Ventricular tachycardia and non-Hodgkin's lymphoma. Syncope in a 33-year-old young

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SOUHRN

Ozařováním vyvolaná ischemická choroba srdeční je v současnosti jednou ze součástí oboru kardioonkologie, která na sebe poutá největší pozornost; případy akutního infarktu myokardu u mladých pacientů po radioterapii totiž nejsou nijak vzácné.
Popisujeme klinický případ synkopy po infarktu myokardu s elevacemi úseku ST (STEMI) zadní stěny vyvolaném komorovou tachykardií u mladého pacienta, který před deseti lety absolvoval radioterapii a chemoterapii při léčbě non-Hodgkinova lymfomu.

ABSTRACT

Radiation induced coronary heart disease is among the most actively studied areas in cardio-oncology today. In fact, cases of acute myocardial infarction in young patients previously subjected to radiotherapy are not rare.
We describe a clinical case of a syncope following an inferior STEMI started with ventricular tachycardia, in a young patient who underwent radio- and chemotherapy treatment 10 years ago for the treatment of non-Hodgkin's lymphoma.

Introduction

In the treatment of non-Hodgkin's lymphomas, radiotherapy still remains one of the fundamental cornerstones of treatment, significantly improving the prognosis of patients with a 5-year disease-free survival of about 85% in the treated subjects.[1]

However, mediastinal irradiation, often with high doses of ionizing radiation, causes different effects on the heart, determining various pathological pictures that interest pericardium, myocardium, systolic ventricular function, heart valves and coronary circulation.[2–9] Population-based studies estimating excess risk to develop ischemic heart disease at 25% and 50% among survivors of breast cancer and HL, respectively.[5–13] For this reason, the interest of the international scientific community in cardio-oncology has grown considerably in recent years. Cardio-oncology has made it possible to provide valid screening programs for patients undergoing oncological treatments that have important repercussions on the cardiovascular system, so as to act in time with preventive measures and therapies.

Clinical case

A 33-year-old young man comes to the Emergency room for a syncopal episode during a dinner. ECG documents sustained VT at 240 bpm (Fig. 1), administered amiodarone without success, when the arrhythmia and hemodynamic instability persisted, electrical cardioversion (200 j) was carried out.

When sinus rhythm was restored, the ECG showed a sopraelevation of the ST segment in DII, DIII aVF, therefore the patient was immediately taken to the hemodynamics laboratory.

Coronary angiography documented chronic occlusion of right coronary (Fig. 2) with indication for medical therapy.

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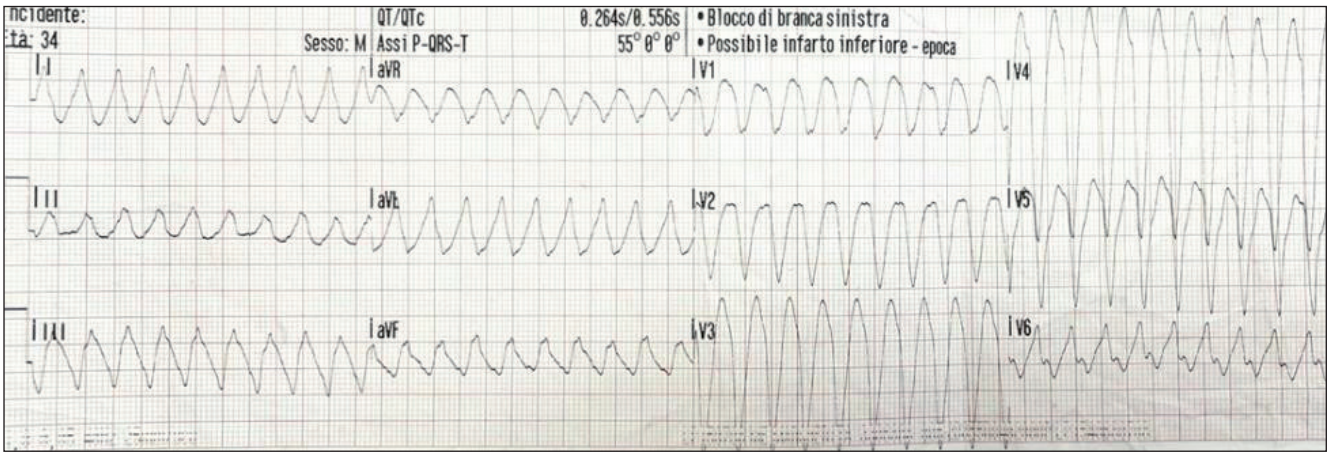

Fig. 1 – Permanent ventricular tachycardia at 240 bpm.

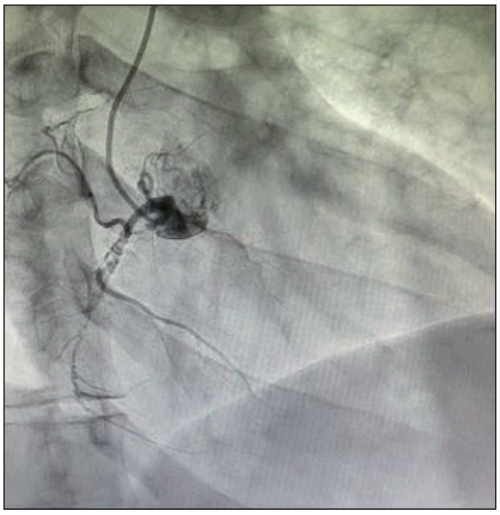

Fig. 2 – Coronary angiography documenting chronic occlusion of the right coronary artery.

From the patient's medical history, it emerged he had undergone splenectomy and radio- and chemotherapy for Hodgkin's lymphoma 10 years ago with complete regression to subsequent oncological follow-up, in the absence of other cardiovascular risk factors except for family history of ischemic heart disease.

The blood chemistry tests at the entrance showed a slight increase in CK-MB and troponin.

The echocardiogram highlighted: hypokinesia of the basal segment of the lower septum, of the lower and inferolateral wall with preserved left ventricular global function (EF 50%). During the hospitalization, amiodarone infusion continued with subsequent switch to oral therapy and after a collegial valuation a subcutaneous ICD implant was chosen. The remaining clinical course was uneventful and the patient was discharged on the eighth day, with a one-month follow-up.

Discussion

Syncope secondary to ventricular tachycardia is a not infrequent event in young subjects, but is generally correlated to conduction system anomalies, reentry circuits or ectopic focus. In the case described above, the trigger of this arrhythmia, which occurred with an episode of loss of consciousness, is attributable to acute myocardial infarction inferior with chronic total occlusion (CTO). Soteriades et al. in a prospective cohort study, showed an increase in mortality over 17 years in patients with cardiac syncope.[14] An article by Elpidoforos published in *New England Journal of Medicine* about incidence and prognosis of syncope said that cardiac syncope doubled the risk of death from any cause and increased the risk of fatal and nonfatal cardiovascular events. Survival of the syncopal episode is an opportunity to prevent future sudden death. In our case, we opted for subcutaneous ICD implant compared to the traditional defibrillator, based on current clinical experiences and scientific evidence, in particular in subjects with a long life expectancy. The patient's clinical history shows how mediastinal radiotherapy can favor a particularly accelerated atherosclerotic process.[13] Many studies report that patients who survived from Hodgkin's lymphoma approximately ten years after the completion radiotherapy, develop cardiovascular disease. It's typical that coronary angiography finds angiographically severe proximal or ostial disease, and this pattern is associated with higher incidences of acute myocardial infarction (MI) and sudden cardiac death.[15–31]

Some studies demonstrated that in patients treated at younger age than in patients treated at older age relative risks of myocardial infarction mortality increased.[32–34] This is due to the fact that arteries in young patients are more susceptible than those in adults to suffering radiation damage. The pathogenesis of coronary artery disease, as a result of local radiotherapy, is essentially based on an accelerated atherosclerotic process by marked inflammation from oxidative stress and secretion of multiple inflammatory and profibrotic cytokines that cause endothelial damage of the coronary arteries.[5] Some studies have examined the histological characteristics of radiotherapy-induced coronary heart disease (RICHD) at autopsy. Plaques of patients undergoing radiotherapy have a greater fibrocalcific component with increased fibrotic content of the intima and media, associated with >50% narrowing of the great

epicardial vessels in 28% of all coronary arteries, while the lipid deposits were very rare.[35]

Heidenreich have reported unexpected early deaths from myocardial infarction at young ages after HL. Serhan Kupeli in an article published in *World Journal of Cardiology* 2014 said that probability of developing a coronary abnormality depends on the radiation dose, because it was 6 to 8 times higher in a group of patients receiving mediastinal radiotherapy more than 2000 cGy in comparison with the other group receiving radiotherapy less than 2000 cGy by multivariate analysis ($p = 0.009$).[36] In our case, we are in front of an advanced stage post actinic coronary artery disease, not susceptible to percutaneous coronary intervention (PCI), which resulted in ischemic suffering of the inferior-posterior wall of the left ventricle with triggering of ventricular tachycardia (VT).

The patient's clinical and anamnestic history shows that a screening program for the evaluation of associated coronary artery disease is essential and necessary for patients undergoing mediastinal radiotherapy for the treatment of HL.

Although research and introduction of new oncological therapies have improved the survival of cancer patients significantly, the adverse events on the cardiovascular system are increasing constantly. So in the international context, the interest in cardio-oncology has grown, making a complete cardiological evaluation essential before the start of each radio- and chemotherapy treatment. Many studies suggest echocardiography for baseline and serial monitoring, though the National Comprehensive Cancer Network recommends stress testing as a reasonable alternative because it could show alterations not visible on the simple echocardiogram suggestive of coronary microcirculation disease.[37] Cardio-oncology must refer to all non-invasive imaging methods in order to provide a valid screening for cardiac pathologies, from simple echocardiography to advanced imaging methods such as cardio computed tomography (CT). In this regard, coronary CT is a minimally invasive and easily reproducible method that can be used in screening.[38,39] Angiography-CT provides information about the vascular wall and soft tissues besides vessel lumen, helps determining the pathologic vessels and additional extra vascular abnormalities in advance and calcium in arterial wall.[40,41] So calcium score is an important parameter to consider, but its low specificity, and without further conditions a conventional angiography, cannot be indicated solely based on coronary calcium scoring. Girinsky et al. in their trial focused on using coronary computed tomography angiography in asymptomatic Hodgkin lymphoma (HL) patients demonstrated an increase in the prevalence of coronary artery abnormalities from 15% in the first 5 years after radiotherapy to 34% at 10 years post-treatment in a cohort of asymptomatic HL survivors, with confirmed diagnosis of obstructive lesions by coronary angiography in 10% of patients and revascularization in 6%.[42] However, it must be considered that the use of cardioTC would expose a patient to a certain dose of ionizing radiation, and should therefore be evaluated in relation to age, comorbidities, renal function, and the pre-test probability of using this method.

Conclusions

Our clinical case, in its complexity, shows how syncope in a young patient can represent only the tip of the iceberg of a multifactorial condition where acute myocardial infarction and the consequent arrhythmia are attributable to coronary artery disease favored by previous cycles of radio- and chemotherapy. Therefore, there is a need for Hodgkin's lymphoma patients receiving radio- and chemotherapy treatment, to undergo a screening program that does not only consider the evaluation of systolic function with repeated echocardiograms, but also the epicardial coronary vessel disease that could result from irradiation of mediastinal.

Today there are numerous studies about cardio-oncology for study valid screening programs, so as to allow cancer patients to obtain the maximum effect from chemotherapy or radiotherapy by limiting the cardiotoxic effects as much as possible. The clinical case we have described is intended as a reminder of how the increase in survival in patients with cancer thanks to the new treatments leads to an increase in the incidence of adverse cardiovascular events. Therefore, cardio-oncology becomes a cornerstone in the therapeutic management of cancer patients and it is essential to continue research in this area.

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