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Pathology in Practice

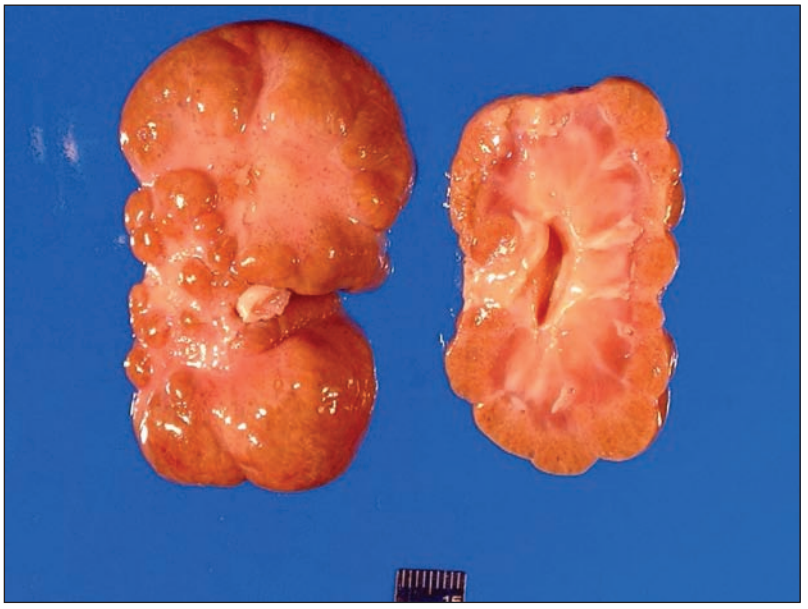

Figure 1—Photograph of the kidneys of a 2-year-old Weimaraner that was evaluated because of vomiting, anorexia, cachexia, and lethargy. Both kidneys are pale with irregularly indented cortices and are smaller than expected for a dog of this breed. In the kidney on the left (cortical surface view), notice the bands of dense fibrous tissue that interrupt and replace normal renal parenchyma and extend into medullary regions. In the kidney on the right (cut surface view), mild dilation of the renal pelvis is evident. Scale bar = 1 cm.

History

A 2-year-old sexually intact female Weimaraner was evaluated because of vomiting, anorexia, cachexia, and lethargy. Two weeks earlier, the referring veterinarian had determined that the dog had whipworm and hookworm infestations; the dog was treated with an anthelmintic. The owner reported that urine had been clear and light yellow but made no mention of polyuria or polydipsia.

Clinical and Gross Findings

The dog had pale mucous membranes, weighed 25 kg (55 lb), and was cachectic with marked muscle atrophy and a body condition score of 3 (9-point scale). A large amount of dental calculus was present and was accompanied by halitosis. Green mucoid ocular discharge was evident bilaterally. Rectal temperature was 37.6°C (99.6°F). Heart rate was 150 beats/min (reference range, 70 to 120 beats/min), and respiratory rate was within reference limits. A CBC revealed normocytic, normochromic anemia (RBC count, 2.2 × 10^6 cells/µL; reference range, 4.8 × 10^6 cells/µL to 9.3 × 10^6 cells/µL); there were no abnormalities in erythrocyte morphology. Serum biochemical abnormalities included hypoalbuminemia (2.5 g/dL; reference range, 2.7 to 4.4 g/dL), azotemia (BUN concentration, 249 mg/dL [reference range, 6 to 25 mg/dL]; creatinine concentration, 24.5 mg/dL [reference range, 0.5 to 1.6 mg/dL]), hyperphosphatemia (26.5 mg/dL; reference range, 2.5 to 6.0 mg/dL), high amylase activity (1,246 U/L; reference range, 290 to 1,125 U/L), and low triglyceride concentration (23 mg/dL; reference range, 29 to 291 mg/dL). Urinalysis revealed low urine specific gravity (1.012; reference range, 1.015 to 1.050) and low pH (5.0; reference range, 5.5 to 7.0); urine protein concentration was 2+ (reference range, negative). Microscopic examination of the urine sample revealed the presence of 51 to 100 WBCs/hpf (reference range, 0 to 3 WBCs/hpf) and bacterial rods and cocci (classified as 4+ on a scale of 0 to 4).

Abdominal radiography and ultrasonography revealed that both kidneys were markedly smaller than expected for a healthy dog of this breed. The longest dimensions of the kidneys were 1.7 and 1.8 times the length of the L2 vertebral body; normal range of kidney size in dogs is 2.5 to 3.5 times the length of L2. Ultrasonographically, the kidneys appeared hyperechoic, compared with the liver, with mild distension of both pelves. Because of the poor prognosis for recovery, the dog was euthanized and necropsied. Grossly, both kidneys were small, irregularly nodular, and pale tan with fibrous bands running through the depressed regions of the cortices (**Figure 1**). Other notable gross lesions included bilateral enlargement of parathyroid glands and a few erosions within the gastric mucosa.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

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Histopathologic Findings

Samples of various tissues were routinely processed for histologic examination. In sections of the kidneys, there was abundant collagen within the cortical and medullary interstitium (**Figures 2 and 3**) that often formed dense, fibrotic bands between remaining nodules of renal parenchyma. In some regions, the interstitium was composed of loosely arranged plump spindle cells in slightly basophilic, undifferentiated mesenchyme; in other regions, the interstitium was composed of hypocellular and faintly fibrillar eosinophilic material. Cortical tubules were dilated and lined by flattened epithelium with mineralization of tubular basement membranes; some ducts appeared primitive and were surrounded by layers of mesenchyme. The appearance of the glomeruli varied from shrunken capillary tufts surrounded by markedly dilated Bowman's spaces to thickened and hypercellular tufts attached to Bowman's membranes by synechiae. There was evidence of moderate lymphoplasmacytic and histiocytic inflammation within the fibrotic renal interstitium. To rule out leptospirosis, sections of kidney tissue underwent *Leptospira*-specific immunohistochemical staining and results were negative. Mild lymphoplasmacytic inflammation (accompanied by a few neutrophils) was evident within the lamina propria of the urinary bladder. Notable microscopic lesions in other tissues included superficial and multifocal necrosis in the gastric mucosa with mineralization of the lamina propria and scattered foci of necrosis and inflammation in the deeper mucosa. Chief cell hyperplasia was present in both parathyroid glands.

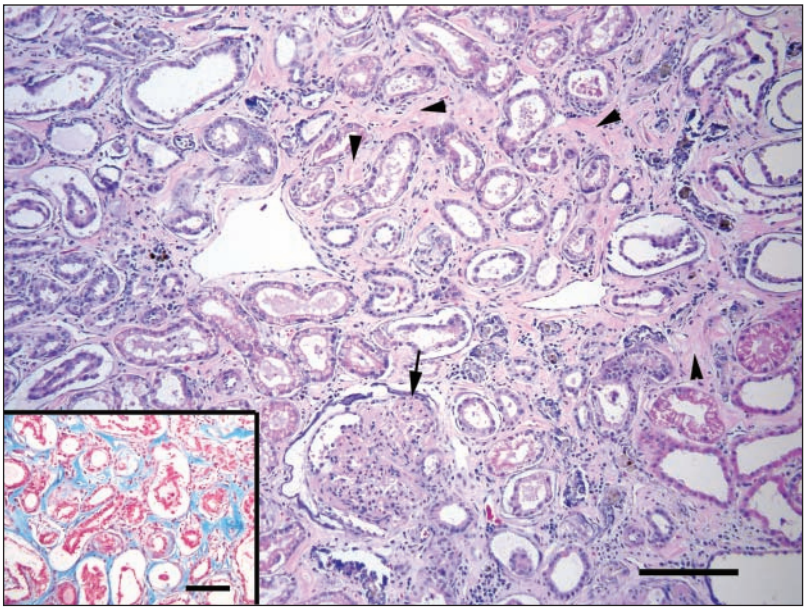

Figure 2—Photomicrograph of a section of a kidney from the dog in Figure 1. In the main image, the cortical interstitium contains abundant dense fibrous tissue (arrowheads) that separates the renal tubules. Glomerular capillary tufts are thickened and hyalinized and often form synechiae with adjacent Bowman's membranes (arrow). H&E stain; bar = 160 µm. In the inset image, the blue-stained areas indicate the presence of collagen. Masson trichrome stain; bar = 160 µm.

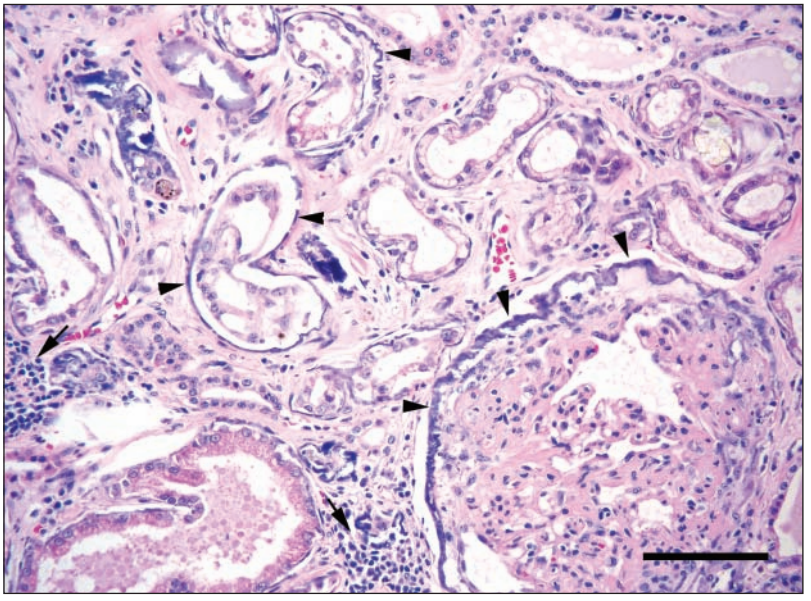

Figure 3—Photomicrograph of a section of the renal cortex of a kidney from the dog in Figure 1. Basement membranes of most tubules and glomerular Bowman's capsules are mineralized, as evidenced by basophilia and fragmentation (arrowheads). Aggregates of lymphocytes, plasma cells, and macrophages are scattered throughout the fibrous tissue within the interstitium (arrows). Moderate numbers of intraluminal crystals, as seen in the upper right portion of the image, are present in scattered renal tubules. The crystals are most consistent with calcium oxalate crystals, which likely developed secondary to compromised renal function. H&E stain; bar = 100 µm.

Morphologic Diagnosis

Severe, diffuse, interstitial renal fibrosis with tubular degeneration, glomerulosclerosis, and multifocal lymphoplasmacytic interstitial nephritis; mild and diffuse lymphoplasmacytic cystitis; erosive gastritis with necrosis and mucosal mineralization; and parathyroid gland chief cell hyperplasia.

Comments

The clinical signs, physical examination findings, and clinicopathologic abnormalities in the dog of this report were all supportive of an antemortem diagnosis of chronic renal failure. Severe azotemia with isosthenuria and accompanying hyperphosphatemia are directly related to decreased renal function. The dog's normocytic, normochromic anemia was most likely attributable to decreased erythropoietin production, which itself is a result of renal impairment. The presence of 2+ protein concentration in the dog's urine was not a definitive indication of glomerular protein loss because of the active urine sediment associated with concurrent cystitis. However, given the other indicators of renal compro-

mise, hypoalbuminemia was suspected to be related to glomerular dysfunction. Other findings associated with renal failure include halitosis (likely secondary to uremic stomatitis), uremic gastritis, and renal secondary hyperparathyroidism with parathyroid gland chief cell hyperplasia. Soft tissue mineralization detected in the dog of this report was likely associated with uremia and hyperphosphatemia that developed as a result of chronic renal failure. Despite apparently normal serum calcium concentration, markedly high phosphorus concentration resulted in a high ratio of these 2 concentrations (expressed as the calcium and phosphorus product), which was associated with soft tissue mineralization. Mild hyperamylasemia, without other indicators of pancreatic disease, was likely the result of decreased renal filtration.

Chronic renal failure is typically considered to be a disease of older animals. When encountered in young animals (< 5 years old), chronic kidney disease is classified as congenital (present at birth), inherited (genetic), familial (develops in a closely related group), or acquired. In young animals, chronic renal lesions that are noninflammatory, degenerative, or developmental and that have an obscure pathogenesis are typically included in the broad category of juvenile nephropathies.[1] Within the general classification of juvenile nephropathies, the microscopic changes in the kidneys of the dog of this report have some, but not all, of the features of renal dysplasia, a more specific and well-defined disease entity. Renal dysplasia refers specifically to anomalous differentiation and disorganized development of renal parenchyma and is typically evidenced by microscopic features such as undifferentiated mesenchyme, immature glomeruli, and primitive ducts.[1] In this dog, immature glomeruli were not observed but undifferentiated mesenchyme was occasionally present, as were a few primitive ducts. Renal dysplasia is typically congenital but may be caused by early neonatal disease that develops within the first few weeks after birth in cats, dogs, and pigs (ie, species in which the subcapsular nephrogenic zone remains active after birth).[1] Some juvenile nephropathies are inherited in dogs and have been reported in families within certain dog breeds, including Golden Retriever,[2,3] Pembroke Welsh Corgi,[4] Cocker Spaniel,[5] and Dutch Kooiker.[6] Juvenile nephropathy in a Weimaraner has been previously reported, although a familial or hereditary association has not been established.[7]

Some of the specific abnormalities that lead to renal failure in young animals, aside from renal dysplasia, have been recognized within families or breeds. Familial renal diseases in dogs and cats include polycystic kidney disease, renal amyloidosis, glomerulopathies involving basement membrane defects, and membranoproliferative glomerulonephritis associated with abnormalities in the complement system.[8]

The renal lesions (interstitial fibrosis accompanied by tubular dilation and degeneration) in a young dog support progressive juvenile nephropathy as a diagnosis. Common gross features of juvenile nephropathies include renal fibrosis, which results in pale, shrunken kidneys that are often irregularly shaped because of the development of dissecting fibrous bands. However, such changes are not specific to juvenile nephropathies, as they may develop as a result of other chronic, destructive disease processes that lead to renal scarring. In the dog of this report, leptospirosis was considered as a possible cause of end-stage renal failure but was thought to be unlikely on the basis of results of immunohistochemical staining of kidney specimens. It is not uncommon that lesions in end-stage kidneys are often so advanced that histologic determination of the underlying pathological process is difficult or impossible.[1] Concurrent urinary tract infections, involving both lower and upper regions of the tract, are relatively common in animals with nephropathies. The risk of bacterial colonization is increased by altered urine flow in patients with ureteral malformations and as a result of urine dilution in patients with compromised renal concentration ability. Therefore, it is not uncommon for juvenile renal disease to be complicated by secondary inflammation. In fact, a diagnosis of pyelonephritis or recurring cystitis may warrant consideration of renal dysplasia or other developmental renal disease as an underlying pathological process in a dog < 5 years old.[2,9]

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