Abnormal Morphological Patterns of the Left Ventricular Myocardium in the Critical Stenosis of the Aortic Valve and the Intact Ventricular Septum

The evaluation of prognostic factors in infants with critical stenosis of the aortic valve and intact ventricular septum is often misleading due to a complex interaction among lesions in the mitral and aortic valves, and the left ventricular myocardium. The clinical parameters on the left ventricular function, such as ejection fraction and left ventricular end-diastolic volume, are of particular interest as their effects on survival are very controversial. We performed a clinicopathologic analysis of two autopsied cases of this disease. Besides the morphological hallmarks of the aortic and mitral valves, these two cases showed two extreme types of pathology in the left ventricular myocardium, which might have significant impacts on the clinical evaluation of the left ventricular function. Case 1 showed endocardial fibroelastosis associated with abnormal intertrabecular spaces (so-called spongy myocardium), obscuring accurate estimation of the left ventricular end-diastolic volume. Case 2 showed ischemic necrosis of the apical part of the left ventricular myocardium. This infarct was associated with acute and chronic subendocardial ischemia and mild endocardial fibroelastosis. Aggravation of the left ventricular failure could be caused by the recent ischemic insult. The evaluation of the left ventricular function, therefore, should include the evaluation of the morphologic status of the myocardium as regards to whether there is ischemia, endocardial fibroelastosis or hypertrophied trabeculae in addition to stenotic lesions in the aortic and mitral valves. *(JKMS 1997; 12: 49~54)*

Key Words : *Spongy myocardium, Endocardial fibroelastosis, Myocardial infarct, Aortic stenosis*

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Received : September 10, 1996
Accepted : November 27, 1996

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* This study was in part supported by Seoul National University Hospital Research fund (94-200).

INTRODUCTION

Neonates or young infants with critical aortic stenosis and intact ventricular septum often present with severe and progressive heart failure which does not respond to medical management (1, 2). Urgent relief of the valve stenosis is required in these cases but the therapeutic options, whether to balloon the valve or to surgery, and their outcomes are still controversial and early hospital mortality is still high up to 52.1% (1~4). Factors related to prognosis have been studied and the size of the aortic valve, ejection fraction, end-diastolic pressure, mean left atrial pressure and presence of endocardial fibroelastosis have been claimed as significant predictors of mortality (5~8). Other recent studies, however, show contradictory results (9, 10). The lower transvalvar pressure gradient was not an indicator of a better outcome, which reflect the fact that they have severely impaired ventricular function at the time of presentation and there is limited antegrade flow through the aortic valve (10). Most of the controversial aspect of the prognostic indicators are those on the left ventricular function, and the reason for poor relation and their significance are yet to be explained.

Clinicopathologic analyses of two autopsied cases of this disease were performed with particular emphasis on the diagnostic and prognostic significance of the abnormal morphological patterns of the left ventricular myocardium.

CASE REPORT

Case 1. Small left ventricle with endocardial fibroelastosis

A 20-day-old male infant was admitted because of profound sweating and mild differential cyanosis. He was born after an uneventful full-term gestation. His body weight was 4.3kg. Grade 2/6 systolic murmur was detected at his left lower sternal border. The second heart sound was accentuated. Liver tip was palpable 3cm below the right costal margin. Arterial pulses at four extremities

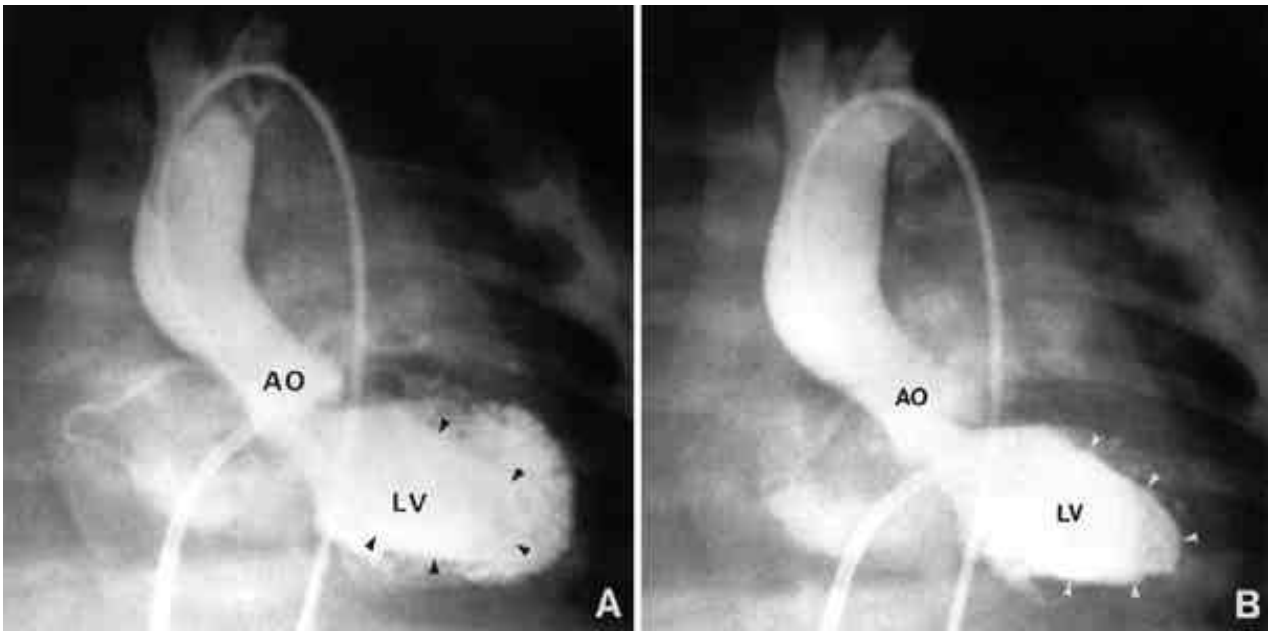

Fig. 1. Frontal left ventriculograms of case 1. In the diastolic phase (A), the left ventricular cavity consists of the central cavity ("LV" surrounded by black arrow heads) and the peripheral zone that represents clefts of intertrabecular spaces. In systolic phase (B), only central part is opacified (white arrow heads) and the peripheral zone is completely obliterated. (AO, ascending aorta; LV, left ventricle)

were well palpable. Echocardiograms showed severe aortic stenosis, a largely patent arterial duct with right-to-left shunt, mild narrowing of the isthmus and poor left ventricular function. The end-diastolic volume of the left ventricle was 10.0ml/m^2 body surface area (BSA) and end-systolic volume was 2.2ml/m^2(BSA). The pulse rate was 150/min. On angiocardiography, the left ventricle showed a double contour, the central functioning part being surrounded by numerous clefts of contrast collections that were obliterated during the ventricular systole (Fig. 1A, 1B). The left ventricular pressure before and after the valvuloplasty were 155 and 88mmHg and transaortic valvar pressure gradient, 46 and 28mmHg, respectively. Left ventricular end-diastolic pressure before and after valvuloplasty were 42 and 33mmHg. Echocardiograms obtained after the procedure showed left-to-right shunt through the arterial duct. Surgical ligation of the arterial duct was performed, and the left ventricular function was improved. The cardiac function was much improved after the surgery, the left ventricular ejection fraction being 70%. There was trivial regurgitation through the aortic valve. At the age of three months he died of severe pneumonia and pleural effusion. Autopsy revealed mixed bacterial and cytomegaloviral pneumonia. The left ventricular myocardium consisted of two distinct layers, the outer compact layer with normal myocardial architecture and inner incompact layer with numerous clefts of intertrabecular spaces. There was an endocardial fibroelastosis and the thick endocardium extended into the incompact layer to line the clefts of the intertrabecular spaces (Fig. 2A, B). The epicardial and intramyocardial coronary arteries were normal and there was no evidence of direct communication of the intertrabecular spaces with the coronary circulation. There was no evidence of recent myocardial necrosis. The aortic valve was dysplastic, unicuspid and unicommissural. The mitral valve was stenotic due to congenital hypoplasia but without parachute morphology (Fig. 2A).

Case 2. Dilated left ventricle with myocardial necrosis

A 45-days-old male infant was admitted because of irritability, dyspnea and mild cyanosis. He was born after the full-term gestation. His body weight was 2.48kg. There was subcostal retraction. Grade 2-3/6 systolic murmur was heard at the right upper sternal border. The tip of the liver was palpable 2cm below the right costal margin. Femoral pulses were slightly weaker than the brachial pulses. Echocardiograms demonstrated a small aortic valve with thick dysplastic cusps, oval fossa defect, largely patent arterial duct, relatively small mitral valve, and poor left ventricular function. Electrocardiograms showed depression of ST segment of aVF lead. Balloon aortic valvuloplasty was attempted. Angiocardiograms showed dyskinetic wall motion of the left ventricle, especially in its apical half (Fig. 3A, B). During the

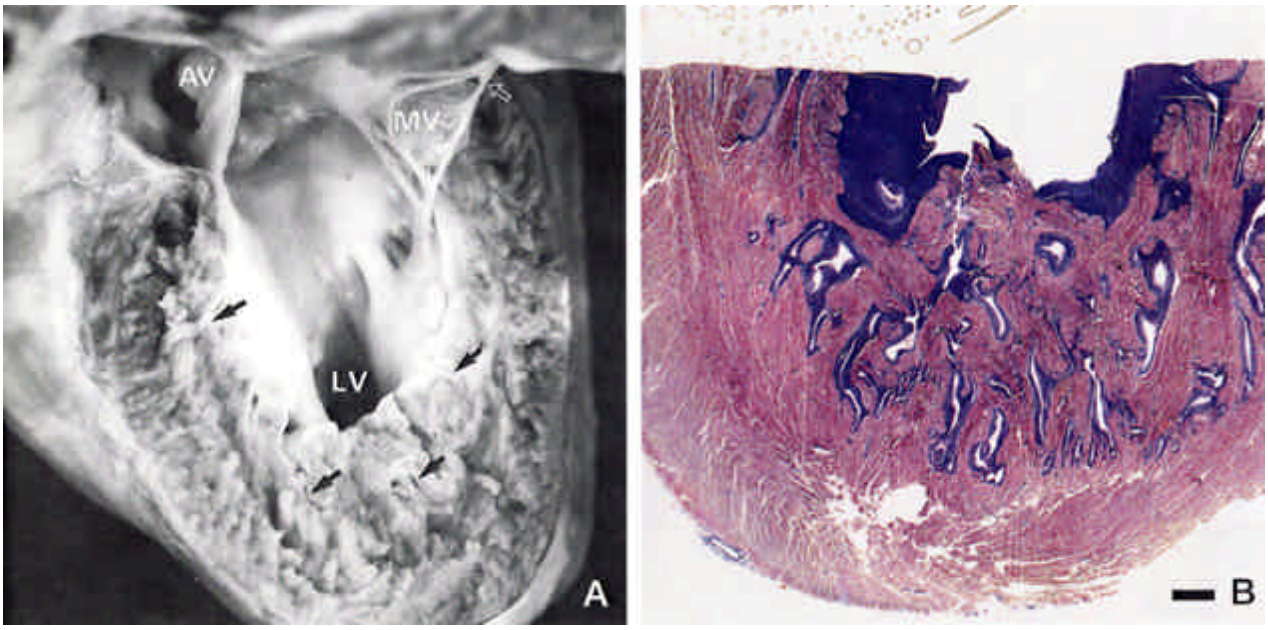

Fig. 2. Autopsied heart specimen of case 1. **A.** Left ventricular view of the heart shows pearly white endocardial surface and slit-like intertrabecular spaces (black arrows) in the inner half of the left ventricular wall. Aortic valve leaflets (AV) are nodular and stenotic. Mitral valve (MV) shows small leaflets and short chordae tendinae. Papillary muscles are hypoplastic (white open arrows). **B.** Scanning power view of a histologic section of left ventricular myocardium at the apical region. Thick endocardium, stained blue, extends to the inter-trabecular space at the inner half of the ventricular wall. The outer myocardial layer is compact and epicardial coronary vessels are normal. (Bar represents 1mm. Masson's trichrome stain)

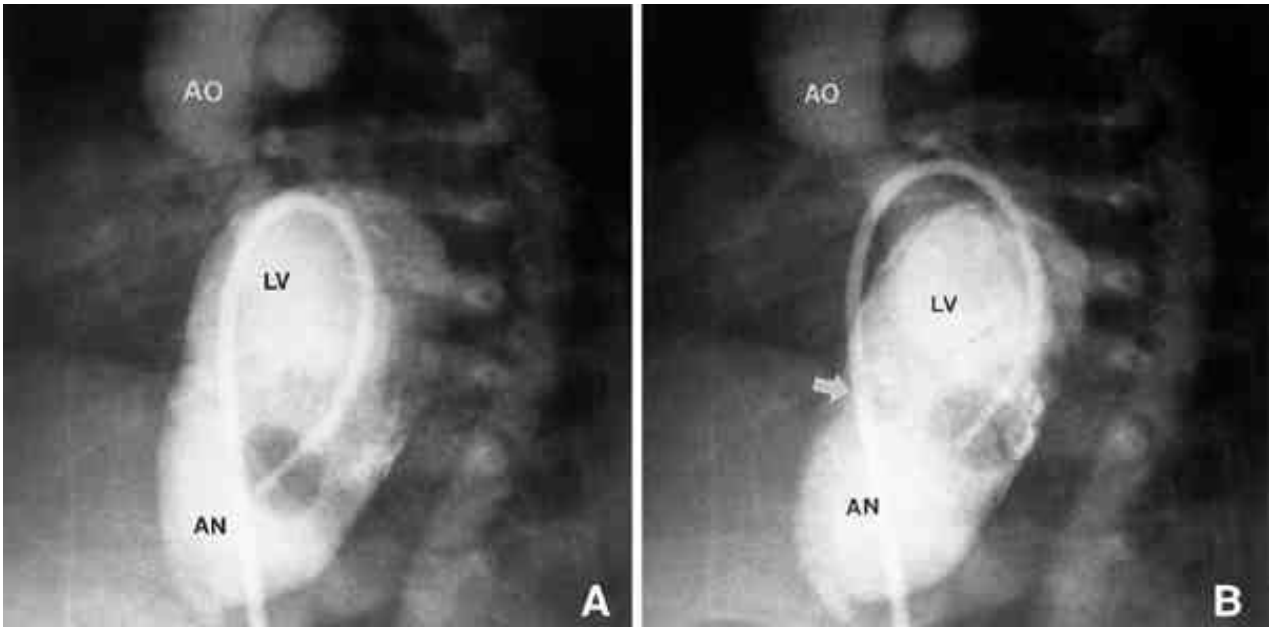

Fig. 3. Left ventriculograms of case 2 in the left anterior oblique view. In the diastolic phase (A), the ventricular cavity (LV and AN) is well expanded. In systolic phase (B), the basal part (LV) is well contracted but the apical part of the ventricle shows aneurysm with decreased contraction (AN). A notch is formed at the middle of the ventricular cavity (arrows). Ascending aorta (AO) shows post-stenotic dilatation.

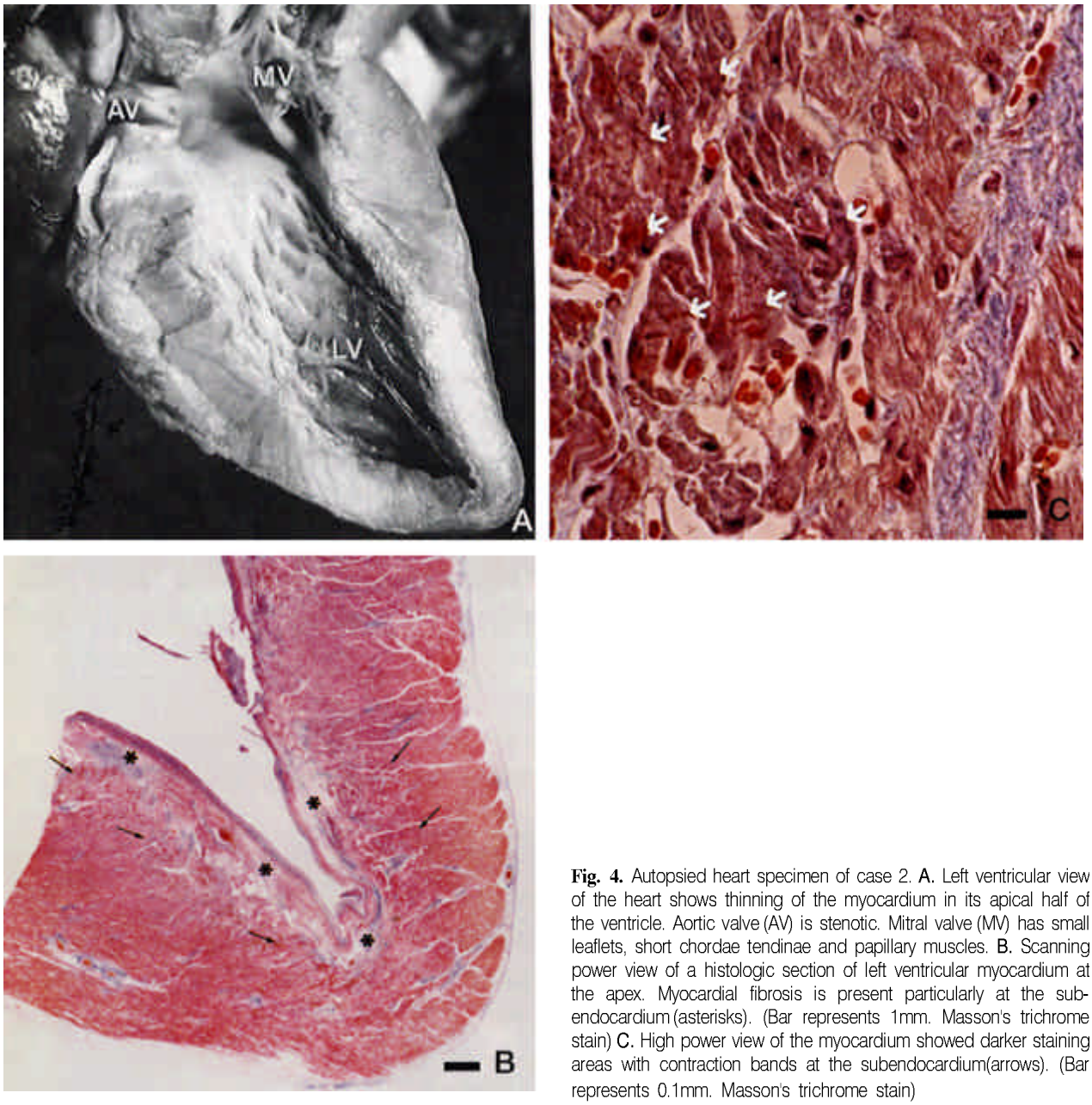

Fig. 4. Autopsied heart specimen of case 2. **A.** Left ventricular view of the heart shows thinning of the myocardium in its apical half of the ventricle. Aortic valve (AV) is stenotic. Mitral valve (MV) has small leaflets, short chordae tendinae and papillary muscles. **B.** Scanning power view of a histologic section of left ventricular myocardium at the apex. Myocardial fibrosis is present particularly at the subendocardium (asterisks). (Bar represents 1mm. Masson's trichrome stain) **C.** High power view of the myocardium showed darker staining areas with contraction bands at the subendocardium(arrows). (Bar represents 0.1mm. Masson's trichrome stain)

procedure, cardiac arrest developed. Emergency operation with aortic valvoplasty, coarctoplasty and ligation of the arterial duct was performed, but he died in the operating room. Autopsy revealed multifocal myocardial necrosis involving inner half of the left ventricular myocardium and aneurysmal dilatation in the apical half of the left ventricular free wall and septum (Fig. 4A~C). Histologic sections showed myocardial fibrosis particularly at the subendocardium. Groups of myocardium showed contraction band necrosis suggestive of a recent additional ischemic insult (Fig. 4C). Coronary arteries were normal. Endocardial fibroelastosis was mildly present. The aortic valve was dysplastic and bicuspid. Mitral valve was mildly hypoplastic.

DISCUSSION

Evaluation of the cardiac function in critical aortic stenosis includes the measurement on the actual size of the mitral and aortic valves and on the functional status of the left ventricle. Clinical assessments based on the hemodynamic and morphologic status of the left ventricle, however, are often misleading (4, 11). Transaortic

pressure gradient as measured by Doppler analysis shows poor correlation with the severity of stenosis due to the left ventricular myocardial failure often present in this disease (7, 12, 13). Moreover, the presence of mitral regurgitation accelerates the left ventricular failure (12~14). The pressure data of the left ventricle, therefore, indicates neither the severity of the aortic stenosis nor the degree of the wall stress of the left ventricle.

The initial clinical assessment of our cases showed relatively well developed left ventricles by echocardiographic and angiocardiographic measurements. But autopsy examination of the left ventricle and retrospective analysis of echocardiograms and angiocardiograms showed that the left ventricular anatomy and function were much worse than expected. The present cases showed two extreme patterns of myocardial abnormalities in critical aortic stenosis, one being abnormal myocardial architecture with numerous clefts of intertrabecular spaces and endocardial fibroelastosis, and the other being myocardial infarction. These two situations would be main organic causes of ventricular dysfunction in this particular disease.

In case 1, endocardial fibroelastosis was responsible for the poor left ventricular function. It also showed abnormal myocardial architecture. Numerous clefts of intertrabecular spaces in the inner layer of left ventricular myocardium was opacified on the left ventriculography, forming a peripheral halo. The ejection fraction derived from the angiocardiograms was misleading, as the peripheral halo, which was hardly a functioning cavity, was included in the calculation of the diastolic volume. Abnormal myocardial architecture of this form is a rare anomaly described in various terms; persistent spongy myocardium (15), myocardial sinusoid (16), deep intertrabecular space (17), or noncompaction of the myocardium (17). Obstructive lesions in the ventricular outflow, such as critical aortic stenosis and pulmonary atresia and intact ventricular septum, are commonly associated with such myocardial pathology. In both situations, the increased ventricular pressure is deemed to be a pathogenetic mechanism (15). Other conditions of this anomaly included abnormal origin of one coronary artery from the pulmonary trunk, but this lesion can also be detected in adulthood as an isolated cause of myocardial dysfunction (16). When examining this anomaly it is important to find any fistulous communication between the intertrabecular space and the coronary vessels, not only because of its functional significance but also because the fistulous communication might be related with the type of myocardial blood supply observed in the early stages of the human embryo (18). Angiographic and pathologic studies demonstrated fistulous communications of this space with the coronary arteries in pulmonary atresia and intact ventricular septum. This communication was also present in some cases with isolated myocardial disease (19). There is no report of this communication in the left ventricular obstructive lesion (16). Histological studies in case 1 showed normal epicardial and intramural coronary vessels and thick endocardium, suggesting a blind intertrabecular pouch without communication.

The left ventricular dysfunction in case 2 was due to dyskinetic wall motion at its apical half. The end-diastolic volume of the left ventricle was not small for body surface area but aneurysmal dilatation of the apical part in systolic phase resulted in low ejection fraction. Postmortem examination of the left ventricle showed old ischemic fibrosis and recent ischemic necrosis with contraction bands particularly in its apical half. The precipitating cause and time of onset of the recent myocardial necrosis was not determined despite the careful retrospective analysis of the clinical course. Electrocardiograms of this patient did not show evidence of recent infarct but histologic features suggested that there were both longstanding subendocardial fibrosis and recent aggravation. It is well understood that the blood supply to the myocardium is often compromised in patients with aortic stenosis despite wide patency of the coronary arteries, because of the increased intramyocardial compressive force and the short diastolic duration in critical aortic stenosis especially at a high heart rate. Moreover, coronary driving pressure is reduced when heart failure or aortic insufficiency is developed [20, 21]. In these patients, myocardial fibrosis is the severest in the subendocardial region, which can be a mechanism of endocardial fibroelastosis [22, 23], ventricular dilatation or rupture and sudden death (24, 25).

In summary, these cases with critical aortic stenosis presented herein showed two distinctive patterns, one being abnormal myocardial architecture with numerous intertrabecular spaces and endocardial fibroelastosis, and the other being myocardial ischemic change. The evaluation of the clinical manifestation and diagnostic findings of critical aortic stenosis, therefore, should include the assessment of the morphological status as well as functional status of the myocardium.

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