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Left Atrial Myxosarcoma with Systemic Metastasis : A Case Report

The term myxosarcoma is currently not used in standard classification for soft tissue tumors, but restricted to cardiac tumors. Primary cardiac myxosarcoma is a very rare disease and is difficult to differentiate from myxoma clinically and pathologically. We report a case of left atrial myxosarcoma with widespread systemic metastasis in a 21-yr-old male. The patient presented with sudden onset of intermittent dyspnea and orthopnea. Echocardiography showed a mobile, pedunculated tumor, 7.5×5×2 cm in size, at left atrium. Histologically, the excised tumor showed an amorphous finely fibrillar and mucinous stroma, in which irregular cords and clusters of lepidic cells and large stellate cells with plump vesicular nuclei resembled the usual type of cardiac myxoma were noted. And it showed focally cellular area with great nuclear pleomorphism and frequent mitoses. The patient received combination chemotherapy, peripheral blood stem cell collection transplantation and operations for systemic metastases in the brain, skeletal muscle and lung. He is alive at present 37 months after initial diagnosis and has no more new metastatic lesion.

Key Words: *Myxosarcoma; Myxoma; Sarcoma; Heart*

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INTRODUCTION

Primary cardiac neoplasms are rare, occurring in 0.002-0.3% of autopsy series (1). Malignant disease is present in 20-30% of these patients and is almost always of sarcomatous nature (1). The term myxosarcoma is currently not used in standard classification for soft tissue tumors, but restricted to cardiac tumors that are myxoid in all areas, without cellular or vascular patterns diagnostic of other sarcomas (2). In a search of the literature, 8 cases of cardiac myxosarcoma reported by AFIP were aged 2-66 yr and were 3 men and 5 women, and 6 cases arised in the left atrium (2) and had poor survival rate with 10 months of mean survival time (3).

We present a case of primary left atrial myxosarcoma with widespread systemic metastasis. The primary and metastatic tumors were removed by operations, and chemotherapy and peripheral blood stem cell collection transplantation (PBSCT) were performed. He is alive 37 months since initial diagnosis and has shown no more new metastatic lesions. The clinical course, pathologic findings and histogenetical aspect are described in an attempt to obtain a better understanding of this rare neoplasm. To the best of our knowledge, this is the first report of cardiac myxosarcoma in Korea.

CASE PRESENTATION

A 21-yr-old man was admitted because of a sudden onset of intermittent dyspnea on exertion, orthopnea and hemoptysis for 15 days. The past history was non-specific. Echocardiography revealed a large, intracavitary, free floating, pedunculated tumor attached to lateral wall of left atrium, extending through the mitral orifice (Fig. 1). The tumor was removed through a standard median sternotomy using cardiopulmonary bypass with bicaval and aortic cannulation. The excised mass, measuring 7.5×5×2 cm in dimension, revealed a friable, gelatinous, multilobulated and polypoid appearance with focal hemorrhage (Fig. 2). Histologically, the tumor had a diffuse myxoid background and showed a weak to moderate positive reaction to PAS and alcian blue and two admixed representative areas. One was usual histologic feature of myxoma, which consists of most of the tumor. The other was a focal more cellular area having pleomorphism and high mitotic activities, up to 8 per 10 high power fields. The cells had moderately clumped chromatin, irregular nuclear membranes, multinucleation and medium-sized nucleoli (Fig. 3). There were no definitive areas of cellular or vascular patterns diagnostic of malignant fibrous histiocytoma, fibrosarcoma, leiomyosarcoma, rhabdomyosar-

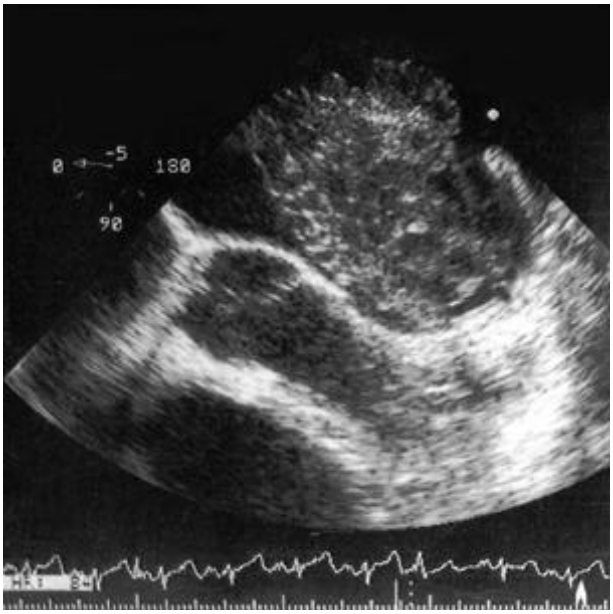

Fig. 1. Echocardiography reveals a free floating, large, pedunculated tumor attached to lateral wall of left atrium.

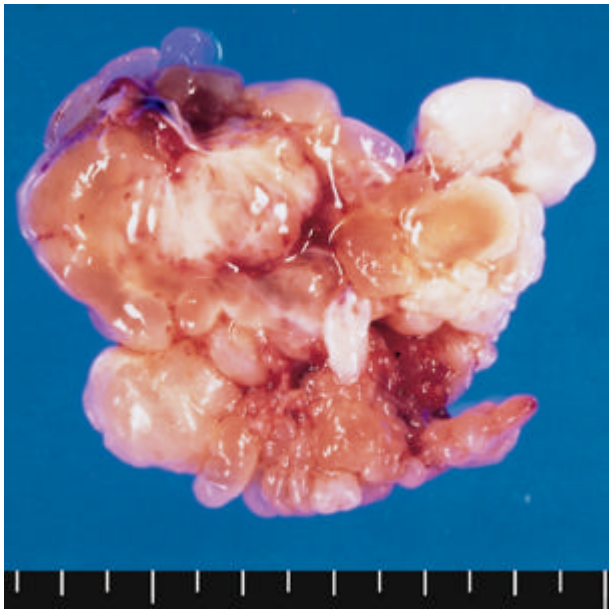

Fig. 2. Excised tumor, 7.5×5×2 cm, reveals a polypoid glistening, myxoid and multilobated appearance with focal hemorrhage.

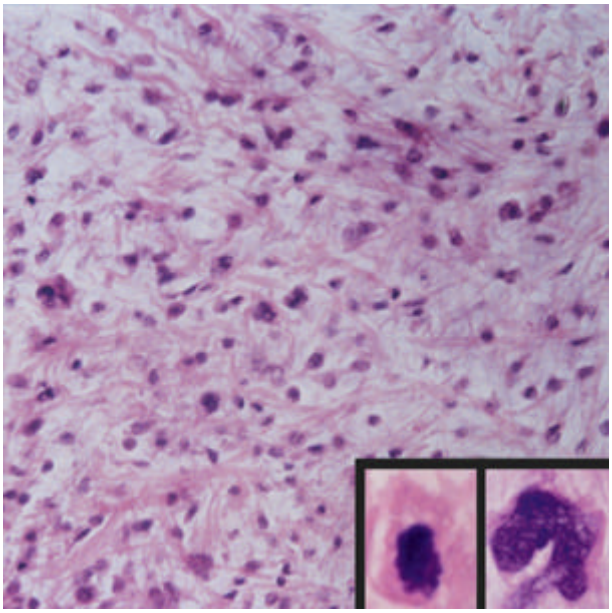

Fig. 3. Cellular area is composed of atypical spindle cells with irregular and hyperchromatic nuclei, multinucleation and occasional mitoses (inset) (H&E, ×200).

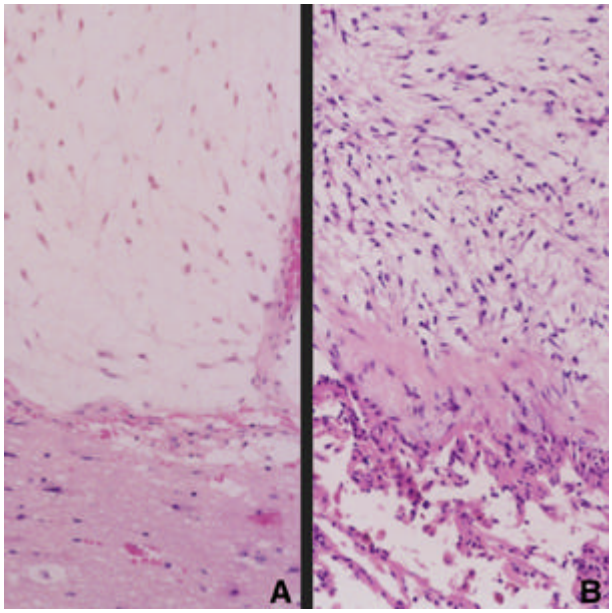

Fig. 4. Systemic metastases of myxosarcoma are noted in the brain (A) and lung (B) (H&E, ×100).

coma, neurofibrosarcoma, or liposarcoma. By immunohistochemistry, the tumor cells were diffuse positive for vimentin and negative for desmin, smooth muscle actin, S-100 protein, and factor VIII-related antigen. The patient received three cycles of adjuvant chemotherapy with VACA (Vincristin, Actinomycin D, Cytoxan, Adriamycin) after operation. On follow-up, metastatic lesions were found at right parietal lobe at 7 months (Fig. 4A) and in right thigh at 9 months after removal of the primary cardiac tumor. The metastatic lesions were removed, and the chemotherapy regimen was changed to VIP (VP-16, Ifosfamid, Cisplan) and PBSCT was done. Fourteen months later, a new metastatic lesion appeared in the right thigh. The regimen was changed to VACA but another metastatic lesion appeared in the lung soon (Fig. 4B). And the regimen was changed to VIP again. The

patient is alive at 37 months since initial diagnosis and no more new metastatic focus has developed for 7 months after removal of the latest metastatic pulmonary lesion.

DISCUSSION

Cardiac tumors are infrequent but potentially life-threatening conditions that necessitate prompt diagnosis and aggressive therapy. Accurate preoperative assessment is particularly crucial in cases of malignant disease, in view of the very poor prognosis of this subset of patients after surgical resection. Despite advances in imaging techniques, pathologic examination of biopsy specimens still appears to be of fundamental importance to fully characterize the cardiac tumors. Because of the gross and histologic similarities, myxosarcoma may be misdiagnosed as myxoma until the tumor recur. So it is important to know the relation between myxosarcoma and myxoma and differentiate them, because both are characterized by accumulations of extracellular proteoglycans and are located in the left atrium. The most important histologic criterion in identifying myxosarcoma is the absence of the typical cords, rings, and capillary structures formed by myxoma cells. The degree of cellularity of myxosarcoma varies and sometimes myxoma also can be quite cellular, but there are invariably foci with atypical hyperchromatic cells in myxosarcoma. Hemosiderin-laden macrophages are usually absent in myxosarcoma but plentiful in myxoma (2). The fact that myxosarcoma corresponds to malignant transformation of myxoma is controversial because there is no solid evidence that supports a sequential transformation of cardiac myxoma to myxosarcoma. And there are several reasons to doubt this transformation. The first, composite tumors consisting of sarcoma and myxoma probably do not exist and the propensity toward recurrence in cardiac myxoma is not a function of histologic appearance or atypia, but depends on hereditary factors. The second, with the exception of angiosarcoma, most cardiac sarcomas, not only myxosarcomas, arise in the left atrium. The third, a myxoid background may occur in all types of cardiac sarcomas and may be a consequence of intracavitary location rather than a reflection of histogenesis (2).

The origin of cardiac myxosarcoma remains unclear. The pathologic material in the presented case showed variable areas of dedifferentiated, as well as differentiated areas that resemble benign atrial myxoma. The cells that are clearly malignant show areas of pleomorphism and hyperchromacity with high mitotic activity. Harris et al. (4) reported that the immunohistochemical and ultrastructural findings of cardiac myxosarcoma indicate a tendency toward smooth muscle differentiation, although undifferentiated cells, best classified as primitive mesenchymal cells, were present. The undifferentiated cells have the capacity to differentiate into mesenchymal cell lines, including endothelial cells, fibroblasts, smooth muscle cells and chondroid cells, suggesting that other histologic variants of atrial sarcoma may be derived from the same group of undifferentiated cells. These tumors may have originated from the same embryonal cell as the myxoma cell, and after differentiation, assumed the histologic picture of fibromyxosarcoma, malignant fibrous histiocytoma, or even chondrosarcoma. Basso et al. (3) reported that the cells positively reacted at immunohistochemistry to factor VIII-related antigen as in myxoma. But our case showed immunohistochemically negative reaction for smooth muscle actin, desmin and factor VIII-related antigen, and we did not perform an ultrastructural study so we cannot define the origin of cardiac myxosarcoma. However, we suspect that undifferentiated mesenchymal cell plays a role in histogenetic origin.

The prognosis of cardiac primary sarcoma is very poor with a mean survival of 9 months after the first symptoms according to Murphy et al. (5), 11 months by Putanam et al. (6), and 16.5 months by Donsbeck et al. (7). And one patient with cardiac myxosarcoma in the AFIP files survived 50 months after several local recurrences (2). Basso et al. (3) reported that mean survival time of cardiac myxosarcoma was 10 months after operation. The exact evaluation of clinical course and treatment modality has not been perfectly evaluated due to the very small number of reported cases of myxosarcoma. Factors apparently associated with an increased survival of cardiac sarcoma are left side location, a mitotic rate of less than 10 per 10 high-powered field and no necrosis, whereas tumor histotype does not seem to affect the prognosis (8). Some authors suggest that adjuvant therapy for cardiac tumors may be only a palliative measure which does not improve survival (6). Donsbeck et al. (7) reported that adjuvant chemotherapy and/or radiation therapy did not prevent local recurrence or visceral metastasis in a study of 24 primary cardiac sarcomas. The present case is alive at 37 months after initial diagnosis in spite of widespread metastasis, thus we think adjuvant chemotherapy is probably helpful, and the left side tumor location and histologic feature with lower mitotic figure than 10 per 10 high power fields and no necrosis may have affected the increased survival time in this case.

It is likely at times that many malignant myxomas are sarcomas with myxoid features which have been misdiagnosed as myxoma. None of the current cardiac imaging techniques is able to provide a definitive diagnosis. So only specimens acquired at the time of endomyocardial biopsy or thoracotomy can yield an in vivo tissue

characterization of cardiac masses. Especially, cardiac mass with myxoid feature should not be diagnosed as benign myxoma when tissue is obtained from endomyocardial biopsy. Prompt histological and immunohistochemical examination are mandatory in order to rule out malignancy and establish the best medical or surgical treatment.

In conclusion, cardiac myxosarcoma is exceptionally rare and a distinct disease entity. Our case is the first reported case in Korea, which also emphasizes that the histologic features of myxosarcoma are distinctive from myxoma. Defining the histogenesis of myxosarcoma and clinical course requires further studies.

REFERENCES

1. Silverman NA. *Primary cardiac tumors. Ann Surg 1980; 191: 127-38.*
2. Burke A, Virmani R. *Tumors of the heart and great vessels. In: Atlas of tumor pathology. Series 3, fascicle #16. Washington, DC: Armed Forces Institute of Pathology, 1996; 127-55.*
3. Basso C, Valente M, Poletti A, Casarotto D, Thiene G. *Surgical pathology of primary cardiac and pericardial tumors. Eur J Cardiothorac Surg 1997; 12: 730-8.*
4. Harris GJ, Tio FO, Grover FL. *Primary left atrial myxosarcoma. Ann Thorac Surg 1993; 56: 564-6.*
5. Murphy MC, Sweeney MS, Putnam JB, Walker WE, Frazier OH, Ott DA, Cooley DA. *Surgical treatment of cardiac tumors: a 25-year experience. Ann Thorac Surg 1990; 49: 612-8.*
6. Putnam JB, Sweeney MS, Colon R, Lanza LA, Frazier OH, Cooley DC. *Primary cardiac sarcomas. Ann Thorac Surg 1990; 51: 906-10.*
7. Donsbeck AV, Ranchere D, Coindre JM, Le Gall FL, Cordier JF, Loire R. *Primary cardiac sarcomas: an immunohistochemical and grading study with long-term follow-up of 24 cases. Histopathology 1999; 34: 295-304.*
8. Burke AP, Cowan D, Virmani R. *Primary sarcomas of the heart. Cancer 1992; 69: 387-95.*