ABSTRACT: Testicular cancer is the most common malignancy in young men (15-29 years old). Combination therapy with bleomycin, etoposide, and cisplatin has been the standard first-line treatment for testicular metastatic disease. We present a case of multicoronary thrombi causing acute inferior myocardial infarction in a patient who recently received chemotherapy for testicular tumor.

Key words: acute myocardial infarction, coronary angiography, GP IIb/IIIa inhibitors, testicular cancer, chemotherapy

Testicular cancer is the most common malignancy in men between 15 and 29 years of age. Two major histologic groups of testicular cancer, seminoma and non-seminoma, have been defined. Seminomas are generally treated with surgical resection, followed by radiotherapy for early-stage disease and chemotherapy for more advanced-stage disease. In contrast, non-seminoma encompasses several histologic types such as teratoma and choriocarcinoma; teratomas do not respond well to radiotherapy and are frequently treated with chemotherapy.

Combination therapy with bleomycin, etoposide, and cisplatin has been the standard first-line treatment for testicular metastatic disease. Nevertheless, these drugs have several adverse effects, such as pneumonitis, Raynaud-like phenomenon, fever, bone marrow suppression, acute leukemia, nephrotoxicity, neurotoxicity, ototoxicity, infertility, and thromboembolic complications.

Here, we present a case of multicoronary thrombi causing acute inferior myocardial infarction in a patient who recently received chemotherapy for testicular tumor.

Case Report. A 36-year-old man was diagnosed with immature teratoma. Semicastration was performed shortly after the diagnosis. At 16 days after the operation, metastases had been detected in several paraaortic lymph nodes, and the patient received a combination of cisplatin (44 mg), etoposide (200 mg), and bleomycin (30 mg) daily for 5 days. The second cycle of chemotherapy was initiated nearly 3 weeks after the conclusion of the last therapeutic cycle, and consisted of cisplatin (44 mg), etoposide (160 mg), and bleomycin (30 mg) daily. Six days after completion of the second cycle, he presented to our hospital with chest pain that had lasted for 6 hours. His previous medical history was unremarkable. He did not have any major coronary risk factors. Physical examination was within normal limits. His electrocardiogram (ECG) showed ST-segment elevation (inferior leads). Coronary angiography showed a large thrombus causing subtotal occlusion in the mid segment of the circumflex artery (CX) and total occlusion in the distal segment of the CX, along with thrombi in the left anterior descending (LAD) artery and first septal (S1) artery (Figures 1 and 2). Due to the sharp angle between the proximal and distal segments of the CX, a thrombus aspiration device was not used. Direct stenting was performed for the mid segment of the CX. Tirofiban infusion was initiated immediately prior to the stenting procedure and continued for 36 hours. The patient reported that the degree of the chest pain was decreased and ECG performed after the procedure showed the regression of ST-segment elevation over 50%. During follow-up, an echocardiogram showed hypokinesia in the inferior, apical, and septal walls. Two days after the first procedure, another coronary angiogram was performed.
showing that the thrombus in the LAD was diminished, the size of the thrombus in the S1 was decreased, TIMI-3 flow was achieved, and the stent in the mid portion of the CX was open, with complete occlusion of the CX in the distal segment (Figure 3). The patient was free of pain and was hemodynamically stable; therefore, no intervention for the S1 and CX arteries was planned. The patient was given aspirin, clopidogrel, metoprolol, and statin, and was discharged in good condition on the 4th day after admission.

Discussion. Adding cisplatin to the combination of bleomycin and etoposide has increased the curative rate of testicular tumor treatment. However, several adverse effects of cisplatin have been reported. The most common side effects of cisplatin consist of gastrointestinal symptoms, neuro-, oto- and nephrotoxicity, and myelosuppression.

Major adverse effects on the cardiovascular system are rarely seen and include arterial occlusion, deep vein thrombosis, transient ischemic attack, stroke, angina pectoris, and acute myocardial infarction. Cisplatin may not only cause acute cardiovascular complications, but also increase the risk of vascular events in the long term, although the exact mechanism of this is unclear. However, patients with an arterial event have elevated levels of von Willebrand factor (a marker of endothelial function), t-PA, platelets, and fibrinogen at baseline and these increase further with chemotherapy. In addition, cisplatin-based chemotherapy increases intima media thickness more than would be expected from an increase in age and may indicate susceptibility to vascular toxicity and be of prognostic significance for cardiovascular complications in the long term. These findings might suggest acute or long-term vascular side effects and are mainly related to effects on the endothelial layer. Nevertheless, cisplatin-based chemotherapy may also cause autonomic cardiovascular dysfunction and this may increase cardiovascular risk in patients during cisplatin-based chemotherapy, as it does in diabetic and postmyocardial infarction patients.

Some of the other possible explanations are prolonged vasospasms, decreased functional protein C levels, hypomagnesemia, hypercholesterolemia, and influences on platelet aggregation. The overall incidence of thromboembolic complications is 10%, occurring in both the venous (8.4%) and arterial systems (1.6%). Although primary coronary intervention (PCI) is generally accepted as the first-line therapeutic strategy for acute myocardial infarction due to its rapid restoration of antegrade flow, differences in etiology and clinical background might cause differences in the clinical outcome of the primary PCI. In previous case reports, no mechanical coronary intervention or thrombus aspiration alone (without any stenting or balloon dilatation) was performed. Our treatment strategy was to use a stent for the mid segment of the CX and pharmaceutical treatment, including tirofiban, for the other thrombi. Intravascular ultrasound was not available at the time of the angiogram to exclude any stenosis beneath the thrombus, and the operator chose to use a stent. In previous case reports, no tirofiban or other glycoprotein IIb/IIIa antagonist was used. Moreover, our case is the first to describe multiple thrombi in multiple coronary arteries. Two days after the procedure, the thrombus in the LAD was diminished, and the thrombus in the S1 became smaller, but the CX remained completely occluded. The patient was free of any pain and clinically stable at the time of second angiography. Thus, no intervention for the LAD or S1 was planned. In previous case reports, the patients suffered from acute myocardial infarction 8 days, 4 days, and 5 days after the second administration of cisplatin. Although our patient
had also received two cycles of cisplatin therapy and suffered from acute myocardial infarction 6 days after the last therapy, the dosage of cisplatin used in this case was lower than used in these previous cases.15,16

To the best of our knowledge, this case is the first description of cisplatin-induced multiple coronary thrombi. The patient was successfully treated with stenting and tirofiban.

We speculate that in the absence of intravascular ultrasound to exclude the presence of coronary atherosclerosis, stents can be used and tirofiban might decrease or even eliminate the thrombus.

References