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Papillary Fibroelastoma of the Heart

Vassil Gegouskov,[1,2] Alexander Kadner,[1] Lars Engelberger,[1] Thierry Carrel,[1] Hendrik Tevaearai[1]

[1]Department of Cardiovascular Surgery, Inselspital, Berne University Hospital and University of Berne, Berne, Switzerland; [2]Department of Cardiac Surgery, University of Heidelberg, Heidelberg, Germany

ABSTRACT

Background: Fibroelastoma is a rare cardiac tumor that was originally described typically from autopsy findings. Thanks to improved imaging modalities, such tumors are today relatively easy to detect and therefore are actively searched for in patients with unclear embolic events. We present the cases of 2 patients recently treated in our clinic and review the recent literature pertaining to fibroelastomas.

Methods and Results: An electronic PubMed search revealed 186 cases reported between 1994 and 2003. Ninety-seven percent of the reported fibroelastomas were diagnosed in living patients in their fourth and fifth decades of life. The majority (86%) were symptomatic, with stroke, transient ischemic attack, myocardial infarction, and angina pectoris being the most commonly described. Echocardiography was the typical diagnosis modality. Surgical resection was completed in 95% of the cases.

Conclusions: Although cardiac papillary fibroelastomas are rare and benign tumors, they cannot be considered as harmless endothelial lesions, because related embolic events are frequent and primarily involve adults in their active period of life. Echocardiography must therefore consider fibroelastoma in the differential diagnosis of every unclear systemic embolic event, especially because surgical resection can be considered as curative.

INTRODUCTION

Papillary fibroelastomas are cardiac proliferations of unclear etiology and represent only 7% of all primary cardiac tumors [Saad 2001]. Fibroelastomas are usually asymptomatic and therefore were reported in the early days only by pathologists as incidental necropsy discoveries [Yater 1931]. In 1856, V.A. Lambl described the first autopsy finding of a papillary structure implanted on an aortic valve. These structures were initially termed *Lambl's excrescences*, and it was not until 1975 that the term *papillary fibroelastoma* was proposed for these tumors [Cheitlin 1975; Gowda 2003]. The same year, Fishbein et al precisely defined the histochemical and electron-microscopical structure of this benign cardiac tumor and confirmed the similarities between fibroelastomas and Lambl's excrescences [Fishbein 1975; Boone 1992].

In 1979, Lichtenstein et al described the first surgical resection of a papillary fibroelastoma [Lichtenstein 1979] as a tumor found incidentally during the surgical closure of an interventricular septal defect. Thereafter and thanks to the multiplication of cardiosurgical interventions and certainly to the increased availability of transthoracic and transesophageal echocardiography, an increasing number of clinical cases were reported. The published reviews of the fibroelastoma literature heretofore have included all identifiable published cases; however, the clinical data drawn from autopsy findings are different from those obtained from patients who have undergone operations. We present a systematic review of the literature published over a 10-year period and report on 2 patients who recently underwent operation in our clinic for a symptomatic cardiac papillary fibroelastoma (Figure 1).

MATERIALS AND METHODS

We used the electronic PubMed advanced search option (http://www.ncbi.nlm.nih.gov/PubMed) and the search terms *fibroelastoma*, *papillary fibroelastoma*, *papillary heart tumors*, *benign cardiac tumors*, and *growths of heart valves* in a search covering the period January 1994 to December 2003. Only case reports published in English, German, or French were considered, and all previous reviews of the literature were excluded to avoid the possibility of including cases twice. We focused our interest on demographic data, tumor location, clinical manifestations, diagnosis, and treatment. Data are expressed as the mean ± SD, and statistical analyses were performed with SPSS for Windows (Release 10.0.5; SPSS, Chicago, IL, USA). Continuous variables were evaluated with the Mann-Whitney *U* test, and categorical variables were analyzed with either the chi-square test or the Fisher exact test. A P value <.05 was considered statistically significant.

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Correspondence: V. Gegouskov, MD, Department of Cardiac Surgery, University of Heidelberg, Im Neuenheimer Feld 110, D-69120 Heidelberg, Germany; 49-6221-566272; fax: 49-6221-565585 (e-mail: Vassil.Gegouskov@med.uni-heidelberg.de).

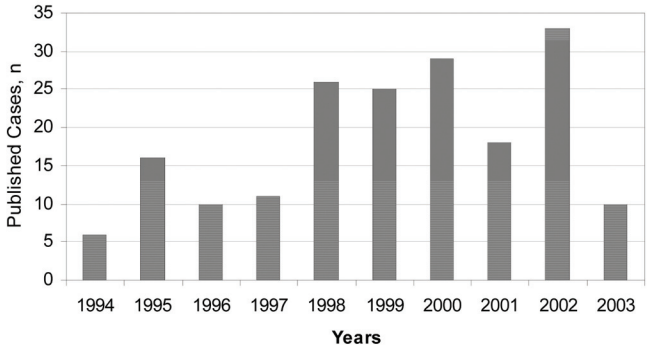

Figure 1. Annual distribution of the number of papillary fibroelastomas reported in the literature between January 1994 and December 2003.

CASE PRESENTATIONS

Patient 1

A 44-year-old woman with a history of hypertension and type I diabetes mellitus complicated by retinopathy, cheiroarthropathy, and nephropathy with the necessity of peritoneal dialysis was hospitalized for recurrent transient ischemic attacks that had occurred over the previous 6 years. Each event was associated with variable clinical manifestations, such as dysarthria, aphasia, and both left- and right-sided sensorimotor hemisyndrome. The physical examination highlighted a 2/6 to 3/6 diastolic murmur at the second right intercostal space without peripheral radiation. After eliminating other potential reasons for such symptoms, we performed a transthoracic echocardiography examination to search for a potential cardiac source of the repeated emboli. This examination revealed a circinate, free, mobile mass (0.6 × 0.7 cm) attached by a short thin pedicle to the right coronary cusp of the aortic valve. Additionally, the patient had a mild aortic insufficiency but no stenosis. The lesion was confirmed by transesophageal echocardiography (Figure 2A). The patient had no fever, and nothing in her history led to a suspicion of endocarditis. A preoperative coronary angiography examination revealed no evidence of coronary artery disease.

Patient 2

A 39-year-old woman was admitted to a division of internal medicine for nonspecific, cervical-accentuated arthralgia that she had experienced for 2 years. She had no history of fever, weight loss, dyspnea, cardiac dysrhythmia, or neurologic deficits. The routine physical examination was remarkable for a 2/6 systolic murmur at the second right intercostal space with radiation to the axilla. This finding prompted first a transthoracic echocardiographic evaluation and then a transesophageal echocardiographic examination, both of which revealed a patent foramen ovale as well as a solitary round mass of 0.5 × 0.6 cm that arose from the noncoronary cusp of the aortic valve. There was no other significant valvular pathology.

Surgical Procedures

Both cases were considered as clear indications for elective surgical resection. The operations were performed under moderate systemic hypothermia (32°C) and extracorporeal circulation with a nonpulsatile flow rate of 2.4 L/min per m^2 body surface area. A standard cannulation technique was used in both cases, with bicaval cannulation used in patient 2. After initiating antegrade cold blood cardioplegia and subsequent cardiac arrest, we performed a transverse aortotomy to allow inspection of the aortic valve. A pedunculated circinate tumor arose from the right coronary cusp of the aortic valve in patient 1, whereas the tumor originated from the noncoronary cusp in patient 2. In both situations, the tumor was excised en bloc, and the valve cusp was repaired with a bovine pericardial patch. In patient 2, we additionally performed a direct closure of the patent foramen ovale. No complications occurred during the postoperative period.

Pathologic Findings

The diagnosis of papillary fibroelastoma was confirmed in both cases by pathologic examination. Macroscopically, the excised sample showed a small, soft structure of a yellowish-gray color attached to the valve cusp by a short central pedicle.

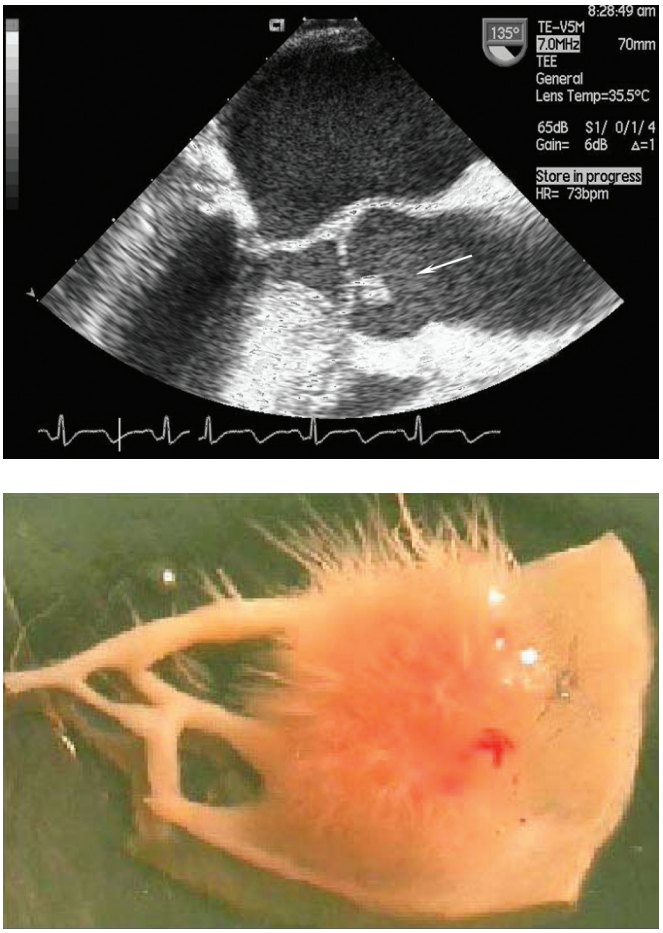

Figure 2. A, Transesophageal echocardiographic long-axis view of the aortic root showing a pedunculated free, mobile papillary tumor (0.6 × 0.7 cm). B, Papillary fibroelastoma (0.6 × 0.7 cm) in physiological saline solution showing the anemone-like appearance.

As others have suggested, we placed the tumor samples in a physiological saline solution, because the aqueous medium best showed the characteristic sea anemone–like appearance of fibroelastoma (ie, a typical central core and multiple papillary fronds; Figure 2B) [Shahian 1995; Minatoya 1996; Gowda 2003]. Microscopically, the central core was composed of thin collagen and elastic fibrils, whereas the peripheral zone surrounding the core consisted of a loose mesh of connective tissue combined with elastic fibers. We also found solitary obliterated vessels in some areas, and a layer of endothelial cells with no thrombotic components covered both tumor masses. There was no evidence of malignancy in either case.

REVIEW OF THE LITERATURE

Patient Data

Descriptions of 186 cases (including our 2 patients) were published over the period between January 1994 and December 2003 (10 years). Almost all (n = 181; 97%) of the fibroelastomas were diagnosed in living patients. Only a few cases were reported from postmortem examinations (n = 5, 3%; $P < .001$). Accurate sex and age data were obtained for 152 cases (82%) and 133 cases (72%), respectively. All age groups were involved, but the fourth and fifth decades of life were predominant, representing 43% ($P = .002$) of the cases reported during this period (Figure 3). The youngest patient was a 3-year-old boy, and the oldest was an 89-year-old woman. The cases were nearly equally distributed between male patients (n = 73, 48%) and female patients (n = 79, 52%; $P = .613$). Demographic data are presented in Table 1.

Tumor Location

In 171 cases (92%), the papillary fibroelastoma occurred as a solitary lesion; multiple fibroelastomas were reported in 15 cases (8%, $P = .026$). The identified tumor lesions affected mainly the left-sided cardiac valves and cavities (n = 154, 83%), compared with right heart structures (n = 32, 17%; $P = .022$; Table 2). Additionally, most of the lesions originated either from the valve leaflets directly or from the valve apparatus (n = 136, 73%); papillary fibroelastomas were more rarely attached to the free wall of the cardiac cavities (n = 50, 27%; $P = .125$; Figure 4). The mean maximum diameter of the reported fibroelastomas was 13.5 ± 9.0 mm (range, 2.0-53.0 mm) (Figure 5).

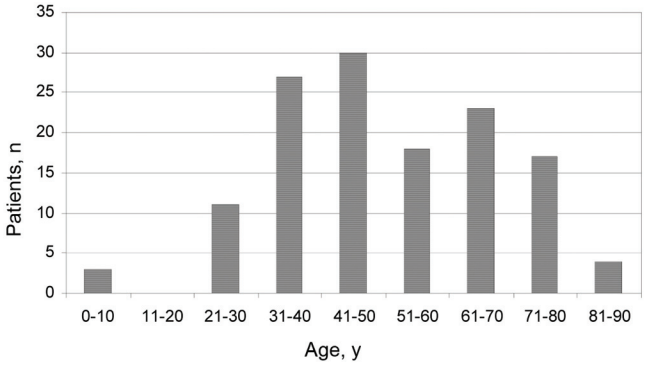

Figure 3. Age distribution of patients having a fibroelastoma reported between January 1994 and December 2003.

Table 1. Demographic Patient Data

Parameter	Value
Fibroelastoma cases, n	
Total	186
Diagnosis in life	181 (97%)
Diagnosis postmortem	5 (3%)
Age, y*	50.6 ± 17.3
Sex, n	
Male	73 (48%)
Female	79 (52%)
Concomitant cardiac diseases, n	
Mitral regurgitation	29 (16%)
Mitral stenosis	5 (3%)
Aortic regurgitation	15 (8%)
Aortic stenosis	6 (3%)
Tricuspid regurgitation	14 (8%)
Pulmonic regurgitation	2 (1%)
Coronary artery disease	21 (11%)
Cardiomyopathy (all forms)	8 (4%)
Congestive heart failure	11 (6%)

*Age data are presented as the mean ± SD.

Clinical presentation

Symptoms could clearly be related to the fibroelastoma in 156 patients (86%). The most common initial symptoms in the diagnosis of papillary fibroelastoma were neurologic in origin, with documented stroke in 57 patients (31%), transient ischemic attack in 41 patients (23%), diplopia/blindness in

Table 2. Tumor Characteristics

Parameter	Value
Patients, n	186
Tumor size, mm*	13.5 ± 9
General localization, n	
Left-sided lesions	154 (83%)
Right-sided lesions	32 (17%)
Involved cardiac structures, n	
Valvular	136 (73%)
Nonvalvular	50 (27%)
Aortic valve	57 (30%)
Mitral valve	62 (34%)
Tricuspid valve	17 (9%)
Pulmonary valve	4 (2%)
Chorda tendinea/papillary muscle	14 (7%)
Left atrium/pulmonary veins	14 (7%)
Left ventricle	16 (8%)
Right atrium	4 (2%)
Right ventricle	2 (1%)
Multiple tumor findings	15 (8%)

*Data are presented as the mean ± SD.

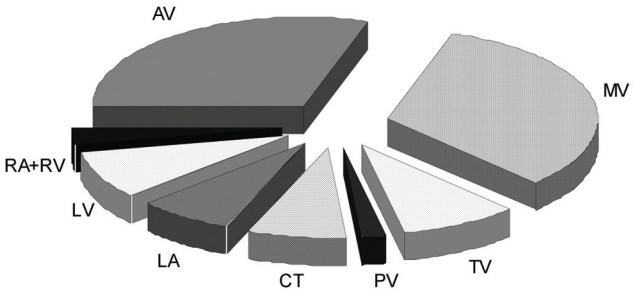

Figure 4. Distribution of tumor locations of fibroelastomas reported between January 1994 and December 2003: aortic valve (AV), 31%; mitral valve (MV), 33%; tricuspid valve (TV), 9%; pulmonary valve (PV), 2%; chorda tendinea (CT), 7% (6% on MV, 1% on TV); left atrium (LA), 7%; left ventricle (LV), 8%; free wall of right atrium and right ventricle (RA + RV), 3%.

10 patients (6%), and syncope in 7 patients (4%). The second most common type of symptoms was related to myocardial ischemia, including myocardial infarction in 18 patients (10%), angina pectoris in 14 patients (8%), and sudden cardiac death in 4 patients (2%). There were 5 cases (3%) with combined cerebrovascular and myocardial manifestations. Occasionally reported were other clinical presentations, such as dyspnea (n = 17, 9%), pulmonary embolism (n = 2, 1.3%), mesenteric ischemia (n = 2, 1.3%), and renal ischemia (n = 1, 0.6%). Paraplegia due to embolization to the spinal cord was reported in a single patient (0.6%). Some patients developed various nonspecific clinical symptoms, such as recurrent fever (n = 9, 5.7%), thyroid dysfunction (n = 3, 1.9%), bleeding disorder due to thrombocytopenia of indefinite mechanism (n = 1, 0.6%). The distribution of the reported clinical symptoms is summarized in Table 3. Systolic or diastolic cardiac murmur was described in 14 cases (7.5%). Protodiastolic tumor plop at auscultation, a phenomenon previously reported as typical for fibroelastomas with an atrial location [Colucci 2001], was reported in only 2 cases (10% of all reported atrial fibroelastomas).

Diagnosis

Transthoracic and/or transesophageal echocardiography was used as the diagnostic tool for cardiac papillary fibroelastomas in 155 (86%) of the 181 living patients.

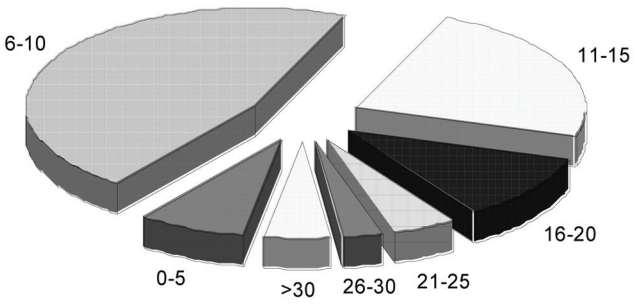

Figure 5. Tumor sizes (in millimeters) of fibroelastomas reported between January 1994 and December 2003.

Table 3. Specific Clinical Manifestations

Parameter	Value
Patients, n	181
Neurologic symptoms, n	
Stroke	57 (31%)
Transient ischemic attack	41 (23%)
Diplopia/blindness	10 (6%)
Presyncope or syncope	7 (4%)
Cardiac symptoms, n	
Myocardial infarction	18 (10%)
Angina pectoris	14 (8%)
Rhythm disturbances	14 (8%)
Sudden cardiac death	4 (2%)
Pulmonary embolism	2 (1%)
Peripheral embolism, n*	6 (3%)
Nonsymptomatic patients, n	24 (13%)

*Limb ischemia (n = 2), mesenteric ischemia (n = 2), renal ischemia (n = 1), spinal cord ischemia (n = 1).

Most lesions were described echocardiographically as small (10 mm or less), pleomorphic, and mobile masses attached by a short pedicle to the cardiac endothelium. In 22 cases (12%), the tumor was found incidentally during a routine echocardiographic examination performed during a cardiac surgical procedure for an unrelated pathology. Cardiac catheterization and coronary angiography examinations were performed in 42 patients (23%), including 2 cases in which the tumor was found incidentally during the cardiac catheterization.

Treatment

A total of 172 cases (95%) were considered as a clear indication for surgical resection under cardiopulmonary bypass. Simple tumor removal was performed in 105 cases (61%), whereas in 67 cases (39%) the valve had to be repaired (n = 55, 32%) or replaced (n = 12, 7%). Valves were repaired by directly suturing the edges of the resected cusp, by using a pericardial patch, or by using a cryopreserved aortic homograft cusp. In 3 patients (2%), a dental mirror and/or a video-assisted cardioscope were used intraoperatively when the lesion was situated deep within the heart cavity.

It was not possible to clearly determine the method of treatment in 3 patients, whereas 6 other patients initially did not undergo operation. Coumadin treatment was initiated for an unknown reason in 2 patients; however, both patients finally underwent operation after recurrent transient ischemic attacks occurred within a 10- to 12-month period. In another case, the echocardiography examination revealed a structure on the aortic valve that was not considered the embolic source; the patient was then initially discharged on Coumadin therapy. Nevertheless, the patient experienced recurring cerebral symptoms over a 2-week period, and the tumor was ultimately removed surgically. Because of very slow tumor growth, another patient was also treated primarily with Coumadin. The echocardiographic follow-up over a 16-year period showed progressive symptomatic mitral stenosis, and the patient then underwent an elective operation. In a single

case, the tumor was initially thought to be an abacterial thrombotic vegetation on the aortic valve. Coumadin treatment was initiated in this case, but the patient underwent an elective operation after 7 uneventful months. Finally, one patient initially refused the operation but underwent an elective procedure 11 months later without any complications.

DISCUSSION

Even though echocardiography has become a routine examination procedure, our analysis confirms the rarity of fibroelastomas. Indeed, only 186 fibroelastoma patients were described over the recent 10-year period; however, in contrast to earlier descriptions in which fibroelastomas were described as incidental findings during autopsies or unrelated cardiac surgical procedures [Eckstein 1995; Shahian 1995; Alawi 2002], almost all recently reported data concern living patients. Between January 1994 and December 2003, we found only 5 articles that reported on autopsy findings. In fact, the recent increase in echocardiographic examinations and the improvements in image quality have contributed to this increased rate of diagnosis in living patients. It is interesting that more than 80% of the patients underwent echocardiographic evaluation as a search was conducted for a potential cardiac embolic cause of their symptoms. The remaining 20% of the reported observations were made incidentally during unrelated surgery or an unrelated echocardiographic investigation. In other words, with the recognition of fibroelastomas as a potential source of microemboli, an echocardiographist certainly is advised to pay special attention to searching for these rare and often small tumors.

Papillary fibroelastoma is the third most common primary cardiac tumor after atrial myxomas and lipomas [McAllister 1978; Chitwood 1988; Georghiou 2003]. The etiology of fibroelastomas remains unclear. Several pathogenic theories have been proposed [Georghiou 2003], including a degenerative process [Heath 1961] or a mechanical endocardial trauma, such as prior open heart surgery [Kurup 2002]. Consequently, an increasing number of fibroelastomas have been suggested to occur in older patients [McAllister 1978; Howard 1999]. We found the fibroelastoma incidence to peak in the fourth and fifth decades, however, with fibroelastomas progressively declining in older patients. Early speculations suggested that papillary endocardial lesions develop from mural thrombi of nonbacterial thrombotic endocarditis [Salyer 1975]. Abnormal hemodynamics may indeed play a role in forming the characteristic papillary structure of these lesions [Lichtenstein 1979]. Other authors proposed that these lesions could be the result of aging of the valvular endocardium [Gully 1998]. Some theories have proposed that fibroelastomas are hamartomas, whereas others have hypothesized an inflammatory source or a congenital origin [Heath 1961; McAllister 1978; Howard 1999]. In 1995, Rubin et al presented an immunohistochemical comparison of papillary fibroelastomas and cardiac myxomas [Rubin 1995] and confirmed their common endothelial origin; however, this study could not clearly distinguish whether cardiac papillary fibroelastomas are hamartomas or reflect reparative processes.

The clinical manifestations of fibroelastomas depend primarily on their localization and mobility [Gowda 2003]. In the majority (83%) of the cases reported during this 10-year period, papillary fibroelastomas were found on the left-sided cardiac valves or in the left heart cavities and thus might have been associated with cerebral, coronary, or peripheral embolic events [Shahian 1995; Georghiou 2003]. Right-sided cardiac fibroelastomas are seldom symptomatic, observations that may explain why they are described more rarely (17%). Nevertheless, right-sided fibroelastomas have been reported to cause pulmonary hypertension, pulmonary embolisms [Neerukonda 1991], or intermittent cyanotic episodes [Anderson 1977] with systemic hypoxia and polycythemia [Savino 1995]. Paradoxical embolic events may also occur in patients with patent foramen ovale and a right-to-left shunt [Gowda 2003]. Furthermore, papillary fibroelastomas can be responsible for right or left ventricular outflow tract obstruction [Anderson 1977; Yee 1997] or even congestive heart failure [Chitwood 1988]. Some lesions sporadically may induce other nonspecific clinical signs and symptoms (eg, recurrent fever, thyroid dysfunction, bleeding disorder due to thrombocytopenia, and so on) [Oostenbrug 2001].

Overall, we found that more than 80% of the living patients presented with cerebral and/or cardiac symptoms. Because these manifestations may be serious, including sudden cardiac death [Howard 1999; Georghiou 2003], the diagnostic identification of papillary fibroelastomas is of absolute importance. Abnormal laboratory findings (such as anemia and/or thrombocytopenia), changes in electrocardiography findings (such as atrial fibrillation, abnormal P waves), chamber enlargement, and signs of pulmonary hypertension in chest radiographs may be characteristic but are obviously not pathognomonic diagnostic criteria [Colucci 2001; Kouchoukos 2003].

The screening and diagnostic modality most frequently used to identify cardiac papillary fibroelastomas is transthoracic and/or transesophageal echocardiography [Yee 1997; Colucci 2001; Meng 2002]. In particular, 2-dimensional echocardiography combined with Doppler color flow measurement provides essential information about tumor size, shape, location, mobility, presence of stalk, and multiplicity [Yee 1997; Colucci 2001; Sun 2001]. The continuing improvement in this diagnostic tool over the last 2 decades and the subsequent increase in its sensitivity certainly have contributed to the increase in fibroelastoma diagnosis, including in neonates and in utero [Anderson 1977; Dennis 1985; Colucci 2001]. In patients for whom transesophageal echocardiography is contraindicated or technically impossible, multislice computed tomography appears to be an appropriate alternative diagnostic method, because of its fast data acquisition and high spatial resolution [Rbaibi 2002]. Invasive diagnostic procedures such as percutaneous transluminal endomyocardial biopsy, cardiac catheterization, and coronary angiography are not absolutely necessary to confirm the diagnosis of papillary fibroelastoma but may be appropriate as part of a preoperative search for

potential associated pathologies, such as coronary artery disease [Colucci 2001; Kouchoukos 2003]. Surgical excision as quickly as possible is indicated, regardless of clinical symptoms or site of origin [Neerukonda 1991; Minatoya 1996; Howard 1999; Alawi 2002]. An involved valve may be repaired, as we have described for our 2 patients. Accordingly, intraoperative use of transesophageal echocardiography is recommended to assess valve function following the repair [Okada 2001]. In the absence of valve repair or replacement, there is currently no evidence for the use of postoperative oral anticoagulation therapy [Howard 1999; Gowda 2003]; however, long-term anticoagulation treatment may be an alternative for patients with inoperable tumors or for patients at high risk for surgery. Today, an absence of recurrence has been reported in almost all cases after surgical excision. The only report of recurrence occurred in a case involving the development of a second papillary fibroelastoma on the mitral valve 9 years after successful excision of a fibroelastoma located on the tricuspid valve [Hynes 2002].

Our review has focused on descriptions of papillary fibroelastomas. We voluntarily did not include a time period longer than 10 years. We considered it important to concentrate on a recent period in which echocardiography constituted a routine examination, not only for assessing cardiology patients but also for use in interventions during cardiac surgery. We found almost no postmortem reports during this period; therefore, the analysis of the data for this 10-year period permits a better comprehensive analysis of the clinical aspects of this rare cardiac tumor, including its diagnosis and treatment. On the other hand, postmortem findings are more objective regarding the description of tumor location. Indeed, we may have underestimated cases involving the right side of the heart in our study because of the limited occurrence of symptoms associated with this location.

In conclusion, fibroelastomas, although rare, have to be seriously considered in the differential diagnosis of every systemic embolic event. For such patients, echocardiography is a key tool in the search for such tumors. With very rare exceptions, fibroelastomas should be surgically excised as soon as possible, regardless of clinical symptoms or site of origin.

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