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CASE REPORT

Companion or pet animals

Epistaxis associated with *Angiostrongylus vasorum* infection in a dog

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Abstract

A 9-month-old, female, entire border collie was presented as an emergency for unilateral epistaxis, rapidly evolving to bilateral, and lethargy of sudden onset. A moderate broncho-interstitial pattern was present on thoracic radiographs, particularly in the caudo-dorsal lung lobes. Haematology and coagulation parameters (prothrombin time, partial thromboplastin time, fibrinogen) were within normal range. Multiple larvae (L1) of *Angiostrongylus vasorum* were identified both on flotation (Ovassay technique) and sedimentation (McKenna technique). The dog was treated with fenbendazole (50 mg/kg) for 15 days. On re-examination, 4 days after completion of treatment, faecal analysis was negative and thoracic radiographs were improved. This case reports epistaxis as the main clinical finding in a young dog infested with *A. vasorum*, in the southwest of France, where this parasite is endemic. If bleeding diatheses are increasingly reported in angiostrongylosis, epistaxis is an unusual presentation, especially as the sole clinical sign of bleeding, in a dog with normal coagulation parameters.

KEYWORDS
Angiostrongylus, dogs, infectious diseases, parasitology

BACKGROUND

Angiostrongylus vasorum is a metastrongylus nematode living in the pulmonary arteries and right heart of domestic and wild dogs whose life cycle has been extensively reviewed.[1,2] It has a recognised worldwide patchy distribution.[3] However, in the past decade, its geographical range has been expanding, particularly across Europe, with numerous new reports of infection in areas previously free from the parasite.[4–7]

Dogs infected with *A. vasorum* present a variety of clinical signs. The most common ones include respiratory disorders (coughing, dyspnoea) and non-specific signs (lethargy, exercise intolerance).[8–10] Bleeding diathesis and coagulopathies are increasingly recognised as possible clinical manifestations.[11] These clotting disorders can manifest as petechia, ecchymoses, continued bleeding following surgery, as haemoptysis or haemothorax, and can occur as a sole clinical sign or in combination.[12–14] The pathophysiological mechanisms underlying the bleeding are not fully established.[11,14,15]

Investigation often involves thoracic imaging with description of non-pathognomonic, unspecific changes, such as diffuse bronchial, interstitial and/or alveolar pattern and pleural effusion.[3,8] Diagnosis relies on identification of first-stage larvae in faecal samples using the Baermann migration method (gold standard), despite recent development of specific immuno-assays and molecular techniques, including a rapid, patient-side test (AngioDetect Test, IDEXX Laboratories).[6,16]

Epistaxis has been reported previously in angiostrongylosis cases, in either retrospective case series offering minimal description of the clinicopathological findings (platelet count, coagulation parameters) and treatments, or in more documented reports.[14,17–19] However, epistaxis was never the main clinical finding nor reported without any concurrent alteration of coagulation parameters.

CASE PRESENTATION

A 9-month-old, female, entire border collie presented out-of-hours to the Emergency and Critical Care Department of the small animal hospital of the National Veterinary School of Toulouse, France, for sudden onset of unilateral epistaxis and lethargy. The dog had just returned from a walk and no trauma was reported. The dog had been in its owners' possession since 3 months of age. The dog was treated monthly against ectoparasites with a spot-on application of fipronil-(S)-methoprene

(Frontline Combo, Mérial), and had been dewormed within the 3 months leading to the consultation with a single dose of a combination of oxantel (24.7 mg/kg), pyrantel (6.2 mg/kg) and praziquantel (6.2 mg/kg) (Dolpac, Vétoquinol).

On presentation, the dog was bright, although extremely anxious. Physical examination did not raise concern for haemodynamic instability, but the dog was panting with increased bronchovesicular sounds on thoracic auscultation. The respiratory rate eventually settled to 44 breaths per minute once acclimated to its environment. A mild left-sided epistaxis was noticed. The remainder of the clinical examination was unremarkable.

INVESTIGATIONS

Based on the presentation, acute onset of unilateral epistaxis occurring 1 hour after a walk, in a bright, young mesocephalic dog, the main suspicion at the time was a nasal foreign body. The dog was admitted to the hospital for monitoring and referred to the Internal Medicine Department for rhinoscopy the next day. Overnight, epistaxis became bilateral, and the patient was transferred to the out-of-hour internal medicine clinician for investigations.

Screening for inciting causes of epistaxis was performed. Blood pressure was measured using a non-invasive method (Doppler), but was deemed unreliable due to the anxious nature of the patient (average systolic of 170 mmHg). Fundic examination was normal, in particular, there were no retinal changes evocative of systemic hypertension (tortuous vessels, haemorrhage, detachment). Radiographs showed an unspecific, mild, broncho-interstitial pattern, peri-hilar and across the caudo-dorsal lung lobes (Figure 1). On haematology, a moderate leukocytosis [24.55×10^9/L (5.05–16.76)] with neutrophilia [16.54×10^9/L (2.95–11.64)] and lymphocytosis [5.9×10^9/L (1.05–5.10)] was present. The remainder of the blood analyses were within the reference interval of the clinical laboratory, in particular haematocrit (Hct = 45% [37.3–61.7]), platelet count (Plt = 263×10^9/L [148–484]) and coagulation parameters (prothrombin time [PT] = 7.7 seconds [7.1–9.0]; partial thromboplastin time [aPTT] = 16.3 seconds [12.8–17.2]; buccal mucosal bleeding time [BMBT] <5 minutes; fibrinogen = 3 g/L [1.3–4.8]; antithrombin III = 129% [109–195]). A rapid test for dirofilariosis (SNAP 4DX Plus, Idexx) was negative. Serum was stored for further testing. Faecal collection (3 consecutive days) was initiated upon admission. Stools were obtained within 12 hours of hospitalisation. Stored serum and the first lot of faeces were submitted on the next working day for immediate coproscopic analysis (Ovassay flotation technique), and for leishmaniasis serology.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for epistaxis is split between localised and systemic causes of bleeding. Local causes include trauma, aspergillosis, linguatulosis, respiratory capillariasis, nasal foreign bodies, canine chronic inflammatory rhinitis, tooth root abscess, oronasal fistula, nasal tumours or more rarely vasculitis. In the present case, in the absence of history of trauma and with unilateral epistaxis rapidly evolving to bilateral, local causes became less likely. Systemic causes include thrombocytopenia, thrombocytopathia, coagulopathies (rodenticide intoxication, haemophilia A, B or C, Von Willebrand disease, disseminated intravascular coagulation [DIC]), systemic hypertension, Scott syndrome in German sheperd dogs and infection with *Ehrlichia canis, Leishmania infantum* or *A. vasorum*. In the present case, with an appropriate platelet count, normal clotting times, a moderate suspected situational hypertension, negative serology for ehrlichiosis, and radiographic changes to the lungs, in an area endemic for *A. vasorum*, the main suspicion would be a bleeding diathesis secondary to parasitic infection.

TREATMENT

While awaiting emission of faeces and subsequent parasitology results, treatment was initiated with amlodipine (0.38 mg/kg/day; Amlor 6.25 mg, Pfizer). Faecal flotation, obtained on the next working day, revealed the presence of numerous larvae. This finding was later confirmed by the McKenna technique for the research of respiratory nematodes larvae (average 85 larvae per gram of faeces). Their size was between 345 and 391 μm in length, and were identified as first-stage larvae of *A. vasorum* due to the presence of a wavy tail presenting a sub-terminal notch with characteristic dorsal and ventral indentations (Figure 2).[20] The epistaxis and broncho-pulmonary abnormalities were attributed to the infestation with *A. vasorum*. Amlodipine was discontinued, and a 15-day course of fenbendazole (50 mg/kg orally [per os]; Panacur 500, Intervet) was implemented. The dog was discharged after 48 hours of observation.

OUTCOME AND FOLLOW-UP

On reassessment, 5 days after discharge, a mild epistaxis was still observed in one nostril (Figure 3). Fewer larvae were visible on faecal analysis (average 17 larvae per gram). On re-examination, 48 hours after finishing the course of treatment, the owner reported a complete resolution of the epistaxis and lethargy. Thoracic auscultation was normal, and repeat chest

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LEARNING POINTS/TAKE-HOME MESSAGES

- Angiostrongylosis is endemic in numerous areas in Europe and appears to be spreading.
- Angiostrongylosis should be considered as a potential differential diagnosis in dogs presented with unexplained bleeding such as epistaxis, even when unilateral.
- Angiostrongylosis can be associated with bleeding diathesis and should not be dismissed on the base of unremarkable routine blood analysis or normal clotting times.
- Clinical signs usually retrocede after prolonged fenbendazole treatment.
- Rapid diagnosis and patient-based supportive care are paramount to prevent potential dramatic complications.
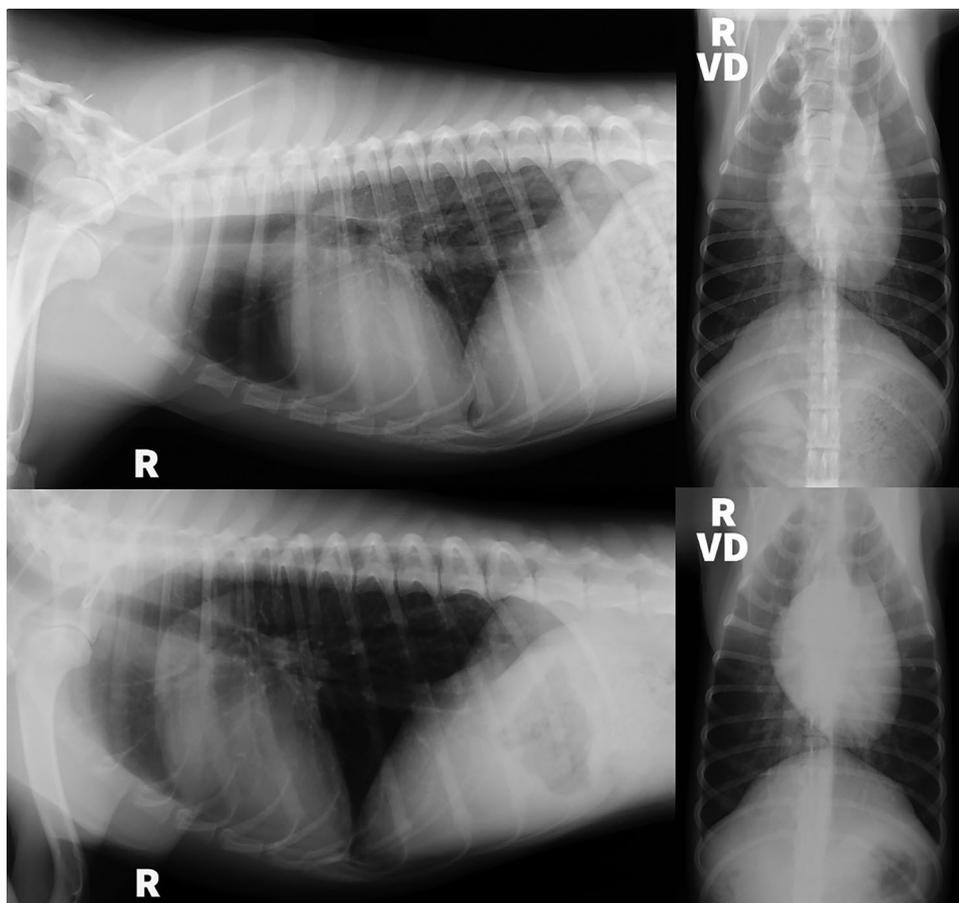
FIGURE 1 Right lateral and ventro-dorsal radiographs of the thorax of the dog (upper: upon admission, before treatment; lower: after treatment). The upper images reveal a mild, broncho-interstitial pattern affecting the peri-hilar area and the caudo-dorsal lung lobes. The lower images show a reduction of the multifocal broncho-interstitial pattern.


FIGURE 2 *Angiostrongylus vasorum* first-stage larvae observed in the faecal material after realisation of the Ovassay technique. The larva presented a characteristic wavy tail with a sub-terminal notch.

radiographs revealed a moderate improvement with only a mild residual patchy interstitial pattern affecting the very tip of the dorsal lung lobes (Figure 1). Faecal analysis (samples from 3 consecutive days, McKenna technique) was negative.

DISCUSSION

This case reports epistaxis as the main clinical finding in a dog diagnosed with *A. vasorum*, living in the South-west of France; the initial historical endemic focus of the
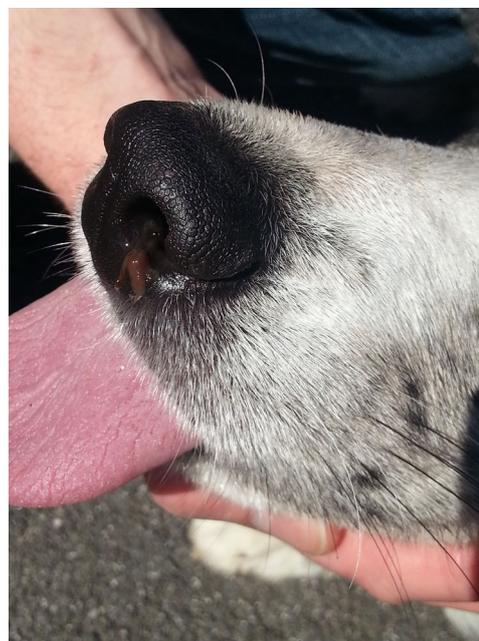
FIGURE 3 Mild unilateral epistaxis observed at the second re-examination visit, 5 days after initiation of treatment.

parasite, but without concurrent clinicopathological evidence of coagulation disorder.[1] Angiostrongylosis is now endemic in numerous areas in Europe, but appears to be spreading and is

considered emergent in a rising number of countries, making this parasitosis increasingly clinically relevant.[2,10,21–45]

The main clinical finding reported here was unilateral epistaxis rapidly evolving to bilateral, and lethargy of sudden onset, with concurrent increased respiratory sounds and tachypnoea. The panting and borderline tachypnoea could be attributed to the anxious nature of the dog. Epistaxis is a rare finding in dogs with angiostrongylosis, often bilateral and, to the authors' knowledge, only reported in six other cases. In these cases, multifocal haemorrhage and concurrent clinicopathological changes were present (thrombocytosis 1/6, thrombocytopenia 5/6, prolonged coagulation times 3/4).[17,19,46] With its initial unilateral onset and absence of clinicopathological changes, the present case is original.

Coagulopathies and bleeding disorders associated with angiostrongylosis have been described since 1986.[47] Bleeding diathesis has been increasingly reported through the years, accounting for, respectively, 35%, 71% and 57% of the presenting complaint in small case series of 23, 49 and 21 dogs naturally infected by *A. vasorum* presented to referral veterinary hospital.[15,18,21] Broad appreciation of unexplained bleed as potential presentation of angiostrongylosis is now widely accepted, but probably lacked at the time of presentation of this case. In general practices, the most common clinical signs remain respiratory in nature (cough and dyspnoea), with bleeding disorders being the chief complaint only in 2.8%–9% of cases.[9,48]

In the present case, haematological and biochemical parameters were mostly unremarkable. This is not an unusual finding, and angiostrongylosis should not be dismissed on the basis of unremarkable routine blood analysis.[49] In contrary, the presence of clinical bleeding in the absence of any coagulation abnormality is unusual. Prolonged aPTT, PT, thrombocytopenia or increased fibrinogen degradation products are commonly reported in dogs with bleeding diathesis.[3,21] In a study investigating the coagulation status of dogs with naturally occurring *A. vasorum*, 96% of the 25 dogs had at least one abnormal coagulation parameter.[11] In another study focusing particularly on unexplained bleeding as the primary complaint in dogs infected with *A. vasorum*, only one dog among the 15 included had unremarkable coagulation times.[14]

The mechanisms underlying the coagulopathies associated with *A. vasorum* are still poorly understood. Some dogs may display severe hypercoagulable state and others hypocoagulable state, based on recent studies using thromboelastometry.[15,50,51] Several hypotheses have been offered, including development of DIC, thrombocytopenia, hyperfibrinolysis or, more recently, complex interactions between host's homeostasis and *A. vasorum* surface proteins.[52–54] Young dogs are more likely to be infected by the parasite, especially due to their exploratory behaviour; however, studies on the impact of age at the time of infestation or parasitic burden on the development of bleeding diathesis are lacking.[5]

DIC is the excessive activation of haemostasis, which can eventually result in haemorrhage by consumption of platelets and coagulation factors. Results of coagulation tests depend on the phase of the disease (compensated phase, overt and hypercoagulable, haemorrhagic and hypocoagulable).

Depletion of coagulation factors, consumption of platelets, as well as possible platelet and endothelial dysfunction are characteristics of the haemorrhagic phase. This phase is easiest to diagnose because concurrent laboratory abnormalities are present. These can include thrombocytopenia, increased PT and aPTT, normal to low fibrinogen, decreased AT III and elevated D-dimers or fibrin degradation products (FDP).[54,55] DIC was deemed unlikely in the present case, based on the absence of supporting laboratory findings.

Thrombocytopenia, particularly immune-mediated, has been reported as a potential cause for bleeding in two cases, with platelet counts of 1 and 28×10^9/L.[17,56] A recent study, conducted on dogs naturally infected with *A. vasorum*, demonstrated significantly lower median platelet count in those with bleeding diathesis, compared to the non-bleeding ones and healthy controls.[51] However, the platelet counts were strictly superior to 81×10^9/L and unlikely to account for the clinical bleeds (spontaneous bleed being normally observed in cases with less than 30×10^9 platelets per litre). Regardless, thrombocytopenia alone is unlikely to be the sole underlying cause of bleeding in dogs infected with *A. vasorum* as diathesis is reported in numerous dogs with normal platelet count.[14,15]

In the present case, tests performed for both primary haemostasis (normal platelet count, BMBT within normal limit) and secondary haemostasis (PT, aPTT, fibrinogen) were within normal limit. Thrombocytopathia has been suggested as a possible cause when confronted to bleeding with normal thrombocyte numbers and secondary coagulations parameters.[15]

Hyperfibrinolysis has recently been brought out in dogs infected with *A. vasorum*.[50–52] Its diagnosis is challenging and relies on unspecific markers (D-dimers, FDP) or the use of techniques not widely available such as thromboelastometry. These were not performed in the present case, and hyperfibrinolysis cannot be formally excluded. However, in a study investigating fibrinolysis in 12 bleeding dogs naturally infected with *A. vasorum*, hyperfibrinolysis was significantly associated with hypofibrinogenemia.[15] Unfortunately, the study did not report the results of routinely available coagulation parameters (PT, aPTT, AT III), which precludes comparison with the present case. Nevertheless, the normal fibrinogenemia makes hyperfibrinolysis less likely.

Finally, the development of secondary vasculitis/arteritis has been brought to light by postmortem examination in dogs infected with *A. vasorum*.[56,57] In these reports, arteritis was present in the lungs and heart, but the nasal mucosa was not surveyed. However, in the absence of severe systemic disease, vasculitis is unlikely to account for the epistaxis in our case.

Diagnosis and treatment were delayed by the unavailability of a bedside rapid test (AngioDetect test) and because the parasitology laboratory was closed at the admission of the dog. Various faecal analysis techniques exist that do not require specific equipment. Confronted with a high suspicion of angiostrongylosis, concurrent coagulopathy and unavailable rapid bedside assays, attempts should be made at identifying L1 larvae with methods increasingly time-consuming and sensitive (faecal smear, flotation, modified Baermann methods with accelerated read and standard Baermann method). If the Baermann method remains the gold standard, the recommendation for collection and storage of 3-day pooled faecal samples has recently been questioned

after a study demonstrated a significant decrease in sensitivity over the 3-day storage period.[16] In the present case, the McKenna technique was used. Like the Baermann one, it is based on hydrotropism and gravity of the larvae, but requires little material (gauze, conical flask). It has shown a better sensitivity in detecting some respiratory nematode larvae (*Dictyocaulus viviparus*) in cattle.[58] Another advantage of standard copromicroscopy over bedside assays is the obtention of information on the adult worm burden through the intensity of excretion of L1 larvae, which can guide treatment considerations.[16]

Fenbendazole (at 50 mg/kg/day) courses for 5–21 days is a recognised treatment option of *A. vasorum* and its efficiency is widely reported in the literature.[21,59] Its popularity is based on an alleged 'slow kill effect' that would prevent serious side effect such as anaphylactic shock that has been reported with levamisole.[60] However, its use remains off-label in many territories.[5,6] Currently, two licensed drugs are widely available for the treatment of *A. vasorum*: milbemycin oxime (Milbemax, Novartis) and moxidectin/imidacloprid (Advocate, Bayer).[6] In the present case, off-label use of fenbendazole (at 50 mg/kg/day) was elected considering the heavy worm burden. A 15-day course allowed rapid improvement of the clinical status and eventually cure of the animal.

Further supportive treatments (oxygen, corticosteroids) can be considered on an individual basis.[5,13,56] These were deemed unnecessary in this case. In cases presenting with coagulopathies, additional therapy (whole-blood transfusion, fresh frozen plasma, antifibrinolytic drugs) can be considered, but patients also improve with treatment of the parasite alone.[3,50,61] However, assessment of clotting with viscoelastic techniques is recommended before treatment.[61] In the present case, thromboelastometry was not available. Nevertheless, with a minimal bleed still present 5 days after initiation of fenbendazole, this dog could have benefited from further supportive care.

Unfortunately, it was not possible to confirm that the nasal bleeding was caused by *A. vasorum*. However, the high blood pressure measurements were believed to be stress related rather than an underlying cause. The resolution of epistaxis while treated solely with fenbendazole reinforced this hypothesis. Additionally, while acknowledging the rather moderate sensitivity and specificity of ocular lesions to identify hypertension (62% and 61%, respectively), the normal fundus examination provided further validation that the high blood pressure measurements were likely situational.[62] Treatment with amlodipine was unnecessary based on the consensus guidelines on management of systemic hypertension. Instead, blood pressure and evidence of target organ damage should have been reassessed on two separate occasions over the following 2 months.[63]

AUTHOR CONTRIBUTIONS
Perrine Henry performed the literature review and wrote the main text. Emmanuel Liénard, Emilie Bouhsira and Michel Franc were involved with the clinical management of the case (performed the parasitology tests, identification of the larvae and treatment of the dog). They equally provided valuable insights on the epidemiology and clinical presentation of the parasite. Emilie Bouhsira supervised this work and corrected the successive drafts.

CONFLICT OF INTEREST STATEMENT
The authors declare they have no conflicts of interest.

ETHICS STATEMENT
The patient was treated per hospital policy in compliance with animal ethics and welfare, minimising pain and suffering.

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REFERENCES
1. Rosen L, Ash LR, Wallace GD. Life history of the canine lungworm *Angiostrongylus vasorum* (Baillet). Am J Vet Res. 1970;31(1):131–43.
2. Bolt G, Monrad J, Koch J, Jensen AL. Canine angiostrongylosis: a review. Vet Rec. 1994;135(19):447–52.
3. Helm JR, Morgan ER, Jackson MW, Wotton P, Bell R. Canine angiostrongylosis: an emerging disease in Europe. J Vet Emerg Crit Care. 2010;20(1):98–109.
4. Morgan ER, Jefferies R, Krajewski M, Ward P, Shaw SE. Canine pulmonary angiostrongylosis: the influence of climate on parasite distribution. Parasitol Int. 2009;58(4):406–10.
5. Di Cesare A, Traversa D. Canine angiostrongylosis: recent advances in diagnosis, prevention, and treatment. Vet Med. 2014;5:181–92.
6. Elsheikha HM, Holmes SA, Wright I, Morgan ER, Lacher DW. Recent advances in the epidemiology, clinical and diagnostic features, and control of canine cardio-pulmonary angiostrongylosis. Vet Res. 2014;45(1):92.
7. Barutzki D, Dyachenko V, Schaper R. Lungworms in Germany 2002–2016: is there an increase in occurrence and geographical spread? Parasitol Res. 2017;116(Suppl 1):11–30.
8. Boag AK, Lamb CR, Chapman PS, Boswood A. Radiographic findings in 16 dogs infected with *Angiostrongylus vasorum*. Vet Rec. 2004;154(14):426–30.
9. Morgan ER, Jefferies R, van Otterdijk L, McEniry RB, Allen F, Bakewell M, et al. *Angiostrongylus vasorum* infection in dogs: presentation and risk factors. Vet Parasitol. 2010;173(3–4):255–61.
10. Traversa D, Di Cesare A, Meloni S, Frangipane di Regalbono A, Milillo P, Pampurini F, et al. Canine angiostrongylosis in Italy: occurrence of *Angiostrongylus vasorum* in dogs with compatible clinical pictures. Parasitol Res. 2013;112(7):2473–80.
11. Adamantos S, Waters S, Boag A. Coagulation status in dogs with naturally occurring *Angiostrongylus vasorum* infection. J Small Anim Pract. 2015;56(8):485–90.
12. Willesen J, Bjornvad C, Koch J. Acute haemoabdomen associated with *Angiostrongylus vasorum* infection in a dog: a case report. Ir Vet J. 2008;61(9):591–3.
13. Sasanelli M, Paradies P, Otranto D, Lia RP, de Caprariis D. Haemothorax associated with *Angiostrongylus vasorum* infection in a dog. J Small Anim Pract. 2008;49(8):417–20.
14. Glaus T, Sigrist N, Hofer-Inteeworn N, Kuemmerle-Fraune C, Mueller C, Geissweid K, et al. Unexplained bleeding as primary clinical complaint in dogs infected with *Angiostrongylus vasorum*. Schweiz Arch Tierheilkd. 2016;158(10):701–9.
15. Sigrist NE, Hofer-Inteeworn N, Jud Schefer R, Kuemmerle-Fraune C, Schnyder M, Kutter APN. Hyperfibrinolysis and hypofibrinogenemia diagnosed with rotational thromboelastometry in dogs

naturally infected with *Angiostrongylus vasorum*. J Vet Intern Med. 2017;31(4):1091–9.

16. Oehm AW, Schnyder M. Adult parasite burden and excretion of first-stage larvae of *Angiostrongylus vasorum* in dogs: methodologically relevant diagnostic aspects and associations with serological detection of parasite antigen and specific antibodies. Vet Parasitol. 2022;312:109814.

17. Jo'neill E, Acke E, Tobin E, McCarthy G. Immune-mediated thrombocytopenia associated with *Angiostrongylus vasorum* infection in a Jack Russell terrier. Ir Vet J. 2010;63(7):434–40.

18. Gallagher B, Brennan SF, Zarelli M, Mooney CT. Geographical, clinical, clinicopathological and radiographic features of canine angiostrongylosis in Irish dogs: a retrospective study. Ir Vet J. 2012;65(1):5.

19. Paradies P, Schnyder M, Capogna A, Lia RP, Sasanelli M. Canine angiostrongylosis in naturally infected dogs: clinical approach and monitoring of infection after treatment. ScientificWorldJournal. 2013;2013:702056.

20. Taylor MA, Coop RL, Wall RL. Veterinary parasitology. John Wiley & Sons; 2015. p. 1032.

21. Chapman PS, Boag AK, Guitian J, Boswood A. *Angiostrongylus vasorum* infection in 23 dogs (1999–2002). J Small Anim Pract. 2004;45(9):435–40.

22. Morgan ER, Shaw SE, Brennan SF, De Waal TD, Jones BR, Mulcahy G. *Angiostrongylus vasorum*: a real heartbreaker. Trends Parasitol. 2005;21(2):49–51.

23. Barutzki D, Schaper R. Natural infections of *Angiostrongylus vasorum* and *Crenosoma vulpis* in dogs in Germany (2007–2009). Parasitol Res. 2009;105(Suppl 1):S39–48.

24. Taubert A, Pantchev N, Vrhovec MG, Bauer C, Hermosilla C. Lungworm infections (*Angiostrongylus vasorum, Crenosoma vulpis, Aelurostrongylus abstrusus*) in dogs and cats in Germany and Denmark in 2003–2007. Vet Parasitol. 2009;159(2):175–80.

25. van Dijk EP, Overgaauw PAM. [Pulmonary problems in dogs in the Netherlands with alarming cause (*Angiostrongylus vasorum*)]. Tijdschr Diergeneeskd. 2009;134(13):575–8.

26. van Doorn DCK, van de Sande AH, Nijsse ER, Eysker M, Ploeger HW. Autochthonous *Angiostrongylus vasorum* infection in dogs in the Netherlands. Vet Parasitol. 2009;162(1–2):163–6.

27. Majoros G, Fukár O, Farkas R. Autochtonous infection of dogs and slugs with *Angiostrongylus vasorum* in Hungary. Vet Parasitol. 2010;174(3–4):351–4.

28. Maksimov P, Hermosilla C, Taubert A, Staubach C, Sauter-Louis C, Conraths FJ, et al. GIS-supported epidemiological analysis on canine *Angiostrongylus vasorum* and *Crenosoma vulpis* infections in Germany. Parasit Vectors. 2017;10(1):108.

29. Garcia-Campos A, Power C, O'Shaughnessy J, Browne C, Lawlor A, McCarthy G, et al. One-year parasitological screening of stray dogs and cats in County Dublin, Ireland. Parasitology. 2019;146(6):746–52.

30. Traversa D, Morelli S, Cassini R, Crisi PE, Russi I, Grillotti E, et al. Occurrence of canine and feline extra-intestinal nematodes in key endemic regions of Italy. Acta Trop. 2019;193:227–35.

31. Carretón E, Morchón R, Falcón-Cordón Y, Matos J, Costa-Rodríguez N, Montoya-Alonso JA. First epidemiological survey of *Angiostrongylus vasorum* in domestic dogs from Spain. Parasit Vectors. 2020;13(1):306.

32. Jolly S, Poncelet L, Lempereur L, Caron Y, Bayrou C, Cassart D, et al. First report of a fatal autochthonous canine *Angiostrongylus vasorum* infection in Belgium. Parasitol Int. 2015;64(1):97–9.

33. Canonne AM, Roels E, Caron Y, Losson B, Bolen G, Peters I, et al. Detection of *Angiostrongylus vasorum* by quantitative PCR in bronchoalveolar lavage fluid in Belgian dogs. J Small Anim Pract. 2016;57(3):130–4.

34. Lempereur L, Martinelle L, Marechal F, Bayrou C, Dalemans AC, Schnyder M, et al. Prevalence of *Angiostrongylus vasorum* in southern Belgium, a coprological and serological survey. Parasit Vectors. 2016;9(1):533.

35. Lempereur L, Nijsse R, Losson B, Marechal F, De Volder A, Schoormans A, et al. Coprological survey of endoparasite infections in owned dogs and owners' perceptions of endoparasite control in Belgium and the Netherlands. Vet Parasitol Reg Stud Reports. 2020;22:100450.

36. Papazahariadou M, Founta A, Papadopoulos E, Chliounakis S, Antoniadou-Sotiriadou K, Theodorides Y. Gastrointestinal parasites of shepherd and hunting dogs in the Serres Prefecture, Northern Greece. Vet Parasitol. 2007;148(2):170–3.

37. Angelou A, Gelasakis AI, Schnyder M, Schaper R, Papadopoulos E. The "French heartworm" in Greece: a countrywide serological survey of *Angiostrongylus vasorum* infection by combined detection of circulating antigens and specific antibodies. Vet Parasitol Reg Stud Reports. 2020;19:100376.

38. Hurníková Z, Miterpáková M, Mandelík R. First autochthonous case of canine *Angiostrongylus vasorum* in Slovakia. Parasitol Res. 2013;112(10):3505–8.

39. Čabanová V, Miterpáková M, Druga M, Hurníková Z, Valentová D. GIS-based environmental analysis of fox and canine lungworm distribution: an epidemiological study of *Angiostrongylus vasorum* and *Crenosoma vulpis* in red foxes from Slovakia. Parasitol Res. 2018;117(2):521–30.

40. Grandi G, Lind EO, Schaper R, Ågren E, Schnyder M. Canine angiostrongylosis in Sweden: a nationwide seroepidemiological survey by enzyme-linked immunosorbent assays and a summary of five-year diagnostic activity (2011–2015). Acta Vet Scand. 2017;59(1):85.

41. Deak G, Gillis-Germitsch N, Ionică AM, Mara A, Păstrav IR, Cazan CD, et al. The first seroepidemiological survey for *Angiostrongylus vasorum* in domestic dogs from Romania. Parasit Vectors. 2019;12(1):224.

42. Schnyder M, Schaper R, Pantchev N, Kowalska D, Szwedko A, Deplazes P. Serological detection of circulating *Angiostrongylus vasorum* antigen- and parasite-specific antibodies in dogs from Poland. Parasitol Res. 2013;112(1):109–17.

43. Demiaszkiewicz AW, Pyziel AM, Kuligowska I, Lachowicz J. The first report of *Angiostrongylus vasorum* (Nematoda; Metastrongyloidea) in Poland, in red foxes (Vulpes vulpes). Acta Parasitol. 2014;59(4):758–62.

44. Tiškina V, Lindqvist EL, Blomqvist AC, Orav M, Stensvold CR, Jokelainen P. Autochthonous *Angiostrongylus vasorum* in Finland. Vet Rec Open. 2019;6(1):e000314.

45. Hajnalová M, Svobodová V, Schnyder M, Schaper R, Svoboda M. Faecal detection of the lungworms *Crenosoma vulpis* and *Angiostrongylus vasorum* and serological detection of *A. vasorum* in dogs from the Czech Republic. Acta Vet Brno. 2018;86(4):393–8.

46. Capogna A, Sasanelli M, Lia RP, Spagnolo PP, Paradies P. Further insights into the clinical aspects of *Angiostrongylus vasorum* natural infection in symptomatic and asymptomatic dogs. Vet Sci Med Diagn. 2012;01(2). https://doi.org/10.4172/2325-9590.1000106

47. Schelling CG, Greene CE, Prestwood AK, Tsang VC. Coagulation abnormalities associated with acute *Angiostrongylus vasorum* infection in dogs. Am J Vet Res. 1986;47(12):2669–73.

48. Colombo M, Traversa D, Grillotti E, Pezzuto C, De Tommaso C, Pampurini F, et al. Highly variable clinical pictures in dogs naturally infected with *Angiostrongylus vasorum*. Pathog Basel Switz. 2021;10(11):1372.

49. Willesen JL, Jensen AL, Kristensen AT, Koch J. Haematological and biochemical changes in dogs naturally infected with *Angiostrongylus vasorum* before and after treatment. Vet J. 2009;180(1):106–11.

50. Cole L, Barfield D, Chan D, Cortellini S. Use of a modified thromboelastography assay for the detection of hyperfibrinolysis in a dog infected with *Angiostrongylus vasorum*. Vet Rec Case Rep. 2018;6:e000554.

51. Sigrist NE, Tritten L, Kümmerle-Fraune C, Hofer-Inteeworn N, Jud Schefer R, Schnyder M, et al. Coagulation status in dogs naturally infected with *Angiostrongylus vasorum*. Pathogens. 2021;10(9):1077.

52. Schmitz S, Moritz A. [Chronic disseminated intravascular coagulopathy in a dog with lung worm infection]. Schweiz Arch Tierheilkd. 2009;151(6):281–6.

53. Gillis-Germitsch N, Kockmann T, Asmis LM, Tritten L, Schnyder M. The *Angiostrongylus vasorum* excretory/secretory and surface proteome contains putative modulators of the host coagulation. Front Cell Infect Microbiol. 2021;11:753320.

54. Ramsey IK, Littlewood JD, Dunn JK, Herrtage ME. Role of chronic disseminated intravascular coagulation in a case of canine angiostrongylosis. Vet Rec. 1996;138(15):360–3.

55. Mrljak V, Barić Rafaj R, Sušić V, Matijatko V, Kučer N, Kiš I. Antithrombin III in healthy dogs and in dogs suffering from babesiosis. Vet Arh. 2005;75(6):477–86.

56. Gould SM, McInnes EL. Immune-mediated thrombocytopenia associated with *Angiostrongylus vasorum* infection in a dog. J Small Anim Pract. 1999;40(5):227–32.

57. Rinaldi L, Cortese L, Meomartino L, Pagano TB, Pepe P, Cringoli G, et al. *Angiostrongylus vasorum*: epidemiological, clinical and histopathological insights. BMC Vet Res. 2014;10:236.

58. McKenna PB. Comparative evaluation of two emigration/sedimentation techniques for the recovery of dictyocaulid and protostrongylid larvae from faeces. Vet Parasitol. 1999;80(4):345–51.

59. Ferdushy T, Hasan MT. *Angiostrongylus vasorum*: the "French Heart-worm". Parasitol Res. 2010;107(4):765–71.

60. Søland J, Bolt G. Hypovolaemic shock after anthelmintic treatment of canine angiostrongylosis. J Small Anim Pract. 1996;37(12):594–6.

61. Birkbeck R, Humm K, Cortellini S. A review of hyperfibrinolysis in cats and dogs. J Small Anim Pract. 2019;60(11):641–55.

62. Leblanc NL, Stepien RL, Bentley E. Ocular lesions associated with systemic hypertension in dogs: 65 cases (2005–2007). J Am Vet Med Assoc. 2011;238(7):915–21.

63. Acierno MJ, Brown S, Coleman AE, Jepson RE, Papich M, Stepien RL, et al. ACVIM consensus statement: guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. J Vet Intern Med. 2018;32(6):1803–22.