Case report

Mitral valve recurrence of a left atrial myxoma

Navid Sadeghi*, Sarmad Sadeghi, Abbasali Karimi

Department of Cardiac Surgery, Dr. Shariati Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran

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Abstract

Recurrence of intracardiac myxoma is unusual, and heart valves are extremely rare locations for this tumor to originate, either as the primary site or the site of recurrence. We present a case of non-familial cardiac myxoma, which after successful resection of the tumor mass from the left atrium, recurred in the atrial surface of anterior leaflet of the mitral valve, along with a review of similar cases in the literature. Myxoma was originally believed to recur due to inadequate resection, but recent data suggest the multicentric disease to be the reason. Mitral valve myxoma mainly presents with symptoms of embolization and appears to affect women more often. It involves both leaflets with the same frequency and usually originates from the atrial side. Transesophageal echocardiography is the gold standard for non-invasive diagnosis and localization. Operative resection of the tumor along with the underlying tissue followed by suture repair of the valve and annuloplasty is recommended as the most appropriate treatment option. Long-term follow-up of patients by echocardiography is advised for early detection of any recurrence.

Keywords: Myxoma; Recurrence; Mitral valve

1. Introduction

Intracardiac myxomas with an estimated incidence of 0.5–1 per million per annum [1,2], constitute about 50% of all primary heart tumors [3–5]; however, this percentages is higher when surgically excised tumors are considered [6]. A total of 75% of myxomas arise in the left atrium, generally in the area of fossa ovalis [7], 20% in the right atrium and, the remaining 5% in the right or left ventricles [5,8].

Heart valves are extremely rare locations for this tumor to originate, either as the primary site or the site of recurrence. The tricuspid valve is the most frequent location of the valvular myxomas followed by mitral valve and the pulmonary and aortic valves [9].

The most common presenting symptoms of cardiac myxomas are obstructive symptoms, embolization, and constitutional symptoms. In the case of mitral valve myxoma, sudden death must be included, as stated by Puff and associates [10].

Since the first successful excision of a left atrial myxoma in 1954 by Crafoord, surgical treatment has become the standard procedure to deal with these tumors [11]. At first, recurrence of myxoma was said to be unlikely [12,13], but after 13 years since the first successful operation, the first case of recurrent left atrial myxoma was reported by Gerbode et al. in 1967 [14]. During the past few decades, many cases of recurrent cardiac myxomas and myxomas of heart valves have been reported. This article presents a case of non-familial solitary cardiac myxoma that after successful resection of the primary tumor mass from the left atrium recurred in the atrial surface of anterior leaflet of the mitral valve. This case, to our knowledge, is the first reported case of recurrent myxoma as a solitary tumor on mitral valve.

2. Case report

A 62-year old woman with no significant risk factors of atherosclerosis presented with exertional dyspnea and chest discomfort that had developed over a few weeks, in April 1996. Physical examination was unremarkable. Patient’s history was negative for occurrence of cardiac tumors in the family. Two-dimensional echocardiography revealed a left atrial pedunculated mobile mass, 5 cm in diameter, attached to atrial septum, which was suggestive of atrial myxoma. The mass caused mild stenosis of the mitral valve. Cardiac catheterization visualized the same mass as a filling defect in the left atrium. Additionally, it revealed a significant stenosis of the obtuse marginalis branch of the left circumflex coronary artery.

At the operation in April 1996, her left atrium was occupied by a 5 × 4 × 3 cm mass originating through a short...
pedicle from fossa ovalis. The tumor was resected together with its pedicle and the area of septum around the tumor base, followed by primary closure of the septal defect. Cardiac chambers were explored for any concurrent tumor. The stenotic obtuse marginalis artery was bypassed by a saphenous vein graft. The tumor consisted of a gray-white round, gelatinous and mottled mass, which was slightly lobulated on the surface, with considerable hemorrhage upon incision. Microscopic examination of the resected mass showed scattered stellate cells with scant pink cytoplasm embedded in a loose myxoid matrix along with abundant red blood cells, consistent with preoperative diagnosis of benign atrial myxoma (Fig. 1).

Patient had an uneventful recovery and was discharged 5 days after surgery. Histopathological examination of the resected mass revealed a myxoid stroma with scattered stellate cells, consistent with benign atrial myxoma (Fig. 1).

Fig. 1. Microscopic view of the first tumor (40× magnification) resected from left atrium. Scattered cells embedded in a loose myxoid matrix. Hemorrhage is present throughout the field.

Fig. 2. Microscopic view of the second tumor (40× magnification) resected from atrial surface of mitral valve. Note that unlike the first tumor, microscopic hemorrhage is not significant and the tumor has higher cellularity.
days after the operation. Since the patient lived in a city in northern Iran (distant from our center in Tehran), she discontinued her follow-up schedule 6 months after the operation; however, during that period she was symptom-free with no evidence of recurrence by echocardiography.

In January 1999, patient developed the same clinical presentation again. The local physician first thought the symptoms are due to graft occlusion, and hence she was referred to our center. On admission, she had the symptoms of exertional dyspnea, chest discomfort and paroxysmal nocturnal dyspnea, which she said started 3–4 months earlier, but had suddenly worsened over the last couple of weeks. On physical examination, she had a loud S1, two/six diastolic murmur, and a tumor-plop, best heard in the apex. Two-dimensional trans-thoracic echocardiography revealed a vague echogenic mass in the left atrium that seemed to be connected to the anterior mitral leaflet. Results of cardiac angiography were consistent with those of echocardiography. No stenoses were observed in coronary vasculature and the coronary graft was completely patent.

At the second operation in February 1999, patient underwent surgical excision of the tumor, which was attached through a delicate stalk to the atrial side of the anterior mitral leaflet, near the annulus. Tumor was removed along with its stalk and a very small part of the leaflet. The resulting defect was closed with a running suture. Cardiac chambers were explored for any concurrent tumoral mass or lesion. Mitral valve apparatus function was normal in post-operative echocardiography.

In macroscopic examination, tumor was a $3 \times 2 \times 2$ cm, gray-brown round gelatinous mass with a smooth surface without any gross hemorrhage. Microscopically, elongated cells, some of them in a chord-like arrangement; and stellate cells were seen in a myxoid stroma, consistent with the diagnosis of myxoma. However unlike the first tumor, microscopic hemorrhage was not significant and the tumor had higher cellularity (Fig. 2).

Patient was symptom free 18-month post-operation, with no sign of tumor recurrence or mitral valve dysfunction in trans-thoracic echocardiography.

3. Literature review and discussion

3.1. Recurrence of tumor

For few years following the first successful resection of a left atrial myxoma in 1954 by Crafoord [11], it was generally believed that myxomas never recur. In 1966, Newman and colleagues reviewed 58 cases of attempted excision of left atrial myxoma and reported no recurrence [12]. In the same year, Filor and colleagues, based on a 5–10 years follow-up of three operative cases concluded that simple excision of atrial myxomas was adequate and resection of the adjacent atrial septum or wall was unnecessary [13]. This idea was supported by others as well. Malm and associates had specifically pointed out that pathologically the tumor does not extend beyond elastic fibers and therefore excision of the septum was not necessary [15].

Not long after the reports of Newman et al. and Filor group, in 1967, Gerbode and colleagues reported a case of recurrent atrial myxoma 4 years after a successful resection that included cauterizing the base of a left atrial myxoma [14] and this way the non-recurring myxoma proved to be recurring.

Myxoma recurrence has been reported to occur at different rates in surgically treated patients: 1–5% [16], 5–14% [3], 0.4–5% [17], and 3% [18]. Gray et al., adding together the results of 16 series of cases of atrial myxoma totaling 194 patients, reported a 7% recurrence rate [8].

Myxomas generally recur at the site of initial localization. Shinfeld et al. in their valuable review of literature on myxoma recurrence in 1998 reported that in 85% of cases the tumor recurred at or close to the original site in the left atrium [18]. Reoperation for myxoma recurrence was performed between 3 month and 14 years after the first operation with an average of 3.9 years [18].

Risk of recurrence is said to be higher in familial myxoma, in presence of multiple myxomas, and in the syndrome of complex myxoma [19].

In Gerbode et al. experience, the tumor recurred at the same origin in the left atrium. Therefore, the authors recommended that in order to ensure against any recurrence, the septum in every case should be resected [14]. Bahl and colleagues in 1969 reported another case of recurrence and concluded that excision of the underlying atrial septum or wall is justified in every case [20]. In 1972, the story became more complicated; Walton and colleagues reported recurrence of a left atrial myxoma despite the complete excision of tumor and the stalk together with a cuff of the atrial septum around the origin of tumor [21]. In this case which could not be explained by inadequate resection theory, authors proposed three other explanations as the mechanism of recurrence; multiple tumors, dumb-bell or bilateral atrial myxoma, and existence of pre-tumor cells in the atrial septum, the latter they stated to be the most likely basis for recurrence of tumor in their case.

Read et al., who reported a case of myxoma recurrence at a site other than the primary location in 1974 added another possible explanation for myxoma recurrence; implantation of tumor tissue from the primary myxoma [22]. Jugdutt and colleagues in 1975 reported multicentric recurrence of a left atrial myxoma [23] which was in favor of multifocal disease theory.

Gray et al. in 1985 suggested that the most probable mechanism for tumor recurrence is multiple foci of tumor growth, considering incomplete resection, seeding of tumor and malignant change as alternative explanations [8].

Putting the available data together, some of these mechanisms and explanations seem rather unlikely. Incomplete resection could be a logical explanation for same site recurrence of tumor, but with septectomy becoming the
standard procedure in every case and recurrence of myxomas at sites other than the primary site, it is rather improbable. There is also little evidence to support seeding or implantation of tumor tissue from the primary site. Interestingly, the evidence like ‘upstream recurrences’ as described by O’Neill et al. [24] and, rare occurrence of myxoma seeding in peripheral vascular beds are against this concept.

The third explanation, which is malignant change, even if true appears to be a very rare occurrence. While there is positive evidence on myxoma’s potential for malignant change [25,26], some authors believe that most, if not all, malignant myxomas were misdiagnosed cardiac sarcomas and that most pathologists lack experience with cardiac tumors [27]. It should also be noticed that even if possible, malignant change is a very rare reason for myxoma recurrence, according to the literature.

We believe, like some of the authors, that multicentric myxomas or multiple tumors are the most likely cause of myxoma recurrences and many second myxomas which originate somewhere other than the primary tumor site, are in fact part of multifocal disease.

3.2. Mitral valve myxoma

Mitral valve myxomas are exceedingly rare [28]. Myxomas may originate from mitral valve either as the primary site or, less commonly, as the site of recurrence. Mitral valve myxomas had been originally reported in autopsy studies. In 1974, Read et al. reported myxomatous implantation of chordae tendineae and mitral leaflets as the recurrence of a previously operated left atrial myxoma [22]. However, the first case of myxoma involving mitral valve as the primary site was reported in 1979 by Sandrasagra and colleagues [29].

Table 1
Reported cases of premortem diagnosed mitral valve myxoma in English-language literaturea

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Location</th>
<th>Size</th>
<th>Valve replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974 – Read et al. [22]</td>
<td>48</td>
<td>Male</td>
<td>Dyspnea, CHF</td>
<td>Recurrence of tumor as myxomatous implantation of mitral leaflets and chordae tendineae</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1979 – Sandrasagra et al. [29]</td>
<td>33</td>
<td>Female</td>
<td>Intermittent attacks of shortness of breath</td>
<td>AML, atrial side</td>
<td>3.5 × 4.5 × 1.5</td>
<td>Yes</td>
</tr>
<tr>
<td>1986 – Gosse et al. [28]</td>
<td>15</td>
<td>Female</td>
<td>Arthralgia and fever</td>
<td>PML, ventricular side</td>
<td>3 × 2</td>
<td>Yes</td>
</tr>
<tr>
<td>1986 – Gosse et al. [28]</td>
<td>63</td>
<td>Female</td>
<td>Right hemiparesis</td>
<td>PML, atrial side</td>
<td>1.5 × 1</td>
<td>No</td>
</tr>
<tr>
<td>1987 – Barold et al. [41]</td>
<td>42</td>
<td>Male</td>
<td>Transient facial and left arm paresis, fever</td>
<td>AML, atrial side</td>
<td>2.3 × 0.6 × 0.5</td>
<td>No</td>
</tr>
<tr>
<td>1987 – Martin et al. [32]</td>
<td>20</td>
<td>Female</td>
<td>Fatigue, intermittent diaphoresis, palpitation, tachycardia</td>
<td>Multiple tumors, with involvement of PML, ventricular side</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>1988 – Ghazi et al. [42]</td>
<td>17</td>
<td>Female</td>
<td>Bacterial endocarditis, cerebral emboli</td>
<td>PML, atrial side</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>1990 – Sellke et al. [35]</td>
<td>38</td>
<td>Female</td>
<td>Stroke</td>
<td>NA, atrial side</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1990 – Sellke et al. [35]</td>
<td>31</td>
<td>Female</td>
<td>Stroke</td>
<td>NA, atrial side</td>
<td>NA</td>
<td>Died of tumor embolization during the op.</td>
</tr>
<tr>
<td>1993 – Zamorano et al. [43]</td>
<td>56</td>
<td>Male</td>
<td>Dyspnea, asthenia</td>
<td>PML, atrial side</td>
<td>3.3 × 3.2</td>
<td>No</td>
</tr>
<tr>
<td>1993 – Meisner et al. [44]</td>
<td>42</td>
<td>Male</td>
<td>Transient right-sided weakness</td>
<td>PML, atrial side</td>
<td>0.5 × 0.5</td>
<td>No</td>
</tr>
<tr>
<td>1995 – Kamata et al. [45]</td>
<td>32</td>
<td>Male</td>
<td>Palpitation</td>
<td>PML, atrial side</td>
<td>1.2 × 1</td>
<td>No</td>
</tr>
<tr>
<td>1995 – Kulshrestha et al. [46]</td>
<td>50</td>
<td>Female</td>
<td>Dyspnea, resting chest discomfort</td>
<td>AML, atrial side</td>
<td>3 × 2.5</td>
<td>No</td>
</tr>
<tr>
<td>1995 – Goldstein et al. [33]</td>
<td>47</td>
<td>Female</td>
<td>Decreased exercise tolerance, amaurosis fugax</td>
<td>Multiple atrial tumors, with involvement of PML, atrial side</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>1997 – Murphy et al. [7]</td>
<td>49</td>
<td>Female</td>
<td>Asymptomatic</td>
<td>AML, atrial side</td>
<td>4 × 3.6</td>
<td>Yes</td>
</tr>
<tr>
<td>1997 – Chakfe et al. [9]</td>
<td>44</td>
<td>Male</td>
<td>Aortic emboli</td>
<td>AML, atrial side</td>
<td>2 × 0.8</td>
<td>No</td>
</tr>
<tr>
<td>1998 – Matsui et al. [36]</td>
<td>25</td>
<td>Female</td>
<td>Asymptomatic</td>
<td>AML &amp; PML, atrial side</td>
<td>NA</td>
<td>Yes</td>
</tr>
<tr>
<td>1999 – Toda et al. [47]</td>
<td>20</td>
<td>Male</td>
<td>Fever, embolism, syncopal attack</td>
<td>PML, atrial side</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>1999 – Roques et al. [48]</td>
<td>27</td>
<td>Female</td>
<td>Transient right hemiplegia, aphasia</td>
<td>AML, ventricular side</td>
<td>0.9</td>
<td>No</td>
</tr>
<tr>
<td>1999 – Handke et al. [37]</td>
<td>39</td>
<td>Male</td>
<td>Left-sided Hemiparesis</td>
<td>PML, atrial side</td>
<td>0.5 × 0.5</td>
<td>No</td>
</tr>
<tr>
<td>1999 – Rocha et al. [49]</td>
<td>49</td>
<td>Female</td>
<td>CHF</td>
<td>AML, atrial side</td>
<td>2.5 × 3</td>
<td>No</td>
</tr>
<tr>
<td>2000 – Keeling et al. [30]</td>
<td>26</td>
<td>Male</td>
<td>Asymptomatic</td>
<td>AML, ventricular side</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>2000 – Prifti et al. [50]</td>
<td>42</td>
<td>Female</td>
<td>Dyspnea, fever, arthralgias</td>
<td>AML, atrial side</td>
<td>3 × 3.5</td>
<td>Yes</td>
</tr>
<tr>
<td>2000 – Ozer et al. [31]</td>
<td>38</td>
<td>Male</td>
<td>Dizziness, loss of balance</td>
<td>AML, atrial side</td>
<td>1.04 × 1.07</td>
<td>No</td>
</tr>
<tr>
<td>2000 – Present case</td>
<td>65</td>
<td>Female</td>
<td>Exertional dyspnea, PND</td>
<td>AML, atrial side</td>
<td>3 × 2 × 2</td>
<td>No</td>
</tr>
</tbody>
</table>

a AML, anterior mitral leaflet; PML, posterior mitral leaflet; NA, not available; and Op, operation. Refs [41–50] are referred to only in the table, not in the text.
The presenting features of mitral valve myxoma are almost the same as left atrial myxomas and clinically are rather indistinguishable [7,28].

Mitral valve myxomas seem to increase the risk for sudden death as in the two cases reported by Puff et al., who had syncopal attacks prior to sudden death and mitral valve myxomas in autopsy [10]. Furthermore, because of the high mobility of mitral leaflets and the high pressure within the left ventricular chamber, patients with mitral valve myxoma are at a higher risk for embolization of tumor fragments [9,30,31].

Table 1 lists the reported cases of premortem diagnosed mitral valve myxoma either as the primary site or the site of recurrence in English-language literature including the present case. From the 25 cases of mitral valve myxoma, 23 were primary; in two of them, mitral involvement was part of a multicentric disease [32,33]. The two remaining cases were recurrent myxomas, which include the case reported by Read et al., and the present case. Mitral valve myxoma appears to affect women more than men (15 women and ten men), even if we exclude multiple tumors and recurrences from data (12 women and nine men). It involves both valve leaflets with almost the same frequency (11 AML and ten PML). Most of the tumors originated from the atrial surface of the valve (80% atrial side). According to the literature, embolic events are expected in about 40% of patients with cardiac myxoma [34]. As mentioned earlier, because of high mobility of mitral valve and the high pressure within the left ventricular chamber, these embolic events are expected to happen at even higher rates in mitral valve myxomas. Among tabulated cases, embolization is the most common clinical feature (48% of cases), followed by cardiac and constitutional symptoms. It is worthy to mention that one of the cases reported by Sellke et al., died in operation because of tumor embolization, coronary artery occlusion and low cardiac output [35]. This fact, again, emphasizes the risk of embolization in this set of patients.

It also should be noted that in three cases, tumor had been found during a routine medical checkup in asymptomatic patients [7,30,36]. As for the treatment, in most of the cases removal of tumor mass and repair of the leaflet, valvuloplasty, and annuloplasty constituted the surgical treatment, but in seven cases (28%), the valve was replaced.

Echocardiography has become the procedure of choice and the most important diagnostic tool for non-invasive detection of cardiac tumors and masses [9,28,37]. Transesophageal echocardiography (TEE) is superior to transthoracic echocardiography (TTE) in many ways. TTE may miss a tumor measuring less than 5 mm in diameter [9] and sometimes even larger tumors [38]. In addition, TTE cannot precisely define the site of the tumor attachment [39]. Therefore, it is recommended to perform TEE whenever cardiac myxoma is suspected [9,38].

TEE not only offers significant enhancement of image quality over TTE [39], but also provides greater anatomic detail regarding size and site of attachment [7,37,39], and exclusion of lesions elsewhere [40].

In the case of valvular myxoma, TEE can guide the surgical approach by revealing the integrity and mobility of the valve prior to operation [9]. Following the surgery of valvular myxoma, TEE is valuable in assessing repair of the valve [40].

For early detection of any recurrence, long-term follow-up of patients by echocardiography is advised [40].

4. Comments

Intracardiac myxomas are of special interest to both cardiologists and cardiac surgeons not only because they constitute half of all primary cardiac tumors, but also because of significant complications they can cause. In dealing with an intracardiac myxoma, certain points should be taken into account: obtaining a careful family history of the patient, intraoperative examination of all cardiac chambers for multifocal disease, resection of the tumor along with the underlying tissue, and long-term follow-up of patients in terms of performing routine echocardiographic tests.

As intracardiac myxoma, especially those involving heart valves, carry a significant risk for embolic events, an early diagnosis and prompt surgical intervention may significantly reduce the possibility of embolism.

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References

