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Cardio-oncology challenges — a case report of de novo heart failure in tongue cancer patient

Wyzwania kardioonkologii — przypadek pacjenta z rakiem języka i niewydolnością serca *de novo*

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Abstract

Nowadays, the role of public education about cancer is increasing. Diagnostic methods are also being improved, which, coupled with increased patient awareness, translates into an increase in the detection of cancer and, therefore, an increased number of patients using oncological therapy. However, this therapy is not without complications, especially in the context of the cardiovascular system. It may lead to certain complications, such as cardiomyopathy, myocarditis, vascular damage, hypertension or the development of heart failure, as was the case in the described case. Even though some forms of therapy have a greater cardiotoxic potential than others. According to the ESC 2022 guidelines, each patient should undergo an appropriate cardiological assessment to determine the level of risk of developing cardiotoxic complications. This constitutes a specific challenge for doctors, and it is even more important because complications may appear even decades after the end of oncological therapy. The case presented below is intended to draw attention to the problems of cardio-oncology patients and contribute to their more effective diagnosis and treatment.

Keywords: radiochemotherapy, heart failure, cardio-oncology

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Introduction

Cardio-oncology is a quite novel cardiologic subspecialty focusing on the detection, monitoring, and treatment of cardiovascular disease (CVD), including heart failure (HF), that may occur in the context of cancer treatment [1]. Cardiac damage may be caused by toxins (including chemotherapeutics) and radiotherapy [2]. The ESC (European Society of Cardiology) guidelines on cardio-oncology published in 2022 emphasize the cardiac assessment of the patient before, during and after oncological treatment. Since the oncological therapy is an inducing factor of cancer therapy-related cardiovascular toxicity (CTR-CVT), it may manifest as HF, myocardial inflammation, vascular damage, arterial hypertension, arrhythmias, or as either valvular or pericardial heart diseases [3]. Any complications that may occur due to the cardiotoxicity of medications or radiotherapy, should be considered. This case report aims to increase the awareness of physicians, in terms of possible cardiac side effects in patients, who underwent radiochemotherapy due

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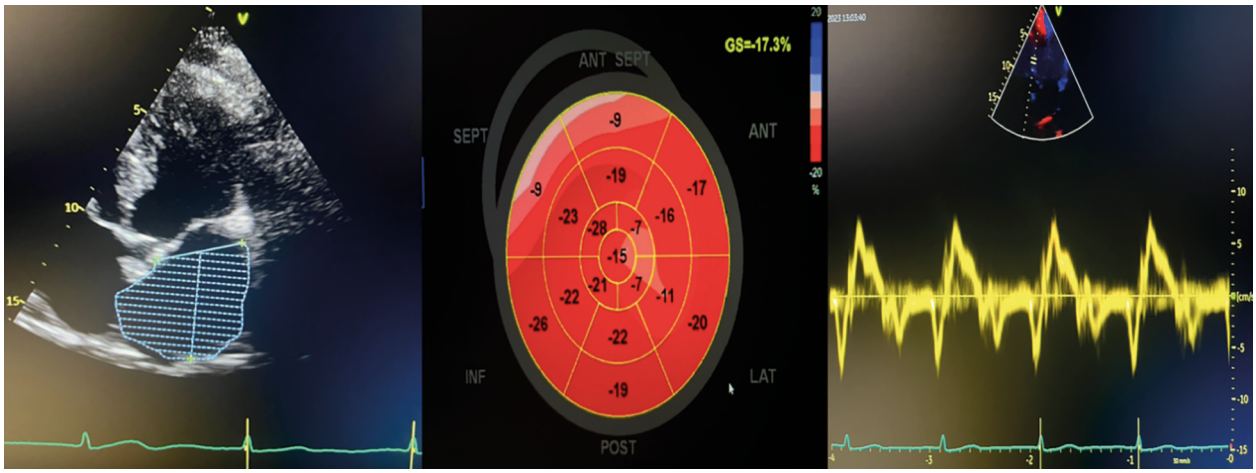

Figure 1. Transthoracic echocardiography (TTE) in four-chamber projection, with visible LAV (left atrial volume) on the left, GLS (global longitudinal strain) in the middle and Tissue Doppler Imaging on the right side.

to its potential to lead to the development of cardiotoxicity and its setbacks, secondary to the ongoing therapy. This is of paramount importance, as in the most severe cases, it may even include a patient's death [4].

Case report

A 77-year-old male, with prior history of 35 radiotherapy exposures and 3 cycles of chemotherapy with cisplatin for tongue cancer and bottom of the mouth cavity with lymph node metastases in October 2022, hypertension, coronary artery disease [in the form of marginal lesions described in computed tomography (CT) angiography], hyperlipidaemia and type 2 diabetes mellitus (T2DM), was admitted to the hospital on the 30th January 2023 due to dyspnoea, peripheral oedema, and impaired exercise tolerance, in the III New York Heart Association (NYHA) class. Laboratory test results showed elevation of the N-terminal B-type natriuretic propeptide (NT-proBNP) — 903 pg/mL on admission and high-sensitive troponine T (hsTnT) = = 39 [ng/L]. The patient was classified as "warm-wet" in Forrester's classification. He received intravenous (IV) loop diuretic treatment, under the control of sodium concentration in urine [5]. The echocardiography (Figure 1) revealed abnormalities of the diastolic function of the hypertrophied left ventricle (LV) with preserved ejection fraction, (EF) = = 55%, global longitudinal strain (GLS) = –17.3, septal mitral annular tissue Doppler = 4 cm/s, lateral mitral annular tissue Doppler = 4 cm/s and early mitral inflow velocity and mitral annular early diastolic velocity ratio = 16. Based on the clinical view, NTproBNP and echo results as presented in Table 1, heart failure (HF) with preserved ejection fraction (HFpEF) was diagnosed.

Table 1. Selected parameters of transthoracic echocardiography (TTE) along with the value.

Selected parameter	Value
TR Vmax	2.5 m/s
PASP	32 mmHg
LAVi	47 mL/m^2
e' sept	4 cm/s
e' lat	4 cm/s
E/e'	16
E/A	0.8
GLS	-17.3

E/A — Early diastolic peak to late diastolic peak ratio; E/e' — early mitral inflow velocity and mitral annular early diastolic velocity ratio; e' lat — lateral mitral annular tissue Doppler; e' sept — septal mitral annular tissue Doppler; GLS — global longitudinal strain; LAVi — left atrial volume index; PASP — pulmonary artery systolic pressure; TR Vmax — maximal velocity of tricuspid regurgitation

The chest X-rays (Figure 2) showed an increased bronchovascular pattern and in the electrocardiogram (ECG) (Figure 3) there was a sinus rhythm with 60 beats per minute (BPM) and intermediate axis, without signs of ischaemia. Holter-ECG also has been performed and revealed both ectopic ventricular beats (ExV) in the number of 241 a day and ectopic supraventricular beats (ExSV) with a frequency of 2133 a day.

Selected laboratory parameters are shown in Table 2. During hospitalization, apart from the mentioned IV loop diuretic treatment, therapy with mineralocorticoid receptor antagonist (MRA) and sodium-glucose cotransporter protein-2 (SGLT-2) inhibitor was implemented. The patient relieved his symptoms by reducing from NYHA III to NYHA II class, peripheral oedema also has been reduced.

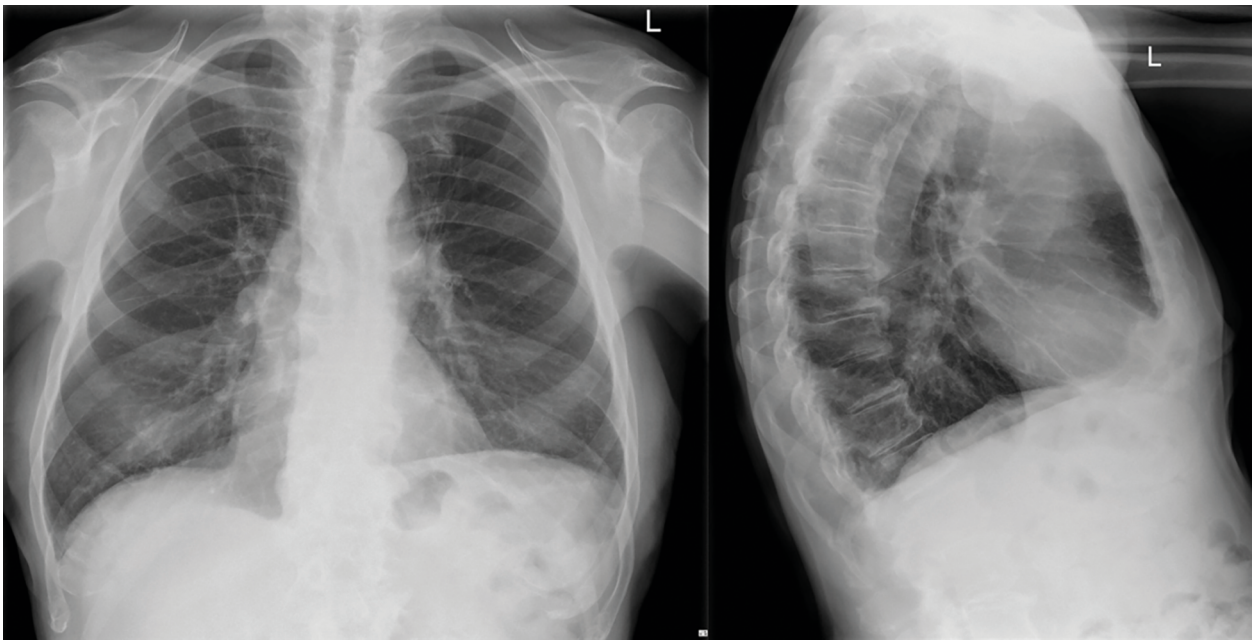

Figure 2. Chest X-rays in two projections including anterior-posterior (AP) on the left side and lateral on the right side, revealing visible interlobar fissures.

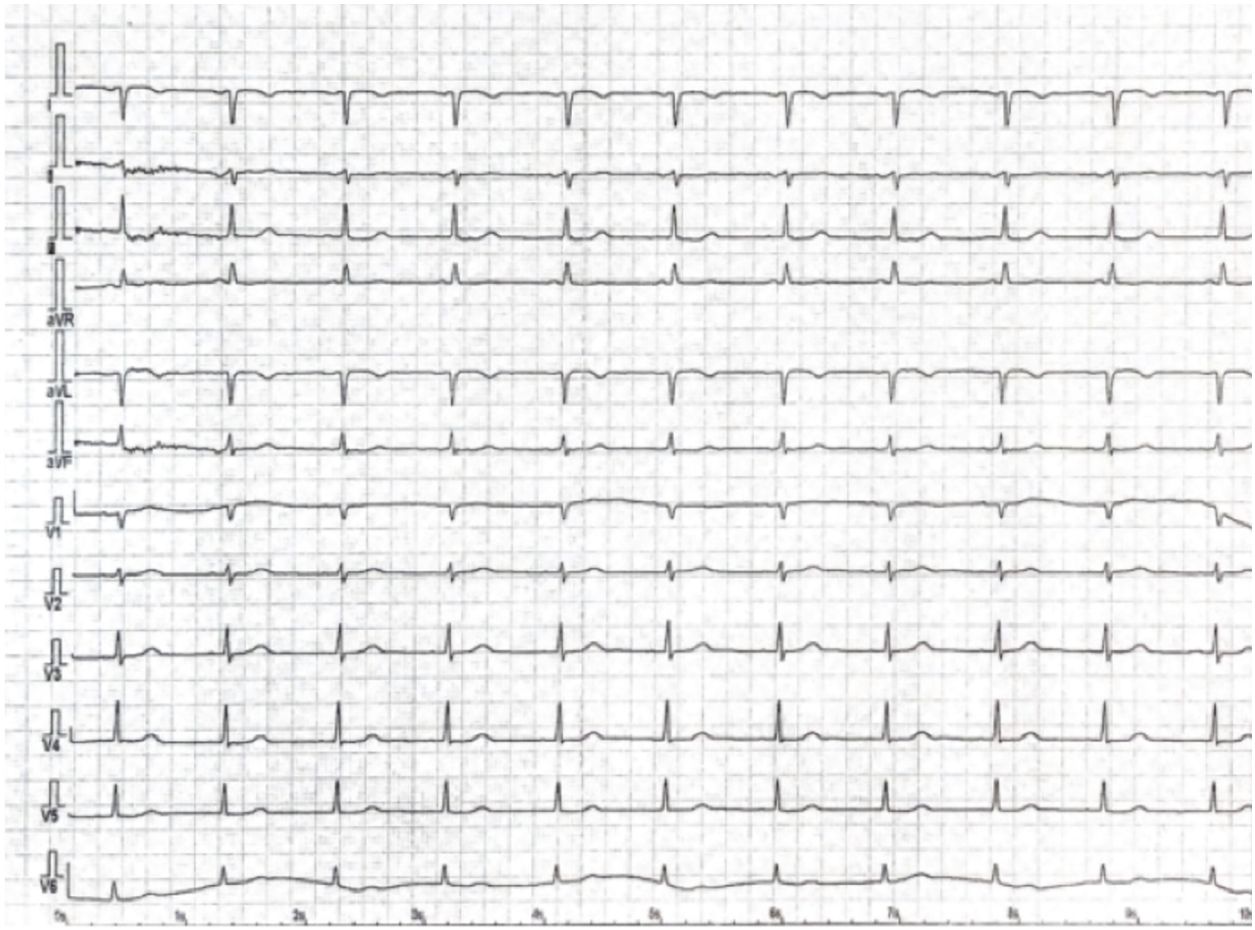

Figure 3. Electrocardiogram (12 leads)

Table 2. Selected laboratory test results

Parameter	Result	Reference range	Unit
NT-proBNP	903	< 125	pg/mL
hsTnT	39	< 14	ng/L
Non-HDLC	2.41	NA	mmol/L
LDLC	1.86	< 3	mmol/L
TG	1.22	< 1.7	mmol/L
Sodium concentration in urine sample (collected 2 hours after first IV torasemide dosage)	110	> 50	mmol/L
CREA (on admission)	109.2	64–104	umol/L
GFR-CKD(EPI) (on admission)	50.2	> 60	mL/min/1.73 m^2
Glucose (in serum)	5.18	4.1–5.5	mmol/L
TSH	0.116	0.3–3.18	uIU/mL

CREA — Creatinine; GFR-CKD(EPI) — glomerular filtration rate chronic kidney disease epidemiology collaboration; hsTnT — high-sensitivity troponin T; IV — intravenous; LDLC — Low Density Lipoprotein Cholesterol; NA — not applicable; NT-proBNP — N-terminal B-type natriuretic propeptide; Non-HDLC — Non-High Density Lipoprotein Cholesterol; TG — Triglycerides; TSH — thyroid stimulating hormone

The patient reached 318 meters at the 6-minute walking test (6MWT). Taking into account the medications that constitute the continuation of previous hypoglycaemic treatment and the HF medications included during hospitalization, the patient was prescribed torasemide, spironolactone and empagliflozin and added rosuvastatin. The patient was under observation, during both the 6 and 12-month follow-ups he remained in a stable condition (NYHA II class), with no hospitalization due to exacerbation of HF, and no presence of lower limb oedema. It is worth emphasizing that the patient did not undergo a cardiological assessment either before, or during oncological treatment. He died in January 2024 due to non-oncological reasons. However, the patient was suspected of having cancer recurrence with lung metastases. Proper cardiological examination took place at the time of hospitalization, due to the HF de novo.

Discussion

To draw the attention of the physicians to the increasing population of cardio-oncologic patients, the study presents a case report of a 77-year-old male, who underwent cardiac assessment later than he should have. Referring to the 2022 ESC guidelines on cardio-oncology, the patient should be assessed for the first time at the moment of cancer diagnosis and the next examination should have taken place during oncological treatment [3]. According to the Polish National Cancer Registry (PLCR) only in 2019 alone, there were over 170,000 new cancer cases reported in Poland [6]. Such a number leads to a subsequent increase in the population with cardiological problems, due to the higher frequency of specific oncological treatment. Depending on the type of neoplasm, cancer therapy usually consists of various treatment protocols, including radiation therapy (RT). In combination, or even separately chemotherapy and RT may lead to the occurrence of severe adverse effects (AEs), including CTR-CVT or to the development of HFpEF, as in the present case. Nevertheless, when it comes to impaired function of the cardiovascular (CV) system, it is necessary to pay attention to the side effects of RT, like radiation-induced heart disease (RIHD). This may happen due to damage to the endothelium of microscopic blood vessels, loss of capillaries, inflammation and fibrosis [2, 7, 8]. Certain platinum-based chemotherapeutics, exemplified by cisplatin administered in this case, exhibit notable interactions with blood vessels, metabolism and cardiac function, thereby increasing the risk of HFpEF development [9]. In the history of the mentioned patient, chemotherapy, as well as RT, occurred, which resulted in HF development. So far it is hard to certainly predict whether HF will develop in any patient during such a treatment [1]. However, it is worth emphasizing that CTR-CVT may occur at any moment, even decades after treatment, such as in the case of CV complications after combined oncological treatment of Hodgkin's lymphoma presented by Stępień et al. In this particular case, the coronary angiography was performed over 20 years after the oncological therapy completion. It revealed 80% stenosis of both the right coronary artery (RCA) and left anterior descending artery (LAD), which finally led to percutaneous coronary intervention (PCI) with implantation of the stent in LAD [10].

Table 3. Division of HF as one of the CTR-CVT based on ESC Guidelines on cardio-oncology [3]

Symptomatic HF	Very severe	Patient requires inotropic or mechanical circulatory support, potentially also a transplantation
	Severe	Patient requires hospitalization
	Moderate	Patient requires escalation of the ambulatory treatment
	Mild	Patient does not require escalation of the therapy and presents mild symptoms of HF
Asymptomatic HF	Severe	New reduction of left ventricle EF below 40%
	Moderate	New reduction of left ventricle EF by at least 10 percentage points to 40-49% or new reduction of left ventricle EF by less than 10 percentage points to 40-49%, but with accompanying new comparative decrease in GLS by over 15% from the base level or new elevation of cardiac biomarkers
	Mild	EF of left ventricle greater or equal to 50% and new comparative decrease in GLS by over 15% from the base level and/or new elevation of cardiac biomarkers

GLS — global longitudinal strain; HF — heart failure. Bond and italic font indicates the state of the patient on admission

CTR-CVT can manifest itself in various ways including HF, which can appear as symptomatic or asymptomatic as presented in Table 3. In this case, on admission patient was presenting severe symptomatic HF and required hospitalization. The severity of the disease, regardless of the presence of symptoms, may exhibit a clinical spectrum with varying intensity, sometimes including requirement of the inotropic or mechanical support or even a heart transplant. In the modern approach, every patient should be evaluated and treated properly to the presenting cardiotoxicity risk level. Each hazard degree has its own management path throughout and subsequently oncological treatment. In accordance with the already mentioned guidelines, TTE remains a key tool for assessing the occurrence of CTR-CVT. Among the parameters evaluated during TTE is GLS. However, in this case, the mentioned parameter remained within the normal range. The criteria, as shown in Table 3, are established based on the decline in left ventricle ejection fraction (LVEF) and/or specific alterations in the aforementioned GLS. Furthermore, before the hospital visit, the study patient had not undergone a cardiological assessment in connection with radiochemotherapy, as he definitely should have. Remembering the frequency of conducting TTE is necessary, which is determined based on the patient's risk level and the received oncological treatment. It standardizes the approach and facilitates the process of detecting de novo HF [3]. In the matter of therapy, the time of hospitalization should be the critical moment to optimize the treatment [11]. It is especially important to consider the incorporation of SGLT2 inhibitors, which not only show a decrease in hospitalization due to HF but also enhance the overall survival in individuals with cancer as well as with HFpEF [12, 13]. In the literature, precise data regarding the frequency of nasopharyngeal carcinoma in adults are lacking. However, in the paediatric population, the incidence is estimated to be 0.5 – 2 per 100,000 individuals per year [14].

Conclusions

Along with the increase of treatment possibilities, such as the usage of RT and chemotherapy, the cardiac side effects always should be considered with the intention of implementing proper cardiac therapy on time. To obtain a comprehensive patient assessment, it is significant to evaluate them before, during and after the course of the radiochemotherapy, in compliance with the ESC protocol. What is more, cardiac AEs can show up at any moment, even decades after treatment completion.

Additional information

Author contributions

PF and MS — writing, ML — writing and supervision with expertise.

Conflict of interest

The authors declare no conflict of interest.

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Streszczenie

W obecnych czasach zwiększa się rolę edukacji społeczeństwa na temat nowotworów. Udoskonalane są także metody ich diagnostyki, co w parze ze wzrostem świadomości pacjentów przekłada się na wzrost wykrywalności chorób nowotworowych oraz tym samym zwiększoną liczbę pacjentów korzystających z terapii onkologicznej. Nie jest to jednak terapia pozbawiona powikłań, szczególnie w kontekście układu sercowo-naczyniowego. Może ona bowiem prowadzić do wystąpienia pewnych powikłań, takich jak między innymi kardiomiopatie, zapalenia mięśnia sercowego, uszkodzenia naczyń, nadciśnienia tętniczego czy do rozwoju niewydolności serca, jak miało to miejsce w opisywanym przypadku. Pomimo tego, że pewne formy terapii mają większy potencjał kardiotoksyczny, a inne mniejszy. Zgodnie z wytycznymi ESC 2022 każdy z pacjentów powinien zostać poddany odpowiedniej ocenie kardiologicznej, w celu ustalenia poziomu ryzyka rozwoju powikłań kardiotoksycznych. Stanowi to więc swoiste wyzwanie dla lekarzy i jest to tym bardziej ważne, iż powikłania mogą pojawić się nawet dekady po zakończeniu terapii onkologicznej. Zaprezentowany poniżej przypadek ma za zadanie zwrócić uwagę na problematykę pacjentów kardioonkologicznych i przyczynić się do ich bardziej efektywnego diagnozowania oraz leczenia.

Słowa kluczowe: radiochemioterapia, niewydolność serca, kardioonkologia

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