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Abstract Aortic dissection (AD) is characterized by bleeding within the aortic wall or a tear in the intimal layer of the aortic wall, resulting in the passage of blood from the aortic lumen into the tunica media. In cases of AD, a floating, intimal flap in the aortic lumen divides the lumen into a true portion, with flow present, and a false portion, with no flow. We describe a series of 4 cats with AD of the ascending aorta and moderate aortic insufficiency. Three cats had an acute onset of clinical signs with pericardial effusion and cardiac tamponade, whereas one cat showed a chronic onset without pericardial effusion. Detailed gross and histopathological characterization is available for two cats, which revealed the typical features of AD. One cat also showed connective tissue abnormalities, microscopically resem- bling Marfan-like syndrome. Concomitant detection of hypertrophic cardiomyopa- thy in 2 cats represents a novel finding in the veterinary literature. Feline AD is generally associated with systemic hypertension. In all the cats of this case series, blood pressure was normal at presentation, although systemic hypertension before the acute dissection cannot be ruled out. In humans, hypotension is more common with AD of the ascending aorta, so the anatomical location could also play a role in cats. Hypertrophic cardiomyopathy in cats could have been a potential trigger of AD through shear stress. Transthoracic echocardiography, as herein demonstrated, can be considered as a rapid, non-invasive and useful method for the diagnosis of dis- section at the level of the ascending aorta.

KEYWORDS: Aorta; Vasculopathy; Feline; Marfan syndrome *

Case 1

An 11-year-old female spayed Persian cat was referred for dyspnoea and severe depression. At admission, the cat was dyspnoeic, tachycardic, extremely depressed and hypothermic. Femoral pulses were weak, and mucous membranes were pale with prolonged capillary refill time. Thoracic radiographs showed a lung alveolar pattern, mild pleural effusion and increased radiopacity of the aortic arch.

Transthoracic echocardiography (TTE) (Table 1) revealed mild left atrial and ventricular enlargement with normal left ventricular (LV) wall thick- ness. A small amount of pericardial effusion (PE) was evident, associated with mild cardiac tampo- nade. The Doppler study showed a moderate aortic insufficiency (AoI). At the level of the ascending aorta, a floating intimal flap divided the aortic cavity into a true and a false lumen. The aortic true lumen was identified by a diastolic collapse and systolic expansion; colour Doppler revealed a bidirectional flow from the true lumen towards the false lumen during systole and from the false lumen to the true lumen during diastole (Fig. 1AeE). The dissected area extended from the non-coronary cusp of the aortic valve along the explorable tract of the ascending aorta; the false lumen surrounded the true lumen, compressing it partially. The diagnosis of severe aortic dissection (AD) associated with moderate AoI and PE with mild tamponade was made. The cat was hospi- talized for intensive care, but died within 1 h. The owners did not give consent for post-mortem examination.

Case 2

A 10-year-old neutered female domestic short- haired cat was presented because she was found lying down in the garden. At admission, the cat was weak, lethargic and hypothermic, the heart rate was 200 beats/min and the femoral pulse was weak. Auscultation revealed a grade III/VI left parasternal systolic murmur. The extremities were cold, and capillary refill time was prolonged. Thoracic radiographs revealed a normal cardiac size (7.5 vertebrae), using the vertebral heart size method (normal range: 6.7e8.1 vertebrae), a normal vascular pattern, but increased opacity of the aortic arch. Serum chemistry revealed an elevated creatinine level of 3.7 mg/dl (0.6e1.5 mg/dl), urea level of 295 mg/dl (25e75 mg/dl) and phosphorus level of 8.5 mg/dl (3.5e5.5 mg/dl). The serum thyroxine level was normal.

Transthoracic echocardiography (Table 1) revealed concentric LV hypertrophy and basal septal bulging. The left atrium was normal in size. Continuous-wave Doppler showed moderate AoI. The aortic root was divided into two portions (a true lumen and a false lumen) by a mobile intimal flap extended from the non-coronary cusp to the right coronary cusp. Colour Doppler demonstrated the presence of flow only within the true lumen (Fig. 1F). A small amount of PE with mild cardiac tamponade was also present. The owner declined further evaluation and therapy, and the cat was euthanized.

At post-mortem examination, severe haemo- pericardium was observed. The aortic arch was diffusely, mildly dilated, with a focal adventitial laceration overlain by a protruding, one-centimetre-diameter region of clotted blood on the cranial surface. On longitudinal sectioning of the heart on its midsagittal plane, a severe blood-filled space dissecting the aortic wall was observed (Fig. 2A and B). The dissection extended from the ascending aorta (immediately above the aortic valve) throughout the aortic arch (where it had the widest extension) and the descending aorta for a total length of 5 cm. The external surface of the pulmonary trunk, as well as the conus arteriosus

Table 1 Signalment, echocardiographic data and histological findings in each of the four cases.

Case	Signalment	Weight (kg)	Onset of clinical signs	SBP (mmHg)	AoI	LA/Ao	LV M-mode	PE	Histological findings
1	Persian cat, F, 11 y	2.1	Acute	100	Yes, moderate	1.60	IVSd: 3.6 mm LVDd: 16.7 mm LVPWd: 4.0 mm	Yes, cardiac tamponade	No
2	Domestic short-haired cat, F, 10 y	4.5	Acute	130	Yes, moderate	1.51	IVSd: 6.7 mm LVDd: 13.1 mm LVPWd: 5.5 mm	Yes, cardiac tamponade	AD of the ascending aorta, pulmonary artery degeneration without dissection, HCM
3	Persian cat, M, 13 y	3.8	Chronic	120	Yes, moderate	1.48	IVSd: 6.2 mm LVDd: 12.8 mm LVPWd: 5.8 mm	No	No
4	Persian cat, M, 12 y	3.6	Acute	135	Yes, moderate	1.61	IVSd: 8.1 mm LVDd: 11.8 mm LVPWd: 7.2 mm	Yes, cardiac tamponade	AD of the ascending aorta, HCM

HCM: hypertrophic cardiomyopathy; AD: aortic dissection; Ao: aorta; AoI: aortic insufficiency; LA: left atrium; IVSd: interventricular septum in diastole; kg: kilograms; LVDd: left ventricular diameter in diastole; LVPWd: left ventricular posterior wall in diastole; PE: pericardial effusion; SBP: systolic blood pressure; y: years.

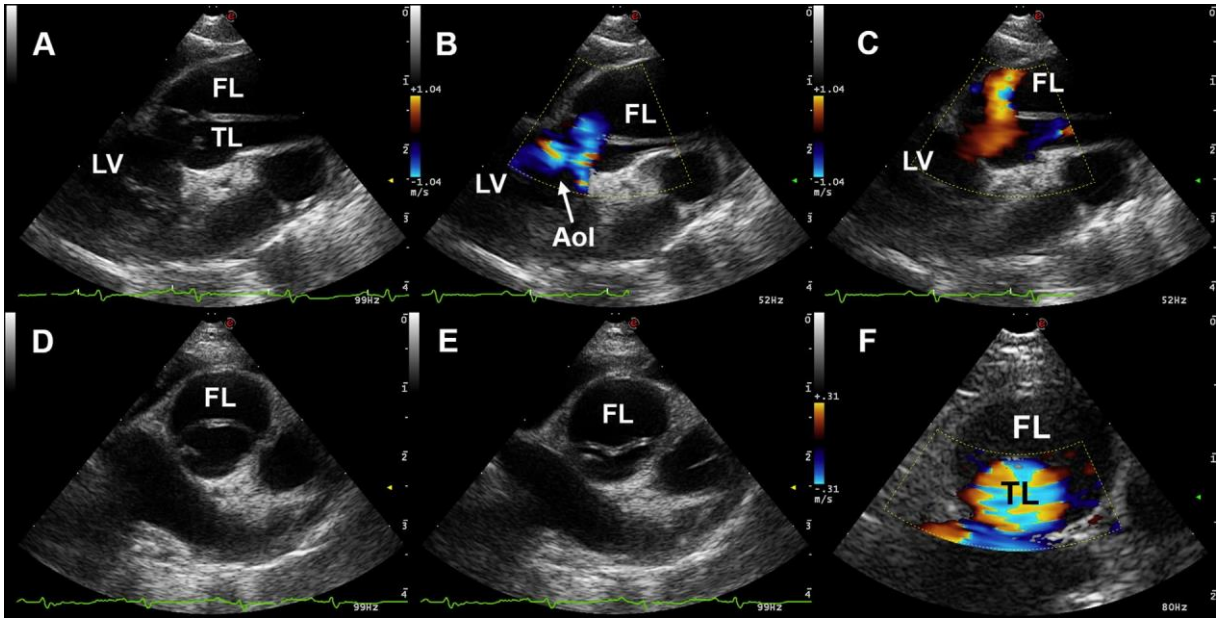

Fig. 1 Case 1 and 2: echocardiographic findings. (AeC) Right parasternal long-axis view, optimized for the aortic root and the ascending aorta: a floating intimal flap divides the aortic cavity into a true lumen and a false lumen (A); colour flow Doppler echocardiography highlights a bidirectional flow between the true lumen and the false lumen during diastole (B) and systole (C). (DeF) Right parasternal short-axis view at the level of the aortic valve: the aortic true lumen is characterized by a systolic expansion (D) and a diastolic collapse (E); colour flow Doppler echocardiography reveals the presence of flow only in the true lumen during systole (F). AoI: aortic insufficiency; FL: (aortic) false lumen; LV: left ventricle; TL: (aortic) true lumen.

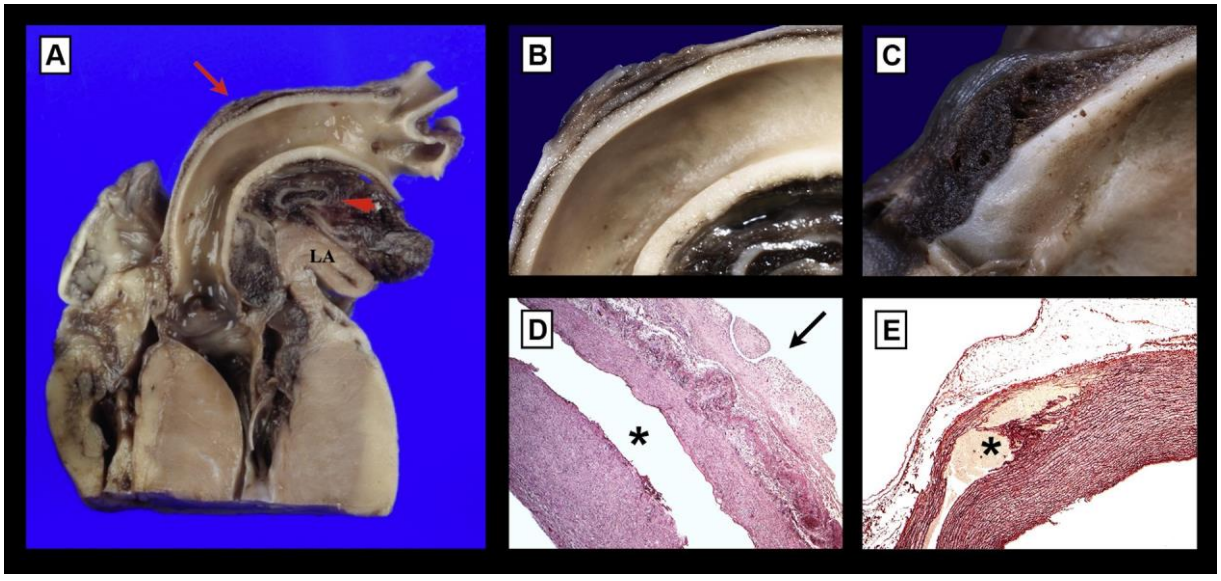

Fig. 2 Case 2: gross and histopathological findings. (A) Longitudinal section of the heart. The aortic wall is split, with haemorrhage (arrow) dissecting into the tunica media. An organized haematoma also encloses the ascending aorta, the aortic arch, the first tract of the descending aorta,

the left branch of the pulmonary artery (arrowhead) and the left auricle (LA). (B) Details of the aortic lesion (photo taken using the stereomicroscope). (C) Details of the large, multifocal to locally extensive adventitial haematomas of the pulmonary artery wall (photo taken using the stereo- microscope). (D) Aortic arch (2.5 , haematoxylin and eosin stain): severe and diffuse dissection of the tunica media with granulation tissue deposition in the tunica adventitia (arrow). *: aortic lumen. (E) Descending aorta (2.5 , Elastic Red Picro Sirius stain): severe and diffuse dissection (*) of the tunica media.

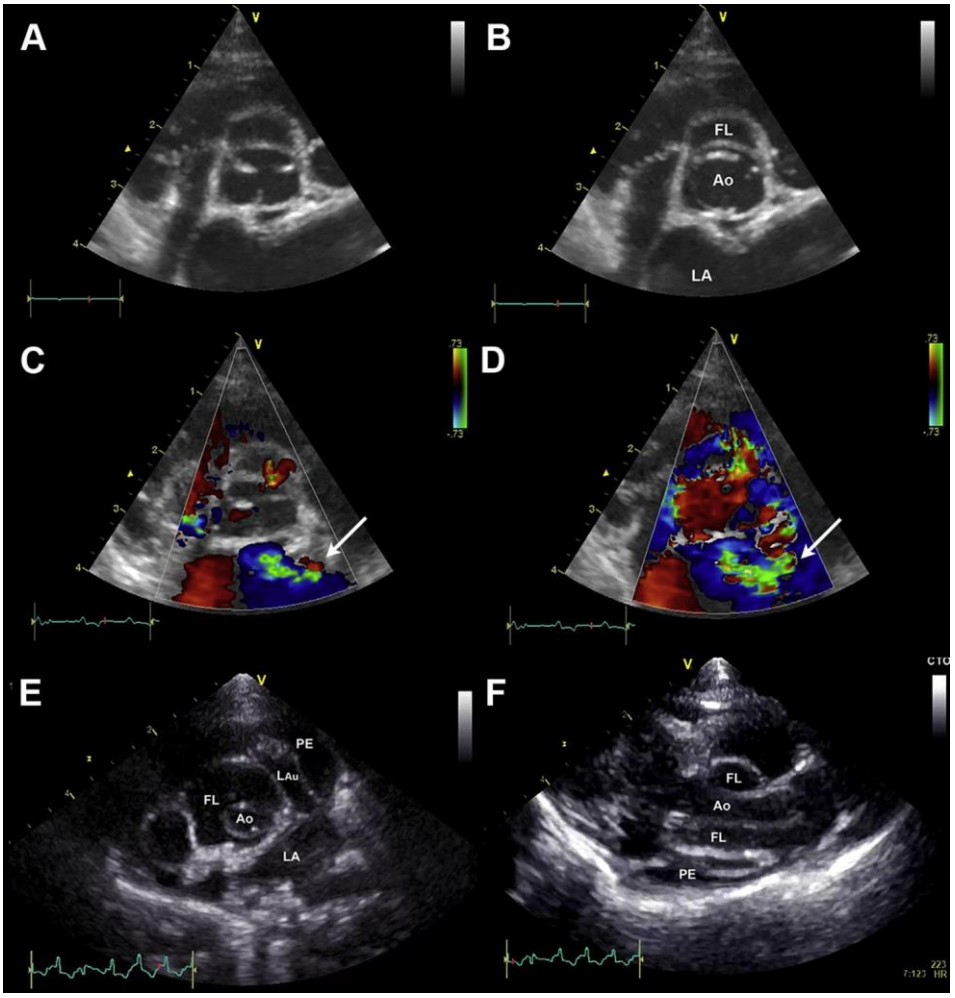

Fig. 3 Case 3 and 4: echocardiographic findings. (AeD) Right parasternal short-axis view at the level of the aortic valve in diastole (A and C) and systole (B and D): images reveal aortic dissection characterized by a false lumen and a true lumen (B), a fistula between the aorta and left atrium is highlighted by colour flow Doppler echocardiography, and a continuous flow in diastole and systole is present (CeD; arrow). (EeF) Right parasternal short- and long-axis views: a severe aortic dissection with pericardial effusion (PE) is highlighted. Ao: aorta; FL: (aortic) false lumen; LA: left atrium; LAu: left auricle; PE: pericardial effusion.

epicardium, appeared diffusely thickened, irregu- lar and brownish red. Longitudinal sectioning of the pulmonary trunk revealed large, multifocal to locally extensive adventitial haematomas (Fig. 2C).

On cross-sectioning of the heart at the level of the middle third of the left ventricle, the wall thicknesses revealed severe concentric LV hyper- trophy (LV free wall thickness: 6.0 mm, interven- tricular septum thickness: 8.0 mm, right ventricular free wall thickness: 3.0 mm). There were no additional intracardiac alterations.

Multiple longitudinal and cross-sectional sam- ples of the aorta and the pulmonary trunk, as well as the ventricles, were collected and fixed in 10% buffered formalin solution. The samples were

successively processed and stained with haematoxylin and eosin. Sections of the aorta and the pulmonary artery were also stained with Elas- tic Red Picro Sirius and alcian blue/periodic acid- Schiff to investigate elastic fibres and collagen as well as mucopolysaccharide deposition, respec- tively. The tissue sections were examined by light microscopy.

On histopathological examination, the aortic wall showed diffuse, severe dissection of the

tun- ica media (Fig. 2D and E) with interposition of an organizing haematoma composed of blood, fibrin, neutrophils and macrophages. Within the tunica media of both the dissected and the non-dissected segments, severe, multifocal fragmentation and/ or loss of the elastic fibres was identified. The retained disorganized elastic fibres were sepa- rated and further disoriented owing to

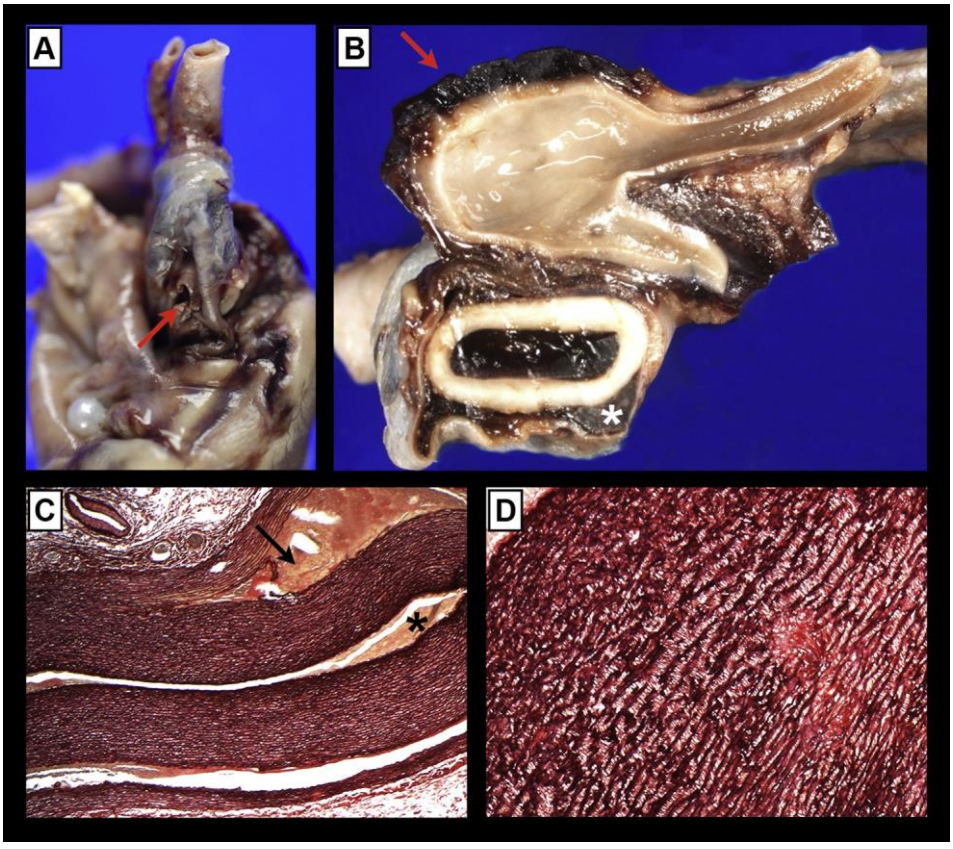

Fig. 4 Case 4: gross and histopathological findings. (A) An irregular full-thickness fissure (2 mm) is identified in the ascending aorta (arrow). (B) Ascending aorta: a large dissecting haemorrhage (*) (dissection) is observed. The lon- gitudinal section of the pulmonary artery shows a wide, periadventitial haematoma (arrow). (C) Ascending aorta (Elastic Red Picro Sirius, 2.5): wide dissection of the wall (tunica media) near the tunica adventitia (arrow); *: aortic lumen. (D) Details of the tunica media of the aortic wall (Elastic Red Picro Sirius, 5): the elastic fibres appear irregular, fragmented and distanced from each other at some points owing to the accumulation of amorphous, eosinophilic material (collagen).

accumulations of acid mucopolysaccharide and fibrous tissue deposition. The tunica adventitia of the aortic arch showed severe, multifocal neu- trophilic, lymphoplasmacytic and macrophagic inflammation, along with granulation tissue depo- sition. Medial elastic fibre alterations and collagen depositiondsimilar to those identified in the aor- tadwere also observed in the pulmonary artery. The pulmonary artery also showed severe, multi- focal haematomas between the tunica media and adventitia. Finally, the left ventricle showed dif- fuse myocardiocyte hypertrophy with marked, multifocal myofibre disarray, severe, multifocal intramural coronary arteriolosclerosis (charac- terized by intimal fibromuscular hyperplasia and medial hypertrophy) and moderate, multifocal interstitial fibrosis.

Based on the gross and histopathological find- ings, a diagnosis of AD with concurrent pulmonary artery degeneration and hypertrophic cardiomy- opathy (HCM) was made.

Case 3

A 13-year-old male neutered Persian cat was pre- sented with a 4-day history of dyspnoea. At admission, the cat was alert but dyspnoeic, and the mucous membranes were cyanotic. The heart and respiratory rates were 180 beats/min and 120 breaths/min, respectively. Auscultation revealed a grade II/VI left parasternal systolic murmur, regu- lar rhythm and pulmonary crackles. Thoracic radiographs revealed generalized cardiomegaly (10 vertebrae, range: 6.7e8.1 vertebrae) and increased lung opacity, consistent with pulmonary oedema. Transthoracic echocardiography and the Doppler study identified concentric LVhypertrophy, left atrial enlargement and moderate AoI (Table 1). A severe AD was highlighted with a false lumen extended from the right coronary cusp (Fig. 3A and B), through the aortic arch. A fistula between the aorta and left atrium at the left coronary cusp level was identified with a turbulent flow from the aorta into the atrium (Fig. 3C and D). Therapy with oxygen, nitroglycerine and furo- semide was initiated, and the symptoms improved. The next day, the cat was discharged with a ther- apeutic plan composed of furosemide and enalapril. After 4 years, the cat returned with dyspnoea and lameness on the right pelvic limb; a diagnosis of arterial thromboembolism and cardiogenic pul- monary oedema was made through clinical examination and radiographs, and the cat was hospitalized. Pulmonary oedema improved with therapy, but the limb remained paretic, pulseless, sore and cold, and creatinine and potassium levels increased in the following days. The cat was euthanized in agreement with the owners, who denied post-mortem examination.

Case 4

A 12-year-old male neutered Persian cat was pre- sented to a referral hospital for dyspnoea. On admission, the cat was alert, with a slightly low rectal temperature (37.1 °C) and a heart rate of 160 beats/min. Auscultation revealed a grade V/VI holosystolic left apical murmur, regular rhythm and muffled lung sounds. The cat was tachypnoeic (48 breaths/min), and the mucous membranes were pale. Serum chemistry revealed a urea level of 184 mg/dl (30e65 mg/dl).

Transthoracic echocardiography (Table 1) iden- tified severe LV concentric hypertrophy and an AD associated with PE and cardiac tamponade (Fig. 3E and F). Left ventricular end-diastolic and end- systolic diameters were moderately decreased. The cat was immediately hospitalized, but after a slight improvement, he died.

On post-mortem examination, severe haemo- pericardium was observed (2 mL). A full-thickness fissure of 2 mm located 1 cm above the aortic wall was also observed on the ascending aorta (Fig. 4A). Serial cross sections of the ascending aorta revealed a longitudinal blood-filled space dissect-

ing more than half of the arterial wall width. This blood-filled space progressively dilated lengthwise for 5 cm distal to its origin immediately above the aortic valve. The pulmonary artery showed a wide, focal periadventitial haematoma (Fig. 4B). Wall thicknesses revealed severe LV concentric hypertrophy (LV free wall: 10 mm, interventricular septum: 6.0 mm, right ventricular free wall:
3.0 mm), and there were no other intracardiac alterations.

The aorta, pulmonary artery and ventricles were sampled and processed as previously reported for case 2.

On histopathological examination, the aorta showed diffuse, severe dissection of the tunica media, with interposition of an organizing hae- matoma composed of blood, necrotic debris, fibrin and neutrophils (Fig. 4C). Within the tunica media of both the dissected and non-dissected segments, severe, multifocal fragmentation and/or loss of the elastic fibres was identified, along with fibrous tissue deposition (Fig. 4D). The pulmonary artery showed severe, multifocal haematomas in the tunica adventitia. Finally, the LV myocardium showed severe, diffuse myocardiocyte hyper- trophy with moderate, multifocal disarray. Mod- erate, multifocal myocardiocyte loss and replacement fibrosis as well as severe, multifocal intramural coronary arteriolosclerosis (charac- terized by intimal fibromuscular hyperplasia and medial hypertrophy) were also observed.

Based on gross and histopathological findings, a diagnosis of AD with concurrent HCM was made.

The systolic blood pressure measured by Dop- pler on the forelimb was normal in all the cats (Table 1).

Discussion

This case series describes four cats with AD, an uncommon but potentially fatal disease with catastrophic complications widely described in humans [1]. In animals, there are only few cases reported in the literature, involving cats [2e6], dogs [7e11], horses [12,13] and cattle [14].

Aortic dissection is characterized by a separa- tion between the aortic wall layers. A degeneration of the aortic medial layer could be a predisposing factor for AD, but an increase in systemic pressure or elevated shear stress on the vessel wall could result in intimal tearing and consequent dissection of the tunica media. Blood pressure usually generates stress on all the wall layers, whereas shear stress is mainly applied on the intimal layer [15]. Furthermore, the rate of acceleration of the pulsatile flow and velocity of the pressure rise, increased, for example, during systemic hypertension, are very important factors in the propagation of the dissection [16]. The ascending aorta, where the pulsatile flow is the greatest [1], is subjected to more stress during LV ejection because of its convexity and its exposure to maximal blood pressure, so it would be more vulnerable [17]. In human patients, AD can be associated with both hypotension, in case of proximal dissections, as happened in our cases, and hypertension, more common when distal dissections occur [1]. Hypotension is often related to cardiac tamponade, AoI and aortic rupture [18], but it is also possible to speculate that during dissection of the ascending aorta, the stiffness of the wall and the compression on the true lumen could create an obstruction to the LV ejection, resulting in hypotension. In contrast, when dis- section of the descending aorta occurs, the stiffness of the vessel may cause increased systolic and pulse pressures. Chronic systemic hypertension is the most common factor predisposing humans to AD [1] and has frequently been reported in cats with AD [2,4,6]. However, although hypertension is a common finding in old cats, AD is rare [4]; therefore, degeneration of the aortic wall may be an additional predisposing factor necessary for AD development. Recently, Kohnken et al. [19] reported vasa vasorum lesions secondary to sys- temic arterial hypertension in cats as a predis- posing factor for damage of the great-vessel wall. It is unclear in cats if systemic hypertension is the main predisposing factor for AD or if the weaken- ing of the aortic wall may be associated with other alterations compared with the vasa vasorum. Scollan and Sisson [4] described a case of AD in a cat with severe hypertension at

presentation, but a computed tomography scan identified a dis- section involving both the ascending and descending aorta. All the cats of this report were not hypertensive at presentation (Table 1), similar to a recent report [3]. Cardiac tamponade, AoI and the anatomic location may explain the lack of systemic hypertension; however, the presence of hypertension before the acute event cannot be ruled out. Two of the four cats had elevated cre- atinine and urea levels, likely owing to a prerenal azotaemia caused by hypoperfusion, but they might have had pre-existing renal insufficiency that predisposed them to systemic hypertension.

Left ventricular concentric hypertrophy was observed in three cats, which may be due to systemic hypertension or could be pseudohypertrophy related to the reduced preload in the cats with cardiac tamponade. However, histopathological examination revealed the typical features of HCM (i.e., myofibre disarray, intramural coronary arteriosclerosis and interstitial and/or replace- ment fibrosis) in two of these cats. These alterations allow us to hypothesize the presence of an obstruction of the LV outflow tract as a poten- tial trigger for AD owing to the increase in shear stress. However, we did not establish whether dynamic outflow tract obstruction was present in these two cases.

All the cats presented with moderate AoI. In humans, proximal dissection may involve the aortic valve, resulting in acute AoI [1]. Several mechanisms have been proposed as the cause of AoI: commonly, there is an incomplete coaptation of the aortic leaflets owing to widening of the sinotubular junction or an intimal prolapse in cases of extensive dissections near the annulus [1].

In humans, degenerative damage of the aortic wall in proximity of the dissection is a common finding [1]. Post-mortem examination has rarely been performed in cats with AD [5,6] with little information about the histopathological findings [6]. In cases 2 and 4, degenerative processes of the aortic tunica media (disorganization, fragmenta- tion and/or loss of the elastic fibres with muco- polysaccharide accumulations) were observed, thus supporting the hypothesis of medial aortic degeneration as a predisposing factor for AD. However, the identification of the aforementioned changes as AD sequelae seems unlikely: AD showed an acute onset of the clinical signs, whereas the histopathological alterations (i.e., adventitial inflammation and medial fibrous tissue deposition) were chronic. Another interesting aspect to con- sider is that the histopathological findings descri- bed in case 2 are similar to those identified for Marfan-like syndrome previously reported in canine aortic aneurysm [20] and dissection [7,9]. Marfan syndrome is a well-recognized connective tissue disorder in both humans [21] and bovines [14], showing the accumulation of acidic mucopo- lysaccharides between the disrupted elastic fibres as main histopathological features [21]. However, because no genetic testing indicative of a fibrillin mutation was herein performed and no other changes associated with connective tissue dis- orders were identified, a diagnosis of Marfan or Marfan-like syndrome cannot be made.

In this case series, three of the four subjects were Persian cats. However, cases reported in the literature include a predominance of mixed-breed cats. More data are needed to consider a breed predisposition.

All the cats with acute AD (cases 1, 2 and 4) had PE with cardiac tamponade, unlike the cat with chronic AD (case 3). Further investigations are needed to evaluate the association between acute onset and PE with cardiac tamponade in cats with AD.

Finally, TTE can be a useful method for diag- nosing AD. Indeed, the identification of a floating, intimal flap in the aortic lumen, which divides the lumen into a true portion where there is flow and a false portion where the flow is absent, is consid- ered diagnostic of AD [22]. However, TTE has low sensitivity in cases of a dissection of the descending aorta, where transoesophageal echo- cardiography is recommended [1]. In all the cats of this report, AD was diagnosed by TTE, which can be considered as an accurate, rapid and non- invasive method for the diagnosis of the dis- section at the level of the ascending aorta.

In conclusion, to the best of the authors' knowledge, the present study is the first case series reporting a detailed clinicopathological characterization of AD in cats. Furthermore, the

concomitant identification of AD and HCM in feline patients represents a novel finding.

Conflicts of Interest Statement

The authors do not have any conflicts of interest to disclose.

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