CASE REPORT

Efficacy of Rituximab Monotherapy for an Elderly Hemodialysis Patient with Primary Cardiac Lymphoma

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**Abstract**

We report a case of primary cardiac lymphoma (PCL) occurring in a 76-year-old man during maintenance hemodialysis. Chest computed tomography (CT) revealed a tumor with pericardial effusion in the left ventricular posterior wall. Cytological examination of the pericardial fluid revealed monotonous lymphoid cells positive for B-cell markers, and clonal immunoglobulin heavy chain gene rearrangement was detected, indicating B-cell lymphoma. Rituximab monotherapy was administered biweekly at the therapeutic level on hemodialysis. The follow-up chest CT showed tumor disappearance with pericardial fluid after two courses of therapy. Rituximab monotherapy was effective for an elderly hemodialysis patient with PCL.

**Key words:** primary cardiac lymphoma, chronic renal failure, rituximab monotherapy, serum rituximab level

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**Introduction**

Primary cardiac lymphoma (PCL) is a rare extranodal non-Hodgkin’s lymphoma (NHL) exclusively located in the heart and/or pericardium with no evidence of extracardiac dissemination (1). This disease accounts for only 1.3% of cardiac tumors and 0.5% of extranodal lymphomas (2). Histopathologic diagnosis is important as it influences treatment and prognosis; however, a definitive diagnosis is not always easy to make from biopsy specimens (3). In some cases, open chest biopsy is difficult to perform especially for older patients. On the other hand, rituximab, a chimeric monoclonal antibody that binds to CD20 antigen, is highly active and well tolerated as a first-line single-agent therapy for indolent NHL (4, 5). Moreover, rituximab monotherapy administered every two weeks has been proven to be highly effective for an older patient with intravascular lymphoma after chemotherapy (6). Here, we report a rare case of PCL in an elderly patient with chronic renal failure (CRF) on hemodialysis who was successfully treated with rituximab monotherapy.

**Case Report**

A 76-year-old man was referred to our hospital in February 2006 because of a mass and fluid retention in the pericardium. The patient was receiving hemodialysis three times a week having developed CRF 5 years previously. While on hemodialysis in the previous hospital, he developed sudden dyspnea due to fluid retention in the pericardium which was detected on ultrasonic cardiography. During pericardial drainage at the previous hospital, he developed no serious cardiovascular or respiratory symptoms. He was transferred to our hospital with the following clinical data: blood pressure, 120/72 mmHg; heart rate, 78 beats/min; oxygen saturation, 98% in room air. He had a performance status (PS) of 3 and was in wheelchair. Chest computed tomography (CT) revealed a mass (6.6x5.4 cm) in the pericardium over the left ventricle, with no enlargement of lymph nodes around

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Figure 1. Diagnostic imaging of primary cardiac lymphoma (PCL). (A) Chest computed tomography (CT) revealed a large mass (arrow) occupying the left ventricular posterior wall (LVPW) before rituximab monotherapy. (B) Transthoracic echocardiography detected an echo free space (arrow), which showed pericardial effusion. (C) Cytological analysis of pericardial fluid revealed an increased number of large lymphoid cells with irregular nuclei (Wright-Giemsa staining, ×400). (D) Expression of CD10, CD79α, CD10, CD20, and CD3 in pericardial fluid as demonstrated by flow cytometric analysis. The number of upper-right corner indicates % positive rate for isotopic antibody. CD: cluster differentiation, FSC: forward scatter, SSC: side scatter. (E) Immunoglobulin heavy chain (IgH) gene rearrangements in pericardial fluid as shown by Southern blotting analysis. The cells were digested with BamHI+HindIII (1) or HindIII (2). The arrows indicate IgH gene rearrangements. (F) Chest CT demonstrated disappearance of the mass (arrow) occupying the LVPW following rituximab monotherapy. RA: right atrium, RV: right ventricle, LA: left atrium, LV: left ventricle, Ao: aorta.

the aorta or trachea or axillary lymph nodes (Fig. 1A). Neck to pelvis CT also revealed no lesions, including nodal lesions, other than the pericardial lesion, suggesting a primary cardiac tumor. Transthoracic echocardiography showed an echo free space in the left ventricular posterior wall (LVPW) suggestive of pericardial effusion (Fig. 1B). Following pericardiocentesis in our hospital, we attempted to confirm a diagnosis of malignant lymphoma based on indirect evidence through morphologic evaluation, use of cell surface markers, and monoclonality of the cytologic specimen. This procedure was adopted because tissue biopsy of the mass in the LVPW was technically difficult and performing thoracotomy in this elderly patient seemed too risky. Cytologic analysis of pericardial fluid revealed increased number of large lymphoid cells with irregular nuclei (Fig. 1C). These cells were positive for CD10, CD19, CD20, CD79α, and negative for CD3 as shown by flow cytometric analysis (Fig. 1D). Moreover, clonal immunoglobulin heavy chain gene rearrangement was detected, indicating B-cell lymphoma (Fig. 1E). Cytogenetic analysis of lymphoma cells from pericardial
Table 1. Serum Rituximab Levels on Hemodialysis

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Patient</th>
<th>Control patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>78.9</td>
<td>30.9</td>
</tr>
<tr>
<td>4</td>
<td>289.3</td>
<td>168.8</td>
</tr>
<tr>
<td>6</td>
<td>324.0</td>
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<td>216.2</td>
<td>150.1</td>
</tr>
<tr>
<td>24</td>
<td>201.3</td>
<td>145.8</td>
</tr>
<tr>
<td>48</td>
<td>141.1</td>
<td>115.6</td>
</tr>
</tbody>
</table>

The rituximab level during hemodialysis in the present patient was compared with that in a control diffuse large B-cell lymphoma (DLBCL) patient with normal renal function. In both patients, rituximab was administered at the same time on the same day, and blood samples were collected at the same time points. Hemodialysis was performed for 4 hours on the first day. The start time of hemodialysis was 1 hour after rituximab administration.

Ceresoli et al reported that cardiac metastasis of malignant lymphoma, as well as a majority of cases of PCL, commonly occurs on the right side of the heart (10). Although the localization of the cardiac tumor was not determined histologically, the present case was a very rare case of PCL localized on the left side of the heart as determined by imaging modalities. PCL is classified mainly as DLBCL (60%-81% of cases) and less frequently as immunoblastic, Burkitt type, or lymphoblastic lymphoma. In more than 90% of cases, lymphoma cells belong to the B-cell lineage (11).

In the present case, since cardiac tumor biopsy via thoracotomy seemed risky in this elderly patient with concomitant morbidity, biopsy was not performed, and the diagnosis of B-cell lymphoma was made by examination of morphologic, cell surface markers, and monoclonality of the cytologic specimen (12). In Japan, only 2 case reports of PCL in the pericardium with no lesions in the myocardium have been reported to date (13).

PCL is considered to have a poor prognosis with a median survival time of 7 months (14). Due to the limited number of cases, no standard therapy has yet been established. However, it has been suggested that PCL should be treated similar to other bulky aggressive NHLs (10). Therefore, we recommended rituximab-containing combination chemotherapy with an anthracycline as the key drug (THP-COP therapy) for the patient. However, the patient refused this combination chemotherapy. Nakagawa et al showed that rituximab monotherapy was safe and effective for primary cardiac B-cell lymphoma (15). In the present case, the patient received rituximab monotherapy at 375 mg/m² biweekly on hemodialysis. The blood level of rituximab during hemodialysis was maintained at a higher level than that in a DLBCL patient with normal renal function, with the peak level reached 6 hours after administration, followed by a similar pharmacokinetic pattern as that in the control pa-
tient. Jillella et al (8) measured the blood level of rituximab before and after each hemodialysis course and showed that rituximab was not removed by hemodialysis. Our data not only support their finding but also provide very valuable information including detailed pharmacokinetic measurements from the start to 48 hours after administration.

The standard treatment for PCL has not yet been established. This case has provided valuable data demonstrating that the mean survival time can be prolonged with rituximab monotherapy. Also, rituximab monotherapy is safe and effective for patients with primary cardiac B-cell lymphoma who are unable to receive chemotherapy because of advanced age and maintenance hemodialysis.

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References