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Iris aneurysm in feline hypertensive oculopathy

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Abstract

Objective: To describe and document the prevalence and cause of iris aneurysm in feline hypertensive oculopathy.

Animals studied: Privately owned cats with systemic hypertension presented for sudden visual deficits and/or hyphema.

Procedures: A retrospective search of medical records of cats with systemic hypertension was performed in a specialized eye practice from October 2001 to August 2016. Inclusion criteria used for further evaluation were (1) systolic blood pressure exceeding 170 mm Hg measured by Doppler ultrasound, (2) typical fundus changes consistent with systemic hypertension (retinal folds, retinal edema, intraretinal bullous fluid accumulation, retinal detachment—partial or total, intra-/preretinal bleeding) in at least one eye, and (3) at least one follow-up visit with documented response to therapy with amlodipine. Cats with bilateral hyphema were excluded.

Results: A total of 206 cats fulfilled the inclusion criteria. Twenty-eight cats (14%) showed an aneurysm of the iridal vessels, 21 75% with some amount of hyphema. In total, hyphema was present in 62 cats (30%). Pearson correlation of fundus changes, hyphema, and aneurysm was performed. A high correlation between fundus changes without posterior segment hemorrhage and hyphema was found. The histopathology of one eye showed iridial vascular changes compatible with an aneurysm. In 75 cats, additional blood analysis was performed. Presumed chronic kidney disease (80%) was the most common cause of systemic hypertension with eye disease, followed by hyperthyroidism (20%).

Conclusion: Vascular changes of the iris compatible with aneurysms were seen in 14% of cats with systemic hypertension and may result in vascular rupture and acute hyphema.

KEYWORDS

feline hypertensive oculopathy, feline systemic hypertension, hyphema, iris aneurysm, iris bleeding

1 | INTRODUCTION

Systemic hypertension is a well-recognized disease in elderly cats and is defined as systolic blood pressure exceeding 168 mm Hg.[1] The main cause for hypertension in cats is chronic kidney disease (CKD), followed by hyperthyroidism.[2,3] Cats are commonly presented to the veterinary ophthalmologist due to blindness or vision deficits. Some cats, however, are presented with partial or unilateral hyphema without significant vision impairment.

Feline ocular findings specific for systemic hypertension are fundus changes including focal or total retinal detachment, retinal edema and hemorrhage (intra- and preretinal, vitreal), retinal folds, and retinal degeneration with typical

hyper-/hyporeflective changes in the tapetal fundus.[2] Less often, blood and fibrin in the anterior chamber are seen (author's observation). Hyphema may lead in the chronic stage to iris synechia, dyscoria, pigment deposits on intraocular surfaces, glaucoma, and vision impairment because of obstruction of the irido-corneal angle and/or pupil.

An aneurysm is defined as a focal sack-like bulging of a vessel with morphologic dilatation of the vessel wall, which can result in rupture.

In human medicine, acquired aneurysms are encountered with arteriosclerosis and hypertension and occur most often in the abdominal and thoracic aorta[4] and intracranial vasculature,[5] but have not been described affecting iridal vessels associated with hypertension.

To the author's knowledge, iris aneurysms in cats in combination with hypertension have rarely been mentioned in the literature.[6]

The purpose of this study was to describe the prevalence of iridal vascular changes (ie, iris aneurysm) with or without hyphema as a manifestation of feline hypertensive oculopathy.

2 | MATERIALS AND METHODS

A retrospective, systematic, and computerized search of the medical records of feline patients with iridal vascular changes presented to an ophthalmological referral practice (Tieraerztliche Spezialisten Hamburg, Rodigallee 49, 22085 Hamburg, Germany) from 2001 to 2016 was performed. Keywords were cat, hypertension, hyphema, and retinal detachment. Cats with elevated systolic blood pressure (over 170 mm Hg) and specific fundus changes in at least one eye, as described below, were included. All records were checked manually reviewed for any type of iris lesion notation. Excluded were cats with ocular signs of hypertension where no measurement of blood pressure had been possible, cats with iridal hyperemia/iridal discoloration as a sign of iridal inflammation (anterior uveitis), and cats where the fundus in at least one eye could not be evaluated due to bilateral complete hyphema.

At least one follow-up, and a positive response to therapy, was necessary for inclusion in the study. Therapy consisted of amlodipine oral 0.125-0.25 mg/kg once per day. Response to therapy was defined as regression of typical ophthalmic signs (resorption of anterior or posterior segment hemorrhage, no recurrence of intraocular hemorrhage, reattachment of retina) and a reduction of blood pressure of at least 40 mm Hg (delta) or under 180 mm Hg.

All cats underwent a complete ophthalmological examination, including slit lamp biomicroscopy (SL 14, Kowa, Japan), indirect ophthalmoscopy (Heine, Omega, Germany), and rebound tonometry (Tonovet, Icare, Finland). Systolic blood pressure was measured with Doppler ultrasound sphygmomanometry (Parks Medical Electronics, Oregon USA) using a special cuff (3.3 × 12 cm UPC3.3, Hokanson WA, USA) placed on the right forearm below the elbow and at heart level. Blood analysis to determine the cause of hypertension was performed in 75 cats.

Fundic changes were categorized as follows:

grade I = retinal folds (Figure 1A),
grade II = focal retinal edema/bullous elevation (Figure 1B),
grade III = retinal detachment segmental/retinal hemorrhage (Figure 1C), and
grade IV = total retinal detachment/retinal hemorrhage (Figure 1D).

The classification of fundus changes was based on the appearance at the first examination.

Iridal aneurysm was defined as vascular engorgement and elevation of a segment of the major iridal arteriolar circle diagnosed by slit lamp biomicroscopy.

One cat was euthanized because of reasons unrelated to the study and the eye with iridal vascular changes was enucleated and histologically examined. Multiple direct cuts through the iris and iris vessels were made and evaluated on hematoxylin- and eosin-stained slides.

2.1 | Statistics

With Pearson correlation coefficient determination, the relationship between iris aneurysm (iridal vessel bulging) and hyphema, aneurysm and fundus changes, and between different fundus changes and hyphema were evaluated. We also looked at possible correlations of systolic blood pressure and fundus changes and systolic blood pressure and hyphema. Further, the influence of age on these parameters was determined.

For the analysis, we conducted a correlation analysis and determined Pearson correlation coefficients with the corresponding *P*-values. The analysis was conducted with the software Stata MP 14.1.

3 | RESULTS

A total of 206 cats met the inclusion criteria. European Shorthair was the main breed with 155 cats, followed by 35 Persian cats, 6 British Shorthair, 3 Maine coon cats, 3 Chartreux, 2 Somali, 1 Siamese, and 1 Russian cat. The age ranged from 8 to 22 years with a mean of 14 years. A total of 178 cats (85.2%) were in the range from 12 to 18 years. A total of 111 cats were female (53.9%) and 95 male cats (46.1%). Systolic blood pressure ranged from 170 mm Hg to

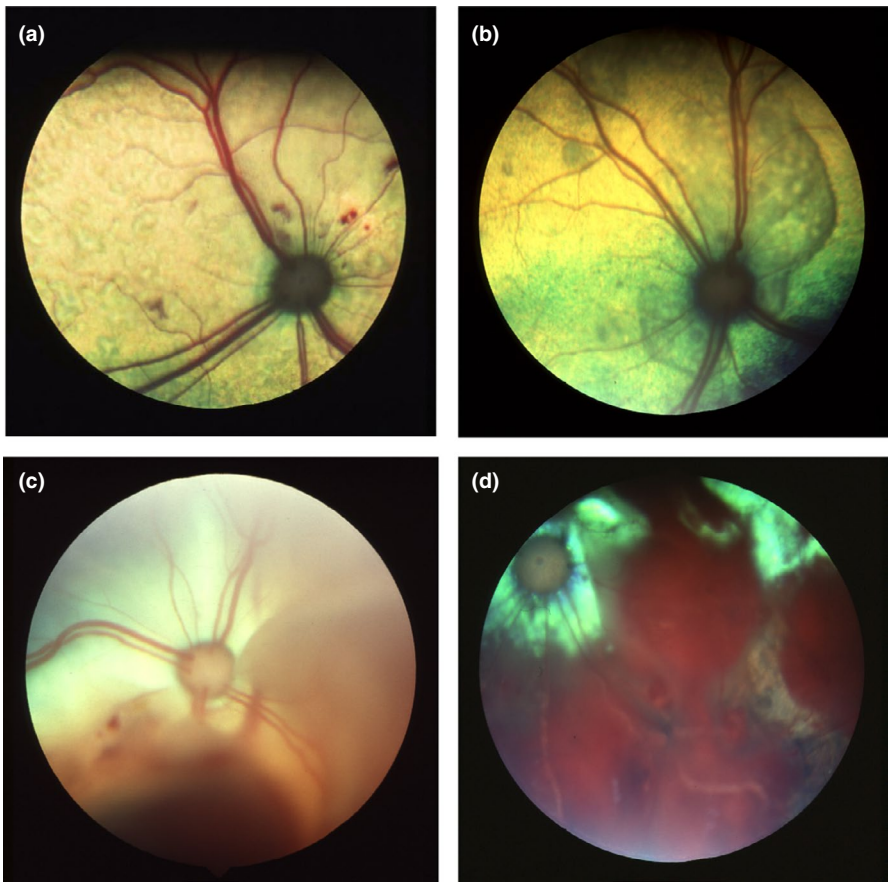

FIGURE 1 A, Fundus changes grd. I: retinal folds, intraretinal hemorrhages. B, Fundus changes grd. II: focal retinal edema, bullous elevation. C, Fundus changes grd. III: retinal detachment segmental/retinal hemorrhage. D, Fundus changes grd. III-IV: retinal detachment/retinal hemorrhage

310 mm Hg with a mean of 231 mm Hg. All cats showed regression of fundus changes (eg, reattachment of the retina, resorption of posterior segment blood) after the initiation of therapy. The normalization of systolic blood pressure under 170 mm Hg was regarded as further proof of correct diagnosis of systemic hypertension associated ocular disease in 203 cats. For three cats with blood pressures between 170 and 180 mm Hg at initial diagnosis, the requirement of post-treatment blood pressure reduction was not applied as they were either under sedation or already under therapy when first presented.

An aneurysm (Figure 2) could be seen in 28 cats (14%). In these cases, hyphema (Figure 3) was present in 21 cats (75%), which signified a high correlation of 0.56 ($P = .000$). In seven cats, an aneurysm without hyphema was diagnosed.

In total, 62 cats (30%) showed hyphema with (n = 21) or without (n = 41) visible aneurysm.

In 41 cats, hyphema (Figure 4) was present and iridal changes could not be reliably excluded. In 23 of them, hyphema impeded the evaluation of the iris (Figure 5), and in 18 cases, it was recorded that there were "no visible iridial changes."

Fundus grade I changes were seen in 14 cats (6.8%); grade II in 37 cats (17.9%); grade III in 71 cats (34.5%); and grade IV in 84 cats (40.8%). 57.1% of cats with grade I and 59.4% with grade II fundus changes showed hyphema, whereas only 23.9% with grade III and 18.8% with grade IV showed hyphema. The correlation coefficient between grade I fundus change and hyphema was 0.15 grade III and IV had a negative correlation coefficient of −0.11 ($P = .109$) and −0.22 ($P = .001$). This indicates that hyphema in systemic hypertension is more likely

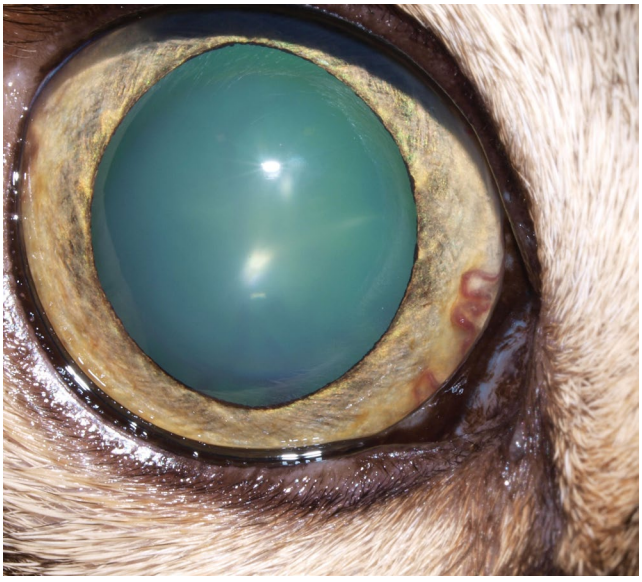

FIGURE 2 Right eye, focal iris aneurysm of the medial greater arterial circle

in cats with less severe fundus changes (grade I and grade II) where no posterior segment bleeding is present.

No significant correlation was found between systolic blood pressure and fundus changes, nor between blood pressure and hyphema. The finding of correlation between fundus changes and hyphema was independent of age and blood pressure.

For the statistical analysis regarding aneurysm, we used a subsample of 165 cats, in which we excluded the above-mentioned 41 cats, where assessment of the iris was either not possible or not seen. All of these may or may not have masked aneurysms. In this subgroup, iridal aneurysm was seen in 38.4% of cats with grade I fundus changes, and in 31.0% of cats with grade II fundus changes, whereas only in 14.5% with grade III and in 6.4% with grade IV fundus changes.

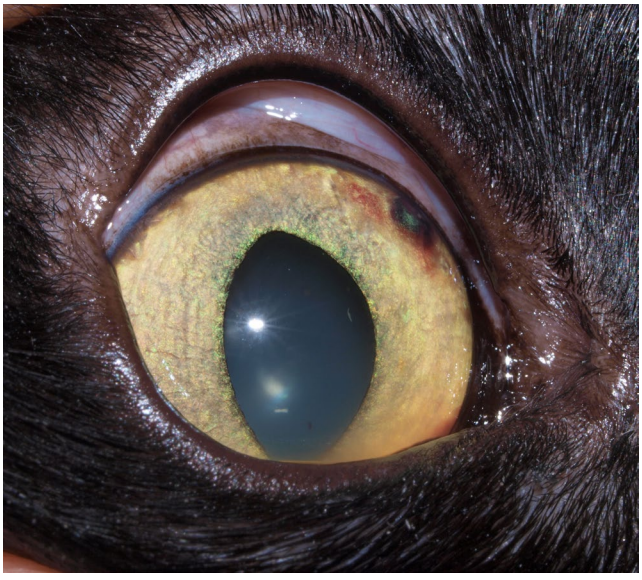

FIGURE 3 Right eye, dorsonasal iridal stromal hemorrhage

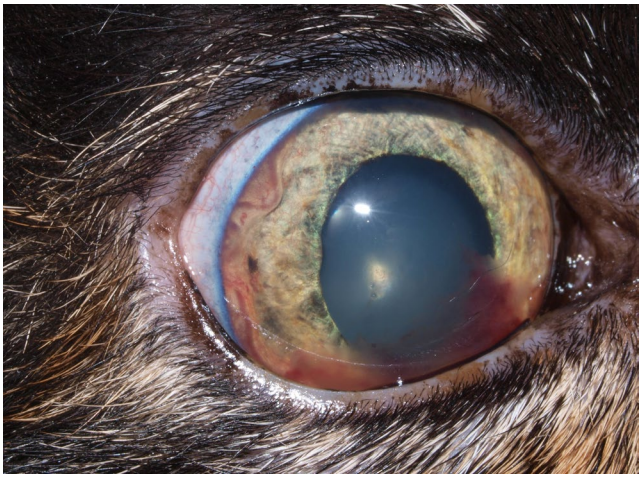

FIGURE 4 Right eye, iris aneurysm of the lateral greater arterial circle, focal fibrinohemorrhagic clot in the ventral anterior chamber

In 75 cats (35.9%), a blood analysis was performed. CKD was regarded as a possible cause for hypertension when BUN and/or creatinine blood levels were elevated. Hyperthyroidism was diagnosed by serum total T4 exceeding 5.0 µg/dL. Sixty cats were diagnosed with presumed CKD (80%). This was the most common cause of systemic hypertension in conjunction with eye disease, followed by 15 cats with hyperthyroidism (20%). The systemic cause for hypertension in the other cats was not further investigated by the author, as work-up was conducted by the referring veterinarian, or a specialist for internal medicine. The follow-up was not the focus of this paper.

We were able to perform histopathology of one enucleated globe and get a cross section of the aneurysm lesion of the iris. The iris showed a large dilated (approximately 1mm in diameter) arterial blood vessel with a thrombus, indicating endothelial damage (Figure 6). The endothelium was largely missing from this section of the vessel (Figure 7). There was no evidence of inflammation of the vascular wall (Figure 8). There was no evidence of arteriosclerosis.

4 | DISCUSSION

Iridal vascular engorgement or iridal aneurysm in association with systemic hypertension in humans has not been described to the author's knowledge. Iridal aneurysm in cats has only been briefly mentioned in the literature, as "some hypertensive cats also have iridal aneurysms and hyphema".[6] One publication exists in rabbits from 1976,[7] where iris aneurysms were described together with cerebral hemorrhage and systemic hypertension. In another study, microradiography was used to detect cerebral and ocular aneurysms in surgically induced hypertension in rabbits.[8] Microaneurysms of the iris and in the brain were correlated with hypertension. However, cerebral bleeding in hypertensive cats has so far only been reported once in 1994.[9] The

FIGURE 5 Right eye, fibrinohemorrhagic clot filling the anterior chamber

two cats in that study had additional neurologic signs, which is not a typical symptom for hypertensive cats.

The author has seen iridal aneurysms thus far only in cats. All were exclusively localized to the tortuous major arterial circle of the iris. This anatomic structure is particularly prominent and exposed in the cat. It is speculated that the major vascular ring may be particularly prone to develop aneurysms under high blood pressure. Regarding the absence of signs of inflammation in the histology performed, it is speculated that the arterial dilation and thrombus formation represent a sequela of aneurysm (ie, a localized thinning of the tunica intima and tunica media with subsequent hemodynamic disturbances and initiation of hemostasis).

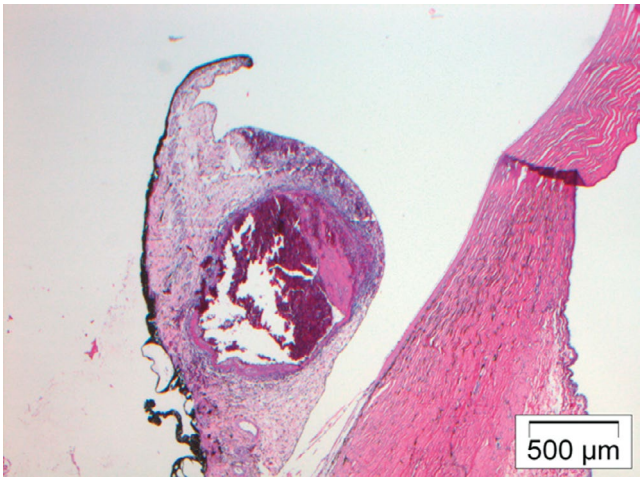

FIGURE 6 Histopathology of iris aneurysm. Low power view of iris with massively dilated artery in the center

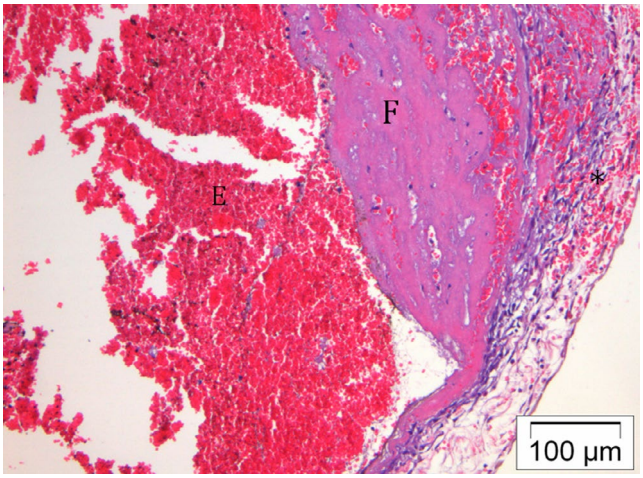

FIGURE 7 High power view of the dilated artery in iris stroma. Note general lack of endothelium (remnant endothelial cell indicated by arrow), thick strands of fibrin (F) covering the arterial tunica media (M), perivascular hemorrhage (asterisk), and scattered pigmented cells in the iris stroma (interpreted as hemosiderin-containing macrophages)

The clinical sign of anterior segment hemorrhage is presumed to be caused predominantly by leakage of iris vessels. Hyphema was seen in 30.1% (62/206) of hypertensive cats in this study, and cats with iridal aneurysm were likely to develop hyphema (75% or 21/28).

In the 23 cats where unilateral hyphema impeded the visualization of the iris, aneurysm might have been the cause for hyphema. A weak point in the study is those 18 cats with hyphema where "no visible iridal vascular changes" were recorded. These cases may also represent hyphema as a result of aneurysm. Therefore, the author hypothesizes that the number of cats with hyphema caused by iridal aneurysm may be underestimated in this report.

Posterior segment bleeding with intraretinal and preretinal (vitreal) bleeding in hypertensive cats is more likely caused by a rupture of retinal vessels. However, we observed in this study that fundus changes associated with retinal bleeding (grade III and grade IV) were significantly less correlated with anterior segment bleeding, whereas cats with fundus changes grade I and grade II were more likely to show hyphema. It seems likely that hyphema results from the iris in the anterior segment. Beyond this, hyphema is more often accompanied with non-hemorrhagic fundus changes as in grade I and grade II.

Also, the grade of fundus changes did not correlate with the level of blood pressure. There were fundus grade IV changes with a systolic pressure of 180 mm Hg. On the other hand, we saw fundus changes grade I with a systolic blood pressure of 250 mm Hg. It can be assumed that in some cats, hypertension targets the posterior segment, and in others the anterior segment.

This retrospective study clearly has limitations, the most relevant being that only data from existing records were available. The author has made the clinical observation that on rare occasions blood (and fibrin) leaks directly out of the aneurysm. This is reinforced by the histologic finding that blood was

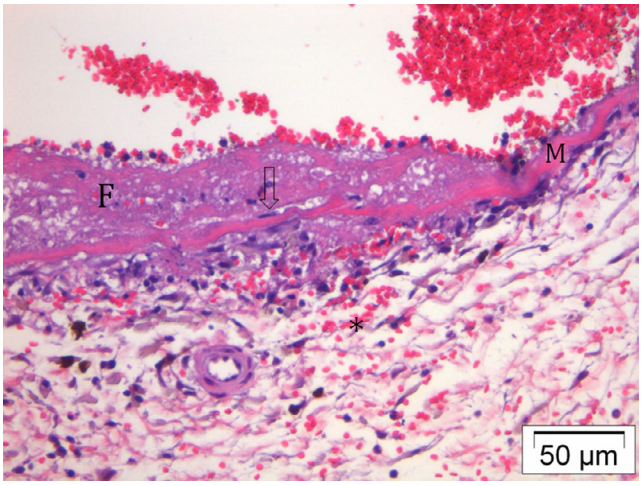

FIGURE 8 Higher power view of dilated artery in iris stroma. Note thick strands of fibrin (F) admixed with erythrocytes (E). Also note perivascular hemorrhage in the iris stroma (asterisk)

found extravascular (Figure 7, asterisk) as indicative of vessel leakage. Further assessment of the integrity of iridal and retinal vessels by more specific diagnostics, such as fluorescein angiography, would be helpful to prove the causality of iridal aneurysm and hyphema. Second, the pathogenesis of arterial aneurysms as a sequela to hypertension may warrant further studies. Also in human medicine, systemic hypertension has long been considered as a risk factor of aneurysmal rupture. However, a causal link between systemic hypertension and the development of aneurysmal rupture has not been established.[4]

Finally, the lack of confirmation of chronic kidney disease as a cause for hypertension in this study is a limitation, as the diagnosis requires urinalysis in combination with BUN and CREAT determination.

In summary, this study aimed to describe iridal aneurysm as an ocular symptom of systemic hypertension in cats. Hyphema was seen in about 1/3 of affected hypertensive cats with ocular symptoms. It is hypothesized that iridal aneurysm is the main cause for hyphema in cats with hypertensive oculopathy, not hemorrhage of the posterior segment migrating through the pupil, as stated in the literature.[2] This is supported by the observation that iridal involvement with hyphema in hypertensive cats was more often seen along with lower grade hypertensive fundus changes which lacked posterior segment hemorrhage.

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