


**CASE REPORT**

# Cardiac biopsy with intracardiac echocardiographic guidance for successful diagnosis of cardiac lymphoma

Seiichiro Katagiri<sup>1</sup>  | Daigo Akahane<sup>1</sup> | Tamiko Suguro<sup>1</sup> |  
 Nahoko Furuya<sup>1</sup> | Hiroaki Fujimoto<sup>1</sup> | Tetsushi Saito<sup>2</sup> | Jun Yamashita<sup>2</sup> |  
 Naoya Nakamura<sup>3</sup> | Kazuma Ohyashiki<sup>1</sup>

<sup>1</sup>Department of Hematology, Tokyo Medical University, Tokyo, Japan

<sup>2</sup>Department of Cardiology, Tokyo Medical University, Tokyo, Japan

<sup>3</sup>Department of Pathology, Tokai University School of Medicine, Kanagawa, Japan

**Correspondence**

Seiichiro Katagiri, Department of Hematology, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan (patchsei@yahoo.co.jp).

**Key Clinical Message**

The diagnosis and appropriate treatment of cardiac lymphoma are often delayed by the difficulty in obtaining heart tissue biopsies. Intracardiac echocardiography-guided biopsy can improve the prognosis of cardiac lymphoma by decreasing post-biopsy complications and increasing biopsy quality, allowing collection of sufficient material for multilateral analysis.

**KEYWORDS**

cardiac lymphoma, flow cytometric analysis, intracardiac echocardiography-guided biopsy

## 1 | INTRODUCTION

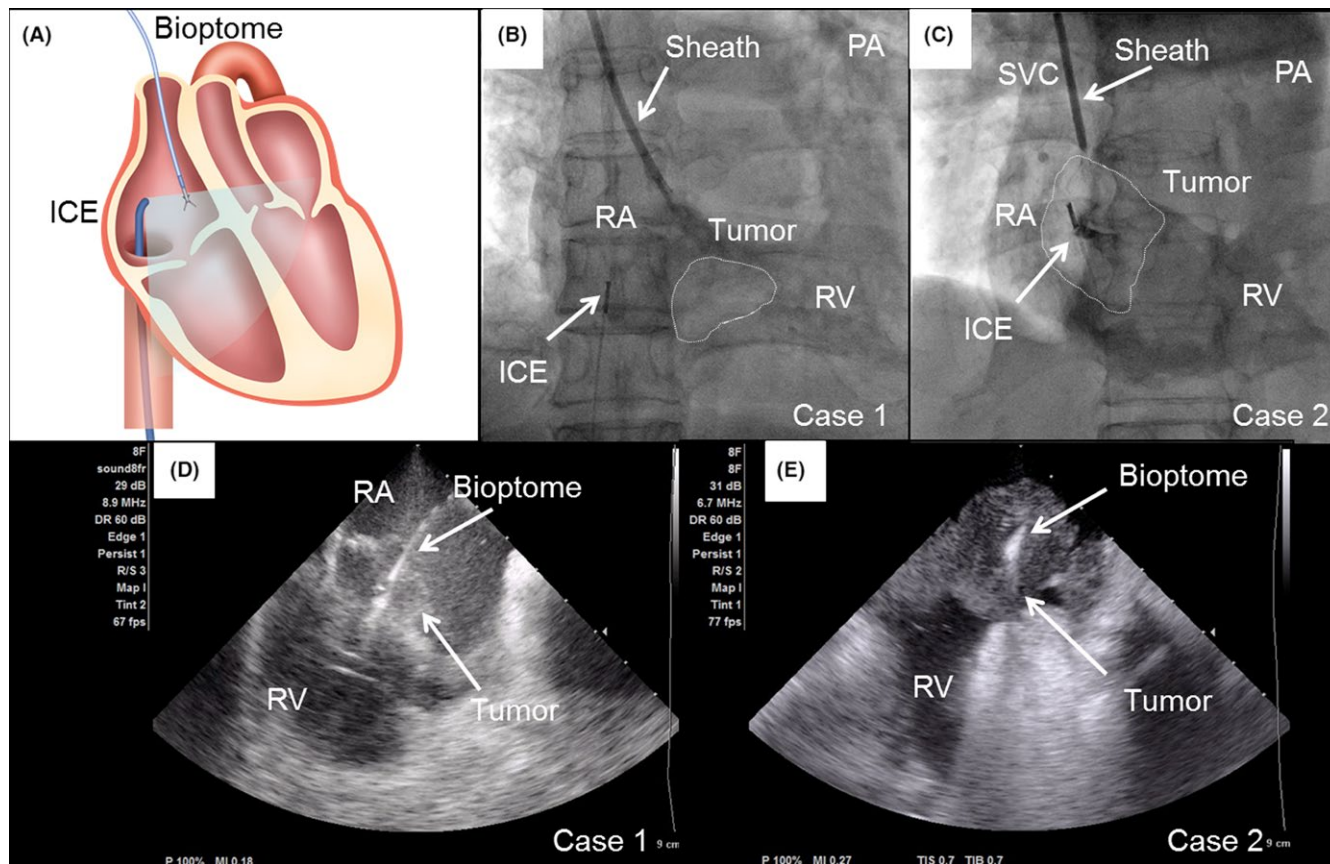
We present two cases in whom endomyocardial biopsy (EMB) was performed safely using intracardiac echocardiography (ICE), allowing collection of sufficient material for multilateral analysis. These findings indicate that ICE-guided biopsy can improve the prognosis of patients with cardiac lymphoma by decreasing postbiopsy complications compared with surgery and by increasing biopsy quality compared with non-ICE-guided EMB procedures.

Primary cardiac lymphoma (PCL) is rare, with an incidence of 0.1%-0.28% according to autopsy reports.<sup>1</sup> As approximately 30%-50% of patients with cardiac lymphoma demonstrate dyspnea, arrhythmia, and heart failure at onset,<sup>2-4</sup> early diagnosis and appropriate chemotherapy are important to improve prognosis. However, the diagnosis of cardiac lymphoma and appropriate treatment is often delayed by the difficulty in obtaining heart tissue biopsies. ICE using a guide for noncoronary interventional procedures can clearly show intracardiac structures and help with EMB.<sup>5</sup> Herein, we report the details of two patients with cardiac lymphoma in whom we successfully obtained early diagnosis

by ICE-guided biopsy with histological and flow cytometric analyses.

## 2 | CASE REPORTS

Case 1 was a 68-year-old woman admitted to hospital with a chief complaint of dyspnea and pretibial pitting edema. Chest X-ray showed cardiomegaly (cardiothoracic ratio: 60%). Transesophageal echocardiography (TEE) showed a 6 × 7 cm right atrium (RA) tumor, while contrast-enhanced computed tomography (CT) showed a cardiac tumor protruding into the RA and right ventricle (RV) wall. As our facility did not have positron emission tomography-CT, gallium scintigraphy was performed and showed increased gallium uptake in the cardiac tumor and mediastinal lymph node. Blood tests revealed elevated levels of serum lactate dehydrogenase (1170 U/L; normal range: 120-240 U/L), soluble interleukin-2 receptor (2760 U/mL; normal range: 145-519 U/mL), and brain natriuretic peptide (91.6 pg/mL). Her hemoglobin level was normal (12.2 g/dL). Case 2 was a 71-year-old woman treated for intraocular lymphoma who



**FIGURE 1** Intracardiac echocardiography-guided biopsy for cardiac lymphoma. A, Intracardiac echocardiography (ICE)-guided biopsy. B, C, Posteroanterior fluoroscopic images of both patients. D, E, ICE images of both patients. RA, right atrium; RV, right ventricle; PA, pulmonary artery; SVC, superior vena cava

had sustained complete remission for 5 years. She was admitted to hospital for atrial fibrillation. Transthoracic echocardiography showed a  $5 \times 6$  cm RA tumor and pericardial effusion. Contrast-enhanced CT also showed a cardiac tumor in the RA. Gallium scintigraphy showed increased gallium uptake in the cardiac tumor and perigastric lymph node. Her serum lactate dehydrogenase level was 390 U/L, soluble interleukin-2 receptor was 1240 U/mL, and brain natriuretic peptide was 32.7 pg/mL. Her hemoglobin level was normal (13.1 g/dL).

For diagnosis, we performed EMB using ICE under short-term heparinization in both patients. A biopptome and an ICE catheter were inserted into the RA via the right jugular vein and right femoral vein, respectively, using fluoroscopy (Figure 1A-C). The biopptome was directed toward the cardiac tumor under ICE image guidance (Figure 1D,E). In both cases, we obtained sufficient samples for flow cytometric, pathological, cytogenetic, and genetic analyses. Flow cytometry showed B-cell markers, including cluster of differentiation (CD) 19 and 20 with light-chain restriction, indicating cardiac B-cell lymphoma. Thus, we prescribed steroid therapy.

Case 1 was diagnosed with diffuse large B-cell lymphoma, which was positive for CD 20, CD10, Bcl-6, and

MUM-1, but negative for CD5, indicating germinal center B type. No metaphases were obtained in G-banding analysis. However, fluorescence in situ hybridization analysis revealed that the lymphoma was negative for *c-MYC* and *BCL-2* gene translocations. Case 2 was diagnosed with diffuse large B-cell lymphoma, which was positive for CD20, Bcl-6, and MUM-1, and negative for CD10 and CD5, indicating nongerminal center B type. Cytogenetic analysis of four metaphases revealed normal results for two and multiple abnormalities without *c-MYC* and *BCL-2* gene translocations for two. Bone marrow examination using pathological and flow cytometric analysis showed no bone marrow involvement in either case. Cerebrospinal fluid examination and magnetic resonance imaging also revealed no central nervous involvement in either case. We encountered no complications postbiopsy including thromboembolism. Case 1 received rituximab, cyclophosphamide, vincristine, and prednisolone, while Case 2 received rituximab, cyclophosphamide, pirarubicin, vincristine, and prednisolone. Following six cycles of rituximab-combined chemotherapy, the tumors were undetectable by imaging tests, including gallium scintigraphy and transthoracic echocardiography, in both patients.

### 3 | DISCUSSION

As approximately 95% of cardiac tumors are diagnosed as sarcoma, cardiac lymphoma is not usually suspected.<sup>6</sup> Previous reports suggest that only chemotherapy is able to improve prognosis of patients with cardiac lymphoma.<sup>4</sup> Thus, a less invasive biopsy approach is required for cardiac lymphoma diagnosis. Generally, biopsy of cardiac lymphoma is performed by surgical approaches, such as thoracotomy or thoracoscopic surgery.<sup>2,7</sup> However, these invasive approaches may delay treatment because of surgical invasion. As approximately 90% of PCL has either RA or right ventricular involvement,<sup>2-4</sup> a transvenous EMB approach is useful. Transvenous EMB is usually safely performed under fluoroscopic guidance, although obtaining sufficient samples for diverse analysis of tumor diagnosis can be difficult. Transvenous EMB under TEE is also useful,<sup>8</sup> but can cause discomfort and requires pharyngeal anesthesia. In our cases, we performed EMB safely and obtained sufficient material for histological and flow cytometric analyses using ICE. Flow cytometric analysis showed that the cardiac tumors had B-cell malignancy, allowing us to start chemotherapy immediately.

#### CONFLICT OF INTEREST

None declared.

#### AUTHORSHIP

SK: treated the patient and wrote the manuscript; DA, TS, NF, HF, TS, and JY: treated the patient and reviewed the manuscript; NN: performed pathological analysis and reviewed the manuscript; KO: treated the patient, reviewed the manuscript, and supervised the project.

#### ORCID

Seiichiro Katagiri  <http://orcid.org/0000-0002-3031-9990>

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