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Vegetative Mitral Valvular Regurgitation Caused by Infective Endocarditis in a Maltese Dog

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Abstract : A 3-year-old intact female Maltese dog (2.5 kg of body weight) with the primary complaint of sudden onset of heart murmur, depression and anorexia was referred to the Veterinary Teaching Hospital of Kangwon National University. The dog was febrile with marked leukocytosis and left apical VI/VI holosystolic murmurs. The electrocardiogram implied the left ventricular enlargement. Diagnostic imaging studies revealed left atrial and ventricular dilation, severe vegetations on mitral valvular cusps with concurrent mitral regurgitation. Based on findings from clinical and diagnostic investigation, the case was diagnosed as vegetative mitral valvular regurgitation caused by infective endocarditis. The dog was successfully treated with broad spectrum antibiotics, diuretics, angiotensin converting enzyme inhibitor and antithrombotics.

Key words **:** infective endocarditis, mitral regurgitation, dog

Introduction

Infective endocarditis (IE) is inflammation of the endocardial structures (e.g. valves or mural endocardium) in dogs. Although all kind of pathogen can become infected, bacterial organisms are major cause for IE(4,5,6,10,11). Bacterial colonization on cardiac valves (commonly in aortic or mitral valves), may produce proliferative lesions (vegetations) and/or destroy valvular tissues, resulting in improper valve coaptation and regurgitation(5,7,8). Acute bacterial endocarditis is usually associated with gram negative rods (e.g. E. coli) and has very short clinical course (~2-3 weeks by death)(4). Much of the disease seen in dogs appears to be acute and commonly follows a malignant course(5). One retrospective study found IE primarily affects the aortic (49%) and mitral valves (36%) in dogs, while the tricuspid valve is rarely affected (2%) and the pulmonic valve is almost never affected(4). It is also rare that both the aortic valve and mitral valve involved (2%)(10). IE is more common in medium-sized to large purebred dogs (e.g. German shepherds or German shepherd crosses, golden retrievers, and Labrador retrievers)(10,11).

Bacteremia is a major cause for bacteria to colonize a heart valve. Physical manipulation of mucosal surfaces (urinary catheterization, dental scaling) produces bacteremia in humans(10). Dental scaling is a primary concern of most veterinary practitioners for producing bacteremia(10). Predisposing factors for IE are preexisting valvular diseases (e.g. subaortic stenosis), systemic illness (e.g. uremia, systemic lupus erythematosus), bacteremia, immune deficiency.

Discovering a new heart murmur in a patient that is febrile is the classic finding to make one suspicious of IE(10,12). Although a systolic heart murmur is the most common, the quality and degree of murmur can be varied by the location and severity of affected valve(s). If the aortic valve is affected, a diastolic heart murmur due to aortic regurgitation is commonly identified in dogs-(12). Diagnosis of IE usually is made by the history (sudden onset of murmur with fever), clinical findings, blood cultures (gram negative rods), and echocardiography (valvular vegetation or regurgitation) (7,8,13). However, blood cultures lack specificity and sensitivity in dogs and cats and are as a result hardly ever solely relied upon to make a definitive diagnosis of bacterial endocarditis in small animals(4,8). Treatment usually directed to control bacterial infection using empirical antibiotic therapy (initially, but later, should be based on the sensitivity test). A fairly aggressive therapeutical approach is ideal to keep the antibiotic serum concentration at the high end of the therapeutical scale for several weeks. Cardiac complications (e.g. heart failure) should be separately addressed using classical heart failure therapy. The prognosis for dogs is generally poor. Although dogs with mitral involvement generally survived longer than those with aortic involvement, all affected dogs will have a certain degree of heart failure in the end, because no definitive treatment for valve destruction exists in veterinary medicine(11,13).

This case study presented clinical and diagnostic features

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of a vegetative mitral valvular diseases caused by infective endocarditis in a Maltese dog.

Case

A 3-year-old intact female Maltese dog (2.5 kg of body weight) was referred at Veterinary Teaching Hospital of Kangwon National University with the primary complaint of sudden heart murmur, depression and anorexia. The dog was healthy and maintained good appetite till she had been trimmed at local pet shop 1 week before. The owner felt sudden loud heart murmur and thrill few days before the presentation at our clinic. According to the referring veterinarian, the dog was febrile (39.5-40.4°C) with marked heart murmur and precordial thrill at the first consultation.

On the cardiac auscultation at our clinic, grade VI/VI holosystolic murmurs were detected all side of chest with severe precordial thrills (Fig. 1). The point of maximal intensity

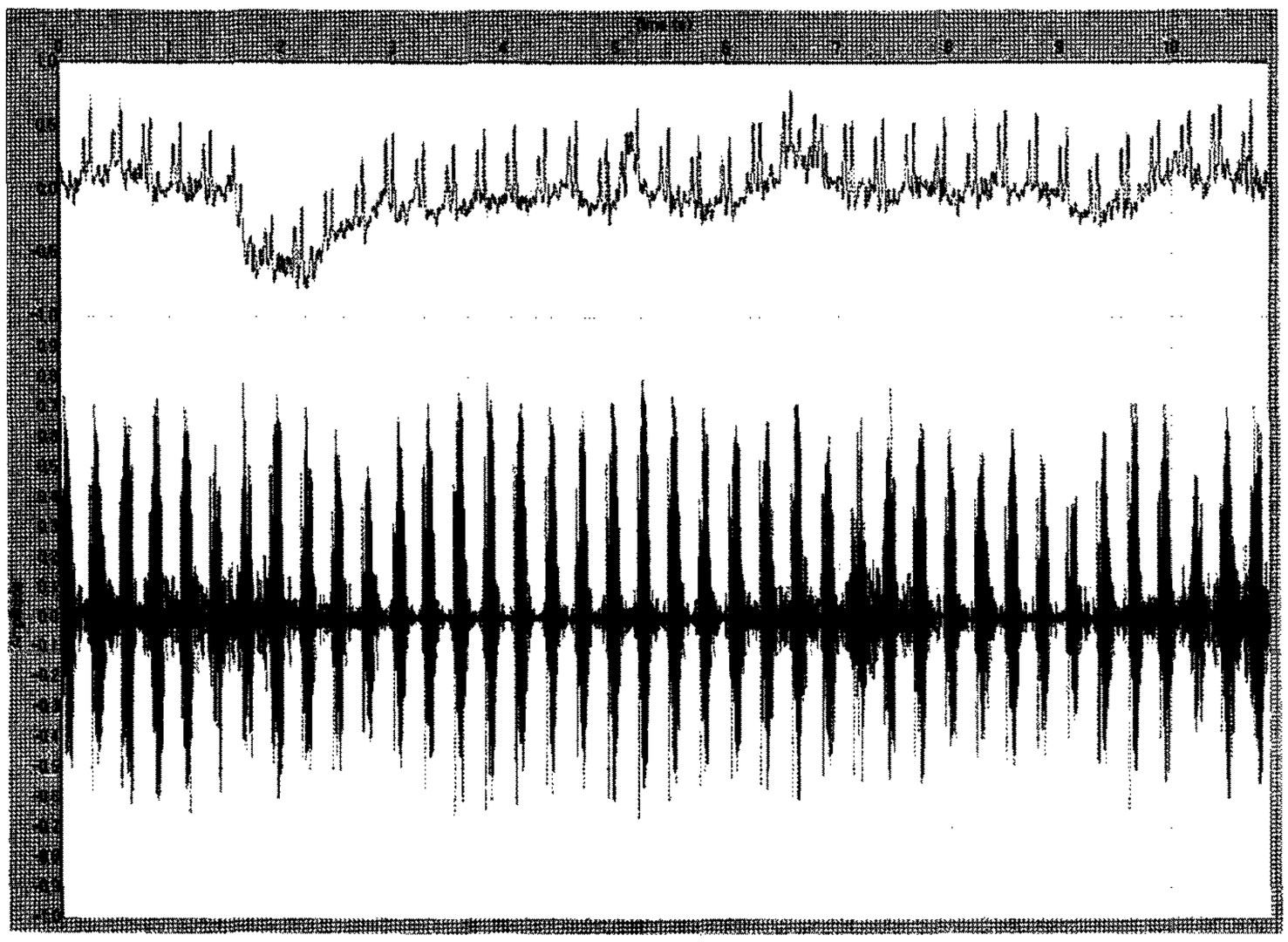

Fig 1. Phonocardiogram of this case. The heart sound was recorded from the left apical area. Phonocardiogram showed a very strong (grade VI/VI) holosystolic (between S1 and S2) murmur without diastolic murmur (no murmur between S2 and next S1), suggesting that murmur might be originated from mitral valve rather than aortic valve.

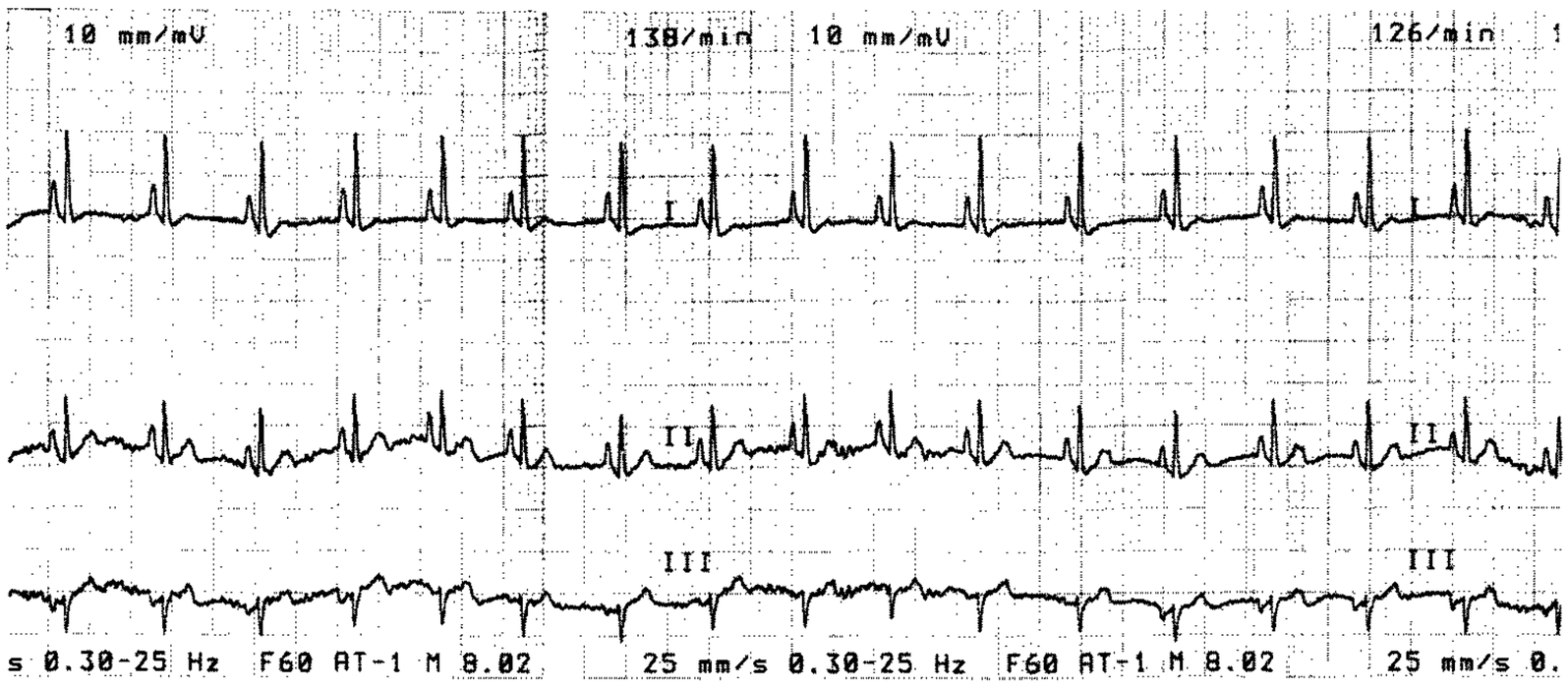

Fig 2. Surface electrocardiogram (ECG) of this case. The ECG revealed the left QRS axis deviation (+25°) suggesting left ventricular hypertrophy. However the heart rhythm was from sinus origin.

(PMI) was the left apical region, although the murmurs were detected even in the clavicular region. The 12-lead electrocardiogram (ECG) showed the left QRS axis deviation (+30°) with sinus origin rhythm, suggesting the left ventricular enlargement (Fig. 2). Complete blood cell count (CBC) found severe leukocytosis ($53.4 \times 10^3/\mu L$; reference range: $6–17 \times 10^3/\mu L$) and neutrophilia with left shift ($34.1 \times 10^3/\mu L$; reference range: $3.0–11.8 \times 10^3/\mu L$), suggesting acute inflammatory process in a certain part of the body. Serum biochemistry showed mildly increased hepatic leakage enzymes (alanine aminotransferase; ALT 128 IU/L, reference range: 3–100 IU/L; aspartate aminotransferase;AST 72 IU/L, reference range: 1–50 IU/L). Based on medical history (sudden onset), physical examination (sudden onset of heart

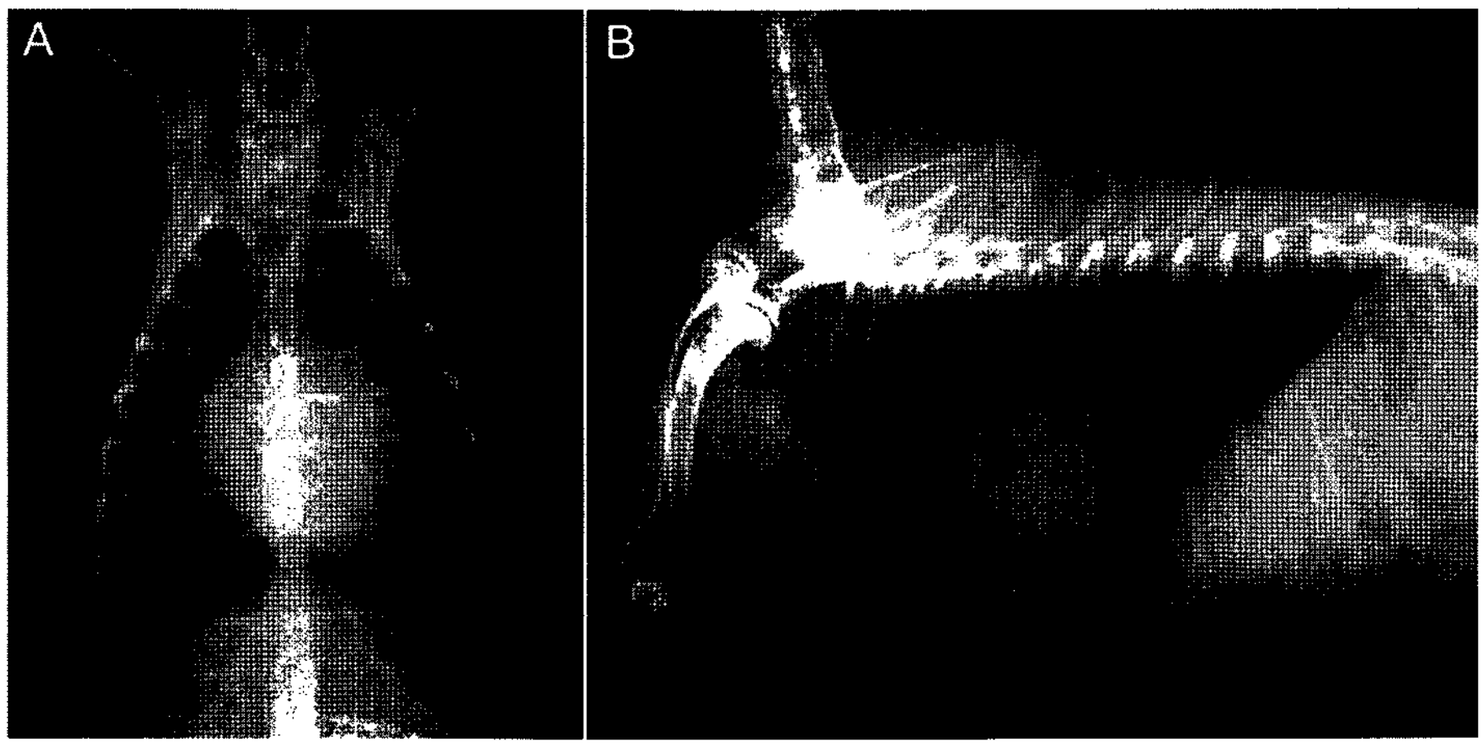

Fig 3. Thoracic radiography of this case. A: Dorsoventral projection. There is mild left atrial dilation, although lung fields are clear. B: Right lateral projection. Although the heart size is not changed, there is a certain degree of dilation at the direction of 1 o'clock (left atrial dilation).

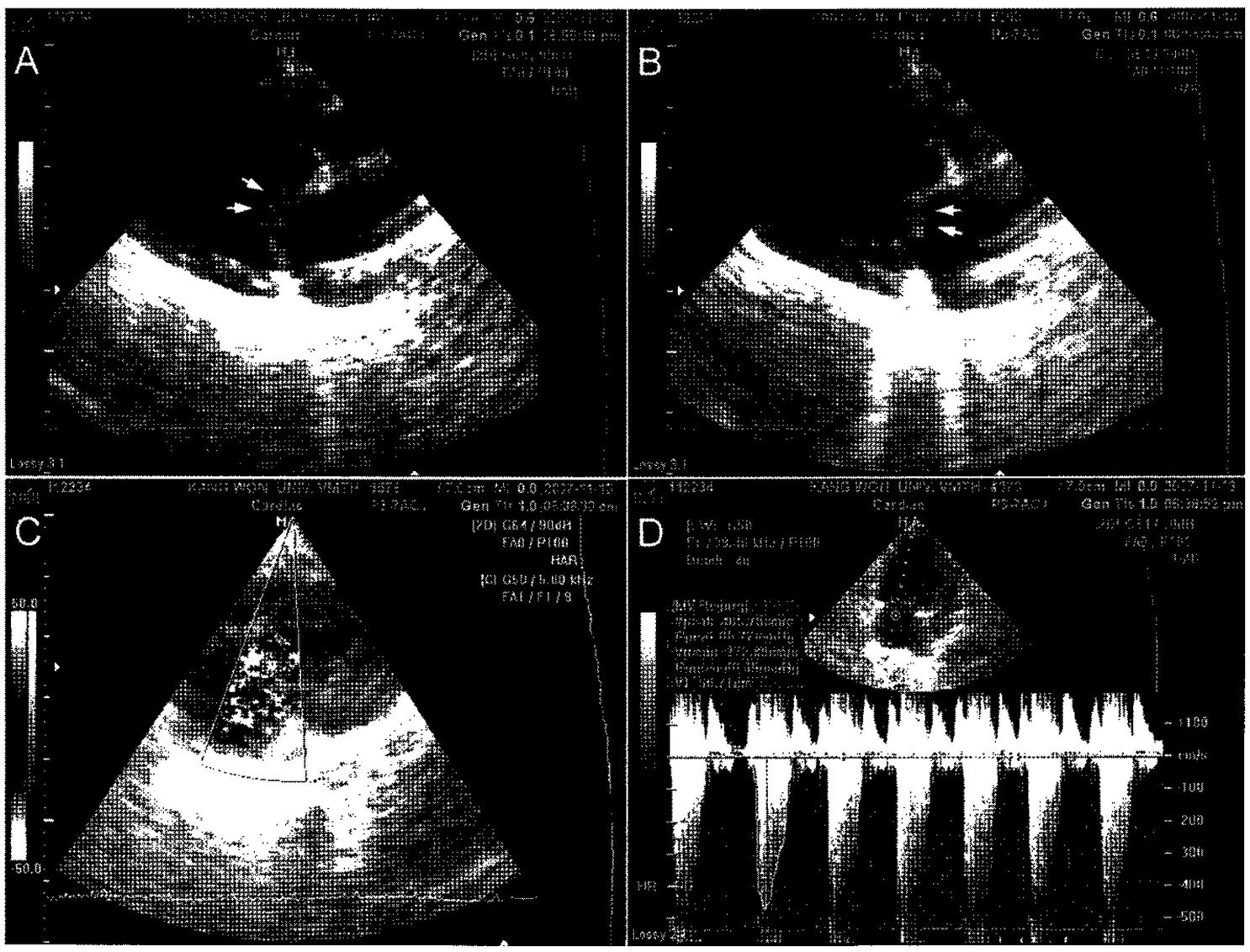

Fig 4. Echocardiography of this case. A-B: The 2-dimentional echocardiography of mitral valvular orifice showed the vegetation (arrow) of mitral valvular cusps. Although both mitral cusps were markedly thickened, there was severe vegetation on the anterior cusps. C-D: The color and continuous wave Doppler echocardiography at the same position revealed severe turbulent backward flow (mitral regurgitation) with a maximal velocity of 5 m/sec.

murmur) and CBC (leukocytosis and neurophillia with left shift), the case was tentatively diagnosed as bacterial endocarditis. Gentamycin (3 mg/kg, IM) and cefazoline (10 mg/kg, IV) were urgently administered for treating potential bacterial infection. Her blood was submitted for bacterial culture.

After emergency antibiotic therapy, diagnostic imaging studies were conducted. Thoracic radiography revealed left atrial dilation without pulmonary infiltration. On the echocardiography, there were vegetations on the anterior cusps of mitral valve (Fig 4A and B). Both mitral cusps were markedly increased in thickness and echogenicity on the 2 dimensional echocardiography (Fig 4A and B). More severe vegetations were observed in the anterior cusp of the mitral valve (Fig 4A and B). The shortening of E-point septal separation (EPSS) and thickening of mitral valvular excursion were obvious in the M-mode echocardiography (Fig 5A). The color and continuous wave Doppler echocardiography at the mitral orifice revealed severe turbulent backward flow (mitral regurgitation) with a maximal velocity of 5 m/sec (Fig 4C and D). The measurement of cardiac dimensions revealed a marked dilation of left ventricular diastolic dimension (LVDd) and thinning of interventricular septum (IVS), suggesting left ventricular eccentric hypertrophy due to severe mitral regurgitation (Fig 5B and Table 1). The left atrium was also moderately dilated in the echocardiography. However, no intra-atrial thrombosis was observed. Furthermore no vegetation or regurgitation were detected at the right and left outflow area (aortic and pulmonic valves). Diagnostic findings (vegetation on mitral valve, severe mitral regurgitation, left ventricular eccentric hypertrophy) from imaging studies supported our initial diagnosis.

The dog was empirically treated with broad spectrum antibiotics (Gentamycin, 3 mg/kg, TID, IM and cefazoline, 10 mg/kg, TID, IV), diuretics (Furosemide, 2 mg/kg, BID, PO), angiotensin converting enzyme inhibitor (ACEi; Enalapril, 0.5 mg/kg, BID, PO) and antithrombotics (Clopidogrel, 18 mg/kg, SID) for 7 days. After 3 days of empirical antibiotic therapy, total number of leukocyte was decreased to $13.4 \times 10^3/\mu L$ and general condition of the dog was gradually improved, although the heart murmur was still audible at the left apex. The dog was released after 7 days with prescription of antibiotics (Amoxicillin-clavulanate, 20 mg/kg BID, PO), furosemide (2 mg/kg, BID, PO), enalapril (0.5 mg/kg, BID, PO), and clopidogrel (18 mg/kg, SID, PO) for 2 weeks, although blood culture failed to identify the pathogenic bacteria.

After 2 weeks of release, the dog was re-examined. Although the heart murmur was still audible and mitral valvular vegetation and regurgitation was persisted, the grade of murmur reduced (grade III/VI) and the condition of the dog returned to normal.

Discussion

Although blood cultures must be obtained to try to identify the offending organism and subsequently to identify the

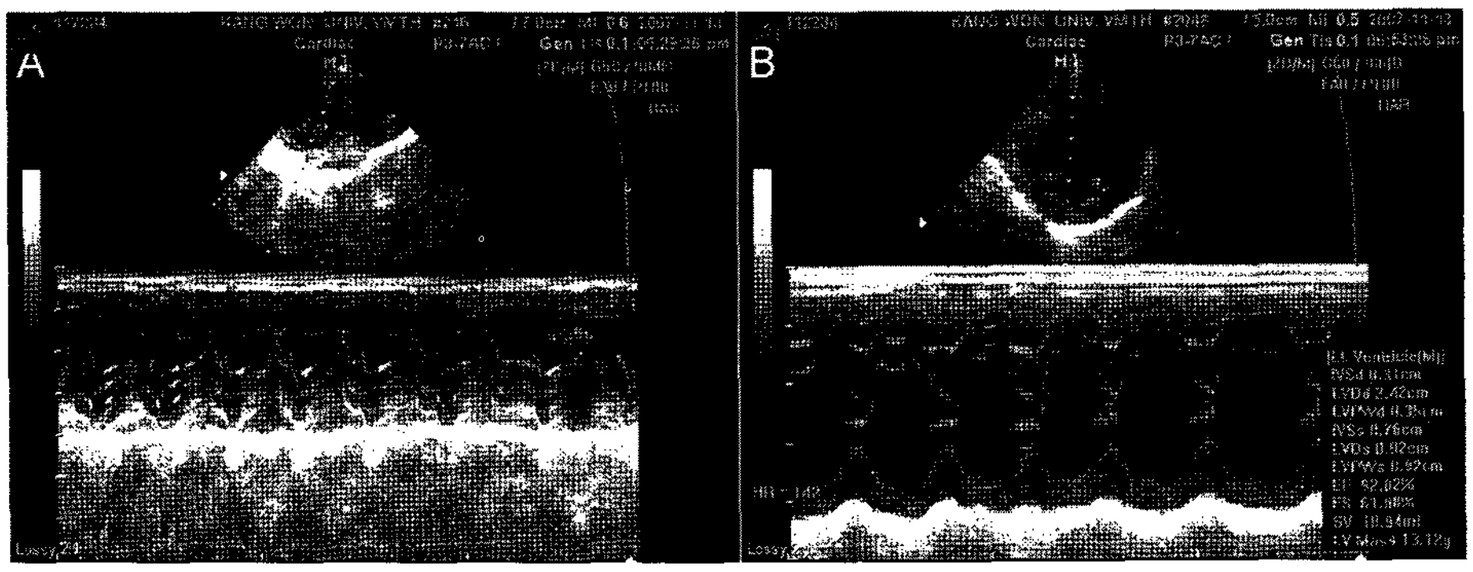

Fig 5. Echocardiography of this case. A: M-mode echocardiography revealed the shortening of E-point septal separation (EPSS) and thickening of mitral valvular excursion. B: There were a marked dilation of left ventricular diastolic dimension and thinning of interventricular septum.

Table 1. Echocardiographic dimensions of this case

	IVSd [a)] (mm)	LVIDd [a)] (mm)	LVPWd [a)] (mm)	IVSs [a)] (mm)	LVIDs [a)] (mm)	LVPWs [a)] (mm)	EF [a)] (%)	FS [a)] (%)
Reference	5.4-7.4	9.2-21.0	4.3-5.9	8.2-10.3	3.0-13.3	7.3-9.3	20-70	28-48
	3.1	24.2	3.5	7.6	9.2	9.2	92.02	61.98

[a)] IVSd: interventricular septal thickness at diastole, LVIDd: left ventricular internal dimension at diastole, LVPWd: left ventricular posterior wall thickness at diastole, IVSs: interventricular septal thickness at systole, LVIDs: left ventricular internal dimension at systole, LVPWs: left ventricular posterior wall thickness at systole, EF:% ejection fraction, FS:% fractional shortening.

appropriate antibiotic in patients with IE, the echocardiography is being more widely used to diagnose IE in dogs and cats, because blood cultures are almost never used to make the definitive diagnosis of IE due to lacking of sensitivity and specificity in dogs and cats(11). Of dogs with IE, blood cultures are positive in 50-90% of the cases (lack of sensitivity; 11). Therefore, currently, most of IE cases are initially diagnosed based on clinical signs (usually fever, leukocytosis with a sudden onset of heart murmur or signs consistent with systemic embolic disease) and echocardiography and then blood cultures are obtained(4,8,9,11). Although the echocardiography is not 100% sensitive or specific, it will be quicker and better to identify dogs with IE, if the dog has detectable valvular vegetation with larger than 1 mm(7,8). Besides identifying vegetations, dogs with destructive lesions of their valves but without vegetations can be diagnosed with IE based on the presence of a regurgitant lesion and the echocardiographic appearance of the valve, especially when the aortic valve is involved(7). The confirmation of bacterial etiology in our case was problematic, because of the negative bacterial culture. However, the acute progression with fever and marked leukocytosis and neutrophillia with left shift on CBC strongly suggested bacterial etiology in this case. Furthermore, rapid recovery without steroidal therapy suggested immune mediated etiology (e.g. autoimmune disease) was unlikely, although immune mediated endocarditis has been reported in association with Bartonellosis in dogs(3). In general, immune mediated glomerulonephritis and/or polyarthritis often accompanied with IE with Bartonellosis. However, Bartonellosis was also unlikely, because no other lesions were detected in this case, except endocaritis. Although vrial endocarditis associated with human immune deficiency virus (HIV) has been reported in human(1), viral etiology associated IE has never been reported in dogs. Therefore viral etiology was also less likely. Our echocardiogram clearly demonstrated vegetative lesions on the mitral valve, which was the most diagnostic finding for IE. Although the sterile left atrial thrombus could be the cause of vegetation on the valves, it was also unlikely, because atrial thrombus generally form the centre of the atrium enlarged markedly. Our case showed typical findings of IE (e.g. acute onset and rapid progression of clinical signs, marked leukocytosis and neutrophillia with left shift, vegetative lesion on mitral valve with severe mitral regurgitation, rapid recovery after antibiotics without steroidal therapy), although we failed to reveal bacterial etiology. Therefore our final diagnosis was infective endocarditis suspecting bacterial etiology.

Generally treatment for IE should be directed to treat offending bacteria and to minimize cardiac complications (e.g. heart failure or embolization). Although the selection of antibiotics should be based on the sensitivity test, basing antibiotic therapy on blood culture results is often not feasible, either because the blood culture is negative or because the blood culture does not identify the organism early enough in a patient with acute bacterial endocarditis(11). Generally, antibiotics for treating a patient with IE should be bactericidal, because bacteriostatic antibiotics will not successfully kill the bacteria inside of vegetation. A combination of the 2nd generation penicillins (e.g. ampicillin) or cephalosporins (e.g. cefazoline) for gram negative bacteria and aminoglycosydes (e.g. gentamicin or amikacin) for gram negative bacteria is the best choice. Steroid therapy should be avoided because it exacerbates the clinical signs and worsens the prognosis in patients with IE. Congestive heart failure, the most common complications, can be managed by standard heart failure therapy (e.g. diuretics, ACEi, inotropics), if valves are not severely affected. In our case, our selection of antibiotics was based on literature and was effectively control bacterial infection. Because blood culture was negative, no further sensitivity test could be performed. Fortunately, the cardiac performance was not much deteriorated by IE in this case. Low dose furosemide and ACEi were enough to minimize cardiac complications. thromboprophylaxis therapy was included for preventing potential thromboembolic crisis.

Although the prognosis for dogs and cats with active IE is generally poor, our case was fairly recovered from IE, due to the early recognition of IE and the early initiation of antibiotic therapy. Mitral involvement might be also contributed for better prognosis in this case.

In conclusion, this case study presented clinical and diagnostic features of a vegetative mitral valvular diseases caused by infective endocarditis in a dog, which was successfully managed by the early empirical antibiotic therapy.

Acknowledgements

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말티스견의 감염성 심내막염에 의한 우상성 이첨판 역류증

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요 약 : 3년령 말티즈 개(2.5Kg)가 갑작스런 심잡음, 의기소침, 식욕결핍으로 내원하였다. 혈액검사상에서 백혈구증가증과 함께 발열이 관찰되었으며 심장청진시 좌측 심첨부에서 VI/VI holosystolic murmurs가 청진되었다. 심전도에서 좌심실의 종대소견이 보였다. 진단방사선상에서 좌심방과 좌심실의 확장, 이첨판 판막의 증식이 보였으며, 이로 인해 이첨판의 역류가 관찰되었다. 이러한 임상증상과 검사 결과를 바탕으로, 본 증례는 감염성 심내막염에 의한 증식성 이첨판 역류증이라 진단하였다. 환자는 광범위 항생제, 이뇨제, 항혈전제로 치료하였다.

주요어 : 감염성 심내막염, 이첨판 역류증, 개