Capecitabine-Induced Takotsubo Cardiomyopathy: A Case Report

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ABSTRACT

Introduction: The medication 5-fluorouracil is known to cause cardiotoxic effects (with an incidence ranging from 5% to 18%), such as rhythm abnormalities and cardiomyopathies, including takotsubo cardiomyopathy. Capecitabine, an oral prodrug of 5-fluorouracil, has rarely been reported to cause cardiotoxic effects compared with its parent drug.

Case Presentation: An 80-year-old woman presented to the hospital with chest pain after recent initiation of capecitabine use for anal cancer. Results of cardiac catheterization revealed moderate nonobstructive coronary disease. Overall, the findings were highly consistent with a clinical diagnosis of takotsubo cardiomyopathy.

Discussion: With the current increasing use of capecitabine, recognizing this agent as a potential risk factor for cardiac-related events is important.

INTRODUCTION

Capecitabine is an oral prodrug of 5-fluorouracil that has been used in different types of cancers, especially colorectal cancers, because of the convenience of administration and comparable efficacy with 5-fluorouracil. Capecitabine metabolizes to 5-fluorouracil at the tumor site, resulting in fewer cardiotoxic effects than are associated with 5-fluorouracil. Common cardiotoxic effects of 5-fluorouracil reported in the literature include angina, rarely rhythm abnormalities, myopericarditis, and well-documented takotsubo cardiomyopathy. However, capecitabine-induced cardiotoxicity is presumed to be more infrequent and less documented. This condition often presents a diagnostic and therapeutic dilemma, mostly because oral capecitabine is preferred over 5-fluorouracil in elderly patients, especially those with colorectal cancers, because 5-fluorouracil causes significantly more toxic effects and is an infusional chemotherapy, whereas capecitabine is in pill form, which is convenient. We present the case of a woman undergoing oral capecitabine therapy who presented with chest pain and dynamic electrocardiographic changes and was found to have takotsubo cardiomyopathy.

CASE PRESENTATION

An 80-year-old white woman of German descent with a medical history of long-standing anxiety who had been taking benzodiazepines long-term and had hypertension and hyperlipidemia presented to the hospital with chest pain. She experienced chest pain 4 hours before admission (midsternal, 8/10 in severity), which she described as a tightness in her chest associated with shortness of breath but without nausea, diaphoresis, or palpitations. She initially thought her pain was related to her anxiety; however, the pain did not subside with her regular medications, which prompted her to seek medical attention. The results of a review of systems were otherwise negative.

The patient had been diagnosed with anal cancer approximately 2 months previously, for which she was prescribed capecitabine 4 days before admission. She denied any other recent stressors. Her current medications also included clonazepam (0.25 mg twice a day), atorvastatin (10 mg once daily), and meclizine as needed. She is a nonsmoker and denied alcohol and recreational drug use. She was independent and lived with one of her children. Her family history was significant for a father with coronary artery disease after the age of 50 years.

On examination, her vital signs were afebrile. She was 160 cm in height and weighed 47.6 kg. Significant cardiopulmonary examination included no jugular venous distension, normal heart sounds without murmurs, and clear lungs to auscultation.

She was noted to have hyperacute T waves in the anterior precordial leads on an electrocardiogram taken at the time of chest pain (Figure 1). There was no prior electrocardiogram for comparison. She was admitted to the hospital for further evaluation and was started on aspirin and clopidogrel.

On the next day, the patient was re-examined and her pain was gone. She had no new onset of symptoms. Laboratory tests revealed a normal cardiac troponin level. A repeat electrocardiogram was obtained and was normal. A cardiac catheterization was performed and showed normal coronary arteries. The patient was discharged home with no new medical issues.

Figure 1. Electrocardiogram performed on presentation showing hyperacute T waves.

Figure 2. Coronary angiogram revealing 40% to 45% coronary artery disease in the left anterior descending and left circumflex territories.

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The pathogenesis of capecitabine-induced cardiotoxicity is largely unknown, but the proposed mechanisms include effects on coronary vasculature and direct toxic effect on myocytes. Coronary continuous intravenous infusion, and estimates of its incidence vary from 1% to 5% to as much as 18%.

Although a prodrug of 5-fluorouracil, capecitabine is less cardiotoxic than 5-fluorouracil, some scattered incidents have been documented in the literature, including angina-like chest pain, myocardial infarction, cardiogenic shock, and sudden cardiac death. The preferential delivery of 5-fluorouracil to tumor tissue is thought to result in a lower risk of cardiovascular adverse events with the use of capecitabine compared with other fluoropyrimidines.

Interestingly, only 1 of 6 reported cases of possible capecitabine-induced cardiomyopathy described the classic apical balloononing characteristic of cardiomyopathy. Our case is the second report of apical balloononing with capecitabine use consistent with cardiomyopathy.

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Table 1. Timeline of the case

<table>
<thead>
<tr>
<th>Date</th>
<th>Visit information</th>
<th>Diagnostic testing</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>August 15, 2017</td>
<td>An 80-year-old white woman with hypertension, anxiety with long-term benzodiazepine use, and recently diagnosed anal cancer presented to the hospital with unrelenting chest pain. She was prescribed oral capecitabine 4 days before admission.</td>
<td>Dynamic changes with hyperacute T waves were noted on electrocardiogram.</td>
<td>Cardiac catheterization revealed moderate coronary artery disease without acute culprit lesion, and a ventriculogram revealed apical balloononing consistent with takotsubo cardiomyopathy.</td>
</tr>
<tr>
<td>August 17, 2017</td>
<td>Postcardiac catheterization follow-up.</td>
<td>Echocardiogram revealed ejection fraction of 55% to 60% with akinetic apex.</td>
<td>Discharged home with aspirin, β-blocker, and statin prescriptions and advised to stop oral chemotherapy.</td>
</tr>
<tr>
<td>March 28, 2018</td>
<td>Telephone call to check on patient, who stated she was doing well and not receiving oral chemotherapy anymore.</td>
<td>Subsequent echocardiogram revealed normal ejection fraction results with no wall motion abnormality.</td>
<td>Continued use of aspirin with no indication for β-blocker use.</td>
</tr>
</tbody>
</table>
vasospasm has also been suggested on the basis of the characteristic electrocardiographic and clinical features that are similar to those of reversible ischemic heart disease.

We could not identify other predisposing factors, such as previous chest radiotherapy and concurrent treatment with other cardiotoxic agents, in our patient. Although she has a long-standing history of anxiety while taking benzodiazepines long-term, she had no inciting events that potentially triggered this event, and we assume that it was merely a confounder in this case. Hence, she was presumed to have chemotherapy-induced takotsubo cardiomyopathy in the setting of recent initiation of chemotherapy. Reviewing the literature, cardiotoxic effects are completely reversible with cessation of capecitabine therapy. As general internists who encounter symptoms of chest pain routinely in clinical practice, it is important to consider medication adverse effects as a source for this pain. Takotsubo cardiomyopathy remains a diagnosis of exclusion in patients who present with ischemic changes on electrocardiography. Also noteworthy is that takotsubo cardiomyopathy is usually reversible with time.

CONCLUSION

In the near future, the incidence of fluoropyrimidine-induced cardiovascular adverse effects is expected to increase worldwide because of the increasing use of these drugs in patients with breast or gastrointestinal cancers, especially common in our aging population. Although the incidence of cardiotoxic effects caused by capecitabine is estimated at 5%, which is lower than the parent drug, we suspect these effects may be underreported. Further studies and clinical experience are needed to determine which patients are at higher risk for cardiotoxic effects. For now, potential cardiotoxic effects and other risk factors vs benefits should be weighed carefully before prescribing capecitabine to any patient. In addition, these adverse effects need to be discussed with patients before use.

Disclosure Statement
The author(s) have no conflicts of interest to disclose.

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References