Folia Cardiologica 2020
tom 15, nr 6, strony 424–427
DOI: 10.5603/FC.2020.0062

ISSN 2353–7752

Sinus node dysfunction as a late complication of Hodgkin lymphoma treatment

Dysfunkcja węzła zatokowego jako późne powikłanie leczenia chłoniaka Hodgkina

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Abstract

Cardiotoxicity and cardiovascular complications associated with radiation therapy can be revealed many years after oncological therapy, most often 15–20 years after this treatment. A 45-year-old man was admitted to hospital due to syncope with accompanying head injury. At the age of 30, he was diagnosed with Hodgkin lymphoma (clinical stage III) and underwent chemotherapy (including doxorubicin), followed by mediastinal radiotherapy. Complete remission of the disease was achieved, and the patient remained under constant haematological control for the following years.

On admission to the hospital, sinus bradycardia up to 25/min was recorded in electrocardiographic (ECG) examination, without other abnormalities. ECG monitoring carried out in the following hours revealed episodes of sinus arrest (up to 17 s). Laboratory test results were in the normal range. Transthoracic echocardiography showed no abnormalities. The oncological treatment has been considered the most likely cause of sinus node damage. Due to symptomatic sinus node dysfunction, the patient was implanted with a dual-chamber pacemaker.

The presented case report confirms the need for indefinite cardiological supervision in patients after oncological treatment in childhood or youth, especially when thorax irradiation and chemotherapy with proven cardiotoxicity were applied.

Key words: Hodgkin lymphoma, sinus node dysfunction, radiotherapy, cardiotoxicity, oncological treatment, cardio-oncology

Folia Cardiologica 2020; 15, 6: 424–427

Introduction

Cancer and cardiovascular disorders are the most common diseases in our population [1]. The Position Paper of the European Society of Cardiology (ESC) of 2016 and the consensus of the European Society of Clinical Oncology (ESMO) of 2020 describe the management of cardiovascular diseases in patients with cancer [1, 2]. The most common complications associated with chemotherapy include left ventricular (LV) dysfunction, heart failure, and arrhythmias. For chest radiotherapy, pericarditis is the most common early complication. Later these are arrhythmias, conduction disorders, valvular heart disease and chronic pericarditis. It is believed that arrhythmias and conduction disorders can affect up to 75% of patients treated for Hodgkin lymphoma and occur 14.3 years (median) after treatment [3].

Case report

A 45-year-old man was admitted to the Cardiology Department because of syncope with a head injury. At the age of 30 due to the diagnosis of Hodgkin lymphoma (clinical

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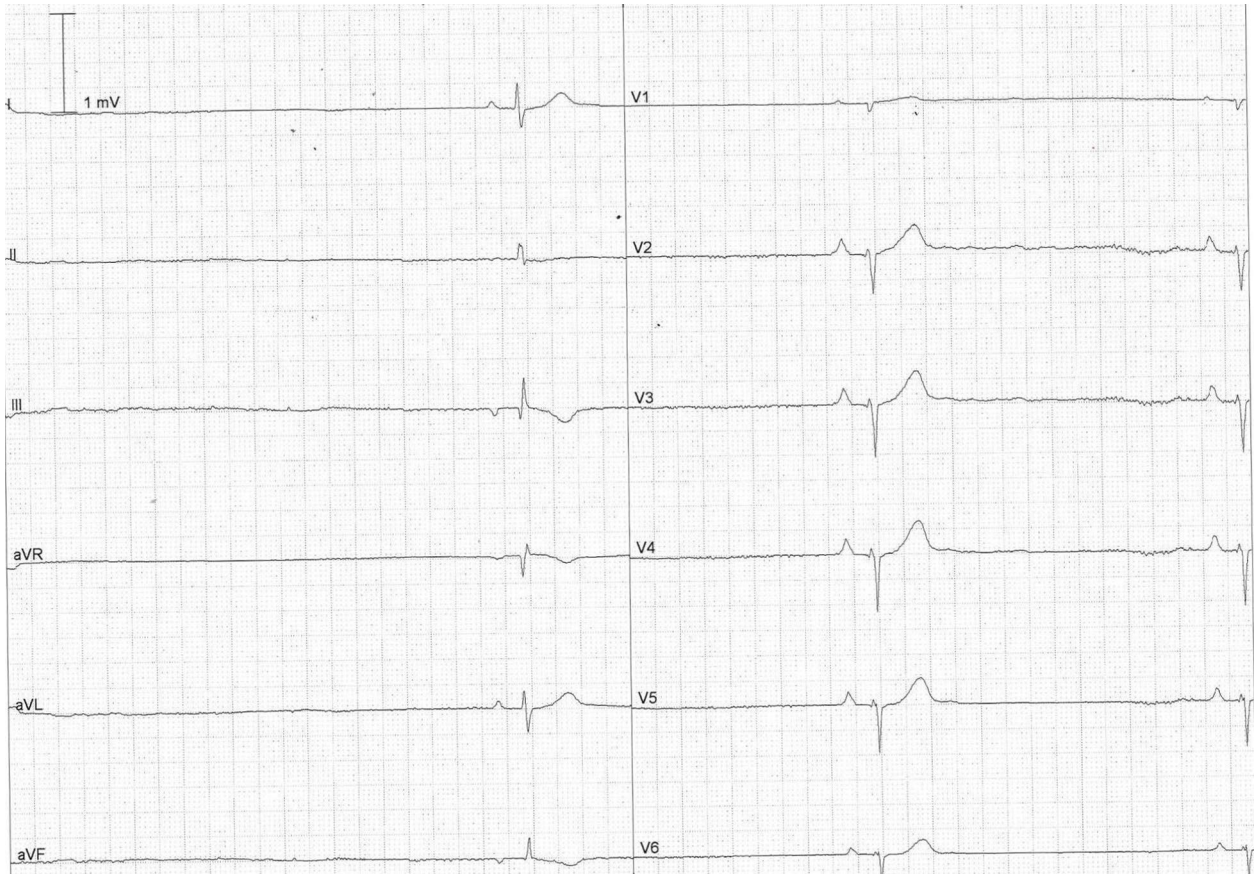

Figure 1. Sinus arrest with pauses — a printout of telemetry ECG monitoring after admission to hospital (Philips Medical Systems, USA). Amplitude: 20 mm/mV, paper speed 25 mm/s

stage III), the patient received 6 cycles of chemotherapy according to the ABVD regimen: doxorubicin, bleomycin, vinblastine and dacarbazine (total cumulative dose of doxorubicin was 150 mg/m^2). It was followed by radiotherapy, which involved the mediastinal and right cervical lymph nodes (total radiation dose was 30 Gy). Complete remission of the disease was achieved, and the patient remained under constant haematological control.

On admission to the hospital, the patient did not report any symptoms, but the electrocardiographic (ECG) examination showed sinus bradycardia up to 25/min, without other abnormalities. The following hours of ECG monitoring revealed sinus bradycardia, transient 1st degree AV block (PR interval up to 230 ms) and recurrent episodes of sinus arrest (Figure 1), with the longest pause of 17 seconds. Transthoracic echocardiography (TTE) didn't show any abnormalities. Laboratory results also were normal. Dobutamine stress echocardiography and computed tomography angiography did not show a coronary reserve reduction or significant narrowing of the coronary arteries. Doppler ultrasound of the carotid arteries did not show any abnormalities. Ultimately, thoracic radiotherapy was considered the most likely cause of sinus node dysfunction. Due to symptomatic and severe sinus node disease, the patient was implanted with a dual-chamber pacemaker (Vitatron G70A2 DR).

Control echocardiography performed 2 years later showed normal LV function with LVEF of 65% and LV global longitudinal strain (GLS) of –19%, with only slightly impaired regional deformation in basal inferoseptal and lateral segments (Figure 2). Pacemaker control revealed its proper function, with no arrhythmias recorded. The patient confirmed well-being, good exercise tolerance and lack of any symptoms, still not taking any medications.

Discussion

Thorax radiation therapy is associated with the risk of arrhythmias and conduction disorders such as sinus arrest, atrioventricular conduction disturbances, right bundle branch block and others [4]. Conduction disturbances after radiation therapy can occur in 5% of patients [5]. Shira et al. [6] showed that patients with Hodgkin lymphoma treated with thoracic radiation twice as often require implantation of a pacemaker or cardioverter-defibrillator compared to the general population. However, atrioventricular conduction

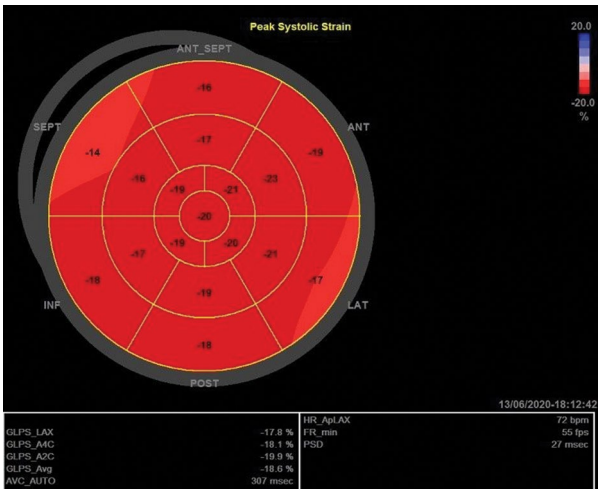

Figure 2. Left ventricular longitudinal strain bull's eye plot derived from the two-dimensional (2D) speckle tracking imaging in echocardiography performed two years after pacemaker implantation (GE Healthcare, Chicago, Illinois, USA)

disturbances are mainly seen after mediastinal irradiation. Sinus node dysfunction is extremely rare. It is postulated that this may be the result of radiotherapy-induced atherosclerosis in the sinoatrial artery, which cannot be assessed in routine computed tomography because of the small size of the vessel. Nabiałek-Trojanowska et al. [7] indicated that sinus node disease may be the result of ischemia, myocardial fibrosis or direct damage to the cardiac conduction system due to radiation therapy.

It has been shown that an independent risk factor for cardiovascular complications caused by oncological treatment constitute the total cumulative doxorubicin dose ≥ 250 mg/m^2 or total radiation dose ≥ 30 Gy when the heart is in the radiation field, or doxorubicin dose ≤ 250 mg/m^2 when combined with the radiation dose ≤ 30 Gy [8]. Cardiovascular complications after radiation therapy may appear late, even after 15–20 years after the end of oncological treatment, which was also observed in the presented patient. Younger age of the patient during oncological treatment is a well-documented risk factor for cardiovascular complications.

Conclusion

The presented case confirms the necessity of lifetime cardiological supervision in patients who underwent oncological treatment at a young age. This is especially true for patients in whom combination therapy was applied: thoracic irradiation and chemotherapy with proven cardiotoxicity. Following current recommendations of scientific societies, life-long cardiac supervision is required in patients after thoracic radiotherapy [9].

Funding

Not declared.

Conflict of interest

The authors declare no conflict of interest.

Streszczenie

Kardiotoksyczność i powikłania sercowo-naczyniowe związane ze stosowaną radioterapią mogą się ujawnić wiele lat po zakończeniu leczenia onkologicznego, najczęściej 15–20 lat po jego zakończeniu. Czterdziestopięcioletni mężczyzna został przyjęty do szpitala z powodu utraty przytomności z towarzyszącym urazem głowy. W wieku 30 lat w związku z rozpoznaniem chłoniaka Hodgkina (stadium III) był leczony chemioterapią z zastosowaniem między innymi doksorubicyny oraz radioterapią śródpiersia. Po leczeniu uzyskano całkowitą remisję, a pacjent był objęty nadzorem hematologicznym; nie zgłaszał alarmujących objawów.

Przy przyjęciu do szpitala w badaniu elektrokardiograficznym (EKG) zarejestrowano bradykardię zatokową około 25/min, bez innych nieprawidłowości. Prowadzone w kolejnych godzinach monitorowanie EKG wykazało epizody zahamowania zatokowego (do 17 s). W badaniach laboratoryjnych nie stwierdzono istotnych odchyleń od normy. Przezklatkowe badanie echokardiograficzne nie ujawniło nieprawidłowości. Za najbardziej prawdopodobną przyczynę uszkodzenia węzła zatokowego uznano przebyte leczenie onkologiczne. W związku z objawową dysfunkcją węzła zatokowego pacjentowi implantowano dwujamowy stymulator serca.

Prezentowany opis przypadku potwierdza konieczność bezterminowego nadzoru kardiologicznego u osób po przebytym w dzieciństwie lub młodości leczeniu onkologicznym, zwłaszcza gdy koniecznie było stosowanie radioterapii klatki piersiowej oraz chemioterapii o udowodnionej kardiotoksyczności.

Słowa kluczowe: chłoniak Hodgkina, dysfunkcja węzła zatokowego, radioterapia, kardiotoksyczność, leczenie onkologiczne, kardioonkologia

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