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Fluorouracil-Associated Coronary Vasospasm and Reversible Cardiomyopathy Mimicking ST-Elevation Myocardial Infarction During a First Cycle of FOLFOX: A Case Report

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 50-year-old
Final Diagnosis: 5FU induced vasospasm
Symptoms: Chest pain
Clinical Procedure: —
Specialty: Cardiology • Oncology

Objective: Unusual clinical course

Background: 5-Fluorouracil (5-FU) is a mainstay chemotherapeutic agent for gastrointestinal malignancies but carries a recognized risk of cardiotoxicity, most often manifesting as coronary vasospasm that can mimic acute myocardial infarction. This report describes the case of a 50-year-old woman with ST-elevation myocardial infarction (STEMI) due to coronary artery vasospasm during continuous infusion of 5-FU as part of the first round of FOLinic acid (leucovorin), Fluorouracil (5-FU), and OXaliplatin (FOLFOX) chemotherapy for colorectal carcinoma.

Case Report: A 50-year-old woman with colorectal carcinoma receiving her first cycle of FOLFOX developed severe chest pain during a continuous infusion of 5-FU. Initial emergency department evaluation was reportedly unremarkable, and she was discharged after symptomatic improvement with ketorolac. She returned emergently with recurrent crushing chest pain; a repeat electrocardiogram showed hyperacute T waves and ST-segment elevation, prompting ST-elevation myocardial infarction activation and transfer for emergent catheterization. Coronary angiography revealed no obstructive coronary artery disease. Echocardiography demonstrated a severely reduced left ventricular ejection fraction (LVEF) of 30% to 35% with apical akinesis, consistent with 5-FU-induced cardiomyopathy. 5-FU was permanently discontinued, and the patient was treated with vasodilator therapy, with complete resolution of symptoms and normalization of ventricular function on follow-up echocardiography.

Conclusions: 5-FU can precipitate life-threatening coronary vasospasm and a fully reversible cardiomyopathy even during a first chemotherapy cycle, in the absence of obstructive coronary artery disease. Early recognition, prompt drug interruption, and a multidisciplinary cardio-oncology approach, including an individualized decision between permanent discontinuation and carefully supervised rechallenge, are essential to guide safe oncologic decision-making.

Keywords: Case Reports • Coronary Vasospasm • Fluorouracil • Colorectal Neoplasms • Cardiomyopathies
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Introduction

5-Fluorouracil (5-FU) is one of the most widely used chemotherapeutic agents in the treatment of solid tumors, particularly colorectal, gastric, and head and neck cancers [1]. It remains a core component of the FOLFOX regimen (folinic acid, fluorouracil, oxaliplatin), a first-line therapy for colorectal carcinoma. While its hematologic and gastrointestinal toxicities are well characterized, cardiovascular toxicity, although less frequently recognized, represents a clinically significant and potentially lethal complication [2].

The reported incidence of 5-FU cardiotoxicity ranges from 1.2% to 18%, with coronary vasospasm being the most commonly implicated mechanism [2]. Affected patients may present across a spectrum ranging from asymptomatic electrocardiographic changes to acute myocardial infarction, arrhythmias, cardiogenic shock, and sudden cardiac death [2,3]. Continuous infusion regimens are associated with higher cardiotoxic risk than bolus dosing, likely because of prolonged endothelial exposure [2,4]. Cardiotoxicity is idiosyncratic and can arise even during a patient's first exposure to the drug [4], as illustrated in the case below.

Coronary artery vasospasm is a transient, reversible constriction of the epicardial coronary arteries that produces myocardial ischemia in the absence of fixed obstructive coronary artery disease [5]. Recognized precipitants include tobacco use, cocaine and other sympathomimetic agents, ergot alkaloids, hyperventilation, cold exposure, and emotional or physical

stress, acting through endothelial dysfunction, impaired nitric oxide-mediated vasodilation, and vascular smooth muscle hyperreactivity. Its clinical effects range from asymptomatic ischemic electrocardiographic changes and stable angina to malignant ventricular arrhythmias, acute myocardial infarction, and sudden cardiac death [6].

This report presents the case of a 50-year-old woman who developed ST-elevation myocardial infarction (STEMI) secondary to coronary artery vasospasm during continuous infusion of 5-FU in the first cycle of FOLFOX chemotherapy for colorectal carcinoma. The purpose of this report is to provide confirmatory evidence rather than to propose novel mechanisms. This case is significant for its detailed documentation of the clinical course, including an initially unremarkable evaluation, recurrent STEMI-like electrocardiographic changes, nonobstructive coronary angiography, severe but reversible ventricular dysfunction, and subsequent modification of oncologic therapy.

Case Report

A 50-year-old woman with newly diagnosed colorectal carcinoma, no known prior cardiac disease or cardiovascular risk factors, and receiving her first cycle of FOLFOX (folinic acid, fluorouracil, oxaliplatin) chemotherapy presented with chest pain. Chest pain developed during the continuous infusion of 5-FU. On initial evaluation, she was hemodynamically stable, and the initial cardiac workup, including cardiac biomarkers,



Figure 1. 12-lead electrocardiogram showing hyperacute T waves and ST-segment elevation.

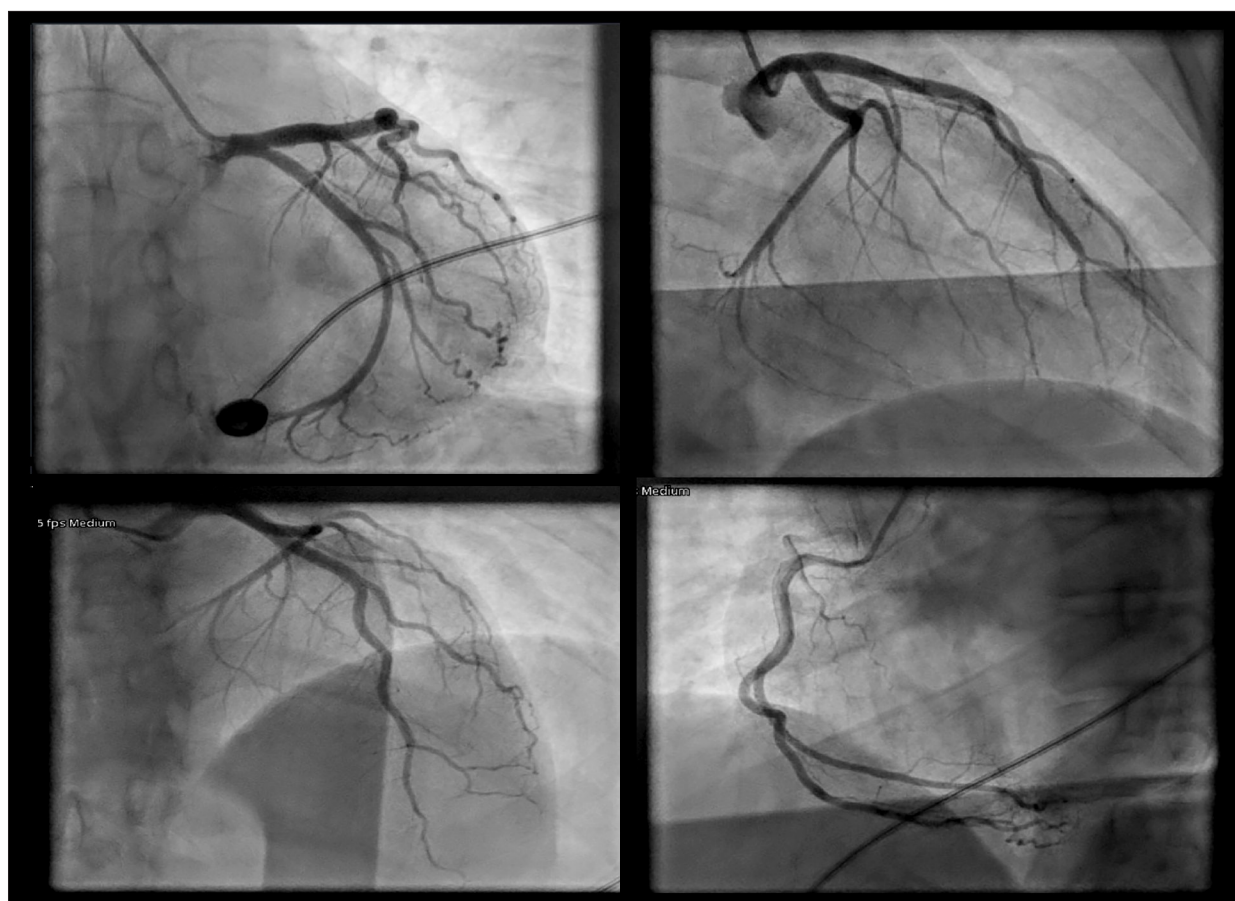


Figure 2. Left heart catheterization demonstrating angiographically normal left and right coronary arteries without evidence of obstructive coronary artery disease, plaque rupture, intraluminal thrombus, or flow-limiting stenosis in the major epicardial vessels.

was reportedly unremarkable. Her symptoms improved after administration of ketorolac (Toradol), and she was discharged from the emergency department.

Approximately 1 hour after discharge, while still in the hospital parking lot, she developed sudden-onset severe crushing sub-sternal chest pain. Emergency medical services were activated, and she returned to the emergency department. A repeat 12-lead electrocardiogram (ECG) demonstrated ST-segment elevation concerning for acute myocardial infarction, prompting immediate ST-elevation myocardial infarction (STEMI) activation and transfer via air transport to a tertiary care center with percutaneous coronary intervention capability. Physical examination on presentation was notable for severe distress due to chest pain; however, she remained hemodynamically stable without signs of cardiogenic shock or overt heart failure. The ECG on arrival showed hyperacute T waves and ST-segment elevation (**Figure 1**).

Serial high-sensitivity troponin rose from 5 ng/L to 25 ng/L (reference range, < 14 ng/L), consistent with acute myocardial

injury. A basic metabolic panel was unremarkable, with normal sodium (142 mmol/L; reference range, 136-145 mmol/L), potassium (4.0 mmol/L; reference range, 3.5-5.0 mmol/L), and creatinine levels (0.70 mg/dL; reference range, 0.6-1.1 mg/dL), and an estimated glomerular filtration rate greater than 90 mL/min/1.73 m². A complete blood count showed mild leukocytosis (white blood cell count $13.5 \times 10^3/\mu\text{L}$; reference range, $4.5\text{-}11.0 \times 10^3/\mu\text{L}$) and mild normocytic anemia (hemoglobin 10.3 g/dL [reference range, 12.0-15.5 g/dL], hematocrit 32.2% [reference range, 36%-46%]), both thought to reflect her underlying malignancy rather than an acute infectious or hemorrhagic process; platelet count was normal.

Emergent left heart catheterization and coronary angiography revealed no obstructive coronary artery disease, plaque rupture, thrombus, or flow-limiting stenosis in the major epicardial coronary vessels (**Figure 2**). Repeat ECG after improvement of chest pain showed resolution of ST-T changes (**Figure 3**). Transthoracic echocardiography demonstrated a left ventricular ejection fraction (LVEF) of 30% to 35%, global left ventricular hypokinesia, and akinesis of the apical wall, with normal

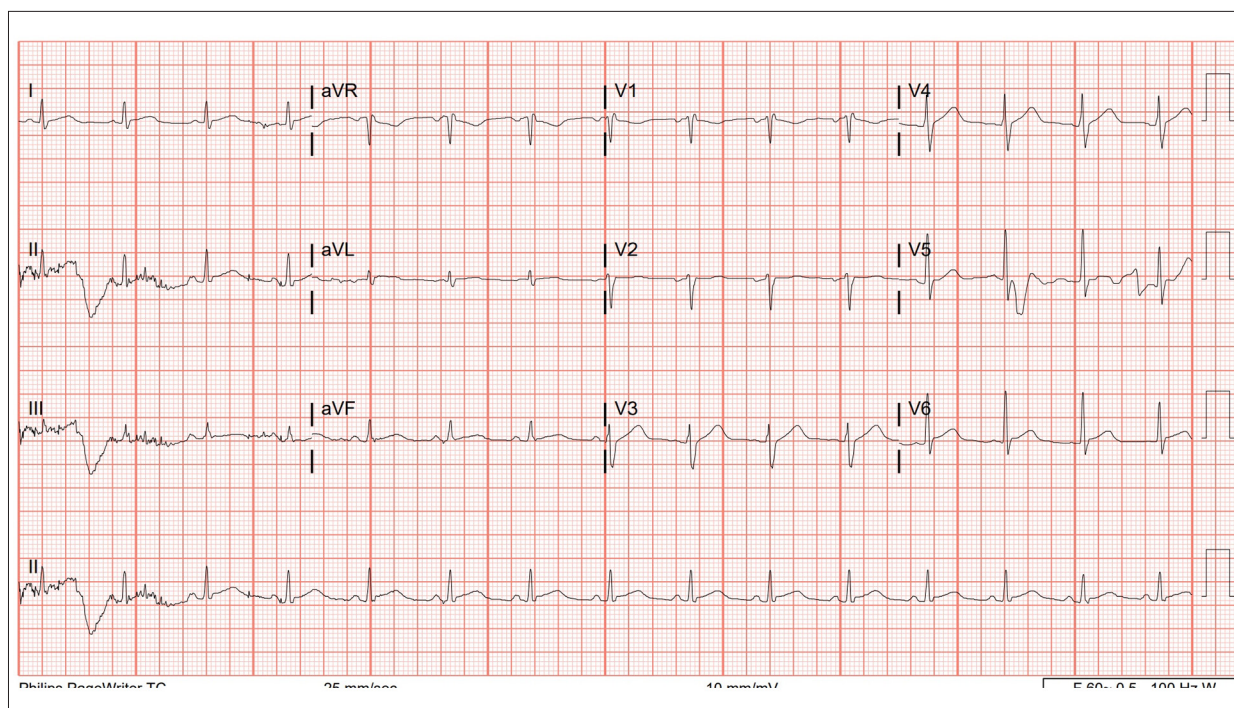


Figure 3. 12-lead electrocardiogram showing resolution of ST-segment and T-wave (ST-T) changes.

right ventricular size and systolic function. These findings were consistent with 5-FU-associated reversible cardiomyopathy, with clinically suspected coronary vasospasm and associated myocardial injury as the leading proposed mechanism, alongside possible direct chemotherapy-related myocardial toxicity.

Cardiology and oncology services jointly recommended discontinuation of 5-FU and, by extension, the FOLFOX regimen, given the high risk of recurrent and potentially fatal vasospastic events; her oncologic treatment plan was subsequently revised to a non-fluoropyrimidine-based regimen. Medical therapy included aspirin 81 mg daily, isosorbide mononitrate, and vasodilatory therapy with diltiazem (Cardizem), which was later discontinued after an echocardiogram showed reduced ejection fraction. The patient's chest pain resolved completely within 24 hours of initiation of vasodilatory therapy. She remained hemodynamically stable, tolerated oral intake, and showed no recurrent ischemic symptoms during hospitalization. She was discharged home in stable condition with outpatient cardiology follow-up arranged. A repeat echocardiogram months later showed normalization of the ejection fraction to 60% to 65%, with resolution of the previously noted global hypokinesis and apical akinesis.

Discussion

The precise molecular mechanism underlying 5-FU cardiotoxicity remains incompletely understood. The leading proposed

mechanisms include endothelial injury with coronary vasospasm, impaired nitric oxide-mediated vasodilation, platelet activation with a prothrombotic state, and direct myocardial injury via oxidative stress [2,6,7]. Coronary vasospasm, as demonstrated in this case, is the predominant mechanism, and its occurrence with angiographically normal coronary arteries supports a vasomotor rather than atherosclerotic etiology.

Continuous infusion protocols of 5-FU carry substantially higher cardiotoxic risk than bolus dosing methods, given that prolonged drug exposure amplifies endothelial injury [2,6]. Pre-existing cardiovascular disease is an additional risk factor. However, 5-FU-related vasospasm frequently occurs in younger patients without known prior cardiac disease [8], as in our patient, who developed this complication during her very first cycle of therapy. The absence of flow-limiting coronary artery disease on angiography is a characteristic finding of vasospasm-mediated injury [8,9].

The cornerstone of management is immediate discontinuation of the offending agent [10,11]. Rechallenge was considered contraindicated [9]; however, the historical prohibition against fluoropyrimidine rechallenge has evolved substantially. A structured protocol from Massachusetts General Hospital, validated in larger cohorts, demonstrates the safety of rechallenge with aggressive vasodilator prophylaxis [12]. In this case, the multidisciplinary team opted for permanent discontinuation, based on the severity of the initial event, the degree of ventricular dysfunction, and the availability of a non-fluoropyrimidine oncologic

alternative. Uridine triacetate is FDA-approved for life-threatening cardiotoxicity occurring within 96 hours of exposure [13]. Long-acting nitrates and calcium channel blockers are the mainstays of vasospasm management, although calcium channel blockers require caution in patients with reduced LVEF [7].

These findings are consistent with previously reported cases of fluoropyrimidine-induced coronary vasospasm. Garbis et al described a case of 5-FU-induced coronary vasospasm characterized by cardiovascular magnetic resonance imaging, providing direct evidence of vasospasm-mediated myocardial injury with subsequent recovery of ventricular function [14]. Similarly, Dimitrova reported a case of 5-FU-induced coronary artery vasospasm in a patient with salivary gland cancer that resolved following cessation of the offending agent and vasodilator therapy [15]. As in these reports, the present case involved a patient without antecedent cardiovascular risk factors who developed vasospasm early in the treatment course, strengthening the idiosyncratic and dose-independent nature of this complication [7,8].

The development of an LVEF of 30% to 35% with global hypokinesis and apical akinesis in this patient raises an important differential diagnosis: ischemic cardiomyopathy secondary to sustained vasospasm, Takotsubo-like stress cardiomyopathy, or direct 5-FU-induced myocardial toxicity. The presence of apical akinesis may suggest a stress cardiomyopathy (Takotsubo syndrome) superimposed on the vasospastic event. Coronary microvascular dysfunction has been increasingly implicated as a potential trigger, rather than only a consequence, of Takotsubo syndrome. Most affected patients show abnormal endothelium-dependent coronary vasoreactivity and impaired microvascular flow during the acute phase, and normalization of myocardial perfusion has been associated with recovery of ventricular function in preclinical models [16,17]. A similar vasospastic or microvascular insult could plausibly have contributed to the reversible apical dysfunction observed in this case. However, as with Takotsubo syndrome more broadly, it remains unclear whether such microvascular dysfunction was a cause or a consequence of the transient ventricular impairment in this instance. The patient's left ventricular dysfunction resolved on repeat echocardiogram. Additional investigation into the mechanisms of 5-FU cardiotoxicity is necessary to prevent cardiovascular events and identify patients who may benefit from prophylactic treatment [9].

References:

- Longley DB, Harkin DP, Johnston PG. 5-fluorouracil: Mechanisms of action and clinical strategies. *Nat Rev Cancer*. 2003;3(5):330-38
- Polk A, Vistisen K, Vaage-Nilsen M, Nielsen DL. A systematic review of the pathophysiology of 5-fluorouracil-induced cardiotoxicity. *BMC Pharmacol Toxicol*. 2014;15:47
- Sara JD, Kaur J, Khodadadi R, et al. 5-fluorouracil and cardiotoxicity: A review. *Ther Adv Med Oncol*. 2018;10:1758835918780140
- Sorrentino MF, Kim J, Foderaro AE, Truesdell AG. 5-fluorouracil induced cardiotoxicity: Review of the literature. *Cardiol J*. 2012;19(5):453-58
- Juricic S, Dobric M, Stojkovic S, et al. Coronary artery vasospasm: Cellular and molecular insights. *Cells*. 2026;15(13):1145
- Zalaquett Z, Shukla N, Hajj J, et al. Cardiovascular toxicity of fluoropyrimidines: What we know. *Mayo Clin Proc*. 2026;101(1):136-55

Conclusions

This case demonstrates that 5-fluorouracil-induced coronary vasospasm is a rare but potentially life-threatening cause of acute cardiomyopathy, capable of mimicking acute coronary syndrome in patients with angiographically normal coronary arteries, even during the initial cycle of therapy. It emphasizes the need for a strong index of suspicion for fluoropyrimidine cardiotoxicity in any oncology patient presenting with chest pain or electrocardiographic changes during or after infusion. Rapid recognition, immediate cessation of the offending agent, and initiation of vasodilator therapy constitute essential components of management. The use of a multidisciplinary cardio-oncology approach is essential to balance the oncologic need for continued fluoropyrimidine therapy against the cardiovascular risk of rechallenge.

Department and Institution Where Work Was Done

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Patient Consent

Informed consent was obtained from the patient for publication of this case report and any accompanying images.

AI Usage

During the preparation of this manuscript, the authors used an artificial intelligence-based language model (ChatGPT, OpenAI) solely for assistance with English-language editing, grammar, clarity, and manuscript organization. The AI tool was not used to generate original clinical content, interpret clinical data, or draw scientific conclusions. All clinical information, interpretations, references, and final manuscript content were reviewed and approved by the authors, who take full responsibility for the accuracy and integrity of the manuscript.

Declaration of Figures' Authenticity

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7. Moghadamnia A, Karim B, Ebrahimi P, et al. 5-Fluorouracil (5-FU)-induced organ toxicities: Mechanisms, management, and prevention strategies. *Toxicol Mech Methods*. 2026;36(1):1-28
8. Zafar A, Drobni ZD, Mosarla R, et al. The incidence, risk factors, and outcomes with 5-fluorouracil-associated coronary vasospasm. *JACC CardioOncol*. 2021;3(1):101-9
9. Faheem B, Kania B, Ashkar H, et al. 5-fluorouracil-related cardiotoxicity with coronary vasospasms. *J Community Hosp Intern Med Perspect*. 2022;12(5):71-74
10. Zafar A, Drobni ZD, Lei M, et al. The efficacy and safety of cardio-protective therapy in patients with 5-FU (Fluorouracil)-associated coronary vasospasm. *PLoS One*. 2022;17(4):e0265767
11. Rana R, Wallace RL, Waksman R, et al. 5-fluorouracil-induced microvascular vasospasm diagnosed by coronary functional testing. *JACC Case Rep*. 2025;30(27):105137
12. Padegimas A, Carver JR. How to diagnose and manage patients with fluoropyrimidine-induced chest pain: A single center approach. *JACC CardioOncol*. 2020;2(4):650-54
13. Raber I, Frazer MB, Zerillo JA, Asnani A. Uridine triacetate for severe fluoropyrimidine cardiotoxicity in a patient with thymidylate synthase gene variants. *JACC CardioOncol*. 2020;2(2):329-32
14. Garbis K, Rafiee MJ, Luu J. 5-fluorouracil-induced coronary vasospasm: A cardiovascular magnetic resonance imaging case report. *Glob Cardiol Sci Pract*. 2023;2023(3):e202316
15. Dimitrova IN. A Case of 5-fluorouracil-induced coronary artery vasospasm in a patient with salivary gland cancer. *Cureus*. 2020;12(10):e10887
16. Y-Hassan S. Coronary microvascular dysfunction in Takotsubo syndrome: Cause or consequence. *Am J Cardiovasc Dis*. 2021;11(2):184-93
17. Caglioni S, Mele D, Milzi A, et al. Impact of coronary microvascular dysfunction in takotsubo syndrome: cause, consequence or both? *Rev Cardiovasc Med*. 2024;25(5):163