Srce i krvni sudovi 2024; 43(4) : 104-107

Case report

Unexpected turbulence: Ventricular tachycardia in a patient with lung cancer on Osimertinib

Marina Ostojić[1], Mladen Ostojić[1], Marko Banović[1,2], Olga Petrović[1,2], Branko Beleslin[1,2], Tomović Sara[1], Katarina Matejić-Gaćeša[1], Marija Ristić[1], Suzana Kostić[1], Nedeljković Ivana[1,2]

[1]Cardiology Clinic, University Clinical Center of Serbia, Belgrade, Serbia, [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Abstract

Background: Ventricular arrhythmias are an uncommon but clinically significant manifestation during targeted therapy of cancer patients. Their occurrence requires careful evaluation to differentiate between therapy-related cardiotoxicity and other cardiovascular causes, while balancing oncologic treatment needs.

Case summary: Our case report presents a 63-year-old physically active man with metastatic lung adenocarcinoma on targeted therapy (osimertinib), who was admitted for recurrent non-sustained ventricular tachycardia (NSVT). He had no prior cardiovascular disease or arrhythmia. Initial echocardiography evaluation revealed preserved biventricular function without structural abnormalities. 24h Holter monitoring documented frequent supraventricular and ventricular ectopy, including NSVT. Malignant ventricular arrhythmias were registered in the recovery of treadmill stress echocardiography, and coronary angiography showed non-obstructive coronary artery disease. Antiarrhythmic therapy with amiodarone and bisoprolol led to complete arrhythmia suppression. Targeted therapy was temporarily withheld during cardiac work-up and subsequently resumed after multidisciplinary discussion. At six-month follow-up, the patient remained asymptomatic and arrhythmia-free under combined cardiology and oncology surveillance.

Discussion: This case highlights the need for a careful and individualized approach to ventricular arrhythmias in patients undergoing EGFR-targeted therapy. In the absence of structural heart disease and with effective pharmacological control, oncologic treatment may be safely continued with close rhythm monitoring. A multidisciplinary approach is crucial to balance cancer control with cardiovascular safety.

Key words Arrhythmias, cancer, therapy, prognosis

Introduction

In recent years, the treatment of lung cancer with biological therapy has significantly advanced[1]. Targeted therapies, such as epidermal growth factor receptor (EGFR) inhibitors[2], have enabled a personalized treatment approach, improving survival rates[3] and quality of life[4]. Osimertinib, a third-generation EGFR inhibitor, has demonstrated remarkable efficacy in treating lung cancer EGFR mutations[5]. However, despite its clinical benefits, this therapy may be associated with serious adverse effects, including rare but potentially fatal cardiotoxic events[5,6]. The arrhythmological disorders reported in the literature most commonly occur due to QT interval prolongation[7]. In this case report, we present a patient with repetitive ventricular tachycardia with a normal baseline electrocardiogram (ECG), which developed during osimertinib treatment.

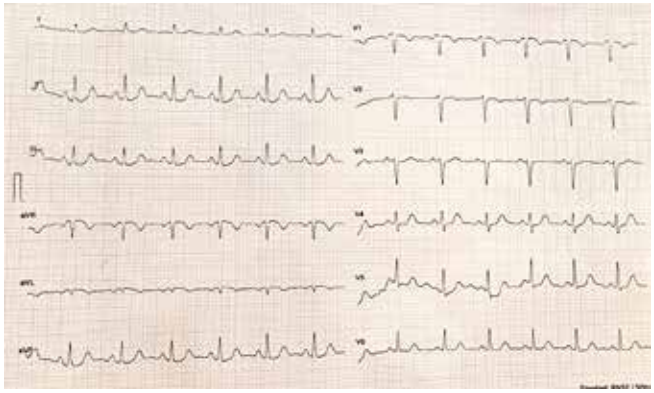
Case report

A 63-year-old man was admitted to the Coronary Care Unit for recurrent episodes of non-sustained ventricular tachycardia (VT). During the month prior to admission, he reported frequent palpitations during physical activity, without syncope or dizziness. He did not experience chest pain or dyspnea. He had no history of cardiovascular disease or previously documented arrhythmia.

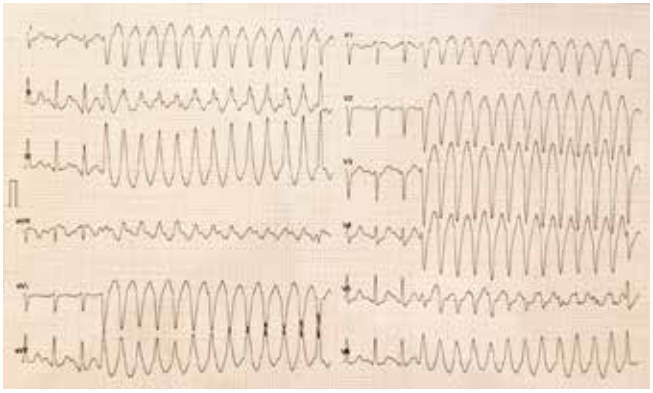
Throughout his life, he was initially engaged in professional football and later in recreational cycling, and he remains physically active. His medical history was notable for metastatic lung adenocarcinoma with spinal and pelvic involvement, diagnosed one and a half years earlier. He had been receiving targeted therapy, initially with erlotinib, later switched to osimertinib.

His initial ECG showed sinus rhythm with no significant changes in the QRS complex, ST segment, or QT interval (Picture 1). Transthoracic echocardiography revealed preserved biventricular size and function, with a left ventricular ejection fraction of 72%, elongated and voluminous mitral valve cusps, mild mitral regurgitation (1–2+), and a small, clinically insignificant pericardial effusion. A 24-hour Holter ECG revealed frequent ectopy: 1,288 isolated supraventricular extrasystoles (SVES), 96 SVES triplets, 177 SVES couplets, and 4 episodes of supraventricular tachycardia (SVT) lasting up to 17 seconds. Ventricular

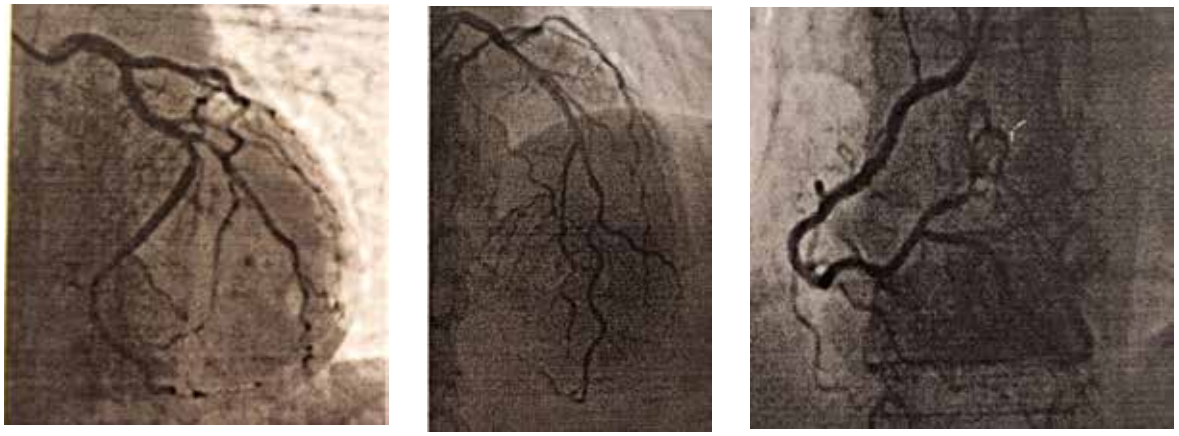
Corresponding author: Marina Ostojic, MD, Cardiology Dpt, University Clinical Center of Serbia, drmarinaostojic@gmail.com



Picture 1. Electrocardiogram at rest



Picture 2. Non-sustained ventricular tachycardia during the recovery phase of the stress test



Picture 3. Coronary angiogram showing nonsignificant coronary disease

ectopy included 418 ventricular extrasystoles (VES), 117 triplets, 49 couplets, and 9 runs of non-sustained VT (longest seven beats at 154 bpm). Amiodarone and bisoprolol therapy was initiated.

For further evaluation of ischemic burden, the patient underwent treadmill stress echocardiography using the Bruce protocol. The test was stopped early, at stage 3, due to fatigue at 90% of the target heart rate (142 bpm). During the test, the ECG showed upsloping ST-segment depression in inferior and lateral leads, which rapidly resolved during recovery. The patient reported no angina, dyspnea, or dizziness. In the first minutes of recovery, frequent supraventricular and ventricular ectopic beats were recorded, including couplets and triplets. From the fifth minute of recovery, frequent episodes of NSVT (up to 22 beats) were observed (Picture 2), prompting administration of lidocaine and amiodarone. Coronary angiography revealed non-obstructive coronary artery disease, with a 30% proximal LAD stenosis and TIMI 3 flow, and otherwise normal coronary arteries (Picture 3). Follow-up Holter monitoring after one month of amiodarone and bisoprolol therapy showed effective arrhythmia suppression, with a sinus rhythm range of 48–94 bpm (mean 65 bpm), 10 isolated SVES, and no recorded ventricular arrhythmias or NSVT episodes.

Notably, biological therapy for lung carcinoma was temporarily suspended during cardiac evaluation. After multidisciplinary discussion, targeted therapy was resumed with careful rhythm monitoring, given the absence of structural heart disease and effective arrhythmia suppression on medical therapy.

At 6-month follow-up, the patient remained asymptomatic and hemodynamically stable, on optimized therapy including amiodarone, bisoprolol, and osimertinib. He was advised to continue close follow-up with both his cardiologist and oncologist, with plans for repeat Holter monitoring and thyroid function testing.

Discusion

Our case report describes a rare presentation of recurrent non-sustained ventricular tachycardia (NSVT) in a patient without structural heart disease but with metastatic lung adenocarcinoma receiving osimertinib therapy. Osimertinib, a third-generation EGFR tyrosine kinase inhibitor, is known to cause cardiovascular adverse effects, including QT interval prolongation and arrhythmias, although clinically significant ventricular tachyarrhythmias are uncommon. In our patient, the baseline QTc was normal, suggesting a mechanism other than QT prolongation, potentially related to drug-induced heterogeneity of myocardial repolarization or other indirect pro-arrhythmic effects.

An experimental study in isolated guinea pig hearts demonstrated that osimertinib produces concentration-dependent prolongation of cardiac conduction intervals (PR, QRS, QTc), with pronounced effects at higher concentrations (24 μM)[8]. It also increased the ventricular effective refractory period and slowed conduction in the left atrium and ventricle. These changes are linked to

inhibition of multiple ion channels, including hERG potassium channels, Nav1.5 sodium channels, and L-type calcium channels. Such electrophysiological effects may precipitate arrhythmias, QT prolongation, reduced ejection fraction, and heart failure, particularly in patients with pre-existing cardiac risk factors. These findings underscore the importance of close ECG surveillance in patients receiving osimertinib[8].

In patients with pre-existing cardiovascular risk factors, careful cardiac monitoring during osimertinib treatment is essential to detect early signs of toxicity[9-12]. Heart failure (HF) is a recognized complication of EGFR inhibitor treatment, including osimertinib. The study by Okutucu S. et al. describes the development of HF in a patient with lung adenocarcinoma after five months of osimertinib therapy, presenting with marked symptoms, significantly elevated NT-proBNP levels, cardiomegaly, and severely reduced left ventricular systolic function (LVEF 27%). Discontinuation of osimertinib and initiation of cardiac therapy led to gradual improvement in left ventricular function and reduction of NT-proBNP. However, despite cardiac stabilization, the patient died six months later due to cancer progression and pulmonary infection. The study also emphasizes that most reported cardiotoxicity cases occurred at the standard osimertinib dose of 80 mg daily, underscoring the need for monitoring cardiac function and biomarkers during treatment13. This case highlights the need to carefully balance the treatment of the underlying malignancy with the prevention and management of cardiotoxicity, as interruption of cancer therapy may compromise oncologic control. In contrast, insufficient management of cardiac complications can substantially affect patient quality of life and survival.

Regular cardiac monitoring is necessary in patients on biological therapy. Regular evaluation should include baseline and periodic assessment, echocardiograms, and ECGs for monitoring cardiac function, with particular attention to left ventricular ejection fraction and QT intervals[14]. Depending on the patient's cardiovascular risk profile, cardioprotective therapies like beta-blockers or angiotensin-converting enzyme inhibitors may be considered[15]. For patients exhibiting signs of cardiotoxicity during treatment, individualized drug adjustments, including dose reduction or switching to alternative agents, may be necessary. A multidisciplinary approach involving cardiologists, oncologists, and primary care providers is crucial to ensure comprehensive management of the patient's health. Implementing these strategies can help minimize the risk of serious cardiac complications during osimertinib therapy while maintaining effective cancer treatment[14].

Conclusion

Close cardiac monitoring combined with a multidisciplinary approach is crucial in managing pulmonary carcinoma patients treated with osimertinib. This strategy helps to prevent adverse cardiac events not only in those with pre-existing structural heart abnormalities but also in patients with structurally normal hearts. Early detection and coordinated care among cardiologists, oncologists, and other specialists optimize patient safety while allowing the continuation of effective cancer therapy.

Reference

1. Zugazagoitia J, Molina-Pinelo S, Lopez-Rios F, Paz-Ares L. Biological therapies in nonsmall cell lung cancer. Eur Respir J. 2017 Mar 2;49(3):1601520. doi: 10.1183/13993003.01520-2016. PMID: 28254765.
2. Stanzione, B.; Del Conte, A.; Bertoli, E.; De Carlo, E.; Bortolot, M.; Torresan, S.; Spina, M.; Bearz, A. Non-Small Cell Lung Cancer with Epidermal Growth Factor Receptor (EGFR) Common Mutations: New Strategies. Cancers 2025, 17, 1515. https://doi.org/10.3390/cancers17091515.
3. Ćeriman Krstić, V.; Soldatović, I.; Samardžić, N.; Gajić, M.; Kontić, M.; Reljić, A.; Savić, M.; Roksandić Milenković, M.; Jovanović, D. Long-Term Outcomes in Patients with EGFR Positive Lung Adenocarcinoma and Subgroup Analysis Based on Presence of Liver Metastases. *Curr. Issues Mol. Biol.* 2024, *46*, 13431-13442. https://doi.org/10.3390/cimb46120801
4. Du R, Wang X, Zhou H, Ma L, Larcher LM, Chen C, Wang T. The health-related quality of life of lung cancer patients with EGFR-TKI-related skin adverse drug reactions and its relationship with coping style and self-management. Support Care Cancer. 2022 Dec;30(12):9889-9899. doi: 10.1007/s00520-022-07451-2. Epub 2022 Nov 19. PMID: 36400979.
5. Kaira, K.; Ogiwara, Y.; Naruse, I. Occurrence of Ventricular Fibrillation in a Patient With Lung Cancer Receiving Osimertinib. J. Thorac. Oncol. 2020, 15, e54–e55. Cancers 2023, 15, 5723 14 of 17.
6. Guo, G.G.; Luo, X.; Zhu, K.; Li, L.L.; Ou, Y.F. Fatal ventricular arrhythmias after osimertinib treatment for lung adenocarcinoma: A case report. J. Geriatr. Cardiol. 2023, 20, 242–246.
7. Ikebe S, Amiya R, Minami S, et al. Osimertinib-induced cardiac failure with QT prolongation and torsade de pointes in a patient with advanced pulmonary adenocarcinoma. Int Cancer Conf J 2021; 10: 68–71.
8. Li P, Tian X, Wang G, Jiang E, Li Y, Hao G. Acute osimertinib exposure induces electrocardiac changes by synchronously inhibiting the currents of cardiac ion channels. Front Pharmacol. 2023 May 30;14:1177003. doi: 10.3389/fphar.2023.1177003.
9. Lu SX, Xing YL, Miao Y, Zhang XJ, Li HW. Osimertinib induced adverse cardiac events: a case report. J Geriatr Cardiol. 2023 Sep 28;20(9):702-706. doi: 10.26599/1671-5411.2023.09.006. PMID: 37840629; PMCID: PMC10568547.
10. Patel SR, Brown SN, Kubusek JE, Mansfield AS, Duma N. Osimertinib-Induced Cardiomyopathy. JACC Case Rep. 2020 Apr 1;2(4):641-645. doi: 10.1016/j.jaccas.2019.12.038. PMID: 34317311; PMCID: PMC8298525.
11. Gawli CS, Patil BR, Nagpure NR, Patil CR, Kumar A, Patel HM. Prevalence of osimertinib-induced cardiotoxicity in non-small cell lung cancer patients: a systematic review and meta-analysis. Lung Cancer. 2025 Jul;205:108629. doi: 10.1016/j.lungcan.2025.108629. Epub 2025 Jun 19. PMID: 40555063..
12. Luo J, Zhou B, Yang J, Qian H, Zhao Y, She F, Liu F, Zhang P. Recurrent ventricular arrhythmias and heart failure induced by osimertinib- a case report. Front Cardiovasc Med. 2024 Aug 29;11:1423647. doi: 10.3389/fcvm.2024.1423647. PMID: 39267801; PMCID: PMC11390421.
13. Okutucu S, Sayin BY, Aksoy H, Oto A Development of heart failure after initiation of osimertinib treatment for Epidermal Growth Factor Receptor (EGFR)-mutant adenocarcinoma of the lung. Am J Cardiol. 2018;121:e160–e161.
14. Lyon AR, López-Fernández T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J et al. ESC Scientific Document Group. 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). Eur Heart J. 2022 Nov 1;43(41):4229-4361. doi: 10.1093/eurheartj/ehac244. Erratum in: Eur Heart J. 2023 May 7;44(18):1621. doi: 10.1093/eurheartj/ehad196. PMID: 36017568.
15. Lin CY, Chang WT, Su PL, Kuo CW, Yang J, Lin CC, Lin SH. Cardiac Events and Survival in Patients With EGFR-Mutant Non-Small Cell Lung Cancer Treated With Osimertinib. JAMA Netw Open. 2024 Dec 2;7(12):e2448364. doi: 10.1001/jamanetworkopen.2024.48364. PMID: 39636639; PMCID: PMC11621985.

Sažetak

Neočekivana turbulencija: Ventrikularna tahikardija kod pacijenta sa rakom pluća na osimertinibu

Marina Ostojić[1], Mladen Ostojić[1], Marko Banović[1,2], Olga Petrović[1,2], Branko Beleslin[1,2], Tomović Sara[1], Katarina Matejić-Gaćeša[1], Marija Ristić[1], Suzana Kostić[1], Nedeljković Ivana[1,2]

[1]Klinika za Kardiologiju, UKCS, Beograd, Srbija, [2]Medicinski fakultet, Univerzitet u Beogradu, Srbija

Uvod: Komorske/ventrikularne aritmije su retka, ali klinički značajna komplikacija tokom lečenja pacijenata obolelih od raka. Njihova pojava zahteva pažljivu procenu kako bi se razlikovala kardiotoksičnost povezana sa terapijom od drugih kardiovaskularnih uzroka, a uz istovremeno razumevanje i prepoznavanje potrebe za onkološkim lečenjem.
Prikaz slučaja: Slučaj opisuje 63-godišnjeg fizički aktivnog muškarca sa metastatskim adenokarcinomom pluća na ciljanoj terapiji (ozimertinib), koji je primljen zbog rekurentne kratkotrajne ventrikularne tahikardije (NSVT). Nije imao ranija kardiovaskularna oboljenja ili aritmije. Ehokardiografski nalaz je pokazao očuvanu biventrikularnu funkciju bez strukturnih abnormalnosti. 24-časovni Holter monitoring ukazao je na česte supraventrikularne i ventrikularne ektopije, uključujući NSVT. Maligne ventrikularne aritmije registrovane su prilikom oporavka od stresehokardiografskog testa na traci za trčanje, a koronarna angiografija je pokazala neobstruktivnu koronarnu arterijsku bolest. Antiaritmička terapija amiodaronom i bisoprololom dovela je do potpune supresije aritmije. Ciljana antikancerogena terapija je privremeno obustavljena tokom kardiološke evaluacije, a potom je nastavljena nakon multidisciplinarne diskusije. Nakon šestomesečnog praćenja, pacijent je ostao asimptomatski i bez aritmija pod kombinovanim kardiološkim i onkološkim nadzorom.
Diskusija: Ovaj slučaj ukazuje na potrebu za pažljivim i individualizovanim pristupom kod pacijenata sa ventrikularnim aritmijama, a koji se podvrgavaju usmerenoj antikancerogenoj terapiji. U odsustvu strukturne bolesti srca i uz efikasnu farmakološku kontrolu, onkološko lečenje se može bezbedno nastaviti uz pažljivo praćenje ritma. Multidisciplinarni pristup je ključan za ravnotežu između kontrole raka i kardiovaskularne bezbednosti.

Ključne reči: *Aritmije, kancer, terapija, prognoza*