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Multiple papillary fibroelastomas attached to left ventricular side and aortic side of the aortic valve: A report of new case and literature review

Toshimitsu Tsugu MD, PhD[1,2,3] | Yuji Nagatomo MD, PhD[4] | Jin Endo MD, PhD[3] | Takashi Kawakami MD, PhD[3] | Mitsushige Murata MD, PhD[5] | Masataka Yamazaki MD, PhD[6] | Hideyuki Shimizu MD, PhD[6] | Keiichi Fukuda MD, PhD[3] | Hideo Mitamura MD, PhD[1] | Patrizio Lancellotti MD, PhD[2]

[1]Department of Cardiology, Federation of National Public Service Personnel Mutual Aid Association Tachikawa Hospital, Tachikawa, Japan

[2]Department of Cardiology, University of Liège Hospital, CHU Sart Tilman, Liege, Belgium

[3]Department of Cardiology, School of Medicine, Keio University, Tokyo, Japan

[4]Department of Cardiology, National Defense Medical College Hospital, Tokorozawa, Japan

[5]Center for Preventive Medicine, School of Medicine, Keio University, Tokyo, Japan

[6]Department of Cardiovascular Surgery, School of Medicine, Keio University, Tokyo, Japan

Correspondence
Toshimitsu Tsugu, MD, PhD, Department of Cardiology, University of Liège Hospital, CHU Sart Tilman, Domaine Universitaire du Sart Tiilman B.35-4000 Liège 1, Liège, Belgium.
Email: tsugu.z7@keio.jp

Abstract

The aortic valve (AV) is the most commonly affected site in multiple papillary fibroelastomas, but the frequency of embolism caused by the attachment side of the AV has not been elucidated. According to the review of the previous literature, 16 cases have been found attached to the AV. Of these, 6 of these have been found to be attached on the aortic side and 4 on the left ventricular side, 1 was bilateral, and 5 cases were unknown. Of the cases found on the aortic side, embolism occurred in 3 of them, and of the left ventricular side cases, embolism occurred in 2 of them. The frequency of embolism is equivalent even if papillary fibroelastoma attached to either side of the AV.

KEYWORDS

aortic valve, cardiac neoplasm, cardiac tumor, double, echocardiography

1 | INTRODUCTION

Primary cardiac tumors are rare with an incidence of 0.001%–0.003%[1] in autopsy series, 75% of which are benign. Papillary fibroelastoma (PFE) accounts for 7.9%, the second most common type of benign primary cardiac tumor.[2] PFE is usually found as solitary tumor, and multiple tumors are relatively rare with an incidence of 7%–13% of all PFE cases.[3-5] The aortic valve (AV) is the most common affected site in multiple PFEs, but it remains to be clarified whether attached side of the AV may affect the incidence of embolism. Here, we present a case of multiple PFEs attached to both the left ventricular (LV) side and aortic side of the AV, and we review the other previously published cases of multiple PFEs.

2 | CASE REPORT

A 70-year-old woman was diagnosed with a parathyroid tumor at an outside hospital. She was admitted to our hospital to undergo surgical resection. The patient had no history of cardiac disease, cardiac surgery, or radiation therapy, and she had taken no medication. Transthoracic echocardiography was conducted to assess the surgical

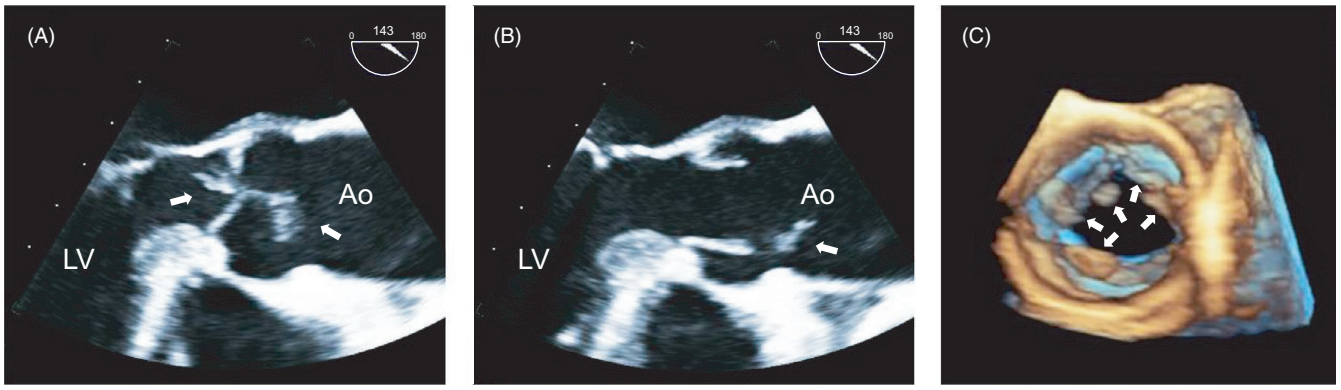

FIGURE 1 Mid-esophageal long-axis view (143° rotation) on transesophageal echocardiography, showing the multiple PFEs. A, Multiple PFEs (arrow) attached to the left ventricular side and the aortic side of the aortic valve during diastole. B, PFE had short pedicle and multiple papillary fronds which attached to the aortic side of the AV during systole (arrow). C, Mid-esophageal short-axis view on three-dimensional transesophageal echocardiography revealed multiple mobile masses attached to the all cusps of the aortic side of the aortic valve during systole (arrow). Ao = aorta; LV = left ventricle; PFE = papillary fibroelastoma

risk for resection of the parathyroid tumor. Transthoracic echocardiography showed multiple mobile low-echoic restiform lesions on the left ventricular side and aortic side of the AV. Transesophageal echocardiography was carried out for further evaluation of the multiple tumors. These tumors had a short pedicle and multiple papillary fronds which attached to aortic side of the noncoronary cusp (4.7 × 2.3 mm), the right coronary cusp (13.0 × 1.9 mm), the left coronary cusp (6.6 × 2.1 mm), and left ventricular side of the left coronary cusp (7.0 × 2.0 mm) during diastole (Figure 1A) and systole (Figure 1B). Three-dimensional transesophageal echocardiography revealed multiple mobile masses attached to the all cusps of aortic side of the AV during systole (Figure 1C). Computed tomography revealed multiple chronic cerebral infarctions of the cerebral hemispheres bilaterally, but no evidence of atheromatous plaques in the carotid artery. Magnetic resonance angiography showed no evidence of significant stenosis or occlusion in intracranial or carotid arteries. From these findings, we suspected that multiple cerebral infarction might be attributed to emboli consisting of multiple fragments of PFE. In this context, surgical extirpation by minimally invasive cardiac surgery through a mini-right thoracotomy was performed to prevent life-threatening additional embolic events induced by these tumors. A surgical view with an approach through the left atrium (Figure 2A) revealed the masses (arrow) adhered to

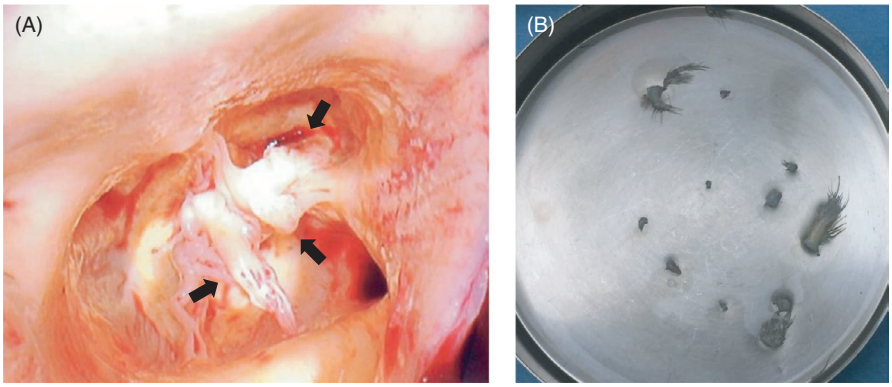

FIGURE 2 Surgical view with an approach through the left atrium in a patient with masses (arrow) adhered on the aortic side of the aortic valves (A). Resected specimen showed multiple papillary frond-like structures (B)

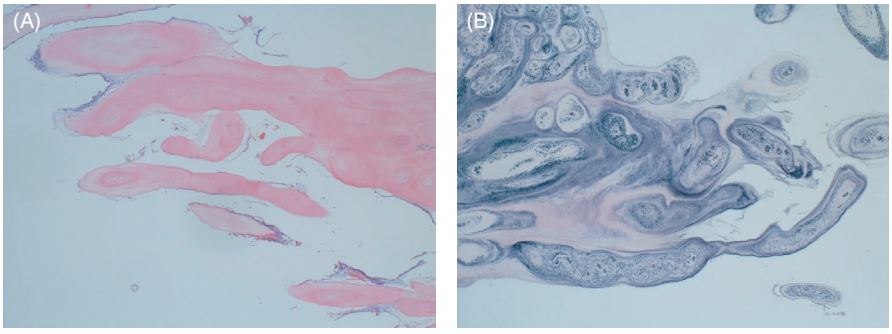

FIGURE 3 A, Multiple avascular hyaline fronds are lined by flattened endothelial cells (hematoxylin and eosin staining, ×10). B, Multiple papillary fronds with a dense core of connective tissue containing elastic fibers (Elastica van Gieson staining, ×10)

TABLE 1 Summary of the 37 reported cases of multiple papillary fibroelastomas

Reference	Age (y), sex	Location: side of the AV: size	Embolism	Treatment	Outcome
Erdogan et al[10]	65, F	RVOT (16 × 12 mm, 5 × 4 mm)	None	Resection	Good
Diplaris et al[11]	46, M	MV (AML: A1: 9 × 9 mm; AML: A2: small), LV	CI	Resection	Good
Floria et al[12]	70, M	AV (RCC: Ao side: 7 mm), MV (AML: 6.6 mm)	None	Resection	Good
Sato et al[13]	59, F	AV (2 on the RCC, 3 on the LCC: 9 mm)	None	AVR	Good
Roque et al[14]	64, F	AV (NCC/RCC: Ao side: 10 mm; NCC: Ao side 9 × 7 mm)	None	Resection	Good
Alozie et al[15]	48, M	AV (LCC: Ao side: 8 × 7 mm; RCC: small: Ao side; NCC: small: Ao side)	MI	Resection	Good
Law et al[16]	25, M	LVOT (9 × 3 mm), AV (NA), MV (LA side)	None	MVR (mechanical valve)	Good
Kumar et al[17]	41, F	RV (5–6 mm), LV (8–10 mm)	PE	Resection	Good
Kobayashi et al[18]	68, M	LV (24 × 11 mm, small)	None	Resection	Good
Truscelli et al[19]	59, F	AV (LCC: LV side: 5 × 5 mm; RCC: small)	MI	AVR (mechanical valve)	Good
Hoashi et al[20]	5, M	MV (AML: LV side)	None	Resection	Good
Hattori et al[21]	71, F	AV (4 cusps: LV side), LVOT	None	AVR (mechanical valve)	Good
Yoda et al[22]	70, F	AV (all 3 cusps: LV side), LVOT (10 × 10 mm)	CI	AVR (bioprosthetic valve), Resection (LVOT)	Good
Asrress et al[23]	72, M	AV (NCC/RCC: Ao side: 14 × 12 mm; LCC: Ao side: small)	MI	Resection	Good
Matsumoto et al[24]	62, F	AV (LCC: Ao side: 8 × 5 mm; RCC: Ao side: small; NCC: Ao side: small)	None	AVR	Good
Fuzellier et al[25]	44, M	MV (AML: LV side: 20 × 15 mm; PML: LA side and LV side), AV (NCC)	None	MVR (mechanical valve), Resection (AV and LV)	Good
Yeo et al[26]	81, F	AV (LCC: Ao side: 7 × 7; RCC: small: Ao side)	MI	Observation (reject surgery)	NA
Irie et al[27]	59, M	LVOT, 6 × 5 mm	CI	Resection	NA
Davoli et al[28]	77, M	AV (LCC: Ao side: 10 × 5 mm; NCC: Ao side: 4 × 2 mm)	None	Resection	Good
Eslami-Varzaneh et al[29]	67, F	AV (11 × 7 mm), MV (AML: 6 × 5 mm), LVOT (20 × 15 × 12 mm)	None	AVR, MVR, Resection	Good
Neuman et al[3]	75, M	AV (NCC: LV side: 15 × 14; RCC: LV side: 9 × 8; LCC: LV side: 2 × 2)	None	Resection	NA
Kanarek et al[30]	41, F	AV (NCC: LV side: >10 mm), MV (AML: LA side: 5 mm; PML: LA side: 10 mm)	CI	AVR, MVR	Good
Kurup et al[31]	35, M	AV (3 × 3 × 1 mm), LVOT (8 × 7 × 7 mm)	NA	AVR, Resection	NA
Kurup et al[31]	47, F	LV (20 × 10 × 8) mm	NA	Resection	NA
Kurup et al[31]	49, F	MV, LV	None	MVR, Resection	NA
Kurup et al[31]	52, M	LVOT (7 × 6 × 2 mm, 3 × 2 × 1 mm), AV (7 × 3 × 1 mm)	NA	Resection	NA
Kurup et al[31]	79, M	LV (5 × 4 × 3 mm)	None	Resection	NA
Touati et al[32]	49, M	AV (NCC: 12 mm, RCC: 2 mm)	CI	NA	NA
Touati et al[32]	64, M	AV (LCC, NCC)	TIA	NA	NA
Touati et al[32]	40, F	AV (LCC, RCC)	NA	NA	NA
LiMandri et al[33]	66, M	TV (posterior leaflet: 10 mm and anterior leaflet: 4 mm)	None	Resection	Good
Lee et al[34]	57, F	LVOT (seven), AV (LV side: small), MV (LV side: small)	None	Resection, MVR	Good
Kalman et al[35]	52, F	MV (AML: LV side: 15 mm), LV (8 mm)	None	MVR (mechanical valve), Excision (LV)	NA
de Virgilio et al[36]	48, F	MV (LV side 5–10 mm), LVOT (5–10 mm)	None	MVR	Good
Levinsky et al[37]	27, F	AV (NCC: 15 mm, LCC: 5 mm), MV (AML)	NA	AVR, MV resection	Good
Cha et al[38]	54, F	LV (32 × 16 × 15), AV (LV side)	NA	AVR (mechanical valve), MVR	Good
Present Case (2018)	70, F	AV (NCC; Ao side 7 mm, RCC; Ao side 5 mm, LCC; Ao side 4 mm, NCC; LV side 4 mm, RCC; LV side 4 mm)	CI	Resection	Good

Abbreviations: AML = anterior mitral leaflet; AV = aortic valve; AVR = aortic valve replacement; CI = cerebral infarction; LCC = left coronary cusp; LV = left ventricle; LVOT = left ventricular outflow tract; MI = myocardial infarction; MV = mitral valve; MVR = mitral valve replacement; NCC = non-coronary cusp; PE = pulmonary embolism; PML = posterior mitral leaflet; RCC = right coronary cusp; RVOT = right ventricular outflow tract; TV = tricuspid valve.

aortic side of the noncoronary cusp (5 mm), the right coronary cusp (7 mm), the left coronary cusp (4 mm), and left ventricular side of the right coronary cusp (4 mm). Gross specimens of the masses all showed multiple papillary frond-like structures (Figure 2B). Histological findings showed multiple papillary fronds which consisted of an avascular collagen matrix and a single layer of endothelial cells, leading to the definite diagnosis of PFE (Figure 3). She had an uneventful course and no recurrence of PFE until 1 year after operation.

3 | DISCUSSION

The majority of PFEs are solitary, but multiple PFEs are found in 7%–13% of all PFE cases.[3,5] In the case report literature from 1981 through 2019, 37 cases of multiple PFEs have been reported including the present case (Table 1). The cases with multiple PFEs consisted of 17 men (46%) and 20 women (54%), age from 5 to 79 years (median 59), and the average size of 12.3 ± 6.3 mm. The size and location of the attachment site of the largest tumor in each case were evaluated. The most common size of PFE was 6–10 mm (49%), and the tumors of more than 21 mm all attached to the LV (Figure 4). Whereas the incidence of embolism was 50% among the tumors of <15 mm, there were no cases that caused embolism among the tumors of more than 16 mm. (Figure 5). The lack of correlation between the tumor size and the risk of embolism is presumed to be because the larger size of tumors adhered to the ventricle broadly. Solitary PFE typically arises from the aortic or the mitral valve endocardium on the flow surface. The AV is the most often affected site (44%) followed by the mitral valve (35%), the tricuspid valve (15%), and the pulmonary valve (8%).[6] Since the pulmonary valve is difficult to visualize by two-dimensional transthoracic echocardiography, the number of pulmonary valve case may be underestimated. As reported by Singh et al,[7] three-dimensional transthoracic echocardiography may have the potential to accurately diagnose them. In our review of multiple PFEs, likewise solitary PFE, the AV was the most commonly involved site with 14 cases (38%), followed by LV 11 cases (30%), mitral valve 3 cases (8%), right ventricle 2 cases (5%), the tricuspid valve 1 case (3%), and not available 6 cases (16%) as shown in Figure 4. The most serious complication is thromboembolism. Its frequency has been reported as high as 53% and is higher than other benign cardiac tumors such as myxoma, lipoma,[8] or even vegetation.[9] The high frequency of thromboembolism in PFE is ascribed to two potential mechanisms that of easily formed tumor fragments of or micro-thrombus attached to the irregular and shaggy surface on the tumor. It remains to be clarified as to whether there is a difference in the incidence of embolism caused by adhesion to the aortic side of the AV. Of 37 cases of multiple PFEs, 16 cases (43%) were

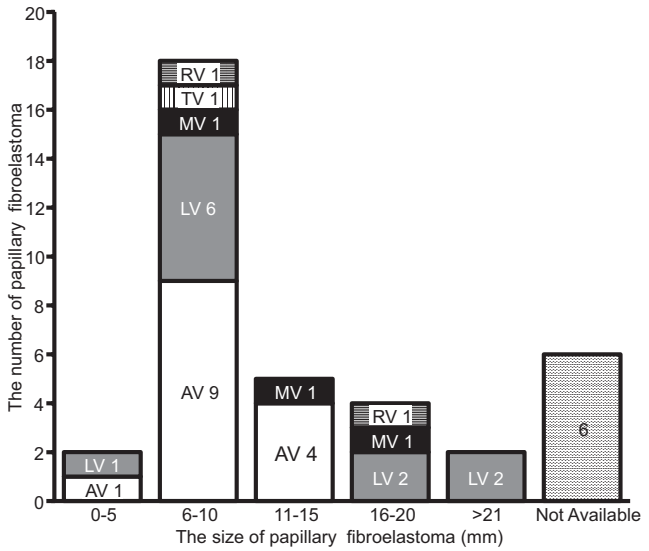

FIGURE 4 The relationship between the number of PFE and the tumor size. AV = atrial valve; LV = left ventricle; MV = mitral valve; PFE = papillary fibroelastoma; RV = right ventricle; TV = tricuspid valve

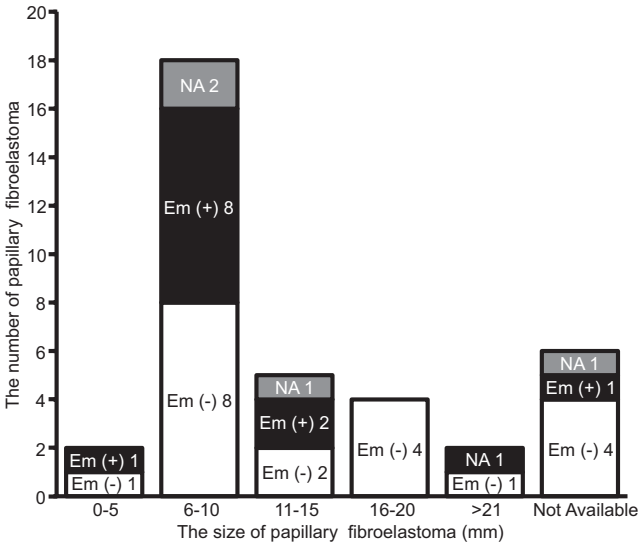

FIGURE 5 The relationship between the frequency of embolism and PFE size. Em = embolism; NA = not available; PFE = papillary fibroelastoma

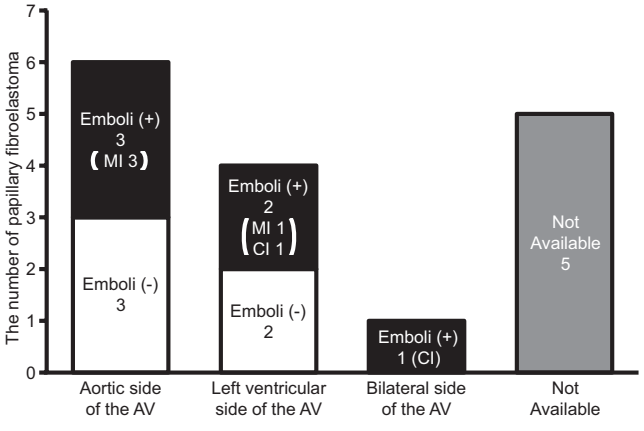

FIGURE 6 The relationship between the frequency of embolism and the attachment side of the aortic valve. AV = aortic valve; CI = cerebral infarction; Emboli = embolism; MI = myocardial infarction

multiple tumors attached to AV. Among them, 6 cases had tumors on the aortic side of AV, 4 cases had those on the left ventricular side, 1 case had those on the bilateral side, and the details were not available for 5 cases. Among 6 cases of aortic side of the AV, 3 cases (50%) suffered from myocardial infarction possibly due to the embolization by fragments of PFE. The tumor size was comparable between the cases with embolization (9.7 ± 3.8 mm) and those without (9.3 ± 1.2 mm). Of 4 cases of left ventricular side of the AV, 2 cases (50%) presented with embolism (cerebral infarction in 1 case and myocardial infarction in 1 case). The size of tumor was not so large (5 mm in myocardial infarction case, and small size in cerebral infarction case). Only our case showed multiple PFEs attached to bilateral side of AV (Figure 6). There was no difference in the likelihood of embolism between PFE attached to aortic side of AV and that on left ventricular side of AV. There are no guidelines for PFE treatment, but therapeutic intervention should be recommended once embolism has occurred. We believe surgical resection is recommended when the tumor is located on the LV side (high flow). Even if tumor is attached to either side of the AV, the risk of embolism is equivalent. Furthermore, complete tumor excision has a high success rate with simple shave excision.[8] If the patient is not a surgical candidate due to a small tumor size or attachment to the nonvalvular side such as the LV, anticoagulation with warfarin or antiplatelet therapy with aspirin should be administered, since platelet clumping within the fronds of the PFE can lead to thromboembolism.[5] Our case was considered to have a high likelihood of embolism, since cerebral infarction had already occurred, and the size of tumor was the most common size which coincided with embolism. In this context, PFE was resected to prevent life-threatening embolic events. To our best knowledge, this is the first report of multiple PFEs attached to both valvular sides (high flow and low flow) of AV. In addition, this is the first study to assess the risk of embolism caused by attachment site of the AV. The number of patients reviewed in the present study was small because of its rarity and findings. And the findings should be confirmed in a larger population.

4 | CONCLUSIONS

We presented a case of multiple PFEs attached to AV. To our knowledge, this is the first report of multiple PFEs attached to both sides of the AV. In addition, this is the first study to assess the risk of embolism is the equivalent regardless of whether the PFE is attached to the LV side (high flow) or Ao side (low flow). Therefore, surgical extirpation should be performed once embolism has occurred, and even in asymptomatic patients, surgical resection should be considered when PFE has an adequate size.

ORCID

Toshimitsu Tsugu https://orcid.org/0000-0002-3399-8757
Mitsushige Murata https://orcid.org/0000-0002-9110-7465

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