Management of hypertension in a geriatric cat

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Abstract — Hyperthyroidism and chronic renal disease occur commonly in geriatric cats, often in association with potentially life-threatening primary or secondary hypertension. Early treatment of hypertension minimizes damage to vital organs. This case illustrates the complexity of managing hypertension in a geriatric cat with both hyperthyroidism and renal disease.


A 16-year-old, spayed female, Persian cat was presented for paresis and difficulty in walking (day 1). The owners also complained that the cat’s urine had a strong odor. Progressive polyuria, polydipsia, and weight loss had occurred over the previous several months, despite the cat’s voracious appetite. Diarrhea had been noticed intermittently and, recently, the cat had been salivating constantly. Activity level had remained normal to increased. The cat was always confined and there was no known exposure to toxicants, including plants and ethylene glycol.

The cat was alert and responsive when touched; however, on the basis of visual and auditory cues, she did not appear to be aware of her surroundings. She exhibited bilateral minimally responsive pupillary light reflexes, no appreciable menace response, and severely dilated pupils. The cat crouched when walking and was generally weak, but apparently not in pain. She was emaciated, weighing 2.5 kg, and exhibited severe muscle atrophy, particularly of the hind limbs. Neck ventroflexion was not observed. Moderate dehydration (5% to 8%) was estimated on the basis of skin tenting and pink, tacky mucous membranes. Capillary refill time was < 2 s. Rectal temperature was 38.8°C and the extremities felt warm. Mild halitosis, associated with severe bilateral gingivitis and dental tartar, was noted. Thoracic auscultation revealed tachycardia (220 beats/min; reference range, 120 to 140 beats/min) and a grade III/VI bilateral holosystolic apical heart murmur. No abnormality of rhythm or pulse deficit was appreciated. Abdominal palpation did not elicit a painful reaction; however, small nodular kidneys were appreciated bilaterally. The thyroid gland was not palpable. Possible differential diagnoses at this time included hyperthyroidism and renal failure, with secondary hypertension, cachexia, and retinal blindness. Diabetes mellitus and hypertrophic cardiomyopathy were also considered.

Further diagnostic testing included a complete blood cell (CBC) count, serum biochemical profile, serum free T4 assay, urinalysis, electrocardiography, and fundic examination. Survey radiographs and echocardiographs to rule out hypertrophic cardiomyopathy and aortic dilatation were declined by the owner. Results of the initial tests (Table 1) revealed an elevated serum free T4 level, suggestive of feline hyperthyroidism; increased serum alanine aminotransferase (ALT); and mild hypokalemia and hypernatremia. Urea and creatinine concentrations were within the normal range. Normal serum glucose ruled out diabetes mellitus. The in-house urinalysis showed trace proteinuria and low specific gravity, but no glucosuria or casts. No other significant clinical findings were noted.

The electrocardiogram revealed only sinus tachycardia, with no evidence of chamber enlargement or left-axis deviation suggestive of hypertrophic cardiomyopathy (1,2). The fundic examination revealed bilateral focal retinal red lesions with mild vascular tortuosity and substantial tapetal hyperreflectivity. The appearance of these lesions was consistent with retinal hemorrhage and partial detachment due to hypertension (3,4).

On the basis of the clinical signs and diagnostic test results, a diagnosis of hyperthyroidism and hypertension was made. Concurrent chronic renal disease could not be ruled out; however, further diagnostic tests were declined. The owners elected for medical therapy to control the hyperthyroidism because of the cat’s age, its
questionable renal status, and their financial concerns. Methimazole (Tapazole; Paladin Labs, Montreal, Quebec), 1 mg/kg bodyweight (BW), q12h, PO, was prescribed to control the hyperthyroidism and 0.9% NaCl solution was to be administered in 100-ml boluses, SC, on alternate days, to optimize renal perfusion and facilitate rehydration. Enalapril maleate (Enacard; Merial Canada, Baie D’urfe, Quebec), 0.5 mg/kg BW, q24h, PO, was prescribed for its antihypertensive and potential renoprotective effects.

On day 15, the cat appeared clinically much improved. She had gained 0.25 kg, was walking with less difficulty, seemed more relaxed and much brighter, and had stopped salivating. Polyuria and polydipsia were unchanged. Tachycardia was still evident; however, hydration was good and there was a normal pupillary light reflex (PLR) and menace response in the right eye. The PLR in the left eye was weak, but the cat easily tracked movements.

Hematologic and biochemical tests and urinalysis were repeated to assess the T4 levels and renal parameters; the results (Table 1) showed a much reduced serum free T4 level and a mildly increased urea, with all other parameters within normal range, and urine specific gravity unchanged. The dosage of methimazole was increased to 1.5 mg/kg BW, q12h, PO. The owners agreed to continue with the SC fluid and enalapril therapies and to repeat the blood tests in 2 wk.

Feline hyperthyroidism, the most common endocrinopathy of cats (5), is associated with spontaneous development of hyperfunctional thyroid nodules. As in this case, clinical signs are variable and widespread. Restlessness, nervousness, weight loss, increased appetite, polyuria, polydipsia, vomiting, tachycardia, and elevated rectal temperature are frequent findings (2). Diagnosis is based on clinical signs and an increase in serum free T4 levels. The origin of increased ALT levels in hyperthyroid cats is unknown (1).

The association between hypertrophic cardiomyopathy and hyperthyroidism has not proven to be causal (1). However, hyperthyroidism induces an increased number and sensitivity of myocardial β-adrenergic receptors (2–4), resulting in an increased response to catecholamines and subsequent tachycardia. In this case, the aorta may contribute to hypotrophy and increased myocardial oxygen demand (3,4). Thyroxine also has a direct effect via an adenylate cyclase-cyclic adenosine monophosphate (cAMP) system, resulting in increased stroke volume and cardiac output (4). Older cats, in which the aorta is less distensible, are unable to accommodate the additional pressure, and hypertension develops.

Left untreated, hypertension inevitably damages delicate capillaries in end-artery organs (the eyes, kidneys, heart, and brain) (3,4). Hypertension may manifest as blindness, polyuria, polydipsia, cardiac irregularities, seizures, nystagmus (neurological signs), and hind limb paresis (3). Retinal detachment and acute blindness, the most common presenting complaints for hypertensive cats (2–4), are recognized by retinal hemorrhages, tape-tal hyperreflectivity, and vascular tortuosity on fundic examination (3), as in this case. Diagnosis of hypertension in cats may be established if systolic blood pressure, measured indirectly, exceeds 170 mm Hg (3,6). Published ranges for cats vary widely, and there is an important “white coat” effect to be considered (6).

Direct blood pressure recordings are unrealistic in practice, and the use of Doppler ultrasonographs, oscillometric devices, and photoplethysmographs are good instruments for indirect assessment (3). In this case, objective blood pressure measurements were not possible. Treatment of hyperthyroidism may be attempted by using medical management, surgery, or radiation (1,5). Methimazole or carbimazole (a prodrug of methimazole) offers control of hyperthyroidism alone, inhibiting synthesis of thyroxine (t4) and triiodothyronine (t3) (5). Adverse reactions include anorexia, vomiting, lethargy, bleeding, and icterus (5).

The lowest possible dose is recommended in order to minimize side effects, as monthly monitoring of thyroidine levels and blood indices (5). Renal parameters should be monitored closely, as hyperthyroidism increases glomerular filtration rate and may mask renal lesions (1,5). This effect might explain the initial normal urea concentration in this cat, prior to methimazole therapy.

Management of hypertensive effects due to increased β-receptor sensitivity may best be achieved with specific beta-blocker therapy (5). The most commonly recommended drug for cats is atenolol (2,3,5,7), which decreases the neuromuscular and cardiovascular effects of hyperthyroidism. The cat in this case might have benefited from a short course of atenolol until euthyroidism was achieved. However, β-blocker therapy might have further compromised kidney perfusion.

It was important to establish the etiology of hypertension in this case in order to pursue proper therapy. The 2 most common causes of hypertension in the cat are renal disease and hyperthyroidism (3). Less common causes include hyperadrenocorticism, pheochromocytoma, and anemia (2,3). Management of this cat was challenging because of concurrent kidney disease.

The pathogenesis of renal-dependent hypertension is thought to be multifactorial, including decreases in ability to excrete sodium and activity of vasodilators (prostaglandins) and increases in renin secretion, norepinephrine (or response to it), and cardiac output or total peripheral resistance (3,8). Increased secretion of renin (which induces increased formation of angiotensin II) may be caused by ischemic damage to kidneys and reduction of pressure, or decreased sodium chloride levels at the macula densa (2,8). An overactive renin-angiotensin-aldosterone system causes hypertension by a combination of volume excess and vasoconstrictor mechanisms, and ongoing hypertension may accelerate renal lesions (8).

Activation of the renin-angiotensin-aldosterone-system

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Day 1</th>
<th>Day 15</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>166</td>
<td>15</td>
<td>5 to 67</td>
</tr>
<tr>
<td>Free T4 (nmol/L)</td>
<td>125.0</td>
<td>72.5</td>
<td>12.9 to 51.5</td>
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<tr>
<td>Urea (mmol/L)</td>
<td>9.1</td>
<td>12.6</td>
<td>4.0 to 10.7</td>
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<tr>
<td>Urine specific gravity</td>
<td>1.018</td>
<td>1.018</td>
<td>1.020 to 1.040</td>
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*Methimazole (1 mg/kg BW, q12h, PO) and enalapril maleate (0.5 mg/kg BW, q24h, PO) were administered daily beginning on day 1.

Table 1. Serum biochemical profile and urinalysis results before and after treatment for hypertension and hyperthyroidism in a 16-year-old, spayed female, Persian cat
may stimulate production of endothelin, a potent vasoconstrictor found in vascular endothelial cells and vascular smooth muscle (2). Future therapies may be directed at countering the ischemia produced by this vasoconstriction.

Hypertension in cats may not always be associated with renin-dependent mechanisms (8,9), explaining the apparent failure of treatments aimed at inhibiting angiotensin II production (7–9). Primary hypertension in felines may be responsible for progression to renal failure, rather than the reverse (4). Angiotensin-converting enzyme inhibitors, including enalapril, decrease blood pressure and increase renal perfusion and glomerular filtration rate (4,9). Enalapril was chosen for management of this case on the assumption that renal disease was a primary contributor to hypertension.

Amlodipine is a calcium channel blocker that relaxes vascular smooth muscle without the myocardial depressive effect of many calcium channel antagonists (4). In cats, amlodipine is long acting (24 h), safe, and effective, and may be renoprotective (9,10). It is reported to be the most effective therapy for hypertensive cats (2,6,7,9). It was not used in this case because blood pressure could not be monitored accurately. There have been recent reports that calcium channel blockers cause renal injury and proteinuria in humans and in diabetic dogs (10). Amlodipine and angiotensin-converting-enzyme inhibitors may be used safely and effectively in combination (7), offering vasodilation of both afferent and efferent arterioles. Although this would have been the best approach for management of hypertension involving several etiologies, as in this case, financial considerations, the practicality of administering multiple oral medications, and the inability to objectively measure blood pressure accurately were deciding factors.

**Acknowledgments**

The author thanks Dr. Danny Butler, Ontario Veterinary College, and Drs. Ines Allin, Kathy Marchildon, and Ian Webb and the staff of the Orillia and District Veterinary Services for their advice and encouragement, also the owners of Muffin.

**References**