Case Report

Gemcitabine-induced supraventricular tachycardia: A rare manifestation

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ABSTRACT

Gemcitabine is a cytotoxic drug with superior toxicity profile and widely used in the management of various solid malignancies. The common side effects associated with gemcitabine are myelosuppression, diarrhea, and flu-like symptoms. Cardiac side effects due to gemcitabine are very rare. We present a case of an elderly female aged 69 years, diagnosed to have metastatic carcinoma gallbladder, and without any cardiac risk factors, who developed supraventricular tachycardia 3 days after gemcitabine infusion. We emphasize the need for careful and routine cardiac monitoring in an elderly patient who develops symptoms of tachyarrhythmia when on gemcitabine therapy.

Key words: Carcinoma gallbladder, cardiac monitoring, gemcitabine, supraventricular tachycardia

INTRODUCTION

Gemcitabine (2′,2′-difluorodeoxycytidine) is widely used in the management of solid tumors. Gemcitabine appears to be relatively safe, but can be associated with some rare serious toxicity. The common side effects associated with gemcitabine are myelosuppression, diarrhea, nausea, vomiting and flu-like symptoms. Cardiac side effects such as ventricular tachyarrhythmias after gemcitabine infusion are relatively uncommon.[1] It is, however, very important to recognize the serious toxicities associated with these medications, and appropriate measures should be taken to avoid and manage such complications. In this case report, we discuss a case of gemcitabine-induced supraventricular tachycardia (SVT) in an elderly female, diagnosed with having metastatic carcinoma of the gallbladder.

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CASE REPORT

A 69-year-old female patient presented to the outpatient department of a Tertiary Care Oncology Hospital with complaints of abdominal pain, fever, nausea and vomiting, persistent over a period of 3 months. On examination, a right hypochondriac mass was detected. Radiological imaging suggested a mass lesion in the gallbladder fundus, extending into segment IVb/V of liver, with associated liver metastasis and enlarged porta hepatis, and sub diaphragmatic lymph nodes. Ultrasonographic-guided fine needle aspiration cytology was suggestive of malignant adenocarcinoma of the gallbladder. The patient was diagnosed to have a metastatic carcinoma of the gallbladder. The prechemotherapy cardiac evaluation of the patient showed a normal electrocardiography (ECG) and a normal echocardiogram (ECHO) with an ejection fraction of 60%. The patient was initiated on injection gemcitabine 1400 mg on D1 and D8 (over 30 min infusion) and injection cisplatin on D1 (over 60 min infusion), repeated over every 3 weeks

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for a total of six cycles. Three days after the last dose of D8 gemcitabine, the patient presented to the emergency with complaints of palpitations, difficulty in breathing, and tiredness. On evaluation, the patient had a pulse rate of 110/min and blood pressure was 130/80 mmHg. ECG showed tachycardia, prolonged PR interval with ST depression in V5-6 leads [Figure 1]. Two-dimensional (2D) ECHO was normal, with an ejection fraction of 58%. Serum electrolytes, thyroid function tests, and renal function tests were normal. Injection diltiazem 15 mg intravenous stat was given and a repeat ECG was done. Repeat ECG showed sinus rhythm with 1st degree heart block [Figure 2]. Patient was discharged on tablet metoprolol 25 mg O.D. No further chemotherapy is being planned for this patient. On review with a repeat positron emission tomography scan, it showed partial response to chemotherapy.

DISCUSSION

Gemcitabine is an analog of deoxycytidine and is a highly lipid soluble molecule, and the intracellular incorporation is mediated by transcellular diffusion. It has a dual mechanism of drug clearance, urinary and hepatic and its product 2′,2′-difluorodeoxyuridine (dFdU) has a half-life of approximately 18–24 h.[2] The toxicities of gemcitabine are dose dependent.[3] Phase I and II trials with gemcitabine have not shown any significant risk of cardiotoxicity, but in literature, several case reports of gemcitabine-induced cardiotoxicities such as acute myocardial infarction, cardiomyopathy, heart failure, and arryhthmias have been recently reported. Atrial fibrillation and SVT are among the arrhythmias reported with gemcitabine use.[4,5] Brady arrhythmias have also been reported.

Various hypothetical mechanisms have been proposed explaining the possible causes of gemcitabine-induced arrhythmias and other cardiac toxicities.

1. Direct myocardial toxicity from the active metabolite of dFdU[5]
2. Inflammatory pathogenic mechanism mediated by cytokine release resulting in myofibroblasts proliferation and collagen deposits was stated as the reason for gemcitabine-induced atrial fibrillation and adult respiratory distress syndrome[6]
3. Influence of various stimuli on sinus node and hyperstimulation of parasympathetic/sympathetic system may lead to abnormal supraventricular and atriventricular conduction
4. Electrolyte imbalances and histamine release
5. Coronary vasospasm.[7]

In this 69-year-old elderly patient, the probable mechanism of the ventricular arrhythmia maybe due to the active metabolite (dFdU)-induced cardiotoxicity. The ECG and 2D ECHO scan done before the onset of chemotherapy was normal and showed no abnormality. Other precipitating causes such as electrolyte disturbances and abnormal thyroid functions were ruled out during the episode of arrhythmia. The patient developed SVT 3 days post chemotherapy. While reviewing the literature, a similar case report was seen where the patient developed SVT 6 days after chemotherapy. There are few other case reports regarding other gemcitabine-induced cardiac abnormalities such as coronary vasospasm,[7] non ST elevation MI,[8,9] cardiomyopathy,[10] atrial fibrillation,[4,11] and even heart failure.[12] Gemcitabine has also been implicated in the development of pericardial effusions in patients who had prior exposure to radiation suggesting radiation recall phenomenon with Gemcitabine.[13]

CONCLUSION

Gemcitabine is a widely used cytotoxic drug and its relatively good safety profile makes it a good option for chemotherapy in elderly patients. Gemcitabine-induced cardiotoxicity is a very rare but serious and deleterious side effect, and further studies are needed to establish the

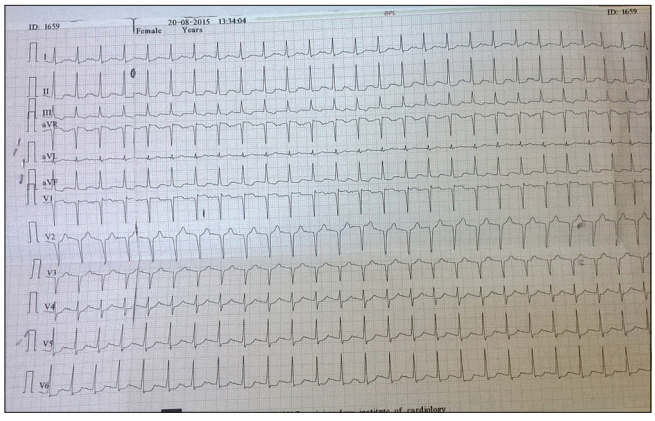

Figure 1: Electrocardiography showing supraventricular tachycardia

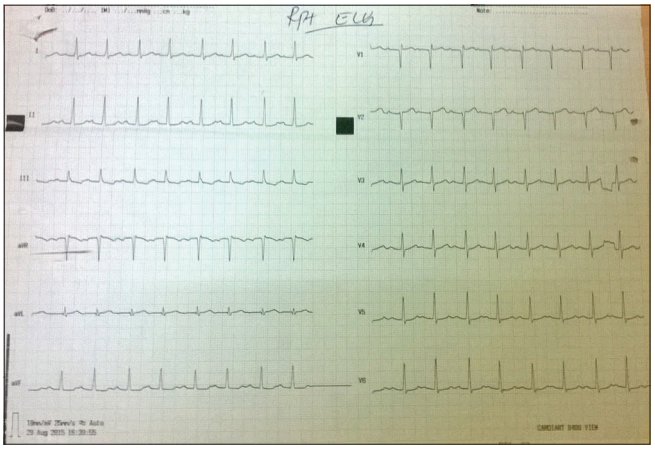

Figure 2: Electrocardiography showing reversion of supraventricular tachycardia with 1st degree heart block

mechanisms of gemcitabine-induced cardiotoxicity and the various predisposing factors causing cardiotoxicity. Careful cardiac monitoring should be done in high-risk cardiac patients. It should also be noted that these tachyarrythmias may occur in patients without any predisposing factors, and early medical advice should be taken if symptoms of tachyarrhythmia develop.

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Conflicts of interest
There are no conflicts of interest.

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