Annals of Hematology (2019) 98:1775–1776
https://doi.org/10.1007/s00277-019-03665-3

LETTER TO THE EDITOR

Isolated extramedullary leukemic involvement of the heart presenting as fulminant heart failure

Maria Stamouli[1] · Konstantinos Gkirkas[1] · Aiantas Antoniades[2] · Loukas Kaklamanis[3] · Konstantinos Gkodopoulos[1] · John Palios[2] · Angeliki Karagiannidou[1] · George Makavos[2] · Ignatios Ikonomidis[2] · Panagiotis Tsirigotis[1]

Received: 27 February 2019 / Accepted: 6 March 2019 / Published online: 11 March 2019

Dear Editor,

Prognosis of patients with acute lymphoblastic leukemia (ALL) relapsed after allogeneic stem cell transplantation (allo-SCT) is dismal with less than 10% long-term survivors [1]. Therapeutic options include blinatumomab, inotuzumab ozogamicin, or chimeric antigen receptor T cells.

A 37-year-old woman with B-(ALL and t(4;11) was referred to our department. She had relapsed ALL after previous allo-SCT performed in CR1. She received salvage chemotherapy without success. Bone marrow examination revealed persistence of leukemia (blasts 6%). Second allo-SCT with the same donor was performed by using a non-myeloablative conditioning. GVHD prophylaxis consisted of a short course (1 month duration) of cyclosporine. Following second allo-PBSC repeated testing showed complete morphological and molecular remission.

Six months after the second allo-PBSCT, she presented with shortness of breath, orthopnea, and edema anasarca. Troponin and NT-pro-BNP levels were markedly elevated NT-pro-BNP = 18.016 pg/ml, (normal < 125 pg/ml) and troponin = 682.4 pg/ml (normal < 14 pg/ml). SO_2 was 89%, while a chest X-ray revealed bilateral pleural effusion and a markedly enlarged heart. An echocardiogram showed mild-to-moderate pericardial effusion with no signs of tamponade. Concentric wall thickening was apparent in both the left and right ventricles, and the left ventricular ejection fraction was 30%. Abdominal ultrasound revealed hepatomegaly, ascites, and inferior vena cava dilatation.

Cardiac MRI revealed increased wall thickness and extensive early and late gadolinium enhancement indicative of infiltrating myocardial disease (Fig. 1a). Total body CT scan did not reveal any abnormal findings except those associated with heart failure (hepatomegaly, pleural fluid, ascites, etc.). Cytospin preparations from both the pleural and pericardial fluid did not reveal the presence of leukemic cells. Blood counts remained normal, and marrow examination with the use of quantitative-PCR confirmed that she remained in complete hematological and molecular remission. A transvenous endomyocardial biopsy and histological examination showed diffuse infiltration of the myocardium by B-lymphoblasts (Fig. 1b). She received treatment with high-dose steroids but her condition deteriorated rapidly and she passed away shortly after histopathology results were obtained.

Differential diagnosis included leukemic infiltration, acute myocarditis, and GVHD-associated cardiomyopathy and cardiotoxity due to chemotherapy [2]. Acute myocarditis is usually associated with viral infections. Clinical manifestations range from asymptomatic cases to severe heart failure and sudden death. Modern imaging techniques such as MRI have become important tools for the diagnosis and follow-up. Myocardial biopsy is necessary for definitive diagnosis [3–5].

Rare cases of heart involvement due to GVHD have been reported, and clinical manifestations include arrhythmias, coronary disease, myocarditis, cardiomyolysis, and heart failure. Concentric wall thickening and decreased ejection fraction are common echocardiographic changes, while histology showed massive heart infiltration by donor lymphocytes [6–8].

Isolated leukemic involvement of the heart is an extremely rare event [9, 10]. Clinical presentations range

✉ Panagiotis Tsirigotis
panagtsirigotis@gmail.com

[1] Second Department of Internal Medicine, ATTIKO General University Hospital, National and Kapodistrian University of Athens, Rimini-1, Haidari, 124 62 Athens, Greece

[2] Second Department of Cardiology, ATTIKO General University Hospital, National and Kapodistrian University of Athens, Athens, Greece

[3] Department of Histopathology, Onasseio Heart Surgery Center, Athens, Greece

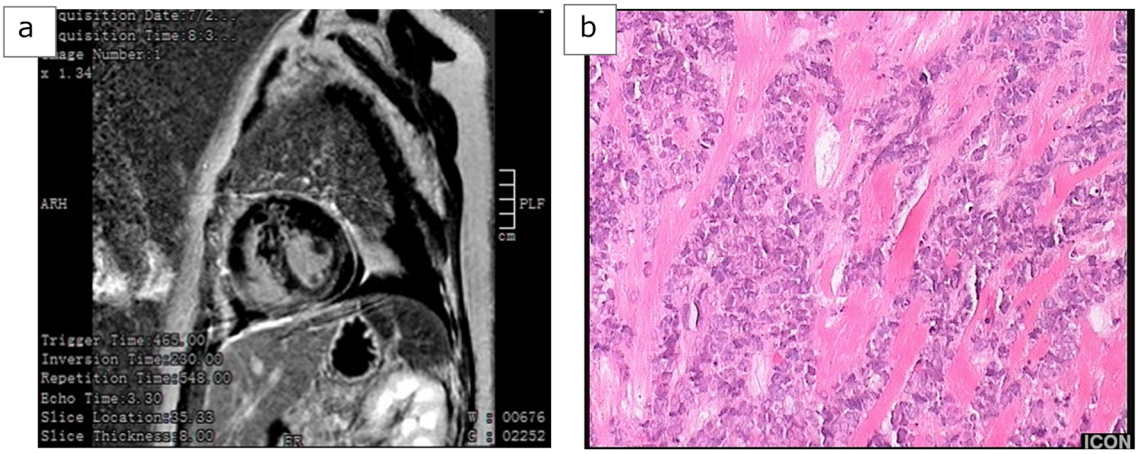

Fig. 1 **a** Cardiac MRI revealed increased wall thickness and extensive patchy early and late gadolinium enhancement with abnormal borders within in the mid- and epicardial layers of the interventricular septum, inferior and posterior wall of the left ventricle indicative of infiltrating myocardial disease. **b** Endomyocardial biopsy revealed diffuse infiltration of leukemic cells

from asymptomatic cases detected in routine cardiac imaging to arrhythmias or even acute heart failure. Prognosis is extremely poor. The absence of systemic leukemia suggests a bone marrow and blood-restricted dynamic of the graft versus leukemia effect.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from the patient included in this article.

References

1. Poon LM, Hamdi A, Saliba R, Rondon G, Ledesma C, Kendrick M, Qazilbash M, Hosing C, Jones RB, Popat UR, Nieto Y, Alousi A, Ciurea S, Shpall EJ, Champlin RE, Kebriaei P (2013) Outcomes of adults with acute lymphoblastic leukemia relapsing after allogeneic hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 19:1059–1064
2. Volkova M, Russell R (2011) Anthracycline cardiotoxicity: prevalence, pathogenesis and treatment. Curr Cardiol Rev 7: 214–220
3. Brennan Y, Gottlieb DJ, Baewer D, Blyth E (2015) A fatal case of acute HHV-6 myocarditis following allogeneic haemopoietic stem cell transplantation. J Clin Virol 72:82–84
4. Ammirati E, Veronese G, Cipriani M et al (2018) Acute and fulminant myocarditis: a pragmatic clinical approach to diagnosis and treatment. Curr Cardiol Rep 26(20):114
5. Caforio AL, Marcolongo R, Jahns R et al (2013) Immune-mediated and autoimmune myocarditis: clinical presentation, diagnosis and management. Heart Fail Rev 18:715–732
6. Rackley C, Schultz KR, Goldman FD, Chan KW, Serrano A, Hulse JE, Gilman AL (2005) Cardiac manifestations of graft-versus-host disease. Biol Blood Marrow Transplant 11:773–780
7. Roberts SS, Leeborg N, Loriaux M, Johnson FL, Huang ML, Stenzel P, Thiede C, Godder KT (2006) Acute graft-versus-host disease of the heart. Pediatr Blood Cancer 47:624–628
8. Platzbecker U, Klingel K, Thiede C, Freiberg-Richter J, Schuh D, Ehninger G, Kandolf R, Bornhäuser M (2001) Acute heart failure after allogeneic blood stem cell transplantation due to massive myocardial infiltration by cytotoxic T cells of donor origin. Bone Marrow Transplant 27:107–109
9. Wright TL, Bardy PG, Disney P, Moore S, Horvath N (2002) Isolated cardiac recurrence of acute lymphoblastic leukemia characterized by t(11;19) two years after unrelated allogeneic bone marrow transplantation. Cancer Genet Cytogenet 137: 146–149
10. Chang K, Kim DY, Lee KH, Huh J, Kang JW, Shin DY, Kim DH (2017) An isolated cardiac relapse after allogeneic hematopoietic stem cell transplantation for acute lymphoblastic leukemia. Korean J Intern Med 32:753–757