HYPERTENSIVE RETINOPATHY IN A CAT

A Case Report and Literature Review

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Introduction

Systemic hypertension in cats is defined as an indirect systolic blood pressure of 160–170 mmHg[16,17]. The prevalence of hypertension in the feline population is poorly defined, but a prospective study of middle-aged and geriatric cats found that 8% of cats exhibited hypertension[1]. Several conditions are well documented to lead to hypertension in the feline patient including: renal disease[2], hyperthyroidism[3], hyperaldosteronism[4], hyperadrenocorticism[5], pheochromocytoma[6], chronic anemia[7], and high salt intake[8]. Of the listed conditions, it occurs most commonly secondary to chronic renal disease with a frequency of up to 65%, or hyperthyroidism with a frequency of up to 23%[16].

Clinical signs of hypertension are recognized as damage to target organs with a rich arteriolar blood supply. The commonly affected "target organs" in cats are the eye, brain, kidney and heart[13]. In the eye, hypertensive changes can manifest in three ways: hypertensive retinopathy, hypertensive choroidopathy, and/or hypertensive optic neuropathy[14]. Ocular lesions associated with hypertensive retinopathies often lead to acute blindness and present veterinarians with an extraordinary opportunity. By incorporating therapy in a time sensitive manner, clinicians have the potential to allow the patient to regain vision.

History and presentation

A 17-year-old, 3.2 kg, female spayed domestic shorthair cat was examined at the Ophthalmology Service at the Mississippi State University College of Veterinary Medicine for evaluation of an acute onset of blindness OU that occurred a few days prior to presentation. Previous medical history included hyperthyroidism, chronic kidney disease, and feline herpes virus. Her hyperthyroidism had been managed with topical methimazole for the past several years at varying dosages based on what the owner thought was needed. Indirect blood pressure,

measured via doppler ultrasonic sphygmomanometry, was elevated at ~243 mmHg. General physical examination revealed a well-hydrated patient with a pulse of 240 beats per minute and respiratory rate of 32 breaths per minute. Temperature was not recorded to avoid stressing the patient. The patient was bright, alert, and responsive with a body condition score of 3/9. Symmetrical appendicular and axial muscular atrophy was noted. On ophthalmic examination of vision, the menace, tracking, and maze responses were absent OU. The dazzle response was present OU. The globe size, position and motility were within normal limits OU. No abnormalities were present upon examination of the nictitating membrane and conjunctiva in either eye. Schirmer tear testing was not performed in an effort to minimize patient stress. Fluorescein stain uptake was negative OU. The intraocular pressure, measured with applanation tonometry, was 9 mmHg OS and 12 mmHg OD. Both pupils were dilated at rest, and the direct and consensual pupillary light reflexes were absent OU. The palpebral reflexes were present OU. Upon examination of the anterior chambers, trace aqueous flare was present in the OS, but none was noted OD. Nuclear sclerosis was present in the lens OU. On indirect examination, billowing, vascularized tissue was visualized through the pupil in each eye, along with retinal edema. Our clinical diagnosis was bilateral serous bullous retinal detachment due to hypertension. Considering the medical history of the patient, the top differential diagnosis was systemic hypertension secondary to a combination of renal disease and hyperthyroidism.

Pathophysiology

Hypertensive retinopathies are not primary disorders, but rather they are manifestations of disease elsewhere in the cat. The disease contributing to the pathologic changes in the retina is most commonly renal disease or hyperthyroidism[16], but can be any combination of renal disease[2], hyperthyroidism[3], hyperaldosteronism[4], hyperadrenocorticism[5], pheochromocytoma[6],

chronic anemia[7], and/or high salt intake[8]. All of these diseases have the potential to cause systemic hypertension and ocular lesions. Whatever the underlying cause, the most common baseline systolic arterial blood pressure value reported in the literature to begin causing ocular lesions is around 160 mmHg. Although 160 mmHg is widely accepted, the American College of Veterinary Internal Medicine (ACVIM) consensus panel correlated risk of target organ damage to various blood pressure values in 2007. The ACVIM consensus panel stated that risk of target organ damage is mild when systolic arterial blood pressure is 150 mmHg to 159 mmHg, moderate when at 160 mmHg to 179 mmHg, and severe when ≥ 180 mmHg[15].

The most commonly described ocular lesions with hypertension are retinal detachment, edema, retinal hemorrhage, hyphema, and retinal degeneration[16-20]. Retinal hemorrhage and edema results from retinal vascular damage alone, while retinal detachment results from both retinal vascular damage and choroidal vascular damage[20,21]. An important aspect in understanding the pathophysiology of hypertensive damage to the eye is held within the vascular system. The vascular system supplying the retina and choroid differ anatomically and physiologically.

Retinal arterioles exhibit autoregulation to ensure a constant blood flow despite changes in intraocular pressure and local arterial blood pressure[22]. Hypertension results in vasoconstriction of the pre-capillary arterioles and the sustained vasoconstriction of these arterioles leads to ischemic damage to the vascular smooth muscle and endothelium[22]. In response to ischemic damage to the vascular endothelium, vasodilation and increased vessel permeability ensues. This response is achieved by the release of vasoactive substances such as nitric oxide[23], prostacyclin[24], and endothelin-1[25], and causes leakage of plasma and cells into the

surrounding retinal tissue. The leakage of these fluids manifests as retinal edema and hemorrhage[20].

Choroidal capillaries supply the outer layers of the retina. These capillaries are called the choriocapillaris and lie just beneath the retinal pigmented epithelium. These choroidal vessels do not exhibit autoregulation; rather, they are under autonomic control[13]. They are fenestrated, allowing leakage of plasma protein into the interstitium. Tight junctions between the cells of the retinal pigmented epithelium normally prevent this fluid from entering the subretinal space (the space between the retinal pigmented epithelium and the photoreceptors of the retina). Retinal pigmented epithelium disruption results in breakdown of the blood-retinal-barrier, fluid leakage into the sub-retinal space, and retinal detachment[21]. This type of retinal detachment is classified as a serous retinal detachment and presents as acute blindness OU in the patient.

Diagnostic approach/considerations

When a feline patient presents for acute blindness, it is profoundly important to initially measure systolic arterial blood pressure. This should be performed prior to physical examination in an effort to minimize artificial elevations in blood pressure due to stress, and performed using a doppler ultrasound device, because doppler blood pressure measurements have the best agreement with invasive measures[27]. Next, any previous medical history should be recorded and a physical examination should be performed.

Combined with blood pressure measurements, an ophthalmic examination can validate a hypertensive retinopathy. The ophthalmic examination should begin by testing the patient's menace, tracking, maze and dazzle responses. The size, position, and motility of the globe should be evaluated next, along with the nictitating membrane and conjunctiva. With hypertensive retinopathies, abnormalities to the globe and eyelids are rare, but they should be evaluated for

any associated comorbidities. The cornea should be examined and intraocular pressures measured using tonometry. Pupil size and pupillary light reflexes should be measured and will often reveal obvious abnormalities. With hypertensive retinopathies, the retinas are often detached and the pupils mydriatic OU with absent pupillary light reflexes. The anterior chamber and iris should be examined for aqueous flare, hyphema, hypopion, iris atrophy, and/or synechia. The lens can be involved in cases of blindness, so pathology in this anatomic structure should be ruled out. The final, and most valuable, step of diagnosing a retinopathy is a thorough fundic examination using a direct or indirect ophthalmoscope. Fundic examination will often reveal retinal edema, hemorrhage, degeneration, tortuous vessels and/or retinal detachment.

Since hypertensive retinopathies are clinical signs of underlying disease(s), investigating the known causes of systemic feline hypertension should be performed. A complete blood count, serum chemistry, urinalysis, and a total thyroxine test are warranted in most cases. Further diagnostics such as abdominal radiographs and abdominal ultrasound may be required in special cases. The bottom line is that investigating the underlying cause(s) of hypertensive retinopathies must not be overlooked.

Treatment and management

The goal of hypertensive therapy is to reduce blood pressure to < 170 mmHg[17]. A variety of anti-hypertensive drugs including angiotensin-converting enzyme inhibitors, beta-adrenergic blockers, diuretics, alpha-adrenergic blockers, and calcium channel blockers can be used to treat hypertension[17]. Amlodipine is a calcium channel blocker, and it's the main treatment of systemic arterial hypertension in the feline patient due to its immediate peripheral and coronary vasodilation combined with its anti-hypertrophic action[28]. Dosing for amlodipine is 0.625 mg/cat PO q24h in general, but 1.25mg/cat PO q24h can be used in larger patients[28]. Once blood

pressure is normalized, follow-up monitoring of blood pressure, target organ damage, and progression of systemic disease should continue quarterly throughout the life of the patient.

Prognosis

In general, prognosis for return of vision in cats with retinal detachment caused by hypertension is guarded. Although the prognosis is guarded, the duration of detachment is highly correlated to the return of vision. Achieving a normotensive state with medical therapy will often lead to retinal reattachment, but unfortunately this doesn't always equal vision. While the retina is detached, ischemic damage causes degeneration of the photoreceptors (retinal degeneration), which cannot be corrected with reattachment[9]. Without these neurosensory cells, the patient will never fully regain vision. Due to the timely nature of this degenerative process, owner compliance, client education, and regular veterinary monitoring heavily dictates the prognosis for return of vision.

Case outcome

In this case, treatment for hypertension was initiated with amlodipine 0.625 mg, PO, q24h. A recheck appointment was scheduled for one week. Upon re-evaluation 7 d later, the systolic blood pressure measurement was improved at ~170 mmHg. The retinal detachments were resolved OU and vision was improving. Urinalysis revealed pale yellow, slightly hazy urine with a specific gravity of 1.014. The pH was 6.5. The urine had trace protein and large blood (50-100 RBC phpf). A urine protein/creatinine ratio measured 0.47 (urine total protein 34.0 mg/dl and urine creatinine 71.8 mg/dl). A total T4 measured 2.1 ug/dl (normal range: 2.0-5.0), and the sample had 2+ hemolysis. Vision continued to improve upon further rechecks, but was never fully regained. Since the owner brought the patient in days after the onset of blindness,

retinal degeneration likely played a role in the incomplete return of vision. The patient eventually succumbed to chronic kidney disease and passed away in the following weeks.

Conclusion

Feline hypertensive retinopathies are a clinical sign of systemic disease(s). Taking a thorough medical history, recording blood pressure measurements upon initial presentation, performing a thorough physical and ophthalmic examination, and routine lab work will often times lead clinicians to a diagnosis. Medical therapy should be initiated immediately and should include amlodipine for the rapid treatment of hypertension. Once systemic hypertension has been addressed, diagnosing the disease caused hypertension is necessary. This disease process should be treated appropriately. While understanding that vision can be regained during acute retinal detachments, it's important to give the pet owner a guarded prognosis for return of vision. Lifelong medical management of the underlying disease is often required, with routine recheck examinations. Owners must understand the entire clinical picture and be compliant to at-home-therapy for the long-term success of the patient. The opportunity to allow a blind patient vision again remains the most admirable aspect of treating feline hypertensive retinopathies.

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