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Torsades de pointes during ibutilide administration in a patient on long-term osimertinib after pulsed field ablation: a case report

Siqi Jiao
State Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College

Kuo Zhang
State Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College

Xiaonan Dong
State Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College

Min Tang
State Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College

Yuhui Zhang
yuhuizhangjoy@126.com

State Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College

Case Report

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Abstract

Osimertinib, a third-generation EGFR-TKI, is the standard of care in first-line therapy for advanced EGFR-mutant non-small cell lung cancer (NSCLC), but with the potential proarrhythmic effects including QT prolongation and atrial fibrillation (AF). We report a 77-year-old woman on long-term osimertinib for non-small cell lung cancer who developed early recurrent AF on postoperative day 1 following pulsed field ablation (PFA). Intravenous ibutilide was administered for cardioversion, during which she developed torsades de pointes (TdP) with transient loss of consciousness that resolved spontaneously after drug discontinuation and electrolyte supplementation. This case highlights the proarrhythmic risk when ibutilide is used in patients receiving osimertinib, particularly in the setting of recent ablation and early post-procedural rhythm instability. Caution is warranted with QT-prolonging agents in this population, and close ECG monitoring is essential.

Background

Osimertinib is a third-generation epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) and first-line therapy for EGFR-mutant non-small cell lung cancer (NSCLC)[1], but carries a risk of QT prolongation that may predispose to torsades de pointes (TdP)[2]. Ibutilide, used for acute cardioversion of atrial fibrillation (AF), also carries TdP risk via IKr blockade[3], yet their electrophysiological synergy is rarely reported. We report an elderly patient on long-term osimertinib who developed TdP after ibutilide for early recurrent AF following pulsed field ablation (PFA).

Case presentation

A 77-year-old woman was admitted due to recurrent episodes of palpitations and dizziness over the past two years. Her medical history included non-small cell lung cancer (NSCLC), for which she was receiving osimertinib 80mg once daily, which was well tolerated and resulted in a sustained clinical response. She had also undergone radiofrequency catheter ablation for atrial fibrillation (AF) at an outside hospital one year prior to this presentation.

Post-ablation ECGs documented recurrent paroxysmal atrial fibrillation. On admission, transthoracic echocardiography showed biatrial enlargement, mild to moderate aortic and tricuspid regurgitation, and a left ventricular ejection fraction of 60%. Laboratory tests revealed mild anaemia with haemoglobin of 112 g/L and an elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) of 652 pg/mL; routine blood count, troponin, and biochemistry were otherwise normal. The patient was continued on rivaroxaban 15 mg once daily for anticoagulation. As admission heart rate was 63 bpm, no antiarrhythmic agents were initiated. She subsequently underwent successful pulmonary vein isolation via pulsed field ablation (PFA) under general anaesthesia. Post-procedural ECG confirmed sinus rhythm, with no procedure-related complications.

On the morning of the first postoperative day, telemetry revealed recurrent AF. Intravenous ibutilide was administered for cardioversion. During infusion, the patient developed dizziness, tinnitus, and diaphoresis, with telemetry showing torsades de pointes (TdP) (Fig. 1A), complicated by a transient loss of consciousness lasting 2–3 seconds with spontaneous recovery. Blood pressure ranged 120–150/80–95 mmHg, heart rate ~ 120 bpm. Ibutilide was immediately discontinued, and potassium and magnesium were supplemented. Approximately 30 minutes later, the rhythm converted to junctional escape at 63 bpm, with a QTc interval of 485 ms (Fig. 1B). On the second day, the rhythm converted to sinus rhythm (Fig. 1C), and atenolol was added before discharge.

Discussion

Osimertinib, a third-generation epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), has demonstrated substantial clinical benefits for advanced or metastatic EGFR-mutant NSCLC[1]. However, it is associated with a significantly higher risk of QT prolongation and other cardiovascular adverse events, including AF, supraventricular tachycardia (SVT), myocardial infarction, and heart failure, compared with other EGFR-TKIs and targeted therapies[2, 4]. A recent in vitro study has shown that osimertinib prolongs the action potential duration by downregulating KCNN1 expression, providing a mechanistic basis for its proarrhythmic effects[5]. Ibutilide, an antiarrhythmic agent, also affects potassium currents and carries a known risk of TdP[3]. In our case, the patient received ibutilide for cardioversion, during which TdP occurred, suggesting a possible synergistic proarrhythmic effect between osimertinib and ibutilide. Similarly, Bian et al. reported a case of an 85-year-old male with advanced NSCLC receiving long-term osimertinib who developed TdP following the addition of moxifloxacin[6]. These observations highlight the importance of identifying cancer patients at high risk of QT prolongation and subsequent TdP, as this population frequently harbours predisposing factors such as targeted therapy, electrolyte abnormalities, organ dysfunction, and drug–drug interactions [7].

Besides its role in QT prolongation, osimertinib may also predispose to early recurrence of atrial tachyarrhythmias (ERAT). PFA has emerged as a promising nonthermal ablation technique that employs electroporation to selectively target cardiomyocytes, reducing complications and ERAT compared with thermal ablation[8, 9]. A recent prospective study reported a median time to first recurrence of 17 days following PFA[9]. However, in the present case, the patient developed early-onset AF on the first postoperative day, which may not only reflect post-ablation electrophysiological instability but also suggest a potential role of osimertinib-related proarrhythmic effects.

This case underscores the need for caution when using QT-prolonging agents in patients receiving long-term osimertinib, and emphasises the importance of collaboration between oncologists and cardiologists in the management of cancer patients.

Conclusions

We have described a case of a 77-year-old female on long-term osimertinib who developed TdP during ibutilide administration for ERAF following PFA. This case illustrates that life-threatening arrhythmias may occur when osimertinib is combined with QT-prolonging drugs. Careful ECG monitoring and appropriate management of risk factors lengthening QT interval are essential in this high-risk population.

Declarations

Ethics approval and consent to participate

This case report was conducted in accordance with the principles of the Declaration of Helsinki. Formal ethical approval was waived by the Research Ethics Committee of Tehran University of Medical Sciences. Written informed consent for the publication of clinical details and accompanying images was obtained from the patient's legal guardians. Patient confidentiality was maintained throughout, and all identifying information has been removed from the article.

Consent for publication

Written informed consent was obtained from the patient's legal guardians for publication of this report.

Competing interests

The authors declare no competing interests.

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Author Contribution

S.J. and K.Z. wrote the main manuscript text and prepared Fig. 1. X.D. collected and interpreted the clinical data. M.T. and Y.H.Z. supervised the clinical management and critically revised the manuscript. All authors reviewed and approved the final manuscript.

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Figures

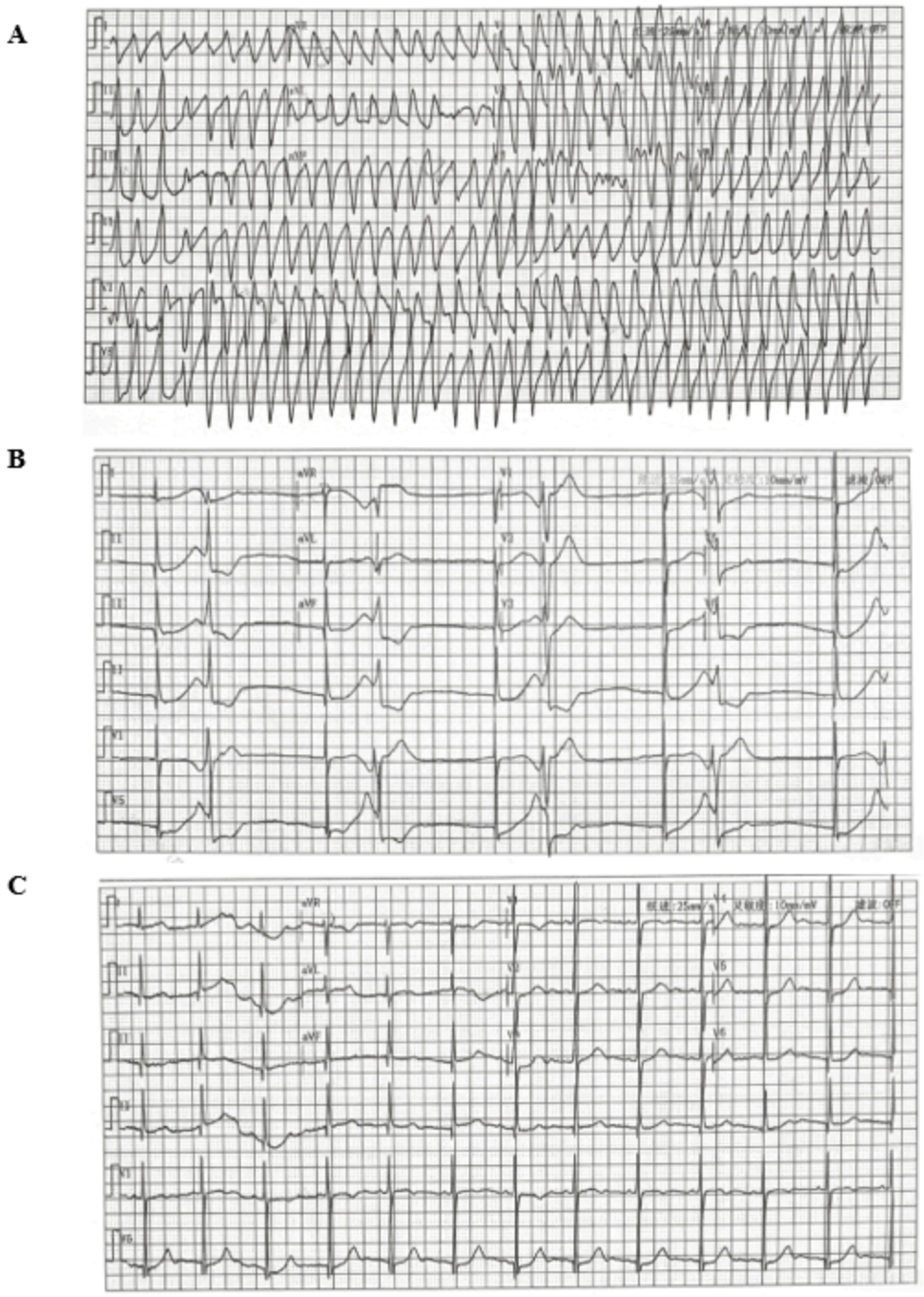


Figure 1

Sequential ECG changes.

A) Torsades de pointes. B) Junctional escape rhythm. C) Sinus rhythm restoration.