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INFECTIOUS DISEASE

Coccidioidomycosis Presenting as a Heart Base Mass in Two Dogs

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Summary

Two atypical cases of canine coccidioidomycosis presenting as heart base masses are described. An echocardiogram performed in one of the two dogs revealed a large mass at the base of the heart and a computed tomography scan showed that the mass compressed the bronchi, left atrium, aorta and pulmonary arteries. A firm, white or pale yellow mass was found at the base of the heart at necropsy examination in both cases. Microscopical examination of the masses revealed severe, chronic, locally extensive granulomatous or pyogranulomatous inflammation with intralesional spherules consistent with *Coccidioides* spp. The diagnosis was further confirmed by immunohistochemistry and in-situ hybridization. *Coccidioides* spp. have been reported to cause pericarditis in dogs, but this is the first description of coccidioidomycosis mimicking a heart-based tumour in dogs.

Keywords: canine coccidioidomycosis; heart; immunohistochemistry; in-situ hybridization

Coccidioidomycosis is a systemic fungal disease of man and animals caused by the dimorphic soil fungi *Coccidioides immitis* and *Coccidioides posadasii* (Fisher *et al.*, 2002). The disease is commonly known as San Joaquin Valley fever, valley fever or desert fever and it exists almost exclusively in the low desert plains of the southwestern USA including Arizona, California, Nevada, New Mexico, Texas and Utah. Other countries where endemic foci exist include Argentina, Brazil, Colombia, Guatemala, Honduras, Mexico, Nicaragua, Paraguay and Venezuela. The disease is rarely reported in the rest of the world. *C. immitis* is geographically restricted to the San Joaquin Valley of California, whereas *C. posadasii* (previously referred to as non-California *C. immitis*) is found commonly in the remaining endemic regions (Fisher *et al.*, 2002). Despite the genetic diversity, these two species are morphologically indistinguishable and cause identical disease. The disease has been reported in many domestic and wild animals including cattle (Maddy, 1954b), sheep (Maddy, 1954a), pigs (Prchal and Crecelius, 1966), horses (Zontine, 1958), dogs (Maddy, 1958), cats (Reed *et al.*, 1963), bats (Krutzsch and Watson, 1978), tapirs (Dillehay *et al.*, 1985), Przewalski's horses (Terio *et al.*, 2003), llamas (Fowler *et al.*, 1992), primates (Rosenberg *et al.*, 1984; Burton *et al.*, 1986), a black rhinoceros (Wallace *et al.*, 2009),a bottlenose dolphin (Reidarson *et al.*, 1998) and sea lions (Fauquier *et al.*, 1996).

Approximately 70% of the infections in dogs are asymptomatic or subclinical (Shubitz *et al.*, 2005); however, severe illness can occur, especially in immunocompromised dogs. The disease occurs in two forms: (1) pulmonary and (2) extrapulmonary or disseminated. The pulmonary form is the most common in dogs and is characterized by coughing (Johnson *et al.*, 2003; Shubitz, 2007). Commonly involved tissues in the disseminated form include bones, joints, heart, brain, eyes, testes, skin, spleen, liver, kidney and subcutaneous tissues. Pericarditis is a common lesion in the heart due to *Coccidioides* spp. infection (Reed, 1956; Shubitz *et al.*, 2001; Heinritz *et al.*, 2005); however, involvement of the base of the heart has not been reported thus far.

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Typically, *Coccidioides* spp. initiate granulomatous or pyogranulomatous inflammation in the target tissue, which usually manifest as numerous small nodules throughout the affected tissue. Solitary nodules of greater size are uncommon. There have been rare case reports of human coccidioidal granulomas mimicking tumours (Petrini *et al.*, 2003; Ellis *et al.*, 2004), but similar reports are lacking in the veterinary literature. The present report describes two unusual cases of canine coccidioidomycosis that mimicked heart base neoplasms.

Case 1 was a 5-year-old male Labrador retriever that was presented to the referring veterinarian with a 6-month history of vomiting, regurgitation, anorexia, lethargy, intermittent fever and syncopal episodes. On referral to the Veterinary Medical Teaching Hospital at Texas A&M University, the dog was febrile (39.8°C) with a pulse rate of 130/min and respiratory rate of 20/min. Auscultation of the thorax revealed a grade 3/6 systolic murmur on the right side and bilaterally increased bronchovesicular sounds. A complete blood count indicated leucocytosis (22.3×10^9/l; reference interval $6-17 \times 10^9$/l) due to neutrophilia (18.5×10^9/l; reference interval $3-11.5 \times 10^9$/l) and monocytosis (3.3×10^9/l; reference interval $0.15-1.2 \times 10^9$/l) and lymphopenia (0.4×10^9/l; reference interval $1-4.8 \times 10^9$/l) were present. Serum biochemical analysis revealed hyperglobulinaemia (52 g/l; reference interval 17–38 g/l). Electrocardiography showed a normal sinus rhythm. A thoracic computed tomography (CT) scan showed an irregular soft tissue mass surrounding the caudal trachea and much of the aortic arch. The mass displaced the heart, pulmonary trunk and pulmonary arteries ventrally and partially compressed the left bronchus. Echocardiographic examination revealed a large soft tissue mass at the base of the heart surrounding the ascending aorta.

The dog was humanely destroyed due to the poor prognosis. At necropsy examination, a very firm, unencapsulated, poorly demarcated and highly infiltrative pale yellow mass ($10 \times 6 \times 8$ cm) was found at the base of the heart (Fig. 1). In the centre of the right caudal lung lobe was a discrete, soft, gelatinous, grey nodule (7 mm diameter). Small, firm, white, scattered nodules were visible throughout the lungs. The left cranial lung lobe was covered with fibrin. The tracheobronchial and cranial mesenteric lymph nodes were enlarged and had a mottled green–black appearance on cut section.

A search of the Texas A&M University pathology archive identified a second similar case of coccidioidomycosis. Unfortunately, a detailed history and clinical findings for this case were not available. This was a 3-year-old male German shepherd dog with a 3-month history of vomiting and anorexia that was humanely destroyed due to a poor prognosis. At necropsy examination, a roughly triangular, firm, white mass ($12 \times 10 \times 5$ cm) was found at the base of the heart. This mass encompassed the bronchi at the level of the tracheal bifurcation, compressed the trachea and extended into the pericardial sac, forming a few nodules. A marked fibrinous pericarditis with tags of fibrin connecting focal masses to the epicardium was noted. One of the caudal lung lobes was firm. No significant gross changes were evident in other organs.

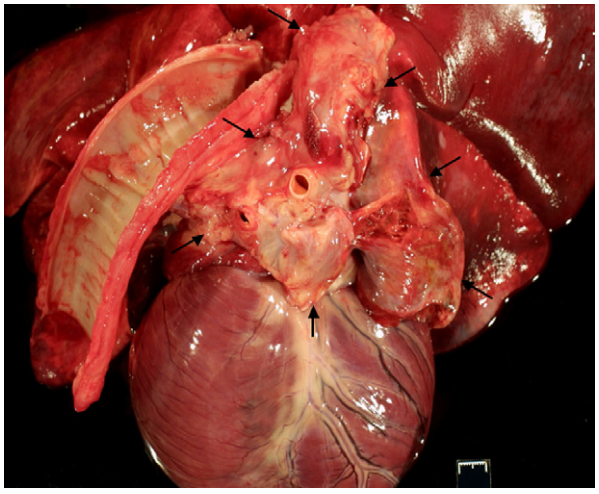

Fig. 1. Case 1. Heart showing an unencapsulated, firm mass measuring $10 \times 6 \times 8$ cm at its base. The boundaries of the mass are marked by arrows.

Tissue sections were fixed in 10% phosphate-buffered formalin, processed routinely and stained with haematoxylin and eosin (HE). Selected tissue sections were also stained with periodic acid–Schiff (PAS).

In case 1, microscopical examination of the mass revealed severe, locally extensive, chronic, pyogranulomatous inflammation composed of a large number of viable and degenerate neutrophils and macrophages and a small number of lymphocytes and plasma cells. The inflammatory cells were surrounded by abundant fibrous connective tissue. PAS staining demonstrated sparse endosporulating, refractile, double-walled spherules consistent with *Coccidioides* spp. The pleura was fibrotic and infiltrated by lymphocytes and plasma cells. In the lungs, the grossly evident nodules were composed of fibrosis and chronic inflammation with lymphocytes and plasma cells. Pyogranulomatous inflammation and fungal spherules were not evident in the lungs. The tracheobronchial and cranial mesenteric lymph nodes were markedly reactive. There was marked diffuse vascular congestion of the centrilobular and midzonal areas of the liver. There was a multifocal lymphoplasmacytic interstitial nephritis.