

Acute Myocardial Infarction Following 5-Fluorouracil Use

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Abstract

Fluorouracil (5-FU) is the most common chemotherapeutic agent suggested for colorectal cancers. Cardiogenic side effects such as coroner artery vasospasm, ventricular dysrhythmia, and cardiac ischemia are also rarely stated. 48-year-old male patient applied to the emergency service with conditions of chest pain, nausea and vomiting. ECG was performed and found to be normal sinus rhythm. In the control ECG of the patient, there were ST elevations in inferior and anterior derivations. The control troponin value for the patient was found to be 0,073 µg/L (normal range 0,010-0,023 µg/L). When the patient expressed that his chest pain aggravated even more as he was being prepared for coroner angiography, control ECG was reperformed and seen that lateral derivations were added to ST elevations in inferior and anterior derivations. The patient, who has started to chemotherapy two days ago and still receives 5-FU infusion, is thought to have myocardial infarction with ST elevation based on the cardiotoxic impact of 5-FU, and he was taken to coroner angiography. His CAG is reported as LAD: Plaque CX: Plaque RCA: 40% lesion observed at CB alignment. 5-FU is a partner medical agent used to treat head and neck, gastrointestinal system, bladder, and chest malignancies. Despite cardiac toxicity being a rare and serious complication, the life-threatening toxicity is observed in 0,5% of the patients. In the previous reports, it is underlined that the only mechanism contributing to STEMI development after 5-FU infusion is vasospasm. In our case, the patient came to us with myocardial infarction with ST elevation resulting from the emergence of chest pain after the use of 5-FU. Patients should be closely followed when receiving 5-FU treatment. Due to the cardiac side effects that may seriously show a fatal course, patients should be examined in detail before the treatment.

Key words: 5-FU, chest pain, MI

Özet

Fluorourasil (5-FU), kolorektal kanserler için önerilen en yaygın kemoterapötik ajandır. Bu ajana bağlı, koroner arter vazospazmı, ventriküler disritmi ve kardiyak iskemi gibi kardiyojenik yan etkiler nadir olsa da bildirilmiştir. 48 yaşında erkek hasta acil servise göğüs ağrısı, bulantı ve kusma şikayeti ile başvurdu. Çekilen ilk EKG'si normal sinus ritmi olarak değerlendirildi. Kontrol EKG'sinde, inferior ve anterior'da ST segment yükselmeleri mevcuttu. Hasta için çalışılan kontrol troponin değeri 0,073 µg/L (normal aralık 0,010-0,023 µg/L) olarak geldi. Hasta, koroner anjiyografi için hazırlanırken göğüs ağrısının daha da şiddetlendiğini ifade etti. Bunun üzerine tekrarlanan EKG'de, anterior ve inferior derivasyonlara, lateral derivasyonda, ST segment yükselmesinin eklendiğini görüldü. İki gün önce kemoterapiye başlayan ve hala 5-FU infüzyonu alan hastanın, 5-FU'nun kardiyotoksik etkisine bağlı ST yükselmeli miyokard enfarktüsü geçirdiği düşünüldü. koroner anjiyografisi alınan hastada. Anjiyografi sonucu LAD: Plak CX: Plak RCA: CB hizasında gözlenen% 40 lezyon olduğu bildirildi. 5-FU,baş, boyun, gastrointestinal sistem, mesane ve göğüs malignitelerini tedavi etmek için kullanılan ortak bir tıbbi ajandır. Kardiyak toksisite nadir ve ciddi bir komplikasyondur ve yaşamı tehdit eden toksisite hastaların% 0,5'inde görülür. Önceki çalışmalarda, 5-FU infüzyonundan sonra STEMI gelişimine katkıda bulunan tek mekanizmanın vazospazm olduğu vurgulanmıştır. 5-FU tedavisi alırken hastalar yakından takip edilmelidir. Ciddi ölümcül seyir gösterebilecek kalp yan etkileri nedeniyle, hastalar tedaviden önce ayrıntılı olarak incelenmelidir.

Anahtar kelimeler: 5-FU, göğüs ağrısı, MI

Introduction

Fluorouracil (5-FU) is the most common chemotherapeutic agent suggested for colorectal cancers^{1, 2}. Its frequently observed side effects include nausea, vomiting, and diarrhea. 5-FU, which is a medicine from antimetabolite group of chemotherapy medicines, can be given as 5-10 min. or 20-60 min. intravenous infusions, as well as 22-24 hrs., 1-4 days and longer periods of continuous infusions. Cardiogenic side effects such as coroner artery vasospasm, ventricular dysrhythmia, and cardiac ischemia are also rarely stated³.

Case Report

48-year-old male patient applied to the emergency service with conditions of chest pain existing since yesterday, as well as nausea and vomiting. In the anamnesis of the patient, it is seen that there is metastatic rectum cancer in his history. The patient was operated 2 months ago had a colostomy. The patient is given his first chemotherapy 2 days ago with Bevacizumab + irinotecan + folic acid and 5-FU. The patient did not have a previously known coroner medical history and his echocardiography test before starting chemo-

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therapy is considered as normal. There were no characteristics found in the physical examination of the patient. The vital parameters of the patient were 36.5 °C, 77/min pulse, TA: 125/85 mmHg, 20/min respiratory rate. The patient was monitored and ECG was performed (Figure 1) and found to be normal sinus rhythm. Hemogram, biochemistry, troponin, d-dimer and artery blood gas are drawn from the patient. The blood tests of the patient are found to be normal. The patient, whose chest pain vaguely continued, is put on follow-up. During this follow up, the patient expressed that his chest pain has aggravated and had tachycardia. Along with control ECG (Figure 2), control troponin was performed for the patient. In the control ECG of the patient, there were ST elevations in inferior and anterior derivations. The control troponin value for the patient was found to be 0,073 µg/L (normal range 0,010-0.023 µg/L). The patient was consulted for cardiology as myocardial infarction with ST elevation. The patient was planned for coroner angiography. When the patient expressed that his chest pain aggravated even more as he was being prepared for coroner angiography, control ECG was reperformed (Figure 3) and seen that lateral derivations were added to ST elevations in inferior and anterior derivations. The patient, who has started to chemotherapy 2 days ago and still receives 5-FU infusion, is thought to have myocardial infarction with ST elevation based on the cardiotoxic impact of 5-FU, and he was taken to coroner angiography. His CAG is reported as LAD: plaque CX: plaque RCA: 40% lesion observed at CB alignment. 5-FU infusion is stopped along with the advice of medical oncology, the patient was taken into intensive care unit after coroner angiography.

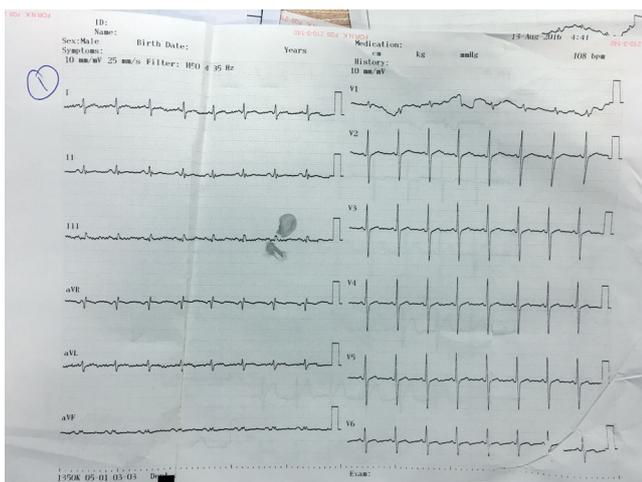


Figure 1. First ECG of the patient

Discussion

5-FU is a partner medical agent used to treat head and neck, gastrointestinal system, bladder, and chest malignancies⁴. Despite cardiac toxicity being a rare and serious complica-

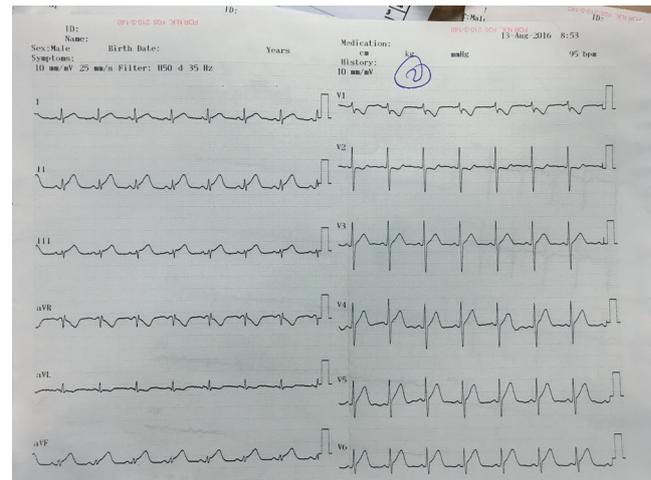


Figure 2. Second ECG of the patient

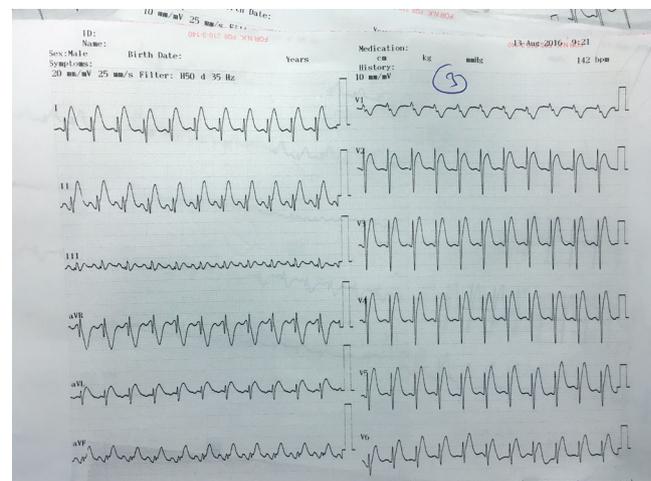


Figure 3. Third ECG of the patient

tion, the life-threatening toxicity is observed in 0,5% of the patients⁵. Generally speaking, cardiac toxicity is the ischemia emerging with angina, vasospasm, myocarditis, ventricular and supraventricular dysrhythmia, vessel dissection and myocardial infarction; or without myocardial infarction⁶. In experimental research, it is found that cardiotoxic effects cause coroner vasospasm by affecting nitric oxide swing directly from endothelium; and independent from endothelium, by causing vasoconstriction through protein kinase C. In the previous reports, it is underlined that the only mechanism contributing to STEMI development after 5-FU infusion is vasospasm. Existing coronary artery conditions in patients lead to increase in the present risk of cardiac side effects^{3, 6}. In a prospective research, angina pectoris attacks, arrhythmia, and LV function decrease incidence are observed for a period of 5 months for 102 patients diagnosed with 5-FU⁷. In our case, the patient came to us with myocardial infarction with ST elevation resulting from the emergence of chest pain after the use of 5-FU. According to another prospective research conducted

by Forni et al.⁸, 7.6% of the treated patients had cardiotoxicity. Some researchers intended to prevent vasospasm by providing calcium channel blocker or nitrate as prophylactic for patients who have CAD and will receive 5-FU⁹. As the treatment is stopped as soon as possible after cardiotoxicity, it is found beneficial to provide calcium channel blocker and nitrate treatments to remove the vasospastic effect.

Conclusion

Patients should be closely followed when receiving 5-FU treatment. Due to the cardiac side effects that may seriously show a fatal course, patients should be examined in detail before the treatment. Moreover, the cardiac performance of the patient should be analyzed in detail and closely monitored during the infusion treatment.

References

1. de Gramont Ad, Figer A, Seymour M, Homerin M, Hmissi A, Cassidy J, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. *J Clin Oncol* 2000;18(16):2938–47.
2. Shimura T, Fuse N, Yoshino T, Minashi K, Tahara M, Doi T, et al. Clinical features of interstitial lung disease induced by standard chemotherapy (FOLFOX or FOLFIRI) for colorectal cancer. *Ann Oncol* 2010;21(10):2005–10.
3. Alter P, Herzum M, Soufi M, Schaefer JR, Maisch B. Cardiotoxicity of 5-fluorouracil. *Cardiovasc Hematol Agents Med Chem* 2006;4(1):1–5.
4. Fidan E, Fidan S, Yildiz B, Durmus I, Kavgaci H, Ozdemir F, et al. Bolus fluorouracil induced syncope and pulseless ventricular tachycardia: a case report. *Hippokratia* 2011;15(1):93–5.
5. Luwaert RJ, Descamps O, Majois F, Chaudron JM, Beauduin M. Coronary-artery spasm induced by 5-fluorouracil. *Eur Heart J* 1991;12(3):468–70.
6. Sorrentino MF, Kim J, Foderaro AE, Truesdell AG. 5-Fluorouracil induced cardiotoxicity: review of the literature. *Cardiol J* 2012;19(5): 453–8. <http://dx.doi.org/10.5603/CJ.2012.0084>
7. Wacker A, Lersch C, Scherpinski U, Reindl L, Seyfarth M. High incidence of angina pectoris in patients treated with 5-fluorouracil. *Oncology*. 2003;65(2):108-12.
8. de Forni M, Malet-Martino MC, Jaillais P, Shubinski R, Bachaud J, Lemaire L, et al. Cardiotoxicity of high-dose continuous infusion fluorouracil: a prospective clinical study. *Journal of Clinical Oncology*. 1992;10(11):1795-801.
9. Kleiman NS, Lehane DE, Geyer Jr CE, Pratt CM, Young JB. Prinzmetal's angina during 5-fluorouracil chemotherapy. *The American journal of medicine*. 1987;82(3):566-8.

