Common Geriatric Disease of Cats

Katrina R. Viviano, DVM, PhD, Diplomate ACVIM (Internal Medicine)
Clinical Assistant Professor
University of Wisconsin
School Veterinary Medicine
Madison WI

Introduction

Aging is an intrinsic systemic process that affects all cells, tissues, and organs of the body resulting in altered homeostasis, decreased ability to respond to environmental stimuli, increased frailty, and predisposition for illness. Therefore geriatric populations are at increased risk for the development of systemic abnormalities including multiple organ abnormalities as well as a population more commonly receiving long-term or multiple medications. Although many factors contribute to the aging process (genetics, nutrition, and environmental factors) each species and individuals within a species age differently.

The classification of geriatric varies with species and each species has their own unique group of chronic diseases that require routine monitoring for early disease recognition, long term management, and to decrease the risk of adverse clinical events. The more common chronic disease of geriatric felines will be reviewed focusing on diseases that have a significant impact on drug disposition (chronic kidney disease, chronic liver disease, and protein losing enteropathy) and the primary metabolic disease of cats, hyperthyroidism, which significantly impacts many of the major organs systems.

Chronic kidney disease

The inherent age-related structural and physiological changes in the functional nephron result in an overall decrease in the renal reserve. Structural changes associated with age in humans include glomerulosclerosis, mesangial expansion, obliteration of juxtamedullary nephrons, dysfunction of autonomic vascular reflex, and tubule-interstitial changes. These structural changes result in altered renal physiology in older adults including decreased glomerular filtration rate (GFR), altered tubular handling of creatinine, reduced sodium reabsorption, and reduced potassium secretion. These age-related changes in the kidney make elderly adults more likely to experience clinical adverse events in association with standard levels of stimuli (stress or illness) and therapeutic dosage regimens. Studies are lacking in our veterinary species but likely these age-related structural and physiological changes also occur in the kidneys of cats with age, making the geriatric feline more susceptible to clinical decompensation in association with standard stresses.

Despite the similarities in the loss of kidney reserve and decreased GFR associated with the aged-kidney and patients with chronic kidney disease (CKD) there are important clinical differences between these two populations. In the “otherwise healthy” aged-kidney the function of the proximal tubules is preserved and serum erythropoietin levels and hematocrit are maintained. In addition serum urea, electrolytes (magnesium, calcium, phosphorus), vitamin D, and parathyroid hormone levels remain normal in the patient with an aged-kidney. Two important clinical consequences of hypofiltration of the aged-kidney patient are their risk of
developing volume overload following a sodium load and the need for drug dosage adjustments based on a decrease in GFR.

The prevalence of chronic kidney disease (CKD) increases with age and in geriatric patients CKD is more often associated with irreversible nephron loss, fibrosis, and progressive disease. Irrespective of the inciting cause the common histopathological changes associated with CKD are non-specific and include tubular loss with associated fibrosis and mineralization, glomerulosclerosis and glomerular atrophy. Inflammatory changes are localized to the interstitium with mononuclear cells (small lymphocytes, plasma cells, macrophages) being the dominate cell types present.

In many geriatric patients subclinical CKD commonly persists without detection because of the large functional reserve of the kidney, compensatory hypertrophy of remaining functional nephrons, and the relatively insensitive markers of kidney function routinely available. When 66% of the kidney’s nephrons are lost the term renal insufficiency is sometimes used as the kidneys have lost their ability to produce concentrated urine but the kidney maintains the ability to excrete wastes. As nephrons are lost the remaining functional nephrons increase fluid excretion per nephron preventing the development of significant clinical signs. Renal insufficiency is commonly not clinically identified as these patients feel well despite being persistently isosthenuric, polyuric and polydipsic, although not azotemic. It is not until 75% of the nephrons are lost that kidneys ability to excrete wastes becomes compromised and patients develop azotemia. As the GFR of the kidney decreases the clinical sequela of CKD begin to emerge including uremia, hyperphosphatemia, metabolic acidosis, systemic hypertension, anemia, and secondary hyperparathyroidism.

In older cats CKD is most commonly acquired due to nephron loss as a consequence of aging or a result of a primary kidney insult of known or unknown etiology. Based on the results of a retrospective study it is estimated that 15% of cats > 15 years of age have evidence of kidney dysfunction. In cats the most frequent histopathological description of either a kidney biopsy or postmortem sample in a cat with CKD disease is diffuse tubulointerstitial nephritis. The more common underlying causes for CKD in cats include infectious triggers (pyelonephritis (E. coli)), nephrolithiasis with or without urethral obstruction, dehydration or hypovolemia, nephrotoxic drugs (NSAIDs), polycystic kidney disease, neoplasia (ex. renal lymphoma), and amyloidosis. Primary glomerular disease and associated proteinuria is not a significant contributor to progressive CKD in cats but proteinuria is a negative prognostic indicator for survival in cats with CKD.

The inciting underlying cause for nephron loss is commonly not identified in cats therefore the management of CKD focuses on reducing the workload of the kidney, controlling clinical signs, and preventing and/or treating complications. Medical management of CKD begins with the pursuit of appropriate diagnostic work-up to stage the disease and identify any known or suspected underlying causes. CKD is staged according to the guidelines developed by the International Renal Interest Society (IRIS). Staging is based on renal function (serum creatinine), proteinuria, and blood pressure. Any identified sequela (dehydration, positive urine culture, hypertension, proteinuria, hyperphosphatemia, hypokalemia, gastrointestinal ulceration, anemia, urethral obstruction) should be appropriately treated and monitored. In addition protein, phosphorus, and sodium reduced kidney diets are recommended and the discontinuation and/or avoidance of any nephrotoxic therapies (NSAIDs) are also recommended.

**Chronic liver disease**
The common age-related physiological changes in the hepatobiliary system with age are a decrease in the numbers of hepatocytes and an increase in hepatic fibrosis. Relative to humans and canines, feline chronic liver diseases tend to be more inflammatory and/or infiltrative than fibrotic with a biliary system component. Often cats that develop chronic liver have other concurrent diseases including inflammatory bowel disease, pancreatitis, and cholecystitis. The more common chronic liver diseases of cats include inflammatory liver diseases (neutrophilic cholangitis, chronic neutrophilic cholangitis, lymphocytic cholangitis, and lymphocytic portal hepatitis) and hepatobiliary neoplasia which can be primary, hemolymphatic, or metastatic in origin.

Cholangitis in cats is differentiated histopathologically by the type of inflammatory infiltrates present in the biliary tree and hepatocytes surrounding the portal triad. Ruling out an extra-hepatic biliary obstruction becomes important in these older icteric cats and a liver biopsy and bile culture are needed to more accurately describe the liver pathology and direct therapy.

Neutrophilic cholangitis is more common in middle-aged male cats associated with an acute onset (lethargy, vomiting, diarrhea, icteric, and febrile) and believed to result from bacteria ascending the common bile duct. Neutrophils are present in bile ducts and portal areas with extension into the hepatic parenchyma.

Chronic neutrophilic cholangitis is usually associated with a mixed inflammatory reaction (neutrophils, lymphocytes, and plasma cells) and has a more chronic clinical course with episodic anorexia, vomiting, or diarrhea and occurs more commonly in older cats. Biliary cirrhosis is associated with end-stage chronic neutrophilic cholangitis and functional liver failure. The hallmark of biliary cirrhosis is bridging portal fibrosis, bile duct proliferation, and minimal inflammatory infiltrates.

Lymphocytic cholangitis differs from neutrophilic cholangitis due to the lack of neutrophilic infiltrates in the portal areas and the lymphocytes present in portal areas do not invade the bile duct lumen or epithelium. Bile duct hypertrophy and fibrosis are often present but lymphocytic cholangitis does not lead to biliary cirrhosis although lesions are slowly progressive with age. Lymphocytic portal hepatitis results in inflammation limited to the portal areas (mild lymphocytic inflammation with some neutrophils and plasma cells) with infiltration of inflammatory cells extending into the hepatic parenchyma, but bile duct involvement is lacking.

Infiltrative diseases of the liver include primary hepatobiliary tumors (biliary adenoma versus carcinoma, hepatocellular adenoma versus carcinoma, hemangiosarcoma, hepatobiliary neuroendocrine carcinoma), hemolymphatic neoplasia (lymphosarcoma, mast cell tumor, and plasma cell tumors) and metastatic neoplasia. A liver biopsy is needed to make a definitive diagnosis and direct therapy to treat the underlying cause.

Protein losing enteropathy

Age-related changes in the gastrointestinal tract based in human and rodent studies include decreased gastric and intestinal mucosal turnover, decreased innervation of smooth muscle, increased motility of small intestine, delayed colonic transit time, and decreased absorption of water, electrolytes, and vitamins. Limited research is available in cats but data supports that fat digestion is decreased in older cats. Altered fat digestibility with age can occur due to physiological and metabolic changes associated with aging. In cats decreased fat
digestibility has been suggested secondary to a decrease in pancreatic enzymes and/or bile acids.\textsuperscript{7,8}

Infiltrative diseases of the gastrointestinal tract (inflammatory bowel disease (IBD) and small lymphosarcoma (LSA)) commonly occur in geriatric cats. In most cases the presenting clinical signs, biochemical changes, and imaging can be identical therefore gastrointestinal biopsies are need to different between the two diseases. Especially in cats, it can be difficult to differentiate between IBD and LSA due to high prevalence of small cell alimentary LSA in cats. Transmural biopsies from all segments of the intestine (especially jejunum and ileum) and collection of extraintestinal biopsies are ideal to provide the most optimal samples for differentiating between IBD and LSA in cats. Although to establish a diagnosis of IBD, endoscopic biopsies are considered adequate in cats but may result in a misdiagnosis of IBD in some cats with LSA.\textsuperscript{9}

Histological changes consistent with IBD include the presence of diffuse mucosal inflammatory cell infiltrates, characterized by lymphocytes, plasma cells, eosinophils, neutrophils, and/or macrophages in various proportions. The presence of inflammatory infiltrates and their mediators result in enterocyte dysfunction, intestinal dysmotility, and clinical signs. The diagnosis of small cell alimentary LSA is based on neoplastic lymphocytes infiltrating the intestinal mucosa. The lymphocytes are irregularly distributed with infiltration may extend to the submucosa, and in some cases infiltration can be transmural. In some cats, especially those cases where the owner maybe interested in pursuing chemotherapy beyond prednisone, immunohistochemistry or PCR may be used to differentiate been small cell LSA versus IBD.\textsuperscript{10,11}

Hyperthyroidism

Hyperthyroidism is the most common endocrinopathy in geriatric cats and occurs due to an increase in the production and secretion of active thyroid hormones thyroxine (T4) and triiodothyronine (T3). The hyperfunctionality of the thyroid gland is most often associated with a functional but benign thyroid adenoma in ~ 98% of cases. Sequela that can occur in association with hyperthyroidism and thyrotoxicosis include tachycardia, hypertension, cardiomegaly with or without signs of congestive heart failure, and concurrent chronic kidney disease.

Thyrotoxicosis significantly impacts the cardiovascular system producing peripheral vasodilation with both ionotropic and chronotropic effects on the heart resulting in increased oxygen consumption and increased circulating volumes. Systemic hypertension not only negatively impacts the cardiovascular system but also contributes to clinically significant end organ damage including ocular, neurologic, and kidney effects. Chronic kidney disease is a common concurrent illness in geriatric cats and the severity of the underlying kidney disease can be masked by the increase in glomerular filtration rate (GFR) associated with hyperthyroidism. In most cases the clinical or biochemical severity of the underlying kidney disease is not fully appreciated until the cats become euthyroid. The common sequela associated with hyperthyroidism should be investigated at the time of diagnosis and if identified treatment should be pursued concurrent with the treatment of hyperthyroidism. Common concurrent therapies may include the use of beta-blockers to control heart rate and/or calcium channel blockers to treat those cats that are hypertensive. Medical therapy is the treatment of choice for hyperthyroidism in cats either with either daily methimazole therapy or radioactive iodine therapy (i.e. I-131).
References