LETTER TO THE EDITOR

ECG Changes in Capecitabine-Induced Takotsubo Cardiomyopathy

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Bhardwaj and colleagues described an interesting case study of Takotsubo cardiomyopathy (TC) in a patient with anal cancer who received chemotherapy with capecitabine, an oral prodrug of 5-fluorouracil (5-FU).1 Cardiac toxicity is a well reported side effect of fluoropyrimidine chemotherapies (5-FU and capecitabine); however, TC is a rare and less commonly known side effect. TC has been previously reported with the use of 5-FU in some case studies, although other cardiotoxic and systemic side effects of fluoropyrimidine therapies have been well described in large studies.

TC is indeed a rare adverse event associated with use of 5-FU, whereas one of the most common forms of cardiotoxicity associated with 5-FU is ischemia, mediated by coronary artery vasospasm (widely reported). Other less common forms of adverse cardiac effects are vascular endothelial damage related to thrombogenicity and direct myocardial toxicity.2,3 In the presented case by Bhardwaj et al., the first electrocardiogram (ECG) on presentation interestingly shows peaked and symmetrical large amplitude T-waves in the setting of chest pain. Although TC may be considered a plausible differential diagnosis in the presented case given the apical wall motion abnormality, the possibility of coronary vasospasm associated with transient myocardial stunning should also be strongly entertained as a primary or co-existing differential diagnosis.3-5 Our reasoning for this is that large amplitude symmetrical T-waves are usually not the typical ECG changes encountered in TC. Typical ECG changes of TC evolve in 3 to 4 different stages that include: ST-elevations in stage 1, followed by ST-normalization often associated or preceded by deep precordial T-wave inversions in stages 2 and 3, and finally, resolution of repolarization abnormalities in stage 4 (Figure 1).6-9 These changes have been previously well described in prior reports including the data from large studies comprising TC patients.6,8 On the contrary, peaked and symmetrical large amplitude T-waves are most commonly observed in coronary vasospasm (>50% patients) and are usually the first finding in vasospasm before the ST elevations that might develop if vasospasm remains persistent.10

The two ECGs presented in the case by the authors demonstrated large amplitude symmetric T-waves in the first ECG followed by complete normalization of these changes on the second ECG, which may support primary (or co-existing) coronary vasospasm, whereas the apical motion abnormality may be attributed to transient myocardial stunning associated with the coronary vasospasm.10 The patient reportedly had negative cardiac biomarkers that are somewhat uncommon for patients of TC. Most often, patients with TC usually have a mild elevation of cardiac troponin levels with the incidence of negative cardiac biomarkers being a rarity (usually <2% to 5%).5

A few other important clinical considerations would be useful for clinicians treating patients with 5-FU use. An assessment to clinical response of patient’s symptoms with use of nitroglycerine may also sometimes help tease out underlying vasospasm.2,3 Although it may not be relevant to the presented case, patients receiving 5-FU may also experience tumor lysis effects that may be associated with electrolyte derangements, such as hyperkalemia, that can thus result in large amplitude T-wave amplitude. Thus, these additional clinical markers may serve as a valuable tool for clinicians in teasing out a clinical diagnosis.

In summary, we want to congratulate the authors for presenting such an interesting case that highlights important cardiotoxic effects of chemotherapeutic agent, 5-FU. Clinicians should remain vigilant about the potential cardiotoxic effects of chemotherapeutic agents such as 5-FU and should entertain all the important differential diagnosis as noted above to deliver the best guideline-directed therapy for the patients.

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Figure 1. Demonstrates ECG changes in evolution in a patient with Takotsubo cardiomyopathy. (A) Demonstrates precordial ST elevations on initial presentation. (B) Demonstrates ST normalization with early appearance of biphasic T waves in V3 and V4. (C) Demonstrates stage 3 changes demonstrating diffuse T-wave inversions. Eventually in stage 4, these ST-changes demonstrate normalization or somewhat delayed persistence of these repolarization abnormalities. Less commonly, transient Q-waves may also be seen (not seen in this patient).
In Response

The authors of the originating article were contacted but did not wish to respond.