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Capecitabine induced coronary vasospasm

Nitish Kumar Sharma, Parth Shah, Sarju Ganatra, Ajay Sharma

ABSTRACT

Introduction: Capecitabine is used for malignancies of the breast, stomach, pancreas and hepatobiliary system. Capecitabine-induced cardiotoxicity has been well described. However, there are few studies showing capecitabine induced coronary vasospastic angina. Here, we describe a case of capecitabine-induced coronary vasospasm. Case Report: A 54-year-old female with a history of metastatic breast cancer on recently started Capecitabine presented with intermittent chest discomfort on exertion. She was ruled out for the acute coronary syndrome. During the hospital stay, the patient had two further episodes of typical chest pain. She then underwent an exercise stress test and was noted to have ST-segment elevation in the inferolateral leads. Given the positive stress test, a coronary angiography was done, that showed no significant obstructive coronary artery disease. Therefore, a diagnosis of Capecitabine induced coronary spasm was made as a diagnosis of exclusion. Capecitabine was stopped and her chest discomfort resolved. The patient was seen as a follow up two months after this episode and she has been chest pain-free after the change in her chemotherapy. Conclusion: Our patient was diagnosed with coronary artery vasospasm secondary to capecitabine and furthermore, discontinuation of capecitabine resolved her symptoms. Recognition of the complication i.e coronary artery vasospasm secondary to capecitabine by the physicians and patients can prevent further adverse events. Also, discontinuation of the drug can further avoid risk for cardiotoxicity.

Keywords: Capecitabine, Chest pain, Coronary angiography, ST-segment elevation, Vasospastic angina

Nitish Kumar Sharma[1], Parth Shah[2], Sarju Ganatra[2], Ajay Sharma[2]

Affiliations: [1]St Vincent Hospital, Worcester, USA; [2]Lahey Hospital and Medical Center, Burlington, MA, USA.

Corresponding Author: Nitish Kumar Sharma, Saint Vincent Hospital, Department of Medicine, 123, Summer Street, Worcester, MA, 01608, USA; Email: nitish.sharma@stvincenthospital.com

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INTRODUCTION

Capecitabine is an oral fluoropyrimidine antimetabolite, which is converted by thymidine phosphorylase to 5-fluorouracil (5-FU). Although it is simply considered an oral version of 5-FU, designed to mimic 5-FU continuous infusion. Capecitabine has the important advantage of being able to concentrate in the targeted tumor [1], resulting in favorable efficacy and toxicity profiles. Moreover, Capecitabine is more convenient for patients, most of whom prefer oral to intravenous treatment, especially in a palliative setting and all these properties justify its increased use [2]. Capecitabine-induced cardiotoxicity is thought to occur through the action of 5-FU on the endothelium resulting in the production of endothelin-1 and subsequent coronary vasospasm. The cardiotoxicity of fluoropyrimidines includes vasospasm, hypertension, ventricular arrhythmias, cardiogenic shock, and even cardiac arrest. The mean reported time interval

between 5-FU administration and the onset of cardiac symptoms is three days (range two to five days) [3, 4]. Symptoms are usually relieved within 48 hours after drug discontinuation, but they usually recur when medication is restarted [1].

CASE REPORT

A 54-year-old female with background medical history of metastatic breast cancer status post(s/p) bilateral mastectomy, s/p chemoradiation with relapse presented with intermittent chest discomfort on exertion. She was started on Capecitabine (1250 mg/m^2) four days prior to admission. She has initially ruled out for an acute coronary syndrome with negative serial troponins and her resting echocardiogram was normal with no wall motion abnormalities and no valvular pathologies. Her baseline electrocardiogram (ECG) did not have any ischemic ST changes (Figure 1). In the hospital, the patient had two further episodes of typical chest pain but her troponin continued to stay negative with a normal EKG. She then underwent an exercise stress test on account of her typical chest pain and after 6 minutes on the treadmill, developed chest discomfort and was noted to have ST elevation in the inferolateral leads consisting of leads II, III, aVF, V5 and V6 (Figure 2). Given the positive stress and a history of radiation to the chest wall, a coronary angiography was considered to evaluate for coronary involvement. Coronary angiography showed no significant obstructive coronary artery disease (Figure 3, Figure 4). The patient did not note any other history of significant medications or drugs or a history of unstable angina in the past. Troponin was checked which was <0.01 ng/dL, creatinine 1.2 mg/dL. Therefore, a diagnosis of Capecitabine induced coronary spasm was made as a diagnosis of exclusion. Capecitabine was stopped and her chest discomfort resolved. After stopping the medication, no testing was repeated as coronary angiogram did not show any obstructive coronary artery disease and her symptoms resolved. The patient was seen in the cardiology clinic as a follow up two months after this episode. Her chemotherapy had been changed since and she had no further episodes of chest pain.

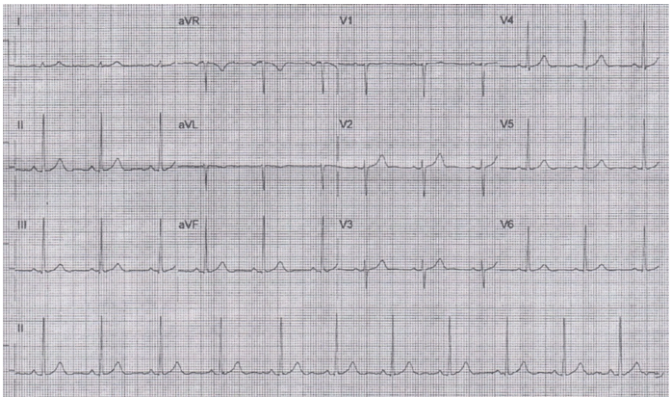

Figure 1: Electrocardiogram at presentation: Normal electrocardiogram.

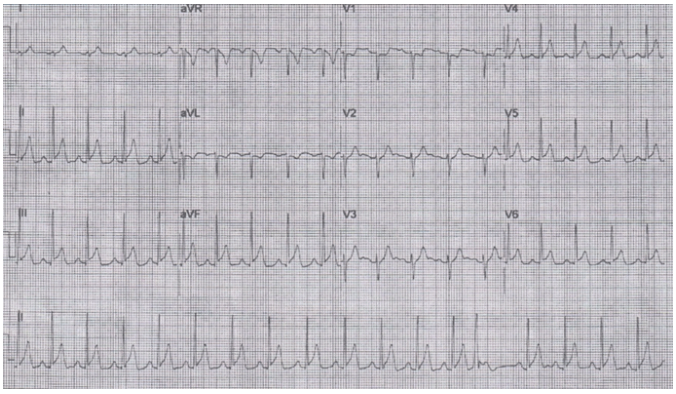

Figure 2: Electrocardiogram after 6 min of treadmill test: ST elevation in the inferolateral leads consisting of leads II, III, aVF, V5 and V6.

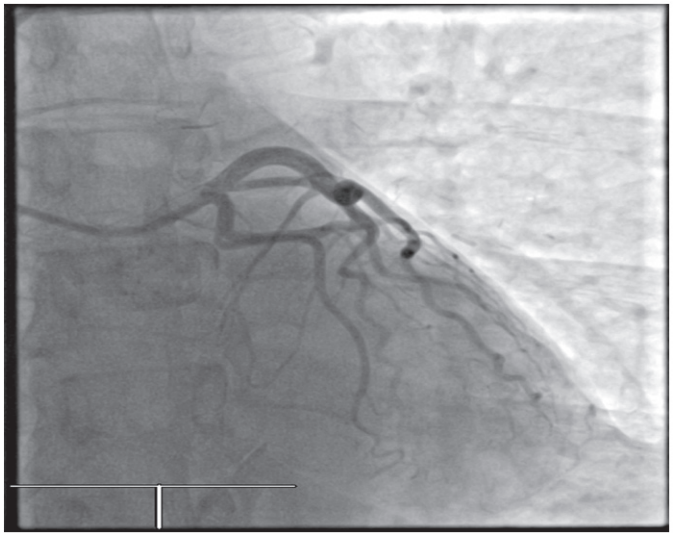

Figure 3: Coronary Angiogram: Normal coronary artery.

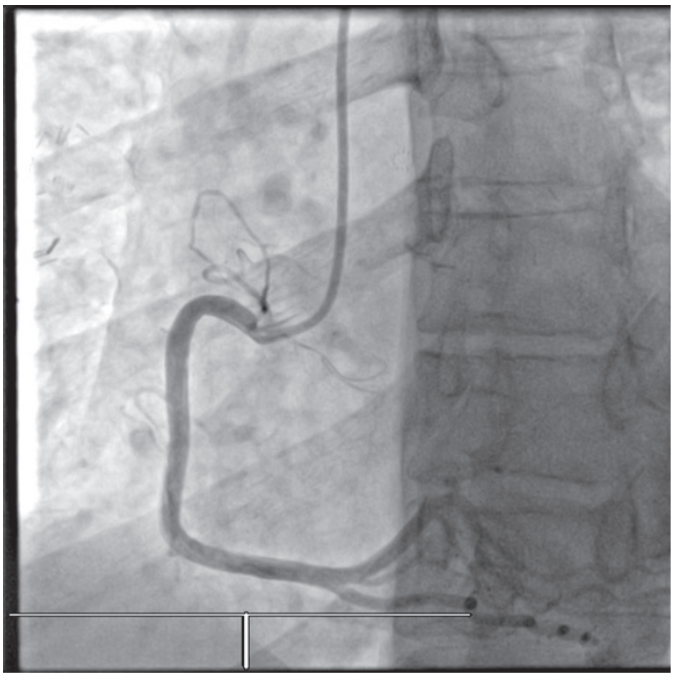

Figure 4: Coronary Angiogram: Normal coronary artery.

DISCUSSION

Capecitabine is used for malignancies of the breast, stomach, pancreas and hepatobiliary system. Capecitabine-induced cardiotoxicity has been well described. The most frequent ECG abnormalities associated with capecitabine are acute ST-segment changes and T wave inversion, mostly resolved from within a few hours to up to three days after withdrawal of the drug. Initiation of capecitabine again at the reduced dose has been studied in the retrospective study of 668 patients [5] and a prospective study of 664 patients [6] reported benefit from dose reduction and initiating antianginal drugs at retreatment in 9 of 12 patients and 12 of 15 patients, respectively with strict cardiac monitoring. Moreover, a retrospective study done by Jensen SA et al, symptoms were abolished by nitroglycerine [5]. Prophylactic use of calcium channel blockers failed to demonstrate any effect on the occurrence of cardiotoxicity [7]. Larger studies regarding capecitabine dose reduction and use of antianginal therapy are warranted.

Prior history of ischemic heart disease is the strongest predisposing factor for capecitabine induced cardiotoxicity [8]. A number of studies demonstrated the importance of preexisting cardiac disorders factor for capecitabine induced cardiotoxicity. Some retrospective studies [5] and a prospective cohort study found that patients with the preexisting cardiovascular disease have a significantly increased risk for cardiotoxicity (risk ratio = 6.83) compared to those without baseline cardiac disease [9].

Fluoropyrimidine-induced cardiovascular side effects are expected to increase worldwide, because of the large use of these drugs in patients with breast or gastrointestinal cancers in the near future [10]. The symptoms of toxicity vary from asymptomatic electrocardiographic changes to life-threatening events. Apart from the past history of ischemic cardiac disorders, no other risk factors have been identified.

CONCLUSION

Fluoropyrimidine rechallenge may be considered after a first cardiac episode, but it should be proposed with great caution. Education regarding the side effects of cardiovascular impairment should be informed to the patients and caregivers about the side effects in order to assess the risks and benefits of the medication.

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Author Contributions

Nitish Kumar Sharma – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Parth Shah – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Sarju Ganatra – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Ajay Sharma – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement
Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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