Case Reports

Primary Cardiac Lymphoma in an Immunocompetent 71-Year-Old Man

Claudia Montanaro, MD
Ferdinando Loiacono, MD
Gabriele Fragasso, MD
Francesco De Cobelli, MD
Marco Foppoli, MD
Alberto Margonato, MD

Isolated cardiac lymphomas are very rare, especially in immunocompetent patients. As a consequence, little is known about the best therapeutic management and about patients' outcomes in these cases. Diffuse large B-cell lymphoma is the most frequent subtype; anthracycline-based chemotherapy has been the most successful treatment. We describe the case of a primary cardiac lymphoma in an immunocompetent 71-year-old man. As of December 2015, the patient had been in clinical remission for 2 years. The most relevant literature on primary cardiac lymphoma is reported and discussed. ***(Tex Heart Inst J 2015;42(6):561-4)***

Key words: *Biopsy, endomyocardial; cyclophosphamide; etoposide; heart neoplasms/therapy; immunocompetence; lymphoma, large B-cell, diffuse/diagnosis/drug therapy; lymphoma, non-Hodgkin/drug therapy; prednisone; rituximab; vincristine*

From: *Heart Failure Unit, Department of Cardiology (Drs. Fragasso, Loiacono, Margonato, and Montanaro), Department of Radiology (Dr. De Cobelli), and Lymphoma Unit, Department of Onco-Haematology (Dr. Foppoli), Istituto Scientifico San Raffaele, Vita-Salute San Raffaele University, 20132 Milan, Italy*

Address for reprints: *Gabriele Fragasso, MD, Heart Failure Unit, Istituto Scientifico San Raffaele, Via Olgettina 60, 20132 Milan, Italy*

E-mail: *gabriele.fragasso@hsr.it*

To date, epidemiologic data indicate that the prevalence of primary cardiac tumors (PCTs) in the general population is between 0.001% and 0.3%.[1] According to most studies, approximately 10% of PCTs are malignant.[1-7] Cardiac involvement can occur in up to 20% of patients with lymphomas, whereas primary cardiac lymphoma (PCL) is rare and accounts for 1.3% of all PCTs.[8] In 1978, McAllister and Fenoglio[9] defined PCL as an extranodal lymphoma involving only the heart, pericardium, or both. Later, Cairns and colleagues[10] proposed to extend the definition of PCL to tumors that present small secondary lesions nearby. Currently, the clinically accepted definition of PCL is "a lymphoma presenting as cardiac disease, especially if the bulk of the tumor is intrapericardial."[11]

A close association exists between PCLs and immunodepression, because most reported PCL cases are in patients who are taking immunosuppressive drugs or are infected with human immunodeficiency virus (HIV). Here we describe a case of PCL occurring in an immunocompetent patient who was otherwise in good health.

Case Report

A 71-year-old man came to our attention when he presented with a 2-month history of fatigue and intense exertion-induced dyspnea. Arterial hypertension, for which he was on drug therapy, was the patient's only known medical condition. Physical examination of the patient was unremarkable. Electrocardiography (ECG) showed a complete atrioventricular block with idioventricular rhythm (45 beats/min). He was transferred to our clinical cardiology ward for further investigation and eventual pacemaker implantation.

The patient's blood count was abnormal. In particular, lymphocytes were fewer than normal (700/mm^3, 9.3% of total leukocytes). Despite that, the patient was considered to be fairly immunocompetent, and his subsequent test for HIV was negative.

Transthoracic (TTE) and transesophageal (TEE) echocardiography—routine before pacemaker implantation—revealed severe pericardial effusion (3 cm posterior, 5–6 cm anterior), with right atrial collapse in diastole; yet the patient's left ventricular (LV) systolic function was normal. Some round, nodular, and variable-in-dimension echogenic masses were present in the atrioventricular sulcus and in the free wall of the right ventricle (RV). The RV had mild systolic dysfunction. The inferior vena cava appeared dilated (2.6 cm), but collapsed normally during inspiration.

We drained 230 mL of pericardial fluid. The results of cytology showed a cellular population compatible with a lymphoproliferative process. Total-body computed tomography (Fig. 1) and cardiac magnetic resonance imaging (Fig. 2) confirmed

the presence of a mass in the atrioventricular sulcus of the RV, surrounding the right coronary artery and infiltrating the posterior interventricular sulcus, the left coronary sulcus, the epicardial adipose tissue, the RV inferior wall, and the LV basal posterior wall. This mass was 3 cm thick and 6 cm long from base to apex; it displayed late enhancement after gadolinium-based contrast administration, compatible with tumor. Some nodules were visible in the visceral pericardium, and the pericardial effusion was still present.

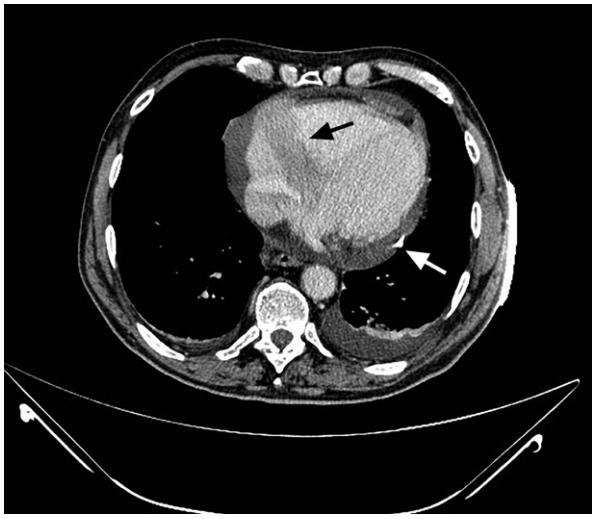

Fig. 1 *Computed tomographic scan of the thorax shows a mass in the cardiac atrioventricular sulcus (black arrow) and pericardial drainage (white arrow). Image artifacts are the consequence of pericardial drainage.*

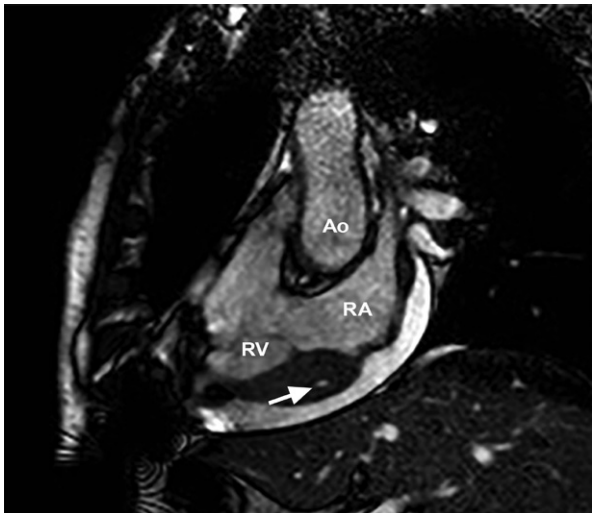

Fig. 2 *Cine magnetic resonance image (right 2-chamber long-axis view) shows a mass in the atrioventricular sulcus surrounding the right coronary artery (arrow). Pericardial effusion is also evident. Image artifacts are caused by pericardial drainage. Because of the patient's precarious clinical condition, breath-hold during image acquisition was not easily obtainable. Therefore, a low-matrix acquisition protocol was adopted, which resulted in greater acquisition speed but lower resolution.*

Ao = aorta; RA = right atrium; RV = right ventricle

We successfully implanted a bicameral pacemaker. Under radioscopic and TEE guidance, 5 samples of RV myocardium were collected for biopsy. Histologic examination yielded a diagnosis of B-cell non-Hodgkin lymphoma-like cellular infiltrate (large and intermediate-to-large dimensions), compatible with diffuse large B-cell lymphoma (DLBCL). The immunophenotype was $CD20^{+}$, $CD10^{+}$, bcl-$6^{+/-}$, $CD3m^{-}$, cyclin $D1^{-}$, $CD56^{-}$, $CD34^{-}$, TdT^{-}. Bone marrow histology produced evidence of minimal lymphoma localization, together with mild reduction of other cellular lineages; ^{18}fluorodeoxyglucose positron emission tomography showed a significant tracer uptake, in correspondence with the cardiac lesion. Our patient's Karnofsky performance status was 80. According to the Ann Arbor staging of non-Hodgkin lymphomas, he presented with stage IV-B DLBCL.

We therefore treated our patient in accordance with the R-CHOP 21 plan, making use of liposomal doxorubicin. R-CHOP 21 provides 6 cycles of drug administration, with 3-week intervals between cycles. It consists of rituximab (375 mg/m^2 on day 1), cyclophosphamide (750 mg/m^2 on day 1), liposomal doxorubicin (50 mg/m^2 on day 1), vincristine (2 mg on day 1), and oral prednisone (75 mg, days 1–5). After the 3rd cycle, TTE documented a significant reduction of LV ejection fraction to 0.40. Our patient's serum troponin T determinations had always been negative. The R-CHOP* plan was therefore converted to R-CEOP**; that is, liposomal doxorubicin was replaced by etoposide (100 mg/m^2 on day 1). Thereafter, his LV ejection fraction increased to 0.53.

After the last of 6 expected cycles of chemotherapy, repeated staging showed evidence of complete clinical remission, which was maintained after 2 years of monitoring.

Discussion

The present report describes a rare case of PCL in an immunocompetent patient who was successfully treated with anthracycline-based chemotherapy. Despite the fact that it is impossible to exclude the possibility of lymphoma localization in other sites, our separate staging of images in other locations did not reveal any other

*R-CHOP: **R** = rituximab; **C** = cyclophosphamide; **H** = doxorubicin hydrochloride (hydroxydaunomycin); **O** = vincristine sulfate (Oncovin); **P** = prednisone

**R-CEOP: Treatment guidelines in British Columbia recommend the substitution of etoposide for doxorubicin in standard R-CHOP patients with DLBCL who have a contraindication to anthracyclines.

detectable disease in our patient. Although PCL is not characterized by specific cardiologic signs or symptoms, the combination of ECG abnormalities, prominent involvement of the right side of the heart by heterologous tissue, and systemic symptoms (such as fatigue) hint that cardiac lymphoma should be considered in the differential diagnosis. Various imaging techniques—together with histologic analysis of the myocardium and eventually of other tissues—are necessary to confirm the diagnosis. Anthracycline-based chemotherapy is the first-line treatment for DLBCLs. Primary cardiac lymphoma presents no exception to this approach: indeed our patient's good outcome at his 2-year follow-up provides reasonable confirmation. No pathognomonic clinical signs set apart PCL. The patient can present with heart failure, pericardial effusion, chest pain, cardiac tamponade, pleural effusion, arrhythmia, superior vena cava syndrome, myocardial infarction, pulmonary embolism, or dyspnea, depending on the location and the extent of the tumor.[12]

In immunocompetent patients, primary cardiac lymphomas (of which DLBCL is the principal subtype) have rarely been reported. Our report thus confirms information already present in the literature. To our knowledge, only 23 cases of PCL in immunocompetent patients have been reported to date (Table I).[13-30] According to these reports, no patient presented with noncardiac lymphomatous localization, but, as in our patient, it was impossible to absolutely exclude noncardiac involvement in the absence of autopsic investiga-

TABLE I. Reports of Primary Cardiac Lymphomas in Immunocompetent Patients

Reference	Age (yr), Sex	Treatment	Outcome and Known Duration	
			Alive	Dead
Daus H, et al.[13] (1998)	69, M	Chemo	After chemo	—
Gosalbez F, et al.[14] (1999)	NA	Surgery and chemo	12 yr	—
	NA	Surgery and chemo	—	After chemo
Ryu SJ, et al.[15] (2001)	64, M	Chemo	3 mo	—
	31, F	Chemo	7 mo	—
Porcar Ramells C, et al.[16] (2002)	46, M	Chemo and autologous peripheral blood stem cell transplantation	29 mo	—
Chalabreysse L, et al.[17] (2002)	72, F	Chemo	—	6 mo
	65, M	Chemo	33 mo	—
	9, M	Surgery and chemo	12 mo	—
Hayes D Jr, et al.[18] (2003)	76, F	Surgery and chemo	—	10 wk
Giunta R, et al.[19] (2004)	58, F	Chemo	—	3 wk
Anghel G, et al.[20] (2004)	52, M	Chemo and autologous peripheral blood stem cell transplantation	24 mo	—
	70, F	Chemo and pericardiocentesis	—	2 wk
Gosev I, et al.[21] (2006)	67, M	Surgery	—	3 d
Santini F, et al.[22] (2009)	67, M	Surgery and chemo	1 yr	—
Ling LF, et al.[23] (2009)	55, M	Chemo	After chemo	—
Johri A, et al.[24] (2009)	60, M	Chemo	22 mo	—
Chin JY, et al.[25] (2009)	42, F	Chemo	4 mo	—
Gadage V, et al.[26] (2011)	38, M	Chemo	—	After relapse
Sharma A, et al.[27] (2012)	38, F	Surgery and chemo	11 mo	—
Crisel RK, et al.[28] (2012)	55, M	Chemo	3 mo	—
Donegani E, et al.[29] (2013)	14, M	Surgery and chemo	6 mo	—
Habertheuer A, et al.[30] (2014)	70, F	Surgery and chemo	At end of 6 cycles	—
Current case (2015)	71, M	Chemo	2 yr	—

Chemo = chemotherapy; F = female; M = male; NA = not available

tion, which was performed in only 2 patients[17,20] and revealed no extracardiac metastasis.

Nine of these patients were treated with surgical excision followed by chemotherapy, and 5 of them survived at least 6 months after treatment. No evidence exists concerning the necessity of surgery as an adjunct to chemotherapy in PCL; moreover, in those 9 cases surgery was the final diagnostic step, along with excision as treatment. Therefore, it is not possible to conclude that ablative surgery leads to better results than chemotherapy alone, which is the gold-standard treatment in lymphomas at other sites.

Patients who died of lymphoma were diagnosed with a clinically advanced disease, which underscores the importance of early diagnosis. In fact, cardiologists are frequently slow to suspect such an uncommon neoplasm, especially in immunocompetent patients in whom PCL is extremely rare. The main aim of this report is to alert cardiologists to the possibility of such a diagnosis.

References

1. Kumar N, Agarwal S, Ahuja A, Das P, Airon B, Ray R. Spectrum of cardiac tumors excluding myxoma: experience of a tertiary center with review of the literature. Pathol Res Pract 2011;207(12):769-74.
2. Basso C, Valente M, Poletti A, Casarotto D, Thiene G. Surgical pathology of primary cardiac and pericardial tumors. Eur J Cardiothorac Surg 1997;12(5):730-8.
3. Blondeau P. Primary cardiac tumors--French studies of 533 cases. Thorac Cardiovasc Surg 1990;38 Suppl 2:192-5.
4. Centofanti P, Di Rosa E, Deorsola L, Dato GM, Patane F, La Torre M, et al. Primary cardiac tumors: early and late results of surgical treatment in 91 patients. Ann Thorac Surg 1999; 68(4):1236-41.
5. Patel J, Sheppard MN. Pathological study of primary cardiac and pericardial tumours in a specialist UK centre: surgical and autopsy series. Cardiovasc Pathol 2010;19(6):343-52.
6. Yu K, Liu Y, Wang H, Hu S, Long C. Epidemiological and pathological characteristics of cardiac tumors: a clinical study of 242 cases. Interact Cardiovasc Thorac Surg 2007;6(5):636-9.
7. Reynen K. Frequency of primary tumors of the heart. Am J Cardiol 1996;77(1):107.
8. Canellos GP, Skarin AT, Klatt MM, Rosenthal DS, Case DC Jr, Pinkus GS, et al. The m-BACOD combination chemotherapy regimen in the treatment of diffuse large cell lymphoma. Semin Hematol 1987;24(2 Suppl 1):2-7.
9. McAllister HA, Fenoglio JJ. Tumors of the cardiovascular system. Fascicle 15, 2nd series. In: Atlas of tumor pathology. Washington (DC): Armed Forces Institute of Pathology; 1978. p. 99.
10. Cairns P, Butany J, Fulop J, Rakowski H, Hassaram S. Cardiac presentation of non-Hodgkin's lymphoma. Arch Pathol Lab Med 1987;111(1):80-3.
11. Chim CS, Chan AC, Kwong YL, Liang R. Primary cardiac lymphoma. Am J Hematol 1997;54(1):79-83.
12. Ceresoli GL, Ferreri AJ, Bucci E, Ripa C, Ponzoni M, Villa E. Primary cardiac lymphoma in immunocompetent patients: diagnostic and therapeutic management. Cancer 1997;80(8): 1497-506.
13. Daus H, Bay W, Harig S, Schneider G, Feiden W, Schieffer H. Primary lymphoma of the heart: report of a case with histological diagnosis of the transvenously biopsied intracardiac tumor. Ann Hematol 1998;77(3):139-41.
14. Gosalbez F, Miralles T, Cofino J, Valle J, Naja J, Llosa J. Primary lymphomas of the heart in immunocompetent patients. Presentation of two cases with one 12 year survival. Analysis of surgical implications. Minerva Cardioangiol 1999;47(3):75-9.
15. Ryu SJ, Choi BW, Choe KO. CT and MR findings of primary cardiac lymphoma: report upon 2 cases and review. Yonsei Med J 2001;42(4):451-6.
16. Porcar Ramells C, Clemente Gonzalez C, Garcia Pares D, Guardia Sanchez R, Perez Ayuso MJ, Garcia-Bragado Dalmau F. Primary cardiac lymphoma: cytological diagnosis and treatment with response to polychemotherapy and hematopoietic precursor autotransplant. Presentation of a case a review of the literature [in Spanish]. An Med Interna 2002;19 (6):305-9.
17. Chalabreysse L, Berger F, Loire R, Devouassoux G, Cordier JF, Thivolet-Bejui F. Primary cardiac lymphoma in immunocompetent patients: a report of three cases and review of the literature. Virchows Arch 2002;441(5):456-61.
18. Hayes D Jr, Liles DK, Sorrell VL. An unusual cause of new-onset atrial flutter: primary cardiac lymphoma. South Med J 2003;96(8):799-802.
19. Giunta R, Cravero RG, Granata G, Sellitto A, Romano C, De Fanis U, et al. Primary cardiac T-cell lymphoma. Ann Hematol 2004;83(7):450-4.
20. Anghel G, Zoli V, Petti N, Remotti D, Feccia M, Pino P, Majolino I. Primary cardiac lymphoma: report of two cases occurring in immunocompetent subjects. Leuk Lymphoma 2004;45(4):781-8.
21. Gosev I, Siric F, Gasparovic H, Ugljen R, Nola M, Jelic I. Surgical treatment of a primary cardiac lymphoma presenting with tamponade physiology. J Card Surg 2006;21(4):414-6.
22. Santini F, Innocente F, Gilioli E, Rossi A, Ferrara A, Brunelli M, et al. Primary bi-atrial Burkitt lymphoma with severe inflow impairment in an immunocompetent patient. Cardiovasc Pathol 2009;18(2):123-5.
23. Ling LF, Chai P, Kee AC, Poh KK, Lim DG, Omar AR. Primary cardiac lymphoma presenting with cardiac tamponade. Am Heart Hosp J 2009;7(2):E125-7.
24. Johri A, Baetz T, Isotalo PA, Nolan RL, Sanfilippo AJ, Ropchan G. Primary cardiac diffuse large B cell lymphoma presenting with superior vena cava syndrome. Can J Cardiol 2009;25(6):e210-2.
25. Chin JY, Chung MH, Kim JJ, Lee JH, Kim JH, Maeng IH, et al. Extensive primary cardiac lymphoma diagnosed by percutaneous endomyocardial biopsy. J Cardiovasc Ultrasound 2009;17(4):141-4.
26. Gadage V, Kembhavi S, Kumar P, Shet T. Primary cardiac diffuse large B-cell lymphoma with activated B-cell-like phenotype. Indian J Pathol Microbiol 2011;54(3):591-3.
27. Sharma A, Minhas HS, Sakhuja P, Satsangi DK. Left atrial primary B cell lymphoma presenting with mitral regurgitation. J Card Surg 2012;27(3):300-3.
28. Crisel RK, Knight BP, Kim SS. Reversible, complete atrioventricular block caused by primary cardiac lymphoma in a non-immunocompromised patient. J Cardiovasc Electrophysiol 2012;23(12):1386-9.
29. Donegani E, Ambassa JC, Mvondo C, Giamberti A, Ramponi A, Palicelli A, Chelo D. Primary cardiac Burkitt lymphoma in an African child [in Italian]. G Ital Cardiol (Rome) 2013;14(6):481-4.
30. Habertheuer A, Ehrlich M, Wiedemann D, Mora B, Rath C, Kocher A. A rare case of primary cardiac B cell lymphoma. J Cardiothorac Surg 2014;9:14.