Myocardial Dysfunction with Delayed Post-chemotherapy Enhancement Assessed in 3 Tesla Cardiac Magnetic Resonance Imaging

Felipe Gomes de Oliveira, Tiago Senra, Luciano Figueiredo Filho, Juliana Horie Silva, Hugo Bizetto Zampa, Ibraim Masciarelli Pinto

Instituto Dante Pazzanese de Cardiologia, São Paulo, SP - Brazil

Introduction

Cardiovascular diseases in patients with cancer are increasingly frequent events because of advances in cancer therapy that resulted in both improved quality of life and increased survival of patients.[1] Progress in cancer treatment in recent years have also resulted in greater exposure of patients with cardiovascular risk factors and chemotherapy with cardiotoxicity potential.[2,3]

Cardiomyopathy induced by myocardial fibrosis resulting from the use of doxorubicin and daunorubicin occurs in about 3% of patients, is dose-dependent, affects all age groups and is often irreversible.[1] Cardiotoxicity can be acute, subacute or chronic.[4] Acute or subacute cardiotoxicity is characterized by sudden changes in ventricular repolarization, changes in the Q-T interval, supraventricular and ventricular arrhythmias, acute coronary syndromes, pericarditis and myocarditis, usually observed from the onset up to 14 days after completion of treatment.[4] The chronic cardiotoxicity can be differentiated into two types, according to the onset of clinical symptoms. The first subtype occurs within one year after the end of chemotherapy and the second usually occurs one year after the completion of chemotherapy. The most typical manifestation of chronic cardiotoxicity is systolic or diastolic ventricular dysfunction that may lead to congestive heart failure and cardiovascular death.[4,5] The emergence of cardiovascular complications can determine interruption of chemotherapy, jeopardizing the cure or adequate control of cancer.[6,7] It is worth noting that heart failure has a worse prognosis than many cancers and may seriously compromise the patient's progress in treatment.[8] The classical cardiotoxic effects are cumulative and are related to the dose, infusion rate, combination of drugs and hepatic and renal failure. In theory, any chemotherapeutic agent has the potential to cause toxicity. The cardiotoxicity of anthracyclines (doxorubicin, epirubicin and idarubicin) is characterized by a decline in left ventricular ejection fraction, occurs in 5% to 25% of the cases, begins with the first doses, and is related to cumulative dose, especially with doses above 400 mg/m^2 of body surface.[9] At this dose, there is a permanent myocardial damage characterized by myocyte apoptosis, resulting in fibrosis and loss of heart function.[3]

In our case report, we seek to show myocardial fibrosis probably generated by chemotherapy (anthracycline) and demonstrate the usefulness of magnetic resonance imaging in the follow-up of patients undergoing chemotherapy.

Keywords

Cardiomyopathies; Neoplasms; Drug Therapy/adverse effects; Cardiotoxicity; Magnetic Resonance Imaging.

Mailing Address: Felipe Gomes de Oliveira •
Instituto Dante Pazzanese de Cardiologia. Av. Dante Pazzanese, 500. Postal Code 04012-909, Vila Mariana, São Paulo, SP - Brazil
E-mail: Lipejf@hotmail.com/ Felipe_gomes@usp.br/ Lipejf10@gmail.com
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Case Report

M.S.A.C., 51 years old, female, was diagnosed with breast cancer in October 2014, when she had left mastectomy followed by chemotherapy with doxorubicin at a dose of 60 mg/m^2, using a total dose of 362 mg/m^2 after six months of treatment. Following the mastectomy, coronary angiography was performed, which showed no obstructive lesions in the coronary arteries. The patient had an echocardiogram scan before the chemotherapy, which showed normal left ventricular ejection fraction (EF = 62%), with normal diastolic and systolic diameters and preserved atrial dimensions. Three months after the end of chemotherapy, the patient developed dyspnea on exertion and paroxysmal nocturnal dyspnea. Physical examination showed regular heart rate, crackles in both lung bases, pathological jugular venous distension and lower limb edema +/4+.In follow-up, a new echocardiogram scan was performed, showing a decrease in left ventricular systolic function (EF = 34%) and increase in ventricular end-diastolic diameter. As a complement, the patient was referred to cardiac magnetic resonance imaging (Ingenia 3T, Philips, Eindhover) to evaluate ventricular diameters, biventricular function and delayed enhancement. Moderate global left ventricular systolic dysfunction with ejection fraction of 32% (Simpson) was evidenced, as well as increased ventricular diameters (indexed end-diastolic volume (iEDVLV) of 128 mL/m^2 and indexed end-systolic volume (iESVLV) of 87 mL/m^2. Mild global right ventricular systolic dysfunction due to diffuse hypokinesia, with indexed end-diastolic volume (iEDVRV) of 121 ml/m^2, indexed end-systolic volume (iESVRV) 74 mL/m^2 and ejection fraction 38% (Simpson). Delayed enhancement evaluation showed lateral wall transmural fibrosis in the left ventricular apical segment (Figures 1 and 2). The patient initiated drug treatment for systolic heart failure with angiotensin-converting enzyme (ACE) inhibitors, aldosterone antagonist, beta-blockers and diuretic drugs. At the moment, the patient is hemodynamically compensated and asymptomatic.

Discussion

Cardiovascular diseases in patients with cancer are becoming more frequent events due to advances in cancer therapy resulting in both improved quality of life and increased survival of patients.[1]

Among the adverse effects of chemotherapy on the cardiovascular system, myocardial injury with systolic ventricular dysfunction and heart failure stand out for their greater frequency and severity. Despite being an infrequent event, myocardial damage evidenced by magnetic resonance imaging with delayed enhancement is a worse prognostic marker with increased cardiovascular mortality.[8]

Cardiac magnetic resonance imaging is a supplementary method of the utmost importance to demonstrate areas of myocardial fibrosis induced by chemotherapeutic agents, especially anthracyclines, defining the etiology of myocardial dysfunction and the prognosis associated with the area of ventricular fibrosis.

In this particular case, magnetic resonance imaging was valuable in demonstrating the presence of myocardial fibrosis in the left ventricle probably related to cardiotoxicity by chemotherapy. Moreover, it enabled ruling out other causes of ventricular dysfunction, such as myocarditis, which shows the distribution pattern of delayed enhancement usually different from this particular case. Although the transmural myocardial fibrosis observed in this case is commonly found in ischemic cardiomyopathies, the patient in question had had a coronary angiography scan less than one year before that did not show any obstructive lesion in the coronary arteries, which makes the ischemic etiology unlikely. In addition, the diffuse character of hypokinesia would not be expected for a minor infarction.

We know that the follow-up of post-chemotherapy ventricular function is usually carried out with echocardiography. However, cardiac magnetic resonance imaging may be useful in this scenario as it accurately measures ventricular function, identifies the presence of myocardial fibrosis and can help plan the treatment of cancer and heart failure.

Authors' contributions

Research creation and design: Oliveira FG, Senra T; Data acquisition: Oliveira FG, Figueiredo Filho L; Data analysis and interpretation: Oliveira FG; Manuscript drafting: Oliveira FG; Critical revision of the manuscript for important intellectual content: Pinto IM, Senra T; Acquisition of magnetic resonance images: Silva JH, Zampa HB.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

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This study had no external funding sources.

Academic Association

This study is not associated with any graduate program.

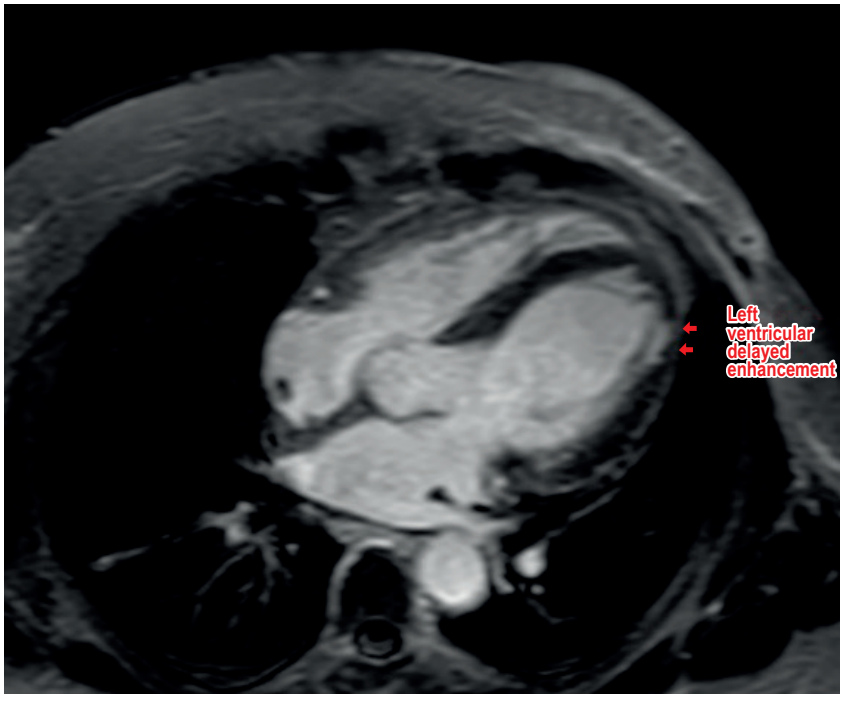

Figure 1 – *Long axis view of delayed enhancement of the heart showing myocardial fibrosis in the lateral wall of the left ventricle in the apical portion (red arrows).*

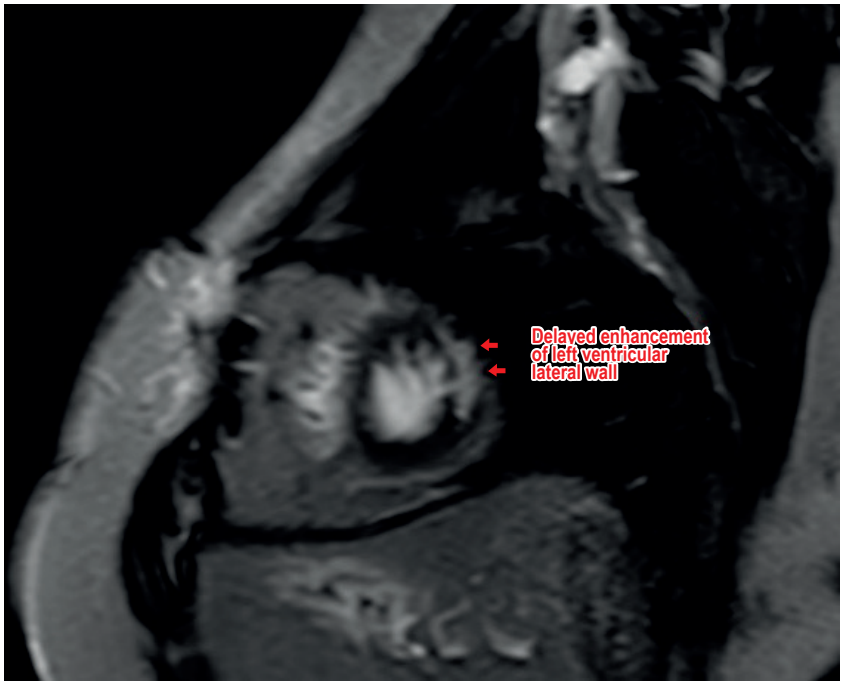

Figure 2 – *Short axis view of delayed enhancement of the heart showing transmural myocardial fibrosis in the lateral wall in the apical segment of the left ventricle (red arrows).*

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Case Report