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Clinical and necropsy evaluation of endocardial fibroelastosis in a mixed-breed cat with left side heart failure

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Abstract: A two-month-old, male intact, mixed-breed cat weighing 0.6 kg was presented with respiratory distress and anorexia. From the transthoracic echocardiographic, reduced fractional shortening (FS) and increased endocardial echogenicity were recognised with severe congestive heart failure (CHF). The kitten was administered an antibiotic and pimobendane under oxygen supplementation in an ICU cage. However, the respiratory condition worsened and the cat died the next day, and the subsequent necropsy and histopathology examinations confirmed endocardial fibroelastosis (EFE). There is a lack of information regarding the antemortem cardiac function evaluated by tissue Doppler imaging (TDI) in EFE cases. We report on the echocardiographic findings including the TDI in the EFE cat with a concomitant necropsy and histopathology confirmation in this paper. The echocardiographic findings showed presence of a ventricular false tendon within the left ventricle, a decrease in the left ventricular contractility (FS 11.1%, and a marked CHF). In this case, the echocardiographic findings were consistent with the human counterpart. However, these findings were like those of dilated cardiomyopathy and, hence, non-specific to EFE. As a result, veterinarians should keep in mind that endocardial fibroelastosis might be a possible reason for respiratory distress resulting from CHF with a low fractional shortening in young cats.

Keywords: echocardiography; endocardial fibroelastosis; kitten; tissue Doppler imaging

Endocardial fibroelastosis (EFE) is a congenital heart disease characterised by the fibrous and elastic thickening of the left-ventricular endocardium (Letteer 1953; Ino et al. 1988). In veterinary literature, genetic factors are thought to play a crucial role, hence, Burmese and Siamese breeds are overrepresented (Paasch and Zook 1980; Zook and Paasch 1982; Rozengurt 1994). In humans,

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EFE reportedly develops frequently in infancy with endocardial proliferation of the elastin and collagen fibres causing a reduction in the left ventricular function and congestive heart failure (CHF) (Greenwood et al. 1976; Nield et al. 2002). A review of past reports reveals similar histopathological findings between human and feline EFE patients (Zook et al. 1981).

While veterinary reports regarding the heritability and post-mortem pathological findings of EFE exist, there is a lack of information about the antemortem cardiac function evaluated by echocardiography, particularly by tissue Doppler imaging (TDI) (Gudenschwager et al. 2019; Schreiber et al. 2020). Here, we report on a conventional echocardiographic evaluation of a kitten with a concomitant necropsy and histopathology confirmation of EFE.

Case description

A two-month-old, male intact, mixed-breed cat weighing 0.6 kg was presented with respiratory distress and anorexia. Since birth, the cat was noticed to have difficulty in breathing and having hyporexia compared to the other littermates. On physical examination, a body condition score of 3 was determined and the cat was lethargic and exhibited a laboured breathing pattern in a prone position (60 breaths per minute), the heart rate was 120 beats per minute with a regular rhythm, a grade II/VI systolic murmur with a point of maximum intensity over the left apex was auscultated, and the rectal temperature was 36.6 °C. The femoral artery could not be palpated in the cat. The thoracic radiography revealed an unclear cardiac silhouette and decreased abdominal contrast details, suggesting the presence of a pleural and peritoneal effusion (Figure 1).

On the transthoracic echocardiography, a pericardial effusion as well as a pleural effusion were recognised. Biventricular enlargement, mild mitral and tricuspid regurgitation (tricuspid regurgitation velocity 230 cm/s), decreased myocardial mobility, and thinning of the left ventricular free wall and interventricular septum were found in the right parasternal long-axis left ventricular inflow view (Figure 2A,B). In the right parasternal short axis view, a marked decrease in the fractional shortening (FS) and increased endocardial echogenicity was noted (Figure 2C). The ratio of the left atrial dimension to the aortic annulus dimension (LA/Ao) was measured at the basal level by two-dimensional echocardiography. The left atrium was remarkably enlarged (left atrium 13.8 mm, left atrium/aorta ratio 3.45). The peak tissue Doppler mitral annular velocities at systole (S'), early diastole (E') in the left parasternal apical four-chamber view were measured by focusing the sample volume

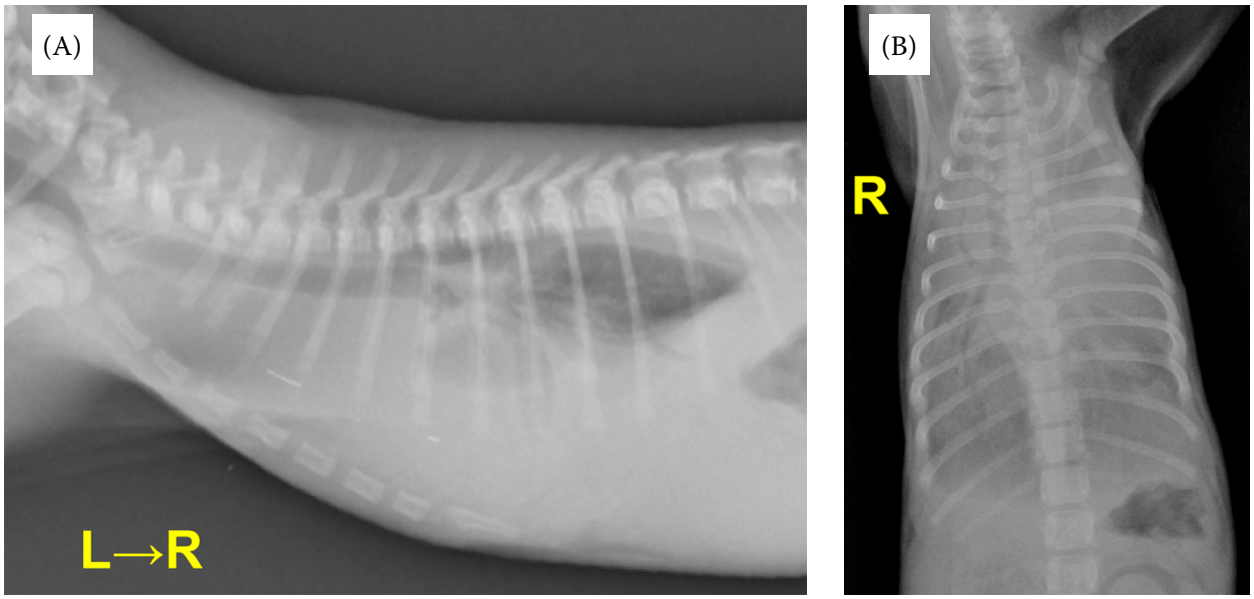

Figure 1. Thoracic radiography in this case

(A) Lateral view. (B) Dorsoventral view. Obscure cardiac margin and decreased abdominal contrast suggested the presence of a pleural effusion and ascites, respectively

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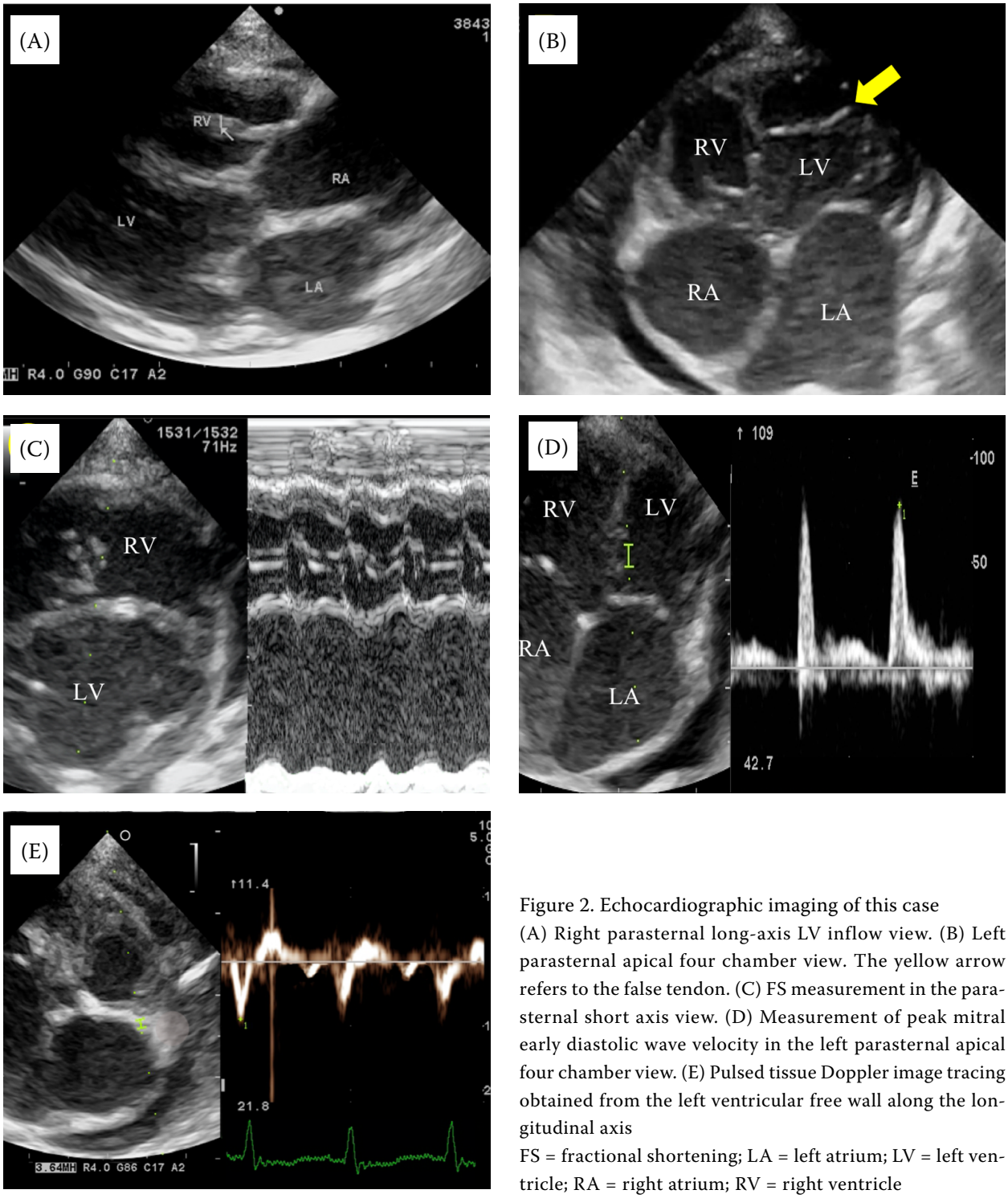

Figure 2. Echocardiographic imaging of this case
(A) Right parasternal long-axis LV inflow view. (B) Left parasternal apical four chamber view. The yellow arrow refers to the false tendon. (C) FS measurement in the parasternal short axis view. (D) Measurement of peak mitral early diastolic wave velocity in the left parasternal apical four chamber view. (E) Pulsed tissue Doppler image tracing obtained from the left ventricular free wall along the longitudinal axis
FS = fractional shortening; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle

on the mitral annulus of the left ventricular lateral wall (Lat) and septal wall (Sep) of the mitral valve annulus, respectively, and the E wave/E' was calculated. The findings from the left parasternal apical four chamber view included the presence of a ventricular false tendon within the left ventricle, a decrease in the left ventricular function, and a marked CHF (Figure 2D,E; peak E 77.7 cm/s, E/É'Lat 39.64, E/E'Sep 27.75).

We provided a reference range regarding the echocardiographic variables in Table 1 (Koffas et al. 2006; Bach et al. 2021). A spontaneous echo contrast that indicated blood stasis in the left atrium was also recognised. The left ventricular outflow

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Table 1. Echocardiographic variables

Echocardiographic variables	Values	Reference range
Peak E (cm/s)	77.7	44–98
S' Lat (cm/s)	4.7	2.8–6.58
E' Lat (cm/s)	1.96	3.94–11.65
E/E' Lat	39.6	8.41–11.16
S' Sep (cm/s)	4.2	3.35–8.09
E' Sep (cm/s)	2.8	3.16–8.42
E/E' Sep	27.75	11.6–13.9
LA/Ao	3.45	0.97–1.28
LVIDd (mm)	16.2	11.59–19.36
LVIDs (mm)	14.4	3.25–5.00
LVPWd (mm)	1.9	3.0–4.97
FS (%)	11.1	31–56
LVOT (cm/s)	24.7	69–91

Ao = aortic annulus dimension; E' = early diastolic wave signal measured by tissue Doppler imaging; FS = fractional shortening; LA = left atrial dimension; Lat = mitral annulus at the left ventricular lateral wall; LVIDd = left ventricular internal dimension in diastole; LVIDs = left ventricular internal dimension in systole; LVOT = left ventricular outflow tract; LVPWd = left ventricular posterior wall in diastole; peak E = early diastolic mitral inflow velocity; S' = systolic wave signal measured by tissue Doppler imaging; Sep = mitral annulus at the septal wall

tract (LVOT) peak velocity was measured (33 cm/s) in the left parasternal apical five chamber view. Table 1 summarises the echocardiographic variables of this case.

Thoracocentesis was performed due to the severe respiratory distress. Analysis of the pleural fluid revealed a slightly white and turbid appearance, with a total protein concentration of 20 g/l and a cell count of 500/µl. The sediment components comprised a few neutrophils and lymphocytes. Feline infectious peritonitis virus (FIPV) was negative by real time polymerase chain reaction [(PCR); FIP Virus Real Time PCR Test; IDEXX Laboratories, Tokyo, Japan].

We suspected dilated cardiomyopathy (DCM) or myocarditis from the findings in which the cat had CHF with a left ventricular (LV) systolic dysfunction and hyperechogenicity of the endocardium. The cat was administered an antibiotic drug [Cefovecin; Zoetis, Tokyo, Japan; 8 mg/kg, subcutaneously (s.c.)] and pimobendan [Vetmedin; Boehringer Ingelheim, Ingelheim, Germany; 0.25 mg/kg, perorally (p.o.), b.i.d.] under oxygen supplementation in an intensive care unit (ICU) cage. The physical examination findings suggested that this case had very low blood pressure. Therefore, we could not administer diuretics because the administration of diuretics would lead to a further decrease in the blood pressure. The respiratory condition deteriorated, and the cat died the next day in hospital. With permission of the client, a necropsy was performed.

Grossly, the heart showed marked enlargement of both atria and the ventricles. There was no dysplastic change observed in the mitral and tricuspid valves. In addition to the severe thinning of the left ventricular free wall and interventricular septum, the endocardial surface of the left ventricle was nearly diffusely thickened having a tinge of greyish white in appearance. Moreover, a false tendon connecting between the left ventricular free wall and the interventricular septum was recognised (Figure 3). The histopathological examination demonstrated a significant deposition of collagen fibres and elastic fibres, mainly in the endocardium. This fibrotic process sometimes involved the subendocardial myocardium layer. In addition, the finding of myocardial fibres travelling in an undulating fashion (attenuated wavy fibres) was observed in almost all of the entire myocardium layers of the left and right ventricles and interventricular septum (Figure 4). EFE was diagnosed based on these findings.

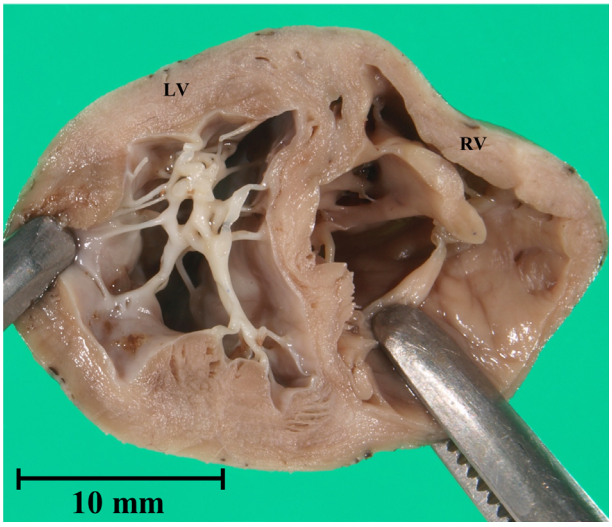

Figure 3. Macroscopic view of the heart with endocardial fibroelastosis

The left ventricle showed the existence of a thick endocardium and false tendon

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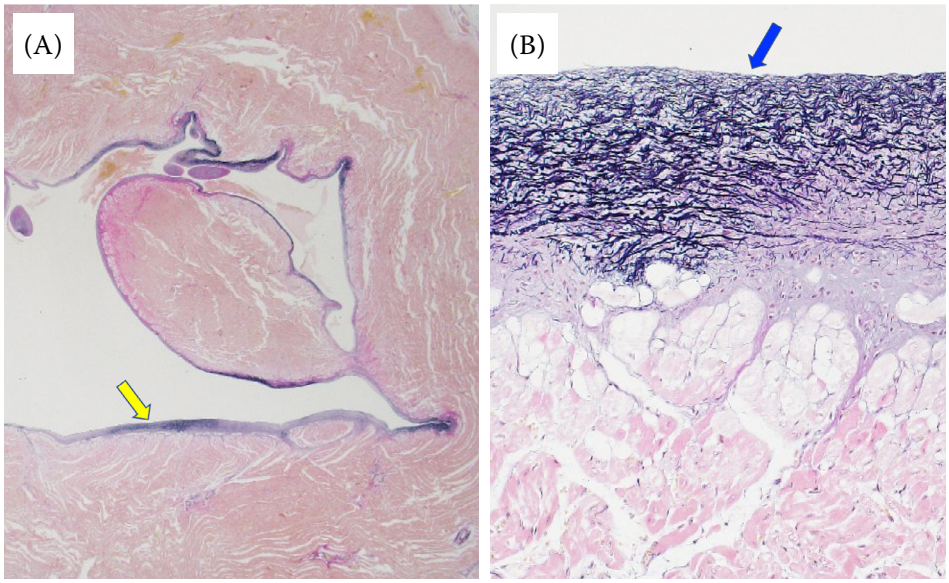

Figure 4. Histopathological sections of the left ventricular endocardial surface
(A) Yellow arrow indicates the thickening of the endocardium (× 100). (B) Special staining with the elastica van Gieson stain was performed and revealed abundant elastic fibres (blue arrow) within the endocardial layer (× 400)

DISCUSSION

Burmese and Siamese cats are known to be genetically susceptible feline breeds to EFE. However, reports regarding feline EFE are limited and remains largely unknown (Paasch and Zook 1980; Zook et al. 1981; Zook and Paasch 1982; Rozengurt 1994). In addition, previous reports in domestic cats mostly regard cases diagnosed post-mortem without documenting ante-mortem echocardiographic findings (Paasch and Zook 1980). EFE is a congenital heart disease that is characterised by the deposition of collagen fibres and elastic fibres, mainly in the endocardium, resulting in the thickening of the endocardium and the consequent ventricular hypertrophy and atrial dilatation (Letteer 1953; Ino et al. 1988). In addition, it is known that EFE occurs secondarily in response to various cardiac diseases, such as cardiomyopathy, endocarditis and viral myocarditis (Ni et al. 1997; Lurie 2010), and autoimmune reactions (Aoki et al. 2011). Although there are some case reports of EFE in cats, it is possible that the EFE occurred secondarily because most of the cats reported with the condition are middle-age cats. In this report, for the first time, we provide echocardiography data including a TDI in a kitten with idiopathic EFE 24 h before death. In humans, echocardiographic findings of EFE include the left ventricular enlargement, reduced ejection fraction, and increased echogenicity of endocardium (Sharland et al. 1991; Clur et al. 2010). In this case, reduced FS and increased endocardial echogenicity were also recognised with severe CHF; therefore, the echocardiographic findings were consistent with the human counterpart. Since these findings were like those of dilated cardiomyopathy and, hence, non-specific to EFE, EFE cannot be diagnosed based purely on the isolated echocardiographic findings (Hambrook and Bennett 2012). In human medicine, EFE is a disease related to early infancy with a poor prognosis (Linde and Adams 1963). It is onsidered that the earlier in life the CHF develops, the worse the response to medical therapy is (Linde and Adams 1963; Ino et al. 1988; Jiao et al. 2010). The onset of symptoms in the current case was at the age of two months. Despite the medical therapy and ICU management, the cat showed a poor response to treatment and eventually succumbed. This suggests that poor responsiveness to medical therapy is also expected after the development of CHF. Moreover, the significantly high E/E', low LVOT peak velocity and low FS noted in this case indicated CHF with a systolic and diastolic dysfunction, which might necessitate utilisation of catecholamines, such as dobutamine and dopamine, and diuretics to improve the failing circulation. While EFE has a poor prognosis, a report stating that with early diagnosis and intervention, prolongation of survival can be anticipated (Trucco et al. 2011). Hence, it is considered that there is a potential for improvement in a prognosis with early diagnosis and treatment.

In conclusion, our report provides a guide to veterinarians to perform a differential diagnosis with EFE when a cat is presented with CHF associated with a low FS and having hyperechogenecity

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of the endocardium, particularly at a young age, as is in this two-month-old cat case. In addition, TDI is a useful indicator to examine the myocardial function of a case and may help with the drug selection.

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Conflict of interest

The authors declare no conflict of interest.

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