Siklofosfamide bağlı supraventriküler ve ventriküler aritmiler sıklıkla gözlenebildiği gibi, kardiyak toksisiteye bağlı ölüm de bildirilmiştir (3). Ando ve ark.nın (4) yüksek doz siklofosfamid ile kemik iliği transplantasyonu yapılan 39 meme kanserli hastayı içeren çalışmalarında hazırlama rejimi olarak siklofosfamid (2000mg/m²) ve thiotepa (200mg/m²) kullanılmıştır. Bu calısmada hastaların birisinde koniestif kalp vetersizliği, 2'sinde sol ventrikül disfonksiyonu, 3 hastada perikardiyal effüzyon, 2 hastada ST-T anormallikleri, aritmi gelişen 9 hastanın 3'ünde atriyal, 2'sinde ventriküler aritmi ve 4'ünde atriyoventriküler blok epizotları izlenmiştir (4). Morandii ve ark.nın (2) yine kemik iliği transplantasyonu yapılan 16 meme kanseri hastasını iceren calısmalarında siklofosfamid dozu 70/m² olarak kullanılmış ve haştaların takibinde kardiyak enzimlerden troponin, kreatin kinaz (CK) ve CK-MB, EKG ve EKO kullanılmış: EKG, 12, 24, 48. ve 72. saatlerde çekilmiş. Hastaların hiçbirinde kardiyak enzimler yükselmezken, sadece 6 hastanın EKG'sinde nonspesifik ST-T değişiklikleri izlendiği ve 6 hastanın EKO'sunda sol ventrikül diyastolik disfonksiyon tespit edildiği bildirilmiştir (2). Goldberg ve ark.nın (5) 84 kemik iliği transplant hastasını iceren, 50 mg/kg/gün/4 gün dozunda siklofosfamidin kullanıldığı calısmasında hastaların 14'ünde siklofosfamidin kardiyak toksisitesine bağlı semptom ve bulgular saptanmış. Hastalar, siklofosfamidin dozuna göre (vücut yüzey alanı göz önüne alınarak) 2 gruba ayrılmış. Günlük 1.55 mg/m²'den yüksek dozda siklofosfamid kullanılan 52 olgunun 13'ünde konjestif kalp vetersizliği gözlenirken, 6 olgu exitus olmuş; günlük 1.55 mg/m²'den daha az dozda siklofosfamid kullanılan 32 olgunun 1'inde konjestif kalp yetersizliği gelişmiş ve hiçbir hasta kaybedilmemiş (5). Olgumuzda da 60 mg/kg/gün dozunda kullanılan siklofosfamid, vücut yüzey alanına göre hesaplandığında, 2.3 mg/m² olup yan etki gözlenmiştir. Olgumuzdaki kardiyak toksisitenin nedeni, vücut yüzey alanına göre hesaplanan yüksek doza bağlı olabilir.

Sonuç olarak; kemoterapiye bağlı olduğu düşünülen, kardiyak yan etki değerlendirmelerinde mutlaka olgunun hikâyesi, semptomları, ilaçları, ilaç dozları, EKG, EKO ve kardiyak enzimleri birlikte değerlendirilmeli ve özellikle siklofosfamidin en sık görülen konjestif kalp yetersizliği toksisitesi dışında MI ile karışabilen vazospastik angina tablosu ile karşımıza çıkan klinik durumu da yapabileceği unutulmamalıdır.

Hava Üsküdar Teke, Alparslan Birdane*, Zafer Gülbaş Eskişehir Osmangazi Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Hematoloji Bilim Dalı, *Kardiyoloji Anabilim Dalı, Eskişehir, Türkiye

Kaynaklar

- Biganzoli L, Cufer T,Bruning P, Coleman RE, Duchateau L, Rapoport B et al. Doxurubicin -paclitaxel: a safe regimen in terms of cardiac toxicity in metastatic breast carcinoma patients. Results from a European Organization for Research and Treatment of Cancer multicenter trial. Cancer 2003; 97: 40-5.
- Morandi P, Ruffini PA, Benvenuto GM, La Vecchia L, Mezzena G, Raimondi R. Serum cardiac troponin I levels and ECG/Echo monitoring in breast cancer patients undergoing high-dose (7g/m²) cyclophosphamide. Bone Marrow Transplant 2001; 28: 277-82.
- Braverman AC, Antin JH, Plappert MT, Cook EF, Lee RT. Cyclophosphamide cardiotoxicity in bone marrow transplantation: a prospective evaluation of new dosing regimen. J clin Oncol 1991; 9: 1215-23.
- Ando M, Yokozawa T, Sawada J, Takaue Y, Togitani K, Kawahigashi N et al. Cardiac conduction abnormalities in patients with breast cancer undergoing high-dose chemotherapy and stem cell transplantation. Bone Marrow Transplant 2000; 25: 185-9.
- Goldberg MA, Antin JH, Guinan EC, Rappeport JM. Cyclophospamide cardiotoxicity: an analysis of dosing as a risk factor. Blood 1986; 68: 1114-8.

Yazışma Adresi/Address for Correspondence: Dr. Hava Üsküdar Teke,

Eskişehir Osmangazi Üniversitesi Tıp Fakültesi İç Hastalıkları Anabilim Dalı, Hematoloji Bilimdalı, Eskişehir, Türkiye

Tel: 0 222 239 29 79 Fax: 0 222 239 37 72 E-posta: havaus@yahoo.com

Dilemma in the strategy of treatment: revascularization or medical treatment?

Tedavi stratejisinde ikilem: Revaskülarizasyon mu, tubbi tedavi mi?

A 43 years old woman presented with chest pain. Because she had no angina and she was in the subacute phase of myocardial infarction neither thrombolytic nor percutaneous coronary intervention (PCI) was done. On the coronary angiography, it was seen that left anterior descending artery (LAD) was totally occluded proximally, there were critically discrete stenoses at the midportion of right coronary artery (RCA). Circumflex artery (Cx) was normal and there was Rentrop 2 collateral flow to LAD from Cx artery and RCA (Fig. 1-4). On the ventriculography the left ventricular sizes were normal, akinesis at the anterior and apical portion of the left ventricle, mild mitral regurgitation were seen. The ejection fraction was measured as 38%.



Figure 1. Angiographic view of totally occluded left anterior descending artery in proximal portion



Figure 2. Angiographic view of critically discrete stenoses at the midportion of right coronary artery

What must be our treatment strategy in this patient?

- 1. PCI to LAD and to RCA
- 2. Coronary artery bypass surgery (CABG) to LAD and RCA
- 3. PCI to RCA to maintain collateral blood flow to LAD from RCA
- 4. Medical follow-up

Recently, in the study of Hochman et al. (1) 2166 patients with acute myocardial infarction with proximal total occlusion and EF<50% were studied, medical therapy versus PCI to the infarct-related artery plus medical therapy was compared. Reinfarction, the NYHA functional status and heart failure and mortality rates were not different between these groups. This study was controversial to the previous studies' results, but it must not be forgotten that most of the previous studies were retrospective and non-randomized contrary to the study by Hochman et al. (1). If we act according to these studies results, it will be wise to choose medical treatment without PCI.



Figure 3 (top) and 4 (bottom). Angiographic view of normal circumflex artery with Rentrop 2 collateral flow to left anterior descending artery from circumflex and right coronary arteries

It's known that the presence of collateral blood flow preserves left ventricular function and patients with collateral flow have better survival rates than those without collateral flow. Overall, 23 cases of totally occluded left main coronary artery with good collateral flow from RCA were reported. Twenty-one of these patients have CABG operation and two of them denied the operation. After mean follow-up of 60 months, all of the patients were alive (2).

Our had collateral blood flow from RCA to LAD and critical stenoses in midportion of RCA. If the critical stenoses occluded totally the RCA, the collateral flow to LAD will be lost. To prevent this we can think of PCI to RCA, but the possibility of total occlusion of RCA during the procedure makes us stay backward. Also there is no any data supporting this thought's accuracy. Then can we increase the existing collaterals? It was shown that exercise and high dose statin usage increases collateral vessel development (3, 4).

Our case is a suitable candidate for CABG. Considering the results of the study by Hochman et al. (1) we must think of CABG operation once more. To my knowledge, there is no any prospective randomized study comparing these kinds of patients.

We are sure that, every clinics decision of treatment approach will change according to its own experience and vision. According to us, in the light of the literatures it will be wise to recommend medical therapy including beta-blocker therapy with high-dose statin.

Ersan Tatlı, Meryem Aktoz, Gökhan Aydın, Mustafa Yılmaztepe, Armağan Altun Department of Cardiology, Trakya University School of Medicine, Edirne, Turkey

References

- Hochman JS, Lamas GA, Buller CE, Dzavik V, Reynolds HR, Abramsky SJ, et al. Coronary intervention for persistent occlusion after myocardial infarction. N Engl J Med 2006; 355: 2395-407.
- Charitos CE, Nanas JN, Tsoukas A, Anastasiou-Nana M, Lolas CT. Total occlusion of the left main coronary artery with preserved left ventricular function.Int J Cardiol 1997; 61: 193-6.
- Dincer I, Ongun A, Turhan S, Ozdol C, Kumbasar D, Erol C. Association between the dosage and duration of statin treatment with coronary collateral development. Coron Artery Dis 2006; 17: 561-5.
- Boluyt MO, Cirrincione GM, Loyd AM, Korzick DH, Parker JL, Laughlin MH. Effects of gradual coronary artery occlusion and exercise training on gene expression in swine heart. Mol Cell Biochem 2007; 294: 87-96.

Address for Correspondence/Yazışma Adresi: Dr. Ersan Tatlı

Department of Cardiology, Trakya University School of Medicine, Edirne, Turkey Phone: +90 284 235 76 41/2100 Fax: +90 284 235 23 05 E-mail: ersantatli@yahoo.com