Acute pericarditis during 5-fluorouracil, docetaxel and cisplatin therapy

Dosetaksel, sisplatin ve 5-florurasil tedavisi sırasında oluşan akut perikardit

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Summary– DCF chemotherapy regimen includes docetaxel, cisplatin, and 5-fluorouracil (5-FU). Cardiotoxicity is one of the well-known side effects of 5-FU, docetaxel, and cisplatin. In addition, the complications and side effects are more apparent when these three agents are given in combination. For the first time we describe a case of acute pericarditis associated with DCF regimen in a male patient. A 55-year-old man recently diagnosed with syncrone nasopharenx and non-small cell lung carcinoma was admitted to the oncology unit for chemotherapy. On the fourth day of infusion therapy with DCF he developed a central chest pain that was in pleuritic character and aggravated by recumbence. On electrocardiography (ECG), there was ST elevation on V2-6, D1, D2, and AVL. The patient was immediately transported to the cardiac catheterization laboratory for primary percutaneous coronary intervention. On coronary angiography, coronary arteries were normal. There was no segmentary wall motion abnormality on left ventricle in transthoracic echocardiography. The patient was diagnosed with acute pericarditis and the DCF regimen was discontinued. After 3 days, chest pain disappeared and ECG was normalized. According to the present case, the management of DCF-induced pericarditis includes stopping the drug and administering supportive treatment. The best method to prevent recurrent pericarditis induced by DCF is to use an alternate chemotherapeutic regimen.

Özet– DCF kemoterapi rejimi dosetaksel, sisplatin ve 5-florurasil (5-FU) ilaçlarını içermektedir. Kardiyotoksisite 5-FU, dosetaksel ve sisplatin tedavisinin bilinen yan etkilerinden biridir. Ayrıca, kardiyotoksisite bu üç ilacın kombine kullanımıyla daha fazla görülebilmektedir. Bu yazıda, ilk defa bir erkek hastada DCF rejimi ile ilişkili akut perikardit olgusu sunuldu. Aynı anda nazofarenks ve küçük hücreli dışı akciğer kanseri tanısı konulmuş 55 yaşında erkek hasta onkoloji kliniğine kemoterapi tedavisi için başvurdu. DCF tedavisinin 4. gününde sırt üstü yatmakla artan ve plöretik tarzda göğüs ağrısı meydana geldi. Çekilen elektrokardiyografide (EKG) V2-6,D1, D2 ve AVL derivasyonlarında ST yükselmesi saptandı. Hasta hemen primer perkütan koroner girişim amacıyla kardiyak kateterizasyon laboratuvarına alındı. Yapılan koroner anjiyografide, koroner arterler normal olarak bulundu. Transtorasik ekokardiyografide sol ventrikül segmenter duvar hareket bozukluğu izlenmedi. Hastaya akut perikardit tanısı konuldu ve DCF tedavisi durduruldu. Üç gün sonra hastanın göğüs ağrısı yakınması kayboldu ve EKG normale döndü. Sunulan olguyla, DCF rejimi ile ilişkili akut perikardit tedavisinin ilaç kesilmesi ve destek tedavisini içerdiğini bildirmekteyiz. DCF ilişkili perikarditin tekrarlamasının önlenmesi için en iyi yol ise uygun başka bir kemoterapi rejimine geçilmesidir.

DCF regimen includes docetaxel, cisplatin, and 5-fluorouracil (5-FU). 5-FU belongs to the anti-metabolite class of chemotherapeutic agents.[1] 5-FU inhibits the thymidylate synthase enzyme in cancer cells, interfering with DNA synthesis. 5-FU is widely used in the treatment of gastrointestinal tract, breast, head, neck, pancreatic, and skin cancers.[2,3] Cardiotoxicity is one of the well-known side effects of 5-FU. Docetaxel is a microtubule targeting agent. Docetaxel and cisplatin also have various effects on electrical activity of heart.[4] In addition, the complication risk and side effects are greater when these three agents are administered in combination.[4]

Abbreviations:

DCF	*Docetaxel, cisplatin 5-fluorouracil*
ECG	*Electrocardiography*

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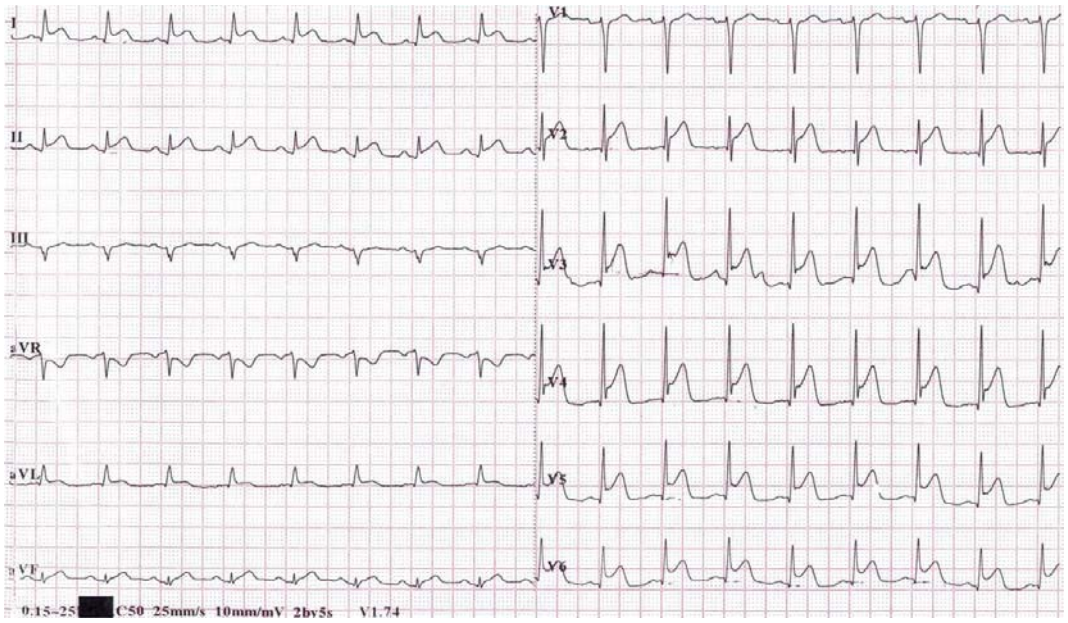

Figure 1. Electrocardiogram on admission.

We described a case of acute pericarditis associated with DCF regimen in a male patient. To the best of our knowledge, there is no reported data about acute pericarditis with 5-FU, cisplatin, or docetaxel treatment in the literature.

CASE REPORT

A 55-year-old man recently diagnosed with syncrone nasopharenx and non-small cell lung carcinoma with bone and lymph node metastasis was admitted to the oncology unit for chemotherapy. DCF (Docetaxel 75 mg/m^2 day 1, cisplatin 75 mg/m^2 day 1 and 5-FU 750 mg/m^2 day 1-5) chemotherapy regimen was planned. He had no significant medical history and no cardiovascular risk factors. On the fourth day of 22 hours infusion therapy with DCF, he developed a central chest pain that was pleuritic in character and aggravated by recumbence. On electrocardiography (ECG), there was ST elevation on V2-6, D1, D2, and AVL (Fig. 1). Although nitrate infusion was started after sublingual

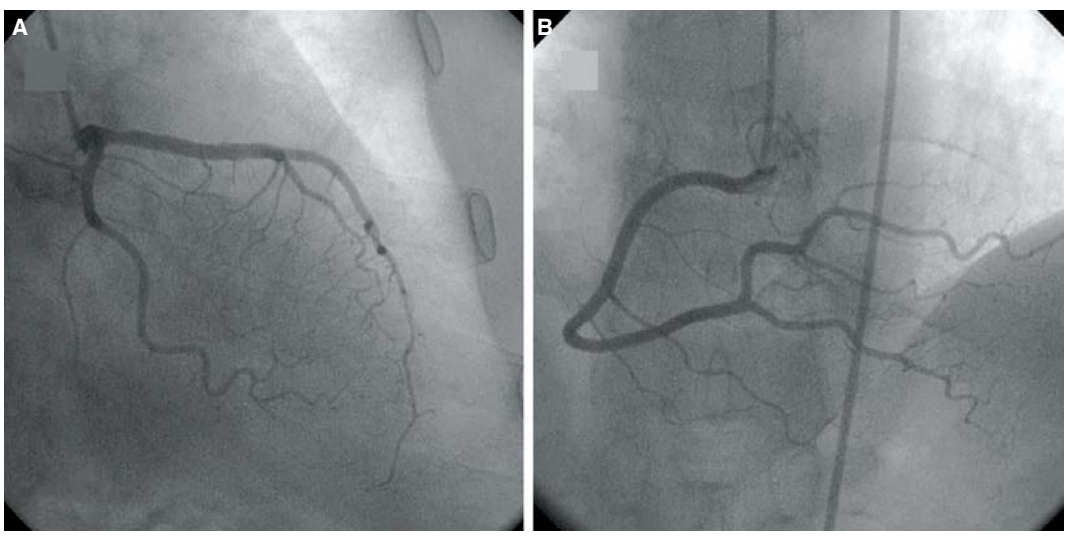

Figure 2. Normal coronary arteries that **(A)** left anterior descending, circumflex, and **(B)** right coronary artery.

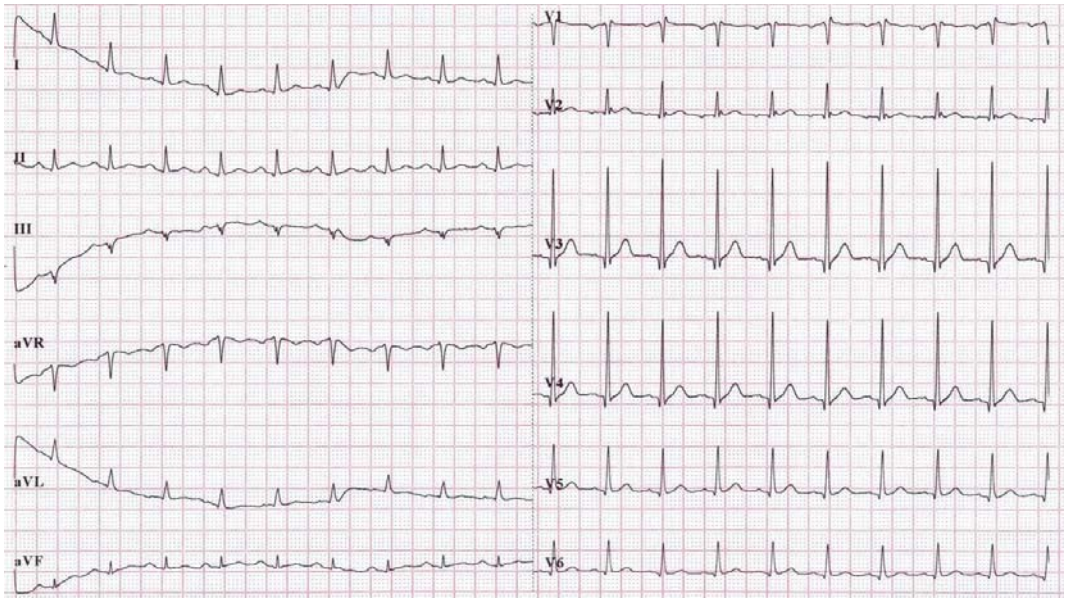

Figure 3. Electrocardiogram on 3rd day.

isosorbid-5-mononitrat, chest pain was not relieved. The patient was immediately transported to the cardiac catheterization laboratory for primary percutaneous coronary intervention. On coronary angiography, all three coronary arteries were normal (Fig. 2). After coronary angiography, we re-performed ECG, ST elevation on V2-6, D1, D2, and AVL leads and the pleurotic chest pain that was aggravated by recumbence was ongoing. There was no segmentary wall motion abnormality on left ventricle in transthoracic echocardiography. DCF was discontinued. In laboratory analyzes, troponin-I was 0.34 ng/ml (N=0-0.04 ng/ml), CK-MB was 18 u/l (N=0-24 u/l) (6 hours after onset of chest pain) and troponin-I was 0.32 ng/ml, CK-MB was 20 u/l (12 hours after onset of chest pain). This patient was diagnosed with acute pericarditis and therefore the DCF regimen was discontinued. After 3 days, chest pain disappeared and ECG was normalized (Fig. 3).

DISCUSSION

DCF regimen includes docetaxel, cisplatin, and 5-FU. All of these three agents have various cardiovascular toxic effects. The complication risk is higher when these three agents are administered in combination.[4]

5-FU therapy associated cardiotoxicity is usually reversible. The incidence of cardiotoxicity with 5-FU treatment varies from 1.6 to 7.6%.[2] The reported cardiotoxicities of 5-FU in the literature are vasospastic angina,[2,5,6] arrhythmias,[5] acute myocardial infarction,[6] dilated cardiomyopathy,[7] cardiogenic shock,[2] cardiac arrest and sudden death.[2] 5-FU induced coronary vasospasm has been well documented in the literature as the most common cardiotoxic side effect of 5-FU. There are a number of cases of transient ischemic attacks during 5-FU therapy that have been reported.[2,5,6]

Docetaxel is a microtubule targeting chemotherapeutic agent.[8] Docetaxel may cause sinus bradycardia, atrio-ventricular blocks, bundle branch blocks, ventricular ectopy, and tachycardia.[4,9,10] However, severe toxicities such as cardiac ischemia and myocardial infarction are rarely seen.[4] Cisplatin may also cause cardiac side effects. Acute symptoms of chest pain, arrhythmias, ST-T changes, left bundle branch block, and occasionally ischemic cardiac events with elevated cardiac enzymes are known to occur with administration of cisplatin. The cardiac side effects of both of cisplatin and docetaxel generally effect electrical activity of heart. Ischemic cardiac events are rarely seen.

In the present case we reported acute pericarditis related to a DCF regimen. The indications for diagnosis of acute pericarditis in this patient are as follows: typical chest pain for pericarditis, drug refractoriness to sublingual and intravenous administration of nitrate, normal coronary arteries in coronary angiogram that was performed immediately after onset of chest

pain, the lack of segmentary wall motion abnormality on the left ventricle in transthoracic echocardiography, ongoing ECG findings after coronary angiogram, absence of reciprocal ST depression in any ECG leads, mildly increased troponin-I levels, the resolution of typical chest pain after three days discontinuation of DCF regimen without any additional therapy.

Docetaxel, cisplatin, and 5-FU regimen related pericarditis has not been reported previously in the literature. Although 5-FU has a wide spectrum cardiac side effects, we can not precisely identify the culprit drug in the DCF regimen in this case. Further experience is needed in order determine the chemotherapeutic agent causing acute pericarditis.

According to the present case, the management of DCF-induced pericarditis includes stopping the administration of the drug and supplying supportive treatment. The best method for prevention of recurrent pericarditis induced by DCF is to use an alternate chemotherapeutic regimen. If an alternative regimen is not available, patients can be treated with a reduced dose of DCF with close monitoring.

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Key words: Antineoplastic agents/administration & dosage/adverse effects; cardiotonic agents/therapeutic use; cisplatin/adverse effects; fluorouracil / adverse effects; heart/drug effects; risk factors.

Anahtar sözcükler: Antineoplastik ajanlar/yönetim ve dozaj/yan etki; kardiyotonik ajanlar/tedavi amaçlı kullanım; sisplatin/yan etki; fluorasil / yan etki; kalp/ilaç etkileri; risk faktörleri.