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CASE REPORT: CLINICAL CASE

SGLT2 Inhibitor for Cardiac Protection in a Patient With Osimertinib-Responsive Advanced EGFR-Positive Lung Cancer

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ABSTRACT

An 85-year-old man with recently diagnosed metastatic EGFR+ lung adenocarcinoma treated with osimertinib presented after 1 month of therapy in decompensated congestive heart failure along with atrial fibrillation, prolonged QTc and acute kidney injury. Osimertinib was held. His hemodynamic status was optimized, and he was started on cardioprotective medications (losartan and metoprolol succinate), and LVEF recovered. However, after reintroducing osimertinib, LVEF reduced, indicating possible osimertinib-induced cardiomyopathy. An SGLT2 inhibitor was added for cardioprotection before another rechallenge of osimertinib. SGLT2 inhibitors are a powerful tool for heart failure and may have a potential secondary benefit in ameliorating cardiotoxic processes. Although their use in osimertinib-induced cardiomyopathy has not been well-established, current heart failure guidelines and emerging research support its use in this setting. This case and the accompanying literature review highlight the novel use of SGLT2 inhibitors coupled with regular clinical and imaging monitoring, as a compelling intervention for osimertinib-induced cardiomyopathy. (JACC Case Rep. 2024;29:102829) © 2024 Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

In this report, we discuss an 85-year-old man with epidermal growth factor receptor (EGFR) positive non-small cell lung adenocarcinoma (NSCLC) treated with osimertinib 80 mg orally. Osimertinib has been shown to significantly prolong disease-free survival in patients with stage IB to IIIA EGFR sequence variant NSCLC compared with placebo in the ADAURA (Adjuvant Osimertinib for Resected EGFR-mutated Non-small Cell Lung Cancer) trial[1] and is considered an ideal therapeutic option for this patient. Within

TAKE-HOME MESSAGES

- Osimertinib causes dose-dependent, reversible cardiotoxicity in patients who can present with symptomatic or asymptomatic HF, reduced ejection fraction, arrhythmias, and prolonged QTc.
- SGLT2 inhibitors for osimertinib-induced cardiomyopathy is a novel use of this class of medications that poses an exciting potential for cardioprotection in the cardio-oncology population.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

EGFR = epidermal growth factor receptor

HF = heart failure

NSCLC = non-small cell lung cancer

LVEF = left ventricular ejection fraction

1 month of treatment, the patient was hospitalized for progressive respiratory distress and volume overload (Figures 1A and 1B) and was in atrial fibrillation (AF) with rapid ventricular response and heart failure (HF) exacerbation. He presented with a B-type natriuretic peptide of 666 pg/mL (reference value <100 pg/mL) and, on point-of-care ultrasound, left ventricular ejection fraction (LVEF) was mildly reduced on visual estimate. High-sensitivity troponins remained normal. He was volume-optimized with diuretic agents, and his AF was aggressively managed with metoprolol succinate 50 mg daily, dronedarone 400 mg twice daily, and apixaban 5 mg twice daily. At discharge, the patient returned to normal sinus rhythm, and a subsequent echocardiogram showed an LVEF of 60% with normalized filling pressures. Given preserved LVEF, his osimertinib was restarted after collaborative decision-making between the medical oncologist and cardiologist. However, within 3 months of continued therapy, the patient demonstrated an LVEF of 46% on echocardiography (Videos 1A and 1B), and osimertinib was held. Arrhythmia monitoring showed normal sinus rhythm, and it was felt that LVEF decline was not secondary to occult AF burden. Three subsequent echocardiograms showed recovered and normalized LVEF, and osimertinib was restarted with losartan 25 mg for cardioprotection. Follow-up echocardiograms demonstrated a stabilized LVEF of 60%. With ongoing osimertinib usage, 11 months after his previous reduction in LVEF, the patient experienced an asymptomatic decline in LVEF to 45%, and osimertinib was held once again.

PAST MEDICAL HISTORY

The patient was previously diagnosed with paroxysmal AF, transient ischemic attack, and hypothyroidism. He maintains an active lifestyle and is a never-smoker. His NSLC was initially diagnosed when he presented for evaluation of a posterior chest wall injury following a mechanical fall while working outdoors. Initial chest radiograph noted a concerning lung opacity. Follow-up computed tomography scan revealed a 2.5 × 3.0 × 2.7 cm mass in the left upper lobe with enlarged mediastinal and hilar lymph nodes without pleural effusion or another metastatic disease. Computed tomography-guided biopsy with subsequent molecular panel revealed a diagnosis of adenocarcinoma positive for EGFR sequence variant L858R on exon 21 and negative for BRAF and KRAS mutations. Given staging and patient focus on quality-of-life measures, osimertinib and denosumab were recommended.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for acute decompensation included atrial fibrillation, ischemia, valvular disease, and uncontrolled hypertension. An electrocardiogram showed AF without ischemic changes, and high-sensitivity troponins were unremarkable on admission. His local electrophysiologist intermittingly monitored AF burden, but he maintained a normal sinus rhythm after adding dronedarone. With each HF exacerbation, the LVEF did not drop below 35%, and it was felt that the benefit of maintaining sinus rhythm outweighed the risk of worsening HF. Clinical

VISUAL SUMMARY. The Course of Events Is Charted From the Onset of Osimertinib Therapy in February 2022 Through August 2024

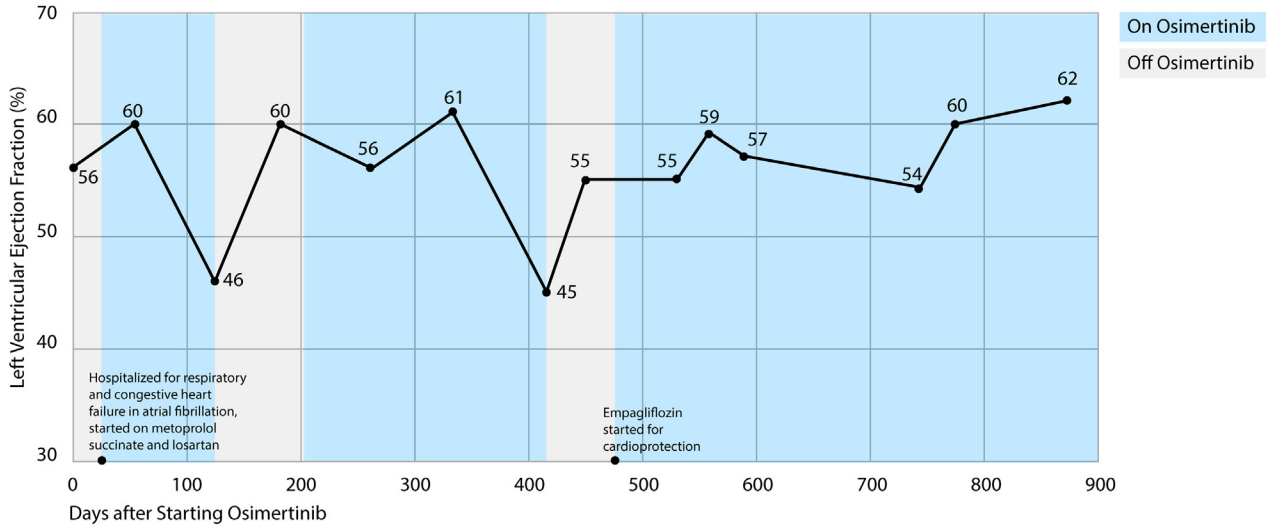
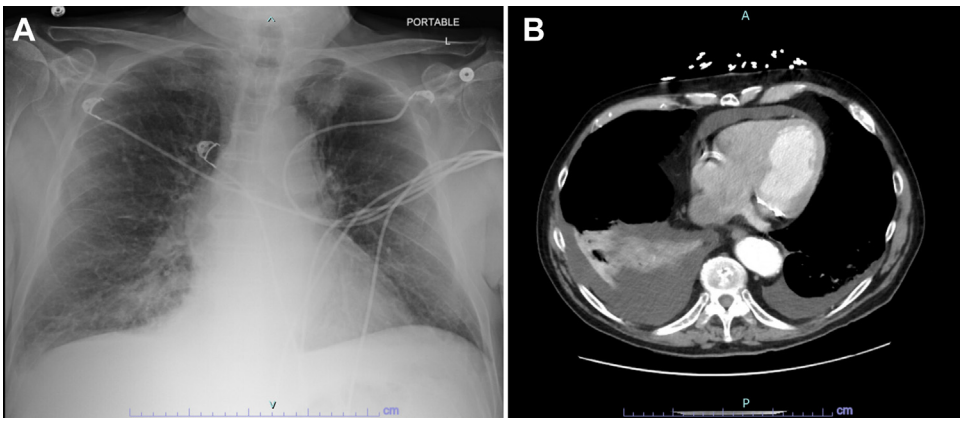


FIGURE 1 Chest Radiograph and Chest Computed Tomography With Intravenous Contrast 1 Month After Starting Osimertinib



(A) Chest radiograph in March 2022, 1 month after starting osimertinib, showed development of right basilar airspace disease and right pleural effusion with stable left upper lobe pulmonary mass. (B) Chest computed tomography with intravenous contrast in March 2022, 1 month after starting osimertinib, showed stable left upper lobe pulmonary mass, new development of a small pericardial effusion, moderate-sized right pleural effusion, and a small left pleural effusion.

history and serial imaging ruled out ischemic or valvular causes for his cardiomyopathy. The patient has remained normotensive.

INVESTIGATIONS

Serial echocardiography and electrocardiograms were performed on the patient. Due to the lower pretest probability of ischemic cardiomyopathy, additional ischemic evaluation was deferred.

MANAGEMENT

A discussion was had on continuing osimertinib vs switching to erlotinib, which has fewer reported cases of cardiomyopathy. Given the superior central nervous system penetration of osimertinib, cardiac function was closely monitored. Traditional cardioprotective agents (metoprolol succinate, losartan) at maximally tolerated doses were insufficient because the patient continued to have LVEF decline. Our patient had marginal blood pressure room for adding sacubitril-valsartan and spironolactone. Atrial fibrillation was well-controlled and was not thought to be the underlying cause. The patient had mildly reduced renal function, with fluctuations correlating with HF exacerbations. A literature review yielded several case reports of patients with reduced LVEF and prolonged QT intervals on osimertinib, similar to our patient's presentation (**Table 1**). SGLT2 inhibitors were considered for guideline-directed medical management for heart failure and renal protection, and given the potential attenuation of cardiotoxic processes, they were the ideal choice for our patient. He was restarted on osimertinib for a final challenge with aggressive protection with empagliflozin 10 mg, losartan 12.5 mg titrated back from 25 mg because of orthostatic hypotension, and metoprolol succinate 50 mg with close echocardiography with strain every 3 months.

OUTCOME AND FOLLOW-UP

At 3-month follow-up, the patient tolerated his medications without reduction in LVEF, QTc prolongation, or other signs of HF. His AF continued to be well-controlled on the existing medication regimen. At 12-month follow-up, the patient remained clinically stable and asymptomatic, having had stable electrocardiographic and echocardiographic examinations (Videos 2A and 2B).

DISCUSSION

NSCLC management has been dramatically advanced with the identification of targeted therapies. The most recent is osimertinib (Tagrisso), which was first approved by the U.S. Food and Drug Administration

TABLE 1 Cases of Osimertinib-Induced Cardiotoxicity

First Author, Year	Age (y), Sex	Cardiovascular Comorbidities	Clinical Presentation and Diagnostic Testing	Time After Initiation	NT-proBNP
Piper-Vallillo et al,[11] 2020	67, F	Hypertension, hypothyroidism, pulmonary embolism	HFrEF with new-onset LBBB, no significant QTc prolongation	7 mo	1,104 pg/mL
Watanabe et al,[12] 2017	78, F	Unknown	Mild exertional dyspnea and accompanying decreasing oxygen saturation, imaging demonstrated bilateral pleural effusions and pulmonary congestion as well as left atrial dilatation	3 wks	224 pg/mL
Okuzumi et al,[13] 2022	91, M	Hypertension, chronic kidney disease	Symptomatic HFrEF, echocardiography showed diffuse hypokinesis with reduced EF	6 wks	321.1 pg/mL
Medepalli et al,[14] 2022	70, F	Former smoker, mild mitral and tricuspid regurgitation	Anorexia, nausea, decreased oral intake, and weight loss, prolonged QTc interval, mild to moderate mitral regurgitation, mild aortic regurgitation, moderate to severe tricuspid regurgitation, and mild pulmonary hypertension	6 mo	680 pg/mL
Reale et al,[15] 2018	70, M	Former smoker, hypertension	HFrEF	3 mo	
	73, F	Intermittent left bundle branch block, hypertension	Asymptomatic LVEF reduction and worsening mitral valve insufficiency	14 mo	
	47, F	None	HFrEF	17 mo	
	71, F	None	Left-sided dilatation and associated dyspnea	11 mo	
	80, F	None	Asymptomatic LVEF reduction and LA volume and LV mass increase	11 mo	
Patel et al,[16] 2020	84, F	Coronary artery disease s/p coronary artery bypass graft, prior ischemic stroke	Pulmonary edema, decreased LVEF with severe global LV hypokinesis	4 wks	22,579 pg/mL
	71, M	Atrial fibrillation, hypertension, hyperlipidemia	Acute-onset dyspnea and peripheral and pulmonary edema, reduction in LVEF with global hypokinesis and moderate LV enlargement	12 d	2,138 pg/mL
	72, F	None	Progressive dyspnea and hypoxia, pulmonary edema and reduced LVEF	1 mo	7,306 pg/mL
Kunimasa et al,[17] 2020	78, F	Hypertension, h/o thoracic aortic aneurysm	Dyspnea, found to have prolonged QTc, severely reduced LVEF with moderate to severe mitral regurgitation	3 mo	18,890 pg/mL
	72, F	Hypertension	Fatigue, severe mitral regurgitation with mitral valve prolapse	3 mo	
	68, M	None	Fatigue and lower extremity pitting edema, QTc prolongation, severe hyponatremia (120 mEq/L), severe tricuspid regurgitation, and mild pulmonary hypertension	3 mo	
	64, F	Moderate mitral regurgitation	Fatigue and lower extremity pitting edema, elevated NT-proBNP	9 mo	227.9 pg/mL
	52, F	Obesity	Asymptomatic reduction in LVEF, normal QTc	2 wks	36 pg/mL
	71, F	Hypertension, diabetes mellitus	Sudden dyspnea and chest pain found to have QS pattern in V_{1-4}, and anteroseptal hypokinesis	2 mo	
Ikebe et al,[18] 2021	84, F	Former smoker, hypertension	Dyspnea and bilateral lower extremity edema, cardiomegaly, bilateral pleural effusion, QTc prolongation and poor R progression, dilated and diffusely hypocontractile LV	2 mo	7,469 pg/mL
Fukuo et al,[19] 2022	74, F	Complete left bundle branch block	QT prolongation	1 mo	1,175 pg/mL
Bardaro and Stirpe,[20] 2022	79, F	Hypertension, type 2 diabetes	Acute respiratory failure and HF with QT prolongation		
Ruiz-Briones et al,[21] 2023	F	Left bundle branch block, dyslipidemia, hypertension	Severe HFrEF		
Ito et al,[22] 2020	73, F	None	Dyspnea on exertion and increased pleural effusion, elevated BNP and reduced EF	6 mo	
Kobat et al,[23] 2023	72, M	Former smoker, type 2 diabetes, hypertension, hypercholesterolemia	QTc prolongation and atrial fibrillation with reduced LVEF	15 mo	
Zhang et al,[24] 2022	62, F	None	Weakness and lower extremity edema, pleural and pericardial effusions, severe LV hypokinesis	6 mo	6,830 ng/L
Fukuda et al,[25] 2022	73, F	None	Progressive shortness of breath, fatigue, and edema, increased LV dimension, right bundle branch block, and prolonged QTc	1 mo	1,002.1 pg/mL
Teran Brage et al,[26] 2022	62, F	None	Acute myocarditis with severe LV dysfunction and cardiogenic shock 24 h after receiving a third dose of the COVID-19 vaccine and the influenza vaccine	2 mo	8.069 pg/mL
Shinomiya et al,[27] 2020	76, F	None	Fever and progressive dyspnea, diagnostic endomyocardial biopsy indicated osimertinib-induced cardiomyopathy	4 mo	1,394 pg/mL
Tanaka et al,[28] 2023	70s, M	Smoker	Bilateral pleural effusion and expansion of the inferior vena cava with cardiac enlargement	6 mo	2,130.1 pg/mL
Patel et al,[29] 2023	63, M	Former tobacco use, hypertension, type 2 diabetes mellitus	Large pericardial, cardiac MR imaging findings showed focal late gadolinium enhancement and myocardial edema	4 wks	666 pg/mL
Saito et al,[30] 2023	66, F	None	Syncope, ECG showed polymorphic nonsustained ventricular tachycardia	10 d	
Xu et al,[31] 2024	62, M	Smoking history, type 2 diabetes mellitus	Respiratory distress, fever, cough, and expectoration, CMR showing LV enlargement, thinning and fibrosis of the lateral myocardial wall without perfusion defects	18 mo, 24 mo	No value, 7,193 pg/mL

BNP = B-type natriuretic peptide; CMR = cardiovascular magnetic resonance; ECG = electrocardiogram; EF = ejection fraction; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; IV = intravenous; LA = left atrial; LBBB = left bundle branch block; LV = left ventricular; LVEF = left ventricular ejection fraction; MR = magnetic resonance; NT-proBNP = N-terminal pro-B-type natriuretic peptide.

Continued on the next page

TABLE 1 Continued

CK-MB	Troponin	LVEF, %	Intervention	Outcomes
		42	Lisinopril later replaced by sacubitril-valsartan; metoprolol later discontinued, discontinued osimertinib	LVEF found to be stable 4 wks after resuming erlotinib, asymptomatic for HF
Not elevated			Diuretic, discontinued osimertinib	Recovered within 5 d of cessation of treatment and diuretic administration, did not require continued diuretic
		48	IV furosemide 40 mg daily for 4 d, discontinued osimertinib	LVEF, BNP, and symptoms normalized 1 wk after treatment discontinuation
	0.062 ng/mL	40-45	Electrolyte replacement focused on optimizing potassium, continued osimertinib	QTc normalized after 72 h
		45	Ramipril 2.5 mg, bisoprolol 1.25 mg, discontinued osimertinib	EF improved after 3 wks of treatment withdrawal, but symptoms and overall clinical condition continued to worsen despite management and patient passed
		58	Bisoprolol 1.25 mg increased to 3.75 mg after the second reduction in LVEF, discontinued osimertinib with each reduction	Recovered EF after 3 incidences with beta-blocker therapy and therapy suspension; however, restarting osimertinib lead to similar reductions
		51	Bisoprolol 5 mg, perindopril 5 mg, osimertinib suspended	Systolic function recovered and osimertinib was restarted; no further reductions were noted
		45	Bisoprolol 2.5 mg, furosemide 12.5 mg, perindopril 2.5 mg, osimertinib suspended	Partial recovery of systolic function with regression of dyspnea was noted and osimertinib was resumed 15 d later without complication
		43	Enalapril titrated from 2.5-5 mg, osimertinib suspended	LVEF improved and left-sided volumes stabilized, osimertinib was restarted but LVEF reduced twice more before being discontinued
	29-31 ng/L	20	Furosemide, losartan, bisoprolol, osimertinib discontinued	Euvolemic after 4 wks with mildly improved EF, initiated on erlotinib
	843 ng/L	39	Diuresis, lisinopril, and metoprolol, osimertinib discontinued	Returned to baseline clinical status and was rechallenged with osimertinib because of confounding cardiac history, has not had further exacerbation
		39	ACEI, beta-blocker, diuretic started, osimertinib discontinued	Normalization of EF 2 mo later, switched to erlotinib
	0.416 ng/mL	28	Furosemide 40 mg, spironolactone 50 mg, tolvaptan 7.5 mg, carvedilol 5 mg, and candesartan 2 mg initiated, osimertinib discontinued	LVEF remained reduced 3 mo after discontinuation but progressively improved after 9 mo
		74	Furosemide 20 mg, osimertinib discontinued	Symptoms improved after 1 mo but mitral regurgitation persisted but did not worsen, switched to gefitinib
			Tolvaptan 3.75 mg, furosemide 40 mg, osimertinib suspended	Fatigue and edema improved after 1 mo, severe tricuspid regurgitation persisted and osimertinib was restarted at lower dose (40 mg)
		50	Furosemide 20 mg, spironolactone 25 mg, osimertinib suspended	Symptoms resolved, LVEF improved, and NT-proBNP reduced after 1 mo, osimertinib was restarted without complication
	<0.01 ng/mL	41	Candesartan 4 mg, osimertinib discontinued	LVEF recovered and patient was treated with afatinib
7.2 ng/mL	2.945 ng/mL	42	Percutaneous coronary intervention of the left anterior descending artery	Switched to erlotinib
Normal	Normal	35	IV furosemide transitioned to oral azosemide and spironolactone; oral enalapril and bisoprolol; osimertinib discontinued	QTc normalized and LVEF improved, passed away from cancer progression 15 mo after therapy discontinuation
	58 pg/mL	31	Telmisartan 20 mg converted to enalapril 1.25 mg, carvedilol converted to bisoprolol 1.25 mg, ivabradine 5.0 mg initiated to modulate heart rate, osimertinib suspended	Improved LVEF and reduced BNP 1 mo after, osimertinib restarted at 40 mg without recurrence
			Diuretic agents, beta-blocker, oxygen, discontinued osimertinib	Required increased therapy because of worsening HF but maintained stable clinical improvement afterwards
			Suspended osimertinib	Resumed osimertinib after stabilization of HF without complication, developed atrial fibrillation during hospital admission for HF
		19	Diuretic, beta-blocker treatment, discontinued osimertinib	Improvement in EF and HF symptoms
		30	Dabigatran, bisoprolol, digoxin, ramipril, and spironolactone were started	Osimertinib was continued without complication after optimizing cardiac management, patient passed because of cancer progression
		36	Furosemide, spironolactone, bisoprolol, valsartan, discontinued osimertinib	LVEF improved after 4 wks and aumolertinib was administered
		58	Spironolactone 25 mg, bisoprolol 1.25 mg, suspended osimertinib	LV motion improved to almost normal kinesis and electrocardiogram changes normalized after 35 d, restarted osimertinib at 40 mg but cardiac complications reappeared 63 d later and treatment was stopped with subsequently improved cardiac function
	12.487,6 pg/mL	Severely depressed	Dobutamine and noradrenaline, glucocorticoids and immunoglobulins, ventricular assist device (Impella) implantation, antibiotics for central catheter infection	Discharged from hospital, unknown outcomes
	40.9 pg/mL	17	Furosemide, carvedilol, enalapril, discontinued osimertinib	Symptoms, cardiac function, and condition improved 3 wks following treatment
39 mg/dL		20	Diuretic and beta-blocker, discontinued osimertinib	Gradual improvement in cardiac function
	2.2 ug/L	30-35	Initiated on empagliflozin, spironolactone, and metoprolol, discontinued osimertinib	Normalization of LVEF and trace pericardial effusion after 3 mo
4.4 ng/mL	0.03 ng/mL		Switched to erlotinib	Osimertinib was trialed at 40 mg every other day before progressing to daily administration without further cardiac events
	Within normal limits	36, 35	Torsemide, spironolactone, metoprolol, and daglitazone improved HF symptoms, osimertinib was discontinued	Follow-up imaging showed no recurrence of primary tumor so osimertinib was not restarted, EF improved with medication

in 2018 for EGFR exon 19 deletions or exon 21 L858R sequence variant NSCLC. Although it has many beneficial therapeutic effects, there are emerging reports of its cardiotoxicity, specifically HF exacerbation, arrhythmias, and QT prolongation (Table 1).

SGLT2 INHIBITORS. SGLT2 inhibitors (ie, empagliflozin, dapagliflozin) inhibit the sodium-glucose cotransporter in the proximal convoluted tubules and are used in the management of type 2 diabetes mellitus, HF, and chronic kidney disease. These therapies are known to improve outcomes and reduce mortality in HF patients regardless of comorbidity status or LVEF, carrying a Class IIa recommendation in similar patients per current guidelines.

In anthracycline- and trastuzumab-induced cardiotoxicity, SGLT2 inhibitor use has demonstrated anti-inflammatory properties, reducing inflammatory markers (interleukin 6, C-reactive protein, tumor necrosis factor-α, and monocyte chemoattractant protein-1) in animal models.[2] Trastuzumab has dose-independent, reversible cardiotoxic properties by blocking EGFR2 on cardiac myocytes. Empagliflozin may attenuate this by suppressing a DNA damage ferroptosis-mediated mechanism in animal models.[3] Conversely, anthracyclines (ie, doxorubicin) typically have dose-dependent, irreversible cardiotoxic properties through a complex interplay of mitochondrial damage and free radical generation. SGLT2 inhibitors may lower the rate of cardiac events and prevent left ventricular dysfunction in cancer patients treated with anthracyclines.[4,5]

OSIMERTINIB. Osimertinib is an effective oral treatment for NSCLC.[1] Ewer et al[6] performed a post hoc analysis of cardiac data from the FLAURA (First-Line Osimertinib in Advanced Non-Small Cell Lung Cancer) and AURA3 (A trial of osimertinib for non small cell lung cancer) studies and did not find a causal relationship between osimertinib and HF. They found a decrease in LVEF of over 10% in 3.9% of all patients, with most of the events being asymptomatic and resolving without further treatment or therapy discontinuation.[6] Although the pharmacokinetic and pharmacodynamic analysis found no relationship between osimertinib exposure and LVEF reduction, the authors note that LVEF decreases were observed in patients with cardiac risk factors before osimertinib treatment; therefore, cardiac monitoring is advised.[6]

Osimertinib has been strongly associated with increased odds of QT prolongation, arrhythmias, and HF compared with other targeted treatments for NSCLC in a large-scale study of 98,765 reported adverse reactions.[7] Another retrospective review of the U.S. Food and Drug Administration Adverse Events Reporting System found the odds for HF, AF, QT prolongation, myocardial infarction, and pericardial effusion were significantly increased with osimertinib use compared with all other drugs in the system and other EGFR tyrosine kinase inhibitors.[8] A study of 58 patients noted reduced LVEF that improved with discontinuation, dose reduction, or switching tyrosine kinase inhibitors in most patients.[9] This data has been supported by several case studies (Table 1).

Osimertinib appears to follow a dose-dependent, reversible model. Trastuzumab has been well-established to have cardiotoxic adverse events, and the mechanism of osimertinib is theorized to share similarities. A study conducted in isolated hearts of guinea pigs found acute exposure to osimertinib blocked hERG, Nav1.5, and L-type Ca channels in a concentration-dependent mechanism, prolonging the QT interval, PR interval, QRS interval, left atrium, left ventricle, and atrioventricular conduction time.[10] Further research is necessary to understand the development of osimertinib-related cardiotoxicity and to determine the most efficacious combination of cardioprotective agents for these cases of cardiotoxicity.

In summary, we recommend that osimertinib-induced cardiotoxicity be managed by first discontinuing osimertinib and then aggressive guideline-directed HF management, with a focus on starting an SGLT2 inhibitor. Close monitoring of clinical signs of HF and serial echocardiograms may be warranted in higher-risk patients with the reintroduction of osimertinib.

CONCLUSIONS

This case highlights the critical need for proactive management mitigating cardiovascular risks associated with anticancer therapies. Given the oncologic impact of osimertinib discontinuation, it is imperative to develop meticulous protocols to monitor cardiovascular complications while allowing for appropriate and necessary oncologic therapies. Permissive cardiotoxicity suggests that specific therapies may indirectly exacerbate cardiovascular risks, necessitating a nuanced approach to intervention balancing the needs for oncologic outcomes with minimizing cardiovascular adverse effects. Adding SGLT2 to traditional guideline-directed medical therapy and regular clinical and imaging monitoring offers a compelling intervention in controlling osimertinib-induced cardiomyopathy. This dual approach holds promise in managing acute

cardiovascular impacts and ensuring the sustained effectiveness of this essential therapy.

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KEY WORDS cardiomyopathy, heart failure, osimertinib, SGLT2 inhibitor

APPENDIX For supplemental videos, please see the online version of this paper.