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Irreversible Ocular Lesions in a Dog With *Angiostrongylus Vasorum* Infection

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A B S T R A C T

This report describes a 10-month-old dog with a sudden loss of vision and severe dyspnoea. The ocular examination revealed bilateral panuveitis, lens subluxation, secondary glaucoma, and retinal detachment. In addition, the ocular ultrasound showed in the vitreous body of the right eye, a small doubled-lined foreign body compatible with an intraocular parasite. Radiographs of the thorax revealed an increased opacity with mixed lung pattern (alveolar and bronchial) and thoracic ultrasonography showed several subpleural nodules. The presence of *Angiostrongylus vasorum* first stage larvae was confirmed with 324 larvae per gram of feces and an antigen test for the parasite (AngioDetect, IDEXX) also yielded a positive result. The severe and irreversible ocular lesions described in this case enhanced the complexity of the clinical picture of canine angiostrongylosis. Infection with the parasite should be included in the list of differential diagnoses for ocular uveitis to avoid potentially serious complications related to a missed or delayed diagnosis.

Introduction

Angiostrongylus vasorum (*A. vasorum*) is a metastrongylid nematode that inhabits the right ventricle of the heart, pulmonary artery, and its branches in domestic dogs and wild canids.[1] As a disease with substantial animal health impact, canine angiostrongylosis remains a high priority for clinicians and researchers.[2,3] Infected dogs usually exhibit signs of respiratory and cardiovascular disease, coagulopathies, and occasionally neurologic signs, with fatal consequences in severe cases.[4,5] However, the variety of the clinical signs, not all correlated with classical respiratory distress, has given canine angiostrongylosis the name of a "great imitator," leading to a delayed diagnosis of the infection.[6-8] Diagnosis of *A. vasorum* in dogs may be challenging due to the presence of subclinical infections and because of the wide range of clinical signs.[4] Ocular manifestations of infection are sporadically reported and have serious implications in infected dogs, although ocular lesions previously reported in the literature have been suggested to disappear after treatment.[9-12] The present report describes a case of angiostrongylosis in a dog with irreversible ocular lesions.

Case Presentation

A 10-month-old female, mixed breed dog was referred to the Veterinary Teaching Hospital of the Department of Veterinary Medicine and Animal Production, University of Naples Federico II, for a 2 week history of lethargy and occasional coughing especially in the evening. Despite antibiotic treatment (marbofloxacin, Marbocyl, Vetoquinol) prescribed by a practitioner, 2 days before, the clinical condition worsened and, moreover, the owners noted a sudden visual loss. The dog had been dewormed and had begun routine vaccinations against geographically common infectious diseases at 8 weeks. He received 2 multivalent vaccinations (including distemper, hepatitis, parvo, and lepto) 4 weeks apart.

At the clinical examination, the dog showed poor general condition, dehydration, dyspnoea, and melena. Mucous membranes were pale and the capillary refill time was normal (<2 seconds). The rectal temperature was 38.9°C. Routine hematology, a biochemical profile, prothrombin time, and active partial thromboplastin time were carried out (Tables 1 and 2). Ophthalmic examination revealed a moderate buphthalmos with marked palpebral and bulbar conjunctival hyperemia and scleral injection in both eyes. Slit-lamp biomicroscopy (SL-15, Kowa) revealed peripheral corneal edema and mild aqueous flare in both eyes; iridal thickening was evident, with pigment dispersion on the anterior lens capsule, and bilateral lens subluxation was present with evidence of an inferior aphakic crescent (Fig 1). The left and right fundus could not be visualized due to marked vitreous opacity. Neuro-ophthalmic examination revealed an absent menace response and dazzle reflex in both eyes. Pupillary light reflexes were absent for both eyes. Tear production (Schirmer tear test strips) was normal with values of 25 mm/min in the right eye (OD) and 18 mm/min in the left eye (OS). Rebound tonometry revealed ocular hypertension with intraocular pressures of 36 mm Hg OD and 32 mm Hg OS. Fluorescein staining was negative for both eyes. Ocular ultrasonography (12.5 MHz probe) revealed bilateral retinal detachment, lens subluxation and, in the vitreal body of the right eye, a small doubled-lined foreign body thought to be compatible with an intraocular parasite (Fig 2).

No 2-dimensional echocardiographic changes, and no relevant arterial pulmonary hypertension were evident. Radiographic examination of the thorax showed an increased opacity of the lungs with mixed pattern: alveolar at the right cranial and caudal lobes, bronchial with interstitial infiltrate at the perihilar regions. A moderate pneumothorax with a radiolucent space between the sternum and the cardiac apex and an enlargement of the cranial mediastinum were present too (Fig 3A and B). Thorax ultrasonography showed several subpleural nodules with a diameter of less than 1 centimeter (Fig 4).

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Abbreviations: OU, both eyes; OD, right eye; OS, left eye

Ethics Statement: All medical procedures were carried with the owner's approval.

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Table 1
Results of Biochemical Profile of "Nala"

Parameter	Nala	Reference range
Urea mmol/L	1.59	0.9-1.9
Creatinine μmol/L	99	20-130
Potassium mmol/L	2.32	3.7-5.8
Lipase IU/L	220	<225
Albumin g/L	38.4	27-35
Globulin g/L	45.7	28-42
Alkaline phosphatase IU/L	78	5-50
Alanine amino transferase IU/L	47	5-20
Bilirubin μmol/L	5.4	0.9-10.0
Calcium mmol/L	2.85	2.3-3.0
Chloride mmol/L	106. 3	99-110

Table 2
Results of Routine Hematology and Measurements of Prothrombin Time (PT) and Activate Partial Thromboplastin Time (APTT) of "Nala"

Parameter	Nala	Reference range
Packed cell volume L/L	0.48	0.37-0.55
Hemoglobin g/L	113	120-180
Red blood cell count x 10^{12}/L	4.5	5.5–8.5
MCHC g/L	427	320-360
MCV fl	75.0	60-77
MCH pg	22.2	19-25
Platelets $\times 10^9$/L	718	200-500
White blood cell count $\times 10^9$/L	45.5	7–17
Neutrophils (mature) $\times 10^9$/L	29.7	3-11.5
Neutrophils (band) $\times 10^9$/L	0	0–0.6
Lymphocytes $\times 10^9$/L	3.4	1-4.8
Monocytes $\times 10^9$/L	2.1	0.2-1.3
Eosinophils $\times 10^9$/L	0	0-1.3
Basophils $\times 10^9$/L	0.2	0-0
Nucleated red blood cells	0	0-0
Prothrombin time (seconds)	16.7 seconds	6-12 seconds
Activate partial prothrombin time (seconds)	23.4 seconds	14-23 seconds

Coprological examination using Baermann and FLOTAC techniques[13] demonstrated the presence of a high load of *A. vasorum* first stage larvae (L1) with 324 larvae per gram of feces. In addition, an antigen test for the parasite (Angio Detect, IDEXX) also yielded a positive result.

Based on findings obtained from clinical and laboratory exams, a diagnosis of *A. vasorum* pneumonia associated to panuveitis, lens subluxation, bilateral retinal detachment and glaucoma was made.

Therapy and Follow-Up

Therapy included systemic fenbendazole (Panacur, Intervet) 50 mg/kg q24h for 3 weeks[14] associated with prednisolone 0.5 mg/kg and systemic antibiotics. A subconjunctival injection of triamcinolone acetonide was performed, and topical prednisolone acetate 1% OU 1 drop q6h, and dorzolamide hydrochloride 2% timolol 0.5% OU 1 drop q8 h, were prescribed for 4 weeks.

Four weeks posttherapy, the dog had a complete resolution of signs of active ocular inflammation, and was negative to *A. vasorum* at coprological and serological tests; however, vision did not return. Intraocular pressures were 22 mm Hg OD and 17 mm Hg OS. Indirect ophthalmoscopy showed bilateral retinal atrophy, with increased tapetal reflectivity, loss of retinal blood vessels and optic atrophy. After 3 months, mild pulmonary changes were still radiographically present, but subpleural nodules were no longer visible via ultrasonography.

No further evidence of systemic clinical signs was observed at another follow-up performed 7 months later.

Discussions and Conclusions

The clinical, hematological, and pathologic changes related to canine angiostrongylosis have been previously described.[15-18] Aberrant larval migration makes the diagnosis of this infection more difficult due to the presenting clinical signs of the affected organ(s) resulting from hemorrhagic and granulomatous conditions.[11] Bleeding, neurologic, ocular, cardiovascular, and gastrointestinal disorders are already reported in the literature[10,19] as well as dermatologic lesions appearing as a crusted papular dermatitis.[20]

The novelty of this case report is the combination of substantial systemic manifestations of disease with devastating and irreversible ocular lesions. Cases of canine angiostrongylosis with ocular involvement have been reported, describing extensive subconjunctival hemorrhage as a common clinical finding, as well as the presence of motile worms in the anterior chamber of the eye, uveitis, hyphema, vitreous herniation, multiple arcuate nonmotile opacities within anterior vitreous or multiple motile larvae in the anterior vitreous, chorioretinitis, retinal hemorrages, and postinflammatory retinal degeneration.[21-23] In all previously reported cases, resolution of ocular signs was obtained and none of the cases that recovered are known to have relapsed. A 20-month-old male Miniature Dachshund previously reported in the literature had impaired vision and was euthanized due to the progression of nervous and ocular diseases caused by migration of parasitic larvae in the eyes, brain, and spinal cord.[24] Interestingly, in the present case, no ocular parasitic stage was detected by ophthalmic examination in the anterior chamber. However, ocular ultrasonography showed a double-lined foreign body into the vitreal body of the right eye suggestive of an aberrant or ectopic migration of *A. vasorum*. Indeed, there are several reports of aberrant migration of *A. vasorum* both with adults and L1.[24,25] However, ocular migration of *A. vasorum* is rarely described and

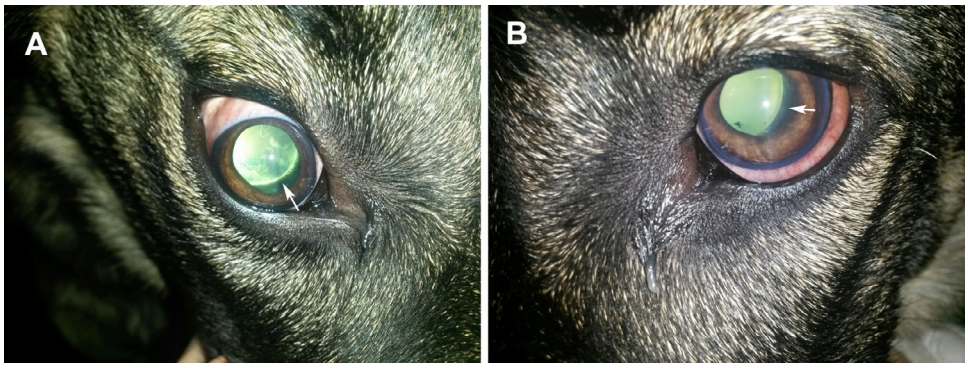

Fig. 1. (A) Right and (B) left eye. An aphakic crescent (white arrow) is visible in both eyes.

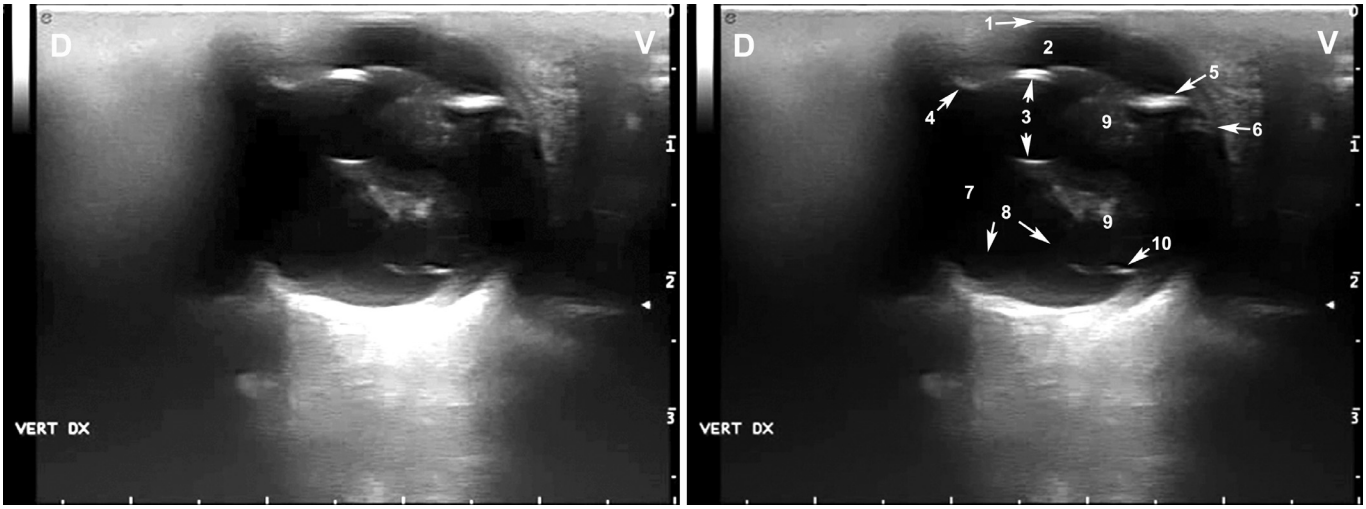

Fig. 2. Ultrasonography of the right eye in a vertical plane. There are severe modifications of the normal echostructure due to the presence of a dorsal subluxation of the lens, an echoic material, ventral to lens and into the vitreal body, and a partial detachment of the retina. A small doubled-lined foreign body, compatible with *A. vasorum* larvae, is visible.

Legend: D = dorsal; V = ventral; 1 = cornea; 2 = anterior chamber; 3 = anterior and posterior capsule of lens; 4 = dorsal iris; 5 = ventral iris; 6 = ciliary body; 7 = vitreal body; 8 = retinal detachment; 9 = exudate or blood cloth; 10 = suspect larvae.

almost all the cases that had been reported until now, confirmed the presence of the parasite in the anterior chamber.[11,21-23]

To the best of our knowledge, severe disseminated larval infection has not been reported previously in naturally occurring or experimentally induced canine angiostrongylosis. Although the mechanism of this ocular migration larval infection could not be determined and confirmed by examining the eye after surgical extraction, the presence of a vitreal linear foreign body suggested that larval parasitemia may have occurred. Ocular penetration of parasitic larvae can stimulate a severe granulomatous uveitis.[11] Therefore, we speculate that in the present case, the infection had caused an inflammatory reaction resulting in panuveitis and inflammation of the iridocorneal angles and ciliary clefts, partial syneresis, infiltration of the vitreous body with inflammatory cells, and retinal detachment. Alternatively, the severity of immunologic response to *A. vasorum* may be an important factor and the present case may be consistent with an immune-mediated uveitis leading to an irreversible ocular tissue damage. In people, it has been reported that ocular damage by parasitic worms can be caused directly by the infectious pathogen, indirectly by the toxic products of the immune response incited by infection, or by ectopic parasitism of preadult or adult stages.[26-28]

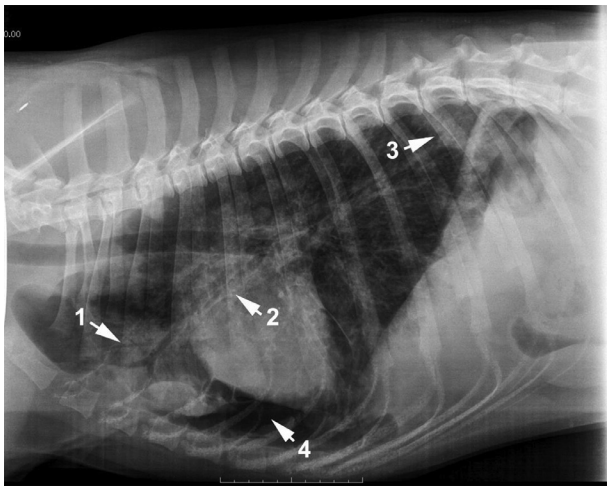

Fig. 3. Latero-lateral radiograph of the thorax of the dog affected by *Angiostrongylus vasorum*. There is an increased opacity of the lungs with mixed pattern, alveolar at the right cranial (1) and caudal (3) lobes, in which multiple air bronchograms are visible, bronchial/interstitial in the perihilar regions (2). These radiographic signs are typical of inflammatory or infectious broncho-pneumoniae. In the pleural space, a moderate pneumothorax (4) with a radiolucent space between the sternum and the cardiac apex is present.

It may be surprising that in this case, although the abnormal radiographic findings still evident after 3 months, no relevant arterial pulmonary hypertension was found. However, several cases of canine angiostrongylosis had been previously described, with severe radiographic changes not associated with pulmonary hypertension.[1,15]

In the present study, despite heavy *A. vasorum* infection load and severe pulmonary changes, only mild hematological and serum biochemical changes were observed; however, prolonged coagulation times were noted. Although peripheral eosinophilia is often reported in dogs infected with *A. vasorum*, its absence should not preclude consideration of infection with the parasite in the differential list.[29-31] The most common causes of blood and tissue eosinophilia are hypersensibility reactions and parasite infection. Based on the host/parasite interaction, it is possible that the peaks in 4 periods, observed for eosinophils in a previous work (on 10, 20, 72, and 160 days after infection) could not be associated in our present study with the initial periods of infection. However, Prestwood et al (1981) did not find any consistent hematological abnormalities in dogs infected experimentally with *A. vasorum*.[32] Moreover, a previous study showed that in dogs experimentally infected with *A. vasorum*, WBC counts and concentrations of neutrophils, eosinophils and monocytes decreased significantly from days 0 to 42, indicating that, even without elevated absolute blood values, a low-grade inflammatory response may be present.

This report, and others recently published, provide important evidence that *A. vasorum* infection has spread in Italy more than expected[5,7,9,13,33,34] probably due to the fact that this infection is still neglected in canine clinical practice. Increasing awareness of the importance of alternative migratory routes of *A. vasorum* in dogs will improve our current understanding of the diagnosis and clinical follow-up of this parasitic condition. Therefore, veterinary practitioners should include canine angiostrongylosis in the differential diagnosis of uveitis, avoiding potentially serious complications, due to a missed or delayed diagnosis.

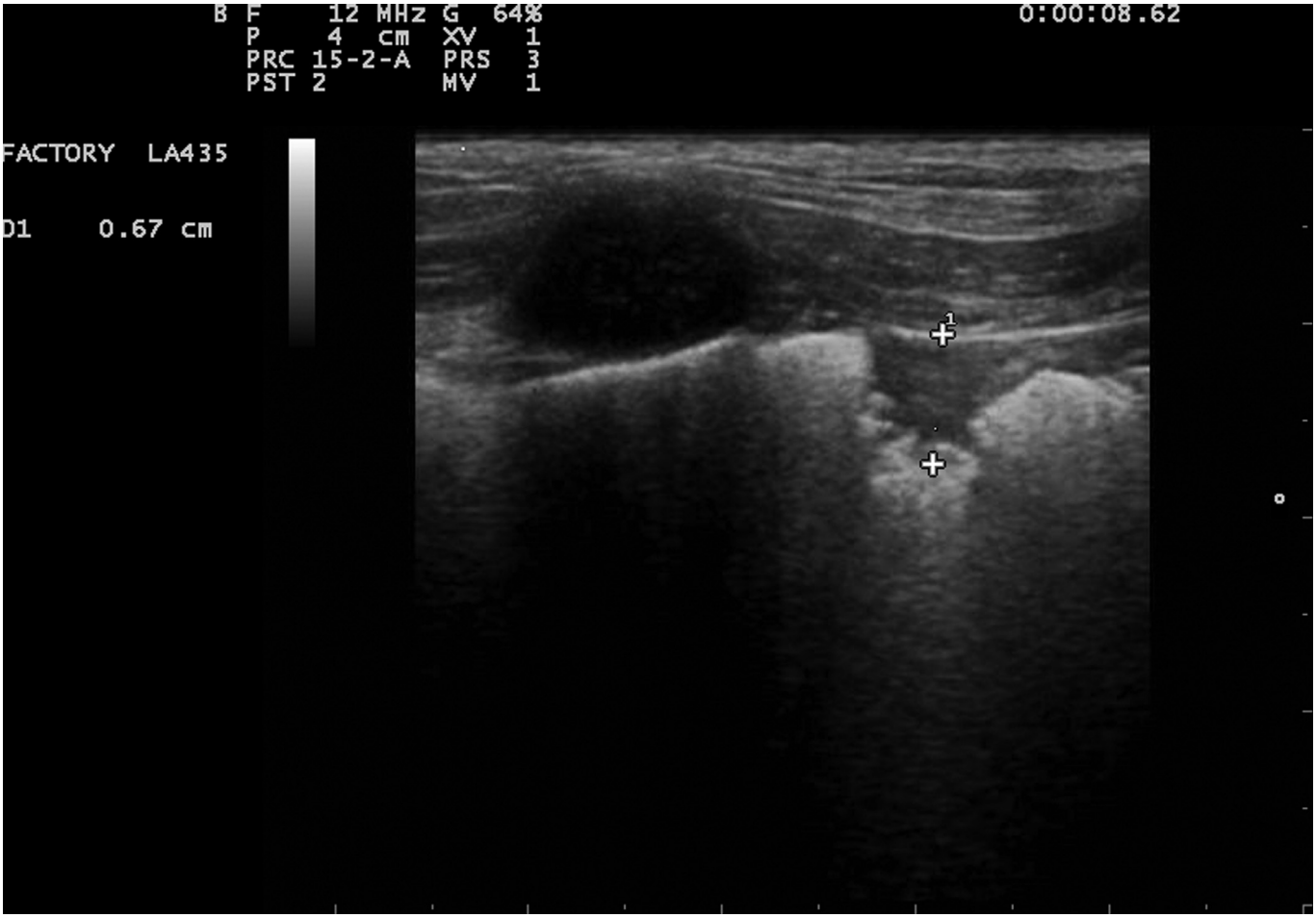

Fig. 4. Right hemithorax – Presence of a subpleural nodule with a diameter of less than 1 centimeter. Similar nodules were visible particularly on the caudo-dorsal region of the lungs.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.tcam.2019.05.001.

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