CASE REPORT

Bleomycin cardiotoxicity during chemotherapy for an ovarian germ cell tumor

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Abstract

Introduction: Platinum-based chemotherapeutic regimens, including BEP (bleomycin, etoposide, cisplatin) represent the standard of care, first line therapy in non-epithelial ovarian tumours. Cardiovascular toxicity is a rare adverse effect of bleomycin.

Case Report: A 41-year-old woman with ovarian granulosa tumor, treated with first line BEP chemotherapy experienced chest discomfort rapidly progressing to severe precordial pain during bleomycin infusion. The infusion was stopped and electrocardiographic changes indicative of myocardial ischemia were revealed. Anti-anginal and anti-thrombotic treatment was introduced. Cardiac enzymes were not elevated and echocardiographic findings showed no wall motion abnormalities. Twenty four hours after the episode the elctrocardiographic changes insisted and chemotherapy was decided to be continued, excluding bleomycin, with no symptom recurrence.

Discussion: Cardiovascular complications pose a rare but potential fatal adverse effect of BEP chemotherapy and should be carefully addressed, especially in patients with additional cardiovascular risk factors. Physicians dealing with bleomycin-based therapies may find this knowledge useful for a more comprehensive evaluation of chest pain syndromes in those patients. Hippokratia 2013, 17, 2: 1787-188

Keywords: BEP chemotherapy, ovarian cancer, cardiotoxicity, myocardial ischemia, chest pain

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Introduction

BEP (bleomycin, etoposide, cisplatin) chemotherapeutic regimen represents the standard of care first line therapy in non-epithelial ovarian tumours[1]. Cardiovascular toxicity is a rare adverse effect of bleomycin and may be expressed clinically as hypotension, pericarditis, acute substernal chest pain, coronary artery disease, myocardial ischemia, myocardial infarction, cerebral vascular accident and Raynaud's phenomenon[2].

Case report

A 41-year-old woman with advanced recurrent ovarian cancer (adult granulosa cell tumor, initial stage pT2b pN1 M0, FIGO IIIC, four years before) was treated with first line platinum-based chemotherapy. Pre-treatment cardiovascular risk factors included arterial hypertension (well controlled with angiotensin II receptor blockers) and obesity (BMI: 40.3 Kg/m^2). Baseline cardiologic evaluation with ECG and echocardiogram just before initiation of chemotherapy was unremarkable. During the first cycle of therapy and during the bleomycin infusion, chest discomfort rapidly progressing to severe precordial pain radiating to the interscapular region emerged. The patient was tachypnoic, in moderate distress. The infusion was stopped and the electrocardiogram (ECG) revealed sinus tachycardia (120 bpm), ST segment depressions (≤2 mm) in leads I, II, aVL, V4-V6 and T wave inversions in leads I, II, aVL, V4-V6 (Figure 1A,B). Anti-anginal treatment with glyceryl trinitrate (5 mg qd) and diltiazem (60 mg tid) as well as acetylsalicylic acid (100 mg qd) and low-molecular weight heparin (bemiparin 3,500 IU qd) were initiated. Symptoms were relieved in about 20 minutes. Cardiac enzymes were not elevated in two serial measurements at 6-hour intervals. Echocardiogram revealed no hypokinetic or akinetic myocardial regions. Left ventricular function was normal and no pericardial effusion or other abnormalities were identified. Twenty-four hours after the episode, T wave inversions insisted in leads I, aVL, V4-V6 and flattened T waves appeared in leads II and aVF (Figure 1C). Bleomycin was discontinued and only etoposide-cisplatin chemotherapy was decided to be continued, without any symptom recurrence.

Discussion

Major cardiovascular toxicity (cerebral ischemic infarction, peripheral arterial thromboembolism, myocardial infarction) of bleomycin appears to be lower than 1%[3]. An acute chest pain syndrome, self-limiting with no apparent etiology or complications, is also described with a frequency of about 3%[4]. Although rare, acute chest pain and myocardial infarction cases during bleomycin chemotherapy have been described in the literature[5-10]. Patients having predisposing risk factors for cardiovascular disease seem to face a higher risk[3].

The pathophysiologic mechanism of the acute chest

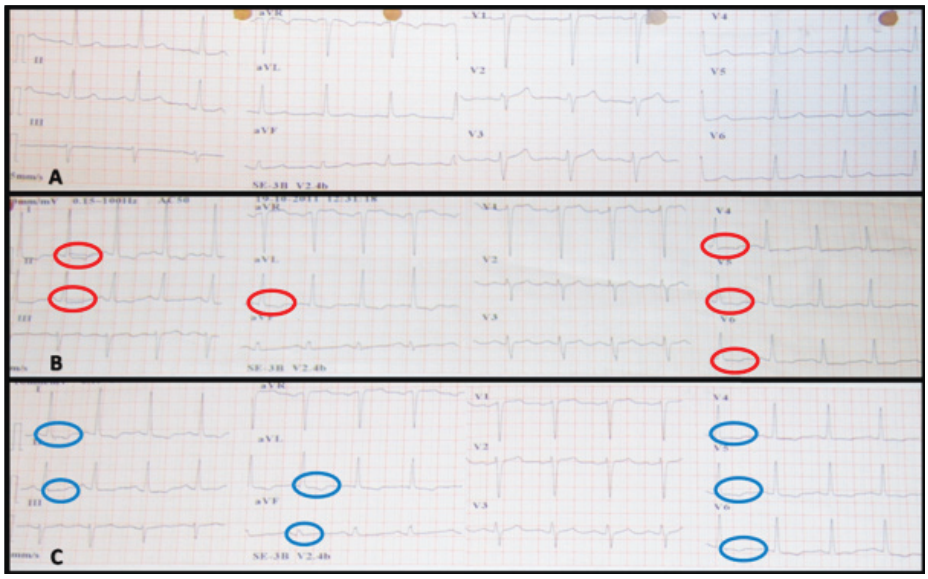

Figure 1: A) admission ECG, **B)** ECG during pain (acute changes marked with red circles), **C)** ECG 24h after the episode (changes marked with blue circles).

pain described during bleomycin infusion remains unclear. Serosal inflammation, manifesting as acute pleuropericarditis as part of the more generalized mucocutaneous toxicity common to bleomycin therapy, could be a possible explanation. A vascular etiology for the pain has also to be considered, since other pulmonary vascular diseases, such as pulmonary hypertension and pulmonary embolism may cause both substernal and pleuritic chest pain even in the absence of infarction[4]. Further courses of bleomycin are not contraindicated, however it seems reasonable to stop the drug in those with intolerable pain or ECG changes[4]. Slowing the rate of infusion, analgesics and (if indicated) anti-ischemic treatment should be applied for relieving the patient and preventing further complications[3,4,6].

We report here a case of a young woman presenting with atypical chest pain during bleomycin infusion and ECG signs of myocardial ischemia. Anti-anginal agents were immediately administered, improving clinical presentation, while antithrombotic treatment was initiated to prevent thrombus formation in the coronary circulation. Cardiac enzymes remained negative and echocardiographic findings showed no regional abnormality. The patient had no recurrence of the chest pain and bleomycin was excluded from future therapy.

Cardiovascular complications pose a rare but potential fatal adverse effect of BEP chemotherapy and should be carefully addressed, especially in patients with additional cardiovascular risk factors[11-13]. Physicians dealing with bleomycin-based therapies may find this knowledge useful for a more comprehensive evaluation of chest pain syndromes in those patients.

Conflict of Interest

The authors declare that there is no conflict of interest.

Acknowledgement

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