

Bolus fluorouracil induced syncope and pulseless ventricular tachycardia: a case report

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Abstract:

5-fluorouracil is an anti-cancer drug commonly used in oncology practice. Typical side effects are myelosuppression, nausea, vomiting, diarrhea and stomatitis. Cardiotoxicity is the other toxicity. Cardiac side effects are ST segment changes, rhythm abnormalities, supraventricular and ventricular dysrhythmias. Pulseless ventricular tachycardia and ventricular fibrillation related with bolus fluorouracil were not detected in the literature. Here we discussed a 46 year-old male patient that has no known cardiac history. After bolus fluorouracil administration, syncope and pulseless ventricular tachycardia developed in this patient. There are a few explanations about the cardiotoxicity of fluorouracil. One of these is the effect on nitric oxide. It causes a reduction in the levels of endothelial NO and this leads coronary vasospasm. Another explanation is protein kinase C mediated vasospasm. In animal studies toxic myocarditis like lesions were detected with fluorouracil infusions. Finally both myocarditis and vasospasm may lead cardiac problems like sudden cardiac deaths. Bolus 5-fluorouracil is as cardiotoxic as 5-fluorouracil infusion and we must be careful about the arrhythmia after the bolus administration. Hippokratia 2011; 15 (1): 93-95

Key words: fluorouracil, arrhythmia, cardiac

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5-fluorouracil is an anti-cancer drug commonly used in oncology practice. It is used in the treatment of various cancers like breast, gastric, colorectal, head and neck, liver cancers. Typical side effects are myelosuppression, nausea, vomiting, diarrhea and stomatitis¹. Cardiotoxicity is the other toxicity¹. Cardiac side effects are ST segment changes, rhythm abnormalities, supraventricular and ventricular dysrhythmias².

Acute myocardial infarction was reported in the literature³. Pulseless ventricular tachycardia and ventricular fibrillation related with bolus fluorouracil were not detected in the literature. Here we discussed a 46 year-old male patient that has no known cardiac history. After bolus fluorouracil administration, syncope and pulseless ventricular tachycardia developed in this patient.

Case report

A 46-year old male patient underwent subtotal gastrectomy because of the adenocarcinoma. He admitted to our out patient clinic postoperatively. Adjuvant chemoradiotherapy was planned due to the pathology report. His cardiological history was negative and he had no cardiac risk factors. In chemoradiotherapy programme 5-fluorouracil dose was 825 mg/day and folinic acid dose was 30 mg/day. The third day of the first cycle chemotherapy was administered to the patient but after 1 hour severe nausea and abdominal

pain developed. He admitted to the clinic and syncope was developed. Pulse was not detected and ECG showed pulseless ventricular tachycardia and ventricular fibrillation (Figure 1).

Defibrillation was performed and normal sinus rhythm was obtained. Physical examination showed an incision scar belonging to the operation. Electrolyte imbalance and hypoxia were not detected and his blood count was normal. Ejection fraction was evaluated by transthoracic echocardiography and it was 15%. After obtaining written consent, coronary angiography was performed in same day. A few plaques but not total occlusion or vasospasm were detected (Figure 2,3). In following days ventricular tachycardia, pulseless ventricular tachycardia and ventricular

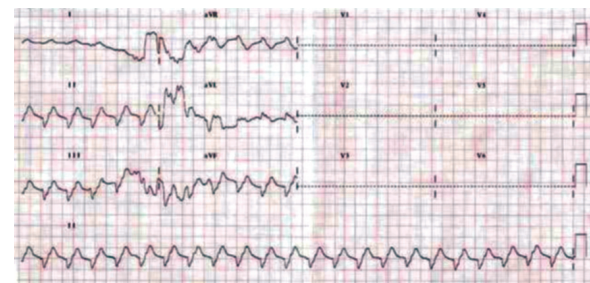


Figure 1: Ventricular tachycardia when syncope was developed.

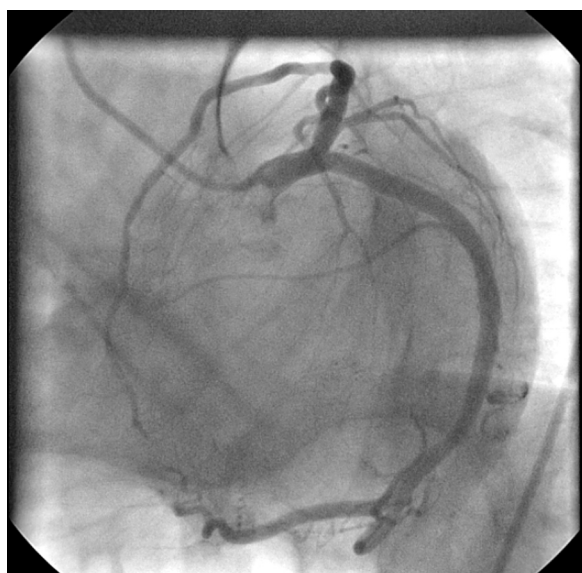


Figure 2: Coronary angiography LAD.

fibrillation attacks were detected and defibrillation was performed 6 times again. Transthoracic echocardiography performed in fifth day of the first event, revealed that ejection fraction was 40%. The medical treatment including carvedilol, amiodarone and trandolapril was composed. One week after the last echocardiography the patient admitted for control. His ECG showed normal sinus rhythm and pulse was 65/ minute (Figure 4). Ejection fraction was 60% and improvement in cardiac functions and diameters were detected. Medical treatment associated with cardiology was prolonged. About this cardiac problems the timing of adjuvant treatment finished so the patient was taken under follow- up for the gastric cancer without any treatment.

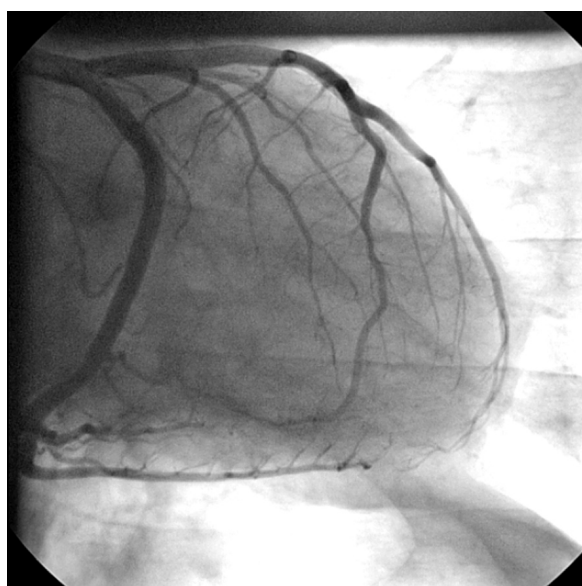


Figure 3: Coronary angiography RAD.

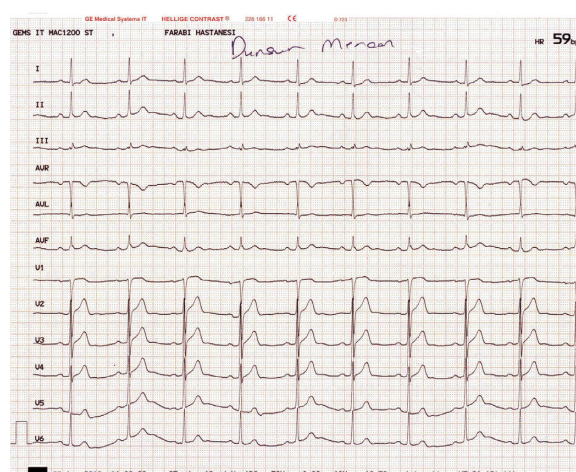


Figure 4: ECG at the time of control.

Discussion

The cardiotoxicity of 5-fluorouracil ranges between 1.2-7.6%¹. Cardiac symptoms are chest pain, ST-T wave changes, arrhythmias, cardiogenic shocks, cardiac failure and acute coronary syndrome. But most common finding is reversible ST-T wave changes⁴.

There are a few explanations about the cardiotoxicity of fluorouracil. One of these is the effect on nitric oxide. It causes a reduction in the levels of endothelial NO and this leads coronary vasospasm. Another explanation is protein kinase C mediated vasospasm¹. In animal studies toxic myocarditis like lesions were detected with fluorouracil infusions³. Finally both myocarditis and vasospasm may lead cardiac problems like sudden cardiac deaths.

Our patient had no cardiac history and pretreatment ECG showed no sinus pathology. In addition syncope, pulseless ventricular tachycardia and ventricular fibrillation were developed just after the bolus chemotherapy. So we can consider that this situation is related with the fluorouracil administration.

Ejection fraction was 15% after the normal sinus rhythm was obtained. In following days ejection fraction developed. In his coronary angiography no occlusion and coronary spasm were detected. So we can think that the cardiac arrhythmia is related with the drug effect especially toxic myocarditis. The patient discharged with the following drugs; carvedilol, amiodarone and trandolapril and at the last administration ejection fraction was 60% and ECG showed normal sinus rhythm. In the literature there are case reports about cardiac side effects related with continuous infusion of fluorouracil but case reports about bolus administration are uncommon^{6,7}. In addition pulseless ventricular tachycardia and ventricular fibrillation were not detected in the literature related with the bolus administration of fluorouracil. So that bolus 5-fluorouracil is as cardiotoxic as 5-fluorouracil infusion and we must be careful about the arrhythmia after the bolus administration.

References

1. Alter P, Herzum M, Soufi M, Schaefer JR, Maisch B. Cardiotoxicity of 5-fluorouracil. *Cardiovasc Hematol Agents Med Chem.* 2006; 4: 1-5.
2. Oztop I, Gencer M, Okan T, Yaren A, Altekin E, Turker S, et al. Evaluation of cardiotoxicity of a combined bolus plus infusional 5-fluorouracil/folinic acid treatment by echocardiography, plasma troponin I level, QT interval and dispersion in patients with gastrointestinal system cancers. *Jpn J Clin Oncol.* 2004; 34: 262-268.
3. Canale ML, Camerini A, Stroppa S, Porta RP, Caravelli P, Mariani M, et al. A case of acute myocardial infarction during 5-fluorouracil infusion. *J Cardiovasc Med (Hagerstown).* 2006; 7: 835-837.
4. Kosmas C, Kallistratos MS, Kopterides P, Syrios J, Skopelitis H, Mylonakis N, et al. Cardiotoxicity of fluoropyrimidines in different schedules of administration: a prospective study. *J Cancer Res Clin Oncol.* 2008; 134: 75-82.
5. Tsibiribi P, Bui-Xuan C, Bui-Xuan B, Lombard-Bohas C, Duperret S, Belkhiria M, et al. Cardiac lesions induced by 5-fluorouracil in the rabbit. *Hum Exp Toxicol.* 2006; 25: 305-309.
6. Tutkun A, Inanli S, Caymaz O, Ayanozlu E, Duman D. Cardiotoxicity of 5-fluorouracil: two case reports. *Auris Nasus Larynx.* 2001; 28: 193-196.
7. Georgieva S, Kinova E, Iordanov V, Gudev A, Tzekova V, Velikova M. *J BUON.* Acute heart failure after treatment with 5-fluorouracil. 2007; 12: 113-116.