

Radiotherapy-Chemotherapy Related Heart Diseases in Surgical Setting

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Received date: March 28, 2016; Accepted date: May 13, 2016; Published date: May 23, 2016

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Abstract

Introduction: The numbers of healed or long term survivors cancer patients are increasing. Radiotherapy and chemotherapy can induce heart damages even after many years. Cancer patient is a chronic patient and frequently requires prolonged anti-cancer therapies and repeated interventions of oncologic surgery during the course of his disease.

According to Guideline on “Perioperative Cardiovascular Evaluation and Management of Patients Undergoing non-cardiac Surgery”, the perioperative cardiologic management can determine changes that can take time and that can include the decision to change medical therapies, the decision to perform further cardiovascular interventions or the decision to recommend alternative therapeutic strategies. The consequent delay of the planned surgery to allow the assessment and significant changes in cardiologic management, will negatively affect outcome also with a negative impact on the costs for the time extension of the hospitalization.

Case report: We present a male caucasian patient of 51 years, smoker, hypertensive, with an history of resection of the right lung for lung microcytoma at age 27 years, treated with chemotherapy and radiotherapy (1988). He was admitted (2012) into our Institute to undergo total surgical laryngectomy for laryngeal cancer. At the perioperative cardiovascular assessment for non-cardiac surgery we found a total atrio-ventricular block and triple vessel coronary artery disease. The planned surgery was delayed, a dual-chamber pacemaker was implanted and the patient underwent surgical myocardial revascularization with triple coronary artery bypass grafting. Consequently, according to the decision of surgeons and oncologists the patient underwent radiation therapy instead of laryngeal surgery.

Conclusion: In cancer patients we recommend the cardiologic surveillance, also for several years, after radiotherapy and chemotherapy to detect and treat in time heart damages. This appears clinically and economically cost-effective because it can reduce the hospitalization time in surgical setting for oncologic time-sensitive procedures.

Keywords: Cardiotoxicity; Radiotherapy; Chemotherapy

Introduction

A considerable amount of literature describes the evidence of heart injuries related to exposure of radiation to the chest. Patient groups in which these cardiac injuries are clinically important is mainly represented by patients with curable malignancies irradiated in childhood or young age, they will have enough time to develop clinically significant late cardiac injury. Such malignancies are mainly Hodgkin's lymphoma and early-stage breast cancer, while there is an increasing number of lung and esophageal cancer patients with long-term controlled disease who could develop post-radiotherapy cardiac sequelae [1].

Radiotherapy and chemotherapy can induce heart damages even after many years. Cancer patient is a chronic patient and frequently requires prolonged anti-cancer therapies and repeated interventions of oncologic surgery during the course of his disease.

According to Guideline on “Perioperative Cardiovascular Evaluation and Management of Patients Undergoing non-cardiac Surgery”, the perioperative cardiologic management it can determine changes that can take time and that can include the decision to change medical therapies, the decision to perform further cardiovascular interventions or the decision to recommend alternative therapeutic strategies. The consequent delay of the planned surgery to allow the assessment and significant changes in cardiologic management, will negatively affect outcome also with a negative impact on the costs for the time extension of the hospitalization.

Case Report

We present a 51 year old male caucasian patient, admitted into our Institute to undergo total surgical laryngectomy for laryngeal cancer (squamous cell carcinoma) of supraglottic portion (2012). Comorbidity: smoker, chronic obstructive pulmonary disease, hypertension, resection of the right lung for lung microcytoma (1988) treated with chemotherapy and radiation therapy, HBV/HCV-related liver disease and a HIV infection from 1993. Home therapy:

raltegravir, tenofovir disoproxil, darunavir, ritonavir, acetylsalicylic acid, nitrates, statins, allopurinol, esomeprazole.

Two weeks before admission into our Institute he showed syncope and it was performed by attending physician an Holter ECG 24 h which didn't show pathological pauses, and it was performed a tilt test which was negative, while the carotid sinus massage triggered complete atrio-ventricular block with pause of 7 seconds without syncope.

Then the patient was admitted into our Institute. In the pre-operative cardiological evaluation for non cardiac surgery the patient reported exertional dyspnea and he didn't report angina. At the auscultation there was S3 gallop. Blood pressure: 110/70 mmHg. Heart rate: 93 b/m. The functional capacity was ≤ 4 METS. The electrocardiogram was normal: sinus rhythm, heart rate 93 bpm, normal atrio-ventricular conduction, no significant abnormalities in the ventricular repolarization. Echocardiogram: It was limited by high acoustic impedance and it showed aortic and mitral valve sclerosis; hypomobility of mitral valve leaflets; moderate aortic and mitral insufficiency; pericardium poorly evaluated; left ventricle size into the normal range; mild hypertrophy of the left ventricle; mild dilatation of the left atrium; normal size of the right cardiac chambers; hypodyskinesis of the interventricular septum; moderate reduction in the left ventricular ejection fraction (LVEF), estimate 40%.

Echo color Doppler of supra-aortic trunks: no evidence of hemodynamically significant stenosis. Chest X-ray: accentuation of bronchovascular drawing right mediastinal enlargement associated with apparent tracheal right traction disventilatory streak with fibrosis.

He was a patient scheduled for surgery with multiple risk factors for coronary artery diseases (CAD) and poor functional capacity (<4 METS). According to Guideline on "Perioperative Cardiovascular Evaluation and Management of Patients Undergoing non-cardiac Surgery" it was decided to submit the patient to further cardiological testing, but there was contraindication to pharmacologic (dipyridamole) stress testing (chronic obstructive pulmonary disease) and there was contraindication to stress echocardiography (high acoustic impedance). For these reasons we decided to subject these patients to coronary angiography directly. The laryngeal surgery was postponed and he underwent to left heart catheterization, coronary angiography and left ventriculography. It was detected a global reduction of the left ventricular systolic function and severe triple vessel coronary artery disease, (left anterior descending artery, circumflex branch of the left coronary artery and right coronary artery). There was indication to surgical myocardial revascularization. According to clinical practice guidelines a myocardial revascularization with triple coronary artery bypass grafting was performed and a dual-chamber pacemaker was implanted. Consequently according to the decision of surgeons and oncologists the patient underwent radiation therapy instead of laryngeal surgery.

Discussion

After radiotherapy can occur complex combined diseases of coronary arteries, heart valves, myocardium and conduction system as well as diastolic dysfunction [2-4].

Risk factors for radiation-associated heart damage include dose $>30-35$ Gy, dose per fraction >2 Gy, large volume of irradiated heart, younger age at exposure, longer time since exposure, use of cytotoxic chemotherapy, endocrine therapy or trastuzumab, presence of other

risk factors such as diabetes, hypertension, dyslipidaemias, obesity, smoking etc [1].

Radiation-associated heart damage includes:

- Arteritis of the endothelium of coronary arteries that can cause premature coronary artery disease and atherosclerosis mainly in left anterior descending and right coronary artery. Time of appearance is 10–15 years after RT.
- Acute pericarditis and symptomatic (haemodynamic compromise with constriction or tamponade) or asymptomatic chronic pericardial effusion, appears usually 6–12 months following RT.
- Myocarditis and congestive heart failure due to non-specific diffuse interstitial fibrosis.
- Valvular stenosis and regurgitation mainly of mitral and aortic valves.
- Fibrosis of the conduction system and complete or incomplete heart block.
- Some indirect implications on the heart may result from irradiation of adjacent structures. Lung and mediastinal fibrosis may result in respiratory insufficiency, pneumonic hypertension and may complicate any potential heart surgery. Hypothyroidism may affect the lipid profile and the cardiovascular function. Mediastinal venous and lymph vessel obstruction may cause pericardial effusion or chylothorax [1,5,6].

The improvements that occurred in the detection and treatment of cancer led to a new cohort of patients achieving a sufficient survival for develop radiation-associated heart damages [7], they might appear thanks to prolonged survival after treatment. The history of radiation therapy is often very distant in time (15-20 years) [8].

It is estimated that the radiation-induced heart disease has a prevalence of 10-30% to 5-10 years after treatment [6], and the number is expected to increase because about 40% of cancer survivors has completed radiation therapy at least 10 years [9].

Thanks to the continuous progress of medicine and the development of more effective therapies we observed an increasing number of healed or long-term survivors cancer patients. However these patients should present cardiovascular complications induced by chemotherapy or radiotherapy even after several years.

In this clinical case the patient developed some heart damages related to radiotherapy: valvular regurgitation and sclerosis, fibrosis of the conduction system and conduction disorders, coronary artery diseases, reduction in left ventricular ejection fraction (LVEF).

However this one is a complex clinical case because this patient received radiotherapy, chemotherapy, antiretroviral drugs and we delayed the surgery for preoperative cardiological management. In cancer patients the cardiological surveillance is necessary during and after radiotherapy and chemotherapy to early detect the therapy that triggered the heart damage, to start an early cardiological therapy of support and to avoid surgical delays related to cardiological management in the preoperative assessment that may occur. The changes in fact can take some time and they can include the decision to change medical therapies, the decision to perform further cardiovascular interventions, or recommendations about alternative therapeutic strategies. This particularly in patients with also HIV and HCV infections. In fact HIV infection is a cardiovascular independent risk factor for the impact that it determines on the metabolic state and for its pro-inflammatory activity. The administration of antiretroviral drugs is associated with a higher risk of cardiovascular events, and the

HCV co-infection determines an increased cardiovascular risk [10]. The delay of the surgery is an unfavorable event in the case of time-sensitive surgical procedures. A time-sensitive procedure is one in which a delay of >1 to 6 weeks to allow for an evaluation and significant changes in management will negatively affect outcome and it has also a negative impact on the costs for the time extension of the hospitalization. Most oncologic procedures would fall into this category.

Conclusions

The numbers of healed or long term survivors cancer patients are increasing, radiotherapy and chemotherapy can induce heart damages even after many years. In cancer patients we recommend the cardiologic surveillance, also for several years, after radiotherapy and chemotherapy to detect and treat in time heart damages to avoid delays in case of future oncologic time-sensitive surgery. This appears clinically and economically cost-effective because it can reduce the hospitalization time in surgical setting for oncologic time-sensitive procedures.

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