An Assessment of Primary Cardiac Lymphoma: A Rare Case in Indonesia

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ABSTRACT

Introduction: Primary cardiac lymphoma (PCL) is an uncommon malignancy with a high mortality rate. The disease is commonly found as non-Hodgkin’s lymphoma (NHL), mainly located in the heart or pericardium. PCL is difficult to diagnose due to its unspecific clinical manifestations. Echocardiography, computed tomography (CT) scanning, and magnetic resonance imaging (MRI) can help in diagnosing PCL, but histopathological examination is the gold standard for a definitive diagnosis. Therefore, this study aimed to compare the case of malignant cardiac lymphoma and MRI with earlier related literature.

Case Presentation: This study reported a case of PCL in 52 years old male who came to Cipto Mangunkusumo Hospital with intra cardiac tumour and underwent surgery with median sternotomy. CT scan of the chest showed a mass in the left atrial and no significant abnormalities in other organs. Histopathological examination showed the morphologic feature of diffuse monotonous proliferation of atypical large B lymphocytes. The lymphoma diagnosis was supported by immunohistochemistry including CD20, MUM1, and Ki67 positivity.

Conclusions: PCL was difficult to diagnose due to nonspecific clinical manifestations. Immunostaining helped to diagnose more specifically and determine the treatment plan. Histologic finding from PCL was mostly Diffuse Large B-cell lymphoma (DLBCL) and the prognosis was poor. Therefore, identifying the subtype of DLBCL was important for prognostic.

INTRODUCTION

Cardiac tumor is divided into two, namely primary and secondary. The primary cardiac tumor is located in the heart and the secondary metastasize to the heart from other parts of the body. Primary cardiac lymphoma (PCL) is a rare disease and the prevalence rate of metastasis is higher than that of primary cardiac tumors in the heart. Approximately, three-quarters of primary cardiac tumors are benign, such as myxoma and others are malignant, the majority of which are sarcomas, including hemangiosarcoma, myosarcoma, and fibrosarcoma [1–3].

Primary cardiac lymphoma (PCL) is an extra-nodal malignant proliferation of lymphoid cells often described as a non-Hodgkin’s lymphoma (NHL) and only found in the heart or pericardium with no evidence of lymphoma in other parts of the body. PCL contributes about 1.3–2% of all cardiac tumors and only 0.5% of all extranodal lymphomas. It is a very rare tumor based on the data from the Armed Forces Institute of Pathology (AFIP) which reported only 38 cases from 1945 to 1994 [2,4–7].

PCL is commonly located in the right atrium and right ventricle, and the majority are found in immunocompromised patients, especially with acquired immunodeficiency syndrome (AIDS). It generally occurs in older patients with a mean age of 62 years and a range between 50 to 90 years, with a male-to-female ratio of 3:1 [7,8]. This disease is difficult to diagnose and usually remains asymptomatic until it produces a mass effect, local invasion, or embolization. Definite diagnosis can be established by pathology examination, such as cytology, histopathology, and immunohistochemistry. According to previous studies, histopathological examination reveals more than 80% diffuse large B-cell lymphoma (DLBCL), and the rest are T-cell lymphomas [4–7].

Most patients die several weeks after being diagnosed with 7 months median survival. Treatment with
chemotherapy and radiation are effective for PCL which could prolong survival when the tumor cannot be resected by surgery. Treatment with chemotherapy and radiation are effective for PCL which could prolong survival when the tumor cannot be demolished by surgery [2–4,9–12]. A case of primary cardiac lymphoma was reported with diffuse monotonous proliferation of atypical large B lymphocytes, which was not associated with acquired immune deficiency. This study aimed to share the knowledge and experience of this rare case in Indonesia.

CASE PRESENTATION

A 52-year-old man experienced epigastric pain, hiccups, cough, and night sweats in August 2012. This patient felt fever without significant cause and also had diabetes mellitus for the last 4 years. There is no history of hypertension and cancer in the family of the patient. Within 10 years, there have been no cases of PCL in Cipto Mangunkusumo Hospital. On 30th April 2013, the patient suddenly had paraparesis, and chest discomfort. After receiving inpatient care treatment, there was an improvement but symptoms persisted. After a week, the patient did a general check-up in Penang. Chest X-ray showed heart enlargement, especially on the left side. CT scan of the thorax revealed a bulky infiltrative mass to myocardium, and attached to the interatrium septum, pulmonary venuses and orificium mitral. There was minimal left pleural effusion and no mass in the lung (Figure 1). Doppler USG examination showed thickening in the tunica media carotid artery but there was no stenosis. Cerebral MRI and MRA did not show focal ischemia, stenosis, or aneurysm. The abdominal CT scan showed no intra-abdominal lymphadenopathy. Furthermore, no metastatic lesion was found in other parts of the body, and myxoma was suspected at first.

A month later, the patient was admitted to Cipto Mangunkusomo Hospital. Vital signs and respiratory sound were clear, and cardiac auscultation was normal. Lung, liver, and spleen were palpated normally, and there was no peripheral edema and no lymphadenopathy. Other physical examinations were essentially normal, and the electrocardiogram showed sinus rhythm with T wave inversion in inferior leads. Echocardiography showed left atrial enlargement due to the presence of a mass which showed a light degree of motion but no free-floating movement.

Laboratory tests showed hemoglobin (Hb) of 10.6 gr/dL white blood cells (WBC) of 6,200/mm3, platelets of 417,000/mm3, and elevated lactate dehydrogenase. Renal and liver function tests showed normal limits. HbsAg, anti-HCV, and anti-HIV test results were negative.

Figure 1. A computed tomogram revealed a bulky mass infiltrative to the myocardium (arrow) and attached to the interatrium septum, pulmonary venuses, and mitral orificium. There was minimal left pleura effusion.

Figure 2. Surgical operation was performed with median sternotomy and there was a mass in the left atrium (arrow).

Figure 3. Macroscopic appearances of heart.
The patient was given heparin anticoagulant therapy before carrying out a median sternostomy. During surgery, left atrial enlargement and infiltrative mass in the left atrium wall were observed. The mass in the left atrium was removed but due to the large size, the tumor was taken out in fragmented pieces. Biopsy with transesophageal echocardiography and cardiopulmonary bypass were also performed. The surgery was successfully performed with good contractility of the heart (Figure 2). Macroscopic appearance showed 20cc of fragmented tissue with homogenous structure, firm in consistency, and yellowish to brown (Figure 3).

Histopathological examination showed tumors with high cellularity and diffuse proliferation of atypical lymphocytes. Focally, they had a starry sky-like appearance, and the tumor cells were infiltrative between myocard cells. The cells were large with mild nuclear pleomorphism, vesicular nuclei with prominent nucleoli, as well as scanty and basophilic cytoplasm. Mitoses were easily identified, and hemorrhagic and necrotic areas were present.

Based on macroscopic and microscopic hematoxylin-eosin (HE) staining, diagnosis of large cell NHL was established. Immunohistochemistry (IHC) stainings showed strong positivity for CD20, MUM1, and Ki67 in about 80% area (Figures 4D, E, and F), and negativity for CD3, CD10, and BCL-6 (Figures 4G, H, and I). The conclusion was DLBCL non-germinal center B-cell-like (non-GCB). After surgery, the condition of the patient was stable, and was referred to another hospital to continue hospitalization. A week later, due to unstable hemodynamic status, the patient died before receiving chemotherapy.

**DISCUSSION**

PCL is a rare but highly aggressive lymphoma, and it is mostly located in the heart/pericardium of men in their 50s [2–7]. Clinical manifestation generally occurs acutely and frequently undetected. The symptoms common to most patients are chest pain, congestive heart failure, pleural effusion, conduction disorder, and pericardial effusion. Tumor in the left atrium caused a mass effect, such as embolism and thrombosis. It may also cause hemodynamic disturbance due to mitral and pulmonary valve obstruction. In this case, paraparesis could be caused by an embolism originating from the atrial cavity. Additionally, emboli have the potential to
Primary Cardiac Lymphoma: Case Report

A previous study showed that malignant cardiac lymphoma has a poor prognosis, with arrhythmia as the common cause of death [1].

The etiology of PCL is unknown and many factors can potentially increase its risk. These factors include iatrogenic etiologies in the setting of transplantation or autoimmune diseases, ultraviolet radiation, pesticides, hair dyes, diet, and infectious agents [2,12]. PCL occurs in immunocompromised patients, especially AIDS [2,3,13,14]. However, in this study, the patient showed negative HbsAg, HCV, and HIV tests.

Some diagnostic tools are needed to diagnose PCL, such as electrocardiography, which shows sinus tachycardia with a complete left bundle branch block, low voltage, and negative T-wave. Furthermore, CT scans and MRIs give more significant information to confirm the location of the tumor. According to previous studies, echocardiography may be a good non-invasive diagnostic tool to demonstrate the tumor [4–7]. In this study, left atrial enlargement, was found in the patient, as well as normal lung, and no metastasis feature in other parts of the body. Faganello et al. [5] stated that the location of PCL is 70% in the right atrium, 33% in the right ventricle, 24% in the pericardium, 14% in the left atrium, 12% in the left ventricle, 9% in superior vena cava, and 6% in inferior vena cava. According to the location, the differential diagnosis of PCL is myxoma, a condition that may affect the left atrium and protrude into the ventricle. In this patient, it was thought to be a cardiac myxoma [1,2].

A definite diagnosis of PCL was made using a tumor biopsy. Macroscopically, PCL showed tissue with a homogenous structure, irregular mass, firm consistency, and white to brown nodular masses. Microscopically, the tumor showed high cellularity and diffuse proliferation of atypical lymphocytes. There was a starry sky-like appearance focally and the tumor is infiltrative between myocardial cells. The cells showed large, mild nuclear pleomorphism, uniform, and vesicular nuclei with prominent nucleoli, as well as scanty and basophilic cytoplasm. Mitoses were easily found and there were numerous mitotic figures, hemorrhagic and necrotic areas. This appearance was consistent with the large-cell NHL. The majority of PCL is DLBCL, constituting over 80%, while the remaining cases are comprised of T-cell lymphomas [13,14].

The immunoblastic variant of DBLCL showed more than 90% immunoblastic with a single, prominent, centrally located nucleolus, scanty cytoplasm, and strongly basophilic. This variant is positive for MUM1 and CD138, while bcl-2 may exhibit either positive or negative expression, correlating with a poorer prognosis [13,14]. Based on molecular study, DLBCL has been classified into two subtypes, namely Germinal Center B-cell-like (GCB) and non-GCB. This classification can be differentiated using immunostaining with anti-CD10, bcl-6, and MUM1 [10,14].

The subtypes demonstrated significant differences in survival, and non-GCB subtypes show poorer prognosis than GCB subtypes. Cases determined as GCB subtypes have 5 years survival about 60 % and 33% for non-GCB subtypes. The poorer prognosis of DLBCL can be determined by markers, including bcl-2, p53 overexpression, high Ki67, and absence of bcl-6 [10]. In this study, the immunostaining result was positive for CD20 which supports B-cell lymphoma, and negative for CD3 excluding T-cell type [9,14]. This case is consistent with non-GCB and may exhibit a poor prognosis.

The International Prognostic Index (IPI), proposed in 1993, has parameters that can determine the survival of lymphoma. Each factor is assigned one point and the low risk of IPI has 5 years of survival, accounting for about 70%, while high risk has 20 % [10,14]. Diagnosis of PCL is usually delayed due to non-specific clinical manifestations. The treatment modalities including surgery, chemotherapy, and radiation were not significantly effective. Furthermore, the median survival without treatment was less than 1 month, while patients treated with chemotherapy and radiation had about 7 months. The patient in this study only survived 1 month, possibly related to the emergence of effects on the location of the mass, local invasion, or embolization, and lack of chemotherapy [15,16]. The study showed no evidence that surgery increases survival as complete tumor resection is difficult to perform. The administration of chemotherapy and radiation proved effective in the treatment of PCL, contributing to a potential extension of survival [8,13].

The patient in this study was referred to another hospital after one week of recovery but passed away due to an unstable hemodynamic condition. Therefore, clarification of any potential cause of death in this case was not possible. In a study by Alicia Xue Fen Chia, the patient underwent a trans-jugular venous biopsy of an RA mass under the guidance of trans-esophageal echocardiography and confirmed the diagnosis of PCL. Following seven cycles of chemotherapy, the individual is presently in remission, 20 months post-diagnosis [16]. Another study described a median progression-free survival (PFS) of 24 months in patients with primary cardiac lymphoma, with a complete response and overall rate of 59% and 79%, respectively. It also shows that patients with arrhythmias have a shorter PFS compared to those without irregularity (hazard ratio (HR): 0.334, 95% confidence interval (CI): 0.112–0.999, P < 0.05) [15]. Petrich et al. [17] reviewed 197 cases of PCL, with half reported since 1995. Survival was affected by 4 factors, namely immune status, left ventricular involvement, presence of extra-cardiac disease, and
arrhythmia. The median overall survival (OS) for immunocompromised and immunocompetent was 3.5 months (m) and “not reached”, respectively (HR 0.29, 95%CI, 0.13-0.68; P = 0.004). However, the duration for immunocompetent patients could not be determined.

CONCLUSIONS

Primary cardiac lymphoma (PCL) was difficult to diagnose due to nonspecific clinical manifestations. CT scan, MRI, and echocardiography were extremely important diagnostic tools for detection. The study showed that a biopsy was mandatory for a definitive diagnosis and immunostaining played a crucial role in providing a more specific diagnosis, contributing to the determination of the treatment plan. Histologic result from PCL was mostly DLBCL and the prognosis was poor. Furthermore, identifying the subtype of DLBCL was important for prognostic.

This study reported a case of PCL in a 52-year-old man with cardiac symptoms. CT scan and echocardiogram showed left atrial enlargement due to left atrial mass and the histopathological diagnosis was DLBCL non-GCB. The duration of symptoms in this patient lasted only one month, possibly related to the impact of mass location, local invasion, or embolization.

DECLARATIONS

Competing of Interest
The authors declare no competing interest in this study.

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REFERENCES