

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 succeeded 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. ♦

Disclosure Statement

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

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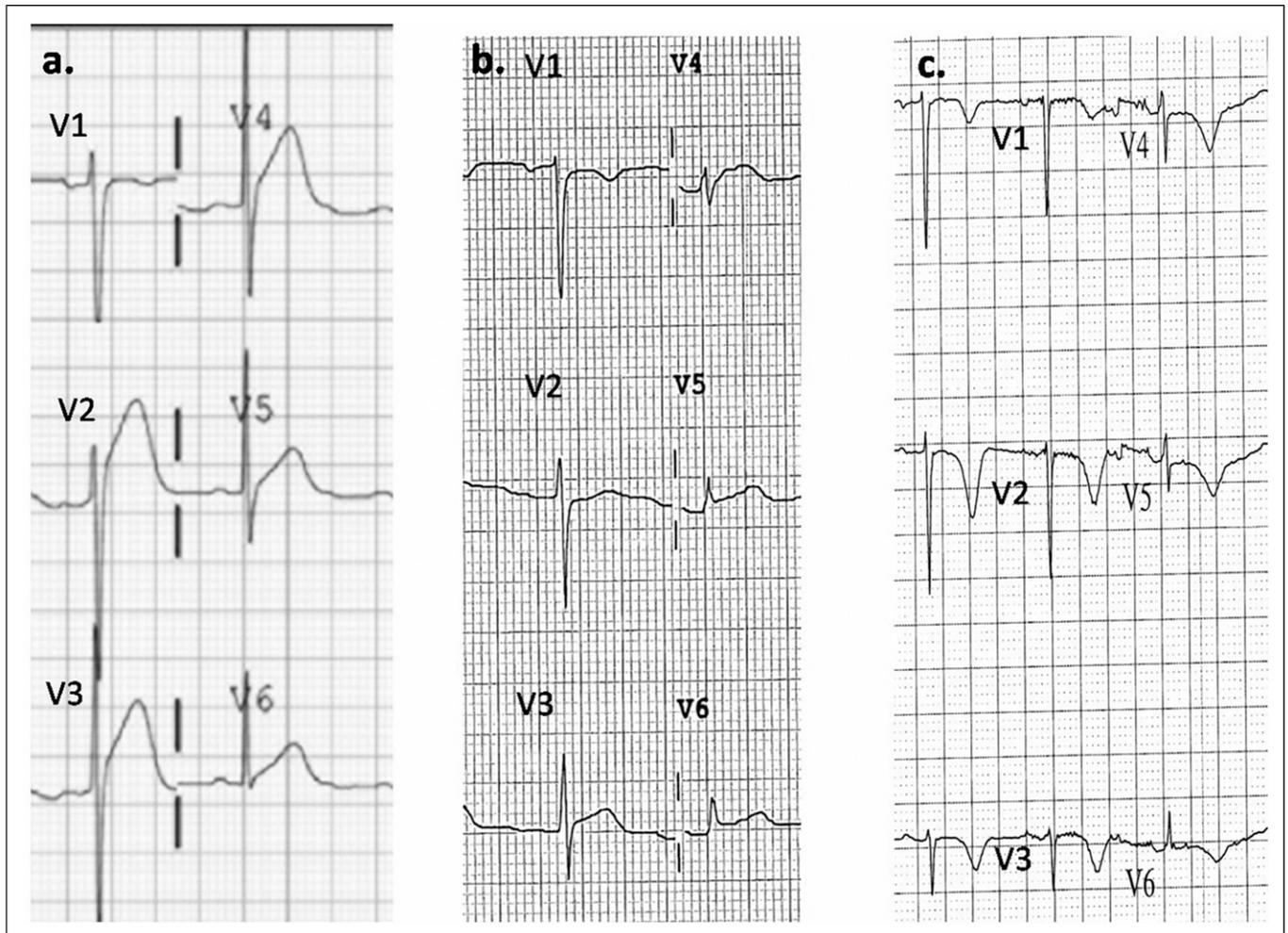


Figure 1. Demonstrates ECG changes in evolution in a patient with Takotsubo cardiomyopathy. (A) Demonstrates precordial ST elevations on initial presentation. (B) Demonstrates ST normalization with early appearance of biphasic T waves in V3 and V4. (C) Demonstrates stage 3 changes demonstrating diffuse 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).

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In Response

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