Papillary Fibroelastoma of the Heart: Report of Two Cases and Review of the Literature

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Abstract. Papillary fibroelastoma is the most common primary cardiac valvular tumor. Historically, papillary fibroelastoma was an incidental autopsy finding, deemed to have no clinical significance. More recently, reports of symptomatic cases of papillary fibroelastoma with complications such as myocardial infarction and stroke have led papillary fibroelastoma to be considered a potentially dangerous lesion. We report 2 cases of symptomatic papillary fibroelastoma, both of which presented with a stroke. Both patients underwent uneventful open-heart surgery. The literature is reviewed, with a compilation of 79 cases. (received 13 April 2001; accepted 15 May 2001)

Keywords: Papillary fibroelastoma, stroke, cardiac valves

Introduction

Papillary fibroelastoma (PFE) is an uncommon primary tumor of the heart. It was an occasional incidental finding at autopsy until the advent of two-dimensional echocardiography. As of 1991, 132 cases had been published in the literature [1]. The earliest reports of symptomatic patients with preoperative diagnosis of PFE were published almost two decades ago [2-5]. The advent of trans-thoracic and trans-esophageal echocardiography (TTE and TEE, respectively) introduced a growing number of cases of symptomatic PFE to the medical literature. Most of these cases presented either with serious clinical complications, such as myocardial infarction (MI) and stroke, or, more ominously, with sudden death caused by embolization to the coronary arteries [6]. Our understanding of PFE has evolved from an innocuous, incidental, postmortem finding to a potentially life-threatening yet easily diagnosed and treatable lesion. We report 2 cases of PFE that were diagnosed by TTE and treated by open-heart surgery. We also present a compilation of 79 cases of PFE, including our cases, with a review of the literature [2-38].

Materials and Methods

Paraffin-embedded sections of formalin-fixed tissue were studied by the hematoxylin-eosin (H & E), Masson's trichrome, Verhoeff-Van Gieson's elastin stain and Alcian blue pH 2.5 methods. Immunohistochemistry was performed with an automated immunostainer (Ventana Corp., Tucson, AZ) by the avidin-biotin technique, using monoclonal antibodies to CD31, CD34, and Factor VIII antigens (all from Ventana Corp.).

Results

Case 1. A 48-yr-old man presented to the hospital's emergency department with ataxia, nausea, vomiting, and vertigo, which started 24 hr prior to admission. Examination of cranial nerves was normal. A computed tomography (CT) scan of the head revealed a cortical hypodense area in the territory of the right middle cerebral artery. During further clinical investigations, a two-dimensional TTE was performed, which showed a solitary 1.5 x 1-cm echogenic mass arising from the chordae tendineae of the posterior leaflet of the mitral valve. An open-heart mitral valvuloplasty was performed with an uneventful outcome. The patient's symptoms resolved within 24 hr; he was discharged from the hospital in stable condition.
Case 2. A 51-yr-old woman developed slurred speech, lightheadedness, and unsteady gait 1 day prior to admission to the hospital. Examination of the cranial nerves was normal. A CT scan of the head revealed a right frontal infarct. After initial clinical investigations, a two-dimensional echocardiography showed a solitary 1 x 1-cm myxomatous-appearing sessile echodensity on the atrial surface of the posterior leaflet of the mitral valve. An open-heart mitral valvuloplasty was performed without replacing the mitral valve. The patient was discharged from the hospital in stable condition.

Pathology. The pathology specimens in both cases were composed of gray-white gelatinous and friable tissues that measured 1.5 x 1 x 0.8 cm and 1 x 1 x 0.5 cm, respectively. On histologic examination, both lesions revealed a papillary configuration, with broad-based fronds arising from a central pedicle and lined by flattened endocardial cells (Figs. 1, 2). The trichrome stain showed thick collagen bands in the papillary cores admixed with elastin fibers, as shown by an elastin stain. The Alcian blue, pH 2.5, staining pattern of the papillae revealed a central white-blue pallor, surrounded by a dark blue condensation of stain, indicating a high...
concentration of mucopolysaccharide around a fibroelastic core. Immunohistochemical reactions for factor VIII, CD34, and CD31 showed positive reactivities of the cells lining the papillary fronds, indicating an endothelial origin. Based on the histology and results of the special stains, a diagnosis of PFE was made in both cases.

Discussion

PFE was first recognized in the 19th century [3]. PFE has been named papillary myxoma, fibroma, hyalofibrome, fibromyxoma, and giant Lambl’s excrescence, among others [1,3]. “Papillary fibroelastoma” is now the preferred terminology. PFE is considered a rare cardiac tumor. In a study at the Mayo Clinic, only 7 of 110 primary tumors of the heart were PFEs [4]. However, PFE is by far the most common cardiac valvular tumor [5,15,44]. In the Armed Forces Institute of Pathology’s [AFIP] file of 42 patients, 39 of 45 PFEs were valvular [1]. In a review of the literature, Ryan et al [15] considered 132 cases of PFE, of which 117 were valvular. In our compilation of 79 cases of PFE in 76 patients, 67 lesions were valvular (84%). The aortic valve was involved in 28 of the cases (35%), followed by mitral valve, which harbored the tumor in 23 cases (29%). In 4 patients, there were more than 1 lesion; 2 had 2 lesions and the other 2 showed multiple lesions [3,7,8,9]. Similarly, in the AFIP’s review, the aortic valve was the predominant site (28 of 76 cases). Grinda et al [10] reported 29% of the PFE lesions on the aortic valve and 25% on the mitral valve [10].

PFEs have a predilection for the left side of the heart. In the AFIP series, 46 of 76 (60%) were left-sided [1]. In our review, 61 of 79 lesions occurred in the left side of the heart, whereas only 18 were right-sided [Table 1].

PFEs are small tumors, which range in diameter from 0.2 to 5.0 cm [7,11,12]. In 79 cases reviewed, the mean estimated diameter was 1.1 cm and 57% of the lesions measured less than one cm [Table 1]. The largest reported tumors measured 4.0 and 5.0 cm in diameter, arising from left ventricular septum and aortic valve, respectively [2,11].

The mean age at diagnosis of PFE was approximately 60 yr, although PFE has been reported in teenagers and children [1,11,13,22]. PFE affects both sexes. In our review, the mean age was 53.9 yr and the male/female ratio was 49 to 27.

The pathogenesis of PFE is controversial. Some authors believe that PFEs represent giant forms of

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### Table 1. Relationship of site versus diameter in papillary fibroelastomas.

<table>
<thead>
<tr>
<th>Site</th>
<th>Diameter of PFE (cm)</th>
<th>&lt;1</th>
<th>1.1-2.0</th>
<th>2.1-3.0</th>
<th>&gt;3.1</th>
<th>NA</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>AV</td>
<td>19</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>MV</td>
<td>14</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>TV</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>PV</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>LV</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>LA</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
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<tr>
<td>RA</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>18</td>
<td>3</td>
<td>3</td>
<td>10</td>
<td>79</td>
<td></td>
</tr>
</tbody>
</table>

NA, not available; AV, aortic valve; MV, mitral valve; TV, tricuspid valve; PV, pulmonary valve; LV, left ventricle; LA, left atrium; RA, right atrium.

### Table 2. Clinical manifestations of papillary fibroelastomas.

<table>
<thead>
<tr>
<th>Clinical manifestation</th>
<th>PFE diagnosed antemortem</th>
<th>PFE diagnosed postmortem</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>11</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>TIA</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>MI</td>
<td>11</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>PE</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>SD</td>
<td>13</td>
<td>20</td>
<td>33</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>28</td>
<td>76</td>
</tr>
</tbody>
</table>

TIA, transient ischemic attack; MI, myocardial infarction; PE, pulmonary embolism; I, incidental finding; SD, sudden death; Others, vague chest discomfort, dyspnea.
Lambl's excrescence, evolving from a thrombotic phenomenon due to traumatization of the endothelial cells [3,16,24]. The latter is postulated to be a result of an increased pressure gradient at the valvular level. The observation that PFE can arise in previously damaged valves (eg, in the setting of rheumatic heart disease) further supports this hypothesis [16]. The presence of fibrin and hyaluronic acid has been shown in both PFE and Lambl's excrescence (LE), although this has been disputed by Fishbein et al [12,16].

LE was first described in 1856 by Lambl [3]. LEs are filiform fronds which frequently occur on the cardiac valves of elderly people, mainly growing along the lines of closure and free cuspal edge in semilunar valves (SLV) and at the site of closure in atrioventricular valves (AVV). LEs are deemed to be a result of traumatic and degenerative processes, leading to fibrin deposition and subsequent organization of the thrombus [12]. PFE, however, is distinct from LE, based on the following considerations [41]:

- LEs do not occur on the atrial side of SLV or on the mural endocardium, whereas PFEs do;
- LEs occur along the lines of closure, but PFEs involve the midportion of the valve away from the lines of closure;
- LEs occur in 70-80% of adult heart valves; PFEs are rare;
- LEs are multiple in more than 90% of cases; PFEs are almost always solitary; and
- LEs invariably contain fibrin deposits; whereas PFEs do not.

Whether or not LEs and PFEs are various manifestations of the same process, it is important that they be clearly distinguished, in view of the potentially life-threatening sequelae of the latter [12].

Raeburn [22] proposed in 1953 a hamartomatous origin of PFEs. He argued that these papillary lesions almost certainly represent only a limited growth potential in pre-existing malformations; hence, hamartoma. He coined the term “papillary fibroelastic hamartomas of the heart valves.” The resemblance of PFEs to chordae tendineae may be additional evidence in support of this hypothesis [22].

The occurrence of PFE in children, albeit rare, has led some to believe that PFEs are congenital. This theory is suggested by the fact that some PFEs arise in congenitally altered valves. In 1980, Flotte et al [2] reported a case of 29-yr-old female with left ventricular PFE who had had a cardiac murmur since birth. Raeburn [22] reported a case of PFE arising in the aortic cusp of mitral valve of a 9-mo-old female. Probably the most compelling evidence favoring the “congenital theory” of PFE was presented by Anderson [42], who reported a case of PFE arising from the tricuspid valve of a neonate, obstructing the right ventricular outflow tract. A case of acute myocardial infarction due to aortic valvular PFE in a 10-yr-old has been reported by Deodhar et al [11].

The view that PFEs are congenital has been disputed by other authors, who have shown that PFEs usually affect congenitally normal valves. In a series of 9 cases reported by Boone [12], 7 lesions arose from normal valves while the other 2 involved pulmonary valves with moderate fibrosis and annular dilation, respectively. Malik et al [14] showed a patient with PFE of the tricuspid valve who had had a normal TEE 10 yr prior to admission. The latter case, as well as the fact that PFE is rare in children, argues against a congenital pathogenesis.

Some authors believe that PFEs are true neoplasms. This view, once in disfavor, is recently supported by the cytogenetic analyses of Speights et al [43]. They showed that the stem line from an atrial papillary fibroelastoma consisted of a complex translocation involving the short arm of chromosome 5, the long arm of chromosome 21, and the short arm of chromosome 15. The side line, on the other hand, had an additional isochromosome for the long arm of chromosome 11 [43]. Endothelial proliferation has been shown to be a major component of PFE. The latter, however, is deemed to be a reactive process rather than a true neoplasm [16].

Grossly, PFEs resemble a “sea anemone.” They usually have a gelatinous membrane on the surface and a stalk with multiple delicate papillary projections, best appreciated by immersing the specimen in water [1,21].

Microscopically, PFEs are composed of a central stalk with radiating villus-like projections. The papillae are avascular structures, containing a core of dense collagen fibers admixed with varying amounts of reticulin and elastin fibers. There is an outer layer of acid mucopolysaccharide, which can be demonstrated by Alcian blue pH 2.5 stain, imparting a darker blue periphery and a pale central core. In contrast, on H&E
stain, the periphery of the papillae reveals a loose pale myxoid tissue surrounding a dark blue core. The cells lining the elongated papillae are hyperplastic endothelial cells, occasionally bulging from the surface [16]. The lining epithelium is contiguous with the rest of the endocardium. The microscopic structure of PFE closely resembles that of chordae tendineae, which prompted some to propose an hamartomatous pathogenesis.

In the reported cases that we analyzed, 48 (63%) were diagnosed antemortem while 28 (39%) were identified at postmortem examination [Table 2]. Eight of the latter died suddenly due to complications of PFE (ie, myocardial infarction subsequent to tumor embolization to coronary arteries). In 48 cases that were diagnosed antemortem, 35 were symptomatic and 13 were incidental findings. Of 35 symptomatic patients, 11 had stroke, 6 had transient ischemic attack, 11 had myocardial infarction, 2 had pulmonary embolus, and 5 had symptoms such as vague chest pain and dyspnea. The symptoms of PFE varied according to location. The feared complications of myocardial infarction and stroke are obviously because of left-sided lesions, whereas right-sided lesions can cause pulmonary embolization.

Howard et al [8] reported that transient ischemic attack/cerebrovascular accident (TIA/CVA) was by far the most common presentation, occurring in 39% of the cases they reviewed. Amr et al [6] discussed 8 patients, including their own single case, who died suddenly due to myocardial infarction as a consequence of PFE. In 7 cases, the tumor involved the aortic valve. In the remaining case, the location was not cited [6].

Since symptomatic PFE carries a definite risk of grave complications, aggressive surgical management is recommended, irrespective of the tumor’s size or the patient’s symptoms[8,39,40,44]. The consensus appears to favor a surgical approach to PFE in symptomatic patients. Conversely, Roberts [45] considers that surgical resection of PFE is rarely warranted in asymptomatic patients.

References


45. Roberts WC. Papillary fibroelastomas of the heart. Am J Cardiol 1997;80:973-975.