

A Case of Biatrial Multiple Myxomas with Glandular Structure

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A 45-year-old male, who had been indicated by brain magnetic resonance imaging to have cerebral infarctions, was found by echocardiography to have a tumor in the left atrium. He had experienced several of the constitutional disturbances associated with myxoma. At the ages of 19 and 35 he had had two episodes associated with embolisms, and at the later one he was diagnosed as having multiple cerebral aneurysms. He received an urgent operation in which three left atrial tumors and one right atrial tumor were resected. Histologically, the tumors were myxomas, and the left atrial main tumor had glandular structure. In view of his clinical history, this patient seems to have had cardiac myxomas for a long period. The multiple growths that occurred in this case may be a good argument for allowing this condition to last for so long. To our knowledge, the present case was the first report of cardiac myxoma with glandular structure in Japan. (Ann Thorac Cardiovasc Surg 2007; 13: 423–427)

Key words: cardiac myxoma, multiple growths, multiple cerebral aneurysms, glandular structure

Introduction

Primary neoplasms of the heart are rare tumors found in only about 0.001–0.03% of autopsy cases.¹ Although approximately 50% of the neoplasms are cardiac myxomas, their nature has not been sufficiently understood. Their natural history is almost unknown because the response to cardiac myxoma is usually an urgent operation.² This case is an extremely rare myxoma, a natural history of which is estimated by its clinical history.

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Case Report

A 45-year-old male, who had no risk factors for atherosclerosis, was admitted to a local hospital because of dysesthesia in his right hand and a gait disturbance. He had had painful erythema in his extremities once or twice a month from childhood. When he was 19 years old, the skin color of his right hand became whitish while he was performing manual labor. His right arm was found to be in a transient condition of being pulseless, and he was diagnosed with Raynaud's disease. At the age of 35, he was admitted to the hospital with right hemiparesis, but he was able to run next day. A cerebral angiography then showed multiple cerebral aneurysms. In present admission, the cerebral angiography was undergone again, and it revealed the same findings as the previous one (Fig. 1).

The patient was then transferred to our hospital for further examinations. Because a magnetic resonance imaging (MRI) showed a fresh cerebral infarction that was suspected of attributing to the embolism, an echocardiography was performed to find out the embolic source. The transthoracic echocardiography revealed a left atrial

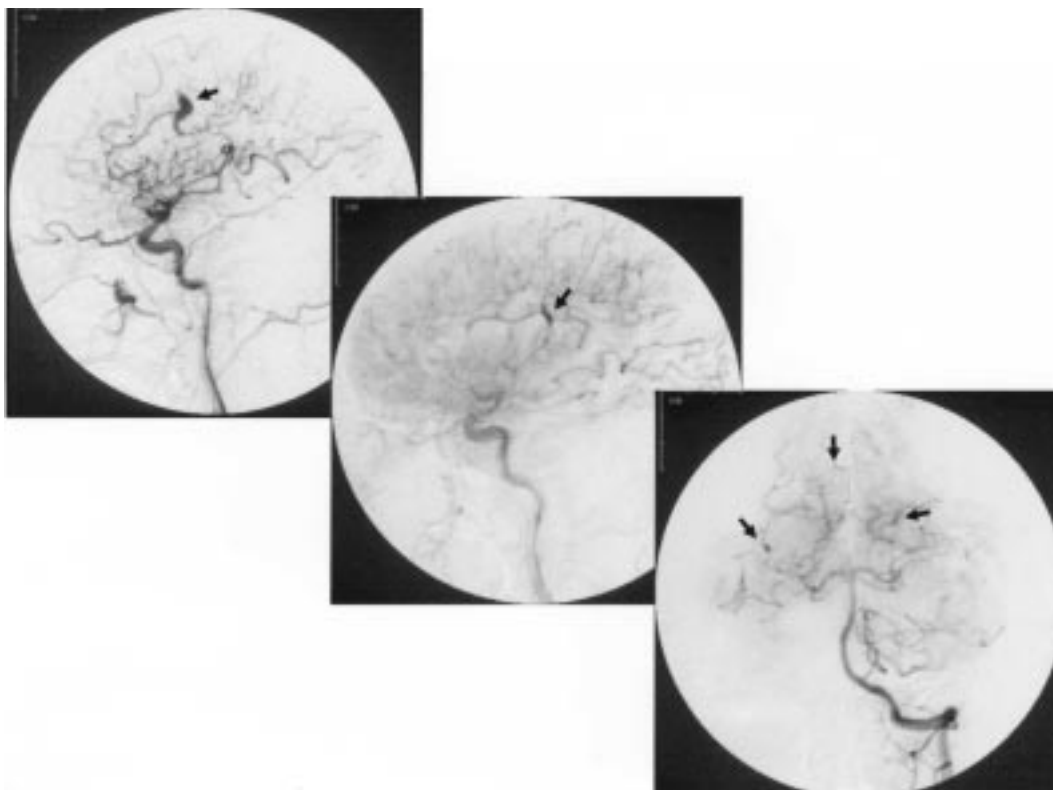


Fig. 1. A cerebral angiogram shows multiple cerebral aneurysms (arrows).

tumor attached to the interatrial septum (Fig. 2). The C-reactive protein (CRP) was 1.2 mg/dL, the sedimentation rate 85 mm in 1 h, and IL-6 3.6 pg/mL. We concluded that the patient had a left atrial myxoma, and he underwent an urgent operation.

In the operation he was placed on a cardiopulmonary bypass with bicaval cannulation, and the heart was arrested with cold blood cardioplegia. When the right atrium was opened, a small nodule was found on the fossa ovalis. As soon as the incision was made into the left atrium just posterior to the interatrial groove on the right side, the myxomatous tissue issued from the left atrium. We resected the left atrial tumor with the interatrial septum and a portion of the posterior wall of the left atrium attached by the tumor. After this tumor was resected, we found two small myxomatous tumors by the right upper pulmonary vein orifice and the mitral annulus, and we also resected these tumors. We reconstructed the interatrial septum and the posterior wall of the left atrium with bovine pericardium (Supple Tissue-Guard™, Bio-Vascular, Inc., Saint Paul, MN).

The patient's postoperative course was uneventful. On his discharge, the Raynaud's phenomenon had improved, and the CRP was 0.2 mg/dL, the sedimentation rate 28

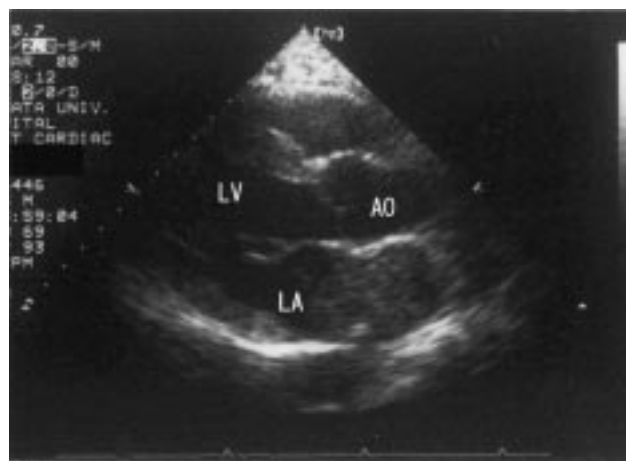


Fig. 2. A parasternal long-axis transthoracic echocardiogram shows a mass in the left atrium (AO, aorta; LA, left atrium; LV, left ventricle).

mm in 1 h, and IL-6 1.0 pg/mL. A macroscopic examination showed that the left atrial main tumor was a globular gelatinous mass with lobulated parts. The main tumor was measured as 5.8×3.3×2.6 cm, and its weight with atrial septum was 25 g (Fig. 3). Histologically, the left atrial main tumor had arisen from the interatrial septum with a

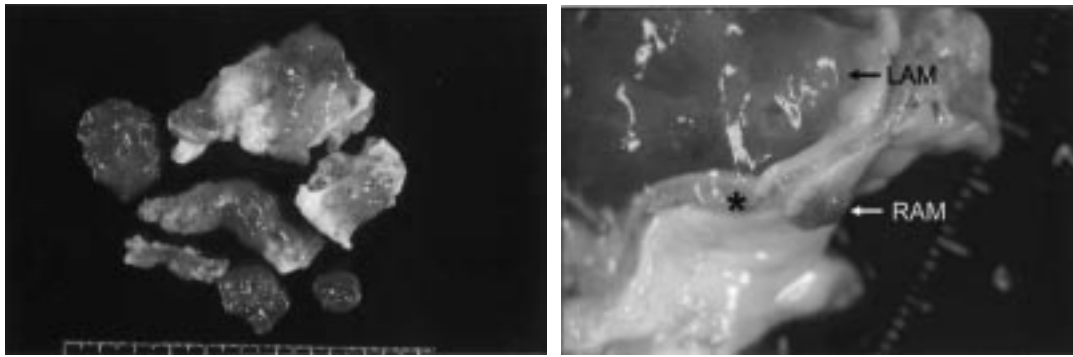


Fig. 3. A specimen of the resected tumor with interatrial septum (LAM, left atrial myxoma; RAM, right atrial myxoma; *, interatrial septum).

A | B

broad stalk and showed lobular proliferation. The tumor was a typical myxoma composed of star-like and pleomorphic cells and capillaries on a background of abundant mucous stroma. Glandular structures were focally observed in the tumor near the septum (Fig. 4).

The glandular structures were similar to those of the gastrointestinal tract and consisted of single columnar epithelium with clear to slightly eosinophilic cytoplasm having small nuclei. Goblet-like cells were found to be sporadically associated. The right atrial tumor had also a myxoid stroma, but with no glandular elements. There was no continuity between the right and left atrial tumors, and there were no malignant cells in any of the tumors.

Discussion

Primary neoplasms of the heart are rare tumors, found in only 0.001–0.03% of autopsy cases. Cardiac myxomas make up about 50% of cardiac neoplasms. Moreover, glandular structures are found in only about 1% of cardiac myxoma.¹⁾ To our knowledge the present case was the 39th case of cardiac myxoma with glandular structure in the world and the first reported in Japan.^{3–27)}

Clinically, this case had two features that are often found in cardiac myxoma. First there were some cerebral aneurysms. The mechanisms of aneurysm formation in cardiac myxoma remain controversial. The vascular damage theory postulates that large tumor emboli could cause perivascular damage with scarring and pseudoaneurysm formation resulting from obstruction.²⁸⁾ A neoplastic process theory postulates that the tumor could remain viable and could penetrate intact or damaged endothelium at the site of final lodgment, with subintimal growth, eventual penetration, and destruction of the entire arterial wall. These developments are associated with some degree of

fibroblastic proliferation.²⁹⁾

In either mechanism, an embolic event initiates the process. Our case had sometimes suffered from embolism-like episodes from youth and was diagnosed with cerebral aneurysms 10 years earlier. Because he was younger and had no risk factors for atherosclerosis, the cause of the cerebral aneurysms could be interpreted as myxoma. It seems likely that he had had the cardiac myxoma for at least 10 years. Moreover, because painful erythema may be considered to be a so-called constitutional disturbance of myxoma,³⁰⁾ cardiac myxoma may have originated in his childhood.

An average growth rate of the left atrial myxoma has been estimated to be 1.8 or 5.7 cm/year.^{31,32)} Because this main tumor for our patient measured 5.8×3.3×2.6 cm and weighed 25 g, if he had had cardiac myxoma for more than 10 years, it would have exhibited an extremely slow growth rate or else a heterogeneous growth rate, as described by Lane et al.³²⁾

Another feature of this case was the occurrence of multiple growths. Assuming that his left atrial myxoma attached to the fossa ovalis was his main tumor, he had sub-myxomas in the right atrium and two left atrial sub-myxomas by the right upper pulmonary vein orifice and the mitral annulus. The mechanisms of cardiac myxoma's multiple growths may be through intracardiac implantation or through growth from a second focus.³³⁾ In our patient, because the right atrial myxoma showed no continuity with the left atrial myxoma, this right tumor may have been a second focus. On the other hand, his left atrial myxomas could have occurred through intracardiac implantation, if one accepts Dang and Hurley's opinion that the multiple growths of recurrent myxoma suggest implantation.³³⁾ Whether or not this is true, the multiple growths may provide evidence that this patient had had

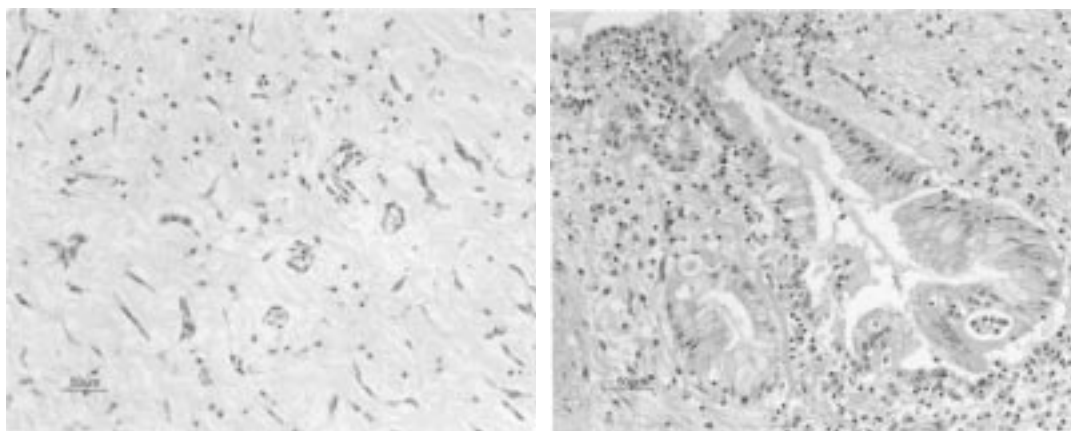


Fig. 4. A histological examination shows typical myxomatous tissue (A), and glandular structures consist of single columnar epithelium and goblet-like cells surrounded with the typical myxomatous tissue (B) (hematoxylin and eosin stain, $\times 200$)

cardiac myxomas for a long period because it would have required significant time for the second tumor to grow.

The histological feature of this myxoma is the glandular structure. A recent immunohistochemical study hypothesizes that myxoma cells originate from remnants of subendocardial vasoformative reserve cells or multipotential primitive mesenchymal cells in the fossa ovalis and the surrounding endocardium.³⁴⁾ There are two hypotheses about the origin of glandular structure. One is that multipotential vasoformative reserve cells differentiate not only into mesodermal cell types, but also into endodermal cell types such as glandular epithelium. The other is that glandular structure might represent entrapped foregut rests in the region of the foramen ovale.²²⁾

Because cardiac myxoma with glandular structure has been reported in only 38 cases in the world, its character has been almost unknown. The presentation of cardiac myxoma with glandular structure seems to be similar to that of classical myxoma,²²⁾ and we have not argued that glandular structure exhibits a special biological behavior. Of course because among the previous 38 cases we do not know how long it took for the cardiac myxoma with glandular structure to develop, we cannot say that glandular structure is associated with slower growth, as we suspected in this case.

Cardiac myxoma is a rare tumor, and this diagnosis has usually been followed by an urgent operation;²⁾ thus its natural history has been almost unknown. The above-mentioned growth rate of left atrial myxoma is taken from only a few cases, so this evidence about its growth rate is inconclusive. Therefore, although the present case might have lasted for a long period, whether this tumor showed

slower growth is not clear. Besides its natural history, cardiac myxoma presents many undetermined issues of interest about its origin and nature as a tumor that has clinical relevance and that also concerns the presence of both sporadic and familial types.³⁴⁾ These justify the need for further studies.

References

1. Burke A, Virmani R. Cardiac Myxoma. In: Rosai J, Sobin LH eds.; *Tumors of the Heart and Great Vessels. Atlas of Tumor Pathology, Third Series, Fascicle 16.* Washington, D.C.: Armed Forces Institute of Pathology, 1996; pp 21–46.
2. Doty DB. Cardiac Tumors. In: *Cardiac Surgery Operative Technique.* Missouri: Mosby-Year Book, Inc., 1997; pp 420–1.
3. Anderson WAD, Dmytryk ET. Primary tumor of the heart containing epithelium-like elements. *Am J Pathol* 1946; **22**: 337–49.
4. Vacek R. Das intracardiale Hamartoblastom. *Zentralbl Allg Pathol* 1963; **104**: 383–91.
5. Frishman W, Factor S, Jordan A, et al. Right atrial myxoma: unusual clinical presentation and atypical glandular histology. *Circulation* 1979; **59**: 1070–5.
6. Song LF, Zhang ZQ, Huang WY. Morphologic study of cardiac myxomas. *Chin Med J* 1983; **96**: 7–12.
7. Widder W, Schneider J, Schanz U. Das Endokardmyxom mit drüsenartige Strukturen und seine Beziehungen zum AV-Knotentumor. Versuch einer histogenetischen Deutung. *Pathologe* 1985; **6**: 303–7.
8. Abenzo P, Sibley RK. Cardiac myxoma with gland-like structures. An immunohistochemical study. *Arch Pathol Lab Med* 1986; **110**: 736–9.
9. Goldman BI, Frydman C, Harpaz N, et al. Glandular cardiac myxomas. Histologic, immunohistochemical,

- and ultrastructural evidence of epithelial differentiation. *Cancer* 1987; **59**: 1767–75.
10. de Moraes CF, Falzoni R, Alves VAF. Myocardial infarct due to a unique atrial myxoma with epithelial-like cells and systemic metastases. *Arch Pathol Lab Med* 1988; **112**: 185–90.
 11. Johansson L. Histogenesis of cardiac myxomas. An immunohistochemical study of 19 cases, including one with glandular structures, and review of the literature. *Arch Pathol Lab Med* 1989; **113**: 735–41.
 12. Tószegi A. Morphology of cardiac myxomas. *Morphol Igazságügyi Orv Sz* 1990; **30**: 43–50.
 13. Schultrich S. Zur Histogenese des kardialen Myxoms anhand eines Myxoms mit drüsenartige Strukturen. *Pathologe* 1990; **11**: 220–3.
 14. Curschellas E, Toia D, Borner M, et al. Cardiac myxomas: immunohistochemical study of benign and malignant variants. *Virchows Arch* 1991; **418**: 485–91.
 15. Schmitt-Gräff A, Borchard F. Cardiac myxoma with a cytokeratin-immunoreactive glandular component. *Pathol Res Pract* 1992; **188**: 217–25.
 16. Burke A, Virmani R. Cardiac myxoma. A clinicopathologic study. *Am J Clin Pathol* 1993; **100**: 671–80.
 17. Thornton CM, Walsh MY. Glandular differentiation in cardiac myxomata. *Ir J Med Sci* 1993; **162**: 95–7.
 18. Wang XY. Immunohistochemical study and evaluation of histogenesis of cardiac myxoma. *Zhonghua Bing Li Xue Za Zhi* 1993; **22**: 262–4.
 19. Deshpande A, Venugopal P, Kumar AS. Phenotypic characterization of cellular components of cardiac myxoma: a light microscopy and immunohistochemistry study. *Hum Pathol* 1996; **27**: 1056–9.
 20. Sipos B, Járay B, Richter T. Glandular myxoma of the heart. *Orv Hetil* 1995; **136**: 1333–5.
 21. Scarpelli M, Montironi R, Ricciuti R, et al. Cardiac myxoma with glandular elements metastatic to the brain 12 years after the removal of the original tumor. *Clin Neuropathol* 1997; **16**: 190–4.
 22. Lindner V, Edah-Tally S, Chakfé N, et al. Cardiac myxoma with glandular component: case report and review of the literature. *Pathol Res Pract* 1999; **195**: 267–72.
 23. Pucci A, Bartoloni G, Tessitore E, et al. Cytokeratin profile and neuroendocrine cells in the glandular component of cardiac myxoma. *Virchows Arch* 2003; **443**: 618–24.
 24. Chopra P, Ray R, Singh MK, et al. Cardiac myxoma with glandular elements: a histologic, histochemical, and immunohistochemical evaluation. *Indian Heart J* 2003; **55**: 182–4.
 25. Eckhardt BP, Dommann-Scherrer CC, Stuckmann G, et al. Giant cardiac myxoma with malignant transformed glandular structures. *Eur Radiol* 2003; **13**: 2099–102.
 26. den Bakker MA, Dinjens WN, Bekkers JA. Cardiac myxoma with atypical glandular component, report of a case. *Histopathology* 2006; **48**: 206–8.
 27. Liu Y, Xu ML. Cardiac myxoma with glandular component: case report. *Chin Med J* 2006; **119**: 174–6.
 28. Stoane L, Allen JH Jr, Collins HA. Radiologic observations in cerebral embolization from left heart myxomas. *Radiology* 1966; **87**: 262–6.
 29. New PFJ, Price DL, Carter B. Cerebral angiography in cardiac myxoma. Correlation of angiographic and histopathological findings. *Radiology* 1970; **96**: 335–45.
 30. Reynen K. Cardiac myxomas. *New Engl J Med* 1995; **333**: 1610–7.
 31. Malekzadeh S, Roberts WC. Growth rate of left atrial myxoma. *Am J Cardiol* 1989; **64**: 1075–6.
 32. Lane GE, Kapples EJ, Thompson RC, et al. Quiescent left atrial myxoma. *Am Heart J* 1994; **127**: 1629–31.
 33. Dang CR, Hurley EJ. Contralateral recurrent myxoma of the heart. *Ann Thorac Surg* 1976; **21**: 59–62.
 34. Amano J, Kono T, Wada Y, et al. Cardiac myxoma: its origin and tumor characteristics. *Ann Thorac Cardiovasc Surg* 2003; **9**: 215–21.