

Persistent metanephric ducts in a geriatric white tiger

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Abstract. An 18-year-old male intact white Tiger (*Panthera tigris*) was euthanized after a clinical diagnosis of severe renal failure. Postmortem macroscopic examination of the kidneys revealed unilateral hydronephrosis with renal calculi and bilateral cortical and medullary fibrosis and papillary coagulation necrosis. Interestingly, multiple large persistent metanephric ducts were found at the corticomedullary junctions accompanied by marked interstitial fibrosis, tubular atrophy, and lymphoplasmacytic interstitial nephritis. To our knowledge, this is the first reported case of persistent metanephric ducts in cats.

Persistent metanephric ducts are structures inappropriate to the stage of renal development and have been reported in cases of renal dysplasia in human and veterinary literature. Renal dysplasia is defined as a disorganized development of renal parenchyma due to an abnormal differentiation.⁷ Microscopic criteria for the diagnosis of renal dysplasia are described and include the presence of metanephric ducts, which are often accompanied by degenerative and inflammatory lesions, sometimes obscuring the dysplastic abnormalities.

An 18-year-old male intact white Tiger (*Panthera tigris*) presented with a 3-month history of partial anorexia, decreased alertness, polydipsia, polyuria, weight loss, and occasional vomiting. During the last 2 weeks the tiger became markedly lethargic and exhibited distension of the abdominal cavity. The animal was euthanized by intravenous injection of Telazol/Beuthanzia-D because of poor quality of life.

Clinical laboratory data demonstrated that during the last year the tiger gradually developed severe azotemia (blood urea nitrogen: 79–135 mg/dl [normal value for adult male tigers: 13–58 mg/dl; International Species Information System]; creatinine: 6.0–10.9 mg/dl [normal value for adult male tigers: 1.5–5.0]). Urine was collected by cystocentesis. Urinalysis revealed yellow cloudy urine with mild hematuria, moderate proteinuria, and marked bacteriuria. At age 14, antibodies against the feline immunodeficiency virus were detected by enzyme-linked immunosorbent assay and Western Blot analysis.

At necropsy, the left kidney was 1.5 times enlarged and fluctuant. It consisted of a large, thin-walled cavity filled with 1 liter of yellow-brown, clear, watery fluid (Fig. 1). The cavity represented a marked dilatation of the renal pelvis accompanied by marked atrophy of the medullary and cortical parenchyma. The pelvis was

covered with moderate numbers of gold-brown renal calculi. The left ureter was not dilated. In addition a few brown, firm nodules of variable size (0.5–2 cm) were found within the pelvis. The renal papillae of both kidneys showed coagulation necrosis characterized by brownish discoloration, softening, and some retraction with preservation of architecture. There were multiple areas of fibrosis (1–3 cm in diameter) in the medulla and cortex of both kidneys, and the surface of the right kidney was irregular with multiple 0.5–1-cm-diameter depressions (Fig. 2). The stomach contained multifocal ulcers accompanied by a strong ammonia odor (uremic ulcers). Multifocal mineralization was present within the lung, pancreas, and adrenal glands. The vertebral spine showed multifocal marked spondylosis with ankylosis.

Several samples of the kidneys were excised, fixed in 10% neutral buffered formalin, and embedded in paraffin. Five-micrometer sections were stained in hematoxylin and eosin (HE) for light microscopy. Histopathologically, both kidneys had multiple areas with marked loss or atrophy of tubules within the medulla and cortex accompanied by marked interstitial fibrosis (Fig. 3). These areas showed multifocal moderate thickening of Bowman's capsule and basement membranes associated infrequently with mineralization. The interstitium was infiltrated with small numbers of lymphocytes and plasma cells. Occasionally glomeruli were shrunken, eosinophilic, and hypocellular, consistent with glomerulosclerosis. Moderate numbers of tubules contained large amounts of granular casts accompanied by moderate flattening of the tubular epithelium. Multiple tubules and renal papilla showed coagulation necrosis. Multiple areas of papillary hyperplasia were identified.

An unexpected histological finding in both kidneys was the presence of persistent metanephric ducts at the corticomedullary junction adjacent to the large blood vessels. These tubular structures were lined by a ciliated tall pseudostratified columnar epithelium (Fig. 4).

The tentative morphologic diagnosis was bilateral

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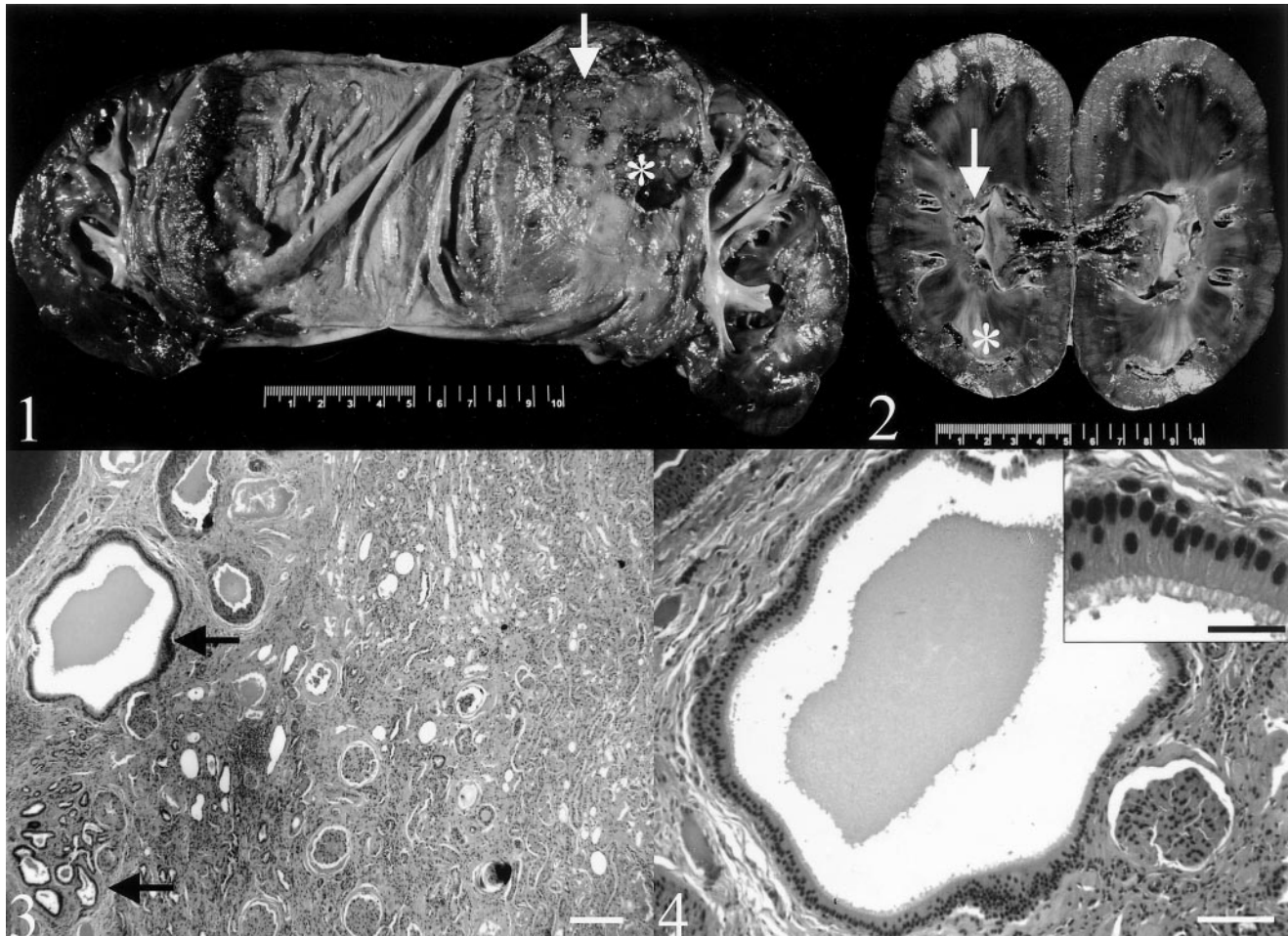


Figure 1. Left kidney; tiger. Hydronephrosis with medullary and cortical atrophy, renal calculi (asterisk) and papillary hyperplasia (arrow).

Figure 2. Right kidney; tiger. Multifocal cortical and medullary fibrosis (asterisk) with papillary coagulation necrosis (arrow).

Figure 3. Kidney; tiger. Cortical interstitial fibrosis with tubular atrophy and metanephric ducts (arrows). HE. Bar = 100 μ m.

Figure 4. Kidney; tiger. Metanephric duct. HE. Bar = 50 μ m. Inset shows higher magnification of the ciliated tall pseudostratified columnar epithelium of the metanephric duct. HE. Bar = 20 μ m.

severe chronic interstitial lymphoplasmacytic nephritis with persistent metanephric ducts, tubular atrophy, tubular and papillary coagulation necrosis, and unilateral hydronephrosis and urolithiasis. A differential diagnosis of renal dysplasia was considered because of the presence of the persistent metanephric ducts.

Although renal dysplasia most often occurs sporadically in neonates and juveniles, occasionally a familial tendency is recognized.⁸ The term dysplasia implies that the branches of the ureteric bud and the metanephric blastema have failed to interact normally. Metanephric ducts in the medulla are thus seen to represent persistent incompletely differentiated ureteric bud branches that did not differentiate into normal collecting tubes.⁸

Most authors in human medicine accept only 2 absolute criteria for dysplasia.^{1,4} Of greater importance is the finding of metanephric ducts. Somewhat less im-

portant, because of its variable presence, is the finding of metaplastic cartilage. Immature glomeruli and tubules may be seen in renal scars and even in tracts of a previous needle biopsy.⁴ The morphologic alterations under these circumstances seem to be acquired, rather than being expressions of dysgenetic development. In veterinary medicine, the term renal dysplasia is often used in a broader sense. The presence of 1 of the following lesions is used to make the diagnosis of renal dysplasia: metanephric ducts, undifferentiated mesenchyme, immature glomeruli/tubules, or metaplastic cartilage.⁷ Renal dysplasia in cats, to our knowledge is only described histologically in kittens that were experimentally infected in utero with panleukopenia virus; however, metanephric ducts were not seen.⁵ Greco's review on congenital and inherited renal diseases mentions cases of renal dysplasia in cats, but references to histologically characterized cases are not pre-

sent.³ The cause of renal dysplasia is uncertain. Mutations (e.g., LIM-homeodomain transcription factor LMX1B, paired-box transcription factor PAX-2), defective regulation of transcription (e.g., PAX-2), and alteration in expression of a number of genes (e.g., tumor necrosis factor receptor, apoptosis regulator BCL-2, fibroblast growth factor, keratinocyte growth factor), have been implicated in the development of renal dysplasia.^{2,9} However, much evidence points to ureteral obstruction in utero as an important element in dysplastic development.⁶

It was surprising to find metanephric ducts within the kidneys of this geriatric tiger because patients with severe renal dysplasia normally die at a young age. It is possible that less severely dysplastic kidneys have normal renal function. The initiation of renal failure might be dependent on the size of the dysplastic lesions or to their increased susceptibility to hydronephrosis, urolithiasis, and infection. Several studies demonstrated that dysplastic renal tissue is unusually liable to ascending infection.^{1,4} Pyelonephritis is found in approximately 65% and lithiasis in 35% of human cases.^{1,4} In this case, the extent of dysplastic lesions was most likely not severe enough to cause renal failure but is possibly attributed to an abnormal susceptibility of the dysplastic tissue to urolithiasis, hydronephrosis, and infection resulting finally in severe renal disease. The unilateral hydronephrosis occurred most likely secondary to ureteral obstruction with the renal calculi.

Alternatively, the metanephric ducts represent an incidental finding, and the cause of the renal disease is not related to the observed dysplastic changes. Because these rare renal lesions appeared in a white tiger, which likely has a higher inbreeding coefficient than other captive tigers, one could envision that white tigers might be predisposed to these dysplastic lesions.

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