

## A Case of Myocardial Ischaemia Induced by 5-fluorouracil

Şevket Görgülü, MD, Enis Oğuz, MD, Ayşegül Zor, MD, Utku Zor,  
MD, Muhammet Gürdoğan, MD, Tuna Tezel, MD.

Siyami Ersek Thoracic and Cardiovascular Surgery Center, Cardiology Department, *Istanbul*

### Introduction

Severe or life-threatening cardiotoxicity is a documented, but rare side effect of intravenous 5-fluorouracil (5-FU) therapy (1). The incidence of angina related to application of 5-fluorouracil ranges from 1.2 to 18% (2). Intravenous infusion of the drug may result in angina (3), myocardial infarction (4), arrhythmias (5) and /or even sudden death (3).

The underlying mechanisms of cardiotoxicity are not yet fully understood, although coronary vasospasm may be responsible (1).

We describe a female patient receiving 5-fluorouracil therapy with typical chest pain and electrocardiographic changes consistent with acute coronary syndrome.

### Case Report

A 47 year old woman who had undergone a colectomy due to adenocarcinoma grade III one month ago, started receiving 5-FU therapy. While no complications had developed at the time of the first two cures, during the third cure typical chest pain of squeezing character, radiating into both arms and associated with sweating, which lasted for 30 minutes was observed. This angina disappeared spontaneously. On the fourth cure of therapy the pain of the same character reappeared again, and the therapy was discontinued because the electrocardiogram (ECG) showed ischaemic changes. At the same day, the patient have applied to

our emergency service due to another pain attack lasting for 20 minutes and associated with 1 mm ST elevation in the leads D1, D2, V4-V6 (Figure1). The pain resolved after treatment with 300mg aspirin and 5mg sublingual nitroglycerin, but the ECG findings persisted. The patient was admitted to the coronary care unit and ECG abnormalities normalized rapidly (Figure 2) after initiation of the intravenous nitroglycerin infusion. Echocardiographic examination didn't show any significant abnormality except diastolic dysfunction grade 1. Serial serum cardiac enzymes and serum troponin T levels were of normal values. Possible reasons for this ST elevation such as pericarditis, hyperventilation, alkalosis were excluded. Coronary angiography was considered appropriate in order to enlighten this event. Coronary angiography revealed normal anatomic features in all coronary arteries, as well as the left ventriculogram was also normal. No recurrence of chest pain and/or ECG abnormalities were observed during the therapy with calcium antagonists and nitrates for one week. A relief of pain and normalization of ECG changes with nitrate therapy and normal coronary arteries indicate that this incident may be due to a coronary spasm caused by 5- FU (6).

### Discussion

The cardiotoxicity of 5-FU has been known for years, but the drug is not familiar to many cardiologists. Therefore, the most important factor determining the recognition of vasospastic angina is the awareness of its existence (7). Furthermore, it should be also emphasized that there is a high risk of relapse when patients are re-exposed to this drug after previous cardiac incidents. Therefore, the

Correspondence address: Şevket Görgülü, MD  
Dumlupınar Mh. Bahtlı Sk. No:65/10  
Kadıköy-Istanbul, TURKEY,  
Telephone: 00-90-216-5665330  
00-90-216-3499120 (1095-1186)  
E-mail: sevket5@yahoo.com

drug should definitely be discontinued and replaced by an alternative regimen (8), as it was the case in our patient.

The precise mechanism by which 5-FU induces a vasospasm remains unclear, but the most plausible explanation for the chest pain with ST elevation on the ECG and normal coronary angiogram in our case seems to be coronary spasm. Since the coronary artery spasm induced by 5-FU administration has been previously documented by angiography (1) and the relief of pain and normalization on the ECG with nitroglycerin, coronary spasm seems to be the main mechanism of this incident.

Although we suppose that coronary spasm to

be the main mechanism, the ST-T changes are not typical for this incident. These changes may be provoked by ischaemia and the suggested mechanism for this is that 5-FU may cause metabolic changes producing hypoxia within myocardial cells, therefore simulating ischaemic heart disease (9). In another study, Porta et al. proposed endothelin-1 as the ultimate mediator of this cardiotoxicity (10).

Whatever the mechanism of this cardiotoxicity, it is of high importance that the cardiologists, not usually involved in the care of cancer patients, should be aware about this life-threatening complication.

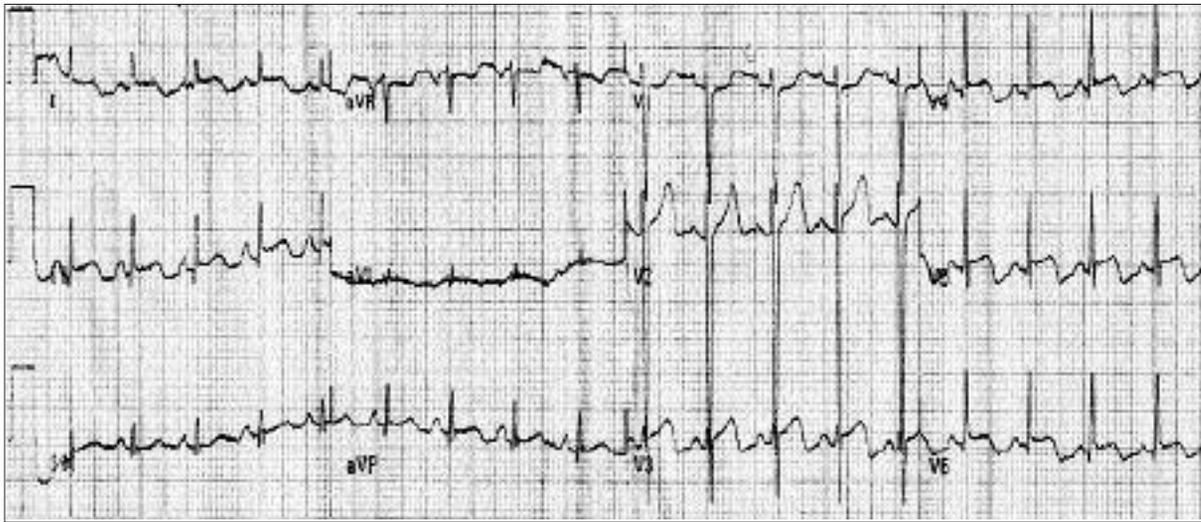


Figure 1- The ST elevation in certain leads associated with typical chest pain (Recorded in the emergency room)

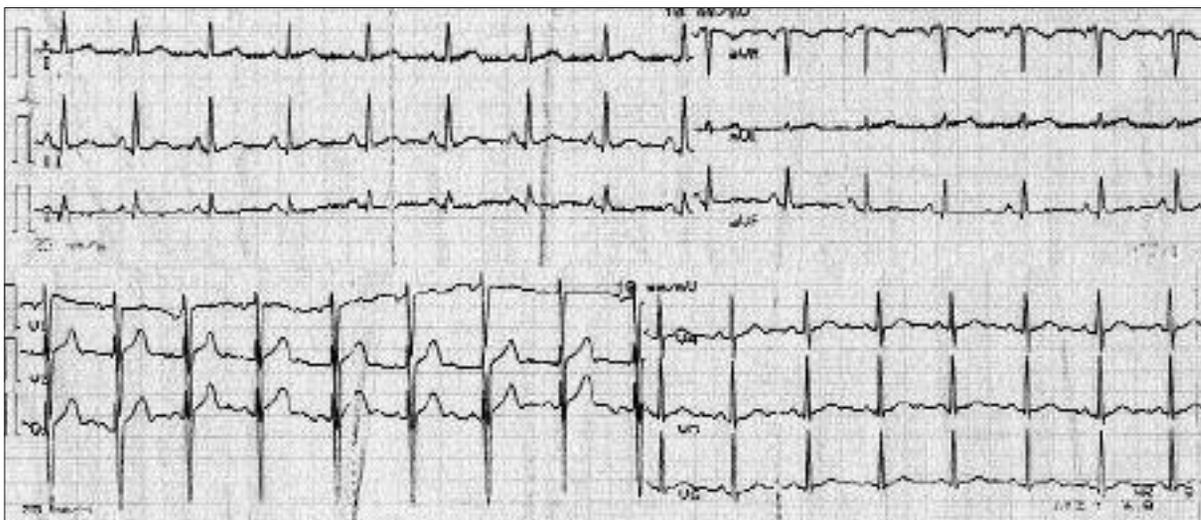
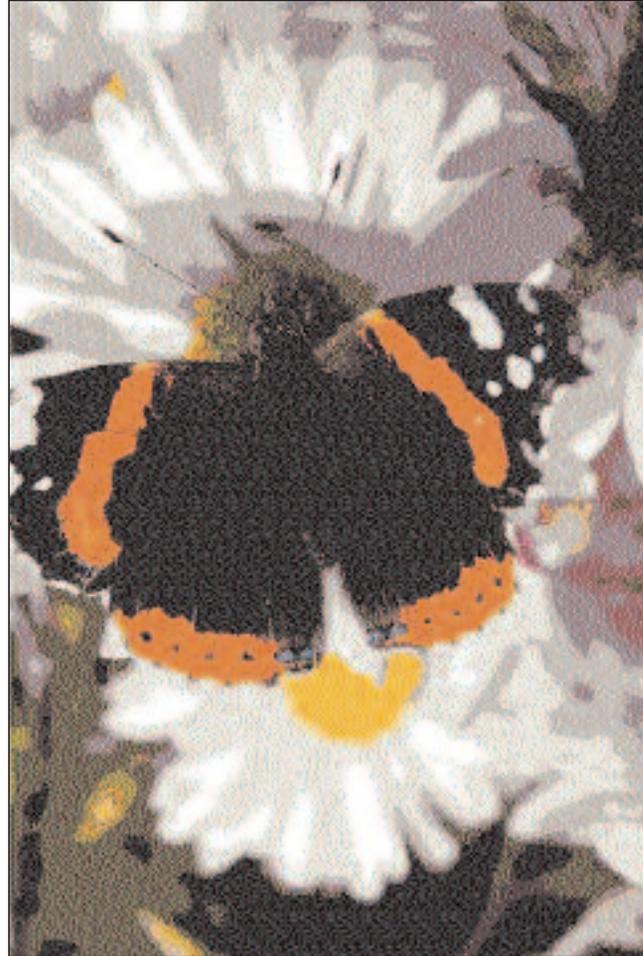


Figure 2- The ST elevation subsided after intravenous nitroglycerin infusion (Recorded in the coronary care unit).

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Prof.Dr. Arif Akşit

Kasımpatı ve Kelebek