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Case Report

Massive Primary Cardiac Malignant Lymphoma found by Occurrence of Cardiogenic Cerebral Embolism

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SUMMARY

A previously healthy 73-year-old woman was admitted to hospital for sudden left hemiplegia, and an electrocardiogram showed transient atrial fibrillation. Transthoracic and transesophageal echocardiography, chest computed tomography, magnetic resonance imaging and ^{18}F-fluorodeoxyglucose positron emission tomography led to diagnosis of a giant right atrial tumor infiltrating the right ventricle. A cardiac tumor was found upon occurrence of cardiogenic cerebral embolism induced by paroxysmal atrial fibrillation. Transvenous atrial tumor biopsy gave a definite diagnosis of Burkitt-like diffuse large B-cell lymphoma, which was improved by THP-COP therapy consisting of cyclophosphamide, pirarubicin, vincristine and prednisolone. Our case shows that early diagnosis and prompt treatment of progressive cardiac lymphoma are important.

Key Words : Cardiac malignant lymphoma, Paroxysmal atrial fibrillation, Cerebral embolism

BACKGROUND

Primary cardiac malignant lymphoma is a rare disease, making up less than 1% of all lymphomas[1] and accounting for 1.3-2% of primary cardiac tumors[2]. We report a case of rapidly growing cardiac malignant lymphoma in the right atrium complicated with paroximal atrial fibrillation and cardiogenic cerebral embolism. The tumor was diagnosed as Burkitt-like diffuse large B-cell lymphoma (Burkitt-like DLBCL) from immunohistological findings in biopsy tissue and was improved significantly by chemotherapy.

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CASE REPORT

A 73-year-old woman experienced sudden left hemiplegia in November 2006. She was admitted to a nearby hospital for treatment and tests for cerebral embolism. Her medical and family history were not particular noteworthy. During hospitalization, an electrocardiogram (ECG) showed tachycardiac atrial fibrillation. Echocardiography was conducted due to suspicion of cardiogenic cerebral embolism and a giant tumor mass was found in the right atrium. After rehabilitation, the patient was referred to Dokkyo Medical University Hospital for a complete examination in May 2007.

At the time of hospitalization, the patient was of height 149 cm, body weight 49 kg, blood pressure 102/64 mmHg, body temperature 36.6℃, pulse 72/min, regular pulse. Left hemiplegia was observed, but the patient was clearly conscious and no anemia or jaun-

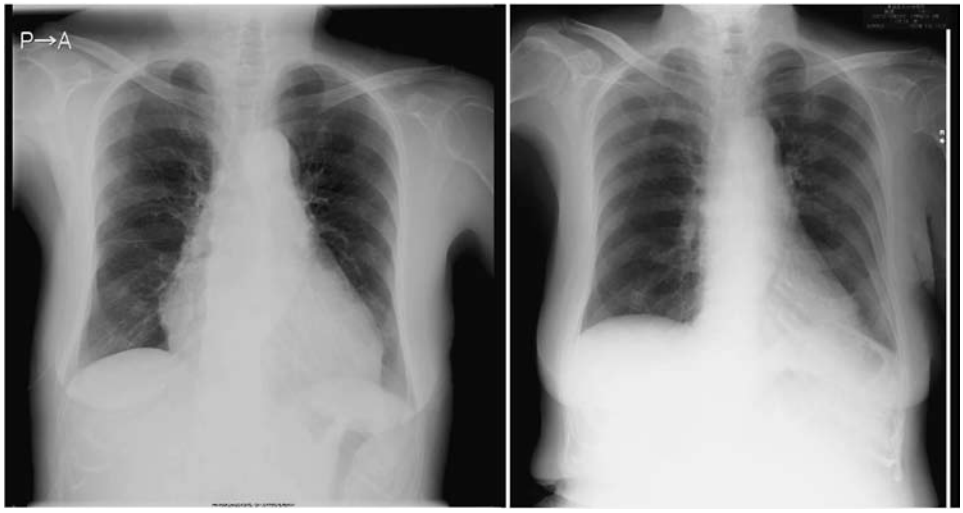

Fig. 1 Chest X-ray before chemotherapy (left), showing the prominence of the right second arch, and after chemotherapy (right).

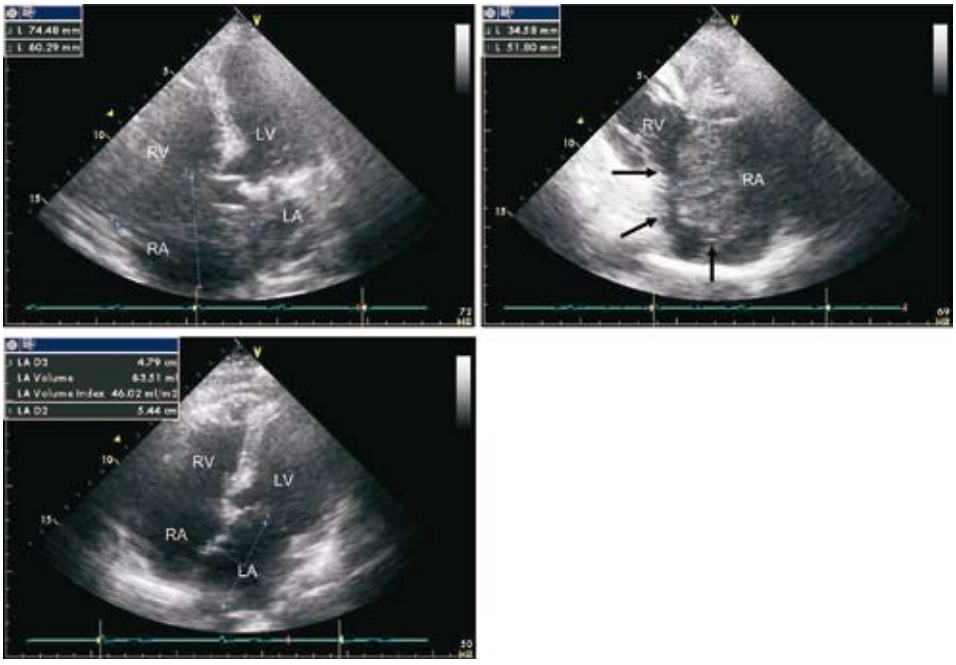

Fig. 2 Transthoracic echocardiographic images before (upper left and upper right) and after (lower right) chemotherapy from apical four-chamber view. Large tumor was in the right atrium (upper right, arrows) and disappeared after chemotherapy. RA, right atrium ; RV, right ventricle ; LA, left atrium ; LV, left ventricle.

dice was found. Heart or pulmonary sounds showed no abnormalities, and the liver, spleen and superficial lymph nodes were impalpable.

After hospitalization, hematological tests showed WBC 4,100/μl, hemoglobin 12.4 g/dl, platelet count 9.4 $\times 10^4/\mu$l, CRP 2.45 mg/dl, lactate dehydrogenase (LDH) 334 IU/l, and soluble interleukin-2 receptor 7,245 IU/ml, all of which were significantly elevated. ECG showed an ectopic atrial rhythm and a pulse rate of 74 beats/min. Chest X-ray showed prominence of the right second arch, a cardiothoracic ratio of 67 %, and a normal lung field (Fig. 1, left).

Transthoracic echocardiography revealed a giant solid tumor-like structure in the periphery of the right atrium to the ascending aorta (Fig. 2, upper left). This tumor filled the inside of the right atrium, had infiltrat-

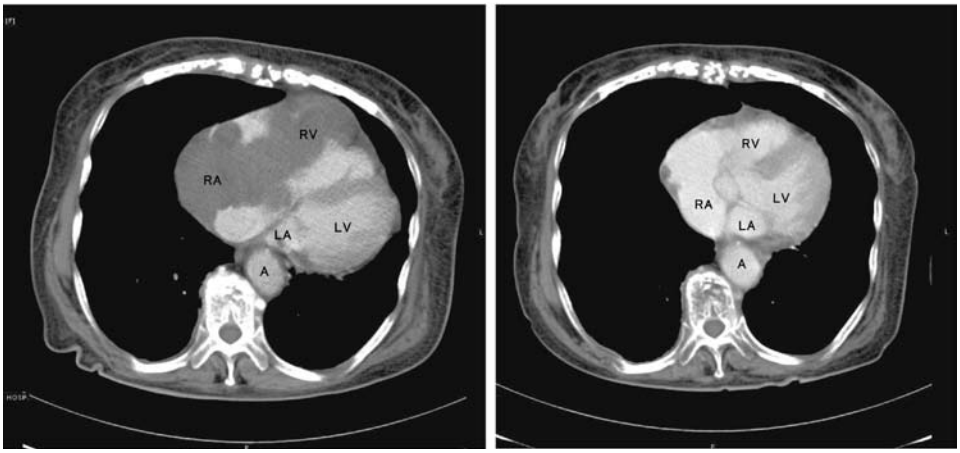

Fig. 3 Computed tomography (CT) before (left) and after (right) chemotherapy. The giant tumor in the right atrium infiltrated into the right ventricle (left). RA, right atrium ; RV, right ventricle ; LA, left atrium ; LV, left ventricle ; A, aorta.

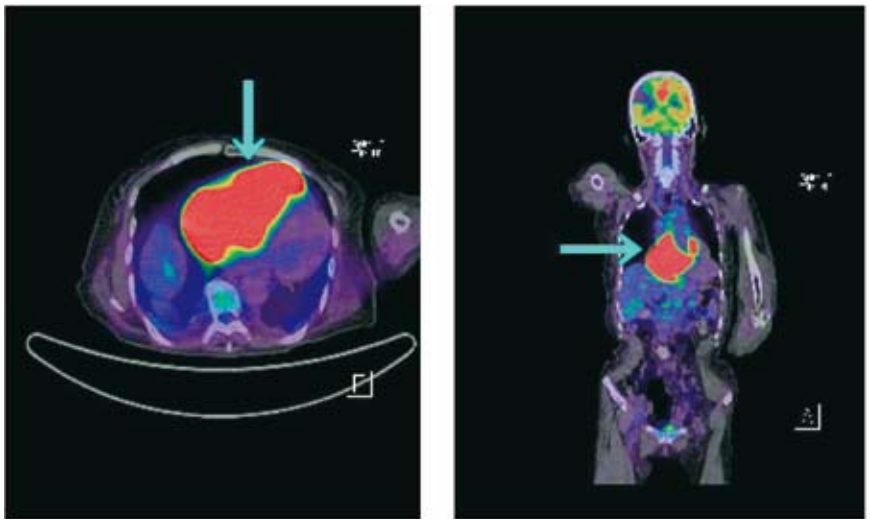

Fig. 4 FDG-PET in coronal (right) and transaxial (left) views before treatment. There was intense FDG uptake (red color area) in the giant mass in the right atrium. The blue arrow indicates the giant cardiac lymphoma in the right atrium.

ed into the interatrial septum and appeared uneven and non-homogenous (Fig. 2, upper right, arrows). Mild aortic valve regurgitation was also recognized. Transesophageal echocardiography (TEE) showed a giant tumor of 6 × 4 cm ranging from the periphery of the right atrium to the superior vena cava, and contrast chest computed tomography (CT) and axial magnetic resonance imaging (MRI) suggested a lobulated giant tumor in the right atrium, which had partly infiltrated into the right ventricle (Fig. 3, left). The tumor occupied the ventral anterior of the right-sided heart and the blood stream ran into the lungs via the dorsal side. The left-sided heart was pressed by the tumor to the left posterior, and the ventral anterior side of the superior vena cava was narrowed and filament-like ; however, there was no stenosis in the inferior vena cava. In ^{18}F-labeled fluorodeoxyglucose (FDG) positron emission tomography (PET) images, FDG was significantly concentrated from the right atrium to the right ventricle, but there was no evidence for a primary or metastatic focus beyond the heart (Fig. 4). A right atrium image in a cardiac catheter examination confirmed that the tumor occupied a large part of the right atrium, and a portion of the tu-

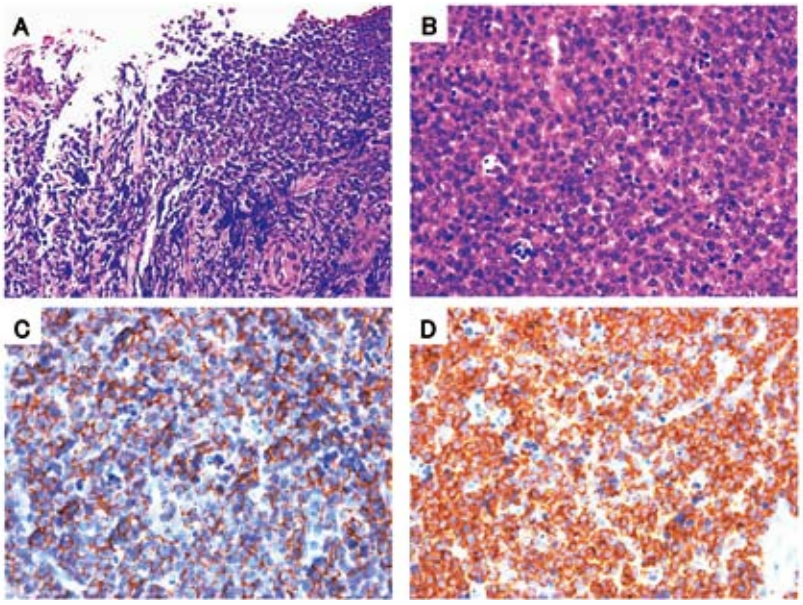

Fig. 5 Histological findings in biopsy tissue. In a hematoxylin-eosin-stained specimen, lymphoma cells had diffusely infiltrated the right atrial muscle fiber (A) and a starry sky appearance of undifferentiated large lymphoid cells was apparent (B). Immunohistological staining was clearly positive for CD20 (C) asnd Bcl 2 (D).

mor mass in the right atrium was collected using a catheter for myocardial biopsy. No abnormalities in the coronary artery were apparent in coronary arteriography.

Images of biopsy tissues suggested infiltration of tumor cells into the atrial muscle fiber (Fig. 5A). The nucleus of each cell differed in size, the nucleolus was clear, and a starry sky appearance characteristic of a Burkitt-type tumor was observed in tumor cells (Fig. 5B). Based on CD20-positive (Fig. 5C), Bcl 2 100% positive (Fig. 5D) and MIB-1 stain index over 90% findings, the tumor was diagnosed as Burkitt-like diffuse large B-cell lymphoma (Burkitt-like DLBCL). Considering the age of the patient and the tumor stage, 5 courses of THP-COP therapy consisting of cyclophosphamide, pirarubicin, vincristine and prednisolone were conducted. The tumor responded to chemotherapy very well : chest X-ray showed a decrease of 54% in the cardiothoracic ratio (Fig. 1, right), and echocardiography and MRI showed a significantly decreased right atrial tumor (Fig. 2, lower left ; Fig. 3, right). After improvement of lymphoma was confirmed, the patient was discharged. Currently, she visits the hospital regularly and has not experienced a recurrence, although an electrocardiogram indicates an ectopic atrial rhythm.

DISCUSSION

Among primary cardiac tumors, 75% are benign and half are myxoma. Of cases of cardiac malignant lymphoma, the peak incidence is at an age of 62-67 years old, the disease occurs more in males than in females, and 69-72% occur in the right-sided heart [2]. The common sites of extra-nodal malignant lymphoma are the mediastinum [3], stomach, skin and central nervous system, with few cases reported in the heart. Cardiac malignant lymphomas are mostly metastatic [4]. Diffuse large B-cell lymphoma (DLBCL) accounts for 30-40% of adult non-Hodgkin's lymphoma cases and extra-nodal lymphoma develops as a tumor mass and grows more rapidly than nodal lymphoma. The tumor can grow to a gigantic size.

Similarly to other tumors, cardiac malignant lymphoma develops asymptomatically and has non-characteristic symptoms such as shortness of breath. Some cases show symptoms of exertional dyspnea, palpitation, syncope, acute heart failure due to atrioventricular block [5~7], and supraventricular arrhythmia such as

atrial fibrillation (as in the current case) and right ventricular failure[8]. Sonoda et al. also reported complete atrioventricular block and superior vena cava syndrome in a patient with giant cardiogenic malignant lymphoma[9]. Cancer is a major risk factors for thrombotic pulmonary embolism[10] and a fatal case of developing pulmonary embolism has been reported[11], but there has been no previous report of cardiac malignant lymphoma complicated with cerebral embolism induced by paroximal atrial fibrillation.

In our case, chest X-ray demonstrated moderate cardiomegaly on the right cardiac side[12]. Transthoracic and transesophageal echocardiography (TEE)[6,13], chest CT and MRI are useful for diagnosis[5,7,12,14], and FDG-PET is effective for examination of metastasis and pathologic conditions[3,15]. Tumor biopsy is essential for definite diagnosis and selection of therapy to confirm whether the lymphoma is highly responsive to chemotherapy and is curable[6,8,12]. Patients have been treated with chemotherapy such as CHOP therapy consisting of cyclophosphamide, adriamycin, vincristine and prednisolone[8,13]. The patient in our case was treated with THP-COP therapy due to her age and this treatment was successful. Other therapeutic methods have been reported, including use of Rituximab-CHOP therapy with addition of an anti-CD20 monoclonal antibody[14] and combination therapy of Rituximab-CHOP and high-dose chemotherapy with autologous peripheral blood stem cell transplantation[15].

Right atrial lymphoma is often accompanied by arrhythmia, as mentioned above, and may damage the stimulus-conducting system by infiltration of atrial tumors into the atrial muscle. Therefore, the system cannot be restored completely in many cases, even after remission of lymphoma. In our case, ectopic atrial rhythm is present currently and we plan a complete follow-up observation of the patient. Primary cardiac malignant lymphoma has also recently been associated with post-transplantation and human immunodeficient virus (HIV) infection[16], suggesting that this disease may occur in several different contexts. Therefore, we report our case as an example of the importance of early diagnosis and prompt treatment of patients with progressive cardiac lymphoma.

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REFERENCES

1) Sutcliffe SB and Gospodarowicz MK. : Primary extranodal lymphomas. in "The Lymphomas". ed by Canellos GP, Lister TA, Sklar JL. Saunders ; Philadelphia, PA. pp449-479, 1998.
2) McManus B and Lee C-H. : Primary Tumor of the Heart. in "Braunwald's Heart Disease. A Textbook of Cardiovascular Medicine. 8th" ed by Libby P, Bonow RO, Mann DL, Zipes DP, Braunwald E. Saunders Elsevier, Philadelphia, PA. pp1815-1828, 2008.
3) Mandysová E, Neužil P, Niederle P, et al : Pulmonary stenosis caused by external compression of non-Hodgkin lymphoma. Echocardiography, **21** : 565-567, 2004.
4) Toko H, Terasaki F, Kawakami Y, et al : A case of malignant lymphoma with diastolic heart failure. Jpn Cir J, **62** : 863-867, 1998.
5) Fujisaki J, Tanaka T, Kato J, et al : Primary cardiac lymphoma presenting clinically as restrictive cardiomyopathy. Circ J, **69** : 249-252, 2005.
6) Tighe DA, Anene CA, Bousou JA, et al : Primary cardiac lymphoma. Echocardiography, **17** : 345-347, 2000.
7) Engelen MA, Juergens K, Breithardt G, Eckardt L. : Interatrial conduction delay and atrioventricular block due to primary cardiac lymphoma. J Cardiovas Electrophysiol, **16** : 926, 2005.
8) Kuo L-T, Hung M-J, Wang C-H, Cherng W-J. : Malignant lymphoma presenting as right heart failure. Echocardiography, **17** : 49-51, 2000.
9) Sonoda H, Jouo K, Umesue M, et al : A case of primary cardiac lymphoma with complete atrio-ventricular block and superior vena cava syndrome. Jpn J Cardiovasc Surg, **35** : 264-267, 2006 (in Japanese with English abstract).
10) Sakuma M, Fukui S, Nakamura M, et al : Cancer and pulmonary embolism —Thrombotic embolism, tumor embolism, and tumor invasion into a large vein—. Circ J, **70** : 744-749, 2006.

11) Skalidis EI, Parthenakis FI, Zacharis EA, et al : Pulmonary tumor embolism from primary cardiac B-cell lymphoma. Chest, **116** : 1489-1490, 1999.
12) Nakagawa Y, Ikeda U, Hirose M, et al : Successful treatment of primary cardiac lymphoma with monoclonal CD20 antibodie (Rituximab). Circ J, **68** : 172-173, 2004.
13) Kang S-M, Rim S-J, Chang H-J, et al : Primary cardiac lymphoma diagnosed by transvenous biopsy under transesophageal echocardiographic guidance and treated with systemic chemotherapy. Echocardiography, **20** : 101-103, 2003.
14) Faganello G, Belham M, Thaman R, et al : A case of primary cardiac lymphoma : Analysis of the role of echocardiography in early diagnosis. Echocardiography, **24** : 889-892, 2007.
15) Nonami A, Takenaka K, Kamezaki K, et al : Successful treatment of primary cardiac lymphoma by Rituximab-CHOP and high-dose chemotherapy with autologous peripheral blood stem cell transplantation. Int J Hematol, **85** : 264-266, 2007.
16) Iwahashi N, Nakatani S, Kakuchi H, et al : Cardiac tumor as an initial manifestation of acquired immunodeficiency syndrome. Circ J, **69** : 243-245, 2005.