The Causes of Glaucoma in Cats

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Abstract. The cause of glaucoma in 131 enucleated eyes from 128 cats was determined in a retrospective histologic study. Obliteration of the ciliary cleft by diffuse iridal melanoma (38 eyes), or other neoplasms (14 eyes), or by the presence of idiopathic lymphocytic-plasmacytic anterior uveitis (53 eyes) were the most frequent lesions likely to explain the development of glaucoma. Secondary changes of inner retinal atrophy, optic disc cupping, scleral thinning with megaglobus, and atrophy of ciliary processes were similar to those described in dogs and human beings with chronic glaucoma. In light of the duration and severity of the glaucoma, the degree of inner retinal atrophy was often less than expected. Diffuse corneal edema and breaks in Descemet’s membrane, changes typical of glaucoma in other species, were rarely detected. Eyes with chronic uveitis and glaucoma had collapsed ciliary clefts, iridocycleral adhesions, and posterior displacement of the iris. We were unable to determine whether these changes were consequences of the uveitis and thus responsible for the development of glaucoma, or if they were merely the result of the chronic glaucoma itself.

Key words: Cat; glaucoma; melanoma; uveitis.

In contrast to the voluminous information about most aspects of glaucoma in dogs, there is scant published information about glaucoma in cats. Accounts in textbooks of ophthalmology, or feline medicine, suggest that glaucoma is infrequent in cats, but that when it occurs it evokes clinical signs similar to those seen in dogs, has an insidious onset, and often is longstanding prior to initial ophthalmic examination. In texts and review articles, the most common causes given for feline glaucoma are ocular neoplasia, lens luxation, and complications of anterior uveitis, but no published data are given to support these claims. In a recent review of 29 cases of feline glaucoma, analysis of clinical histories, results of ophthalmic examinations and ancillary laboratory tests, and results of five histopathologic examinations failed to reveal a cause for the glaucoma in 27 of the 29 cats. One had iridal melanoma, and another had mycotic endophthalmitis. In the only other published report we were able to find, bilateral glaucoma in a 3-year-old Siamese cat was associated with chronic anterior uveitis and peripheral anterior synechia.

In this study, we examined 131 glaucomatous, enucleated eyes from 128 cats in an attempt to determine the causes of glaucoma in cats and to characterize the ocular changes caused by the glaucoma.

Materials and Methods

Enucleated eyes, fixed in 10% neutral buffered formalin, or in Zenker’s or Bouin’s fluid, were submitted by general veterinary practitioners or by veterinary ophthalmologists for histologic evaluation. Most specimens were known to be glaucomatous (as determined by measurement of intraocular pressure) prior to enucleation, but some eyes with suspected uveal neoplasia were identified as glaucomatous only upon histologic detection of optic disc cupping and ganglion cell loss. Each globe was hardened in ethyl alcohol and was sliced to remove a central sagittal calotte for routine paraffin embedding. Sections were stained with hematoxylin and eosin or with periodic acid-Schiff reagent and luxol fast blue and were examined with a light microscope. Patient data and clinical history were summarized from the information accompanying each submission.

Results

Sixty-eight eyes had microscopic changes that readily explained the development of glaucoma: obliteration of the ciliary cleft by diffuse iris melanoma (38 cats) or other neoplasia (14 cats), corneal perforation with extensive anterior synechiae (8 cats), posterior synechiae and pupillary block following traumatic lens rupture (4 cats), fibrovascular pre-iridal membrane with angle overgrowth (3 cats), and anterior entrapment of the iris by an intumescent lens (1 cat) (Figs. 1, 2). The glaucoma in the remaining 63 eyes was less easily explained. Four had anterior luxation of the lens but no detectable change in the filtration angle other than collapse of the ciliary cleft attributed to the glaucoma itself. Three cats had bilateral glaucoma with no observed primary lesion and were classified as open-angle, open-cleft primary glaucoma. The largest group (53 cats) had lymphocytic-plasmacytic anterior uveitis.
Fig. 1. Cat with diffuse iridal melanoma and secondary glaucoma. Note obliteration of the ciliary cleft. HE.

Fig. 2. Cat with intumescent, cataractous lens. Note the anterior displacement of the iris, narrowing of the filtration angle, and secondary glaucoma. HE.

Fig. 3. Lymphoid aggregates in iridal stroma, typical of most cases of uveitis in this study. HE.

Fig. 4. Normal configuration of the filtration angle in a healthy, normotensive cat eye. The trabecular meshwork is lacey and the iridocorneal angle is acute. The termination of Descemet’s membrane (arrow) marks the most anterior insertion of the pectinate (trabecular) fibers. HE.
Table 1. The causes of glaucoma in cats.

<table>
<thead>
<tr>
<th>Primary Ocular Change</th>
<th>Number of Eyes*</th>
<th>Mechanism of Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic uveitis</td>
<td>53</td>
<td>Occlusion of trabecular meshwork by cellular exudate, lymphoid nodules, or peripheral anterior synechiae</td>
</tr>
<tr>
<td>Iridal melanoma</td>
<td>38</td>
<td>Tumor obliteration of trabecular meshwork</td>
</tr>
<tr>
<td>Uveal lymphoma</td>
<td>8</td>
<td>Occlusion of trabecular meshwork</td>
</tr>
<tr>
<td>Corneal ulceration and/or perforation</td>
<td>8</td>
<td>Extensive anterior synechiae</td>
</tr>
<tr>
<td>Lens rupture</td>
<td>4</td>
<td>Pupillary occlusion by perilenticular inflammation and fibroplasia</td>
</tr>
<tr>
<td>Primary ocular sarcoma</td>
<td>4</td>
<td>Pupillary and angle obstruction</td>
</tr>
<tr>
<td>Anterior lens luxation</td>
<td>4</td>
<td>Unknown</td>
</tr>
<tr>
<td>Rubeosis iridis</td>
<td>3</td>
<td>Angle traversed by fibrovascular preiridal membrane</td>
</tr>
<tr>
<td>Primary open angle</td>
<td>3</td>
<td>Unknown—angle and cleft histologically normal</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>2</td>
<td>Uveal fibrinous inflammation posterior synechiae</td>
</tr>
<tr>
<td>Intumescent cataract</td>
<td>1</td>
<td>Anterior iris entrapment</td>
</tr>
</tbody>
</table>

*128 eyes from 131 cats: three had bilateral open angle glaucoma.

No etiologic agent was seen, and no cat was systemically ill (Table 1).

Histologically, the uveitis had two major patterns that were not necessarily mutually exclusive. The most frequent pattern was a diffuse lymphocytic-plasmacytic anterior uveitis. The leukocytes were most prominent in perivascular locations within iridial stroma and anterior ciliary body, but occasionally could be found perivascularly within choroid and retina. A second pattern, usually superimposed on the first, was the presence of discrete lymphoid aggregates within the iris, trabecular meshwork, and ciliary body (Fig. 3).

The clinical histories for 21 of the 53 eyes with uveitis revealed that the uveitis preceded the onset of glaucoma. None of the histories stated that the glaucoma preceded the uveitis, and most of them simply recorded a long history of glaucoma and uveitis with no proof of which had occurred first. The histologic lesions support speculation for three mechanisms by which the uveitis may have caused glaucoma, and in cats with complex lesions, there may have been more than one contributor to the glaucoma. In ten eyes, the accumulation of leukocytes on the face of the pectinate ligament or within the trabecular meshwork was sufficient to justify speculation that outflow had been impaired (Figs. 4, 5). In eight eyes, the obstruction was attributed to numerous lymphoid aggregates within the trabecular meshwork and adjacent uveal stroma. In 28 eyes, there was collapse of the ciliary cleft, adherence of the peripheral iris to the sclera or (rarely) peripheral cornea, and formation of a false angle within the midperiphery of the iris (Figs. 6, 7). In seven eyes with uveitis, there was no lesion that we were able to identify as a probable cause for the glaucoma.

Many of the structural alterations attributed to the chronic glaucoma were similar to those seen in other species: atrophy of ciliary processes and inner retinal layers, cupping of the optic disc, scleral thinning, megaloglobus, and corneal stromal vascularization. The corneal vascularization was usually subtle, except in 14 eyes that had corneal ulceration. In seven, the ulceration was the primary lesion, usually in young cats and usually associated with a history of ocular trauma. Corneal perforation, iris prolapse, and complete anterior synechiae resulted in glaucoma. In the remaining seven eyes, the ulceration was a complication of the glaucoma (presumably because of megaloglobus, corneal protrusion, and increased susceptibility to trauma or desiccation), and in five of the seven it was responsible for the decision to enucleate.

The atrophy of the nerve fiber layer and loss of ganglion cells characteristic of glaucoma were seen in 110 of the 113 eyes. In three cats with unequivocal clinical diagnoses of glaucoma, we could not confirm retinal atrophy. The atrophy was often subtle despite the fact that most of these eyes had glaucoma for several months or even years (Fig. 8). Usually, the retina overlying the tapetum was less severely affected than the retina from the ventral, non-tapetal fundus. Diffuse corneal edema, a hallmark of uncontrolled glaucoma in dogs and human beings, was not seen in any of our feline specimens except in those in which it was attributed to concurrent corneal ulceration. Similarly, the multifocal breaks in Descemet's membrane caused by pressure-induced corneal stretching (striate keratopathy) were seen only in two cats despite what, in many eyes, was a marked megaloglobus.

Discussion

Review articles based upon clinical experience with feline glaucoma list the following as the most frequent causes of glaucoma in cats: angle obstruction by inflammatory debris or by post-inflammatory synechiae, angle occlusion by primary or by metastatic uveal neoplasia, and lens luxation. The last is controversial because of the difficulty of establishing whether the...
Fig. 5. Leukocytes are on the anterior face of the iris and within the ciliary cleft, a possible cause of obstruction to aqueous outflow.

Fig. 6. Ciliary cleft, filled with leukocytes; iridal root is displaced posteriorly, creating a false angle (arrow). HE.

Fig. 7. Collapse of the ciliary cleft and formation of a false angle within the peripheral iris. The altered angle between the iris and sclera deepens the anterior chamber. Note that the new “angle” is very posterior to the termination of Descemet’s membrane (arrow). HE.

Fig. 8. Loss of ganglion cells and nerve fiber layer in glaucomatous retina 1 mm dorsal to the optic disc. Nerve fiber loss has resulted in unusual prominence of the Mueller fibers (arrow). HE.
that lymphocytic-plasmacytic uveitis is the cause of a disease. This belief is supported by the experimental evidence for outflow obstruction caused directly by the leukocytes is weak and mostly arises (as in our series) allowing vitreous prolapse (pupillary block). Some of these clinical impressions are substantiated by this retrospective histologic study.

Diffuse iridal melanoma is a leading cause of glaucoma in cats, accounting for one-third of our cases. The tendency for these tumors to infiltrate the ciliary cleft and to cause glaucoma has previously been reported. In 15 of the 37 eyes in our study, it was the glaucoma rather than the clinically undetected neoplasm that prompted enucleation.

Our results support the clinical observation that many cats with glaucoma have concurrent anterior uveitis, yet we cannot confirm that there is a causal relationship between the two. In most instances, the first detailed ophthalmic clinical examination was of an eye with longstanding disease, so that most of the histories accompanying our specimens had noncommittal statements such as “chronic glaucoma” or “chronic uveitis and glaucoma.” Nonetheless, 21 histories specifically stated that the uveitis preceded the glaucoma, and none specifically stated that the uveitis followed the observed onset of the glaucoma. Our inclination to accept that the uveitis somehow causes the glaucoma is further supported by histopathology. Six eyes with primary glaucoma, four eyes with anterior lens luxation, and most of the eyes with uveal melanoma had no inflammation. This suggests that in cats, as in dogs and human beings, glaucoma per se does not cause uveitis and that the uveitis must be considered either as the primary lesion or a concurrent, independent event. Because it was not seen as a concurrent lesion in the other categories of glaucoma in this study, we conclude that lymphocytic-plasmacytic uveitis is the cause of a substantial proportion of the cases of glaucoma in cats.

The pathogenesis of the uveitis in virtually all of these cases is unknown. Most histories did not specify the extent of testing for such agents as feline leukemia virus, toxoplasma, or the coronavirus of feline infectious peritonitis, which are all frequent causes of uveitis in cats. Because none of these cats was systemically ill, and because the uveitis was reported to be unilateral in 50 of the 53 affected cats, we conclude that these agents are unlikely to have been the cause of the uveitis. As in cats, the pathogenesis of most examples of lymphocytic-plasmacytic uveitis in human beings and other animals is unknown. Failure to identify an etiologic agent, dominance of lymphocytes and plasma cells, and at least partial suppression by corticosteroids or other immunosuppressive agents support speculation that most cases are the result of immune-mediated disease. This belief is supported by the experimental induction of similar lesions by intraocular instillation of a wide variety of antigens, including those native to the eye itself. Unmasking these sequestered (or partially sequestered) antigens of lenticular, uveal, or retinal origin is thought to be critical to the development of nonsuppurative uveitis following a wide range of traumatic, inflammatory, or degenerative ocular disorders. In human beings and domestic animals, the syndrome is only partially controlled by anti-inflammatory and immunosuppressive therapy, with eventual enucleation justified by intractable ocular pain, glaucoma, or blindness.

Although we believe that the uveitis caused the eventual glaucoma, how it did so is not clear, partly because most of the eyes had longstanding disease with secondary compression of the filtration angle that made evaluation very difficult. In the 25 eyes with uveitis that still had open angles, ten had enough entrapped leukocytes to justify speculation that the leukocytes themselves may be obstructing the passage of aqueous humor through the trabecular meshwork. Eight more had lymphoid aggregates within the trabecular meshwork as well as in the more usual location within the iridal stroma, and we believe that such lymphoid proliferation could also be obstructive. The remaining seven eyes with lymphocytic-plasmacytic uveitis and open ciliary clefts had no histologic lesion to explain the development of glaucoma, although we must admit that the number of leukocytes within the trabecular meshwork sufficient to cause obstruction is unknown. Our decision as to what number qualifies an eye for placement in our “cleft occlusion” category is admittedly arbitrary. Our experience with glaucoma in dogs had not prepared us to seriously consider cleft occlusion by leukocytes as a major category in carnivores since, in dogs, the way in which uveitis causes glaucoma is almost always via posterior synechia with or without iris bombé. In our series, only one kitten with corneal perforation and fibrinopurulent endophthalmitis had posterior synechia as the cause for glaucoma.

Idiopathic, lymphocytic-plasmacytic uveitis, virtually identical to that seen in our series of cats, is the most frequent type of uveitis in human beings. When it leads to glaucoma, it does so via posterior or anterior synechiae, overgrowth of the filtration angle by preiridal vascular membrane or corneal endothelium, or by filling the trabecular meshwork with mononuclear leukocytes. After reviewing some of the photographs of that last group (trabecular filling), it seems to us that the evidence for outflow obstruction caused directly by the leukocytes is weak and mostly arises (as in our cats) from the inability to histologically identify any other cause.

Twenty-eight of the 53 glaucomatous eyes with lymphocytic-plasmacytic uveitis had adhesion of the iridal...
root to adjacent sclera, thereby obliterating the ciliary
cleft and, frequently, creating a false angle within the
peripheral iris. Unlike a typical anterior synechia, the
adhesion was not to the peripheral cornea but to the
sclera posterior to the termination of Descemet's mem-
brane, and there was no other evidence of a resolved
fibrinous exudate (such as posterior synechia or ectro-
pion uveae) that presumably would have preceded the
mature adhesion. Cats seem quite resistant to any type
of iridal adhesion as evidenced by their rarity even in
such exudative uveal diseases as cryptococcosis and
feline infectious peritonitis.12 It is possible that the
iridoscleral adhesion is really just angle compression,
which may occur as a result of chronically elevated
intraocular pressure.13 Based upon our histologic stud-
ies, we are convinced that the iridoscleral adhesion in
most of these cats is the result of a local sclerotic pro-
cess that is limited to the trabecular meshwork, rather
than a result of a generalized exudative process. The
sclerosis draws the root of the iris against the sclera
and thereby eliminates the ciliary cleft. The free por-
tion of the iris is thereby shortened and the iridocorneal
angle rendered more obtuse, giving the clinical impres-
sion of a dilated pupil and a deepened anterior chamber
that were typical clinical observations in this series of
cats.

Our observation of histologically normal iridocor-
neal angles and ciliary clefs in three young cats with
bilateral glaucoma is, to our knowledge, the first his-
tologic evidence to support the clinical evidence for
the existence of primary open-angle glaucoma in
cats.11,13

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