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Grain-free diet-induced dilated cardiomyopathy with atrial fibrillation in a Labrador Retriever: a case report

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Abstract

We describe the first reported case of grain-free diet-induced dilated cardiomyopathy (DCM) in a dog in Korea. An 11-year-old female dog was referred with abdominal distention, anorexia, and vomiting, having been fed a grain-free diet for more than 5 years. Thoracic radiography revealed cardiomegaly and pulmonary edema. Atrial fibrillation was detected using electrocardiography. The dog was tentatively diagnosed with congestive heart failure (CHF) secondary to grain-free diet-induced DCM, and its diet changed to contain grain. Digoxin and diltiazem were prescribed for the atrial fibrillation, and pimobendan, enalapril, and furosemide for CHF. Significant improvements in echocardiographic indices were confirmed after 3 months.

Keywords: dogs; dilated cardiomyopathy; diet; atrial fibrillation

Dilated cardiomyopathy (DCM) is a cardiac disorder primarily observed in specific dog breeds, characterized by diffuse left ventricular systolic dysfunction and enlargement [1]. DCM is serious and leads to congestive heart failure (CHF) or sudden death, with survival times typically < 1 year after onset of heart failure, and echocardiographic improvement unlikely [2]. While genetic background is suspected to be the primary etiology, outbreaks linked to nutrient deficiencies [3,4] and concurrent diseases including hypothyroidism [5], myocarditis [6], and chronic tachycardia [7] have also been reported.

In 2018, the US Food and Drug Administration (FDA) released a report describing a potential association between diet and DCM [8]. Diets reported to be associated with DCM are often marketed as "grain-free" and contain ingredients that became part of commercial foods relatively recently (e.g., pulses, potatoes, and sweet potatoes) and lack others (such as rice or corn) [9]. Although DCM typically progresses rapidly in dogs and is associated with short survival times, dogs affected by diet-induced DCM experience substantial enhancement in echocardiographic parameters and extended survival following dietary modification and medical intervention [10]. However, there are no reported cases of grain-free diet-induced DCM in dogs in Korea. Here, we describe the clinical course and successful management of atrial fibrillation (AF) and CHF in a dog with grain-free diet-induced DCM.

An 11-year-old spayed female Labrador Retriever weighing 31 kg was referred with abdominal distention, anorexia, and vomiting. Three years before presentation, the dog showed normal cardiac structure and function on echocardiography.

The dog had also been fed a grain-free diet for more than 5 years.

Physical examination revealed tachycardia (up to 280 beats/min) and tachypnea with respiratory effort. Complete blood cell counts and blood electrolyte analysis revealed mildly decreased packed cell volume (32.9%, reference interval [RI], 37.3%–61.7%) and hyponatremia (Na^+, 131 mmol/L; RI, 141–152 mmol/L). Serum brain natriuretic peptide (proBNP, 1,424.81 pmol/L; RI, 0–900 pmol/L) and cardiac troponin I (cTnI, 1.105 ng/mL; RI, 0–0.2 ng/mL) were increased. Hypothyroidism was ruled out based on the normal thyroid panel results. Electrocardiography revealed AF with an absent P wave and a wide QRS complex interval (0.08 seconds) (Supplementary Fig. 1). Thoracic radiography showed an increased vertebral heart size (12; RI, 10.4–11.4), vertebral left atrial (LA) enlargement (2.7; RI, ≤ 2.3), and increased opacity in the lung fields (Fig. 1), indicating cardiomegaly and pulmonary edema. Echocardiography showed increased LA:aortic (AO) ratio (LA:AO ratio), left ventricular internal diameter in diastole and left ventricular internal diameter in systole (LVIDs) and thinning of interventricular septal thickness in systole and left ventricle posterior wall thickness at systole. Decreased ejection fraction (EF) and fractional shortening were also identified. The E point septal separation was measured at 7.7 mm (Table 1, Fig. 2). Abdominal ultrasonography revealed a large amount of ascites and the fluid was a modified transudate.

Based on these findings, the dog was diagnosed with DCM and concurrent AF induced by a grain-free diet. Treatment was initiated with a prescribed diet containing grains (Royal Canin Cardiac diet; Royal Canin, France), and taurine and L-carnitine

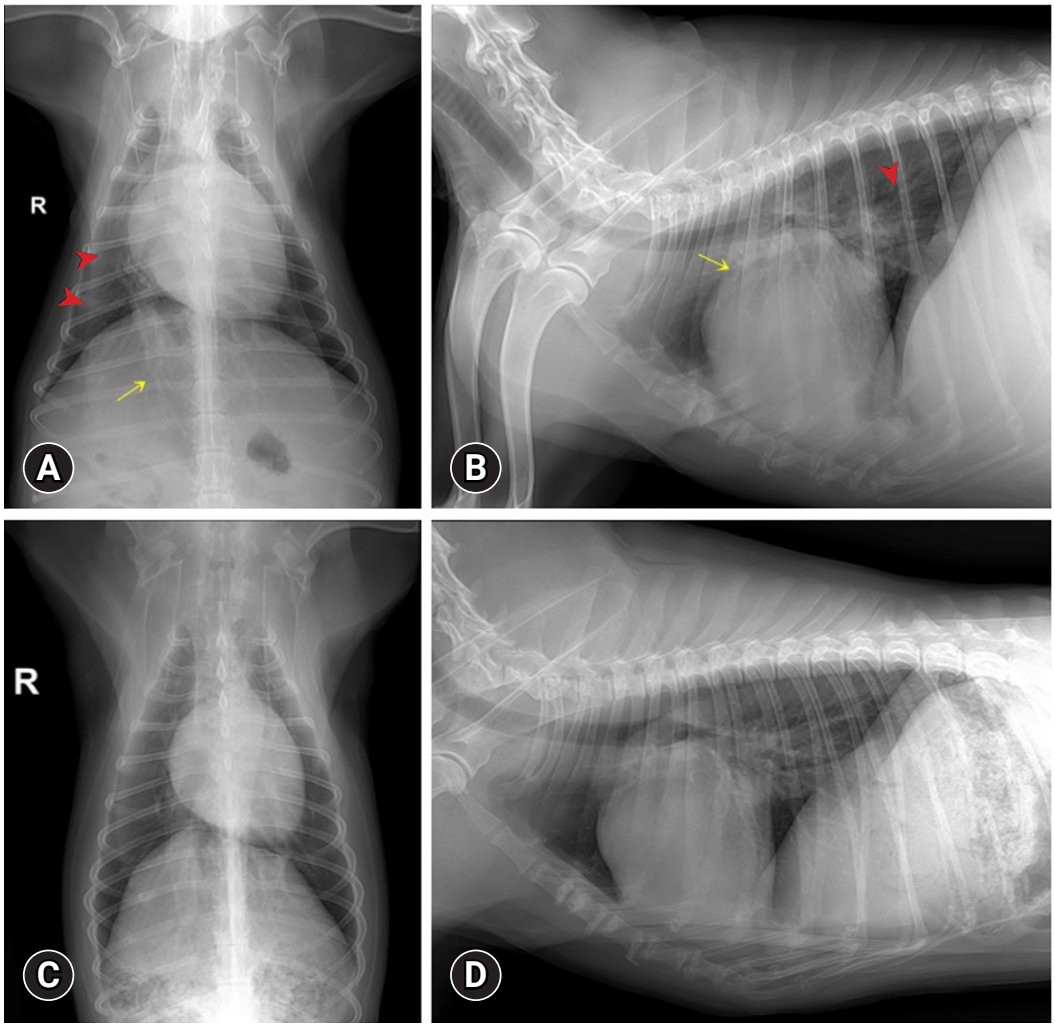

Fig. 1. Ventrodorsal and lateral thoracic radiograph of canine dilated cardiomyopathy. Thoracic radiography revealed enlargement of the globoid cardiac silhouette, broncho-interstitial pattern (red arrowheads) and pulmonary venous dilation (yellow arrows) on day 1 (A, B). At 207 days after treatment, the thoracic radiograph revealed no pulmonary edema and a reduced heart size (C, D).

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Table 1. Serial changes in cardiac biomarker and echocardiographic values in the present patient

Note	Day 0	Day 88	Day 207	Day 410	Reference
cTnI (ng/mL)	2.5	< 0.2	< 0.2		0–0.2
proBNP (pmol/L)	1,424.81	-	-		0–900
LA/AO ratio	1.94	1.80	1.76	2.23	< 1.6
LVIDd (mm)	65.7	58.7	44.6	44.3	29.4–45.3
LVIDs (mm)	56.2	35.2	29.8	28.5	14.5–36.8
IVSs (mm)	13.1	19.5	12.3	10.7	14.72–15.82
LVPWs (mm)	13.0	19.1	16.1	128	12.65–13.70
EDVI (ml)	230	212	136	77.3	< 100
ESVI (ml)	171	74	57	29.6	< 30
EF (%)	29.9	69.6	65.3	65.3	40–75
FS (%)	14.5	39.86	36.0	32.9	30–49
EPSS (mm)	7.7	-	7.0	2.5	0.30–7.70

cTnI, cardiac troponin T; BNP, brain natriuretic peptide; LA, left atrial diameter in systole; LV, left ventricle; AO, aorta; LVIDd, left ventricular internal diameter in diastole; LVIDs, left ventricular internal diameter in systole; IVSs, interventricular septal thickness in systolic; LVPWs, left ventricle posterior wall thickness at systole; EDVI, end-diastolic volume index; ESVI, end-systolic volume index; EF; ejection fraction; FS, fractional shortening; EPSS, E point septal separation; –, not applicable.

were administered as supplements. Pimobendan (Vetmedin; Boehringer, Germany) 0.25 mg/kg, enalapril (Lenipril; JW-Shinyak, Korea) 0.5 mg/kg, and furosemide (Laxis; Handok, Korea) 2 mg/kg twice daily were prescribed to treat CHF, and digoxin (Digoxin; innoN, Korea) 0.05 mg/kg and diltiazem (Herben; innoN) 2 mg/kg twice daily were prescribed to treat AF. However, because diarrhea occurred, suspected to be an adverse effect of digoxin, the treatment was discontinued. Clinical symptoms including increased respiratory rate and open-mouth breathing disappeared during 3-day hospitalization after the first visit, and symptoms of exercise intolerance improved after 1 week and were well maintained. However, tachyarrhythmia (heart rate [HR] > 150 beats/min) persisted, so diltiazem was sequentially increased by 10% to 4.31 mg/kg twice daily, but tachyarrhythmia persisted. Digoxin 0.0074 mg/kg was reintroduced again, resulting in a decrease in the HR to < 125 beats/min, and the previously identified diarrhea was not confirmed. After 3 months of follow-up, the HR was confirmed to be < 125 beats/min, showing a good response to rate control for AF [11], but electrocardiography still showed loss of the P wave and wide QRS complex. When the digoxin blood concentration was measured, it exceeded the therapeutic range at 2.3 ng/mL but did not reach the toxic range, and no adverse effects were observed. With the gradual tapering of diltiazem, the patient discontinued diltiazem on day 123 of treatment and is now solely managing AF with digoxin. On echocardiographic follow-up at 88 and 207 days after treatment, a decrease in the LA:AO ratio and LVID was noted, confirming improvement in left heart hypertrophy, and fractional shortening returned to normal (Table 1, Fig. 2). Serum cTnI concentration also decreased to the normal range (Table 1). Therefore, pimobendan was discontinued on treatment day 267. Currently, 5 months have passed since discontinuation of pimobendan, and there has been no recurrence of clinical symptoms, and no decrease in systolic function was observed during echocardiographic follow-up at 5 months after discontinuing pimobendan (Table 1).

A recent study showed that experimental feeding with a grain-free diet for 28 days resulted in subclinical DCM-related changes. These changes included an increase in LVIDs, a decrease in stroke volume, and an increase in serum NT-proBNP concentration. This finding supports the hypothesis that a grain-free diet contributes to the development of DCM [12]. This patient had been consuming a grain-free diet for 5 years, but no structural or functional problems were detected on echocardiography 3 years prior to presentation. This is the case for naturally occurring, grain-free diet-induced DCM. This suggests that the time required for naturally occurring grain-free diet-induced DCM may differ from that observed in experimental studies.

Dogs with DCM who consume grain-free diets can experience improvements in cardiac function after a diet change, as shown in the present case. The median survival time was significantly longer in dogs with DCM consuming nontraditional diets whose diets were changed (337 days) than in dogs consuming nontraditional diets without dietary modification (215 days) [2]. Moreover, dogs with DCM fed grain-free diets exhibited higher CHF rates than those fed grain-containing diets. Dogs with DCM fed a grain-free diet, such as in this case, should be considered at high risk for heart failure if diet modification is not made early enough, and should be carefully moni-

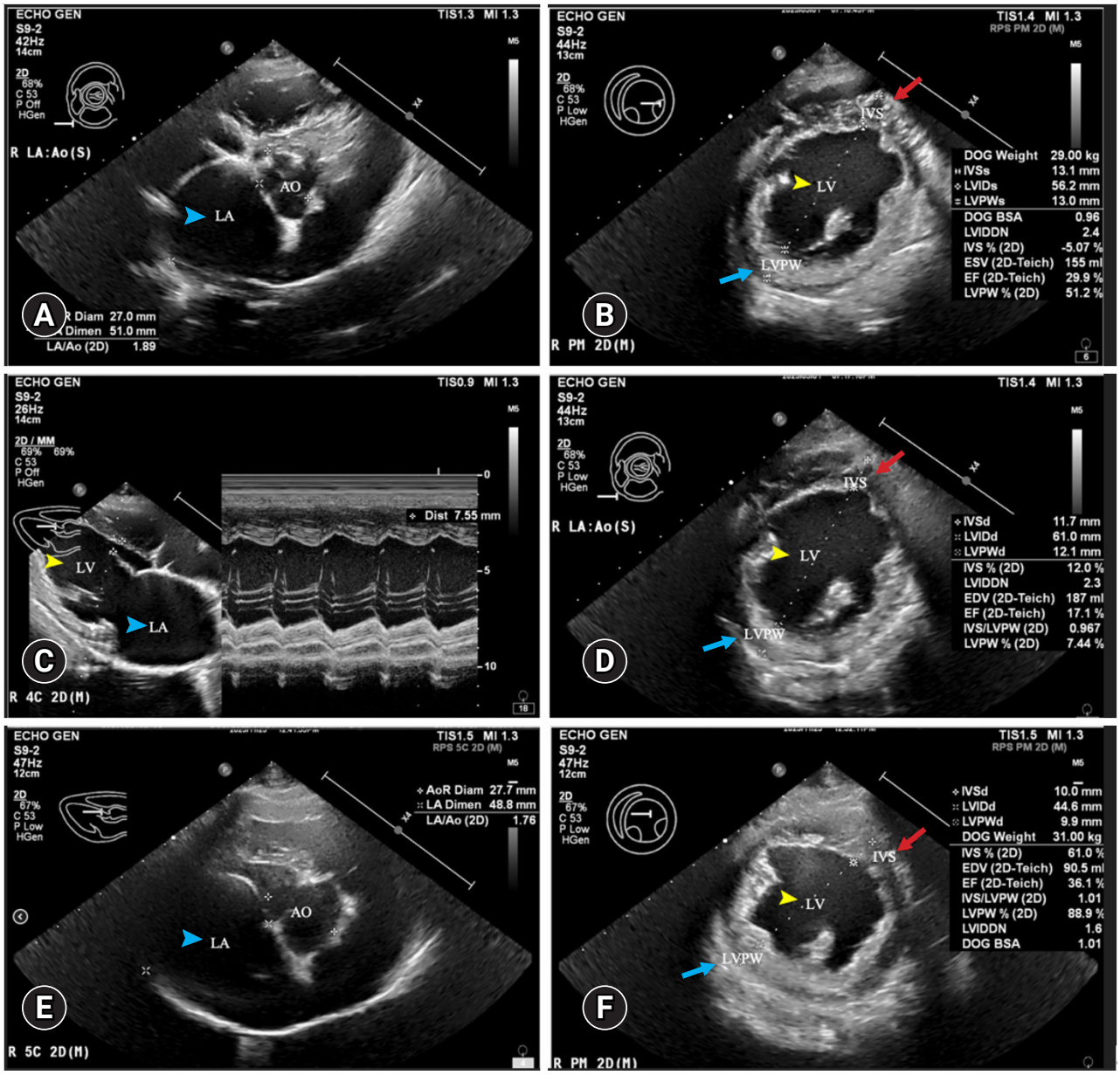

Fig. 2. Echocardiography of canine dilated cardiomyopathy at diagnosis (A-D) and 207 days after diagnosis (E, F). This patient demonstrates an increased LA:AO ratio at the aortic (AO)/LA level (A) with increased E point septal separation on M-mode images of long-axis echocardiographic views from right parasternal position (C). Right parasternal short axis views reveal marked increased left ventricular end diastolic diameter normalized for body weight and thinning of the LVPW and IVS at systole. (B, D). At 207 days after diagnosis, the LA:AO ratio decreased (E) compared to the initial diagnosis and left ventricular end diastolic diameter normalized for body weight exhibit near normal values (F). LA, left atrium (blue arrowheads); LV, left ventricle (yellow arrowheads); AO, aorta; LVPW, left ventricle posterior wall thickness (blue arrows); IVS, interventricular septal thickness (red arrows).

tored. Heart failure, ascites, end-systolic volume index (ESVI) greater than 140 mL/m^2, and EF < 25% had significant negative relationships with survival time. The median survival time for dogs with ascites was 114 days, and that for dogs with ESVI >140 mL/m^2 was 208 days [13]. In this case, the EF value was slightly above 25%, ESVI exceeded 140, and the prognosis was expected to be poor because of heart failure and ascites symptoms.

In addition, this patient had AF, another poor prognostic factor for DCM [14]. The treatment goals for AF are divided into rate and rhythm control [11]. By the time AF is diagnosed, myocardial remodeling is already evident; therefore, rhythm control may be less effective, and the risk of recurrence may be higher in dogs with AF and underlying heart disease. Therefore,

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realistically, rhythm control may be challenging, and focusing on appropriate HR control is necessary, as there is a report that good rate control with an average HR ≤ 125 beats/min reduced the risk of mortality [11]. HR is an important prognostic indicator of DCM. The patient was managed with appropriate HR control by using a combination of diltiazem and digoxin. Despite having poor prognostic factors, the patient is currently surviving beyond the median survival time of other patients with DCM, which surpasses 359 days. Therefore, if grain-free diet-induced DCM is managed with an appropriate diet and medication, as in this patient's case, sufficient improvement can be achieved, and the prognosis is expected to be more favorable than that of dogs with idiopathic DCM.

However, this case report has several limitations. The FDA's data and research evidence published thus far support an association between nontraditional diets and DCM; however, the specific cause is not yet known. A number of nutritional deficiencies, such as those of taurine, thiamine, carnitine, and vitamin E, can cause DCM, but deficiencies have not been identified in published studies. Taurine deficiency can cause secondary DCM and is one of the first suspected causes of this current problem, but it has not been found in most dogs with diet-associated DCM (except in one study on golden retrievers) [10,15]. In other studies, after 28 days of feeding each diet, plasma levels of taurine observed in dogs were not significantly different among diets [12]. However, blood levels of taurine may not be the best indicator of taurine status; therefore, further research is required. Even in this case, the carnitine and taurine concentrations in the tissue were not measured, preventing the exclusion of carnitine or taurine deficiencies as potential factors. Additionally, although primary AF is rare, whether the AF in this patient was primary or caused by DCM remains unknown. Therefore, it is described as AF concurrent with DCM.

This is the first domestic case report of DCM induced by a grain-free diet, and describes a series of clinical courses of DCM induced by a grain-free diet. As in this case, in DCM-related to a grain-free diet, a good long-term prognosis can be expected if appropriate diet and drug management are performed along with active management of poor prognostic factors.

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Author's Contributions

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Supplementary Materials

Supplementary data are available at https://doi.org/10.14405/kjvr.20240025.

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