Circ J 2004; **68:** 172 – 173

Successful Treatment of Primary Cardiac Lymphoma With Monoclonal CD20 Antibody (Rituximab)

Yukinori Nakagawa, MD; Uichi Ikeda, MD; Masahiro Hirose, MD; Satoshi Ubukata, MD; Taka-aki Katsuki, MD; Yuichiro Kaminishi, MD*; Tsutomu Saito, MD*; Mitsugu Hironaka, MD**; Tohru Izumi, MD†; Kazuyuki Shimada, MD

Primary cardiac malignant lymphoma is extremely rare and almost all patients die within weeks. Monoclonal CD20 antibody (rituximab) was administered to a patient with primary cardiac B-cell non-Hodgkin's lymphoma expressing a CD20 molecule. The results suggest that rituximab may be a safe and effective new therapy for primary cardiac B-cell lymphoma. (*Circ J* 2004; **68:** 172 – 173)

Key Words: Antibody; B cells; Cardiac tumor; Lymphoma

Primary cardiac malignant lymphoma, which is defined as a lymphoma involving only the heart or pericardium, is extremely rare. Patients may present with signs of heart failure, cardiac tamponade, or arrhythmias, depending on the site of the tumor, and tumors are rarely detected before death! Almost all patients die within weeks. We report a case of primary cardiac B-cell non-Hodgkin's lymphoma in which lymphoma cells expressed a CD20 molecule and the patient was treated successfully with monoclonal CD20 antibody (rituximab).

Case Report

A 42-year-old man was referred to Jichi Medical School Hospital in July 2001 for further examination of cardiomegaly. On admission, his blood pressure was 140/60 mmHg with an irregular pulse rate of 56 beats/min. There was no peripheral lymphadenopathy or hepatosplenomegaly. Heart murmurs and lung rales were not heard. Biochemical tests were normal, except for elevated concentrations of uric acid (8.6 mg/dl) and γ-glutamyltranspeptidase (253 mU/ml). Electrocardiography on admission showed atrial fibrillation, and the chest X-ray demonstrated moderate cardiomegaly (cardio-thoracic ratio of 67%). Echocardiography and chest magnetic resonance imaging revealed a giant abnormal mass in the antero-lateral and posterior walls of the left ventricle and the posterior wall of the right ventricle, with massive pericardial effusion. Chest computed tomography showed no abnormal lymph node swelling (Fig 1). Abnormal uptake of gallium was detected in the right and left sides of the heart (Fig 2), but not outside the heart. Cytology of the pericardial effusion revealed no abnormal findings (class II).

Despite conducting several minimally invasive examinations, we were not able to diagnose the cardiac mass lesion and so we performed an open biopsy of the lesion. On pathological examination, diffuse large-type lymphoid cells were observed, which were positive for the B-cell marker CD20 (Fig 3). Bone marrow aspiration and biopsy showed no infiltration of the lymphoma cells.

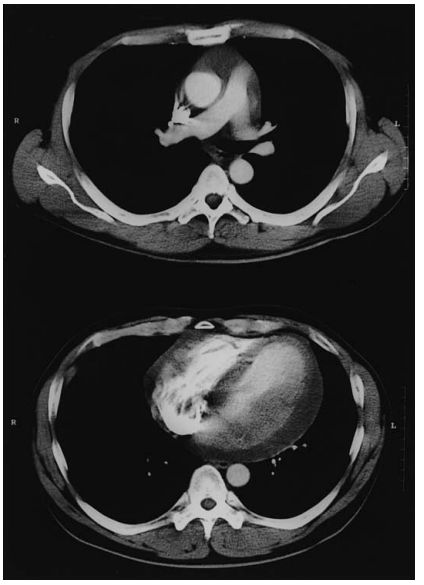

Fig 1. Chest computed tomography showed no abnormal lymph node swelling with the massive pericardial effusion.

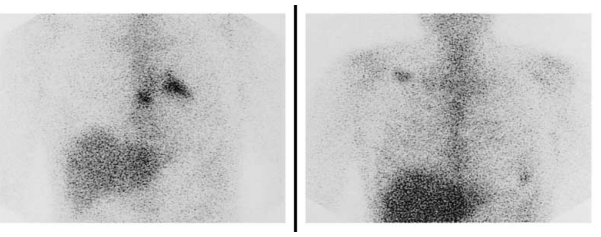

Fig 2. Gallium scintigraphy on admission (Left panel) and 6 months after 4 cycles of treatment with rituximab (Right panel). The abnormal uptake seen in the left and right sides of the heart on admission had almost disappeared after the treatment.

(Received May 29, 2002; revised manuscript received July 12, 2002; accepted July 23, 2002)
*Divisions of Cardiovascular Medicine, *Cardiovascular Surgery, **Pathology, and †Hematology, Jichi Medical School, Tochigi, Japan*
Mailing address: Uichi Ikeda, MD, Department of Organ Regeneration, Shinshu University Graduate School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan. E-mail: uikeda@sch.md.shinshu-u.ac.jp

In October 2001, after informed consent was obtained from the patient, a 4-cycle administration of standard doses (375 mg/m^2) of the monoclonal CD20 antibody rituximab was started. The only complication of the therapy was a low-grade fever after the first injection. After 4 cycles of the rituximab therapy, echocardiography showed a marked reduction of the mass volume of the tumor, and the abnormal uptake of gallium scan in the heart had almost disappeared. The patient was discharged in good general health in December 2001, and remains in remission 6 months later (Fig 2). Careful follow-up examinations will continue.

Discussion

Primary cardiac lymphoma diagnosed antemortem is extremely rare, accounting for only 1.3% of primary cardiac tumors[2] In a review of 12,485 autopsies, there were only 7 cases of primary cardiac tumors with an autopsy incidence of primary cardiac tumors of 0.056%, and yet none of the 7 was lymphoma[3] In 21 reported cases of cardiac lymphoma, only 5 were diagnosed before death[4] Most cases of primary cardiac lymphoma present with signs of heart failure, conduction disturbances, arrhythmias, cardiac tamponade or superior vena cava syndrome. The antemortem diagnosis of primary cardiac lymphoma is very difficult and there has not been effective therapy for this disease.

Rituximab is a monoclonal antibody directed against CD20 and frequently induces regression in a variety of B-cell non-Hodgkin's lymphomas[5,6] Its mechanism of action seems to involve induction of antibody-dependent, cell-mediated cytotoxicity, complement-mediated lysis, phagocytosis of antibody-coupled tumor cells, and induction of apoptosis. The clinical response to rituximab is dependent on the lymphoma subtype and response rates are higher (up to 70%) for newly diagnosed patients treated with rituximab monotherapy.

Rituximab therapy is effective for CD20-positive lymphoma with the advantage of few serious complications. Adverse systemic events are seen in approximately 90% of patients, but are mainly associated with the first infusion and comprise fever, shivering, headaches, eruptions, tachycardia, nausea, leukocytopenia and liver dysfunction. The side effects become less frequent during subsequent infusions and in the present case, rutiximab was well tolerated.

To the best of our knowledge, this is the first report of the administration of rituximab to a patient with primary cardiac lymphoma. We have shown that rituximab can be a safe and effective new therapy for primary cardiac B-cell lymphoma.

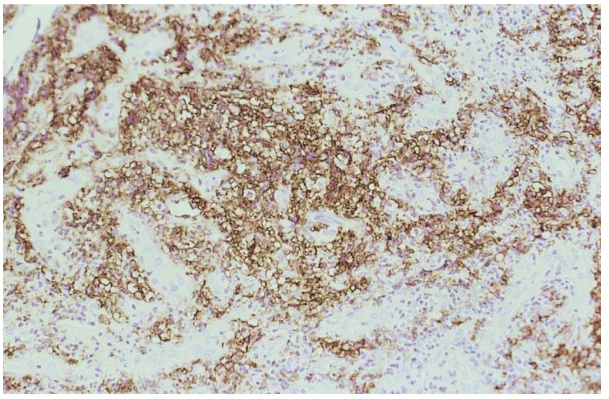

Fig 3. Histological section of the biopsy specimen. Medium-sized and atypical lymphoid cells diffusely proliferated. Immunohistochemical studies with CD20 antibody indicated that the lymphoma cells were CD20-positive B-cells (×100).

References

1. Miyashita T, Miyazawa I, Kawaguchi T, Kasai T, Yamaura T, Ito T, et al. A case of primary cardiac B cell lymphoma associated with ventricular tachycardia, successfully treated with systemic chemotherapy and radiotherapy: A long-term survival case. *Jpn Circ J* 2000; **64:** 135–138.
2. Ceresoli GL, Ferreri AJM, Bucci E, Ripa C, Ponzoni M, Villa E. Primary cardiac lymphoma in immunocompetent patients: Diagnostic and therapeutic management. *Cancer* 1997; **80:** 1497–1506.
3. Lam KY, Dickens P, Chan ACL. Tumors of the heart: A 20-year experience with a review of 12,485 consecutive autopsies. *Arch Pathol Lab Med* 1993; **117:** 1027–1031.
4. Roller MB, Manoharan A, Lvoff R. Primary cardiac lymphoma. *Acta Haematol* 1991; **85:** 47–48.
5. McLaughlin P, Grillo-Lopez AJ, Link BK, Levy R, Czuczman MS, Williams ME, et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: Half of patients respond to a four-dose treatment program. *J Clin Oncol* 1998; **16:** 2825–2833.
6. Coiffier B, Haioun C, Ketterer N, Engert A, Tilly H, Ma D, et al. Rituximab (anti-CD20 monoclonal antibody) for the treatment of patients with relapsing or refractory aggressive lymphoma: A multicenter phase II study. *Blood* 1998; **92:** 1927–1932.