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Overview of chronic renal disease in cats

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Chronic renal disease (CRD) is commonly observed in older cats (those > 7 years of age), and it has been estimated to have a prevalence of between 1 and 3% in the geriatric cat population. On histopathologic examination of the kidneys, slightly more than half of older cats with CRD have chronic tubulointerstitial nephritis of unknown etiology characterized by interstitial infiltration of lymphocytes and plasma cells, interstitial fibrosis, tubular atrophy, tubular dilatation and glomerular sclerosis. This diagnosis is relatively non-specific and may include a number of different diseases that are difficult to distinguish histopathologically from one another. For example, chronic pyelonephritis and chronic glomerulonephritis are two renal diseases of cats that can have end-stage renal lesions that are difficult to distinguish from chronic tubulointerstitial nephritis of unknown etiology.

Acute glomerulonephritis is relatively uncommon in cats, but is relatively easy to recognize clinically due to the presence of severe proteinuria, hypoalbuminemia, hypercholesterolemia and often ascites or subcutaneous edema. Most cases of acute glomerulonephritis in cats are idiopathic, but a search for underlying infectious, inflammatory or neoplastic diseases associated with chronic immune complex production is recommended. Clinically, acute pyelonephritis is readily suspected by the presence of fever, normal-sized but painful kidneys, a high white blood cell count, pyuria and a positive urine culture. Chronic pyelonephritis however can be much more challenging to identify because many of the clinical features of acute pyelonephritis are lacking, and the situation is complicated by the fact that many cats with CRD due to chronic tubulointerstitial nephritis of unknown etiology also have lower urinary tract infection (UTI).

Reactive amyloidosis is a relatively uncommon renal disease of cats that affects primarily the Abyssinian, Siamese, and Oriental shorthair breeds. This disorder is characterized by the deposition of amyloid AA fibrils in the kidneys and many other tissues including the thyroid gland, adrenal glands, heart, liver, gastrointestinal tract, pancreas, and spleen. Although amyloid deposits are not restricted to the kidneys, chronic renal failure (CRF) is the main clinical presentation of amyloidosis in the Abyssinian cat. In Oriental shorthair and Siamese cats however severe hepatic deposition of amyloid can result in liver rupture and acute hemoabdomen. Amyloid deposits in cats with renal amyloidosis predominantly are found in the medullary interstitium, and less consistently in the glomeruli. Thus, the absence of marked proteinuria and even a negative renal cortical biopsy do not necessarily out the diagnosis. The medullary interstitial amyloid deposits can interfere with medullary blood flow by compressing the vasa recta and lead to papillary necrosis, a gross necropsy finding that should prompt suspicion of amyloidosis. Congo red staining should be requested on the collected renal tissue to allow a conclusive diagnosis to be made. Polycystic kidney disease is inherited as an autosomal dominant trait in Persian cats, and it has been reported to affect approximately 25-30% of Persian cats. It is caused by a mutation in the gene for polycystin 1 (PKD1), and the mutation can be identified by a PCR test that identifies a single nucleotide polymorphism in exon 29 of the feline PKD1 gene. From a clinical perspective, renal ultrasound examination is highly sensitive and specific for this disease if performed when the suspected cat is at least 9 months of age or older. Renal lymphoma and feline infectious peritonitis (FIP) are two systemic diseases of cats that can involve the kidneys to a sufficient extent to cause CRF. Normal cat kidneys are approximately 4 cm in length, and although many cats with CRD have small irregular firm kidneys, cats with polycystic kidney disease, renal lymphoma and occasionally those with granulomatous interstitial nephritis due to FIP often have enlarged kidneys on presentation. Potassium depletion nephropathy in cats is of historical interest because it was observed during a time when commercial cat foods were high in protein and acid content but deficient in potassium (< 0.4% on a dry matter basis). Potassium depletion nephropathy was characterized by lymphoplasmacytic interstitial nephritis with vacuolar degeneration of tubular cells. Clinical signs were primarily related to muscle severe weakness and rhabdomyolysis associated with potassium depletion and characterized by marked hypokalemia (< 3.0 mEq/L) and increased serum creatine kinase activity.

The prevalence of nephrolithiasis in cats has increased dramatically in the past 25 years. During this time, there also was a shift in the type of uroliths observed in cats (in all locations) from struvite to calcium oxalate. CRD occurs in approximately 75% of cats with nephrolithasis and persists after resolution of obstruction by surgery in 50% of affected cats. Progressive renal damage by nephroliths may occur as calculi move back and forth between the renal pelvis and ureter causing chronic intermittent renal obstruction. Normal urine flow tends to propel calculi into the ureter causing obstruction whereas the calculi may move retrograde into the renal pelvis and spontaneously relieve obstruction when the cat jumps down from high places. This sequence of events may contribute to so-called “big

kidney–little kidney" syndrome in which one kidney is enlarged from obstruction and the other is small and irregular from chronic interstitial nephritis.

The most common clinical findings in cats with CRF are anorexia, lethargy, and weight loss. Owners frequently do not recognize polyuria and polydipsia, and vomiting is less common in cats with CRF than in dogs. Common findings on physical examination are dehydration and poor body condition. Depending on the stage of disease at presentation, laboratory findings in cats with CRF include nonregenerative anemia, azotemia, hyperphosphatemia, and metabolic acidosis. The severity of anemia may not be appreciated on presentation due to the effect of dehydration. Between 20 and 30% of cats with CRF have hypokalemia, which contrasts with approximately 5 to 10% of older dogs with CRF. Mild hypercholesterolemia occurs in many cats with CRF and does not correlate well with the presence of glomerular disease. Urine specific gravity typically is in the isosthenuric range in cats with CRF. Some cats (10-15%) with CRF however retain substantial concentrating ability, which can cause confusion with pre-renal azotemia. Mild proteinuria (urine protein/creatinine ratio < 1.0) is common in cats with CRD and has been correlated with survival. Proteinuria however may be a marker of severity of CRD rather than a causative factor in its progression. The urine sediment of cats with CRF should be examined carefully for pyuria and bacteriuria because approximately 30% of cats with CRF have UTI, and most of these do not have clinical signs of lower urinary tract disease. The most commonly cultured organism is *E. coli*.

Approximately 30% of cats with CRD are non-azotemic and have International Renal Interest Society (IRIS) stage 1 disease with serum creatinine concentrations (SCr) < 1.6 mg/dl, 40% have IRIS stage 2 disease (SCr 1.6-2.8 mg/dl), 15% have IRIS stage 3 disease (SCr 2.9-5.0 mg/dl), and 15% have IRIS stage 4 disease with SCr > 5.0 mg/dl. Overall, approximately 85% of cats with CRD have renal secondary hyperparathyroidism based on serum parathyroid hormone concentration, and the presence of hyperparathyroidism is correlated with the severity of the CRD. The prevalence of hypertension in cats with CRD is unclear, and may be between 20% and 30%. Ocular (e.g., retinal hemorrhage, retinal edema, retinal detachment, vascular tortuosity) or cardiac (e.g., gallops, murmurs, arrhythmias) indicate morbidity. Although it is difficult to judge the clinical relevance of systolic blood pressure between 140 and 150 mmHg (due to "white coat artifact"), systolic blood pressure > 175 mmHg warrants treatment.

Hyperthyroidism and CRD often occur concurrently in older cats. The presence of CRD makes hyperthyroidism more difficult to diagnose because it acts as a non-thyroidal illness that decreases serum total T4 concentration. Clinicians should trust their identification of a thyroid nodule on physical examination in making the diagnosis of hyperthyroidism. The effect of hyperthyroidism on renal function also is a concern in diagnosis and treatment. Hyperthyroidism increases renal blood flow and glomerular filtration rate (GFR), making renal function (based on SCr) look better than it actually is. When hyperthyroidism is treated, azotemia can become apparent and the cat may deteriorate. Hence a "methimazole challenge" (in which the cat is treated with 2.5 mg methimazole once a day and SCr monitored as the dose is slowly increased over several weeks) is recommended before more definitive treatment of hyperthyroidism is carried out. If renal function remains stable, more definitive therapy may be safe. There also is concern that hyperfiltration associated with increased GFR may predispose the cat to additional renal injury and progression of renal disease. Thus, although unproven, hyperthyroidism itself may be injurious to the cat's kidneys.

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