Papillary fibroelastoma of the pulmonary valve: a case report

ADRIAN MOLNAR1), SVETLANA ENCIĆ2), EMES KOVÁCS3), SIMONA MANOLE4), DIANA SĂCU1), IOAN MUREŞAN1), TRAIAN SCRIDON1)

1) Clinic of Cardiovascular Surgery, "Niculae Stâncioiu" Heart Institute, Cluj-Napoca, Romania
2) Department of Pathology, "Niculae Stâncioiu" Heart Institute, Cluj-Napoca, Romania
3) Clinic of Cardiology, "Niculae Stâncioiu" Heart Institute, Cluj-Napoca, Romania
4) Clinic of Radiology, Emergency County Hospital, Cluj-Napoca, Romania

Abstract
Papillary fibroelastoma is a rare, benign cardiac tumor typically found on the heart valves, which is usually discovered incidentally on echocardiography. The clinical presentation of cardiac papillary fibroelastoma varies from no symptoms to severe embolic sequelae. We report the case of a 55-year-old female patient, with a suspicion of pulmonary embolism one year before, presently admitted to the hospital for mild respiratory symptoms; the trans-esophageal echocardiography (TEE) revealed a 10/10 mm tumoral mass attached on the pulmonary valve, confirmed also by the contrast-enhanced magnetic resonance imaging (MRI). Considering the embolization risk, we decided surgical removal, with favorable outcome. The pathologic exam of the removed tumor established the diagnosis of papillary fibroelastoma. The clinical and imaging assessment one month after surgery were within normal limits. The surgical removal of the papillary fibroelastoma of the pulmonary valve is mandatory for the elimination of embolization risk. The intervention is relatively secure, with low rates of morbidity and mortality.

Keywords: papillary fibroelastoma, pulmonary valve, echocardiography, cardiac magnetic resonance.

Introduction
Primary tumors of the heart are rare, ranging from 0.002% to 0.02% in prevalence, according to large autopsy series.

Papillary fibroelastoma is the third most common primary cardiac tumor (after myxoma and lipoma), accounting for 7% to 9% of benign primary tumors [1, 2]. It usually involves the aortic or mitral valve, and less frequently the pulmonary or tricuspid valve; fibroelastoma can also develop from the papillary muscles, chordae tendineae, ventricular septum, or endocardial surface. Men and persons older than 40-year-old are chief among those who are diagnosed with papillary fibroelastoma; however, this tumor has also been described in neonates with congenital cardiac abnormalities [1].

In some surgical series, papillary fibroelastoma was classified as the second benign tumor of the heart in order of incidence. Even if it can be found anywhere on the endocardium surface, it is most frequent location is on the cardiac valves, usually on the aortic valves; the localization on the pulmonary valve is rare, in the literature being described in 13% of cases [3].

As described in some studies, most of them arise in the left heart, and the vast majority are clinically silent; though occasionally such lesions when on the aortic valve may produce symptoms of myocardial or cerebral ischemia. None has been known to cause symptoms when in the right side of the heart [4].

Most patients with this tumor are asymptomatic. Clinical presentation varies, depending upon which side of the heart is involved. Right-side papillary fibroelastomas are asymptomatic and rarely cause pulmonary embolism [1].

Patient, Methods and Results
A 55-year-old woman was admitted to the hospital for frequent episodes of mild dyspnea and reduced compliance to moderate physical activity. A year ago, she was clinically diagnosed with pulmonary thromboembolism, and accordingly treated with oral anticoagulants; however, this diagnosis was afterwards infirmed by the thoracic CT-angiography. The patient had a medical history of stage III hypertension, and dyslipidemia; also, she presented a first grade obesity, with a body mass index (BMI) of 32.5 kg/m². Due to persistence of respiratory symptoms, the decision for further investigation was taken.

The trans-thoracic echocardiography (TTE) showed no pathologic changes, but the trans-esophageal echocardiography (TEE) revealed a 10/10 mm hyperechogenic mass attached on the ventricular side of pulmonary valve, on the aortic adjacent cusp, prolapsing in the RVOT (right ventricular outflow tract), but not interfering with the valve function (pulmonary valve without stenosis and without first grade regurgitation) (Figures 1 and 2).

These findings led to the recommendation to perform a cardiac magnetic resonance, in order to improve both the structural and functional diagnosis. The contrast-enhanced MRI showed a well-described, polylobate, hypercaptant tumoral lesion on the right anterior pulmonary cusp, without pulmonary stenosis or regurgitation, and without alteration of cardiac function (Figures 3–6).
At this point, considering the embolization risk, the indication for surgical removal of the tumor was established. We performed the excision of the entire mass after opening the pulmonary artery trunk; the procedure required 35 minutes of cardiopulmonary bypass, and aortic cross-clamping for 25 minutes (Figures 7 and 8). Following tumor removal, the pulmonary valve function and structure remained unaffected.

After surgery, the patient was hemodynamically stable with minimal inotropic support, interrupted 24-hours postoperatively. The control trans-thoracic echocardiography revealed a systolic pressure in the pulmonary artery of 35–40 mmHg, with a $v_{max}$ of 2.3 m/s. The patient was discharged nine days later, with an uncomplicated postoperative course.

At the pathologic exam, the removed mass had the characteristics of a papillary fibroelastoma. Macroscopically, the tumor resembled a sea anemone when viewed under water (Figure 9). It was whitish, it measured 1.5/1.0/0.5 cm outside the water, and it was attached to the endocardial surface by a single, thin pedicle.

The mass was fixed in 10% formalin, embedded in paraffin and cut serially into cross-sections (5 μm thick).

Sections were stained with Hematoxylin–Eosin, Masson’s trichrome and Taenzer–Unna Orcein.

Immunohistochemistry was performed in paraffin-fixed tumor sections using LSAB DAKO system. Endogenous peroxidase was blocked with H2O2 3%. Immunohistochemical staining for CD31, CD34 and vimentin were made with DAKO primary monoclonal antibodies in dilution 1/20 for CD31, 1/50 for CD34 and 1/100 for vimentin (clone 9). Finally, the tissues sections were reacted with 3,3’-diaminobenzidine and counterstained with Hematoxylin.

Microscopic aspect of the papillary fibroelastoma is characterized by numerous branches, with a dense collagen core surrounded by a myxoid mantle (Figure 10a). The Masson’s trichrome stain (Figure 10b) and Taenzer–Unna Orcein stain (Figure 10c) showed some fragmentary elastic fibers and collagen fibers; each branch had CD31-positive endothelial cells on the surface (Figure 10d).

On routine follow-up 30-days after discharge, the ECG and thoracic X-ray were within normal limits, and the trans-thoracic echocardiography showed no signs of pulmonary valve dysfunction (Figure 11).
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Discussion

Papillary fibroelastomas are benign endocardial papillomas that mainly affect the cardiac valves and account for approximately 75% of all cardiac valvular tumors [5]. A papillary fibroelastoma situated at the level of a cardiac valve is a serious condition that may ultimately determine emboli formation followed by subsequent migration in any body segment; particularly from the pulmonary valve, these emboli can migrate into the lungs, with serious consequences for vital functions.
Therefore, any of these intracardiac papillary fibroelastomas should be resected by urgent indication [6].

The majority (over 55%) of papillary fibroelastomas are diagnosed at an average age of 60 years [7], ranging between 6 and 92 years [3]. They can be situated anywhere on the endocardium, and rarely there are multiple sites of the tumor [8]. Most frequently papillary fibroelastomas are found on the cardiac valves (90%), mainly on the atric valve (29% of cases) and mitral valve (25% of cases), as shown by some studies; other unusual localizations are the tricuspid valve (17% of cases) and pulmonary valve (13% of cases) [3]. Usually (69.5% of the patients), the tumor appears on affected valves: rheumatic disease and calcific fibrosis are documented in 37.8% and 62.2% of cases, respectively. Beside cardiac valves, papillary fibroelastoma can be found on rete Chiari, coronary ostia, and the atrial or ventricular free wall. They are attached by a single pedicle (rarely by multiple pedicles) on the surface endocardium, and their dimensions range between 2 and 50 mm, usually being smaller than 10 mm [9].

**Histogenesis**

The tumor resembles to Lambi excrescences, but it is quite different. The Lambi excrescences appear at advanced age, on the semilunar valves at the Arantius nodules level, on the valve closing line and the free edges of the valve cusps; on the atrio-ventricular valves, they are situated on the atrial surface of the closing line. The Arantius nodules are also age-dependent and appear as thick masses situated in the centre of the semilunar valves, at the closing line and free edge junction, in contrast to papillary fibroelastomas, which are localized at greater distance from the valve closing line. Also, unlike Lambi excrescences, papillary fibroelastoma can reach bigger dimensions, and can be found on any valve surfaces or in any endocardial tissue. The average dimensions are of approximately 1 cm, but there are reports of papillary fibroelastomas with a diameter of 5 cm [10].

In time, it was developed the idea that papillary fibroelastomas are organized thrombi, due to their contents of fibrin, hyaluronic acid, and elastic fibers; however, their localization in areas with low hemodynamic stress led to abstention from the organized thrombi theory [10].

The histological aspect that suggests a proliferation of miniature chordae tendinea, and the existence of possible congenital cases with the onset if symptoms at a young age, leaded to the formulation of hamartomatous theory.

A recent study [9] showing the presence of dendritic cells and of the cytomegalovirus in the intermediate structures in some papillary fibroelastomas, suggested the idea of a possible connection between these tumors and chronic viral endocarditis.

The repeated hemodynamic trauma can contribute to papillary fibroelastoma appearance, as shown in some studies that correlate the tumor with rheumatic valve disease, hypertrophic cardiomyopathy, or the mitral valve prolapse.

As described by some studies [7], the endocardium seems to react to the flow stress or congenital factors in a unique way. At least a subset of these tumors (18%) develops in relation with iatrogenic factors as radiation therapy, or open-heart surgery; the relationship with these conditions determined the concept that papillary fibroelastoma can be a reactive degenerative process, but the histogenesis remains still unclear. Unlike sporadic cases of papillary fibroelastoma, the iatrogenic tumors are usually multiple and seem to appear outside the cardiac valves, close to the predisposing factor (e.g., near the incised chamber).

Structurally, the tumor seems to contain elastic fibers more prominent in the core and rare or even absent in the distal part of the papillae; the mantle is made up of lax tissue composed by hyaluronic acid, proteoglycans, smooth muscle cells, dendritic cells, and fibroblasts [9].

The expression of vimentin, CD34 and CD31 in the tumor endothelium cells is positive [7, 9]. The endothelial cells that cover the papillary branches are in continuity with endocardial endothelial cells. The structure of papillary branches is microscopically similar to chordae tendinea [7]. This reduced expression of endothelial markers is thought to be linked to a trauma or an endothelial dysfunction; also, the presence of acute or chronic thrombosis can modify the macroscopic aspect of the tumor. Usually, the vast majority (80–90%) of papillary fibroelastomas are unique, but the ones linked to iatrogen conditions can be multiple, varying between two and 40 in the literature [9].

The confusion over the pathogenesis of papillary tumors of valves is reflected in the number of names, which they have been given [10–12]: myxofibroma, papilloma, papillary fibroma, hamartoma, fibro-angio-myxoma and hemangio-elastomyxoma. Accordingly, the surgical removal of these masses should be performed as soon as possible.


Papillary ‘tumors’ arise most often on the left side of the heart, frequently in association with hypertension, but have been observed on all valves. They are usually asymptomatic incidental findings at post mortem or, increasingly often, at cardiac surgery [10–13]. Rarely, when on the aortic valve they may cause angina by occluding the coronary ostia. Emboli into the coronary arteries and cerebral arteries have also been described [5, 14].

Cardiac tumors can present a significant diagnostic challenge causing symptoms and signs that mimic other cardiac diseases. Main symptoms include breathlessness, fever, weight loss, syncope, hemoptysis, and sudden death. Cardiac tumors may also cause embolization, arrhythmias (atrioventricular block and ventricular tachycardia), or obstruction of the outflow tracts. Diagnosis depends on a high index of suspicion and can almost always be made by echocardiography [12, 15–18]. In the detection of papillary fibroelastoma, the sensitivity and specificity of TTE are 88.9% and 87.8%, respectively, when the tumor is larger than 2 mm. However, when the tumor is smaller, the overall sensitivity of TTE is only 61.9%, compared with 76.6% for TEE. Newer imaging techniques, such as contrast echocardiography, can help to better
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Adrian Molnar, Assistant Professor, MD, Clinic of Cardiovascular Surgery, "Niculae Stănciulescu" Heart Institute, 19–21 Moților Street, 400001 Cluj-Napoca, Romania; Phone +40264–591 941/220, e-mail: adimolnar45@yahoo.com

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References


Conclusions

We consider that surgical removal of the papillary fibroelastoma of the pulmonary valve is mandatory in order to prevent the embolization risk. The intervention is relatively secure, with low rates of morbidity and mortality.

delineate cardiac masses [1, 12, 14]. Over the last 10 years, the development of newer pulse sequences and applications in new clinical areas has enabled cardiovascular magnetic resonance (CMR) to emerge as a powerful tool for the physician to both diagnose and guide treatment of various cardiac pathologies [13].

In our patient, the symptoms were non-specific and mild, and the trans-thoracic echocardiography was non-conclusive, therefore more sensitive and specific tests were necessary in order to establish the correct diagnosis. The trans-esophageal echocardiography managed the primary diagnosis of the existence of the tumoral mass at the level of pulmonary valve, whereas the cardiac MR was helpful in the tumoral mass characterization (dimensions, localization, delimitation, mobility, vascularization), and cardiac function evaluation; however, the final diagnosis was made only by the pathologic exam of the resected tumor.

Papillary fibroelastomas are treated curatively by surgery, whether there are preexisting embolic symptoms or a lesion is incidentally discovered [12]. Depending on the intraoperative findings, the resection of the tumor should be sufficient if the cardiac valve is unaffected (as happened in the reported case), but in the case of altered function, the valve replacement should be considered.

Benign tumors normally carry a good prognosis with normal life expectancy after resection. Patients who have had benign tumors resected are usually followed up with regular echocardiography and cardiologic supervision [12]. Re-growth of the tumor after resection has not been reported, and it requires long-term TEE follow-up studies to confirm [14].

Corresponding author

Adrian Molnar, Assistant Professor, MD, Clinic of Cardiovascular Surgery, "Niculae Stănciulescu" Heart Institute, 19–21 Moților Street, 400001 Cluj-Napoca, Romania; Phone +40264–591 941/220, e-mail: adimolnar45@yahoo.com