



## Takotsubo Syndrome Associated With Osimertinib In A Patient With Non-Small Cell Lung Cancer: A Case Report

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Osimertinib is a mono-anilino-pyrimidine compound that specifically binds to the EGFR kinase domain irreversibly by targeting the cysteine-797 residue in the ATP binding site via covalent bond formation.

In 2018 osimertinib was approved by the US food and drug administration (FDA) For the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations.

In the phase III FLAURA trial, 556 patients with treatment-naïve, egfr-mutated advanced nscl were randomly assigned to osimertinib versus standard of care EGFR TKI (Gefitinib or Erlotinib). Osimertinib showed superior efficacy in the first-line treatment of EGFR mutation-positive advanced NSCLC, with a similar safety profile and lower rates of serious adverse events. on regard to tolerability, the trial.

demonstrated a generally manageable tolerability in adults with previously untreated, EGFR mutation-positive advanced NSCLC.

some adverse effects have been reported, such as prolongation of the qtc interval, as well as

decreased left ventricular ejection fraction, which are reversible with drug discontinuation.

Herein, we present a rare case of a patient with takotsubo syndrome in a patient with non-small cell lung cancer during treatment with Osimertinib. we want to describe it to be aware of this entity and thus identify it in a timely manner, to have better results.

**Case Presentation:** A 78-year-old patient presented in 2018 with EGFR mutation-positive (Exon 19 Deletion) IIIA NSCLC, PDL-1 less than 15%. upper left pulmonary lobectomy and mediastinal lymph node dissection was performed followed by adjuvant radiotherapy and 4 cycles of cisplatin and vinorelbine. In July 2021 multiple brain metastases were found. brain metastases were treated with radiosurgery and Osimertinib was initiated. The patient presented to our emergency department 4 weeks after initiation of osimertinib complaining of oppressive chest pain associated with nausea. electrocardiogram showed sinus tachycardia without other alterations. laboratory tests revealed elevated troponin I (1112 Ng/L). A

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transthoracic echocardiogram revealed akinesia of all apical segments, septum, anterior and lateral wall, the other walls appeared hypokinetic. apical aneurysmal dilatation was seen without thrombus inside. the ejection fraction was 25-30% cardiac MRI was consistent with takotsubo cardiomyopathy.

Beta-blocker, aldosterone antagonist, statins and colchicine are initiated and osimertinib is discontinued. at 6 weeks, a cardiac resonance is performed showing no alterations and recovery of cardiac function. therefore, takotsubo syndrome secondary to osimertinib is considered subsequently, afatinib is started with adequate tolerance. currently, her cancer is under control.

**Discussion:** takotsubo syndrome is a cardiomyopathy characterized by transient alterations in the contractility of the left ventricle. It is more common in postmenopausal, who present to the emergency room with chest pain, EKG changes and increased cardiac enzymes mimicking an acute coronary syndrome. however, when studied, no significant coronary disease is found. The pathophysiology is not fully elucidated. There are several proposed mechanisms: coronary vasospasm, production of reactive oxygen species, and catecholamine cardiotoxicity.

The occurrence of this cardiomyopathy is higher in cancer patients, mainly due to the cardiotoxicity associated with oncospecific treatment. Many chemotherapeutic agents have been linked to this complication .

The goal of treatment is support, optimal management of heart failure, and identification of stress factors. triggers should be removed as much as possible.

Our patient presented this complication 4 weeks after starting treatment. Despite being a hypertensive patient, the functional cardiac resonance showed no areas of late enhancement with gadolinium that suggested the presence of foci of necrosis or macroscopic scars. The most important criterion for diagnosis is normalization of cardiac function upon removal of the triggering factor. Our patient recovered cardiac function after discontinuation of Osimertinib and exhibited a favorable outcome.

**Conclusion:** Takotsubo syndrome is a complication that can occur in cancer patients given physiological stress and the administration of systemic cancer therapies which increases this risk. Although Osimertinib has been associated with cardiotoxicity, this is mainly represented by arrhythmias, specifically qt prolongation. this is a rare case of takotsubo syndrome associated with Osimertinib, highlighting the importance of being aware of this entity. Timely identification and early interventions are the basis of management that guarantee a favorable outcome.

**keywords:** GFR Inhibitor; cardiotoxicity; case report; cardiomyopathy.