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Infectious disease

Dissecting aortitis in a goat associated with *Pasteurella multocida* and *Staphylococcus* spp infection

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ABSTRACT

Reports of primary cardiovascular disease in goats are rare and most commonly include ventricular septal defect, valvular endocarditis, traumatic pericarditis, ionophore poisoning and nutritional cardiomyopathies. We now report the pathological findings in a 67 kg, 6-year-old, adult female Boer goat that presented with neurological signs (ie, head pressing, unsteadiness and paddling) and hyperthermia 2 days prior to death. Lack of therapeutic response to meloxicam and penicillin–streptomycin and poor prognosis led to euthanasia of the animal. At necropsy, the main findings included severe aortic dissection with luminal thrombosis and stenosis, and pulmonary congestion and oedema. Histological examination of the aorta revealed severe chronic granulomatous and fibrosing dissecting aortitis with mineralization. Bacterial culture of the affected aortic segment resulted in isolation of a profuse growth of *Pasteurella multocida* and a moderate growth of *Staphylococcus* spp. Histopathological findings in the central nervous system were consistent with neurolisteriosis.

Cardiovascular disease (CVD) is the main cause of morbidity and mortality in humans worldwide. The main pathological entities affecting the aorta include atherosclerosis, aortic aneurysm, aortic dissection (AD) and aortitis [1–3]. AD involves the tearing of the tunica intima and media and is associated with cystic medial degeneration [4]. This entity has been correlated with hypertension, degenerative changes (such as atherosclerosis), aortitis, inherited connective tissue disorders resulting in defective collagen synthesis (such as Marfan and Ehlers–Danlos syndromes), vitamin C deficiency and defects in copper metabolism [1,3].

In domestic and non-domestic animals, CVD types and incidences vary among species. The most common types include degenerative valvular disease and cardiomyopathies in dogs and cats, as well as inflammatory processes (eg, bacterial endocarditis), nutritional diseases (mainly vitamin E and selenium deficiency) and toxic cardiomyopathies in horses and production animals [5]. In small ruminants, particularly goats, CVD typically includes ventricular septal defect, valvular endocarditis, traumatic pericarditis and ionophore poisoning, and appears to have a relatively low incidence [6,7]. Furthermore, goats appear to be resistant to degenerative arterial changes such as atherosclerosis [8]. Common causes of vascular disease in animals include copper deficiency in pigs, *Spirocerca lupi* infection in dogs and *Strongylus vulgaris* migration in horses [8]. AD and aneurysm have been rarely reported, with a few cases involving cats [9], dogs and cattle affected by Marfan syndrome [10,11] as well as turkeys [12]. The incidence of this disease in non-human primates also appears to be low; however, spontaneous lesions have been reported in gorillas, a squirrel monkey and in howler, capuchin, patas, spider and owl monkeys [13,14].

We now present a case of chronic bacterial dissecting aortitis with aortic obliterative thrombosis in a 67 kg, 6-year-old adult female Boer goat with concomitant presumptive neurolisteriosis. Clinical signs included head pressing, unsteadiness and paddling, and hyperthermia 2 days prior to death. The goat had been administered meloxicam and penicillin-streptomycin without clinical improvement. Due to the poor prognosis, euthanasia was elected.

The main necropsy findings involved the intrathoracic aorta and consisted of dissecting aortitis with severe obliterative thrombosis (Fig. 1). Starting at the aortic root, a 7 cm × 1.5 cm × 1.5 cm mass extended distally and expanded the wall of the ascending aorta, aortic arch and descending aorta. On cut surface, the mass was white to yellow and creamy to gritty in the proximal (intramural) portion. It had progressively thickened the aortic wall and

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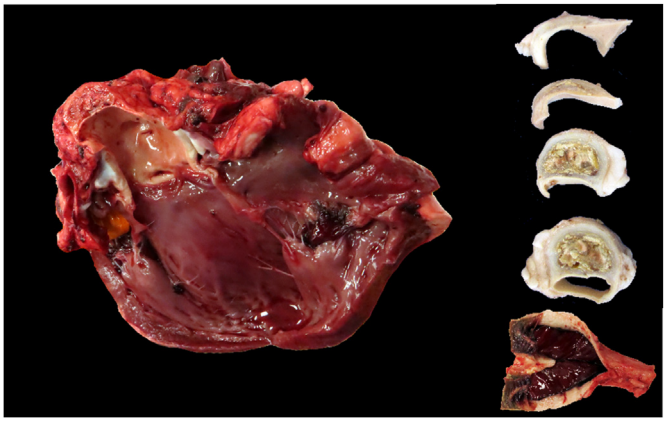

Fig. 1. Dissecting aortitis, *Pasteurella multocida* and *Staphylococcus* spp infection, aorta, goat. Open left ventricle and aortic trunk (left). Proximodistal tangential sections of dissecting aortitis (right).

produced severe luminal stenosis, reducing the lumen to only 0.5 cm in diameter. In the distal portion, the mass transitioned to become intraluminal, gelatinous and yellow to red (Fig. 1). Other gross post-mortem findings included moderate, diffuse pulmonary oedema and mild, acute aspiration pneumonia.

Samples from the intrathoracic aorta, lungs, liver, kidneys, spleen, small intestine, large intestine, adrenal glands, thyroid glands, parathyroid glands and central nervous system (cerebrum, cerebellum and brainstem) were collected. Tissues were fixed in 10% neutral buffered formalin and routinely processed and embedded in paraffin wax. Sections (5 μm) of selected tissues were stained with haematoxylin and eosin (HE) for histological examination. In addition, sections of aorta were stained with Warthin–Starry, periodic acid–Schiff (PAS), Ziehl–Neelsen and Gram stains. Sections of brain were also stained with Gram stain. Bacterial culture was performed at the Veterinary Diagnostic Services Laboratory of the School of Biodiversity, One Health and Veterinary Medicine, University of Glasgow, on a frozen sample of aorta to characterize the suspected bacterial aetiology of the aortic changes.

Microscopically, the aortic media had locally extensive and marked expansion by dense, paucicellular fibrous tissue, with interspersed slender fibrocytes and small scattered foci of osseous metaplasia. This fibrous tissue was multifocally dissected by cores composed of granular to amorphous eosinophilic material with karyorrhectic debris surrounded by a few lymphocytes and macrophages and multinucleated giant cells. Often, necrotic cores were replaced by deeply basophilic granular crystalline material consistent with dystrophic mineralization. Throughout the vessel wall were multifocal, variably sized areas of disarray and loss of elastic fibres that were replaced by paucicellular, pale basophilic material (Fig. 2). No pathogens were identified by Gram, Warthin–Starry, PAS or Ziehl–Neelsen stains in sections of inflamed aorta. Based on these features, a diagnosis of marked, locally extensive, chronic, granulomatous and fibrosing dissecting aortitis with mineralization was determined. Bacteriology of the affected portion of the aorta resulted in dense growth of *Pasteurella multocida* (+4) and moderate growth of *Staphylococcus* spp.

In the brain, primarily within the pons and medulla oblongata, there were multiple foci of liquefactive necrosis with abundant microabscesses containing degenerate and viable neutrophils along with fewer Gitter cells and lymphocytes. Suppurative inflammation also multifocally expanded and disrupted the fourth ventricle and the cerebellar meninges. Numerous intraphagocytic (within histiocytes and neutrophils) and extracellular gram-positive short bacilli were seen in affected areas. A diagnosis of multifocal, moderate to severe, subacute necrosuppurative meningoencephalitis and ventriculitis (rhombencephalitis) with microabscesses and gram-positive rods was made.

To the best of our knowledge, this is the first report of dissecting aortitis in a goat. The bacterial isolates identified in the inflamed aorta of this goat have been previously linked to aortitis, infectious aneurysm (IA) and AD in humans [15] and could be implicated in the pathogenesis of the aortic lesion in this case.

Aortitis can be categorized into two main groups according to the presence or absence of an infectious agent. In humans, non-infectious causes predominate and are associated with rheumatological conditions and systemic lupus erythematosus [16]. Currently, infectious aortitis is most commonly associated with *Salmonella* spp, *Staphylococcus* spp and *Streptococcus* spp infections but a variety of microorganisms can infect vessels [17,18]. In western countries, rare cases of aortitis due to *Mycobacterium tuberculosis* have been reported [19]. Chronic Q fever (*Coxiella burnetii* infection) is also frequently associated with cardiovascular complications, mainly endocarditis, and aortic aneurysms [20].

Infectious aortitis in humans, if left untreated, often progresses to IA and, less commonly to AD. Predisposing factors may include immunosuppression, atherosclerosis, pre-existing aneurysm, arterial medial degeneration, diabetes, vascular/valvular malformation, medical devices or vascular surgery [16]. This disease is associated with a high mortality rate and is usually caused by *Staphylococcus* spp and *Salmonella* spp. However, in rare cases, *P. multocida* may be involved [21,22]. Routes of bacterial invasion of the aorta include implantation on the intimal surface, direct extension of infection from contiguous extravascular sites, traumatic inoculation of contaminated material into the vessel wall and embolization of bacteria into the vasa vasorum. The latter is the most common cause of bacterial seeding leading to aortitis [23]. The isolation of *P. multocida* and *Staphylococcus* spp suggests a bacterial aetiology in this case, although, given the chronicity of the changes, it is not possible to assess whether any particular bacteria caused the lesion or implanted at the site as secondary invaders. Sites of pre-existing aortic wall damage, such as atherosclerotic plaques or aneurysms, can be prone to haematogenous seeding of microorganisms; alternatively, microorganisms can spread from an adjacent site of infection [16,24]. It is noteworthy that no evidence of an underlying injury affecting the aorta or the adjoining tissue was found in this case. Nonetheless, conditions that may have predisposed to bacterial seeding cannot be completely excluded.

In humans, aortitis and IA represent rare and potentially deadly complications of *P. multocida* infection, which can be transmitted from animals to humans through bites, licks or scratches [17,21,22]. It is worth noting that *P. multocida* and *Staphylococcus* spp also represent commensal, notably oropharyngeal, bacteria in animals. However, culture of these bacteria from the site of the AD suggests potential pathogenicity of these organisms in the aortic lesion. The route of infection, as well as the role played by each of these bacteria in the pathogenesis of the disease, were not determined; primary considerations for the site of entry include respiratory or skin infections. Additional testing, such as immunohistochemistry for *P. multocida* and *Staphylococcus* spp, could be used to identify the location of bacteria within the lesions and could help to elucidate the potential pathogenic roles of these bacteria; however, this testing was not pursued in this case.

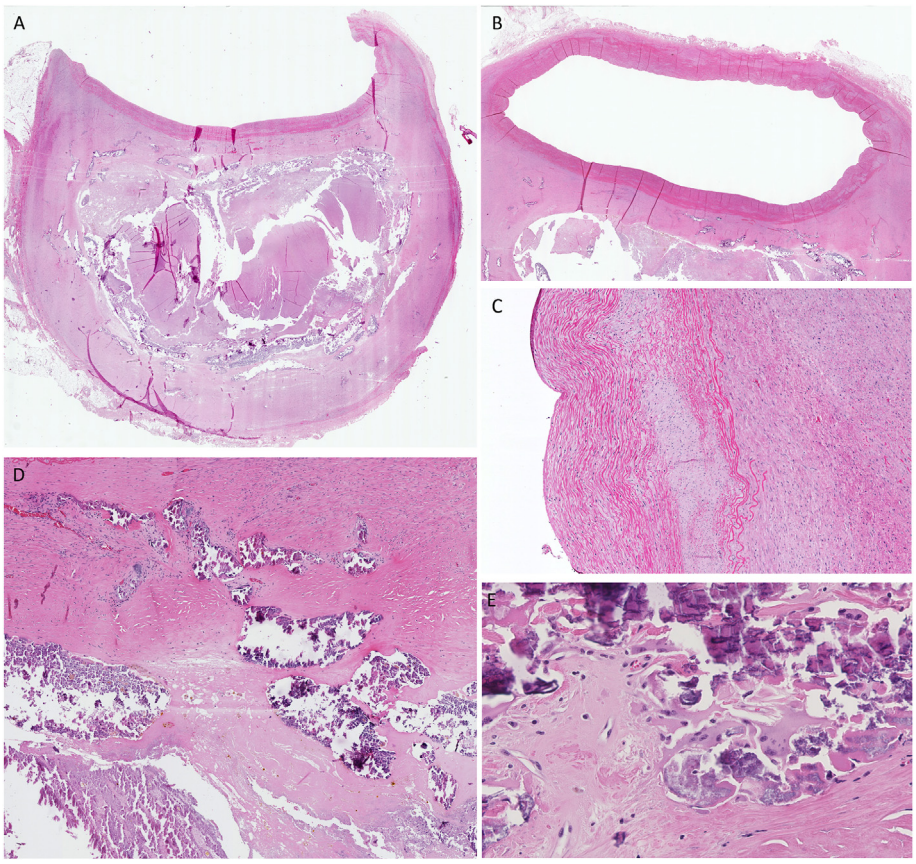

Fig. 2. Dissecting aortitis, *Pasteurella multocida* and *Staphylococcus* spp infection, aorta, goat. (**A**–**C**) Tunica media of aorta disrupted by regionally extensive, disorganized, dense fibrous tissue expanding collagen and elastic fibres. HE. **A**, ×0.5; **B**, ×0.8, **C**, ×10. (**D**) Fibrosis surrounding area of necrosis (1.5 cm × 1 cm) with small foci of haemorrhage. Multifocal to coalescing dystrophic mineralization at periphery of necrotic area and within surrounding fibrous tissue. HE. ×5. (**E**) Macrophages, multinucleated giant cells and rare lymphocytes also present. HE. ×40.

In contrast to the human condition, no aneurysmal dilation was observed in this case. However, locally extensive necrosis that disrupted and dissected the aortic tunica media, yet not forming a false lumen, was present. The significant degree of necrosis associated with a giant cell reaction resembled features of human giant cell aortitis [25], a non-infectious form of aortitis. Although this condition is most commonly associated with systemic arteritis, which was not present in this case, it is plausible that a non-infectious form of aortitis may have contributed to development of the aortic lesions. Non-infectious causes of aortitis have not been well described in goats and investigation of this broad category of vasculitides in animals, in particular goats, is a potential area for future research.

The histopathological findings in the central nervous system in this goat were consistent with neurolisteriosis, one of the most frequent causes of neurological disease in small ruminants, caused by *Listeria monocytogenes*. Although bacteriology was not performed on the central nervous system tissue, the gram-positive intraphagocytic bacilli seen histologically in tissues in association with the brain lesions is pathognomonic for listerial encephalitis. The severity of these lesions could explain the reported neurological signs that led to euthanasia. However, it is also possible that the severe aortic lesions could have aggravated neurological disease by aortic dysfunction including central nervous system hypoperfusion.

In conclusion, the similarities between this case and reports of aortitis and infectious aneurysms in humans suggest a common pathogenesis. This case expands the literature on cardiovascular disease in goats.

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Statement of author contributions

C. Gola, J. Diaz-Delgado, S. Fingerhood: Contributed to the conception or design of the article and the acquisition image data. **C. Gola, J. Diaz-Delgado, S. Fingerhood, N.M. Parry:** Drafted the manuscript and reviewed it critically for important intellectual content. All authors contributed to the article and approved the submitted version to be published.

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Declaration of competing interests

The authors declared no conflicts of interest in relation to the research, authorship or publication of this article.

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