Intraocular Tumors in Animals

II. Primary Nonpigmented Intraocular Tumors

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The present authors (14) have recently discussed intraocular tumors in animals, in a report restricted to primary pigmented neoplasms and based on fifteen such cases in dogs. This was the first comprehensive study of spontaneous intraocular tumors in animals, but because of its restricted scope there remain for consideration other primary and various secondary intraocular tumors. In the present study we are concerned with primary nonpigmented tumors. Secondary tumors will be discussed in a companion paper.¹

Review of literature.—Published reports on primary intraocular tumors in animals are rather scanty. Those on pigmented tumors have already been reviewed (14).

There are three reports on retinoblastomas in horses (2, 6, 10) and one each in a calf (8), a dog (4), a cat (7), a monkey (2), and a chicken (5). Of these, only the reports of Fjellér (6) dealing with horses and of Cole (5) with the chicken are sufficiently detailed to permit appraisal, and both meet the diagnostic criteria for retinoblastomas.

A hemangioma of the iris of a dog was reported by Magrane (9) and submitted by him to the Armed Forces Institute of Pathology. Another case of vascular tumor was seen in the iris of a chicken by Ball (1) and termed by him hemangiendothelioma. Such tumors occur rarely in man; Reese (11) stated that only nine cases have been reported but that six of these are not acceptable. Since so few cases of hemangioma are on record, either from animals or man, we are redescribing (with his permission) Magrane’s case herein in somewhat greater detail.

Tumors of smooth muscle arising from the intraocular structures appear to be rare in man. Reese (11) accepted only three reports unequivocally, and several others with reservations.


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He considered all as benign, i.e., leiomyomas. We have found no report of an intraocular tumor of smooth muscle in an animal. The case of Röder (13), which has been cited by several authors as leiomyoma in the eye of a horse, actually involved the lower lid rather than the globe. A case of muscle tumor of the iris in a dog is described herein.

One of the three cases described here is a tumor of cartilaginous tissue. We have found no report of such a neoplasm in our search of ophthalmic literature. In the veterinary literature there is only the report of Renner (12), who described bilateral “enchondromas” in the eyes of a foal with various other ocular malformations. While his description contained neither a histologic work-up nor illustrations, he was obviously dealing with a group of congenital anomalies, of which the cartilage deposits formed a part, rather than with neoplasms, as he implied.

MATERIALS AND METHODS

The material consisted of three cases submitted to the Armed Forces Institute of Pathology. Embedding and staining technics were as outlined in our previous report (14).

Case 1 (AFIP 59566).²—A 5-year-old male Doberman pinscher dog was presented that had a lesion of the right iris which had been progressively enlarging over a period of 6 months. Clinical examination revealed a swelling of the dorsal portion of the iris that extended anteriorly to the corneal endothelium, filling the dorsal half of the anterior chamber. It extended ventrally half-way down and all the way across the pupil, leaving the latter in the shape of a half-moon (Fig. 1). The unaffected ventral portion of the iris reacted to stimulation by light. The refracting media and fundus were normal, and the dog exhibited no apparent discomfort.

The iridal growth was darkly pigmented, and,
since a malignant melanoma was suspected, it was removed by iridectomy. The extirpated growth measured 10 × 5 × 4 mm. The artificial coloboma of the iris that resulted from the surgery healed well, and there was no recurrence 8 months later.

Histologically, the normal architecture of the iris was obliterated by a mass of vascular spaces separated by a loose collagenous stroma (Fig. 2), in which many pigment-bearing cells were scattered (Fig. 3). No sphincter-bearing muscle fibers were demonstrable (by trichrome staining), but the dilator muscle was largely intact. The majority of the vascular spaces, including some of the largest ones, were lined with only a single layer of mature endothelial cells (Fig. 4), but in some this layer was invested by a few concentric collagen fibers. In one area, near the posterior border of the iris, there was a group of redundant arterioles (Fig. 5). No evidence of mitosis was seen in the lesion. It was diagnosed as a hemangioma.

We have already mentioned that vascular tumors in the eye are a very rare occurrence in man. The tumor reported by Ball (1) from the iris of a 6-month-old chicken was of more solid architecture than the present one, with much smaller vascular spaces and a different cell type. The cells lining the vascular spaces in the avian case were pleomorphic, and mitotic figures were seen. The anaplastic appearance of the cells in Ball's illustration indicates a tumor that may have malignant potentialities, whereas no such possibility could be entertained in our case.

Because of its benign nature, as well as the lack of published cases or similar material for comparison, it is pertinent to consider whether the lesion in our case is a neoplasm at all. Willis (18) states: "Before assuming, then, that any given mass of highly vascular tissue is a truly neoplastic angiomia, the question should be asked: can this be either a vascular malformation, altered maybe by supervening accidental changes, or an extravagant mass of post-traumatic or post-inflammatory reparative tissue, or merely a varicosity or ectasia? The answer will usually be in the affirmative."

In the present case there was no history of trauma or of inflammation, and no histologic evidence was found of either of these conditions. The small group of redundant arterioles seen in one area was probably a vascular malformation, but was totally unlike the bulk of the growth.

Willis admits that "no structural distinction is possible between 'angiomias' and acknowledged vascular malformations..." but states that, "Above all, the common vascular hamartomas have no powers of progressive disproportionate growth. Like any other malformation, the birthmark grows along with the tissues of which it is a blemish; then, unless accidents occur in it, it usually ceases to increase." In our case, the history of 6 months of growth of the tumor in a 5-year-old dog would tend to rule out the type of lesion which is growing concurrently with the normal tissues in a young host. Either the lesion had been growing slowly for 5 years—which would indicate power of "progressive disproportionate growth"—or else, assuming that the history was based on accurate observation, it had been growing for only 6 months in a dog which had been adult for some 4 years. Having duly considered Willis' views, we feel that the data in this case warrant a diagnosis of hemangioma.

Case 2 (AFIP Acc. 125461).—A 2½-year-old male cat was presented for treatment of an unspecified ocular condition which had been present 2 months or longer. The eye was enucleated. The cat died the following week, but no post-mortem examination was made, and the cause of death remains undetermined.

In the gross specimen, the cornea was noted to be opaque. The posterior sclera and optic nerve had been cut off prior to submission for sectioning. Upon incision of the eye, a pale, firm mass streaked with pigment and filling the anterior half of the globe was noted; the lens was not seen.

Histologically, there were three zones in the tumor, which completely filled the globe (Fig. 6). The outermost zone was composed of spindle-shaped cells, an inner one of islands of cartilage, and the central area was occupied by amorphous necrotic material which had presumably been cartilage but was devoid of identifying features. The tumor had destroyed the iris, and the lens was recognizable only by a remaining fragment of capsule. It had infiltrated the cornea on one side, separating Descemet's membrane from the tunica propria; the latter was heavily pigmented. The ciliary processes were firmly entrapped by the surrounding neoplastic growth (Fig. 7). A portion of detached retina was present in the sections. Tumor cells were present in a choroidal vein and in several scleral veins but were not seen in arteries. The peripheral areas of the tumor were composed of spindle-shaped cells, which showed a transition to recognizable chondroblasts as one looked more centrally in the growth. Numerous islands of cartilage were present in which a homogeneous matrix was being deposited (Fig. 8). A few of these showed calcium deposits, i.e., had progressed toward ossification, but the tumor was predominantly composed of cartilage. Mitotic figures...
were numerous in the more actively growing cells near the periphery of the neoplasm (Fig. 9). The tumor was diagnosed as a chondrosarcoma, primary in the eye, probably arising from connective tissue of the uveal tract.

It may appear presumptuous to make a diagnosis of primary uveal chondrosarcoma, and we must concede that such a diagnosis is partly speculative. The evidence for a diagnosis of chondrosarcoma is adequate; however, without an autopsy the possibility that the tumor arose elsewhere in the body and metastasized to the eye cannot be conclusively ruled out. The fact that a relatively slow-growing neoplasm had filled so much of the globe without affecting the general health of the cat is significant. One would expect that, if the ocular tumor were metastatic, the primary neoplasm might have killed the animal before a slow-growing metastatic tumor could have occupied so much of the eye. Also, the absence of involvement of the posterior uvea and its arteries lessens the possibility of intraocular metastasis. We have found no instance on record of a chondrosarcoma with metastasis to the eye in any domestic animal or man. This does not mean that it cannot happen, but it is safe to say that the eye is not a site of predilection for those few chondrosarcomas which do metastasize.

What evidence do we have that the reverse can happen—and that a primary chondrosarcoma can arise from the uvea? Heterotopic ossification has occurred in human eyes in association with inflammation. Sorokoliet (15) found bone in the choroid, lens, or sclera of several enucleated eyes with a history of trauma and cited similar cases from the Russian literature. Reese (11) illustrates a case and cites a personal communication from Ewing of an intraocular osteosarcoma which arose in such an eye. Stow (17) found bone formation in the choroid of a human eye in association with massive hyperplasia of the retinal pigment epithelium. In addition to such spontaneous occurrences, Sorokoliet (16) was able to cause intraocular formation of osteoid tissue in rabbits by experimental intraocular trauma. He stated that the bone arose by metaplasia from pre-existing intraocular connective tissue. Admittedly our thesis would be strengthened by a history or histologic evidence of pre-existing inflammation or trauma, neither of which is available. However, we feel that the demonstrated propensity of the uvea to osteoid formation (neoplastic and otherwise), under the conditions mentioned above, indicates that a closely related primary growth of cartilaginous tissue can arise from the uvea. Whether ours did so we cannot prove; but neither can anyone disprove it.

Case 3 (AFIP Acc. 604524).—The eye of a dog was submitted for sectioning without clinical history or information on its age, sex, or breed. Inside the globe, a tumor had caused considerable thickening of the iris, and an extensive area of necrosis was visible within the neoplasm (Fig. 10). Histologically, the tumor extended posteriorly to involve the base of the ciliary body as far back as the ora serrata, but only the anterior ciliary processes were appreciably thickened by neoplastic infiltration. Anteriorly, the tumor was adherent to Descemet's membrane but had not penetrated it. The constrictor muscle of the iris was almost entirely destroyed by neoplastic cells, but the dilator muscle was preserved.

The cell types in the tumor were similar in both the iris and the ciliary body. Densely packed, spindle-shaped cells, regular in appearance and arranged in whorls or in parallel sheets, predominated (Fig. 11). These surrounded and blended into the large area of necrosis; the edge of this area was vascularized by thin-walled vessels containing blood (Fig. 14). Elsewhere in the tumor the spindle-shaped cells were arranged more loosely, and some plump, oval cells with round or ovoid nuclei were scattered among them (Fig. 13). In such areas of pleomorphism, mitotic figures were observed among the more neoplastic-appearing cells. In areas where the predominating type of cells (i.e., the elongated spindle-shaped ones) were arranged in parallel, the nuclei were elongated, with parallel sides, rounded ends, and finely stippled nucleoplasm (Fig. 12), the hallmarks of smooth-muscle nuclei.

Reese (11) has stated that the criteria which must be present to justify a diagnosis of leiomyoma include: (a) a structure of interlacing, closely packed bundles of elongated, spindle-shaped cells and (b) long, oval nuclei tending to arrange themselves in palisade formation. The appearance of the typical cells in this case conforms to both of these criteria, and the morphology of the nuclei to the distinguishing features of smooth muscle. In addition, the destruction of the constrictor muscle suggests the possibility that the tumor may have arisen from this site. The presence of vascularization, necrosis, and active mitosis in the tumor is indicative of malignancy, and it was therefore interpreted as a leiomyosarcoma of the iris with the extension to the ciliary body and cornea.

We found but one report in the literature of a malignant tumor of muscle in an intraocular site, by Bossalino (3). He described a smooth-muscle
tumor in a 68-year-old woman that arose in the ciliary body and extended to the iris. While Reese (11) lists this case among the leiomyomas, we believe Bossalino's diagnosis of a "malignant leiomyoma," i.e., a leiomyosarcoma, is supported by his histologic evidence.

DISCUSSION

It appears from our previous study (14) that the majority of tumors which arise from a primary site in the eye are either uveal melanomas or tumors of iridal or ciliary epithelium. We stated in our earlier work, based on fifteen pigmented tumors and considerable literature, that the data were as yet too few to disclose the comparative incidence of primary intraocular tumors in animals. This statement regarding the pigmented tumors applies even more strongly to the nonpigmented ones, of which we have only three cases, all different, and on which there are very few published reports. If the situation in animals emulates that in man, it is unlikely that the accumulation of more cases will upset the present preponderance of pigmented over nonpigmented tumors in favor of the latter; but only an awakening of interest in intraocular tumors of animals and the passage of time will tell.

It is unfortunate that the absence of follow-up data in two of our three cases makes it impossible to correlate the histologic appearance of the tumors with their biologic activity. In case 2, diagnosed as a malignant tumor, there was circumstantial evidence that it might have metastasized, since tumor cells were found in the scleral veins and the cat died 1 week following enucleation of the eye.

All the cases in our first paper (14) were in dogs, as well as two out of three in this paper. However, this should not at present be construed as indicative of a higher incidence of intraocular tumors in dogs than in other species of animals. Most of the few veterinarians who are interested in ophthalmology are numbered among those who work with dogs; hence, the material available to us at the AFIP represents their contributions rather than the incidence of intraocular tumors among various animals.

SUMMARY

A review of the literature on primary nonpigmented intraocular tumors of the eye in animals yielded eight reports of retinoblastomas, of which we accepted two unequivocally. One hemangioma of the iris of a dog was on record and is redescribed in detail here. To these are added a case of chondrosarcoma of the globe in a cat and a leiomyosarcoma of the iris and ciliary body in a dog. The former has not been previously reported in an intraocular site. An iridal leiomyosarcoma in a woman is the only prior report of the latter.

ACKNOWLEDGMENT

Thanks are due to Mr. D. K. Winter, who drew the illustration for Figure 1 from a Kodachrome transparency.

REFERENCES

3. BOSSALINO, G. Di una non comune osservazione di leiomma maligno del corpo ciliare e dell'iride. Boll. ocul., 73:392-8, 1934.
FIG. 1.—Tumor of the iris obliterating the dorsal half of the pupil. Case 1. AFIP Neg. 58-3777.

Fig. 2.—Section of iris showing replacement of normal architecture by numerous vascular spaces. Case 1. H & E, X25.

Fig. 3.—Posterior border of iris, from area indicated by arrow in Figure 2, showing group of redundant arterioles. Case 1. H & E, X50. AFIP Neg. 58-3787.

Fig. 4.—Vascular spaces lined by a single layer of endothelial cells. Case 1. H & E, X450. AFIP Neg. 58-3787.

Fig. 5.—Melanin-containing cells in the loose collagenous stroma between endothelial-lined spaces filled with blood. Case 1. H & E, X510. AFIP Neg. 56-11669.
FIG. 6.—Section of eye of cat filled with neoplastic tissue. Case 2. H & E, ×3. AFIP Neg. 59-1440.

FIG. 7.—Intraocular neoplasm surrounding and invading the ciliary body. Case 2. H & E, ×50. AFIP Neg. 58-283.


FIG. 9.—Spindle-shaped neoplastic cells, some of which are in mitosis. Case 2. H & E, ×300. AFIP Neg. 59-1405.
Fig. 10.—Section of iris which is thickened by neoplasia. The lighter area is necrotic tissue. Case 3. H & E, X8. AFIP Neg. 58-14563.

Fig. 11.—Tumor of iris with densely packed cells arranged in whorls and parallel sheets. Case 3. H & E, X100. AFIP Neg. 58-244.

Fig. 12.—Predominating type of neoplastic cells with characteristic smooth-muscle type of nucleus. Case 3. H & E, X1000. AFIP Neg. 58-14560.

Fig. 13.—Area of pleomorphism in iridal tumor. Case 3. H & E, X600. AFIP Neg. 58-14561.

Fig. 14.—Edge of neoplastic tissue blending into area of necrosis, with vascularization of junctional zone. Case 3 H & E, X125. AFIP Neg. 58-14562.
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