Precursor B-lymphoblastic Lymphoma Involving an Intracardiac Mass and Myocardial Infiltration: A Case Report

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Abstract

We report the case of a 17-year-old man with precursor B-lymphoblastic lymphoma involving an intracardiac mass and myocardial infiltration. Intensified chemotherapy followed by autologous peripheral blood stem cell transplantation resulted in long-term complete remission for over 5 years. As the most frequent sites of B-lymphoblastic lymphoma involvement are the skin, soft tissue, bone, and lymph nodes, reports of cases harboring cardiac involvement are relatively few. This is a rare case of B-lymphoblastic lymphoma displaying cardiac involvement, in which cardiac infiltration was one of the initial manifestations.

Key words: precursor B-lymphoblastic lymphoma, cardiac mass, myocardial infiltration, autologous stem cell transplantation

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Introduction

B lymphoblastic lymphoma (LBL) is a neoplasm affecting precursor lymphoblasts that have committed to the B-cell lineage; it accounts for approximately 10% of LBL (1). The most frequent sites of B-LBL involvement are the skin, soft tissue, bone, and lymph nodes (2, 3); only a few cases displaying cardiac involvement have been reported.

Here, we present a B-LBL case involving an intracardiac mass and myocardial infiltration that was successfully treated with intensified chemotherapy including autologous peripheral blood stem cell transplantation (aPBSCT).

Case Report

A 17-year-old man with a one-month history of chest pain and shortness of breath on exertion was referred to our hospital in July 2005. On admission, he was subfebrile, with a pulse rate of 88/min and a blood pressure of 112/68 mmHg. He was not suffering from hypoxemia. A physical examination detected a systolic murmur, but no lymph node swelling or skin rashes were found. His laboratory values on admission included a white blood cell count of 6,960/μL (76% polymorphonuclear leukocytes, 20% lymphocytes, 3% monocytes, and 1% eosinophils), a hemoglobin concentration of 14.6 g/dL, and a platelet count of 22.8×10⁴/μL. His lactate dehydrogenase level was 189 IU/L, and his soluble IL-2 receptor level was 770 U/mL (normal range 135-483 U/mL). A urine dipstick indicated neither proteinuria nor glycosuria, and the specific gravity of his urine sample was 1.016. Electrocardiography (ECG) demonstrated a regular sinus rhythm with inverted T waves in the I, aV₁, and V₅-₆ leads (Fig. 1A). In addition, transthoracic echocardiography revealed a hypoechogenic mass lesion measuring 51×68 mm and a thickened hypoechogenic ventricular wall demonstrating...
mild hypokinesis. The thickening was especially marked in the posterior wall, where it displayed a focal distribution, probably due to the invasion of the mass (Fig. 2A, B). Computed tomography demonstrated abnormal masses in the right atrium, pancreas, twelfth thoracic vertebral bone, and bilateral kidneys. In the heart, the mass produced focal bulging in the right atrium and was uniformly enhanced on computed tomography (Fig. 2C). 18F-Fluorodeoxyglucose-positron emission tomography (FDG-PET) detected a strong accumulation in the same organs as computed tomography. A bone marrow examination revealed no evidence of bone marrow involvement. Surgical biopsy of the kidney was performed and demonstrated the diffuse proliferation of medium-sized cells with irregular nuclei (Fig. 3). Immunohistochemical tests were positive for CD10, CD79a, MIC2, and TdT and negative for CD3, UCHL-1, CD56, and CD34. Southern blot analysis of the surgical biopsy specimen showed gene rearrangement of the immunoglobulin H chain; on the other hand, no gene reconstitution of the T-cell receptor Cβ chain was seen. A diagnosis of precursor B-LBL was made. As his left ventricle (LV) ejection fraction was relatively well maintained (61%) and only focal asynergy was noted, the patient was administered induction chemotherapy without any dose reduction, involving 1,200 mg/m² cyclophosphamide on day 1; 60 mg/m² daunorubicin on day 12 to 13; 1.4 mg/m² (up to 2.0 mg) vincristine on day 3, 10, 17 and 24; 60 mg prednisolone on days 1 to 28; and 12 mg/m² intrathecal methotrexate on day 4, 31, and 35 [based on the modified LSA2L2 protocol (4)]. After induction chemotherapy, he achieved a partial response, and his chest pain and dyspnea on exertion disappeared. Echocardiography showed that the mass had reduced to 14×29 mm. Thereafter, the patient underwent consolidative chemotherapy involving 100 mg/m² cytosine arabinoside on days 1 to 5 and days 8 to 12, 50 mg/m² 6-mercaptopurine on days 1 to 5 and days 8 to 12, 6,000 IU/m² L-asparaginase on days 22 to 35 (7 doses were skipped due to serum ammonium elevation), 60 mg/m² ranimustine on day 44 and 12 mg/m² intrathecal methotrexate on days 35 and 41, which resulted in the disappearance of the remaining tumor: i.e., an echocardiogram and computed tomography showed that the mass had disappeared, that the patient’s thickened LV wall had normalized (Fig. 2D, E, F), and that his LV function had improved without asynergy. On ECG, we found that the inverted T waves observed in the I, aVL, and V₄-₆ leads had disappeared (Fig. 1B). Then, aPBSCT followed by conditioning chemotherapy involving 300 mg/m² ranimustine on days -8 and -3, 300 mg/m² carboplatin on days -7 to -4, 500 mg/m² etoposide on days -6 to -4, and 50 mg/kg cyclophosphamide on day -3 and -2 [the MCEC regimen (5)] was performed (Fig. 4). There has been no evidence of relapse for 5 years since the transplant, and the patient has remained free of symptoms including LV dysfunction.

Discussion

In the past, most cases involving lymphoma infiltration into the myocardium were diagnosed during autopsy (6). However, such cases are now typically diagnosed antemortem due to the recent progress in diagnostic technology. Although cardiac lymphoma is classified into primary cardiac lymphoma and secondary cardiac infiltration, secondary infiltration into the heart is seen in about 20% of cases that display lymphoma at autopsy (7) and it is more frequent than primary cardiac lymphoma, which represents 1.3% of primary cardiac tumors (8).

Precursor B-LBL is estimated to account for about 10% of all LBL cases, and it is most commonly found in the skin, bone, and soft tissue at diagnosis. Previous studies reported that patients with B-LBL displayed involvement at various extranodal sites such as the breast, colon, stomach, ovary, pancreas, or kidney (2, 3, 9). However, cases of B-

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Figure 1. (A) Electrocardiography on admission detected negative T waves in leads I, aV₆, and V₄-₆. (B) After consolidative chemotherapy, the abnormal T waves disappeared.
FIGURE 2. (A) The parasternal long-axis view showed a mass lesion (*asterisk*) and a thickened ventricular wall (arrow) at the initial diagnosis. (B) The parasternal short-axis view showed a markedly thickened left ventricular myocardium. (C) The computed tomography revealed an enhanced mass in the right atrium. (D-F) After consolidative chemotherapy, the mass disappeared, and his ventricular thickening was almost normalized.

LBL involving cardiac infiltration are relatively rare (10-14). Furthermore, not only in LBL patients but also in those with other lymphomas, it is rare for cardiac involvement to be present at the initial presentation (15); rather, cardiac involvement is usually a late manifestation of lymphoma with a median onset of 20 months after the initial diagnosis (16). Further accumulation of cases is necessary to evaluate whether cardiac involvement is truly rare in LBL or rather it is under-recognized.

As for its manifestations, the cardiac infiltration of lymphoma is complicated by a variety of symptoms such as congestive heart failure, arrhythmia, heart rupture, chest pain, and dyspnea. The present patient suffered from chest pain and shortness of breath on exertion. As his LV ejection fraction was only slightly reduced but echocardiography displayed LV wall thickening even at rest, we thought that his symptoms might have been caused by myocardial ischemia, resulting in a falling ejection fraction on effort. On the other hand, cases involving a mediastinal mass or pericardial effusion present with similar symptoms and are associated with latent cardiovascular events, which can cause sudden death. Hence, from the clinical point of view, it is important that clinicians are aware of any cardiac, pericardial, or mediastinal involvement when patients present with the above-mentioned symptoms.

Concerning treatment, LBL patients tend to be treated...
with an acute lymphoblastic leukemia (ALL)-type regimen because LBL is clinically aggressive and is similar to ALL in many aspects. A long-term disease-free survival rate of about 40% to 60% has been reported in LBL patients after intensive chemotherapy, such as treatment with the LSA-L2 protocol (4), which consists of several cytotoxic agents. As for transplantation, many institutions prefer allogeneic stem cell transplantation (SCT) to autologous SCT because of the aggressiveness of the disease. However, it was reported that survival did not significantly differ between patients treated with allogeneic SCT and those treated with autologous SCT (5-years overall survival: 39% versus 44%, p=0.47) because allogeneic SCT is associated with fewer relapses than autologous SCT, but its higher treatment-related mortality offsets any potential survival benefit (17). Furthermore, it was also reported that bone marrow involvement at SCT was associated with inferior outcomes (17). In a previous comparison of autologous SCT and conventional consolidative chemotherapy, although no significant difference was seen because of the small size of the trial, the use of autologous SCT in the first remission resulted in a trend towards improved 3-year relapse-free survival (55% versus 24%, p=0.065) (18). The present patient displayed no evidence of bone marrow invasion, and autologous SCT resulted in
long-term remission. Therefore, powerful modalities including autologous SCT might be a suitable treatment for LBL patients with advanced stage disease, such as extranodal disease without bone marrow invasion.

The authors state that they have no Conflict of Interest (COI).

References