Ischemic Mimics in Cardio-Oncology: Post-Chemotherapy MINOCA dilemma

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Abstract

Advances in neoadjuvant therapies for breast cancer have increased the incidence of acute cardiotoxicity, often presenting as a diagnostic challenge in the emergency setting. We report the case of a 35-year-old female with invasive breast carcinoma, currently receiving neoadjuvant chemotherapy, who presented with acute retrosternal chest pain and ST-segment elevation in the anterior leads. Initial laboratory findings revealed a massively elevated cardiac troponin I level (5,830.60 ng/L) and severe chemotherapy-induced neutropenia. Emergency coronary angiography demonstrated unobstructed epicardial coronary arteries, establishing a working diagnosis of Myocardial Infarction with Non-Obstructive Coronary Arteries (MINOCA).
Subsequent transthoracic echocardiography revealed apical and periapical akinesia, a phenotype consistent with Takotsubo cardiomyopathy. In the context of active oncological treatment, the diagnostic crossover between stress-induced cardiomyopathy and therapy-related myocarditis, particularly immune checkpoint inhibitor-associated myocarditis is critical. While Takotsubo syndrome is primarily managed with supportive care, acute myocarditis mandates immediate cessation of antineoplastic agents and the initiation of high-dose corticosteroids. This creates a formidable therapeutic paradox in the setting of severe neutropenia, where systemic immunosuppression poses a high risk of life-threatening sepsis.

This case underscores that in patients presenting with a STEMI-like MINOCA during chemotherapy, clinical and echocardiographic findings may be insufficient for differentiation. Early Cardiac Magnetic Resonance (CMR) imaging is the definitive arbiter required to distinguish between these entities. Accurate diagnosis is essential to balance the management of fulminant cardiovascular events with the safe continuation of life-saving oncological care.

Keywords: Myocardial Infarction with Non-Obstructive Coronary Artery, Takotsubo Cardiomyopathy, Cardiotoxicity, Breast Neoplasms, ST Elevation Myocardial Infarction

Introduction

The improvement in breast cancer survival rates, driven by advances in neoadjuvant and adjuvant therapies, has unveiled an emerging challenge: acute cardiotoxicity. While historical focus in cardio-oncology has predominantly centered on the chronic, dose-dependent left ventricular dysfunction induced by anthracyclines and HER2(Human Epidermal Growth Factor Receptor 2) (targeted therapies, acute cardiovascular events present an immediate diagnostic difficulty in the emergency department (1).

When a patient undergoing active oncological treatment presents with acute chest pain and ST-segment elevation, the clinical dogma strongly favors acute coronary occlusion. However, the angiographic finding of unobstructed coronary arteries abruptly shifts the paradigm to Myocardial Infarction with Non-Obstructive Coronary Arteries (MINOCA), as defined by the Fourth Universal Definition of Myocardial Infarction (2). In the specific context of cardio-oncology, MINOCA is not a benign condition, but a critical diagnostic challenge where Takotsubo syndrome, coronary vasospasm, and acute myocarditis overlap (3).

This case report shows the challenge of diagnosing MINOCA with an ST-segment elevation, highlighting the need for a multimodal approach to guide life-saving treatments and safely continue her oncological care.

Case presentation

A 35-year-old female with no known cardiovascular risk factors presented to the emergency department with acute and constricting retrosternal chest pain of 3 hours' duration. Her medical history was notable for invasive carcinoma of no special type of the breast HER2 negative and hormone receptor, currently being treated with a neoadjuvant chemotherapy type sequential Anthracycline followed by Taxane regimen. Her most recent cycle of Epirubicin and Cyclophosphamide had been administered 2 weeks prior to presentation. Upon admission, the patient was hemodynamically stable, with a blood pressure of 110/70 mm Hg symmetrical in the two arms and a heart rate of 95 beats per minute. Also, respiratory stable, with no signs of congestive cardiac failure. The patient was very anxious. The pain was graduated as 8 out of ten using the numerical pain scale.

A standard 12-lead electrocardiogram (ECG) (Figure 1) revealed a 4-mm ST-segment elevation in the anterior leads.

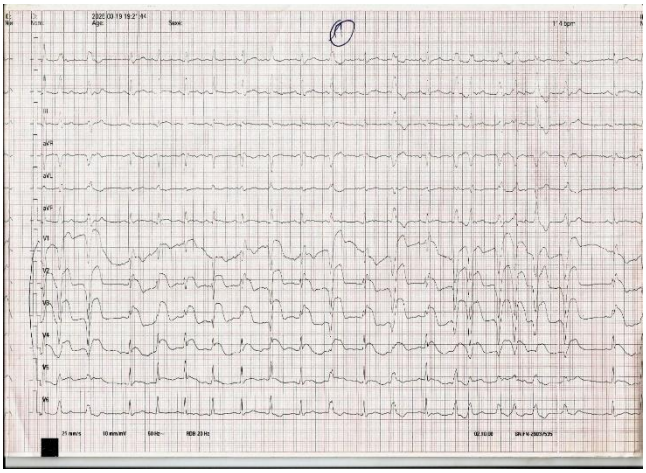

Figure 1: ECG at admission

Initial laboratory investigations confirmed acute myocardial injury, with a cardiac troponin I level massively elevated at 5,830.60 ng/L. Concomitant hematological assessment underscored the systemic impact of her recent cytotoxic therapy, demonstrating marked leukopenia (white-cell count, 1,980 per cubic millimeter) with severe neutropenia (absolute neutrophil count, 520 per cubic millimeter), alongside a mild normocytic anemia (hemoglobin, 10.4 g per deciliter; mean corpuscular volume, 81.5 fL). Her platelet count was preserved at 265,000 per cubic millimeter. We noticed mild hypokalemia (potassium, 3.20 mmol per liter), renal function (creatinine, 62.6 Umol per liter) and coagulation parameters (aPTT ratio, 0.91) remained within normal limits. An acute ST-segment elevation myocardial infarction (STEMI) was the first diagnosis suspected and the patients was emergently transferred to the cardiac

catheterization center. Coronary angiography revealed a strictly normal epicardial coronary tree, with no angiographic evidence of atherosclerosis, intraluminal thrombus, or spontaneous coronary artery dissection (SCAD). An urgent transthoracic echocardiogram (TTE) performed immediately revealed akinesia of the apex and periapical segments with a conserved ejection fraction. Faced with the triad of severe myocardial injury, unobstructed coronary arteries, and profound apical dysfunction, a working diagnosis of MINOCA was established. The primary differential diagnosis hinged between classic Takotsubo cardiomyopathy and an acute, focal post-chemotherapy myocarditis. Patients was admitted to the emergency department, with continuous monitoring of vital signs and pain, treated with beta-blockers and ACE inhibitors with favorable evolution and resolution of chest pain at the second day following admission. No administration of antithrombotic treatment since the coronary angiography was normal. Patient was discharged on day 5.

Figure 2 showed the ECG at discharge.

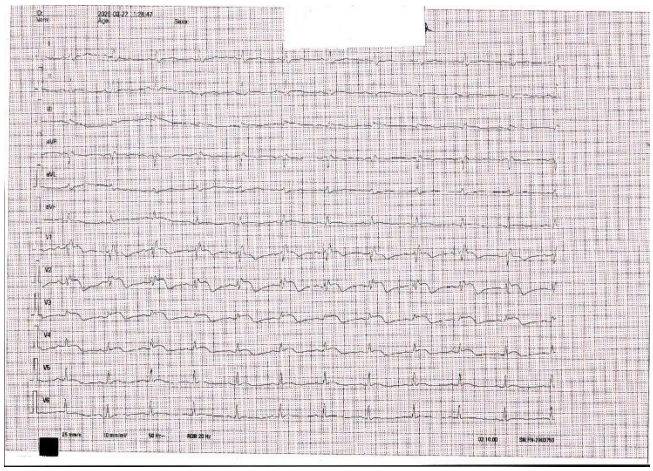

Figure 2: ECG at discharge

For the follow up, the patients was seen by cardiologist 15 days after the episode than seen at emergency department at one month. She reported episods of chest pain scaled 2 out of 10 on numerical pain scale. Laboratory investigations at one month showed white-cell count, 6,660 per cubic millimeter with absolute neutrophil count, 3480 per cubic millimeter, herplatelet count was preserved at 294,000 per cubic millimeter. The other parameters were stable.

Discussion

The presentation of this young patient highlights an increasingly prevalent clinical dilemma in modern emergency care units: the management of Myocardial Infarction with Non-Obstructive Coronary Arteries (MINOCA) in the actively treated oncological patient. According to the Fourth Universal Definition of Myocardial Infarction, MINOCA is not a definitive clinical endpoint but rather a preliminary "working diagnosis" that requires an exhaustive etiologic investigation(2). In the cardio-oncology setting, this diagnostic imperative is amplified. As highlighted by the American Heart Association and the 2022 European Society of Cardiology (ESC) guidelines, cancer patients experience a significantly higher incidence of MINOCA and face worse short- and long-term cardiovascular outcomes compared to the general population(1,4).

Diagnosing MINOCA is exceptionally unreliable when a patient presents with a classic ST-segment elevation. In the context of traditional acute coronary syndromes, ST-segment elevation is the electrocardiographic signature of transmural ischemia driven by acute epicardial vessel occlusion(2). However, in MINOCA, this classical ischemic sign serves as a diagnostic trap, masking a complex pathophysiological crossroads. Transmural myocardial edema whether resulting from intense neurogenic stunning or active inflammation can produce identical repolarization abnormalities (5)

In an oncological patient, the initial evaluation of MINOCA must navigate the risks of the malignancy itself and its treatments. The

prothrombotic state inherent to active breast cancer, combined with systemic endothelial dysfunction, lowers the threshold for transient thrombotic events that may spontaneously lyse prior to angiography (6). As well, the clinician must exclude Spontaneous Coronary Artery Dissection (SCAD), a condition prevalent in young women (7), and coronary vasospasm, a well-documented acute toxicity of antineoplastic agents such as fluoropyrimidines and taxanes. Yet, the echocardiographic revelation of profound acute apical dysfunction in this patient redirects the diagnostic trajectory away from the epicardial vessels and toward direct microvascular or myocardial injury.

The echocardiographic phenotype observed apical akinesia with compensatory basal hyperkinesia is the classic feature of Takotsubo (stress) cardiomyopathy(8). Recent large-scale registry data, including the International Takotsubo Registry, have firmly established a bidirectional relationship between malignancy and stress cardiomyopathy(9). Approximately 1 in 6 patients with Takotsubo syndrome has a concomitant or recent history of cancer (10).

The pathophysiology of Takotsubo in oncology have many sides. It is driven not only by the profound psychological distress of a cancer diagnosis but also by the intense physiological stress of cytotoxic chemotherapy, which acts as an exogenous trigger for a massive catecholamine surge (9). This surge induces diffuse microvascular spasm and direct catecholaminergic myocyte toxicity, preferentially affecting the apex due to the higher density of beta adrenergic receptors in this region(10). While Takotsubo syndrome is often considered a transient and benign condition, its occurrence during active chemotherapy is associated with a high risk of cardiogenic shock and arrhythmias, requiring vigilant intensive care management (10).

While Takotsubo syndrome fits the echocardiographic pattern, acute focal myocarditis can perfectly mimic this clinical and imaging phenotype. Historically, cardiotoxicity in breast cancer was synonymous with the chronic, cumulative, and dose-dependent left ventricular dysfunction induced by anthracyclines or the reversible dysfunction linked to HER2-targeted therapies (1,11). However, the landscape of neoadjuvant therapy for high-risk or triple-negative breast cancer has been revolutionized by the incorporation of immune checkpoint inhibitors (ICIs), such as pembrolizumab, during conventional chemotherapy (12).

This therapeutic evolution has introduced the specter of ICI-associated myocarditis a rare but fulminant autoimmune toxicity. ICI myocarditis typically presents early in the treatment course and frequently mimicking an acute coronary syndrome with ST-segment elevation and massive troponin release(13)**.** The underlying mechanism involves a breakdown of immunological tolerance, leading to aggressive clonal T-cell infiltration into the myocardium, targeting antigens shared between the tumor and the cardiomyocytes(14).In the context of recent chemotherapy, severe interstitial edema and intense focal inflammation can transiently paralyze the myocardium, rendering the initial presentation unclear from the apical ballooning of Takotsubo syndrome.

In the acute phase of a MINOCA presentation featuring ST-segment elevation and regional wall motion abnormalities, early Cardiac Magnetic Resonance (CMR) imaging is the definitive arbiter (15). Relying solely on clinical presentation and echocardiography is insufficient to distinguish between stress cardiomyopathy and acute myocarditis.

Differentiating between acute myocarditis and Takotsubo syndrome dictates a highly divergent and high-risk therapeutic trajectory. Takotsubo syndrome generally warrants supportive care (e.g., beta-blockers, ACE inhibitors) and often allows for the cautious, multidisciplinary-guided

resumption of chemotherapy once the ejection fraction recovers**.**

In contrast, a diagnosis of acute ICI or therapy-induced myocarditis mandates the immediate and absolute cessation of the antineoplastic agents(1,13). The standard of care for ICI myocarditis requires the urgent initiation of high-dose intravenous corticosteroids, potentially escalating to second-line immunosuppressants like mycophenolate mofetil or alemtuzumab if the patient is refractory(14). In this specific case, the hematological panel reveals severe chemotherapy-induced neutropenia. This creates an extreme therapeutic paradox: administering massive doses of immunosuppressive steroids to halt a fatal autoimmune cardiac attack in a patient who is already profoundly immunocompromised and at imminent risk of overwhelming sepsis**.**

Conclusion

Diagnosing MINOCA with an ST-segment elevation in a patient undergoing chemotherapy is a critical clinical challenge. It requires rapid identification between Takotsubo syndrome and therapy-induced acute myocarditis. Early Cardiac Magnetic Resonance (CMR) imaging is essential to make this distinction.

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