

Occurrence and diagnosis of intraocular melanomas in dogs: 6 clinical cases

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Summary

In the present article we report clinical cases of benign and malignant intraocular melanomas in six dogs, two females and four males, of the following breeds: Hovawart, English Cocker Spaniel, American Staffordshire Terrier, Middle Asian Shepherd, and a mix breed. Their age ranged from seven to eleven years. Changes in the eye, observed by the owner before the first contact with a veterinary doctor, persisted for a period of two weeks to six months. All dogs underwent complete ophthalmological examination, ultrasound examination, and, in the cases of enucleation, histological examination. The most common clinical findings were ocular pain, buphthalmos, iris thickening, presence of a mass confined to the iris, irregular pupil, blindness, and secondary glaucoma. Ultrasound examination showed intraocular masses of different size. Another frequent findings were lens subluxation and retinal detachment. According to histological examination, in two out of three enucleated eyes there were benign tumours, and in one, a malignant melanoma. During a period of 9.6 months after surgery we did not observe any recurrence.

Keywords: intraocular melanoma, metastases, dogs, diagnosis

Melanomas belong among the most frequent primary intraocular tumours in dogs (9, 10). They can be histologically malignant or benign. On the basis of a comprehensive study of intraocular melanomas, Wilcock et al and Giuliano et al established a classification, terminology and characteristics of these tumours. The term melanocytoma denotes a benign melanoma in the anterior uvea, limbus and choroidal area. Benign melanocytomas are distinguished from malignant melanomas by nuclear polymorphism, the nucleo-cytoplasmic ratio and the mitotic index (7, 13). A large number of ocular melanomas originate from the anterior uvea, either from the iris or the ciliary body. In the case of large melanoma masses, it is often impossible to histologically determine the primary tumour site (8).

Melanomas are usually distinctly pigmented. In some cases, however, they occur as non-pigmented masses in one of the areas of the uveal apparatus. Iridal thickening, an irregularly shaped pupil, blindness, and severe ocular pain are the most common clinical signs of intraocular melanomas in dogs. Among other effects, massive reproduction of neoplastic cells and their infiltration in the iridocorneal angle result in a secondary glaucoma (5, 12).

Intraocular melanomas are most common in older dogs with an average age of 9 years, but can be found in a rather wide age range of two months to seventeen years. In terms of breed predisposition, a relatively frequent occurrence of melanomas has been reported in German Shepherds and Retrievers. Predisposition with respect to canine sex has not been established (3, 4).

Material and methods

Six dogs (two females and four males) of different breeds (Hovawart, English Cocker Spaniel, American Staffordshire Terrier, Middle Asian Shepherd, German Shepherd, and a mix breed) with intraocular melanomas were diagnosed at the University of Veterinary Medicine and Pharmacy in Košice, Slovakia. Their age ranged from six to eleven years. Data obtained from the medical records included historical information, such the duration of clinical signs, presence of pain and blindness; clinical findings from ophthalmic and general examination; and results of histological examination (Tab. 1). Ocular ultrasonography was performed in all affected eyeglobes by a transcorneal approach using a linear transducer with a frequency of 7.5 MHz (Mindray, DC-6Vet, China). The method of treatment was also reviewed. In all cases, follow-up information was obtained by re-examination. Histological examination was performed in 5 out of 6 eyes: four formalin-fixed globes and one excised

Tab. 1. Characteristics of patients with intraocular melanomas; ocular findings, ultrasonography findings, therapy, histological results and the follow-up period

| Case no. | Breed | Sex Age | Eye | Ocular findings | USG findings | Therapy | Histological results | Follow-up (months) |
|----------|------------------------|---------|-----|--|--|---|--|---------------------|
| 1 | Hovawart | F 7 | OS | Darkly pigmented iris mass (position 10-12 o'clock) with partial deformity of the pupillary opening | Echogenic mass in an area of dark pigmentation | No | No | 6 No progression |
| 2 | English Cocker Spaniel | M 10 | OS | Slight exophthalmos, strabismus, buftalmia; IOP 59 mm/Hg, total corneal opacity | Iris with a hyperechogenic mass causing lens position to change towards the vitreous | Enucleation | Benign melanoma of the iris, ciliary body, and partially choroidea | 15 Clear |
| 3 | Staffordshire Terrier | F 11 | OD | Exophthalmos, buftalmia, eyeglobe deviation, total corneal opacity; IOP 65 mm/Hg | Hyperechoic rounded mass in the vitreous – 19 mm | Enucleation | Benign melanoma with a large number of fusiform cells | 18 Clear |
| 4 | Middle Asian Shepherd | M 8 | OD | Protrusion of the 3 rd eyelid, buftalmia, slight corneal oedema, hyphema, an asymmetric pupillary opening; IOP 60 mm/Hg | Whole iris hyperechogenic, posterior synechia, a mass occupying ¼ of the vitreous | Enucleation | Malignant melanoma with large nuclei; high mitotic activity | 10 Clear |
| 5 | Mix breed | M 10 | OS | Buftalmia, deep scleral vascularization, slight corneal oedema; a darkly pigmented mass on the iris – position 1-5 o'clock; IOP 56 mm/Hg | Hyperechoic iris mass (5 × 8 mm) protruding in the anterior chamber | Local anti – inflammatory + antiglaucomatic therapy | Malignant melanoma | 17 Euthanasia |
| 6 | German Shepherd | M 6 | OS | On the limbus, position 1 o'clock, darkly pigmented and prominent sclera; IOP 17 mm/Hg | Echogenic mass in a darkly pigmented area 3 × 6 mm | Surgical extirpation | Malignant melanoma | 17 Clear |

Explanations: F – female, M – male, OS – left eye, OD – right eye, IOP – intraocular pressure

portion of a globe. Each specimen was dehydrated in 60% ethanol and sliced to give two or more calottes containing the neoplasm and stained with hematoxylin and eosin. Each tumour was classified according to routine histological criteria for melanoma and melanocytoma (mitotic index, pigmentation, tumour cell necrosis and growth pattern).



Fig. 1. A dog, Hovawart, female, 7 year old; on the iris of the left eye, within the area between 10 and 12 o'clock is darkly pigmented mass, with its border partially extending also into the area of pupillary opening; pupillary opening is partially deformed

Clinical case no. 1. A 7-year-old female Hovawart. The owner stated that the colour of the dog's left iris had been changed for approximately 6 months (Fig. 1).

Clinical examination. Ophthalmological examination revealed a darkly pigmented mass (opaque under intensive light) in the area between 10 and 12 o'clock, with its border partially extending also into the area of the pupillary opening. The pupillary opening was partially deformed. The cornea, anterior chamber, and posterior segments were free of



Fig. 2. Usg findings in a Howawart dog: occurrence of an echogenic mass in the area where the tumour was localized, without overgrowth or deformation of the posterior wall of the iris or the ciliary body

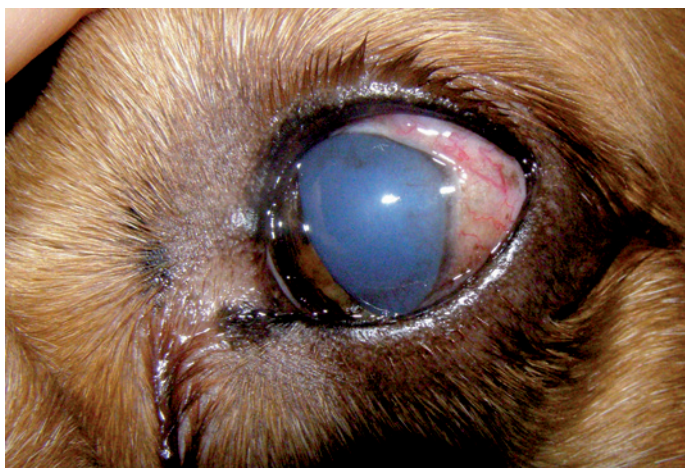


Fig. 3. A dog, English Cocker Spaniel, male, 10 year old; left eye with the slight exophthalmos, strabismus and buphthalmia; deformity of the sclera at 2 o'clock position; cornea is completely opaque, occurrence of deep vascularization penetrated into the cornea along the entire perimeter of the limbal ring

pathological findings. The intraocular pressure was 25 mm/Hg. Ultrasound examination (7.5 MHz probe) revealed an echogenic mass in the area where the tumour was located, without overgrowth or deformation of the posterior wall of the iris or ciliary body.

Given the results of the clinical examination, the owner was advised to monitor the changed site and have the patient examined without delay in case any change was detected.

No further growth of the mass in the area of the iris had been observed since the initial diagnosis made 6 months earlier.

Clinical case no. 2. A 10-year-old male English Cocker Spaniel. According to the owner, the dog had suffered from pain in the left eye for approximately one month, and the colour of the cornea had gradually changed (Fig. 3).

Clinical examination. Ophthalmological examination showed a slight exophthalmos, strabismus and buphthalmia in the left eye, as well as a deformed sclera at 2 o'clock. The cornea was completely opaque because of endothelial oedema, and deep vascularization penetrated into the cornea along the entire perimeter of the limbal ring. The conjunctivas were strongly hyperaemic, and deep vessels could be observed in the sclera. The eye was affected by a secondary glaucoma; the intraocular pressure was 59 mm/Hg. The other segments of the eye could not be examined ophthalmologically because of the opaqueness of the cornea. An ultrasound examination was performed with a 7.5 MHz probe, by which an 8 mm × 15 mm hyperechoic mass was identified in the area of the iris. The mass was causing the position of the lens to change towards the vitreous humour.

The patient underwent enucleation. Histological examination confirmed the presence of a benign melanoma developing through the tissue of the iris and ciliary body, and reaching the choroidea.

The last check-up of the patient – 15 months after the surgery – showed no recurrence.

Clinical case no. 3. An 11-year-old female Staffordshire Terrier. Having been diagnosed with a glaucoma of the right eye, not responding to therapy, the dog was referred by the

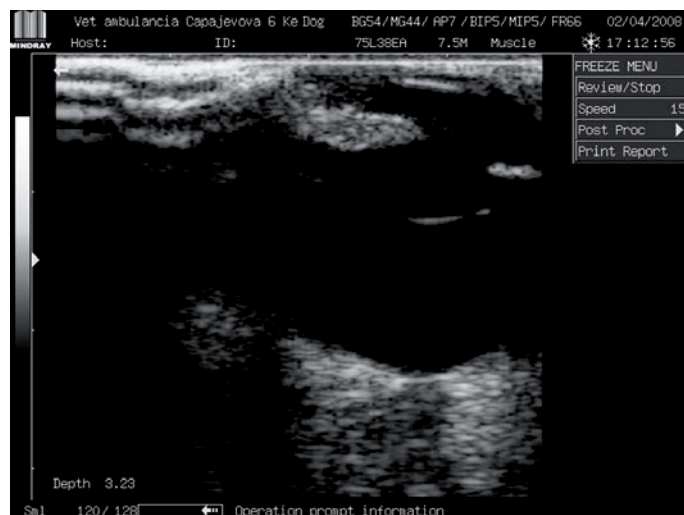


Fig. 4. Usg findings in a English Cocker Spaniel; in the area of iris is present hyperechoic mass, which cause changes in lens position to the vitreous

veterinarian for a specialist eye examination. The eye condition lasted for approximately 3 months.

Clinical examination. Even by unaided visual examination, a right-sided lateral deviation of the eyeball with exophthalmos and buphthalmia were clearly identifiable. The eye was painful, diffusely opaque with the presence of deep vascularization around the entire perimeter, about 1 cm from the limbal ring. The lower third of the cornea showed pigmentation. A slight protrusion of the third eyelid and intense conjunctival hyperaemia combined with deep scleral vascularization indicated a serious intraocular problem. The measured intraocular pressure was 65 mm/Hg.

To identify precisely the dimensions and location of the mass, an ultrasonographic examination was performed with a 7.5 MHz probe. A hyperechoic rounded mass with a di-

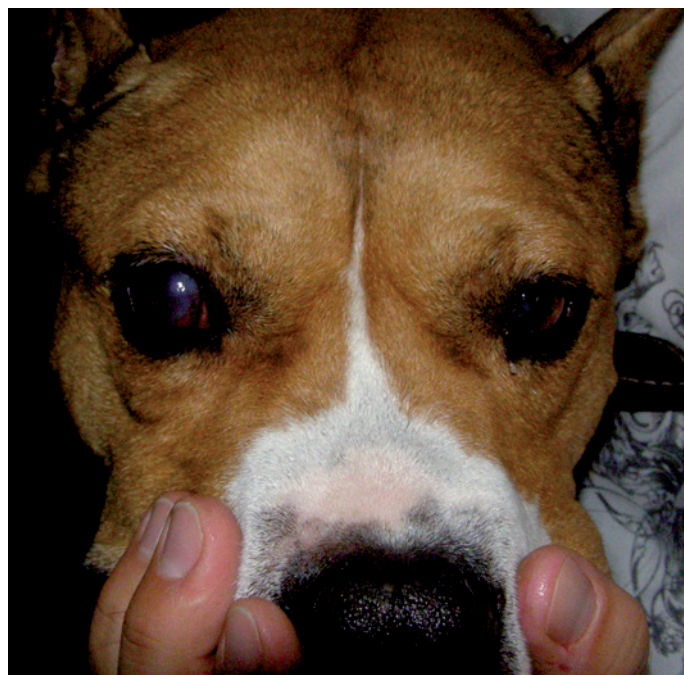


Fig. 5. A dog, Staffordshire Terrier, female, 11 year old; right-sided lateral deviation of the eyeball with exophthalmos and buphthalmia



Fig. 6. Detailed picture of the right eye of Staffordshire Terrier: cornea is edematous not transparent, partially pigmented; conjunctiva with chemosis and hyperemia

ameter of 1.9 cm was detected in the area of the vitreous humour. It was touching the posterior lens capsule, pushing it slightly towards the anterior chamber of the eye. The lens was affected by a cataract. The rest of the vitreous humour was altered in terms of echogenicity as a result of bleeding from the retinal area and tumour. The retina was partially detached (Fig. 5, 6).

Owing to the adverse condition the eye was subjected to enucleation.

Histological examination showed a melanoma developing through the entire retina. Although it was a benign tumour, given the large number of fusiform cells, an inconclusive prognosis was determined (a less differentiated form of neoplasm).

No recurrence was observed in the patient 18 months after the surgery.



Fig. 8. Macroscopic picture of enucleated eye of Staffordshire Terrier; in the vitreous is visible pigmented mass

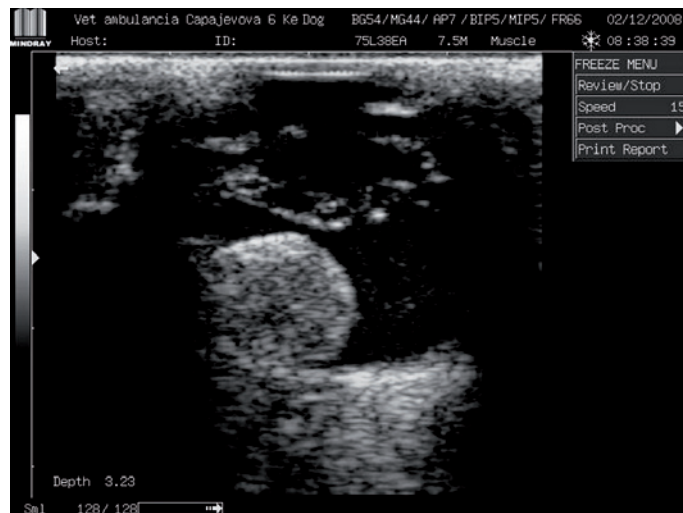


Fig. 7. Usg findings in a Staffordshire Terrier – in the vitreous is hyperechoic rounded mass, touching the posterior lens capsule; changes in vitreous echogenicity due to bleeding from the retinal area and tumour; retina is partially detached

Clinical case no. 4. An 8-year-old male Middle Asian Shepherd. The owner consulted a veterinarian because of a change in the size of the dog's eye that he had noticed two weeks earlier (Fig. 9).

Clinical examination. Ophthalmological examination revealed buphthalmia of the right eye with a mild protrusion of the third eyelid. The eyeball was severely painful, with hyperaemic and swollen conjunctivas. It was possible to perform an examination of the anterior chamber of the eye through slight oedema, showing a shallow anterior chamber with the presence of minor hyphaema. The iris was irregularly thickened, apparently adherent to the anterior lens capsule (posterior synechia, which caused the "iris bombé"), the pupillary opening was asymmetric, and the eye did not respond to direct or indirect pupillary reflexes. The measured intraocular pressure was 60 mm/Hg;



Fig. 9. A dog, Middle Asian Shepherd, male, 8 year old; left eye is buphthalmic, with slight protrusion of the third eyelid; conjunctiva is hyperemic and swollen; cornea is slightly edematous, anterior chamber is shallow, with hyphema; iris with irregular surface, and pupillary opening is asymmetric



Fig. 10. Usg findings in a Middle Assian Shepherd: the whole iris tissue is hyperechoic, with posterior synechia (causing „iris bombé“); in the medial part of vitreous is mass occupied $\frac{1}{4}$ of the vitreous

the eye was affected by a secondary glaucoma. The other parts of the eye could be examined only by an ultrasound device with a 7.5 MHz probe. The ultrasound examination showed an iris altered hyperechoically around its entire perimeter, as well as posterior synechia. The echogenicity of the vitreous humour was also altered, and the lens was affected by a cataract.

The patient underwent enucleation. Histological examination confirmed a malignant melanoma in the area of the iris, ciliary body, and choroidea. A massive invasion of the entire intraocular space by the tumour made it impossible to identify the primary site.

This malignant tumour of the iris was characterized by the presence of large irregularly shaped nuclei with abnormal chromatin clumping and a number of mitotically active nuclei.

The next check-up of the patient was performed 10 months after the surgery, showing no signs of recurrence.

Clinical case no. 5. A 10-year-old male mix breed. The owner had observed gradual enlargement of the left eye for about two months (Fig. 11).

Clinical examination. A visual examination of the dog clearly showed buphthalmia of the left eye. The eye was severely painful, with strongly hyperaemic conjunctivas and the presence of deep vessels in the sclera. A slight degree of oedema in the entire corneal stroma made it possible to perform an examination of the other intraocular structures. The eye did not react in terms of the defensive reflex, and direct and indirect pupillary reflexes were absent as well. The pupil was dilated and had an irregular shape. The anterior chamber was shallow, and a darkly pigmented mass was observed in the iris between one and four o'clock, partially extending into the pupillary aperture in the three o'clock area. The intraocular pressure in the left eye was 56 mm/Hg. The eyeground showed changes caused by persistently elevated intraocular pressure, namely the optic nerve atrophy with changed colour and retinal vessel attenuation. An ultrasound examination with a 7.5 MHz probe revealed a 0.5 mm thick and 8 mm long hyperechoic mass in the area of the iris between one and five o'clock, protruding only



Fig. 11. A dog, mix breed, male, 10 year old; left eye is buphthalmic, conjunctiva with severe hyperemia, occurrence of deep scleral vascularization, cornea affected with slight diffuse oedema; pupil is in mydriasis with irregular shape; anterior chamber is shallow, on the iris – position 1 o'clock the iris between one and four o'clock, partially extending into the pupillary aperture in the three o'clock area

into the area of the anterior chamber and slightly extending over the pupillary aperture. The other parts of the eye showed no pathological ultrasonographic findings.

As the owner refused enucleation, a suggestion was made to proceed with antiglaucomatic and anti-inflammatory local therapy. Seventeen months after the ophthalmological examination, the dog was euthanized because of gastric volvulus and unfavourable prognosis. The owner agreed to a histological examination of the eye. The histological sample showed a 2nd grade malignant melanoma present in the area of the iris with a 0.5×0.2 cm penetration into the corpus ciliare.

Clinical case no. 6. A 6-year-old male German Shepherd. The owner had observed changes in the sclera and in the iris of the left eye for about two months (Fig. 12).

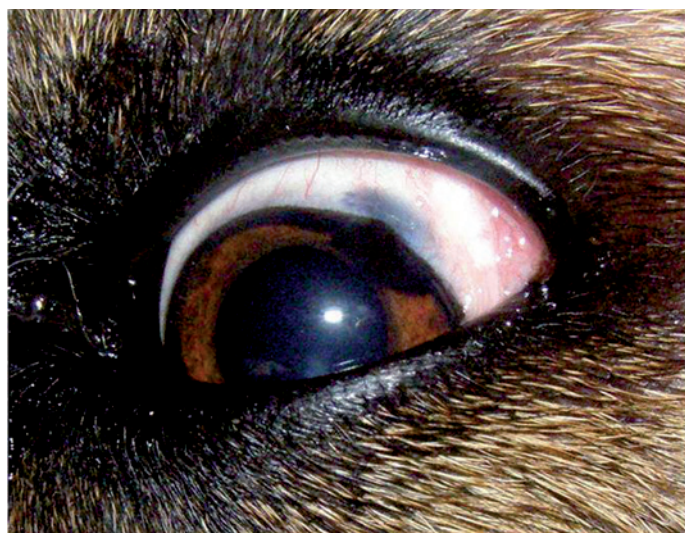


Fig. 12. A dog, German Shepherd, male, 6 year old; sclera of the left eye in area of one o'clock at the level of limbus is darkly pigmented and slightly prominent; in the area of one o'clock a darkly pigmented mass protruded from the iris to the anterior chamber of the eye; cornea is slightly opaque at the affected part



Fig. 13. The same dog as on the fig. 12, 2 weeks after the surgery; presence of the conjunctival flap, around the flap cornea is slightly opaque with vascularization; no evidence of other anterior uveitis

Clinical examination. The colour of the left eye sclera in the area of one o'clock at the level of the limbus was changed – darkly pigmented – and it was slightly prominent. The extent of the lesion was 3×1.5 mm. In the area of one o'clock, a 4×2 mm darkly pigmented mass protruded from the iris into the anterior chamber of the eye. The cornea was slightly opaque at that site. The anterior chamber was shallow at the affected site. The pupil was in medium mydriasis. The eyeground showed no pathological changes. The intraocular pressure in the left eye was 17 mm/Hg. An ultrasound examination with a 7.5 MHz probe revealed a 3×6 mm mass in the area of one o'clock, growing out of the ciliary body. No infiltrates were identified in the area of the vitreous humour. The rest of the iris was intact. Given a favourable evaluation of the operability of the tumour, a recommendation was made to resect it. The surgery was performed at the Veterinary University of Vienna, where the tumour was successfully removed (Fig. 13). Histological examination confirmed an iridocilliary malignant melanoma.

Subsequent check-ups of the dog were performed at our clinic. No signs of recurrence were clinically identified for a period of 1.5 years after the surgery.

Discussion

Intraocular tumours are relatively infrequent eye diseases in dogs. When they do occur, they can be primary or secondary – metastasising from other organs – or locally invasive (2). Although all uveal melanomas and melanocytomas are potentially malignant, most are benign. Metastases from primary intraocular melanomas are quite rare too, although they result in significant damage to that tissue and a secondary glaucoma in the eye itself (10).

With regard to differential diagnosis, intraocular melanomas must be distinguished from other intraocular masses, such as iris cysts, granulomatous lesions and staphylomas. Clinical differentiation is important because the prognosis and therapy of iris cysts are different from those of melanomas. A characteristic feature

of cysts is that they are translucent. Another supportive examination is an ultrasonographic examination, which – in the case of larger masses – makes it possible to distinguish a cyst from a tumorous tissue, as well as to evaluate the extent of the tumour (9, 11). Potential occurrence of tumours must also be considered in all patients with glaucoma and corneal opacity.

The first clinical signs observable by the owner include a changed iridal colour and the presence of a mass in the affected eye. If the owner does not notice these initial changes, and the development of malignant changes causes uveitis and glaucoma, the history will then include information about a “red eye” or enlarged eyeball. Changed iridal colour and the presence of masses in the iris are sometimes detected by a veterinarian in the course of a normal clinical examination.

Unlike in cats and humans, melanomas in dogs have a tendency towards nodular growth rather than diffuse infiltration. Clinical examination may show them focal, but only in the iris, or having an extensive character (12). Large masses often cause bulging in the area of the pupillary aperture (clinical cases no. 1, 4 and 5), pushing the iris forwards and causing dyscoria. Regular findings by clinical examination include focal or diffuse iridal thickening, irregularly shaped iris, blindness and eye pain of various intensity. Although the melanomas were pigmented in all patients, melanomas in dogs may, in rare cases, also be amelanotic. In addition to the above, the clinical signs observed in the patients also included keratitis, anterior uveitis, hyphaema, secondary glaucoma, buphthalmia and retinal detachment.

Intraocular melanomas of the anterior uvea are often locally invasive, with a tendency to grow over to the choroidea, sclera, iridocorneal angle or the orbit. Findings frequently include lens subluxation caused by massive tumour growth.

Tumour cells – melanocytes or melanin containing cells – often float in the anterior chamber, giving rise to a secondary glaucoma due to the infiltration or obstruction of the iridocorneal angle (8, 10).

In terms of histological characteristics of tumours, it has been reported that malignant melanomas constitute approximately 20% of all intraocular melanomas. Malignant tumours are characteristic for their less distinct pigmentation (13).

Metastases occur by way of hematogenous spread and can be microscopically identified as neoplastic cells in the sclera and optic disc. Similarly to other tumours, cytological characteristics (i.e. the mitotic index, nuclear pleomorphism and the nucleus to cytoplasm ratio) are also important in the case of uveal melanomas, indicating the degree of their malignancy.

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