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CASE REPORT

Safe application of extensive radiotherapy to a cardiac resynchronization device

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Abstract

Patients with cardiac implantable electronic devices undergoing radiotherapy (RT) are prone to the risk of device failure. Guidelines and manufacturer's instructions are lacking practical recommendations for cumulative radiation doses to pacemakers or implantable cardioverter defibrillators. The present case demonstrates the effect of RT of a Merkel cell carcinoma near the location of a cardiac resynchronization therapy pacemaker. Despite guideline recommendations, surgical relocation or *de novo* implantation of the device on the contralateral side was avoided to prevent the dissemination of tumour cells, inflammation, and wound healing complications. A total dose of 47.25 Gy applied in very close proximity to the cardiac resynchronization therapy pacemaker was carried out safely without jeopardizing the patient and any device malfunction during and after treatment within >1.5 years of follow-up period. The present case demonstrates that high-dose RT near to a cardiac resynchronization therapy device can be carried out safely. Special precautions during RT as well as close device follow-up interrogations are mandatory. Large-scale studies are needed for the true frequency of adverse events.

Keywords Resynchronization therapy; Radiotherapy; Cardiomyopathy

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Introduction

Patients with cardiac implantable electronic devices (CIEDs) undergoing radiotherapy (RT) are prone to the risk of transient or permanent device failure such as reset to the backup pacing mode, inappropriate pacing inhibition, or inappropriate antitachycardia therapies in implantable cardioverter defibrillators. Guidelines and manufacturer's instructions are lacking practical recommendations for cumulative radiation doses to pacemakers (PMs) or implantable cardioverter defibrillators.[1–3]

Case Report

A 63-year-old man was referred to our outpatient clinic diagnosed with a histologically confirmed Merkel cell carcinoma with a huge lymph node metastasis conglomerate in the right axilla (*Figure 1*). The tumour infiltrated parts of the pectoralis major musculature and the neighbouring nerves and vessels. The origin of the Merkel cell carcinoma was unknown.

The patient has a long-standing history of symptomatic paroxysmal atrial fibrillation and atrial flutter (*Table 1*). He underwent a cavotricuspid isthmus ablation and two pulmonary vein isolation procedures. Over the following years, biatrial electrical disease progression led to persistent atrial fibrillation with rapid ventricular conduction. Eight years later, atrioventricular (AV) node ablation was performed for permanent rate control, and a single-chamber PM was implanted. Because of the worsening of heart failure and New York Heart Association Class III symptoms, the device was upgraded to a cardiac resynchronization therapy pacemaker with a new atrial and a left ventricular lead (Boston Scientific®, Marlborough, MA, USA) a few months later. The device was programmed to ventricular demand pacing (VVIR) mode

Figure 1 (A) Chest X-ray in posterior-anterior projection showing the atrio-biventricular pacemaker implanted from the right side, including one abandoned lead in the right ventricle. (B) The 18-fluorodeoxyglucose positron emission tomography/computed tomography scan demonstrates tumour-related fluorodeoxyglucose uptake in a lymph node conglomerate in the right axilla (arrow) close to the cardiac resynchronization device.

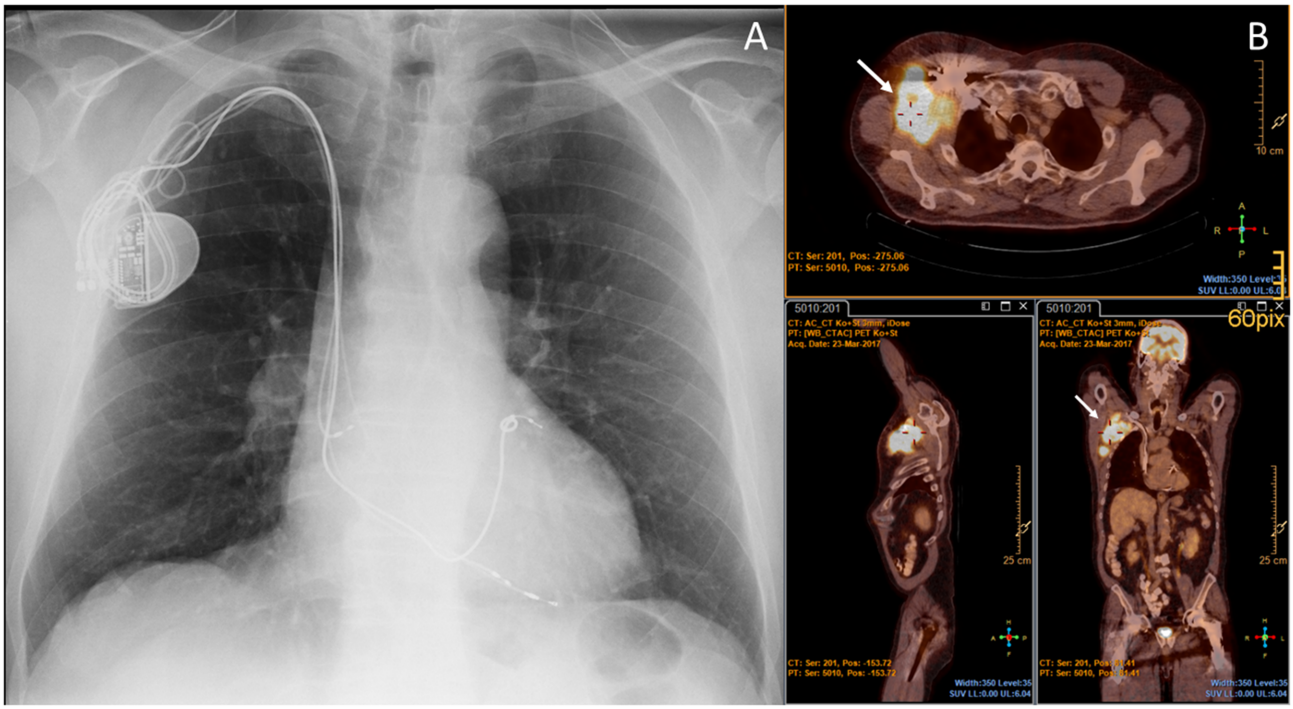

Table 1 Chronological medical history

Chronology of events (years prior to last follow-up)	Clinical disorder	Therapy	Complications
20	Paroxysmal atrial fibrillation	Rhythm control with a variety of antiarrhythmic drugs including amiodarone	Amiodarone-induced thyrotoxicosis
18	Paroxysmal atrial flutter	Cavotricuspid isthmus ablation	
14	CHF	Optimal medical treatment with ACE-Inhibitors and beta-blockers	
13	Aggravation of atrial fibrillation	PVI	
12	Recurrences of atrial fibrillation	PVI redo ablation	Pericardial tamponade
11.5	Progression to persistent atrial fibrillation with rapid ventricular conduction refractory to drugs	Rate control with AVN ablation and implantation of a single-chamber pacemaker (ablate and pace)	LV dyssynchrony soon after device implantation, NYHA Class III symptoms, presyncopal episodes
11	Progression of CHF (LVEF <30%)	Upgrade to CRT-PM	
1.5	Merkel cell carcinoma with a huge lymph node metastasis conglomerate in the right axilla	RT and chemotherapy	No device-associated complications occurred during and after RT
1	Major depressive disorder	Antidepressant therapy	Suicide despite psychological and medical treatment

ACE, angiotensin-converting enzyme; AVN, atrioventricular node; CHF, congestive heart failure; CRT-PM, cardiac resynchronization therapy pacemaker; LV, left ventricular; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PVI, pulmonary vein isolation; RT, radiotherapy.

with a base rate of 60 ppm. The echocardiogram showed a dilated cardiomyopathy with an ejection fraction of 30%. During PM inhibition, the underlying rhythm was permanent atrial fibrillation with a complete atrioventricular block and a stable intrinsic ventricular escape rhythm of 35–40 b.p.m. In a tumour board conference, a primary (neoadjuvant) RT was recommended. A multidisciplinary group of oncologists, dermatologists, radiation oncologists, specialists in nuclear medicine, and cardiologists carefully planned the treatment strategy. According to literature, a cumulative radiation dose

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to PMs exceeding >10 Gy (1 Gy = 1 J of absorbed energy of ionizing radiation per 1 kg of matter) justifies preventive device relocation.[1,2] However, because of the infiltration of the PM pocket and the right vena subclavia, a relocation of the device to the contralateral side implicated the risk of dissemination of tumour cells, as well as inflammation and wound healing complications. *De novo* device implantation from the left subclavian side was considered but refused by the patient because of the unclear progression of the disease. Consequently, the PM was left in the site, and the patient received RT with volumetric-modulated arc therapy technique 2.25 Gy daily/5× weekly to a total dose of 47.25 Gy; RT was delivered using an equally weighted 6 MV photon beam. The applied intensity-modulated RT is based on combinations of multiple intensity-modulated fields coming from different beam directions. This technique produced a customized radiation dose that maximizes the tumour dose while also minimizing the dose to adjacent normal tissues. During RT, the patient was connected to continuous ECG monitoring showing no rhythm abnormalities or loss of stimulation. For high-energy RT in PM-dependent patients, the use of magnet or device reprogramming has been recommended.[3] As the patient was not strictly PM dependent (escape rhythm 35–40 b.p.m.), we decided to have a magnet ready to use in the radiation room in case of inappropriate pacing inhibition. A cardiologist was in a standby position for optional transcutaneous pacing in case of a device failure. Weekly follow-up visits were scheduled in the PM clinic throughout the application of RT. The calculated maximum, minimum, and mean doses to the PM were 47.26, 8.73, and 29.16 Gy, respectively. *In vivo* dosimetry has not been carried out in this case. Following RT, the patient was treated with chemotherapy (carboplatin/etoposide) for 4 cycles. Interestingly, the last positron emission tomography scan 12 months after RT showed no local tumour left. The cardiac resynchronization therapy pacemaker was checked with periodic device interrogations during a follow-up of >1.5 years and showed no malfunctions at all.

Discussion

In the present case, the effective radiation dose at the location of the PM was excessively high as the cardiac resynchronization therapy device was directly exposed to the primary radiation field. This case is in line with other experiences reported in the literature demonstrating the resistance of some devices to considerably higher doses than officially recommended.[4] Modern devices with contemporary complementary metal oxide semiconductor components in the electrical circuit are more robust to damage by RT than earlier designs, which had bipolar transistor-based technologies.[5] Furthermore, modern volumetric-modulated arc therapy techniques leading to low scatter radiation to normal tissue may have contributed to the functional resistance of the cardiac resynchronization therapy device.[3] Expert consensus currently considers a threshold of <2 Gy as low risk,[1,6] but in the literature, this cut-off is discussed as too stringent and impractical. Cumulative research has generally reported that radiation dose does not correlate with device malfunction as shown by the wide range of doses at which CIEDs failed within these studies. On the other hand, even very low cumulative doses may lead to device malfunction such as inappropriate pacing inhibition, PM program resetting, or PM battery depletion.[5,7] In contrast, Bagur *et al*. identified in a large population cohort that the total dose prescribed to the tumour is the only independent predictor for dysfunctions of CIEDs (7%). Furthermore, neither the radiated zone nor the cancer location side was associated with increased rates of dysfunction, and their results suggest that relocation did not protect the occurrence of malfunctions. Future prospective randomized studies have to clarify whether the current practice of CIEDs relocation will remain as general recommendation.[8] Yeung *et al*. proposed in his review the implementation of a clinical approval system for CIEDs exposed to RT similar to magnetic resonance conditional labeling.[5] However, the management of patients with CIEDs undergoing RT must be planned carefully in a multidisciplinary approach between radiation oncology and cardiology with a special focus on individualized risk assessment to carry out a safe and effective treatment.[3,4]

Conclusions

Leaving the CIED in place during high-dose RT may be considered instead of complex device relocation in selected patients under preventive safety measures.

Conflict of interest

None declared.

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