J S Afr Vet Assoc. 2022;93(2):151-155
https://doi.org/10.36303/JSAVA.509

J S Afr Vet Assoc
ISSN 2224-9435 EISSN 1019-9128

CASE REPORT

The clinical presentation and management of a naturally occurring Bluetongue virus infection in a pregnant Rottweiler dog

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Few reports of clinical Bluetongue virus (BTV) infections have been described in dogs. Most cases were linked to inoculation with a BTV-contaminated canine modified live vaccine. In dogs, cases have only been described in pregnant females with clinical signs of fever and abortion followed by severe dyspnoea and death.

A pregnant Rottweiler dog was presented with a three-day history of progressive lethargy and anorexia. The patient was a guard dog living in an enclosure where sheep were kept at night. High mortalities had been experienced in the sheep but had not been investigated. On presentation, the major clinical findings were dyspnoea and hypoxia. Clinicopathological tests showed hypoxia and systemic inflammation. Radiological findings were consistent with non-cardiogenic pulmonary oedema. The patient was treated symptomatically and recovered but did not retain the pregnancy. BTV was identified in the patient's blood using BTV RT-PCR (Ct value 24.7). At a follow-up farm visit, an ongoing BTV outbreak in the sheep was diagnosed with affected sheep testing positive for BTV on RT-PCR.

This report describes the clinical presentation, diagnostic investigations and successful treatment of a dog with BTV infection. This is the first case report of a naturally occurring clinical BTV infection in a dog. Possible routes of infection were direct contact, midge-borne, or ingestion of infected afterbirth or abortus from sheep.

Keywords: canine, abortion, *Orbivirus*, dyspnoea, cross-species infection, sheep, viral pneumonia

Introduction

Bluetongue (BT) is a vector-borne World Organization for Animal Health (founded as the OIE) listed disease, primarily affecting ruminants, caused by the Bluetongue virus (BTV), which belongs to the genus *Orbivirus* of the family *Reoviridae* (OIE 2019). BTV is mainly transmitted by *Culicoides* biting midges but vertical, oral, venereal, and indirect transmission have also been described (Maclachlan et al. 2009). Clinical signs of BTV in ruminants include fever, widespread oedema, serous nasal discharge and, in severe cases, a cyanotic (blue) tongue and dyspnoea with variable mortality rates (Erasmus 1990). BTV can cross the placental barrier and has an affinity for cells in the undeveloped foetal brain causing abortions, malformations and reproductive failure (Osburn 1994).

Subclinical seroconversion occurs in dogs following experimental BTV exposure (Oura et al. 2014). High proportions of BTV seropositive dogs (up to 39%) without clinical signs have been reported with the route of natural exposure regarded as midge-borne or through ingestion of BTV-infected meat (Alexander et al. 1994; Oura & El Harrak 2011).

To the authors' knowledge, there are only five published reports of clinical BTV infection in dogs. These cases were mostly related to BTV contamination of live attenuated canine vaccines in the United States of America in 1992–93, resulting in abortion and death in pregnant dogs (Akita et al. 1994; Evermann et al. 1994; Wilbur et al. 1994;). BTV has also been isolated in two aborted canine foetuses (Dubovi et al. 2013). Midge-borne transmission to the dams or iatrogenic venereal transmission through artificial insemination using BTV-contaminated semen extender was suspected (Dubovi et al. 2013; Evermann 2013; Gaudreault et al. 2015).

For unknown reasons, clinical BTV infections have only been reported in pregnant dogs (Osburn 1994). Reported clinical signs include fever and abortion, followed by severe acute dyspnoea and death or humane euthanasia within two to three days. Necropsy findings of BTV cases in dogs are akin to those described in sheep (Akita et al. 1994; Brown et al. 1996; Wilbur et al. 1994).

To the authors' knowledge, there are no reports of spontaneous naturally-occurring clinical BTV infection in dogs. This publication aims to describe the clinical investigation, diagnosis and treatment of a pregnant dog surviving a naturally occurring case of clinical BTV infection. Survival of clinical BTV infection in dogs following the development of dyspnoea has not previously been reported.

Patient presentation

A 3.5-year-old pregnant intact female Rottweiler was presented to the Onderstepoort Veterinary Academic Hospital (OVAH), Pretoria, South Africa, with a three-day history of progressive lethargy, weakness and inappetence with acute onset dyspnoea.

The patient lived on a farm on the border of Gauteng and North West Province, South Africa, with a flock of approximately 200 sheep, five other dogs and two horses. The farmer had experienced a high mortality rate in the sheep, the cause of which had not been ascertained. The patient was housed with the sheep at night.

The patient had been naturally mated to a Rottweiler dog residing on the same property, approximately one month before presentation. No other dogs were known to be pregnant at the time. Flea and tick control, deworming, and routine vaccinations were current, and the last vaccination was given more than three months before presentation. The patient was fed a commercial pelleted dog food only, had no known access to rodenticides, electrical cables, or large bodies of water, and had no history of trauma.

The patient had a good general body condition. On clinical examination, the patient was lethargic, dull and had a mild bilateral serous nasal discharge. Severe, mixed, inspiratory-expiratory dyspnoea with costoabdominal breathing and moderate tachypnoea (72 breaths per minute). Harsh inspiratory lung sounds, and moderate tachycardia (160 beats per minute) were detected on auscultation. Mild discomfort and moderate abdominal distention were noted on abdominal palpation. The rectal temperature was normal (38.8 °C), and no heart murmurs were detected on auscultation.

The dog was hypoxic, with low peripheral oxygen saturation (SpO_2) (85%; reference interval [RI] 95–100%) on presentation.

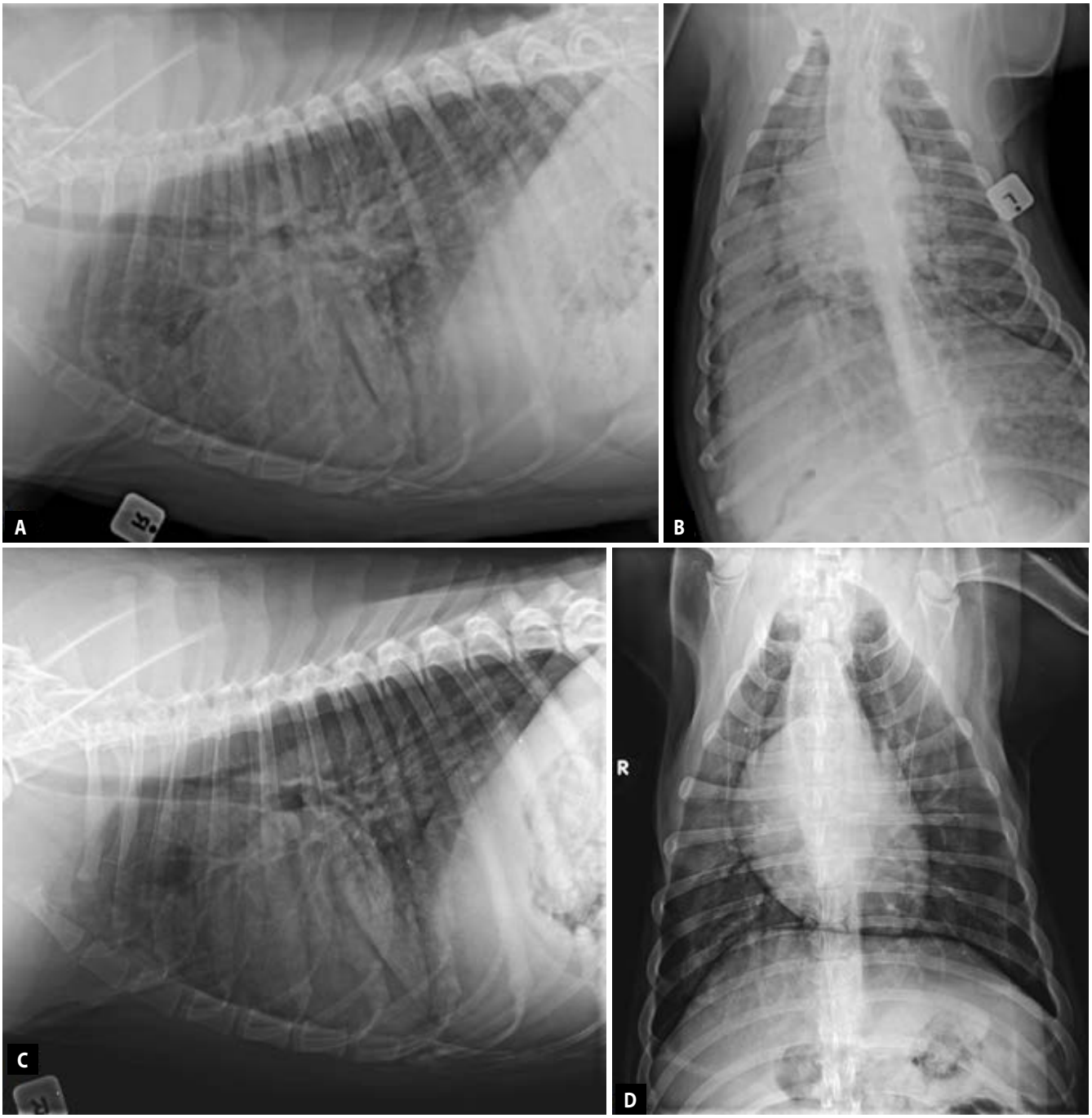

Figure 1: Dorsoventral and right lateral recumbent thoracic radiographs of a pregnant Rottweiler bitch taken on presentation (A, B) and 48 hours later (C, D). Images A and B show a moderate to severe diffuse broncho-interstitial to alveolar pattern. The alveolar component had a ventral distribution on Image A, affecting the right middle and caudal lung lobes with a perihilar extension to the left on Image B. Follow-up radiographs (C, D) showed marked improvement, with patchy remnants, most notably as a caudoventral lobar sign on Image C. These radiographic findings are similar to what was seen in canine African horse sickness cases described elsewhere (Whitehead et al. 2018).

All SpO_2 measurements were taken by pulse oximetry on the lips, tongue, or vulva (Nonin Model 9847V, Nonin Medical Inc).

Radiographs revealed a moderate to severe diffuse broncho-interstitial to alveolar pattern (Figure 1). The patient had a normal vertebral heart score (10.5 vertebrae; RI 8.7–10.7 vertebrae). Abdominal ultrasound confirmed pregnancy with multiple foetal heartbeats seen.

Arterial blood gas analysis (RAPIDPoint 500, Siemens) indicated marked hypoxaemia (PaO_2 54.1; RI 81–103 mmHg) and normolactataemia (1.65 mmol/L; RI 0.43–2.1 mmol/L). There was also a mild mixed acid-base disturbance characterised by metabolic acidosis and respiratory alkalosis.

On haematology (ADVIA 2120i, Siemens), there was a mild leukocytosis (18.2 x 10^9/L; RI 6–15 x 10^9/L) secondary to mild lymphocytosis (5.28 x 10^9/L; RI 6–15 x 10^9/L) and monocytosis (1.82 x 10^9/L; RI 0.15–1.35 x 10^9/L), and a mild thrombocytopenia (131 x 10^9/L; RI 200–500 x 10^9/L). Marked monocyte activity and lymphocyte reactivity and mild toxic change in the neutrophils were noted on blood smear examination. These findings were attributed to acute systemic inflammation, confirmed by a markedly increased canine C-reactive protein (CRP) (226 mg/L; RI in pregnant dogs 70.2–90.4 mg/L [Kuribayashi et al. 2003]).

Clinical chemistry abnormalities (Cobas Integra 400 Plus Analyser, Roche) of note were mild hypoalbuminaemia (26.9 g/L; RI 28–41 g/L) and mild hyponatraemia (137 mmol/L; RI 142–151 mmol/L). Thromboelastography, prothrombin time, activated partial thromboplastin time, urinalysis and faecal floatation were unremarkable. A lateral flow canine distemper antigen ELISA (Antigen rapid CDV Ag Test Kit, BioNote Inc) was negative using conjunctival swabs.

The observed presentation, especially the radiographic changes, resembled previous cases of African horse sickness (AHS) seen at OVAH, and thus AHS was suspected in this patient. BTV testing was also included because of the history of direct exposure to sheep experiencing high mortalities and published reports of BTV infection occurring in pregnant dogs.

Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) testing for AHS virus (AHSV) and BTV (Vetmax reagents, Life Technologies) was performed on EDTA whole blood. The patient tested negative for AHSV and positive for BTV, with an amplification threshold cycle (Ct) value of 24.7.

Management and outcome

Treatment was symptomatic and details of all administered treatments can be seen in Supplementary Table I. Oxygen supplementation was started soon after presentation via free flow close to the nose. This was changed to an indwelling nasal cannula. Broad-spectrum antibiotics were given as per recommended empirical guidelines for suspected bacterial pneumonia (BP) in systemically ill dogs, except for amikacin given once (Lappin et al. 2017). A diuretic was added 12 hours after presentation and was subsequently continued for five days as the patient's SpO_2 gradually normalised to 98% (RI 95–100%) following oxygen supplementation and observed respiratory effort subjectively decreased. After cessation of oxygen therapy, 36 hours after presentation, the SpO_2 remained above 90% (RI 95–100%) until discharge. Follow-up radiographs taken 48 hours after admission revealed significant improvement in the degree of pulmonary oedema (Figure 1 C and D).

The patient was discharged 62 hours after presentation and was clinically normal at a follow-up examination two weeks later. Although ultrasound on the day of discharge detected foetal heartbeats (foetal number and heartrates not recorded) the patient subsequently aborted.

The positive BTV RT-PCR result was received four days after the patient had been discharged. A farm site investigation was done a week after the BTV result was received and multiple sick sheep with BTV symptoms tested positive on BTV RT-PCR. A BTV outbreak was diagnosed, and the state veterinary services were informed.

Eleven months after presentation, the patient whelped a healthy litter with no apparent complications. No other dogs on the farm developed symptoms related to BTV infection.

Discussion

The clinical and clinicopathological findings were consistent with hypoxaemia from inflammatory pulmonary disease. Of note, extremely high CRP concentrations (> 100 mg/L) are indicative of severe inflammatory disease but are not useful to determine the aetiology of a disease (Hindenberg et al. 2020). Increased CRP concentrations may occur during normal pregnancy, trauma, viral diseases, and BP (Kuribayashi et al. 2003; McClure et al. 2013; Viitanen et al. 2014). In this patient, the increased CRP concentration was attributed to marked acute systemic inflammation, likely due to the BTV infection but possible BP, and a normal pregnancy may also have contributed to this marked increase.

The radiographic findings were consistent with pulmonary oedema. The rapid resolution of radiological signs made BP less likely in this patient, but BP could not be excluded due to a ventral alveolar distribution and pattern.

Cardiogenic pulmonary oedema was presumptively excluded as the cause based on the radiological findings of a normal vertebral heart score and an inconsistent distribution of the radiological pattern. The clinical absence of arrhythmias, heart murmurs and strong rhythmic pulses further suggested that the patient's circulation was not compromised. Possible causes of non-cardiogenic pulmonary oedema such as near-drowning, electrocution, severe thoracic trauma, and pulmonary haemorrhage due to rodenticide toxicity (vitamin K antagonism) were excluded from history and testing. The remaining possible differentials were bacterial and viral pneumonia (canine distemper virus, AHSV and BTV).

Bacterial pneumonia (secondary to BTV or as a comorbidity with BTV) may have been present and contributed to the clinical findings in this dog. Due to the severity of the disease and as BP was not fully excluded, antibiotics were used during the treatment of this patient. Lower airway cytology and culture may have been helpful to exclude the presence of BP.

Canine distemper virus (CDV) infection was presumptively excluded based on a good vaccination history, the absence of interaction with new dogs, and a negative ELISA test. Acute catarrhal distemper typically presents with nasal, ocular, and gastrointestinal signs which were mild/absent in this patient.

The AHSV belongs to the same genus of *Orbivirus* as BTV and clinical canine cases have been recently diagnosed at the same institution (O'Dell et al. 2018; Whitehead et al. 2018). The treating clinicians had strongly suspected AHS, which has a remarkably similar presentation, but was excluded with a negative RT-PCR in this case (Whitehead et al. 2018).

A BTV RT-PCR Ct value below 40 amplifications is regarded as positive (Hoffmann et al. 2008). In RT-PCR, Ct values are inversely and logarithmically related to viral RNA concentration and the low Ct value (24.7) in this patient indicated a viraemia with a high viral load (Lakshmi et al. 2018). The patient had a significantly lower Ct value (higher viral load) than those reported in dogs experimentally infected with BTV (Ct values > 30) where viral replication and clinical disease did not occur (Oura et al. 2014).

The diagnosis of BTV infection in this patient was unexpected but could explain all the abnormal findings alone (or in combination with a BP). The clinical findings were consistent with previously described cases of BTV infection in dogs, with the notable exception of the patient's survival and delayed onset of abortion.

Although considered unlikely, cardiogenic pulmonary oedema and CDV infection were also not definitively excluded as causes or contributors to the findings in this patient. Measurement of cardiac troponins and echocardiography may have been useful to further exclude a cardiac cause and further serological or molecular testing may have further supported CDV exclusion.

A BTV outbreak was diagnosed in the flock of sheep as a direct consequence of this patient. The sheep were the likely source of infection with possible routes of vector-borne or oral transmission through the ingestion of sheep placenta, foetal membranes and/or aborted material.

Naturally occurring BTV infections and detectable viraemia have not been reported in dogs. Transport of viraemic dogs into non-endemic areas could represent a risk of BTV transmission to susceptible ruminants in those areas (Oura & El Harrak 2011). This warrants further investigation and serological studies of this outbreak are planned. Bluetongue viral infection should be considered as a possible differential diagnosis for acute dyspnoea in pregnant bitches in BTV-endemic areas, even in the absence of abortion, which may be delayed.

Acknowledgements

The authors would like to thank Heidi and Mark Shippon; Professor Alan Guthrie; Professor Geoffrey Fosgate; the Onderstepoort Veterinary Institute; the OVAH, the Companion Animal Clinical Studies Department, and the Equine Research Center of the University of Pretoria for their assistance and support in making this case study possible.

Conflict of interest

The authors declare they have no conflicts of interest that are directly or indirectly related to the research.

Funding source

Costs related to the treatment were paid by the dog's owner. Costs of further testing were paid by the department of Companion Animal Clinical Studies, University of Pretoria.

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Supplementary Table I: Details of the successful treatment of a pregnant Rottweiler bitch diagnosed with clinical BTV infection. The inclusion of the trade name and manufacturer are not to be seen as an endorsement of the product but reported for clinical completeness.

Therapy type	Drug	Trade name, manufacturer	Route	Dose	Frequency	Notes
Fluid therapy	Lactated ringers solution	Ringer-Lactate solution, Fresenius Kabi SA (Pty) Ltd	Intravenous	61 ml/hr	Constant rate infusion	Maintenance rate for 44 hours then stopped
Oxygen	100% oxygen	Afrox Oxygen, SA (Pty) Ltd	Indwelling nasal cannula	3 l/minute	Constant rate	Started immediately on presentation and stopped at 36 hours
Antibiotic	Amikacin sulphate	Amikacin Fresenius, Fresenius Kabi SA (Pty) Ltd	Intravenous	15 mg/kg	Given once	This was replaced by enrofloxacin to minimise the potential of foetal renal injury, which can occur with aminoglycosides
	Amoxicillin-clavulanic acid	Sandoz® Co-amoxyclav 0.6 g 20 ml, Sandoz SA (Pty) Ltd	Intravenous	20 mg/kg	Every 8 hours for 2 days	Replaced by oral amoxicillin when appetite returned
	Amoxicillin trihydrate	Austell-amoxicillin 250 mg, Austell Laboratories SA (Pty) Ltd	Oral	20 mg/kg	Every 12 hours for 5 days	
	Enrofloxacin	Baytril® 5%, Bayer SA (Pty) Ltd (Animal Health Division)	Subcutaneous	5 mg/kg	Once-daily for 2 days	Replaced amikacin at 24 hours after admission
		Baytril® Flavored 50, Bayer SA (Pty) Ltd (Animal Health Division)	Oral	5 mg/kg	Continued for 5 days	Oral meds replaced subcutaneous injection
Diuretic	Furosemide	Salix® Injection, MSD Intervet SA (Pty) Ltd	Intravenous	2 mg/kg	Initially every 8 hours for 32 hours	Initiated 12 hours after presentation with good response
		Mylan furosemide 40, Mylan SA (Pty) Ltd	Oral	1 mg/kg	Every 12 hours for 5 days	
Anti-emetic	Maropitant citrate monohydrate	Cerenia™ Injection, Zoetus SA (Pty) Ltd	Subcutaneous	1 mg/kg	Once	This was given once on the day of discharge when the dog appeared nauseous and refused a meal; appetite returned later that day