Familial Cardiac Myxoma
A Study of Relatives of Patients With Myxoma

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Purpose: Cardiac myxomas are rare benign tumors of the heart. Although most cases are sporadic, rare familial occurrence has been described. The aim of this study was to evaluate tumor involvement in family members of patients with cardiac myxoma and to compare familial vs nonfamilial cardiac myxoma in relation to age, sex, site and multichamber involvement, endocrine abnormality, embolism, presence of vascular aneurysms, and tumor recurrence.

Patients and methods: We studied 38 family members of 14 patients with cardiac myxoma by two-dimensional echocardiography and whenever possible on an annual basis. Patients with cardiac myxoma were then divided into familial cardiac myxoma (6 patients) and nonfamilial cardiac myxoma (12 patients) for the above comparison. Results: Four family members (10.5 percent) were found to have cardiac myxoma from two different families. The first included a brother and a sister, both with acromegaly, and the second included a mother, daughter, and two sons, in one of whom the tumor was detected on the second annual sons, in two-dimensional study. The patients with familial cardiac myxoma were younger (34.5 years vs 54 years, p < 0.001) than the nonfamilial cases. Right chamber involvement was more common in the familial cases (67 percent vs 8 percent, p < 0.05) and had more frequent recurrence (67 percent vs none, p < .05). There was no difference in endocrine abnormality, vascular aneurysms, or embolism between familial and nonfamilial cases.

Conclusion: Cardiac myxoma is relatively frequent in family members with a higher yield of detection in family members of patients with right-sided or bilateral myxoma. Patients with familial cardiac myxoma are younger and have more frequent right-side involvement and long-term recurrence. Screening by echocardiography of family members of patients with cardiac myxoma is recommended. Annual studies are recommended for relatives of patients with familial cardiac myxoma.

Methods

During the 12-year period between July 1, 1975 and June 30, 1988, 14 patients with cardiac myxoma had their conditions detected by echocardiography and they were treated at University Hospitals of Cleveland, Case Western Reserve University. The patients ranged in age at the time of diagnosis from 26 to 86 years (mean = 52.1 years) with 5 male patients (36 percent) and 9 female patients (64 percent). Eleven patients had left atrial myxoma, one had right atrial myxoma, one had right ventricular myxoma, and one had bilateral myxomas. Thirteen patients were operated on successfully; one patient (86 years old) refused surgery and later died of congestive heart failure. One patient who had successful surgery was unavailable for follow-up. Forty-two percent of the patients presented with obstructive symptoms and 50 percent presented with embolic events, mainly cerebral. In one patient, left atrial myxoma was an incidental finding on an echocardiogram performed to rule out mitral valve prolapse. Patients with cardiac myxoma were studied by two-dimensional echocardiography annually after surgery for tumor recurrence.

Thirty-eight family members with a mean age of 31.2 years (3 parents, 6 siblings, 9 sons, 9 daughters, 8 grandchildren, and 3 nephews and nieces) of the 14 patients with cardiac myxomas were evaluated by two-dimensional echocardiography for evidence of tumor. Most individuals had follow-up annual echocardiographic studies whenever possible. None of the family members had skin tumors, abnormal pigmentation, other tumors or evidence of endocrine disease.

Two-dimensional echocardiography was performed using phased-array ultrasound devices (Hewlett Packard and Diasonics Medical Products) with a 2.5-MHz transducer. The patients were studied in the parasternal long- and short-axis views and apical four-chamber and two-chamber views. A few initial studies in the 1970s were limited to M-mode echocardiographic studies.

All chambers were evaluated for presence of tumor, size, and function. If a myxoma was detected, its site and pedicle attachment

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were determined. The attending physician was informed of any
tumor detected and arrangements were made for surgical excision.

**Statistical Methods**

The data were analyzed by the Wilcoxon Rank Sum test (age) and the \( x^2 \) test. \( p \) values of \(< 0.05\) were considered statistically significant.

**RESULTS**

Four of the 38 family members (10.5 percent) were found to have cardiac myxoma from two different families. The first family included a brother (right atrial myxoma) and a sister (left atrial myxoma) and both were associated with acromegaly. A complete study of all members of this family was not possible because some members refused the echocardiographic studies provided free. The second family included a 50-year-old mother and a 30-year-old daughter (both with bialtral myxoma), a 23-year-old son (right atrial myxoma), and another 40-year-old son studied 8 years later (left atrial myxoma) who 1 year earlier had a normal two-dimensional echocardiographic study. All members of that family were studied and most of them were studied annually. A pedigree of that family is shown in Figure 1.

All myxomas were resected successfully. The likelihood of finding cardiac myxoma in another family member was higher in patients with right or bilateral cardiac myxoma (80 percent) than those with left cardiac myxoma (15 percent) (\( p < 0.05 \)).

**Table 1—Familial vs Nonfamilial Cardiac Myxoma**

<table>
<thead>
<tr>
<th></th>
<th>Familial (n = 6)</th>
<th>Nonfamilial (n = 12)</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>3 (50)</td>
<td>8 (67)</td>
<td>NS</td>
</tr>
<tr>
<td>Age, yr, mean</td>
<td>34.8</td>
<td>54</td>
<td>(&lt; 0.001)</td>
</tr>
<tr>
<td>Right chamber</td>
<td>4 (67)</td>
<td>1 (8)</td>
<td>(&lt; 0.05)</td>
</tr>
<tr>
<td>Multiple chamber</td>
<td>2 (33)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Recurrence</td>
<td>4 (67)</td>
<td>0</td>
<td>(&lt; 0.05)</td>
</tr>
<tr>
<td>Endocrine abnormality</td>
<td>2 (33)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Vascular aneurysm</td>
<td>2 (33)</td>
<td>4 (33)</td>
<td>NS</td>
</tr>
<tr>
<td>Embolism</td>
<td>2 (33)</td>
<td>6 (50)</td>
<td>NS</td>
</tr>
</tbody>
</table>

\*Data are presented as number (percent) of patients in total group. NS = not significant.

Patients with cardiac myxoma were then divided into familial cardiac myxoma (6 patients) and nonfamilial cardiac myxoma (12 patients). The two groups were compared in relation to age, sex, site, multiple chamber involvement, recurrence, endocrine abnormalities, vascular aneurysms, and embolic events (Table 1). Familial cardiac myxoma was defined as a condition in any patient with cardiac myxoma with at least one other family member with cardiac myxoma.

Patients with familial cardiac myxoma were younger (Fig 2) with equal sex involvement; they had significantly more frequent right chamber and/or bilateral chamber involvement (Fig 3). Vascular aneurysms were seen equally in patients with familial (two patients with cerebral, coronary, and pulmonary aneurysms) and nonfamilial (four patients with cerebral and coronary aneurysms) cardiac myxomas.

Patients with familial cardiac myxoma were followed up for a mean of 8.1 years and the patients with nonfamilial myxoma were followed up for a mean of 7.8 years following resection of the initial tumor. Four patients, all from the familial myxoma group who had...
successful resection of the initial tumor, had recurrence of cardiac myxoma, the earliest 4 years after the detection of the first tumor. In two patients the tumor recurred at a different site of attachment. In the two patients with bialtrial myxoma, one had recurrence in the left atrium and the other had recurrence at a different site of origin from the right atrium. There were no differences on microscopic examination between the familial and nonfamilial cases.

DISCUSSION

Cardiac myxomas are the most common primary tumors of the heart. Although most cases are sporadic, familial occurrence has been described in a few reports \(^1\) with myxomas involving siblings of both sexes or parent and child suggesting that the genetic transmission is most likely an autosomal dominant mode of inheritance.\(^{17,23}\) Some families with cardiac myxoma (syndrome myxoma) are associated with cutaneous myxoma, mammary myxoid fibroadenoma, mucocutaneous pigmentation, adrenal and pituitary overactivity, and testicular tumors.\(^{13,83}\)

Review of the literature suggests that patients with familial cardiac myxoma are likely to be younger than sporadic cases with more frequent multiple site involvement, more frequent right chamber involvement, and recurrence.\(^{1,43,25}\)

This study of relatives of patients with cardiac myxoma revealed two families with tumor involvement; one family had two siblings with acromegaly and in both patients, this was the only other manifestation of syndrome myxoma. In the other family, four patients (a mother, daughter, and two sons) had cardiac myxomas involving variable cardiac chambers. To our knowledge, this is the first report of patients discovered to have cardiac myxoma as part of screening with one patient having had a normal two-dimensional echocardiogram 1 year earlier.

Cardiac myxoma in sporadic cases is more frequent in women (3:1 ratio);\(^{26}\) familial cardiac myxoma is more likely to involve both sexes equally.\(^{16,26}\) In our study, the patients with familial cardiac myxoma involved both sexes equally. Women were more involved in the nonfamilial myxoma group (two thirds of patients), but with these small numbers, no statistical significance was found, and the tendency was for equal involvement of male and female subjects in familial cases of myxoma.

In this study, patients with familial myxoma were found to be 19.2 years younger than those with nonfamilial myxoma (p < 0.001) (Fig 2). McCarthy et al\(^{16}\) reviewing their patients and familial patients described in the literature, found the familial patients to be 27.4 years younger than sporadic cases. Right chamber involvement, including patients with bilateral myxomas in this study, was more frequent in the familial cases (67 percent) vs nonfamilial patients (8 percent) (p < 0.05) (Fig 3); and the likelihood of finding cardiac myxoma in a family member was much higher if the patient had right or bilateral cardiac myxoma. Other families described in the literature\(^{1-12}\) showed right-sided involvement in 45 percent of patients with familial myxoma.

Cardiac myxoma is most commonly a single tumor involving the left atrium.\(^{39}\) Multiple chamber involvement is rare and involvement of chambers other than the left atrium is less common. In this study, 33 percent of the patients with familial myxoma had multiple chamber involvement and none of the patients with nonfamilial myxoma had it; the numbers were too small to achieve statistical significance. The left atrium was the only site of involvement in 92 percent of the patients with nonfamilial myxoma and only in 33 percent of patients with familial myxoma.

Cerebral coronary and pulmonary aneurysms are complications of cardiac myxoma with systemic emboli.\(^{37,39}\) The myxomatous embolus can cause, as seen by arteriography, irregular filling defects of fusiform and saccular aneurysms. At pathologic study, in some vessels showing aneurysms, myxomatous tissue is seen to invade the internal elastic lamina and the full thickness of the muscularis, producing dilatation and weakening of the arterial wall. In this study, vascular aneurysms were present equally in the patients with familial and nonfamilial myxoma.

Recurrence of cardiac myxoma is rare. At one time it was suspected that recurrence is related to the surgical approach and more likely to occur if the tumor was removed with normal endocardial tissue vs total resection of the wall at the site of the tumor. However, recent reports (McCarthy et al\(^{16}\) and Hanson et al\(^{26}\)) showed no recurrence of tumor in large groups of sporadic patients with cardiac myxoma with follow-up of 10.5 years and 6.5 years, respectively. McCarthy et al reported recurrence in three of four patients with
familial cardiac myxomas. In this study, patients were followed up for 8.1 years in the familial group and 7.8 years in the nonfamilial group. Recurrence occurred only in the patients with familial cardiac myxoma (66 percent), the earliest being 4 years. In 50 percent of the patients, the tumor recurred originating from a different site of the same chamber.

CONCLUSIONS

Cardiac myxoma is relatively frequent in family members with an autosomal dominant mode of inheritance. There is a higher yield of detection in family members of patients with myxoma with right-sided or bilateral involvement and cardiac myxoma in a family member may be detected on subsequent echocardiographic study.

Patients with familial cardiac myxoma are younger and have more frequent right-sided involvement and long-term recurrence.

To our knowledge, this is the first report of detecting cardiac myxoma as part of a study or screening program in patients who are otherwise normal and asymptomatic.

RECOMMENDATIONS

Screening two-dimensional echocardiography should be performed for all first-degree relatives of patients with cardiac myxoma and in particular younger patients and those with right-sided and/or bilateral involvement.

If a patient is identified as having familial cardiac myxoma, then the patients and family members should be evaluated by two-dimensional echocardiography annually.

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