CASE STUDY:

A persistent, treatment-resistant case of *Bordetella bronchiseptica* infection

This case study was prepared by Dr. Robert Shiel MVB DECVIM PhD, Associate Professor of Small Animal Medicine and Dr. Oliver Waite BVSc MRCVS, Small Animal Medicine Intern, UCD Veterinary Hospital.

Signalment:

Ruby was a six-month-old Cavalier King Charles spaniel that presented with a history of daily coughing for approximately three months. The cough was described as dry and sometimes associated with exercise. Several courses of antibiotics, antiparasitic, non-steroidal anti-inflammatory and glucocorticoid therapies had been prescribed with limited improvement.

Ruby was otherwise healthy and a primary puppy vaccination course (distemper, canine parvovirus-2, canine adenovirus-2, parainfluenza and leptospirosis) had been completed when 11 weeks old.

Physical examination:

Ruby was bright, alert and responsive. Body weight was 5.1 kg and body condition score was 4/9. The mucous membranes were pink with normal capillary refill time. Heart rate was 120 beats per minute. Respiratory rate was 28 breaths per minute. Tracheal pinch testing was negative. Thoracic auscultation and abdominal palpation were unremarkable. Rectal temperature was 38.6°C.

Diagnostic tests:

Haematology, serum biochemistry and urinalysis were performed. No significant findings were identified. Mild lymphocytosis and increased ALP activity are commonly observed in young healthy animals. Faecal parasitology and patient-side serum testing for *Angiostrongylus vasorum* were negative. Thoracic computed tomography was unremarkable, although the thymus was still visible, which is common in healthy dogs of this age (Figure 1). Tracheobronchoscopy revealed mild generalised erythema of the trachea and bronchi, with small amounts of mucoid discharge within the lower airways (Figure 2). Bronchoalveolar lavage was performed, revealing a predominance of large neutrophils, most of which were mildly-to-moderately degenerate (Figure 3). Occasional pyknosis and karryorrhexis were observed. Large numbers of bacteria were identified in the extracellular space and rarely in the intracellular space. These changes were considered consistent with moderate-to-marked predominantly neutrophilic, apparently septic inflammation. Degenerate changes were present within most neutrophils. Bacteriological culture revealed a pure growth of *Bordetella bronchiseptica*, susceptible to gentamicin and tetracycline. Mycoplasmal and fungal cultures yielded no growth.

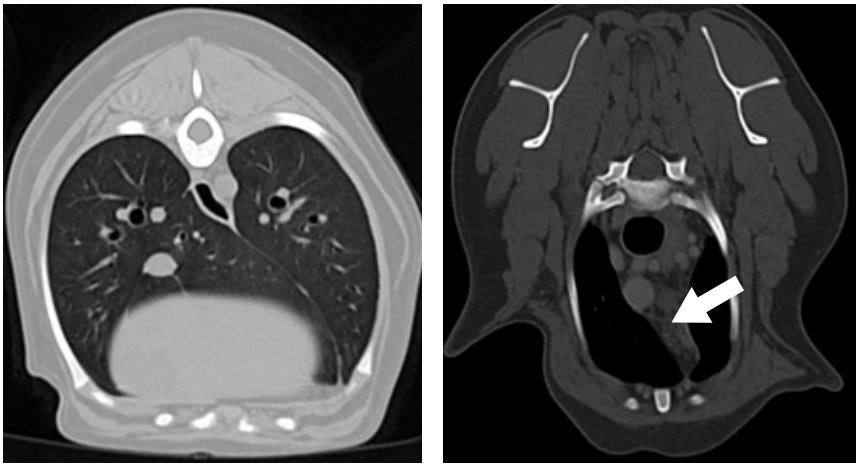

Figure 1: The pulmonary parenchyma appeared unremarkable on thoracic computed tomography (a). Residual thymic tissue was visible within the cranial mediastinum (b, arrow)

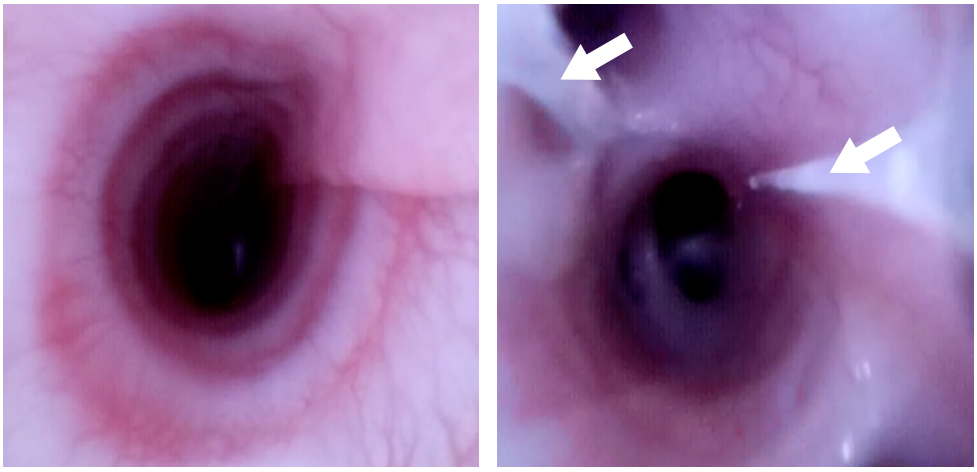

Figure 2: Erythema of the trachea (a) and increased mucus within the lower airways (b, arrows) were visible on tracheobronchoscopy.

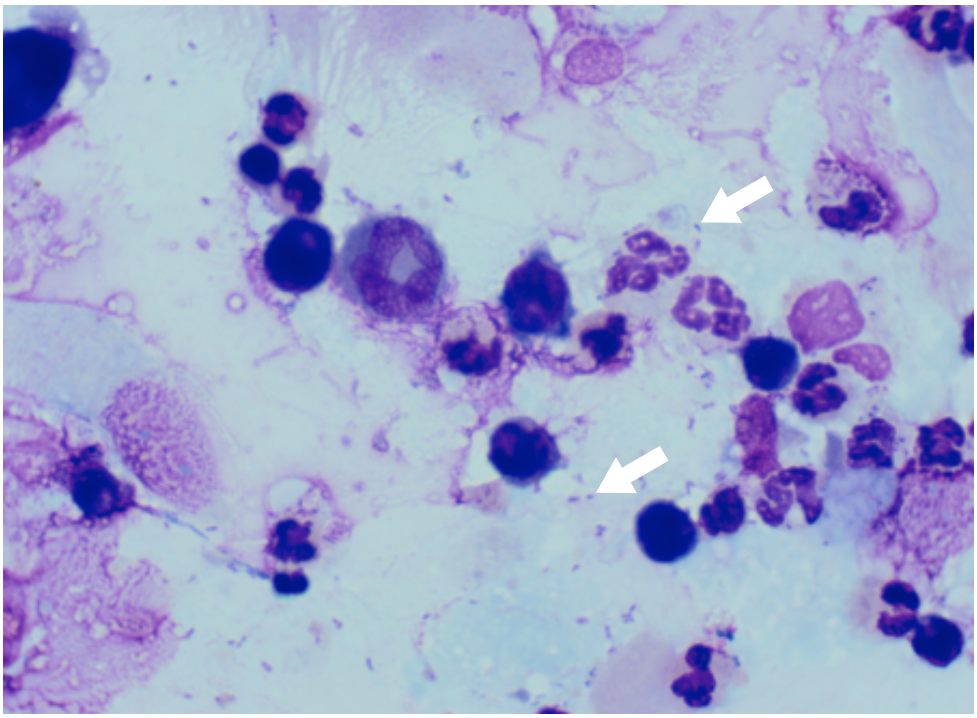

Figure 3: Predominantly neutrophilic inflammation was identified on the bronchoalveolar lavage. Multiple extracellular and intracellular bacteria are also visible (arrows).

Treatment and outcome:

As Ruby had previously received multiple courses of antibiotics, treatment with a combination of nebulised gentamicin (6.9 mg/kg injectable gentamicin in 3 mL of sterile saline, administered twice daily over five days) and oral doxycycline (5mg/kg BID for two weeks) was administered. This resulted in a rapid resolution of clinical signs. The cough had resolved and weight gain was observed at the next visit, two weeks after completion of the antibiotic course. Bronchoalveolar lavage was repeated at this visit. Although cytological changes had resolved, a persistent pure culture was identified. Due to previous episodes of partial improvement and relapse, twice daily nebulisation of gentamicin was recommenced over a period of four weeks. Ruby was re-examined two weeks after completion of this course. No coughing had been observed at home. Bronchoalveolar lavage was repeated, and revealed a possible slight increase in number of well-preserved neutrophils, but no bacteria were identified and culture was negative. No further treatment was recommended.

Discussion:

Canine infectious respiratory disease complex (CIRDC), also known as kennel cough or canine cough, is a condition typically characterised by a dry, hacking cough that can be acute or chronic in nature. Signs vary in severity from mild to life-threatening, depending upon the agents involved, infectious load, immune status of the host, concurrent airway diseases and environmental factors. Multiple agents can be involved, and mixed infections are common. *Bordetella bronchiseptica* remains the most commonly isolated bacterial pathogen amongst symptomatic dogs. Canine parainfluenza virus (CPIV), canine adenovirus type 2 (CAV-2) and canine herpesvirus 1 (CHV-1) are also commonly identified. Concurrent infection with *Mycoplasma cynos* has also been reported, and may be associated with a poorer outcome.

Bordetella bronchiseptica is reported in 5.2-78.7% of CIRDC cases. Although occasionally found as a commensal organism within the respiratory tract of healthy dogs, this bacterium has several virulence factors that allow it to become a primary pathogen. Virulence determinants include filamentous haemagglutinin, fimbriae, pertactin, and a variety of toxins (including dermonecrotic toxin and tracheal cytotoxin) that can cause localised immunosuppression, respiratory epithelial injury, and persistent colonisation. Clinical signs are further complicated in the presence of concurrent airway comorbidities such as structural laryngeal and tracheal disease. *Bordetella bronchiseptica* is not species specific, with reported spread to in-contact cats and immunosuppressed people.

In most cases, clinical signs of bordetellosis are self-limiting and resolve within approximately two weeks. Bacteria can be shed for 2-3 months following recovery. However, in other cases, refractory infection can develop causing persistent clinical signs, and increasing the risk of irreversible sequelae such as chronic bronchitis or pulmonary fibrosis. In Ruby's case, a cough had persisted for several months, and further investigations were recommended to determine the underlying cause, particularly following a lack of complete response to empiric therapy. Although computed tomography revealed no significant findings, *B. bronchiseptica* was identified in addition to cytological evidence of airway inflammation, and clinical signs resolved with clearance of the bacterium.

Cases of CIRDC are often treated empirically without diagnostic testing with a variety of medications including antimicrobials, antitussives and glucocorticoid or non-steroidal anti-inflammatory drugs. Treatment decisions in individual cases can be challenging. Antibiotics are frequently unnecessary; indeed, bacterial pathogens may not be involved, and inappropriate use may contribute to antimicrobial resistance. Antitussive drugs may impair mucociliary clearance in cases with a productive cough. Glucocorticoids can have an immunosuppressive effect which can exacerbate infection.

Once confirmed, treatment of *B. bronchiseptica* can be challenging. Despite apparent susceptibility, a poor response is commonly observed. This may reflect the inability to achieve therapeutic concentrations within affected respiratory tissues, as well as the virulence factors described above. In Ruby's case, several courses of antimicrobials had been administered prior to referral, but the infection persisted. The use of aerosolized gentamicin has shown promise for treatment of persistent respiratory bordetellosis. Such treatment allows high concentrations to be achieved in the respiratory tract, whilst avoiding the adverse effects of systemic aminoglycoside therapy such as renal injury. Traditionally, this low dose was recommended once or twice daily over a period of 5-7 days. However, recently a 3-4 week, higher dose protocol has been shown to result in clinical cure in most dogs. However, it has been advised to reserve its use for refractory bordetellosis only.

Doxycycline was also initially advised in Ruby's case. Doxycycline is a tetracycline antimicrobial recommended as a first line option for the treatment of CIRDC, bacterial bronchitis, and pneumonia in dogs with no systemic manifestations of disease. This antimicrobial offers several advantages compared to other commonly used antimicrobial therapies including concentration in respiratory secretions and its dual action against both *B. bronchiseptica* and *M. cynos*.

Further reading:

- Day, M. J., et al. "Aetiology of canine infectious respiratory disease complex and prevalence of its pathogens in europe." Journal of comparative pathology 176 (2020): 86-108.
- Ford, R.B. "*Bordetella bronchiseptica*: Beyond Kennel Cough" In: Kirk's Current Veterinary Therapy, 14th edition. Eds: Bonagura, J.D. and Twedt, D.C. Saunders Elsevier, St Louis (2009) pp 646-649.
- Lappin, M. R., et al. "Antimicrobial use guidelines for treatment of respiratory tract disease in dogs and cats: antimicrobial guidelines working group of the International Society for Companion Animal Infectious Diseases." Journal of veterinary internal medicine 31.2 (2017): 279-294.
- Morgane Canonne, Aude, et al. "Clinical response to 2 protocols of aerosolized gentamicin in 46 dogs with *Bordetella bronchiseptica* infection (2012-2018)." Journal of Veterinary Internal Medicine 34.5 (2020): 2078-2085.
