Right Atrial Myxoma: Unusual Clinical Presentation and Atypical Glandular Histology

WILLIAM FRISHMAN, M.D., STEPHEN FACTOR, M.D., ALPHONZO JORDAN, M.D., CHARLES HELLMAN, M.D., URI ELKAYAM, M.D., THIERRY LEJEMTEL, M.D., JOEL STROM, M.D., HAL UNSCHULD, M.D., AND RONALD BECKER, M.D.

SUMMARY A 57-year-old black female presented with a 1-month history of right-sided congestive heart failure and clinical evidence of pulmonic and tricuspid valvular stenosis and insufficiency. The echocardiographic examination and ventriculography demonstrated a large right atrial tumor interfering with the function of both right-sided valves. The patient underwent successful surgical resection of the tumor. Histologically, the tumor had cellular areas typical of myxoma, as well as glandular areas, a feature which has been described very rarely in this lesion. Electron microscopy of the glandular zones, which has never been reported previously, showed cells having essential homology with the usual myxoma elements. The atypical histopathology of this lesion supports the theory that atrial myxomas are true neoplasms, and are not derived from unusually organized mural thrombi.

ATRIAL MYXOMAS ARE UNCOMMON but often curable tumors that may produce atypical cardiac symptoms. Approximately one-fourth of myxomas are right-sided, and the majority of patients with these lesions have right-sided congestive heart failure. These tumors can now be diagnosed with reasonable accuracy by cardiac catheterization and angiography.

The pathogenesis of the cardiac myxoma is controversial. Although most observers agree that the myxoma is a true neoplasm derived from a subendocardial reserve cell, a recent report attempted to resurrect the theory that myxomas are derivatives of unusually organized atrial mural thrombi. Despite several recent ultrastructural studies, the thrombus theory has not been unequivocally refuted.

The case described here, a 57-year-old female with right atrial myxoma, sheds some light on this pathological question; the patient’s clinical manifestations are also of interest. She presented with signs of right-sided congestive heart failure and physical findings suggestive of tricuspid and pulmonic valve disease. The echocardiographic examination, although initially unrevealing, showed a lesion so large that it obstructed and interfered with both the tricuspid and pulmonic valves, an unusual presentation for this rare tumor.

Case Report

A 57-year-old black female was admitted to the Bronx Municipal Hospital Center on November 7, 1976 with a 1-month history of anasarca. She previously had been in good health except for some mild blood pressure elevation. She had no known history of congestive heart failure, liver disease, kidney or endocrine disorders, or of chest pain, Raynaud’s phenomenon, fevers, orthopnea or paroxysmal nocturnal dyspnea. She did complain, however, of increasing abdominal girth and a 40-lb weight gain in the 2 months before admission.

Physical examination revealed a blood pressure of 125/80 mm Hg and an irregular pulse rate of 80 beats/min. Tense anasarca was observed, especially on the extremities, back and abdomen. Jugular venous distention to 5 cm was noted on the left with minimal jugular venous distention on the right. The chest examination was clear to percussion and auscultation. The cardiac examination revealed no heaves or thrills, but soft first and second heart sounds and a loud early third heart sound were heard. There was a grade 2/6 systolic murmur heard best in the pulmonic area, and a loud, blowing, grade 3/6 systolic murmur heard along the left sternal border in the fourth intercostal space. A diastolic rumbling murmur was heard along the left sternal border in the fourth intercostal space, and a higher pitched early decrescendo diastolic murmur was also audible over the pulmonic area.

Initial laboratory data revealed a white blood cell count of 7200 mm<sup>3</sup>, a hematocrit of 43 vol%, and a hemoglobin of 13.9 g/100 ml. The erythrocyte sedimentation rate was 28 mm/hour. Latex fixation and fluorescent antinuclear antibody tests were negative. The ECG revealed atrial fibrillation with a ventricular response of 80 and low voltage. The chest roentgenogram showed diffuse cardiomegaly.
Further diagnostic studies included a negative lung scan. Carotid pulse tracing revealed a normal carotid upstroke, while jugular venous pulse tracings had prominent V waves without a marked Y collapse. On phonocardiographic examination, diastolic murmurs were noted over the pulmonic area and along the left sternal border. Systolic murmurs were also recorded from this region. There was an accentuation of all murmurs with inspiration.

An echocardiogram was performed with the patient recumbent at a 30° angle. Marked right ventricular enlargement was observed with normal left ventricular and left atrial indices. A normal mitral valve echo was noted. The aortic root and valve were normal in appearance. A band of wavy-lined echoes could be seen in the area of the right ventricular outflow tract, predominantly during systole (fig. 1). A cloud of wavy echoes was also noted prolapsing behind the tricuspid valve during diastole. The band of echoes did not disappear with systole but remained in the area of the right ventricular outflow tract. The pulmonic valve was not seen. No abnormalities of the ventricular septum were noted.

The patient underwent right- and left-sided cardiac catheterization and cineangiography which revealed an extensive filling defect in the right atrium which prolapsed into the right ventricle (fig. 2). The tumor was so large that it remained in the ventricle during diastole and systole causing insufficiency of both the tricuspid and pulmonic valves. Gradients across the tricuspid and pulmonic valves were also detected.

The patient underwent surgical exploration through a median sternotomy. The pulmonary artery, right ventricle and right atrium were grossly enlarged and extremely tense. The right atrium was opened with a horizontal incision, revealing a huge tumor which protruded across the tricuspid valve and pulmonary outflow tract. The tumor, which was attached by a short stalk to the free atrial wall, was easily resected after dividing its flimsy atrial attachment. The atrial septum was entirely free of tumor. Moderate tricuspid insufficiency was noted after discontinuation of cardiopulmonary bypass. The patient made an uneventful recovery and was discharged. The tricuspid insufficiency spontaneously resolved, with all murmurs and the peripheral edema disappearing within 1 month. Follow-up right-sided cardiac catheterization revealed no pressure gradients or valvular insufficiency.

Pathology Findings

The surgical specimen consisted of a soft, semitranslucent, polypoid mass of gelatinous tissue measuring 9 × 8 × 4 cm in greatest dimension and weighing 109 g. One end of the main tumor mass was irregular and friable, while the other end had grooves corresponding to atrial trabeculations. The tumor had both typical glistening myxomatous areas and more opaque, solid tissue. Small cysts, measuring up to 1 cm in diameter, were noted throughout the central portion of the tumor. Foci of old hemorrhage were present, while organized, recent thrombus adhered to the surface. No areas of necrosis, calcification, ossification or cartilage formation were observed.

Histologically, the predominant cell type was ovoid, spindle or polygonal. In hypocellular areas, individual cells were surrounded by abundant, loose, myxomatous stroma. In scattered foci, the cells were arrayed in irregular masses or were present around thin-walled capillaries (fig. 3). These foci had less myxomatous stroma and abundant hemosiderin-laden macrophages, lymphocytes and plasma cells.

In other foci, numerous cystic spaces were present in the midst of typical myxoma cells intimately associated with capillaries. The cystic spaces ranged from microscopic to macroscopic, and were lined by

**Figure 1.** Echocardiogram through the right ventricle (RV) at the level of the tricuspid valve (TV) leaflets. Note the dense clusters of echoes behind the TV arising from the myxoma (MX) in the RV during diastole. The cluster of echoes persists during systole.
flattened spindle or cuboidal cells which focally demonstrated transition into typical tall, columnar, goblet cells (fig. 4). The stroma in the cystic and glandular portion of the tumor was more collagenous than elsewhere and contained a heavy infiltrate of lymphocytes, plasma cells, histiocytes, and rare multinucleated foreign body type giant cells associated with extravasated mucin. Goblet and transitional cells stained with PAS, mucicarmine, and alcian blue, and the stroma throughout the tumor was strongly alcian blue positive.

Electron microscopy of grossly identified cystic tumor fixed for 1 week in 4% phosphate-buffered formaldehyde and embedded in Epon revealed that the tumor was composed of a variably differentiated cell type, although cells with features of endothelium and histiocytes were also recognized. The myxoma cell, in noncystic areas, contained a large, irregularly indented nucleus and had few cytoplasmic organelles (fig. 5). The most striking cytoplasmic component was a large number of thin filaments coursing irregularly through the cytosol. The plasma membrane displayed...
FIGURE 4. An area of the tumor demonstrating glands or gland-like structures. The bubbly stroma is identical to that seen in figure 3, including the presence of inflammatory cells. Also noted are individual or groups of myxoma cells, a capillary (C) surrounded by a cuff of myxoma cells, a small gland-like structure (G) lined by flat and cuboidal cells, and two large glands (G1 and G2) lined by goblet cells (arrowheads). In gland G1, there appears to be a transition between the flattened and spindled myxoma cells and the plump glandular cells (arrows) (hematoxylin and eosin, × 240).

FIGURE 5. Two individual myxoma cells with focal adherence (arrow). The cells have few cytoplasmic organelles, but the cytoplasm is filled with fine filaments (F) typical of myxoma cells. Thin cytoplasmic processes extend into the stroma which is composed of electron-dense material and collagen fibers. The nuclei are focally indented and have prominent nucleoli. Cells such as these were observed singly or in groups within the stroma, as well as surrounding stromal capillaries (× 17,100).
many thin projections and occasional microvilli. Aggregated myxoma cells had interdigitated projections attached by desmosomes. The extracellular space contained collagen fibrils and electron-dense granular precipitate which was focally condensed along the plasma membrane. No basement membrane was observed around the myxoma cells.

Ultrastructure of the tumor glands revealed that these structures were composed of cells which closely resembled the myxoma cells described previously (fig. 6). In general, these cells had more numerous mitochondria, rough endoplasmic reticulum, and vesicles, possibly reflecting active secretion. The plasma membrane lining the gland spaces was raised into microvilli. The cytoplasm was filled with large numbers of thin filaments which in some areas appeared focally condensed. Numerous desmosomal attachments were noted between cells, and electron-dense cytoplasmic material was frequently associated with areas of attachment. Structures interpreted by light microscopy as mucin vacuoles within goblet cells, were noted to be extracellular spaces enveloped by cytoplasmic processes. The presence of collagen fibrils within these spaces confirmed this interpretation (fig. 6).

Discussion

Atrial myxoma is the most common benign tumor of the heart, occurring 25% of the time on the right side. Early diagnosis of these cardiac tumors is important so that they can be removed before the development of serious sequelae, such as emboli or atrioventricular valvular obstruction. For the most part, surgical resection is completely curative.

The patient described in this report had many unusual manifestations of right atrial myxoma. She had signs of right-sided congestive heart failure, with no evidence of pulmonary emboli. The normal sedimentation rate and hematocrit were atypical findings. The echocardiogram demonstrated clouds of echoes in the right ventricular outflow tract during systole and behind the tricuspid valve during diastole. These observations suggested that the tumor did not...
tricuspid cardiac myxoma the tricuspid valve closure during prolapse into the right atrium during systole, but remained in the right ventricle obstructing the tricuspid valve during diastole and interfering with tricuspid valve closure during systole. At the same time, the tumor interfered with pulmonic valve function, a finding usually seen with right ventricular myxoma, but not described with right atrial myxoma.10

Recent investigators5, 6-7, 11-13 generally agree that the cardiac myxoma represents a true neoplasm. Light microscopic, histochemical and ultrastructural evidence has been presented that the myxoma arises from a multipotential endocardial or subendocardial reserve mesenchymal cell which can differentiate into fibrocytes, myocytes or endothelium. 3, 5-7, 11-13 Salyer et al.4 challenged this traditional view, however, pointing out that organizing cardiac mural thrombi and papillary endocardial lesions have histological features similar to those in the atrial myxoma. These authors therefore proposed that the myxoma is not a true neoplasm, but is the result of an unusually organizing mural thrombus. Their position is supported by the findings of Stovin et al.,1 who were unable to differentiate ultrastructurally a cardiac myxoma and a papillary tumor of the heart, a lesion which is generally accepted as arising from organizing endocardial vegetation. Thus, there is still some question regarding the histogenesis of the cardiac myxoma.

Individual or groups of ovoid, stellate, or spindled mesenchymal cells lying in pools of acid mucopoly saccharide, or the intimate association of these cells with capillary channels, are characteristic of atrial myxoma.5-8, 11-13 These patterns were present throughout the tumor in this case. In addition, the ultrastructural appearance of the nonglandular areas is in accord with many previous descriptions.5-7, 11, 12

There is essential identity between the variably differentiated myxoma cells in our case, containing few cytoplasmic organelles and large numbers of intracytoplasmic filaments, and the myxoma cells illustrated by Ferrans and Roberts in their comprehensive review of the ultrastructure of these tumors.7 The presence of glands and cystic structures in this case, lined by cells demonstrating a transition from more typical myxomatous tissue, is strong support for the neoplastic origin of these tumors. Although these glandular elements have been reported in other myxomas by several authors,15, 16 we are unaware of any published ultrastructural study of these glands. Glandlike, epithelial-lined cystic and tubular spaces are features of the mesothelioma of the atrioventricular node;15, 16 however, the appearance is clearly different from the glands and cysts in our case, and those reported by Fine et al.13 and Anderson et al.14

The ultrastructure of these glands established that they were lined by cells having features of the myxoma cells seen in the more typical portions of the tumor. With the exception of a slight increase in the number of cytoplasmic organelles, and a transformation of the cell surface membrane into numerous microvilli, there were no basic differences. These glands provide further evidence for the multipotentiality of the undifferentiated cell which has been proposed as the progenitor of the myxoma. We are unaware of similar glandular structures being described in cardiac or extracardiac organizing thrombi. Therefore, the demonstration that these glands are derivatives of typical myxoma cells is evidence for the neoplastic origin of these tumors.

References
Right atrial myxoma: unusual clinical presentation and atypical glandular histology.
W Frishman, S Factor, A Jordan, C Hellman, U Elkayam, T LeJemtel, J Strom, H Unschuld and R Becker

_Circulation._ 1979;59:1070-1075
doi: 10.1161/01.CIR.59.5.1070
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1979 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/59/5/1070

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/