

Journal of the Hellenic Veterinary Medical Society

Vol 70, No 1 (2019)



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doi: [10.12681/jhvms.20355](https://doi.org/10.12681/jhvms.20355)

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To cite this article:

PAPAVASILEIOU, E., & DURIEUX, P. (2019). Ciliary body cysts associated with glaucoma in a Great Dane. *Journal of the Hellenic Veterinary Medical Society*, 70(1), 1455–1460. <https://doi.org/10.12681/jhvms.20355>

Ciliary body cysts associated with glaucoma in a Great Dane

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ABSTRACT. An 8-year-old female Great Dane, was referred to the Ophthalmology Unit of the Centre Hospitalier Vétérinaire (CHV) des Cordeliers, for corneal opacity of the left eye that did not respond to topical treatment, administered by the referring vet. On initial examination, bilateral ciliary body cysts were noticed. Lens subluxation, pseudo-plateau iris and glaucoma were observed on the left eye. The diagnosis was confirmed by applanation tonometry and high resolution ocular ultrasonography. Medical treatment resulted in temporary clinical improvement of the left eye. No signs of glaucoma were observed on the right eye upon the last re-check examination.

Keywords: glaucoma, ciliary body cyst, Great Dane.

ΠΕΡΙΛΗΨΗ. Σκύλος οκτώ ετών, θηλυκός ακέραιος, φυλής Great Dane, παραπέμφθηκε στην Οφθαλμολογική Μονάδα του Centre Hospitalier Vétérinaire (CHV) des Cordeliers με συμπτώματα θόλωσης του κερατοειδούς του αριστερού οφθαλμού, μη ανταποκρινόμενη σε τοπική αγωγή, που χορηγήθηκε από τον θεράποντα κτηνίατρο. Κατά την κλινική εξέταση, παρατηρήθηκαν κύστεις του ακτινωτού σώματος αμφοτερόπλευρα. Επιπλέον ο αριστερός οφθαλμός παρουσίαζε υπεξάρθρωμα του κρυσταλλοειδούς φακού, ίριδα ψευδο-plateau και γλαύκωμα. Η διάγνωση επιβεβαιώθηκε με μέτρηση της ενδοφθάλμιας πίεσης και υψηλής ευκρίνειας οφθαλμολογικό υπέρηχο. Μετά την έναρξη της φαρμακευτικής αγωγής παρατηρήθηκε παροδική ύφεση των συμπτωμάτων στον αριστερό οφθαλμό, ενώ δεν παρατηρήθηκε εικόνα γλαυκώματος στον δεξιό οφθαλμό έως και κατά την τελευταία επανεξέταση.

Keywords: γλαύκωμα, κύστη ακτινωτού σώματος, Great Dane

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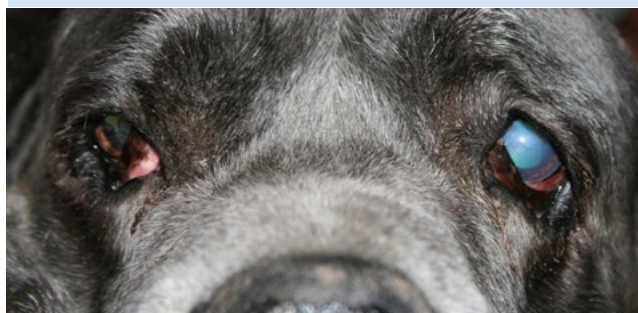
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Date of initial submission: 01-05-2018
Date of revised submission: 01-05-2018
Date of acceptance: 28-08-2018

CASE HISTORY

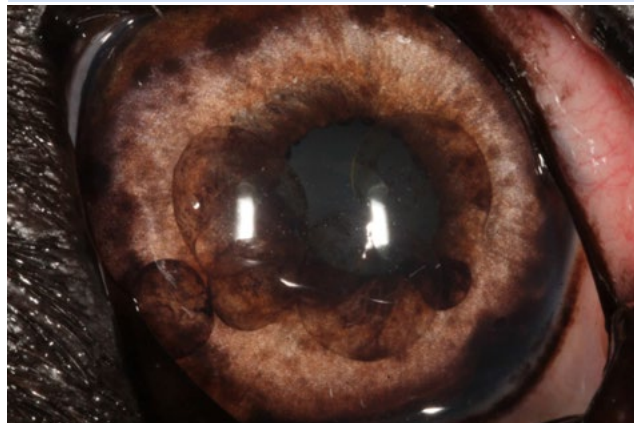
An 8-year-old female Great Dane was referred to the Ophthalmology Unit of the CHV des Cordeliers for corneal opacity of the left eye (OS) evolving over the last month. Topical treatment with framycetine and dexamethasone ointment (Fradexam®, TVM) prescribed by the referring veterinarian did not lead to clinical improvement. No history of uveitis or trauma was reported. An ophthalmic examination was performed. The OS was buphthalmic. Visual loss of the OS was evidenced during the obstacle course. Menace response, dazzle reflex and direct pupillary reflex were negative on the left eye (OS), and positive on the right eye (OD). The indirect pupillary reflex was negative in both eyes (OU). At slit lamp examination (SL-15, Kowa, Torrance, CA, USA) of the OD, multiple ciliary cysts were noticed in the anterior chamber and in the posterior chamber after dilation with tropicamide (Tropicamide®, VIDAL). Iris discoloration was evidenced (Figure

Figure 1. Buphthalmos and corneal oedema are noted on the OS. Ciliary body cysts are visualised in the anterior chamber of the OD.



1). Incipient cataract was noticed. The intraocular pressure (IOP), as measured by applanation tonometry (Tono-pen Vet, Medtronic Solan, Jacksonville, FL, USA), was 12 mmHg on the OD, as opposed to 56 mmHg on the OS. The OS presented buphthalmos. At slit lamp examination, conjunctival and episcleral vessels were hyperaemic and tortuous and diffuse endothelial oedema was also seen in the cornea (Figure 2). Multiple ciliary cysts were visualized in the anterior and posterior chamber. Mydriasis and dyscoria were also noted.

Figure 2. The OD presents multiple ciliary body cysts in the anterior chamber. Note the iris depigmentation.



Lens subluxation was evidenced. The lens was displaced towards the nasal quadrant, without any significant anterior or posterior displacement. Pigment deposition on the anterior capsule of the lens was noticed. Fundus examination with indirect ophthalmoscopy showed media opacity. Gonioscopy (Koeppe pediatric lens) was not easily performed on the OD since it was impeded by the uveal cysts; however, a narrow angle was evidenced.

High resolution ocular ultrasonography (MyLab Sat, Esaote, Genova, Italy, linear 22 MHz probe) was performed on both eyes (OU). The antero-posterior axis measured was 22mm and 26mm on the OD and the OS, respectively. Multiple ciliary cysts, measuring between 2 and 5 mm, were present in the anterior and posterior chamber OU. Cysts located on the level of the iridociliary junction led to anterior displacement of the iris, and consequent angle closure and ciliary cleft collapse (pseudo-plateau iris) on the temporal quadrant of the OS (Figure 3). The OS presented increased corneal thickness and hyper-echogenicity and the anterior chamber was hyper-echogenic. The lens presented cortical hyper-echogenicity. The increased distance between the lens and the ciliary body, the flattened ciliary body and the round silhouette of the lens in the temporal quadrant confirm the zonule rupture and lens subluxation. The vitreous presented hetero-echogenicity and excavation of the optic disc was noted. On the OD, cysts were also located in the posterior segment (Figure 4). Hyper-echogenicity of the anterior lens pole and equator was observed.

Due to the severity and chronicity of glaucoma

Figure 3. US image of the temporal quadrant of the OS. Note the increased corneal thickness and hyperechogenicity, the cysts in the posterior chamber, the iris angulation, the lens subluxation and hyperechogenicity and the hyperechogenic vitreous chamber.

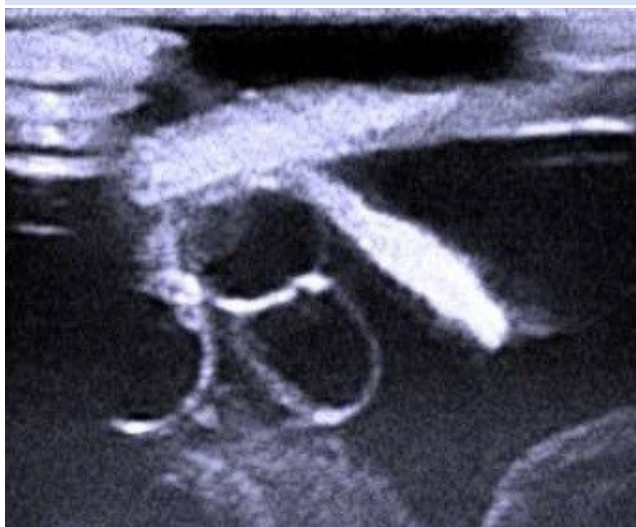
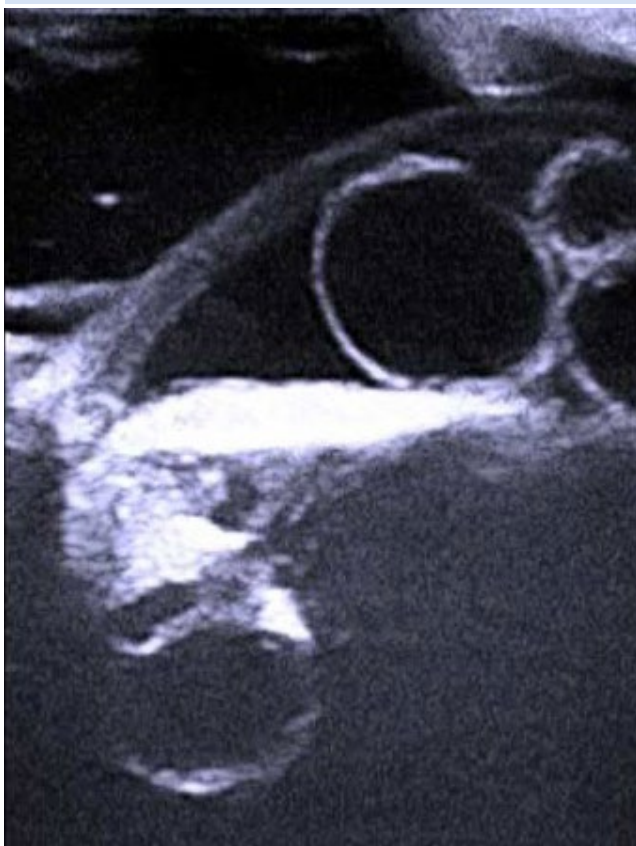


Figure 4. US image of the temporal quadrant of the OD. Multiple cysts are present in the anterior and posterior chamber. Note the presence of one cyst in the posterior segment.



on the OS, the options discussed included intrascleral prosthesis, cyclodestructive procedures, or enucleation. For the OD, needle-aspiration of the cysts and regular follow-ups were suggested. However, the owner did not opt for the surgical recommendations and medical treatment was initiated. Prednisone (Dermipred 20®, VIDAL) at an initial dose of 1 mg/kg PO q 24 h followed by gradual reduction over a three-week period, dorzolamide and timolol ophthalmic solution (Cosopt®, VIDAL) OS TID, travoprost ophthalmic solution (Travatan®, VIDAL) OS BID and retinol and lanoline ophthalmic ointment (Vitamine A Dulcis®, VIDAL) OS BID were prescribed.

Upon the three-week recheck examination, the IOP was 18 mmHg on the OS and 12 mmHg on the OD. The corneal oedema previously reported on the OS had resolved and buphthalmos was less evident. However, vision loss was still evidenced. Prednisone was discontinued. The prescription of local treatment was renewed and a recheck examination in three weeks was recommended.

The patient was re-presented two months later. The OS presented ocular hypertension at 43 mmHg, while the IOP of the OD was of 12 mmHg. Buphthalmos, corneal oedema and vision loss of the OS were noticed. Surgical options were discussed and a date was set for the enucleation of the OS. However, the dog was not presented for surgery on the fixed date.

DISCUSSION

This is the second report in the literature of glaucoma associated with ciliary body cysts in the Great Dane (Spiess et al., 1998). Although uveal cysts are a frequent incidental finding in veterinary ophthalmology, especially in Golden Retrievers, Labrador Retrievers and Boston Terriers (Hendrix, 2013), there are only a few reports of cystic glaucoma. Three breeds have been reported to develop cystic glaucoma: the Golden Retriever (Plummer et al., 2013), the American Bulldog (Pumphrey et al., 2013), and the Great Dane (Spiess et al., 1998). In the Great Dane, glaucoma appears as a result of pseudo-plateau iris, due to mechanical anterior displacement of the iris by multiple ciliary body cysts located in the posterior chamber, and pre-iridal fibrovascular membranes (PIFMs) (Spiess et al., 1998).

On high-resolution ocular ultrasonography, pseudo-plateau iris configuration was evidenced on the temporal quadrant of the OS. Plateau iris configuration consists of anterior displacement of the peripheral iris, placing it in apposition with the trabecular meshwork and leading to angle narrowing or closure, with a flat iris plane from pupil to periphery and a normal central anterior chamber depth (Stamper et al., 2009). Plateau iris syndrome is defined as the persistence of this configuration following patent iridotomy (Stamper et al., 2009). Pseudo-plateau iris refers to plateau iris configuration that is caused by cysts in the posterior chamber (Stamper et al., 2009). It is among the most probable etiopathogenic mechanisms of cystic glaucoma in the Great Dane. Ciliary body cysts have been associated with plateau iris syndrome and glaucoma in humans (Azura et al., 1996; Crowston et al., 2005; Le corre et al., 2009; Kitouni et al., 2015). In human medicine, whether or not cysts are inclined to cause angle closure depends on the number, size and location of the cysts. It has been reported that only an angle closure greater than 180° may lead to glaucoma (Ispa-Callen et al., 2009). Moreover, cysts larger than 0.8 mm located at the iridociliary sulcus may also be responsible for angle closure (Wang and Yao, 2012), and among eyes with angle closure, cyst size in patients with multiple cysts was significantly smaller than in patients with a single cyst (Maraone et al., 2014). To the authors' knowledge, there is no data regarding the extent of closure necessary to affect the IOP in dogs.

Pre-iridal fibrovascular membranes (PIFMs) have been associated with glaucoma in human and animal patients (Plummer et al., 2013). They were histologically identified in all eyes of the Spiess et al. study (1998) and were considered another possible etiopathogenic mechanism of glaucoma in association with pseudo-plateau iris. A study showed that in human patients with neovascular glaucoma, the non-pigmented ciliary epithelium has been identified as an essential source of synthesis of vascular endothelial growth factor (VEGF) (Chalam et al. 2014), which is also the predominant vasogenic protein responsible for PIFMs in dogs (Grahm and Peiffer, 2013). Further research would be needed to evaluate the effect of ciliary body cyst formation on the synthesis of VEGF.

Lens subluxation was observed on the OS. In glaucomatous eyes with lens luxation, it may be challenging to precise if glaucoma is primary or secondary to the lens luxation. Various changes associated with lens luxation, such as pupillary block or substantial amounts of prolapsed vitreous obstructing the aqueous outflow and secondary uveitis, may be responsible for the development of glaucoma, and lens luxations are among the most frequent causes of secondary glaucoma in the dog. However, Great Danes are not predisposed to lens luxation (Davidson and Nelms, 2013) and the contralateral lens was not luxated, neither presented instability. Moreover, subluxations, as observed in our case, are more commonly secondary to buphthalmia, due to stretching and eventual rupture, tearing or disinsertion of the ciliary zonules (Plummer et al., 2013). Thus, the lens subluxation on the OS appears to be secondary to glaucoma rather than the primary cause. However, three voluminous cysts were located on the temporal quadrant and may also be responsible for the zonule rupture [a rare complication reported in human literature (Lois et al., 1998)].

Diagnosis of ciliary body cysts in this case report was based on clinical appearance and was confirmed by high-resolution ocular ultrasound. Transillumination of the cysts with a bright light source is another method to differentiate cysts from neoplasms, and was performed for cysts in the anterior chamber. However, high-resolution ocular ultrasound presents higher sensitivity and sensibility (Hendrix, 2013). Ultrasound biomicroscopy has been reported as effective in the diagnosis, size evaluation and localisation of ciliary body cysts in humans (Maraone et al., 2014) and more effective than standard ocular ultrasonography (7 to 12 MHz) in the detection of canine uveal cysts (Taylor et al., 2015); thus, it may consist the method-of-choice for early diagnosis of cyst formation or detection of small-size cysts on the contralateral eye, especially in human patients that usually present smaller-size cysts [0.6547 ± 0.2319 mm (Wang and Yao, 2012), 0.81 ± 0.35 mm (Maraone et al., 2014)]. However, its use may be impractical for animal patients, as heavy sedation or general anaesthesia may be required. To the authors' knowledge, this is the first report that provides ultrasound images for ciliary

body cysts associated with pseudoplateau iris and glaucoma in the Great Dane.

Several treatment options are available depending on the stage of the disease, but they can be divided in three large groups: treatment addressing the cysts, the plateau iris configuration and the glaucoma.

Uveal cysts are usually benign, however, in case of pupil occlusion or angle closure, cyst removal is necessary. Cyst puncture and aspiration of the cyst content resulting in cyst wall collapse can be performed using a small-gauge needle (Hendrix, 2013), especially if few large cysts are responsible for the angle closure (Stamper et al., 2009). Ciliary body cysts are usually not amenable to deflation by semiconductor diode lasers (Hendrix, 2013). However, in human literature, it has been suggested that Nd-YAG laser cystotomy may be effective (Stamper et al., 2009). There is no data in the literature regarding the incidence of glaucoma among Great Danes that present ciliary body cysts. The report of Spiess et al. (1998) and a recent human study (Xue et al., 2017) showed correlation between cysts and glaucoma, and uveal cysts and elevated IOP, respectively, indicating that extended follow-up would be appropriate for these patients and should include IOP monitoring.

Argon laser iridoplasty (Crowston et al., 2005; Ang et al., 2008; Ispa-Callen et al., 2009) and endocycloplasty (ECPL) (Pathak-Ray and Ahmed, 2016) are both techniques that alter the iridocorneal

apposition observed in pseudo-plateau iris, and they have been documented as effective in some human patients. However, recurring cysts and secondary angle closure following laser iridoplasty have been reported (Ispa-Callen et al., 2009; Pathak-Ray and Ahmed, 2016), and anatomical differences between dogs and humans, such as Schlemm's canal, may result in different success rates.

Medical glaucoma therapy alone for the narrow- or closed-angle glaucomas is usually ineffective in the long term (Spiess et al., 1998; Hendrix, 2013; Plummer et al., 2013), but, it is often necessary pre- and post-operatively (Plummer et al., 2013), in order to maintain the IOP within the target levels, after pseudo-plateau iris has been addressed. Surgical techniques, such as gonio-implants, trans-scleral laser cyclophotocoagulation or cyclocryotherapy, may consist alternative or adjunctive therapeutic choices (Hendrix, 2013).

In summary, although uveal cysts are a common incidental finding, they may be associated with glaucoma in the Great Dane. High-resolution ocular ultrasound is useful in the diagnosis of cysts and pseudo-plateau iris.

CONFLICT OF INTEREST

None of the authors of this article has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper. ■

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