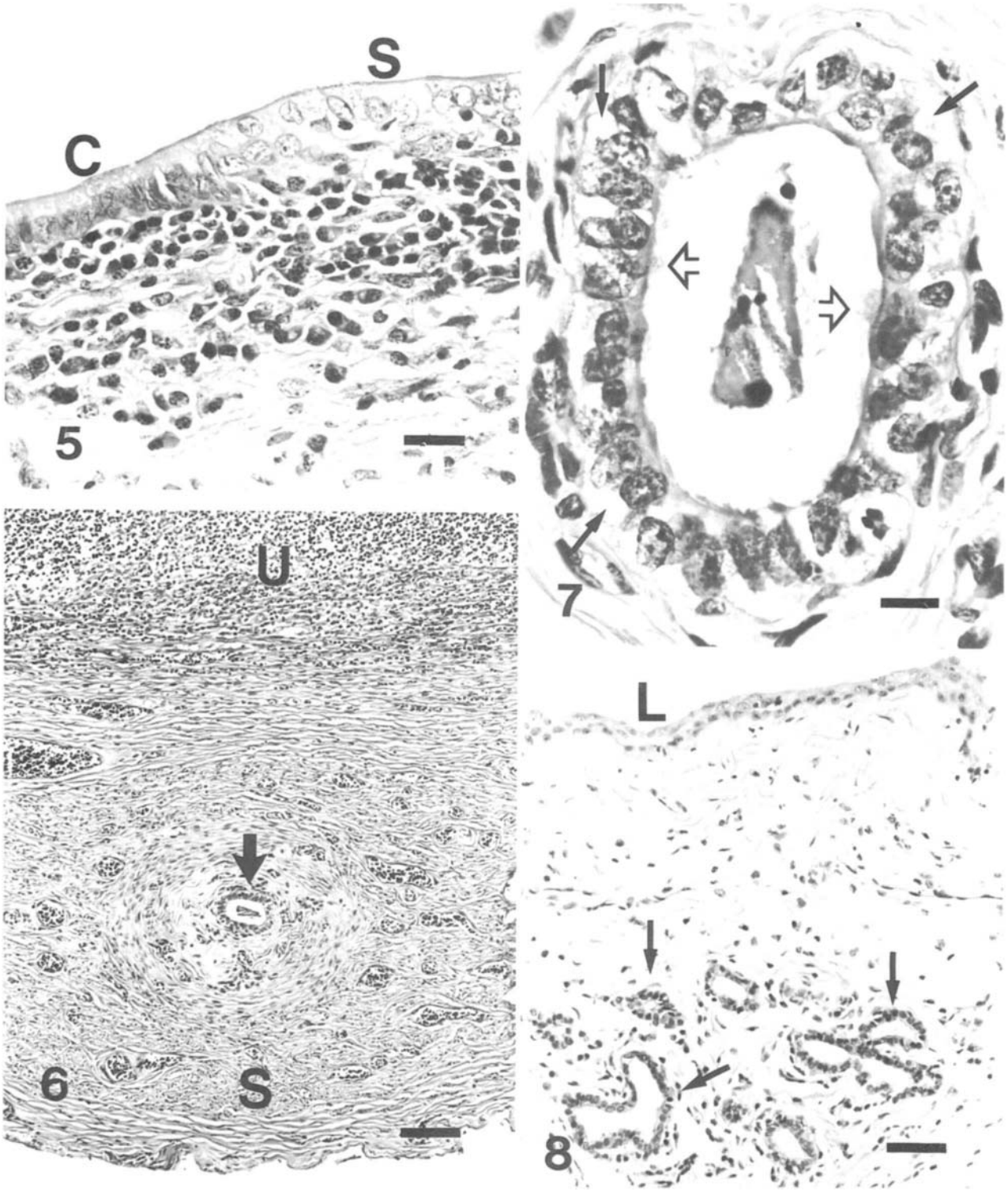

Fig. 5. Cyst on the urinary bladder; ferret No. 4. Transition from columnar (C) to squamous (S) epithelial cells occurs within a single cyst chamber, with infiltration of plasma cells, lymphocytes, macrophages, and few neutrophils in the mucosa. Bar = 26 μm.

Fig. 6. Cyst on urinary bladder; ferret No. 4. Severe focal necrosis is accompanied by accumulation of neutrophils, necrotic debris, bacteria, and other degenerating cells on the ulcerated mucosal surface (U). A tubulelike structure (arrow) is present in the serosal stroma (S). Bar = 80.7 μm.

in ferret No. 4 was lined with transitional epithelium with multifocal squamous metaplasia (Fig. 4). The multiloculated cyst in ferret No. 5 was lined with cuboidal to columnar to keratinized or nonkeratinized squamous epithelial cells in different chambers and even within a single chamber (Fig. 5). The columnar epithelial cells had basally located nuclei and contained PAS-positive material in the apical cytoplasm. Keratinization of the squamous epithelium (ferret Nos. 1, 2, 5) was often associated with a fibrous cyst wall that was poorly vascularized, and the subjacent abutting stroma consisted of dense collagen bundles. The muscle layer consisted of intermittent bundles or single to double discontinuous layers of smooth muscle in large or markedly distended cysts (ferret Nos. 1, 4, 5) or double continuous layers of smooth muscle in small or empty cysts (ferret Nos. 2, 3). Muscle bundles were oriented in diverse directions, whereas when both muscle layers were present they were oriented perpendicular to each other (Figs. 3, 4). The cyst walls had more abundant fibrovascular tissues near the cystic apex and more smooth muscle components near the attachment to the bladder necks. The serosal layer consisted of loose fibrovascular stroma of variable thickness and was covered by flattened mesothelial cells (Figs. 3, 4). In three ferrets (Nos. 1, 3, 4), duct- or acinuslike structures in the serosal stroma (Figs. 6, 7) were lined by cuboidal to low columnar epithelial cells, with subnuclear vacuoles and apical ciliumlike structures in some cells (Fig. 7). PAS-positive granules were present in some of the vacuoles.

Urethral cysts in ferret No. 1 consisted of fibrotic walls lined with stratified squamous epithelium, with abundant intraluminal keratin debris. The cyst in ferret No. 4 had multifocal ulceration and necrosis with full-thickness infiltration of predominantly neutrophils, some lymphoid cells, and macrophages (Fig. 6). Necrotic debris, bacteria, and degenerating cells were present on the necrotic surface. In ferret No. 5, mild multifocal erosion and infiltration of plasma cells, lymphocytes, macrophages, and a few neutrophils were observed subjacent to the transitional and/or columnar epithelia (Fig. 5). Irregular tubuloglandular structures were present around and/or between the urethral cysts in ferret No. 1 and within the fibrovascular septa of the multiloculated cyst in ferret No. 5 (Fig. 8). Multifocal erosion, ulceration, and squamous metaplasia were observed in some cystic chambers, with intraluminal accumulation of keratin, degenerating neutrophils, and debris in ferret Nos. 1 and 5.

Adrenal cortical cell hyperplasia (ferret No. 3) or neoplasia (ferret Nos. 1, 2, 5, 6) were observed in all of the five ferrets examined (Table 1). The hyperplastic cortical cells resembled the normal cortical cells and presented as nodules or in a more diffuse arrangement. The neoplastic cells consisted of irregular cords, nests, or lobules, with fibrovascular stroma of variable abundance. The adrenal architecture was effaced to variable degrees. The cells were predominantly polyhedral and had round nuclei, single nucleoli, and eosinophilic to basophilic cytoplasm. Smaller and darker cells were also interspersed between the polyhedral cells.

Mild to moderate, focal to multifocal epithelial erosions, ulcerations, and infiltration of a mixed population of inflammatory cells were observed in the urinary bladder mucosa of ferret Nos. 1, 2, and 5. Additionally, in ferret No. 1 multifocal interstitial fibrosis and mononuclear cell infiltration with glandular atrophy were observed in the prostate gland. Squamous metaplasia and keratinization occurred in distal ureters and the proximal urethra of this ferret. Additional pathologic findings for these ferrets are summarized in Table 1.

Other findings

Steroid hormone assays performed on two of these ferrets revealed an elevated level of serum estradiol in ferret No. 1 and of estrone in ferret No. 2. The serum estradiol level in ferret No. 1 was 26.6 pg/ml, whereas those of the sex- and age-matched control ferrets were <10 pg/ml (normal = 4.5 ± 0.7 pg/ml[8]). In ferret No. 2, serum estrone levels ranged from 26 to 98 pg/ml (normal = 72.4 ± 10.1 pg/ml), but the serum levels of cortisol, estradiol, testosterone, dihydroxytestosterone, and androstenedione were all within normal limits.[7,8,13,22,34,39]

The cyst fluid aspirated from ferret No. 1 was amber and cloudy, with a specific gravity of 1.017, whereas the fluid in the bladder was cloudy and yellow, with a specific gravity of 1.023. The fluid from both the cyst

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Fig. 7. Cyst on urinary bladder; ferret No. 4. Higher magnification of Fig. 6. The tubule is lined by cuboidal to low columnar epithelial cells, with subnuclear vacuoles (thin arrows) and apical ciliumlike structures (open arrows) in some cells. Bar = 10.6 μm.

Fig. 8. Cyst on urinary bladder; ferret No. 5. Tubuloglandular structures of various sizes and shapes are lined by simple cuboidal or glandular epithelial cells within the fibrous septum (arrows). Located above the septum is one of the cyst chambers (L). Bar = 62 μm.

and the bladder had a high protein content and contained many epithelial cells, white blood cells, and bacteria, trace amounts of blood and urobilinogen, but no glucose, ketones, or bilirubin. Hemolytic *Escherichia coli* was cultured from both the cyst and bladder fluid. Serum biochemistry results were unremarkable for ferret No. 1. Urinalysis for ferret No. 2 revealed a moderately elevated urine protein. *Proteus* sp. and group D *Streptococcus* sp. were cultured from the urinary bladder fluid of this ferret. Bladder stones were present, and chemical analysis indicated that the stones were composed mainly of struvite.

Discussion

Abnormal development of the urogenital glands and/or ducts results in a variety of anomalies in humans and animals that may be diagnostically challenging.[1,3,5,6,10,11,14,23,27,32,33,37,42] Although many urogenital organs or ducts have distinctive histologic or ultrastructural morphology and express different proteins, the majority of the urogenital anomalies are advanced when finally detected and various secondary changes have occurred.[4,10,14,18,19,21,25,28,36,38] Based on the history, clinical presentation, cystograms, involvement of both sexes, and pathologic findings, cystic urogenital anomalies were diagnosed in these six ferrets. The cystic structures were similar in terms of their anatomic location and/or histologic features. The anomalies may represent one single entity, with a slight variation in their clinical and/or pathologic presentations. Alternatively, they might represent several distinct entities, with similar clinical and/or pathologic manifestations. Metaplasia and keratinization of the lining epithelia and/or inflammation, fibrosis, and necrosis of the cyst walls could have occurred under various conditions or stimuli and may mask the original diagnostic features in the present cases.[4,11,14,19,25,28,36] Differential diagnoses included urethral gland or prostatic cysts, mesonephric or paramesonephric duct cysts, urinary bladder diverticula, bladder duplication, or urachal cysts.

Similar cystic structures have been observed in the proximal urethra of female mink (*Mustela vison*), where large cystic masses protruded into the neck of the urinary bladder.[15] The proximal urethras were variably distended and sometimes occluded, with occasionally urinary incontinence or urine retention. The cysts became larger and more prevalent as the mink aged. The authors proposed that the cysts arose by expansion of small urethral glands that are normally present in female mink.[15] Although ferrets and mink are closely related phylogenetically, the glandular structures suggestive of the urethral glands have not been observed around the urethra in normal female ferrets that we have examined histologically (unpublished observations). Embryologically, urethral glands and prostatic glands are derived from the urogenital sinus.[5,24] Pluripotent sinus cells in the urethral epithelium may have been the progenitors of the cysts in female ferrets. In male ferrets, the cysts could have originated from the prostatic glands. The cyst formation in these ferrets could similarly be age and/or hormone related as in mink and other ferrets.[15,39] Elevated serum estrodiol in ferret No. 1 could have partially stimulated cyst development.

Cystic structures in male ferret Nos. 1 and 5 are suggestive of prostatic cysts. Several types of prostatic cysts have been described, but their precise origin is unclear.[20,23] True prostatic cysts should be of epithelial origin and are often located within the prostate. The prostate gland in the ferret is a fusiform enlargement around the proximal urethra near the bladder neck and consists of tubuloalveolar glands surrounded by a fibromuscular capsule and divided by fibrovascular septa.[18] The glandular epithelial cells are cuboidal to columnar and have basal nuclei and intracytoplasmic PAS-positive materials, as observed in the cysts in male ferret Nos. 1 and 5. Prostatic cysts may be congenital or secondary to inflammation, hyperplasia, or neoplasia.[20,23,35,40] Estrogens and/or androgens have been suspected as predisposing factors for prostatic hyperplasia and neoplasia.[35] Periprostatic or paraprostatic are terms that often refer to various cystic anomalies around or adjacent to the prostate, including the prostatic cysts themselves and other glandular or ductal cysts.[14,20,23,40] Thus, the terms periprostatic cyst or paraprostatic cyst should be avoided when the nature and/or the origin of the cysts are known.

The location of the cysts on the dorsal aspects of the urinary bladder and/or proximal urethra in the affected ferrets of both sexes suggests that the cysts might have originated from the mesonephric or paramesonephric duct remnant. Embryologically, the distal mesonephric duct that connects both the ureters and proximal mesonephric duct to the urogenital sinus, also known as trigone precursor, is resorbed into the dorsal wall of the urinary bladder, the trigone mucosa, and the proximal urethra in both males and females.[5,24,32,37,42] Incomplete resorption of the trigone precursor may leave ductal or vesicular remnants on the dorsal aspect of the bladder, the trigone, and/or the urethra.[5,24] Histologic structures of the mesonephric duct, i.e., simple cuboidal to columnar epithelial cells with subnuclear glycogen granules or vacuoles and rudimentary cilia, were seen in the cystic serosa of ferret Nos. 3 and 4.[10,14,18,21] Anatomically, the fused terminal portion or the remnant of the paramesonephric duct forms the utricle on the dorsal urethra within the prostate in males.[5,20,23,24] The histologic features of the paramesonephric duct, e.g., pseudostratified columnar epithelial cells with microvilli, intracytoplasmic mucins or

polysaccharides, and occasional cilia, were observed in the cyst in ferret No. 5.[17,21,33] Under certain circumstances, the remnants may enlarge into cysts that project onto the dorsal aspects of the urethra and/or bladder, as seen in ferret Nos. 1 and 2.[5,20,23]

Cysts on the dorsal bladder neck or trigone have also been diagnosed as bladder diverticula or duplication.[12,16] Bladder diverticula are saclike evaginations of the urinary bladder wall.[1,3,12] The diverticula are congenital or secondary to irregularities or weakness of the bladder walls or chronic urethral obstruction. Bladder diverticula are composed of the same histologic elements as the bladder, including double muscular layers and uroepithelium, as seen in ferret Nos. 3 and 4. In ferret No. 3, iatrogenic hydroureter and hydronephrosis were observed following neutering. It was uncertain whether the cyst formation in ferret No. 3 was associated with accidental trauma to the bladder wall or the urethra. Bladder diverticula, however, occur in random locations and are not consistently located on the dorsal aspect of the bladder or urethra. True bladder duplication is rare and may result from doubling of the endodermal allantoic analog with the development of a midsagittal wall.[1,5,24,41] In such cases, two bladders often lie side by side laterally with each bladder draining the ipsilateral kidney and emptying through its own urethra. Doubling of other caudal abdominal structures is often associated with these anomalies[41] but was not observed in this series of ferrets.

Cystic growth of the urachal remnants could also have the same macroscopic and microscopic appearance as observed in these ferrets.[6,24,29,31] However, the urachal cysts are often located on the apex of the urinary bladder and lack a consistent location on the dorsal aspect of the bladder or urethra. Ureterocele, ureteral duplication, or megaureter could also be considered, but the ureters were not significantly affected in these ferrets.[11,37,42]

The adrenal cortical lesions present in all of the five ferrets examined deserves further comment. In mice, early gonadectomy results in adrenal cortical hyperplasia or tumors and other endocrine-associated lesions.[9,26] In the present study, all of the ferrets with adrenal cortical and cystic lesions were neutered, although their ages at neutering were not determined. It is common, however, to have ferrets neutered at 4–6 weeks of age, prior to their shipment to pet stores. Normal, hyperplastic, and neoplastic adrenal cortical cells produce both androgens and estrogens in humans and other animals.[2,7,8,22,30,34,39] In ferrets, hyperplastic or neoplastic cells of the adrenal cortex can produce estrogens, and high levels of serum estradiol have been reported with adrenal cortical neoplasia in ferrets.[22,34,39] Cystic enlargement of the prostate and prostatitis were also observed in some of these ferrets.[39] The hyperplastic or neoplastic adrenal cortical cells should be considered as a potential endogenous source of estrogen, androgen, or the related sex hormones in the ferrets in this study. Sexual hormones are known to affect the development of the urogenital system both prenatally and postnatally, especially the mesonephric duct and paramesonephric duct.[27,43] An axis of neutering–adrenal cortical neoplasia–estrogen/steroid hormone elevation could thus play a role in the cyst development and/or their growth under certain circumstances.

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