Ischemic Heart Disease Due to Compression of the Coronary Arteries by Malignant Lymphoma

Yuki Nagasako¹, Shun Akaeda¹, Fumitaka Yanase¹, Ryosuke Koyamada¹, Atsushi Mizuno², Takakazu Higuchi¹ and Sadamu Okada¹

Abstract

A 76-year-old man presented with a two-month history of angina pectoris. Computed tomography (CT) revealed a serial enlargement of the supraclavicular and mediastinal lymph nodes compressing the heart, pulmonary artery and aorta. CT angiography (CTA) showed stenosis of the coronary arteries as a result of compression by the enlarged lymph nodes. First-pass contrast-enhanced cardiac magnetic resonance imaging (MRI) at rest revealed a perfusion defect, thus indicating myocardial ischemia. Diffuse large B-cell lymphoma was diagnosed and multidrug combination chemotherapy led to prompt improvement of the symptoms. Relief of the stenosis in the coronary arteries and improvements in myocardial perfusion were noted on follow-up CTA and MRI.

Key words: malignant lymphoma, diffuse large B-cell lymphoma, cardiac magnetic resonance imaging, computed tomography angiography, ischemic heart disease

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Introduction

While primary cardiac lymphoma, defined as extranodal lymphoma involving the heart and/or pericardium only, is very rare (1), secondary cardiac involvement is found in approximately 10% of all patients with malignant lymphoma at autopsy (2). The clinical manifestations of lymphoma of the heart vary widely among patients and are generally non-specific or insufficient to allow for the recognition of cardiac involvement antemortem. Ischemic heart disease sometimes occurs after or during therapy for malignant lymphoma (3-5). However, patients with lymphoma very rarely present with symptoms of ischemic heart disease.

We herein report a rare case of malignant lymphoma in which the patient presented with symptoms of angina pectoris due to direct extension of the anterior mediastinal lymph nodes that compressed the coronary arteries. Non-invasive cardiac imaging was useful for both the diagnosis and follow-up of the patient.

Case Report

A 76-year-old man presented with aggravating chest pain and dyspnea on exertion with a duration of five to ten minutes that had started two months previously. He had undergone subtotal gastrectomy at the age of 48 for a duodenal ulcer. He had received interferon-α therapy for chronic hepatitis C when he was 57 years old. He was currently taking amlodipine for high blood pressure prescribed by his family doctor. At presentation, he was afebrile with a blood pressure of 152/84 mmHg and a heart rate of 83 beats per minute. A physical examination revealed multiple enlargement of the cervical and right supraclavicular lymph nodes up to 1.5 cm. The patient’s heart sounds were distant on auscultation.

An electrocardiogram (ECG) at rest showed negative T waves in II, III and aV₅ and flat T waves in V₅ and V₆ (Fig. 1). Chest X-ray revealed cardiomegaly, an enlargement of the right upper mediastinum and left hilar lymphadenopathy (Fig. 2). A complete blood count was normal. The blood chemistry revealed a lactate dehydrogenase level of 611 IU/
L (normal range: 118-223), an asparate aminotransferase level of 43 IU/L (normal range: 9-32), an alanine aminotransferase level of 23 IU/L (normal range: 3-38) and a creatine kinase level of 87 IU/L (normal range: 57-218). The serum troponin-T value was 0.017 ng/mL (normal range: 0-0.014), the B-type natriuretic peptide (BNP) level was 73.3 pg/mL (normal range: 0-18.4) and the N-terminal pro-BNP level was 712.9 pg/mL (normal range: <125.0). The soluble interleukin-2 receptor level was 2,380 U/mL (normal range: 124.0-466.0). Two-dimensional and doppler echocardiography showed preserved left ventricular contractions with mild diastolic dysfunction. Masses spreading from the right atrium to the aorta and pulmonary artery and a small amount of pericardial effusion were also noted. Computed tomography (CT) revealed the serial enlargement of the lymph nodes from the right supraclavicular region to the mediastinum that compressed the right atrium, right ventricle, pulmonary artery and aorta. CT angiography (CTA) showed the distal right, left main, proximal left descending and left circumflex coronary arteries to be encased and compressed by the enlarged mediastinal lymph nodes resulting in stenosis of the arteries (Fig. 3, left). First-pass contrast-enhanced cardiac magnetic resonance imaging (MRI) at rest revealed a perfusion defect involving the right ventricle and the inferior portion of the ventricular septum that indicated myocardial ischemia (Fig. 4). Delayed MRI imaging was negative, thus indicating that the viability of the myocardium was not impaired. A right supraclavicular lymph node biopsy was performed and diffuse large B-cell lymphoma was diagnosed. Further examinations failed to detect any lymphomatous lesions in any other sites and the clinical stage was judged to be IIA according to the Ann Arbor staging system.

Multidrug combination chemotherapy consisting of cyclophosphamide, pirarubicin, vindesine and prednisolone (THP-CVP) was started. The patient’s symptoms resolved promptly and the negative T waves in II, III and aVF on ECG became positive (Fig. 1). Two more courses of THP-CVP were given with rituximab followed by radiotherapy to the mediastinum. ECG showed further evolution of the ischemic changes during the course of the therapy (Fig. 1). CTA and cardiac MRI showed a marked reduction in the size of the mediastinal lymph nodes with improvement in the stenosis of the coronary arteries and the myocardial ischemia (Fig. 3, right). The patient is presently asymptomatic without any signs of recurrence of lymphoma nine months after the completion of the therapy.

**Discussion**

It is well known that patients with malignant lymphoma occasionally experience ischemic heart disease related to the therapies administered to treat the lymphoma. A causative link between radiation therapy to the mediastinum and coronary artery disease is well recognized in patients with Hodgkin lymphoma (3), and vinca alkaloids and granulocyte-
nodes (11, 12) have been reported. Lymphoma may cause myocardial injury caused by bulky masses (10) or compression resulting from intravascular lymphoma (9), direct compression of the coronary arteries by enlarged lymph nodes (6-8). Much rarer cases of ischemic heart disease related to the lymphoma itself. Lymphoma may cause such patients. The present case demonstrates the usefulness of non-invasive cardiac imaging in the management of ischemic heart disease, performing such invasive procedures is often not feasible in patients with lymphoma. The present case demonstrates the usefulness of non-invasive cardiac imaging in the management of such patients.

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

References
4. House KW, Simon SR, Pugh RP: Chemotherapy-induced myocardial stimulating factor, both of which are frequently given to lymphoma patients, are suggested to be associated with ischemic heart disease (4, 5). However, it is very rare that patients with lymphoma present with ischemic heart disease related to the lymphoma itself. Lymphoma may cause ischemic heart disease due to myocardial necrosis secondary to the direct invasion of the lymphoma into the myocardium (6-8). Much rarer cases of ischemic heart disease resulting from intravascular lymphoma (9), direct compression myocardial injury caused by bulky masses (10) or compression of the coronary arteries by enlarged lymph nodes (11, 12) have been reported.

While primary cardiac lymphoma is a very rare occurrence (1), secondary cardiac invasion to the heart and/or parietal pericardium is observed in approximately 10% of lymphoma patients at autopsy (2). Three patterns of cardiac spread have been suggested: retrograde lymphatic spread, hematogenous spread and direct extension from intrathoracic masses, the first pattern being the most frequent (2). The present patient was considered to have the third pattern of spread along with the enlarged lymph nodes that compressed the coronary arteries and caused ischemic heart disease with clinical features similar to angina pectoris. He was evaluated at diagnosis and during follow-up with non-invasive cardiac imaging, coronary CT and MRI for stenosis of the coronary arteries and perfusion of the myocardium. While coronary angiography is an indispensable procedure in the management of ischemic heart disease, performing such invasive procedures is often not feasible in patients with lymphoma. The present case demonstrates the usefulness of non-invasive cardiac imaging in the management of such patients.

Figure 3. Computed tomography angiography (CTA) at presentation (left) and after two courses of therapy (right). CTA at presentation showed pericardial masses (bordered by dotted line) that encased and compressed the coronary arteries. CTA taken after two courses of therapy showed a marked reduction in the size of the pericardial masses and amelioration of the compressed arteries. RCA: right coronary artery, LV: left ventricle, RV: right ventricle, PA: pulmonary artery, A: aorta, LMT: left main trunk, LAD: left anterior descending artery, LCX: left circumflex artery.

Figure 4. Magnetic resonance imaging (MRI) at presentation (short-axis view). First-pass contrast-enhanced cardiac MRI at rest showed a perfusion defect involving the right ventricle and the inferior portion of the ventricular septum (arrows) and mediastinal masses that compressed the right atrium (arrowheads). LV: left ventricle.