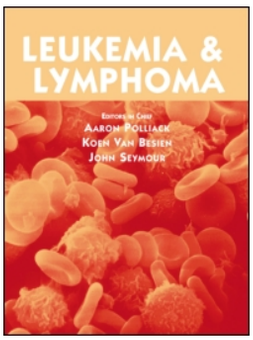

Leukemia & Lymphoma

ISSN: 1042-8194 (Print) 1029-2403 (Online) Journal homepage: http://www.tandfonline.com/loi/ilal20

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To cite this article: Salvatrice Mancuso, Melania Carlisi, Matteo Sarocchi, Mariasanta Napolitano & Sergio Siragusa (2017): Cardio-oncology in multiple myeloma: is it time for a specific focus?, Leukemia & Lymphoma, DOI: 10.1080/10428194.2017.1393674

To link to this article: http://dx.doi.org/10.1080/10428194.2017.1393674

LEUKEMIA & LYMPHOMA, 2017
https://doi.org/10.1080/10428194.2017.1393674

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Cardio-oncology in multiple myeloma: is it time for a specific focus?

Salvatrice Mancuso[a], Melania Carlisi[a], Matteo Sarocchi[b], Mariasanta Napolitano[a] and Sergio Siragusa[a]

[a]Department of Oncology, Haematology Unit, University of Palermo School of Medicine, Palermo, Italy; [b]Department of Internal Medicine and Cardionephrology, University of Genova, Genoa, Italy

ARTICLE HISTORY Received 28 September 2017; revised 9 October 2017; accepted 14 October 2017

It has been known for some time that some oncologic drugs can cause heart damage. The term 'cardiotoxicity' just refers to the presence of a cardiac event during therapy or at least related to therapy.

As a matter of fact, cardiovascular complications may be due to cancer itself and to cancer treatment, ranging from hypertension to asymptomatic left ventricular dysfunction, arrhythmias, myocardial ischemia, peripheral artery disease, thromboembolism, heart failure (HF) and even sudden cardiac death. Therefore, detecting and managing cardiac effects of cancer therapies have become an important issue in oncology.

The remarkable impact of cardiovascular complications, especially in patients receiving cardio-toxic therapies, also led authoritative cardiologic society (ACC/AHA/ASE) to consider these as class-A patients for HF (at risk) and to develop a class I recommendation for their regular monitoring [1]. More recently, dedicated guidelines and position papers considered a wide spectrum of cardiovascular toxicity [2,3].

As a result, cardio-oncology is a new multidisciplinary approach that, due to the best knowledge of the cardio-toxic effects of many antineoplastic therapies, focuses on screening, monitoring, preventing and treating cardiovascular disease in cancer patients. It may identify patients with pre-existing cardiac abnormalities that are especially susceptible to therapy-related cardiotoxicity, and facilitate early therapeutic measures providing optimal care to patients [4].

So far, despite the sensitivity to this topic and the extensive literature, cardio-oncology has been approached focusing primarily on individual drugs with a high risk of cardiovascular toxicity, and in the context of hematological diseases, the focus has been on lymphoma treatment, especially monitoring the left ventricular ejection fraction (LVEF) in anthracycline-based therapy. In addition, even if many recommendations are available, in the real life few cancer patients are subjected to appropriate monitoring programs and do not always receive specific therapy according to ACC/AHA guidelines [5].

Multiple myeloma (MM) is a plasma cell disorder that accounts for around 10% of all hematological malignancies, the second following non-Hodgkin's lymphomas. This neoplasia is often associated with high prevalence of cardiovascular complications resulting from several factors, either unrelated and related to the disease. Among those unrelated to the cancer, generally previous to diagnosis, there are diabetes, hypertension, dyslipidemia, smoking habit and mostly, for the greater incidence in elderly patients, older age. Beyond that, MM may lead to several cardiac effects, through disease-related and treatment-related factors. Underlying cardiac amyloidosis, often not detected at diagnosis, together with hyperviscosity, arteriovenous shunting, high-output failure, anemia and renal dysfunction, are cardiac risk factors related to multiple myeloma [6,7]. Many are also the therapy-related risk factors. For example, the use of corticosteroids, especially for a long time, might cause arrhythmias, hyperglycemia, hypertension, diabetes and obesity. Alkylating agents may lead to myopericarditis, cardiomyopathy, thrombosis and reduced left ventricular ejection fraction. Immunomodulatory drugs can induce arrhythmias and myocardial ischemia. The therapy with proteasome inhibitors may result in congestive heart failure (CHF), myocardial ischemia, arrhythmias, atrioventricular block and hypertension [8]. Furthermore, the transplant patients are at risk of developing HF, cardiomyopathy, myocardial ischemia and rhythm disorders [9]. Finally, the risk of cardiac effects associated with supportive therapies should

CONTACT Melania Carlisi melania.carlisi@unipa.it Department of Oncology, Haematology Unit, University of Palermo School of Medicine, Via del Vespro 129, 90127, Palermo, Italy

also be taken into account. For example, some antibiotics (e.g. macrolides, quinolones) or antifungal agents (e.g. fluconazole, pentamidine) can cause the QT prolongation.

In our opinion, it is time to create a new chapter of cardio-oncology which is entirely devoted to multiple myeloma and adopts a disease-oriented approach rather than a therapy-oriented one.

Indeed, multiple myeloma is a complex and heterogeneous disease in which, as stated above, the CV risk is inherent in the pathophysiology. Therefore, a different management is necessary, as it is in the case of thromboprophylaxis for which Khorana score does not apply, but a specific approach is recommended according to the individual risk factors and the type of therapy [10].

In addition, it should be noted that multiple myeloma remains an incurable disease, with frequent relapses in the natural history. The development of new effective drugs has improved the clinical outcomes and increased life expectancy, but on the other hand, many patients receive numerous treatment lines. All this results in a greater risk of significant cumulative toxicity, especially in people younger than 65 years old who represent approximately 37% of all patients with MM and are also candidates for bone marrow transplant.

For this reason, we are proposing a comprehensive cardiologic evaluation, already at baseline. Firstly, an accurate assessment of cardiovascular risk factors and comorbidities should be performed at diagnosis, along with potential corrective actions (blood pressure control, lipid level reduction, smoking cessation, etc.). This needs to be combined to a clinical, ECG and imaging evaluation. With respect to imaging techniques, baseline echocardiography is crucial not only for LVEF evaluation, but also for the assessment of any alteration, including findings of amyloidosis (increased left and right ventricular wall thickness, diastolic dysfunction with a restrictive pattern, pericardial effusion, etc.). In addition, serum cardiac biomarkers, B-type natriuretic peptide (BNP) and troponins, are likely to serve as earlier markers of cardiac toxicity, when carefully interpreted. This assessment should also be carried out at the end of treatment and repeated for any subsequent therapy line. To this end, a multidisciplinary approach involving cardiology plays a key role, being critical for the optimal management of the patient.

Acknowledgements

English language was revised by Francesco Moscato, University of Glasgow.

Potential conflict of interest: Disclosure forms provided by the authors are available with the full text of this article online at https://doi.org/10.1080/10428194.2017.1393674.

Funding

The authors received no specific funding support for this work.

ORCID

Salvatrice Mancuso http://orcid.org/0000-0002-7926-090X
Melania Carlisi http://orcid.org/0000-0002-5641-2974
Matteo Sarocchi http://orcid.org/0000-0002-8132-8715
Mariasanta Napolitano http://orcid.org/0000-0001-8934-2936
Sergio Siragusa http://orcid.org/0000-0002-1641-6508

References

[1] Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): Developed in Collaboration With the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: Endorsed by the Heart Rhythm Society. Circulation. 2005;112: e154–e235.

[2] Zamorano JL, Lancellotti P, Rodriguez Muñoz D, et al. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). Eur Heart J. 2016; 37:2768–2801.

[3] Maurea N, Spallarossa P, Cadeddu C, et al. A recommended practical approach to the management of target therapy and angiogenesis inhibitors cardiotoxicity: an opinion paper of the working group on drug cardiotoxicity and cardioprotection, Italian Society of Cardiology. J Cardiovasc Med (Hagerstown). 2016; 17(suppl 1):S93–S104.

[4] Domercant J, Polin N, Jahangir E. Cardio-oncology: a focused review of anthracycline-, human epidermal growth factor receptor 2 inhibitor–and radiation-induced cardiotoxicity and management. Ochsner J. 2016;16:250–256.

[5] Hung OY, Brown JR, Dai T, et al. Pattern of cardiac surveillance among patients with lymphoma receiving anthracycline-based chemotherapy. BMJ Open. 2015; 5:e008350.

[6] Kistler KD, Kalman J, Sahni G, et al. Incidence and risk of cardiac events in patients with previously treated multiple myeloma versus matched patients without

multiple myeloma: an observational, retrospective, cohort study. Clin Lymphoma Myeloma Leuk. 2017;17: 89–96.

[7] Inanir S, Haznedar R, Atavci S, et al. Arteriovenous shunting in patients with multiple myeloma and high-output failure. J Nucl Med. 1998;39:1–3.

[8] Siegel D, Martin T, Nooka A, et al. Integrated safety profile of single-agent carfilzomib: experience from 526 patients enrolled in 4 phase II clinical studies. Haematologica. 2013;98:1753–1761.

[9] Sureddi RK, Amani F, Hebbar P, et al. Atrial fibrillation following autologous stem cell transplantation in patients with multiple myeloma: incidence and risk factors. Ther Adv Cardiovasc Dis. 2012;6: 229–236.

[10] Palumbo A, Cavo M, Bringhen S, et al. Aspirin, warfarin, or enoxaparin thromboprophylaxis in patients with multiple myeloma treated with thalidomide: a phase III, open-label, randomized trial. J Clin Oncol. 2011;29:986–993.