5-FU Re-challenge after Cardiotoxicity

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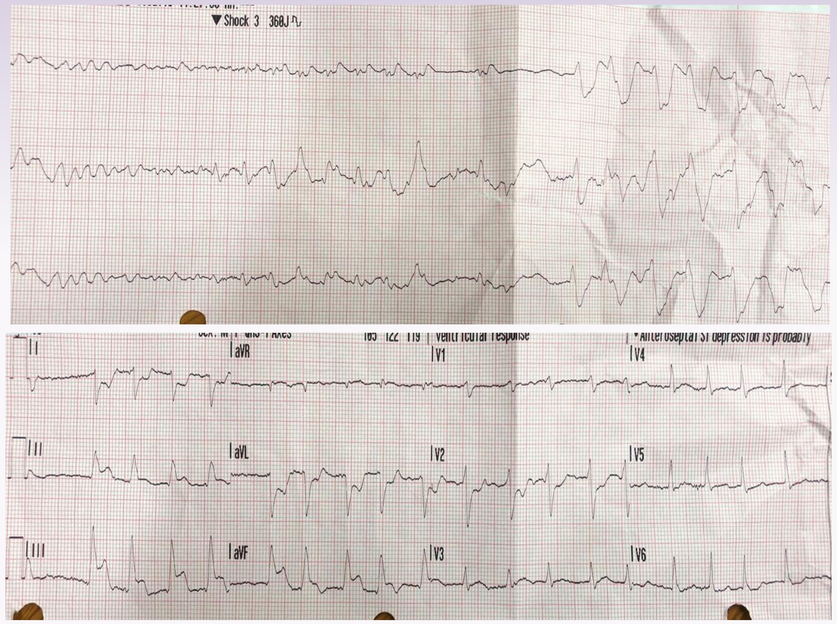
INTRODUCTION

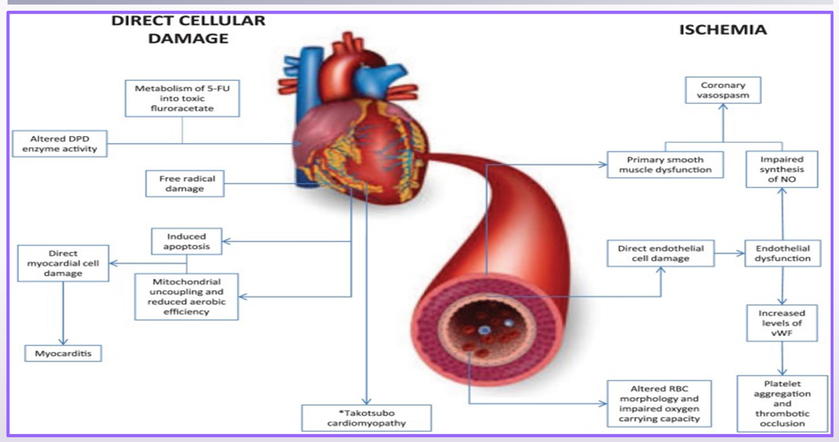
5-Fluorouracil (5-FU) re-challenge following cardiotoxicity is a topic without consensus. Existing literature reveals both cases of recurrent cardiac complications as well as cases of successful re-challenge. Whether a patient who experienced cardiotoxicity from 5-FU can safely receive this drug again is a commonly encountered clinical dilemma that requires further investigation. Here, we report a difficult case involving 5-FU re-challenge.

CASE DESCRIPTION

66-year-old Caucasian man with a history of atrial fibrillation and venous thromboembolism on Xarelto, hypertension, peripheral vascular disease, and heart failure with preserved ejection fraction was diagnosed with stage III colorectal adenocarcinoma. He was treated with FOLFOX regimen in the adjuvant setting. During infusion, he sustained sudden collapse secondary to VT & VF which was successfully terminated by cardioversion. ECG immediately after the cardiac arrest revealed ST-segment elevation in the inferior leads with lateral ST depressions. Emergent cardiac catheterization did not reveal evidence of obstructive atherosclerotic coronary artery disease. Echocardiogram demonstrated preserved EF with no significant wall motion abnormalities or valvular heart disease. Following this event, the decision was made to hold 5-FU. At 3-month follow-up, CT scan revealed extensive metastatic disease. After lengthy multidisciplinary discussion, decision was made to proceed with palliative chemotherapy using 5-FU/leucovorin to slow disease progression. He was premedicated with isosorbide mononitrate, metoprolol succinate, and diltiazem. He tolerated chemotherapy well without complication in the inpatient setting while on continuous telemetry.



EKGs above showing VF while 5-FU infusion and ST elevation in inferior leads and with lateral ST depressions after successful cardioversion.



Possible mechanisms of 5-FU induced cardiotoxicity.

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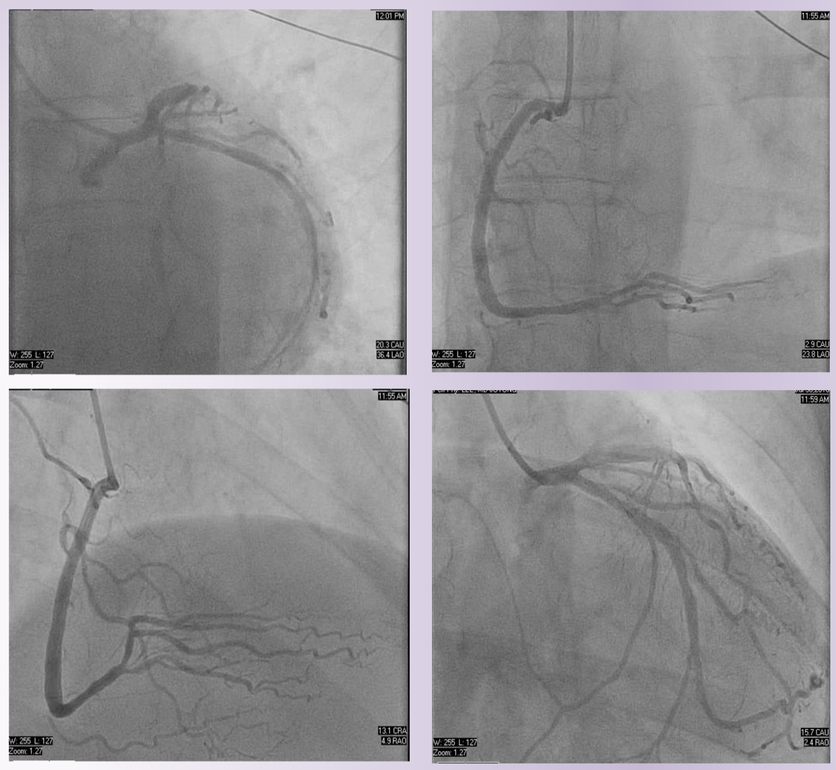

cardiac catheterization did not reveal evidence of obstructive atherosclerotic coronary artery disease.

DISCUSSION

We report a patient who developed cardiac arrest presumably due to fluorouracil-induced coronary vasospasm. When further doses of 5-FU are required, the literature is mixed regarding the safety of 5-FU re-administration. In all cases, clinicians should proceed cautiously and only after extensive multidisciplinary discussions on the risks/benefits of re-challenge. If the drug is being re-administered, adequate pre-treatment with “anti-spasm” therapy, which includes calcium channel blockers (nifedipine and diltiazem) and long-acting nitrates (isosorbide dinitrate), is important in conjunction with telemetry monitoring. Additional strategies for safe re-challenge include dose reduction and switching from infusion to bolus regimen.

Disclosures: The presenting author and lead investigator have no conflict of interest.