CASE REPORT

Doxorubicin-induced ventricular arrhythmia treated by implantation of an automatic cardioverter-defibrillator

Tomasz Rudzinski*, Michal Ciesielczyk, Wojciech Religa, Zbigniew Bednarkiewicz, and Maria Krzeminska-Pakula

2nd Department of Cardiology, Medical University of Lodz, Kniaziewicza 1/5, 91-347 Lodz, Poland

Received 12 October 2006; accepted after revision 9 February 2007; online publish-ahead-of-print 23 March 2007

Anthracyclines are a group of potent antitumour agents and cardiotoxicity is an important factor limiting their therapeutic effectiveness. Although cardiomyopathy is the most widely recognized type of cardiotoxic reaction, early arrhythmia following anthracycline administration may be of clinical significance as well. We report a case of ventricular tachycardia causing cardiac arrest in a female treated with doxorubicin as adjuvant therapy of breast cancer. Due to recurrence of the arrhythmia and a desire to continue chemotherapy, an automatic cardioverter-defibrillator was implanted with excellent effect.

KEYWORDS
Anthracyclines; Cardiotoxicity; Arrhythmia

Introduction

Anthracyclines represent a group of potent antineoplastic agents used in the treatment of haemopoetic malignancies and solid tumours. Unfortunately, significant cardiotoxic side-effects limit their therapeutic effectiveness. Four types of anthracycline cardiotoxicity have been described: acute, subacute, chronic, and late-onset.1 The latter two are manifested by cardiomyopathy leading to heart failure and are probably the most common types.2 Nevertheless, acute cardiac side-effects occurring during or directly after anthracycline administration might be clinically important as well.1 We present a case of a patient who developed life-threatening ventricular arrhythmia during doxorubicine chemotherapy for breast cancer.

Case report

A 48-year-old female was referred to the cardiology department from the oncology ward after an episode of cardiac arrest treated successfully on-site with external defibrillation. Three months earlier the patient had been diagnosed with T1N1M0 cancer of the right breast. She was treated with upper-lateral quadrantectomy and axillary lymphadenectomy and scheduled for adjunctive chemotherapy consisting of four pulses of doxorubicine 90 mg/m² iv. and cyclophosphamide 600 mg/m² iv. Cardiac arrest occured during administration of doxorubicine in the first cycle of chemotherapy. Although no electrocardiogram was recorded during the episode, successful defibrillation suggested a ventricular fibrillation/ventricular tachycardia mechanism.

On admission to the cardiology department the patient was asymptomatic. She was in good health until being diagnosed with the malignancy and had no history of cardiac arrest, syncope, or palpitations. The physical examination was unremarkable. An electrocardiogram revealed normal sinus rhythm with a rate of 88 bpm with no ST and T wave changes. All laboratory studies including electrolyte levels were within normal range. An echocardiogram did not reveal any abnormalities. Twenty-four electrocardiographic monitoring showed normal sinus rhythm ranging from 52 to 123 bpm and 275 single monomorphic ventricular premature complexes. Cardiac catheterization was performed, which showed normal coronary arteries.

The patient was scheduled to receive the next pulses of chemotherapy under continuous electrocardiographic monitoring. Doxorubicin infusion was completed with no complications, but 2 h later the patient developed regular monomorphic ventricular tachycardia with a rate of 205 bpm with cardiac arrest (Figure 1). External cardioversion was performed immediately. Due to necessity to continue chemotherapy, implantation of an automatic cardioverter-defibrillator was proposed to the patient. The procedure was performed on the next day without complications—a single chamber device (GEM III VR, Medtronic, Minneapolis, USA) was implanted in the left prepectoral site and connected to one quadrupolar double coil defibrillation lead (Sprint Quattro, Medtronic, Minneapolis, USA). Interrogation of the device after 3 months revealed two episodes of ventricular tachycardia terminated by

© The European Society of Cardiology 2007. All rights reserved. For Permissions, please e-mail: journals.permissions@oxfordjournals.org
antitachycardia pacing. These episodes did not occur during infusion of doxorubicin. The patient completed her chemotherapy and was in full remission after 12 months.

Discussion

Anthracycline-induced cardiotoxicity is a major clinical problem. It has been shown to be dose-dependent and therefore is the most significant factor limiting cumulative drug dose which can be administered during chemotherapy. As a result, cardiac side-effects directly compromise anti-cancer effectiveness of anthracyclines. Chronic and late-onset toxicity manifested by dilated cardiomyopathy are the most commonly recognized types of toxicity and may occur years after completion of therapy.1,2 Acute side-effects are probably at least as frequent but rarely lead to clinically important complications. They usually appear as electrocardiographic abnormalities, such as sinus tachycardia, non-specific ST and T wave changes, decreased QRS voltage, and prolongation of the QT interval.3,5 However, symptomatic arrhythmias have also been described, such as supraventricular and ventricular tachycardia, antiarrhythmic or bundle-branch block.6

Single cases of sudden cardiac death were reported in early clinical studies on adriamycin but the electrophysiologic mechanism was not evaluated. Furthermore, Wortman, Couch, and Lacasse documented cases of cardiac arrest following anthracycline treatment. Ventricular fibrillation was recognized as the underlying mechanism in some of these cases. On the basis of such reports, numerous studies have been performed to assess the arrhythmogenic effect of anthracyclines. Most of them utilized Holter electrocardiographic monitoring during and after administration of the drug. In general, it was shown that a high proportion of patients developed ventricular ectopy directly after anthracycline administration. One of these studies also demonstrated a statistically significant increase of the risk of QT interval prolongation and development of ventricular tachycardia. Unfortunately, no definite risk factors predisposing to ventricular arrhythmia have been proven to be clinically valuable in this population of patients.

The mechanism of early arrhythmia following anthracycline administration is not clear. A direct cytotoxic effect of either the agent or its metabolites may play a role, but other possible pathways have been proposed as well. These include generation of free radicals, release of vasoactive mediators, intracellular calcium overload, or adrenergic imbalance. Established proarrhythmic factors, especially hypokalaemia, not suprisingly promote acute arrhythmogenic toxicity of anthracyclines. In fact, close monitoring of electrolyte levels is to date the only method of primary prevention of this type of reactions.

It is important to distinguish early arrhythmic complications, which occur during or directly after administration of anthracyclines, from late-onset arrhythmias. The latter are usually presumed to be secondary to anthracycline-induced cardiomyopathy.

In this report, we describe a case of life-threatening ventricular tachycardia during doxorubicin administration for adjunctive chemotherapy of breast cancer. The patient had no history of cardiovascular disease, cardiac arrest, syncope, or palpitations. Other potential causes of arrhythmia, including electrolyte imbalance and coronary artery disease, were ruled out during excessive diagnostic evaluation of the patient. Because of the recurrence of ventricular tachycardia and a necessity to continue doxorubicin therapy, the patient was scheduled for automatic cardioverter-defibrillator implantation. This allowed the planned chemotherapy to be continued, thus increasing the chances of successful treatment of breast cancer.

In conclusion, anthracycline cardiotoxicity is not confined to late-onset cardiomyopathy. These highly effective drugs may also lead to dangerous early complications manifested by life-threatening arrhythmia. In such cases, all available therapeutic options, including implantation of an automatic cardioverter-defibrillator, should be considered.

References


