Relapsed acute myeloid leukemia presenting with myocardial hypertrophy and constrictive pericardial physiology

Aynur Acıbuca*, Mahmut Yeral, Nazım Emrah Koçer***, Zafer Koç****, Hakan Güllü***
Departments of *Cardiology, and **Hematology, ***Pathology, ****Radiology, Faculty of Medicine, Başkent University, Dr. Turgut Noyan Practice and Research Center; Adana-*Turkey*

Introduction

Extra medullary relapse (EMR) after stem cell transplantation can be seen up to 20% of acute leukemia patients (1). Moreover, EMR rarely occurs in the heart and there are few cases reporting cardiac relapses in leukemia (2-5).

Despite exceedingly rare incidence during clinical follow-up, cardiac leukemic involvement can frequently detected microscopically in up to 40% of patients on postmortem examination (6). The ante mortem diagnostic process can be challenging because cardiac symptoms secondary to infections or chemotherapeutics are similar to the symptoms related with leukemic cardiac infiltration (7). We report a case of cardiac relapse in myeloid leukemia presenting with myocardial hypertrophy and constrictive cardiac physiology, that was diagnosed by pericardial biopsy.

Case Report

A 54-year-old male presented to our cardiology department with new onset dyspnea and lower extremity swelling for 3 weeks. There was no history of heart disease. The patient had undergone allogenic peripheral blood stem cell transplantation because of acute myeloid leukemia (AML) type M4 nearly one and a half years ago. Thereafter, he had suffered from EMR and graft versus host disease (GVHD) and had received proper treatment. The bone marrow was in remission during clinical visits.

On admission, electrocardiography (ECG) revealed T-wave inversion in the precordial and inferior leads (Fig. 1). The chest radiogram showed increased cardiothoracic ratio. There was no remarkable abnormality except thrombocytopenia (40.00×10^3/μL) in blood tests. The troponin level was normal. Transthoracic echocardiography (TTE) displayed new extensive myocardial hypertrophy, increased pericardial thickness, massive pericardial effusion, and left ventricular systolic dysfunction compared with TTE done 10 months previously, which showed no evidence of structural heart disease. Pericardiocentesis was performed because of tamponade signs. The effusion was an exudate and atypical cells were not detected during cytologic examination.

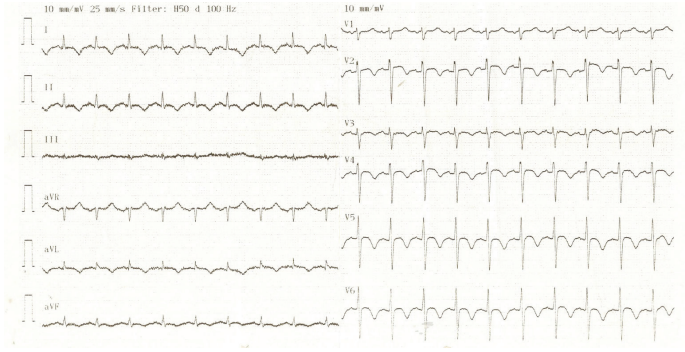

Figure 1. Electrocardiogram illustrate T wave inversion in precordial and inferior leads

Despite the removal of pericardial effusion, myocardium was observed to be constrictive as if surrounded by a shield leading to systolic dysfunction in echocardiographic views (Video 1-3). The most striking point was diffuse myocardial hypertrophy with no clear reason. Also, the patient was still suffering from shortness of breath and pedal edema. Therefore, a cardiac magnetic resonance imaging (MRI) was planned to differentiate opportunistic infection, storage disease, or other possible etiologies. The MRI illustrated pericardial and bilateral pleural effusions, pericardial thickening, diffuse left and right ventricular hypertrophy, myocardial and pericardial late gadolinium enhancement, and diffuse left ventricular hypokinesis (Fig. 2 a-2g), which signs were interpreted by the radiologist to may appear as a result of GVHD, leukemic infiltrates, or infectious diseases. Therefore, a pericardial biopsy was performed to make an accurate diagnosis. While awaiting the results of pericardial biopsy, blood smear unexpectedly showed atypical mononuclear cells; therefore, a bone marrow biopsy was performed. Pathologic examination of pericardium displayed extensive leukemic infiltration. Thereafter, microscopic examination of bone marrow confirmed the recurrence of AML. Despite reinitiation of chemotherapy, the patient died 10 days after the diagnosis.

Discussion

The signs and symptoms of leukemic cardiac involvement are nonspecific and can change according to the infiltrated part of the heart. Therefore, diagnostic process can be challenging. Leukemic infiltration can be presented with heart failure, pericardial effusion, and rarely constrictive pericarditis (4, 5, 8). Cardiac infiltrates of AML can be diffuse as well as massy (3, 9).

In this case, we suspected myocarditis because of systolic dysfunction and remarkable cardiac hypertrophy.

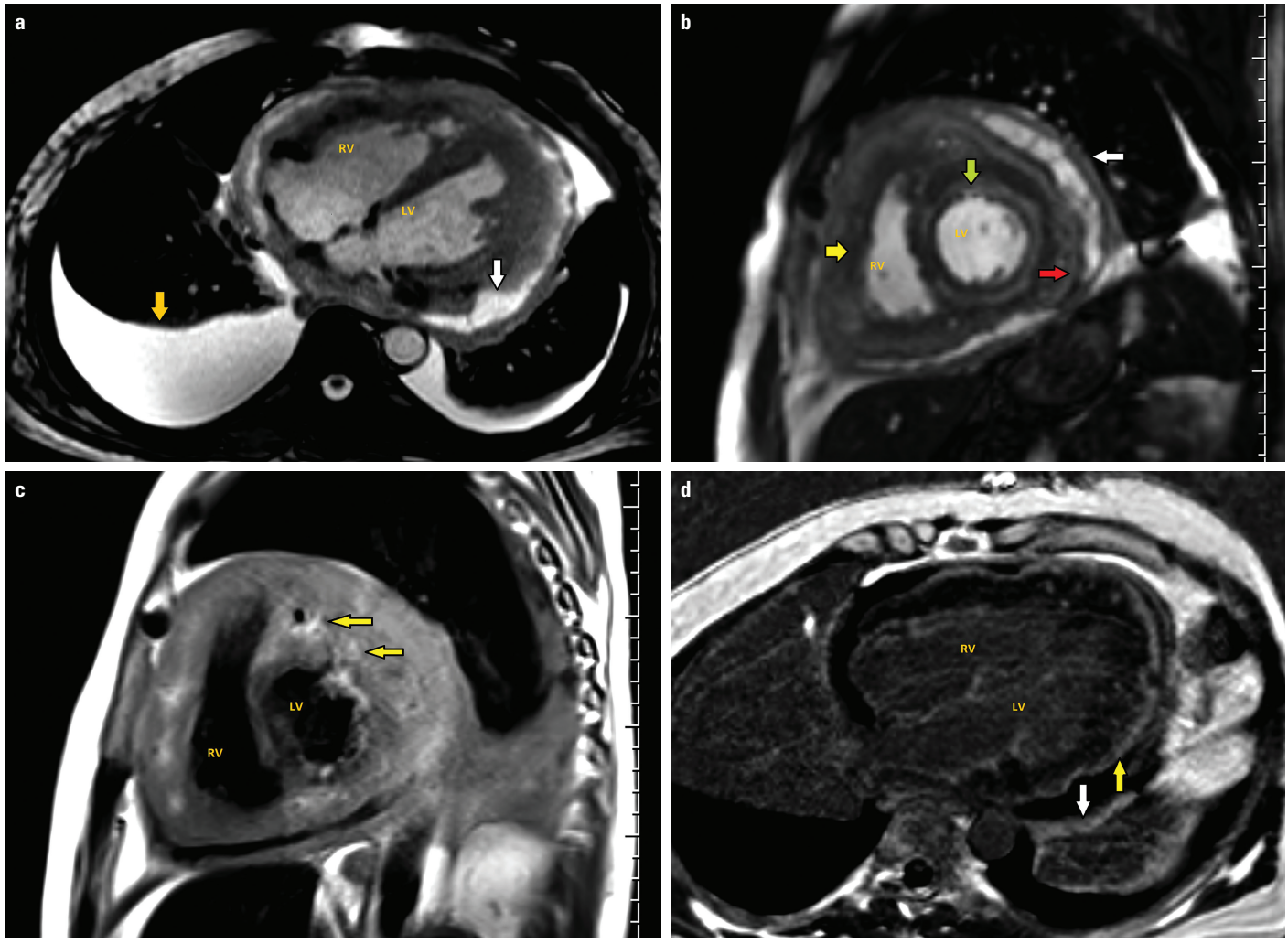

Figure 2. (a) Axial GE T2 weighted image shows pericardial [yellow arrow] and bilateral pleural [yellow arrow] effusion.
(b) Cine short axis view shows biventricular myocardial [yellow arrow], parietal [white arrow] and visceral pericardial thickening and subendocardial [green arrow] and subepicardial [red arrow] hyperintense rim related with myocardial invasion.
(c) Short axis TSE T2-weighted image shows midwall hyperintense areas [yellow arrow] related with myocardial invasion.
(d) Late gadolinium-enhanced four-chamber view shows epicardial [yellow arrow] and pericardial [white arrow] rim enhancement.
LA - left atrium, LV - left ventricle, RA - right atrium, RV - right ventricle

Also, concomitant pericarditis could explain pericardial signs. However, polymerase chain reaction analysis of common isolated cardiotropic viruses was negative and the troponin level was normal. Therefore, we ruled out active viral myocarditis.

The second likely cause of cardiac signs and symptoms was chemotherapeutic agents. However, he had not been exposed to cardiotoxic chemotherapeutics. His MRI images, illustrating abnormal heterogeneous myocardial infiltration with late gadolinium enhancement can provide a hint to rule out cardiotoxicity that cause diffuse homogenous myocardial involvement (4).

Cardiac amyloidosis was also considered in the differential diagnosis, but it was ruled out because there was no sign of low-voltage in ECG, TTE did not show "speckled" pattern, and MRI findings were not consistent with those of amyloidosis (10). Besides, new myocardial hypertrophy could not be explained by hypertensive heart disease, aortic stenosis, or hypertrophic cardiomyopathy, when considering clinical and imaging features.

Our case differs from the other cases in terms of the use of only pericardial biopsy to reveal the diagnosis of AML relapse. We preferred pericardial biopsy to endomyocardial biopsy (EMB) because myocardial involvement was heterogeneous and EMB might not reveal a definitive diagnosis in case of being taken from an area without leukemic infiltrates. Besides, myocardial invasive procedures have more potential complications compared to pericardial interventions.

Conclusion

To sum up, when we encounter a patient with hematologic malignancy presenting with heart failure, we should consider leukemic cardiac involvement in addition to cardiotoxic drugs

or opportunistic infections. Also, leukemic infiltration should be considered in differential diagnosis of cardiac hypertrophy in this patient group. Repetitive cases with different clinical futures will increase our awareness and improve our understanding about leukemic heart disease. Prompt accurate diagnosis and urgent therapy may improve the clinical process of this disease.

Informed consent: An informed consent was obtained from the patient's wife.

Video 1. Parasternal long axis view illustrating severe myocardial hypertrophy, moderate pericardial effusion, and limitation of myocardial motion.

Video 2. Parasternal short-axis view showing extensive myocardial hypertrophy, moderate pericardial effusion, and systolic dysfunction.

Video 3. Apical four-chamber view displaying disproportionate myocardial hypertrophy, and limitation of diastolic expansion movement of the ventricles.

References

1. Clark WB, Strickland SA, Barrett AJ, Savani BN. Extramedullary relapses after allogeneic stem cell transplantation for acute myeloid leukemia and myelodysplastic syndrome. Haematologica 2010; 95: 860-3.
2. Jung MH, Lee YH, Lee KY, Jung HO, Youn HJ. Leukemic infiltration presenting as myocardial hypertrophy after complete remission of acute myeloid leukemia. Echocardiography 2017; 34: 136-8.
3. Facenda-Lorenzo M, Sánchez-Quintana A, Quijada-Fumero A, Laynez-Carnicero A, Breña-Atienza J, Poncela-Mireles FJ, et al. Cardiac Relapse of Acute Myeloid Leukemia after Allogeneic Hematopoietic Stem Cell Transplantation. Case Rep Oncol Med 2016; 2016: 5091021.
4. Chang K, Kim DY, Lee KH, Huh J, Kang JW, Shin DY, et al. An isolated cardiac relapse after allogeneic hematopoietic stem cell transplantation for acute lymphoblastic leukemia. Korean J Intern Med 2017; 32: 753-7.
5. Hori T, Suzuki N, Mizue N, Hatakeyama N, Takamuro M, Tsutsumi H. Relapse of T-cell all after stem cell trans- plant presenting as hypertrophic cardiomyopathy: the value of non-invasive diagnostic imaging in detecting cardiac leukemia. Pediatr Blood Cancer 2006; 46: 108-11.
6. Roberts WC, Bodey GP, Wertlake PT. The heart in acute leukemia: A study of 420 autopsy cases. Am J Cardiol 1968; 21: 388-412.
7. Barbaric D, Holley D, Lau KC, McCowage G. It is ALL in the heart: A patient with acute lymphoblastic leukemia and cardiac infiltration at time of diagnosis. Leuk Lymphoma 2002; 43: 2417-9.
8. Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumours: diagnosis and management. Lancet Oncol 2005; 6: 219-28.
9. Makaryus AN, Tung F, Liu W, Mangion J, Kort S. Extensive neoplastic cardiac infiltration in a patient with acute myelogenous leukemia: role of echocardiography. Echocardiography 2003; 20: 539-44.
10. Mohty D, Damy T, Cosnay P, Echahidi N, Casset-Senon D, Virot P, et al. Cardiac amyloidosis: updates in diagnosis and management. Arch Cardiovasc Dis 2013; 106: 528-40.

Address for Correspondence: Dr. Aynur Acıbuca,
Başkent Üniversitesi Tıp Fakültesi,
Dr. Turgut Noyan Uygulama ve Araştırma Merkezi,
Kardiyoloji Anabilim Dalı,
01250 Adana-*Türkiye*
Phone: +90 322 327 27 27/12094
Fax number: +90 322 327 12 74
E-mail: aynuracibuca85@gmail.com

DOI:10.14744/AnatolJCardiol.2019.64011