

# Cisplatin and bleomycin-induced acute peripheral-vascular stenosis in patient with testicular cancer

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## Abstract

After cisplatin and bleomycin-containing chemotherapy (CTx) for testicular cancer, part of the patients may develop acute or long-term cardiovascular toxicity. In the present case, we reported that a 58-year-old male patient presenting with testicular tumors who developed acute peripheral arterial disease during combination CTx with bleomycin, etoposide, and cisplatin. Superficial femoral artery occlusion not responded to structure thrombolytic and anticoagulators treatment. Left lower extremity was amputated below knee. In patients with high risk of cardiovascular disease, prophylactic anticoagulation may be recommended. The risk of causing factors of thromboembolism in patients with testicular cancer under cisplatin and bleomycin-containing CTx should be evaluated.

**Key Words:** Chemotherapy, testicular neoplasm, thromboembolism

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## INTRODUCTION

Three-drug combination chemotherapy (CTx) for testicular tumors (bleomycin, etoposide, and cisplatin [BEP] therapy) is performed as standard treatment in many hospitals. The side effects of anticancer drugs include vascular toxicity.<sup>[1]</sup> In this report, we present a patient with testicular tumors who developed acute peripheral arterial disease during combination CTx.

## CASE REPORT

A 58-year-old male patient presented with a mixed germ cell neoplasm (GCN) (seminoma and yolk sac tumor).

Postoperative BEP treatment was started. The patient did not have a history of vascular diseases. No sign or symptoms related with vascular diseases at the initial visit. After 1<sup>st</sup> cycle of BEP, bilateral lower extremities (LE) were mildly cyanotic, cold, and hyperemic. Circulations of both LE were normal in Doppler ultrasound (US). Raynaud's syndrome was diagnosed and calcium channel blocker diltiazem 30 mg started. After 2<sup>nd</sup> cycle of BEP, the main complaints were severe pain and coldness on the bilateral LE. A Doppler US showed acute bilateral popliteal artery thrombosis. Bilateral popliteal arterial embolectomy was performed, and LE reperfusion have been completely restored [Figure 1]. Low molecular

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**Figure 1:** Peripheral angiography; after popliteal arterial embolectomy

weight heparin (LMWH) prophylaxis started. Our patient has cardiovascular disease (CVD) risk factors such as smoking, hyperlipidemia, hypertension, and diabetes mellitus. A coronary angiography was normal. In follow-up, LE circulations were normal before and after 3<sup>rd</sup> cycle of BEP CTx under LMWH medication. LMWH was stopped the 4<sup>th</sup> cycle of BEP CTx was administered by a different medical center. Patient presented to our center with acute left LE ischemia and pain. Superficial femoral artery occlusion was detected in peripheral angiography. Depending on late ischemia, superficial femoral arterial occlusion, poor distal artery structure thrombolytic, and anti-coagulators treatment was started [Figure 2]. Patient did not respond to medical treatment. Left LE was amputated below the knee.

## DISCUSSION

Testicular germ cell cancer is the most common malignancy in men between 20 and 40 years of age. Approximately, half of these germ cell tumors are nonseminomas. Nonseminomas are disseminated in approximately 50% of the patients at presentation. After an orchidectomy, standard treatment of disseminated nonseminoma consists of CTx with a combination of BEP.<sup>[2]</sup>

Cisplatin- and bleomycin-containing CTx for testicular cancer has been associated with both acute and long-term vascular toxicity. Endothelial injury has been described after the administration of cisplatin and bleomycin *in vitro*.<sup>[3]</sup> Raynaud's phenomenon, believed to be a vascular toxic effect of bleomycin, has been reported in up to 37% of patients.<sup>[4]</sup> Several patients have also been reported in whom myocardial infarction occurred during or shortly after the administration of cisplatin.<sup>[5]</sup> Furthermore, long-term survivors of disseminated testicular cancer have an increased risk for CVD.<sup>[6]</sup>



**Figure 2:** Peripheral angiography; superficial femoral arterial occlusion

*In vitro* endothelial injury has been shown by cisplatin (CP) and bleomycin.<sup>[7]</sup> When cisplatin added to vinblastine and bleomycin combination Raynaud's syndrome was observed in 41% of patients. These findings support the endothelial injury and vasospasm in the pathogenesis.<sup>[8]</sup> Cardiac risk factors such as hypercholesterolemia, dyslipidemia, and hypertension are more common in patient (ptx) treated with CTx in testicular cancer.<sup>[9]</sup> Cheng *et al.* had reported arterial thrombosis in metastatic testicular germ cell tumors in two patients. In this study, they reported that there is no recommendation for thromboembolic event prophylaxis in oncological guidelines.<sup>[10]</sup>

Physicians should be careful regarding cardiovascular symptoms in a patient treated with CP. Any new onset of cardiovascular symptoms, extremity pallor, paresthesia, pain, and pulselessness is taken into account. Although it is not presented in the guidelines, ptx may be evaluated for CVD. Angiographic evaluation may be performed in patients with the presence of atherosclerosis. In patients with high risk of CVD prophylactic anti-coagulation may be recommended. Further prospective studies are needed to evaluate the risk of causing factors of thromboembolism in patients with GCN.

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## Conflicts of interest

There are no conflicts of interest.

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