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Diffuse Large B-Cell Lymphoma of the Heart

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Abstract

Background: Diffuse large B-cell lymphoma (DLBCL) of the heart accounts for only 1% of primary cardiac tumors. Histopathology examination becomes the primary key for diagnosis and immunohistochemistry evaluation for defining non-Hodgkin lymphoma (NHL) subtype is able to predict the patient prognosis and treatment modality options.
Case description: 70-year-old man complained of shortness of breath. Echocardiographic examination revealed mass occupied the left atrium measured 5.9 x 2.9 cm inherent with interatrial septum and mass with a stem in the right atrium measured 4.6 x 2.4 cm. Intraoperative, considerable amount of extracardiac mass was found, mass extension was unable to be determined. Thoracic surgeon decided to sample the extracardiac mass without performing cardiac surgery. The histopathologic features showed round blue cell tumor resembling a NHL. Immunohistochemical staining were consistent with diffuse NHL, large cell, high grade lymphoma, suitable for DLBCL.
Discussion and conclusion: Round blue cell tumor of extracardiac mass with positive expression of LCA and CD 20 is suitable for B-cell non-Hodgkin lymphoma. Ki-67 immunohistochemical staining revealed a 70-80% proliferation index which indicates a high-grade lymphoma and defining diagnosis and treatment of DLBCL.

Keywords: Cardiac Lymphoma; DLBCL; Heart

Abstrak

Latar belakang: Diffuse large B-cell lymphoma (DLBCL) jantung hanya menyumbang 1% dari tumor jantung primer. Pemeriksaan histopatologik menjadi kunci utama untuk diagnosis dan evaluasi imunohistokimia untuk menentukan subtipe limfoma non-Hodgkin (NHL) mampu menentukan prognosis dan pilihan modalitas terapi.
Deskripsi kasus: Pria berusia 70 tahun mengeluh sesak napas. Pemeriksaan ekokardiografi mengungkapkan massa menempati atrium kiri berukuran 5,9 x 2,9 cm yang melekat dengan septum interatrial dan massa dengan batang di atrium kanan berukuran 4,6 x 2,4 cm. Intraoperatif, sejumlah besar massa ekstrakardiak ditemukan, perluasan massa tidak dapat ditentukan. Ahli bedah toraks memutuskan untuk mengambil sampel massa ekstrakardiak tanpa melakukan operasi jantung. Fitur histopatologis menunjukkan tumor sel biru bulat menyerupai NHL. Pewarnaan imunohistokimia konsisten dengan NHL difus, sel besar, limfoma kelas tinggi, cocok untuk DLBCL.
Diskusi dan kesimpulan: Sel tumor bulat biru dari massa ekstrakardiak dengan ekspresi LCA dan CD20 positif sesuai dengan limfoma non-hodgkin sel B. Pewarnaan immunohistokimia Ki-67 membuktikan 70-80% proliferasi indeks yang mengindikasikan limfoma kelas tinggi dan menentukan diagnosis dan terapi dari DLBCL.

Keywords: Limfoma Jantung; DLBCL; Jantung

1. Background

Diffuse large B-cell cardiac lymphoma (typically non-Hodgkin) accounts for only 1% of primary cardiac tumors.[1] Primary cardiac lymphoma remains asymptomatic until it produces a mass effect by obstructing cardiac chambers and great vessels or until it causes pulmonary or systemic embolization, complete atrioventricular (AV) block, and cardiac tamponade.[2] Its rarity and heterogeneous clinical presentation make the diagnosis difficult.[2] Prognosis is poor due to diagnostic delay and the relevance of the site of the disease.[2-3] In this report, the case of a 70-year-old male with diffuse large B-cell lymphoma (DLBCL) involving the heart is presented.

2. Case Report

A 70-year-old man presented with chief complaint of shortness of breath. The patient was referred from another institution with diagnosis of intracardiac mass in the right and left atria accompanied with atrial fibrillation showed in Figure 1.

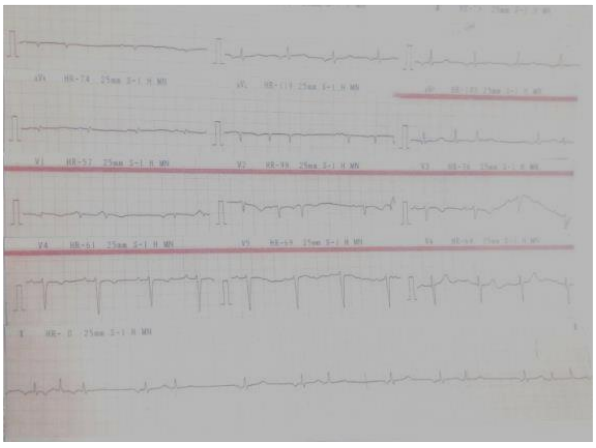


Figure 1. ECG Examination Result.
ECG showed atrial fibrillation with normal ventricular response (68 bpm), right axis deviation, poor R wave progression and right ventricular hypertrophy.

On admission, his respiratory rate increased up to 28x/minutes, with blood pressure of 115/72 mmHg, irregular heart rate of 67 bpm, body temperature of 36.9ºC and 97% peripheral oxygen saturation (8 lpm non-rebreathing mask). Laboratory examination was significant for normocytic anaemia, hypoalbuminemia, and elevated lactate dehydrogenase level (727 U/L).

Chest radiograph revealed pulmonary emphysematous features, cardiomegaly along with left ventricular hypertrophy, left atrial hypertrophy and elongated aorta. No pulmonary or skeletal metastasis visualized, as shown in figure 2.

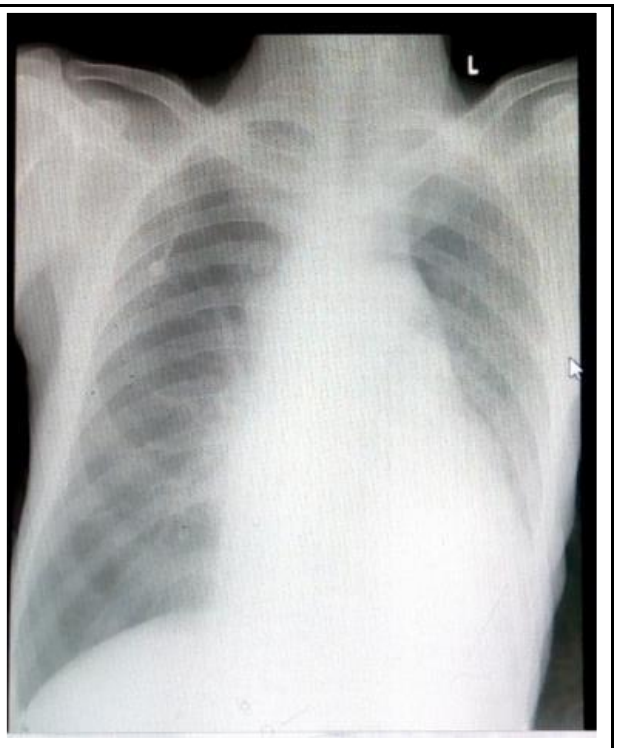
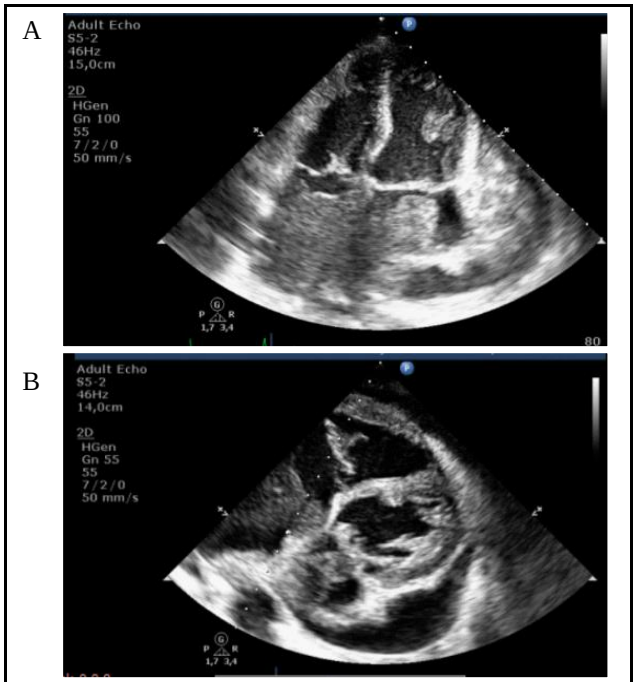


Figure 2. Chest Radiography Examination.
Chest radiograph revealed pulmonary emphysema, cardiomegaly with configuration of left ventricular hypertrophy and left atrial hypertrophy with aortic elongation, no pulmonary metastasis, no skeletal visualization of bone systema.

Echocardiographic examination was immediately performed and revealed a mass in the left atrium measured 5.9 cm x 2.9 cm, attached to the interatrial septum and a mass with a stalk in the right atrium measured 4.6 x 2.4 cm (suspicious for myxoma). Bilateral atrial dilatation and right ventricle dilatation observed with atrial size of 47 mm, left atrium of 43 mm and right ventricle of 31 mm. The left ventricular global and segmental function was unremarkable, with ejection fraction of 74%. Left ventricular diastolic function was unable to be determined due to atrial fibrillation experienced by patient. Right ventricular systolic function decreased, with tricuspid annular plane systolic excursion (TAPSE) of 12 mm. Moderate mitral regurgitation with mild aortic regurgitation observed, with pressure half time (ARPHT) was 531 m/s and severe tricuspid regurgitation with a gradient of 47 mmHg and a speed of 3.43 m/s is consistent with pulmonary hypertension. Normokinetic heart muscle movement with moderate to massive pericardial effusion is shown in figure 3.



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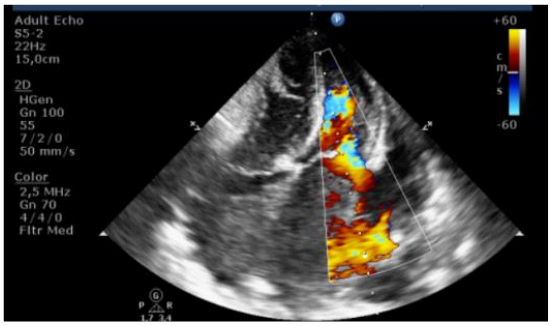

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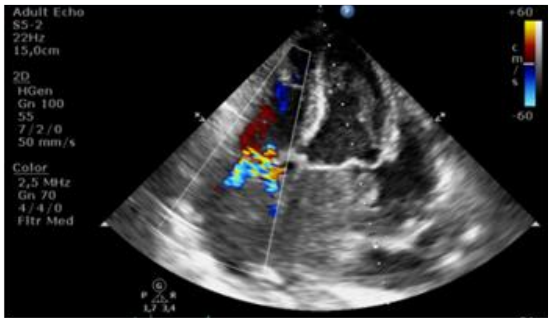
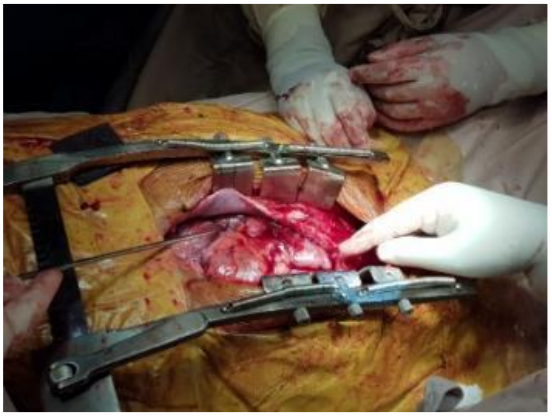


Figure 3. Echocardiography.
(A)-The apical 4 chambers picture shows a large mass in the right and left atria (intracavity). (B)-Subxhyphoid picture shows moderate to massive pericardial effusion. (C)-Apical 4 chambers with color doppler mode showed mitral regurgitation. (D)-Apical 4 chambers with color doppler revealed tricuspid regurgitation.

Based on history taking, physical examination and supporting investigations, patients was diagnosed clinically as right and left atrial masses with moderate to massive pericardial effusion, functional Congestive Heart Failure (CHF) class II et causa anatomical diagnosis: cardiomegaly, mitral regurgitation, tricuspid regurgitation, intracardiac mass, and etiologic diagnosis of right and left atrial masses, chronic obstructive pulmonary disease (COPD) with secondary infections (pneumonia), paroxysmal atrial fibrillation, type 2 diabetes mellitus, and ulcer type dyspepsia. Blood cultures and sensitivity of sputum are also performed to determine the ongoing lung infection etiology. Blood cultures revealed no bacterial growth and sputum culture was positive for *Klebsiella pneumonia ssp* growth that sensitive to meropenem.

C Intraoperatively, substantial amount of extracardiac mass was found. Whether the mass extends from intracardiac or extracardiac was unable to be determined. Considering the difficulty of identifying the vena cava and the right atrium due to massive tumors, the surgeon decided not to perform cardiac surgery but proceed to sample the tissue of the tumor followed by sternal closure as shown in figure 4.

A



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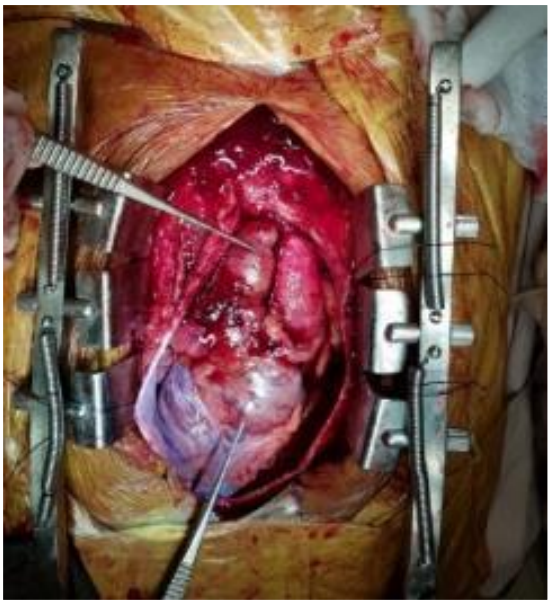


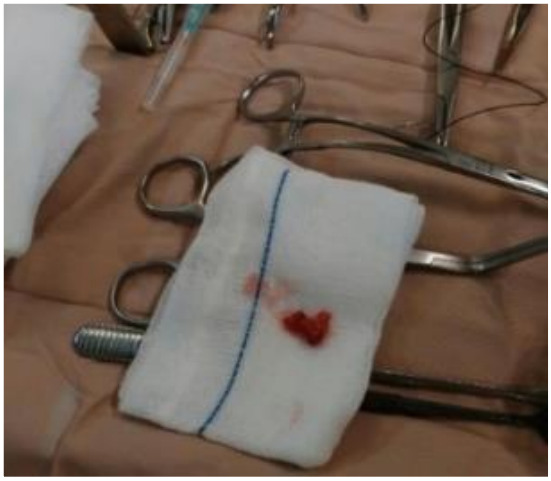


Figure 4. Extracardiac Mass Sample.
(A and B)-Extracardiac mass. (C)-Pieces of mass biopsy.

Gross examination revealed a brownish to white rubbery tissue sample, size of 1.7 x 1.4 x 0.6 cm. Microscopically, cellular tissue sample obtained, composed of cellular, diffuse, cells relatively monotonous with medium to large cell size and scanty cytoplasm. Nuclei are round, oval and partially curved, with coarse chromatin, some with nucleoli located centrally, some located peripherally, with presence of apoptotic bodies and numerous mitosis showed in figure 5.

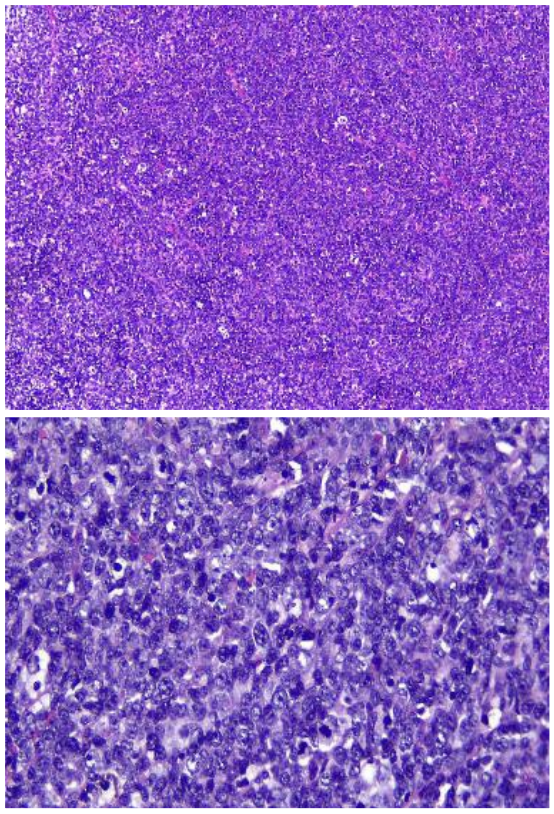
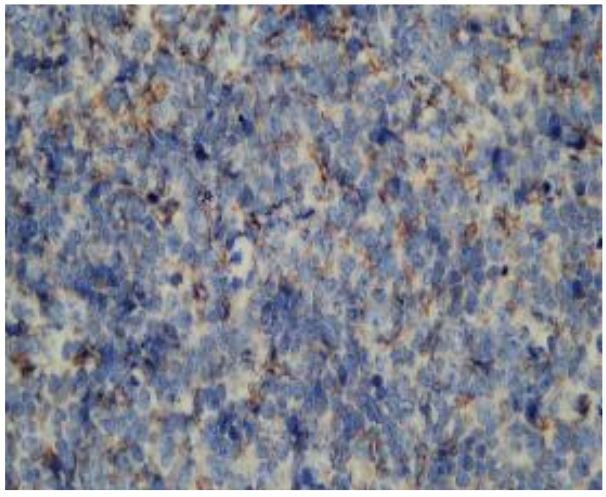
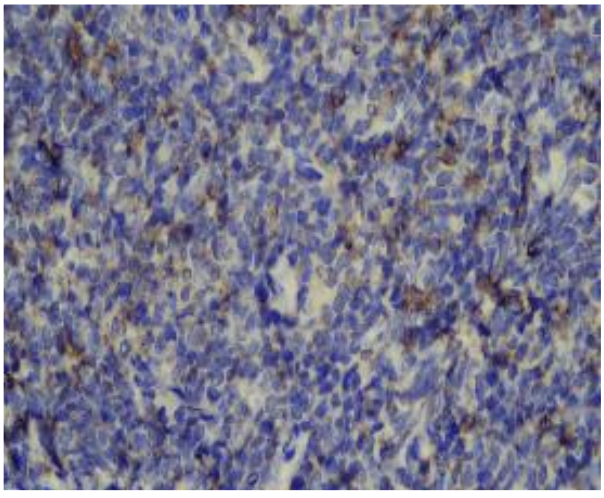


Figure 5. Microscopically Examination.
(A)-Low power magnification (HE staining 100x) revealed cellular, diffuse and relatively monotonous cells. (B)-High power magnification (HE staining 400x) revealed medium to large cell size with scanty cytoplasm, apoptotic bodies, and significant number of mitotic activity.

In conclusion, microscopically the case is consistent with round blue cell tumor resembling a non-Hodgkin lymphoma (NHL). IHC panel consisted of LCA, myogenin, CD 56, CD 99 and Ki67 were recommended to confirm the diagnosis. If later the LCA result is positive, then immunohistochemistry examination of CD 3 and CD 20 are needed to determine lymphoma cell type.

Immunohistochemistry examination of CD45 or LCA revealed moderate positive staining in some tumor cells and CD20 showed moderate to strong positive staining on almost all tumor cell membranes showed in figure 6.





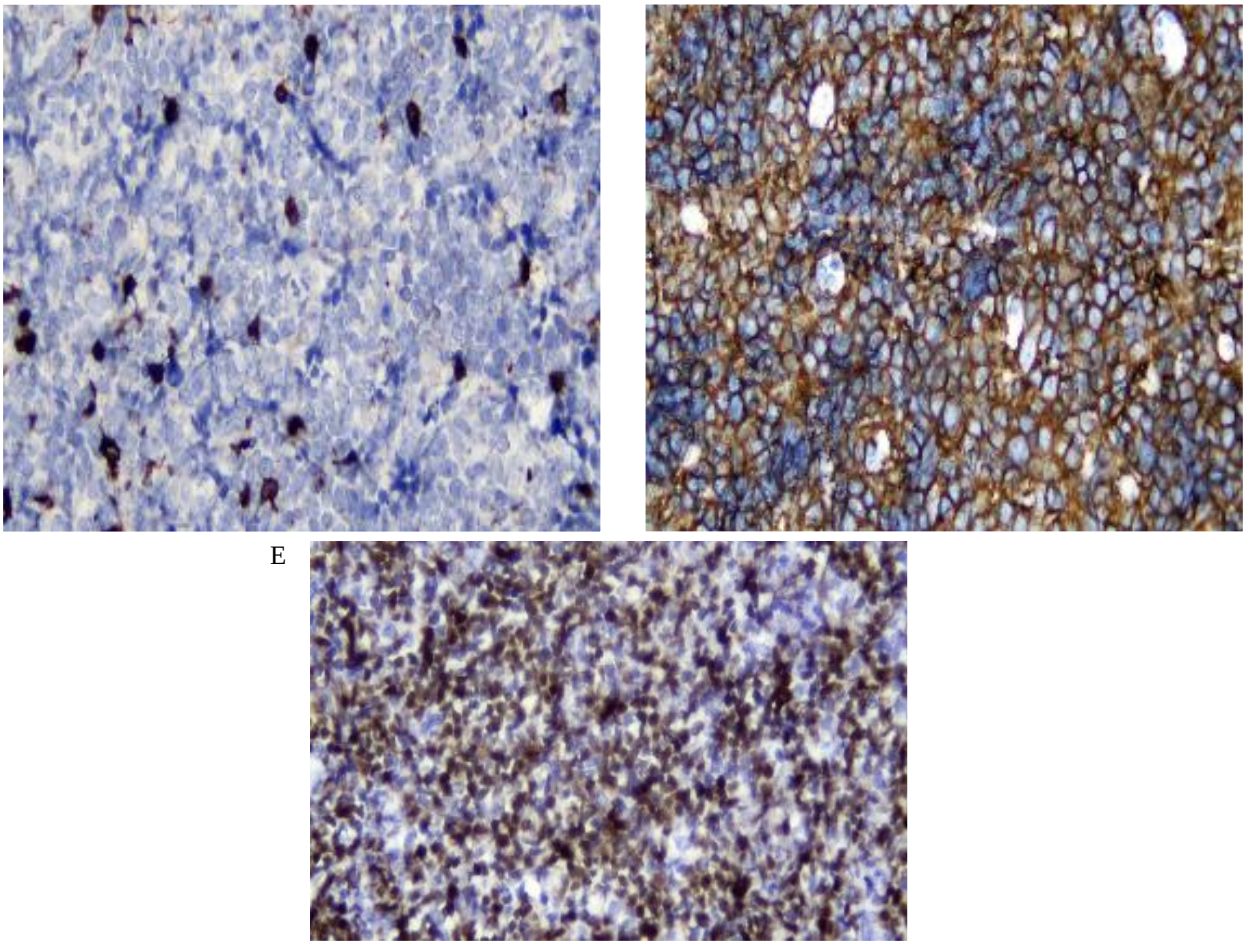


Figure 6. Immunohistochemistry staining with LCA, CD3, CD20, and Ki67 (400x).
(A and B)-LCA stained moderately positive. (C)-CD3 showed negative appearance in all tumor cells. (D)-CD20 showed moderate to strong positive staining on almost all tumor cell membranes. (E)-Ki67 showed positive staining in tumor cell markers.

CD3 negatively stained in all tumor cells, but positively stained on reactive lymphocyte infiltrate (Figure 6). Ki-67 was positively stained in tumor cell nucleus with proliferating index of 70-80% (Figure 6). Other markers such as myogenin, CD56, and CD99 were negatively stained (Figure 7). Diagnosis of DLBCL was then established.

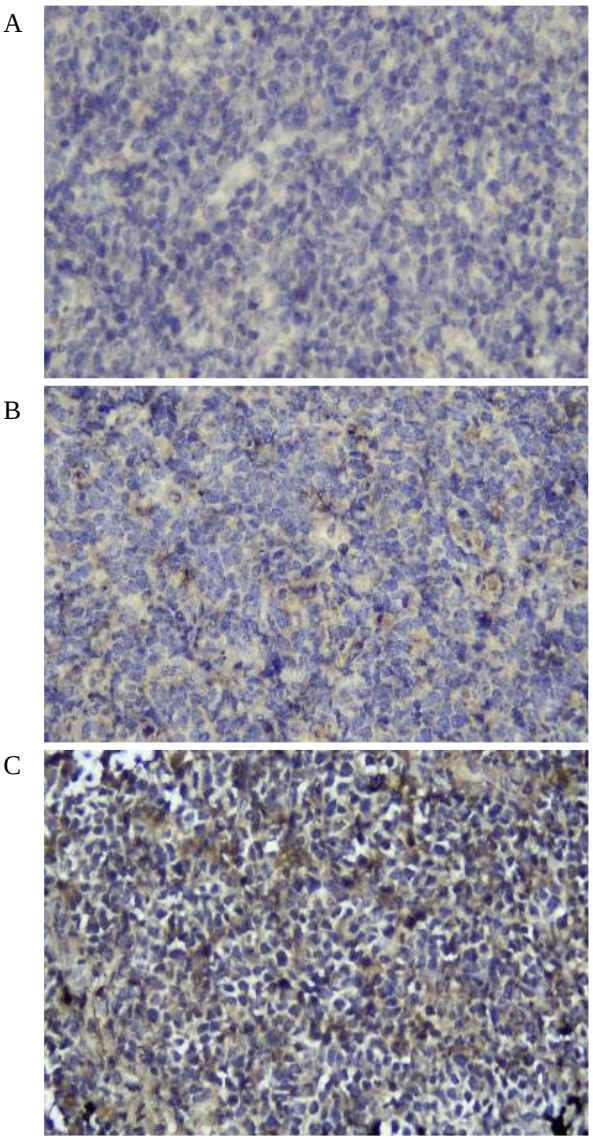


Figure 7. Immunohistochemistry staining with Myogenin, CD56, and CD99.
(A)-Myogenin. (B)-CD56. (C)-CD99. (A, B and C)-Showed negative staining.

3. Discussion

DLBCL is the most common of NHL (31%), and is rapidly fatal if left untreated. Its clinical presentation is determined by several factors: site, size, growth rate, degree of invasiveness, and tumor friability. DLBCL is characterized by high growth rate, presenting as a mass that causes symptoms when infiltrating tissues or organs.[3]

Cardiac involvement may occur in three manners: by contiguity from intrathoracic lesions involving the parietal pericardium and then the heart; by retrograde lymphatic dissemination; or by hematogenous dissemination. The spectrum of cardiac manifestations is broad, going from the absence of symptoms to heart failure, pericardial effusion or arrhythmias. Cardiac involvement is rarely the initial presentation of lymphomas; in average it starts 20 months after the initial diagnosis.[3]

Chest radiography shows low sensitivity and specificity as a diagnostic tool; however, it may reveal tracheal deviation; cardiac enlargement; signs of heart failure; and abnormal cardiac silhouette. Transthoracal echocardiogram is a sensitive method for the identification of cardiac involvement by lymphomas, which more commonly present as nodular or polypoid masses in right chambers, with variable myocardial infiltration. There are few cases in the literature reporting the restrictive/constrictive action of the neoplasm, thus conditioning diastolic heart failure as the underlying pathophysiological mechanism. The pathological diagnosis of cardiac masses is essential. Traditionally, it required thoracotomy, but less invasive procedures such as fluoroscopy-guided endomyocardial biopsy and percutaneous intracardiac biopsy are currently available.[3]

DLBCL is a frequent lymphoma subtype with a heterogeneous behavior and a variable response to conventional cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP)-based regimens. The golden standard for prognostic risk stratification is based upon the

assessment of clinical variable, such as age, stage, performance status, lactate dehydrogenase (LDH). However, whereas these parameters can reliably distinguish between low, intermediate, and high-risk groups of patients, they are less helpful for predicting treatment response in individual patients. Furthermore, they provide no information about the molecular risk factors that determine the clinical diversity of the disease.[4]

In general diagnostic practice, the commonest differential diagnosis is not with other lymphoma entities but with anaplastic tumors of non-lymphoid origin especially carcinoma and melanoma. Positivity for the leucocyte common antigen (CD45 molecule) is very useful for excluding carcinoma except that about 10% of large B-cell lymphomas do not express it.[5] In this case immunohistochemistry of CD45 or LCA had positivity result that suitable for lymphoma. DLBCLs express pan-B markers, e.g. CD19, CD20, CD22, CD75 and CD79a, but there may be an ‘‘aberrant’’ lack of staining with one or more of these, especially in diffuse large B-cell lymphomas expressing the full-length ALK protein (CD20, CD79a, IgAþ). In our institution, we use CD3 and CD20 to determine the cell type. In this case CD20 had a strong expression that signifies the B cell type subtype. Approximately 10% of diffuse large B-cell lymphomas, particularly those with anaplastic morphology express CD30 and EMA. These tumors are, however, negative for ALK protein and in the REAL and WHO classifications are just considered as morphological variants of diffuse large B-cell lymphomas.[5]

Immunostain CD56 stained neuroendocrine cells, schwann cell, and NK cells. CD99 stained immature T cells including cortical thymocytes, various epithelial cells, and endothelial cell. Myogenin stained skeletal muscle differentiation.[6] All of the myogenin, CD56, and CD99 were not expressed in this tumor cell. The proliferating fraction, as detected by Ki-67 or mib-1 staining, is usually high (more than 40% of neoplastic cells).[6] Ki67 showed positivity in tumor cell nucleus and had high proliferating fraction equals to 70-80%.

This case is the first case in our institution. The patient's health condition worsens and eventually he passed away 2 week after surgery. We were unable to perform complete examination to determine the origin of the tumor. We found difficulty to determine whether the tumor is primary cardiac lymphoma or it is a secondary cardiac involvement.

Cardiac involvement was rare as an initial presentation of malignant lymphoma and has often been subclinical. These tumors have seen more common in the right side of the heart and echocardiogram is an effective tool for initial patient assessment. Pathological diagnosis is essential for prognosis determination and further management of cardiac masses. The only effective treatment modality for the given case is chemotherapy.

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