Acute Aortic Thrombosis during Cisplatin Based Chemotherapy for Gastric Cancer

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Abstract

The development of aortic thrombosis without the presence of atherosclerosis, dissection, or aneurysms is rare. A cancer-related hypercoagulable state is a well-known risk factor for venous thrombosis, however, atrial thrombosis has rarely been reported in cancer patients. Cisplatin-based chemotherapy is known to cause various side-effects. Detecting aortic thrombosis is important because it is a fatal condition. We herein present the first reported case of endo-aortic thrombosis occurring during cisplatin-based chemotherapy for gastric cancer.

Key words: aortic thrombosis, cisplatin, chemotherapy, S-1


Introduction

The development of aortic thrombosis without the presence of atherosclerosis, dissection, or aneurysms is relatively rare. Uncommonly, aortic thrombosis may be related to an identifiable hypercoagulable state or factors that promote clot formation, such as sepsis, polycythemia, disseminated intravascular coagulation, and autoimmune disease (1).

Cisplatin-based chemotherapy has been reported to cause a variety of vascular side-effects. Only a few case of cisplatin-associated arterial thrombosis have been documented in patients with small cell lung cancer (2), testicular seminoma (3), esophageal adenocarcinoma (4), and cervical cancer (1).

We herein present the case of a patient with a localized aortic thrombus who had received cisplatin-based chemotherapy for gastric cancer.

Case Report

A 66-year-old woman presented with a decreased appetite and an enlarged infraclavicular lymph node. Computed tomography (CT) showed enlarged Virchow’s and para-aortic nodes. Upper gastrointestinal endoscopy revealed an ulcerative lesion in the gastric antrum. A biopsy revealed that the lesion was signet-ring cell cancer. Therefore, the lesion was diagnosed as gastric cancer stage IV.

The patient’s history included radical hysterectomy performed 12 years earlier, however, there was no history of chemotherapy. Five years previously, she had been a 20 pack-year smoker. She had no history of cardiovascular factors such as hypertension, hypercholesterolemia, or diabetes. Coagulation markers such as the platelet count, prothrombin time, and activated partial thrombin time were within the normal limits. Electrocardiogram was normal without arterial fibrillation, and echocardiography showed a normal cardiac status. Staging CT revealed no vascular anomalies, thrombosis, or a compressed aorta (Figure A).

The patient was treated with chemotherapy consisting of one cycle of cisplatin at a dose of 60 mg/m² administered intravenously on day 8 and S-1 at a dose of 100 mg/day administered orally on days 1 to 21. Although the patient was routinely administered dexamethazone at a dose of 8 mg on day 8 and 5 mg on days 9 and 10, she experienced anorexia and vomiting of grade 3 during her clinical course. However, she was able to complete the first cycle of cisplatin administration.

Restaging on chest and abdominal CT revealed regression of metastases and, unexpectedly, endo-aortic thrombotic de-
Deposits in the descending arch of the thoracic and abdominal aorta. Surprisingly, another thrombotic deposit was found in the infrarenal abdominal aorta (Figure B). Although approximately 30% of the abdominal aorta was occluded by the thrombotic material, no significant clinical symptoms were noted.

The level of fibrin degradation product was elevated to 3.4 μg/mL and the von Willebrand factor was 201% (normal range: 100-170%). The level of anti-thrombin III, the prothrombin time and the activated partial thrombin time were normal. Echocardiography showed the absence of pulmonary hypertension. Although no pulmonary embolisms or deep vein thrombosis were evident, to prevent further complications, the patient immediately received heparin at a dose of 10,000 U/day administered intravenously for seven days and warfarin administered orally. After two weeks, the thrombi in the thoracic and abdominal aorta had nearly completely resolved (Figure C). The patient did not experience any difficulty or discomfort related to the cancer or thrombi. Treatment with cisplatin + S-1 chemotherapy and warfarin was continued until the chemotherapy regimen was changed due to severe nausea.

Discussion

The development of aortic thrombosis without the presence of atherosclerosis, dissection, or aneurysms is rare. Uncommonly, aortic thrombosis may be related to an identifiable hypercoagulable state or factors predisposing patients to clot formation, such as sepsis, polycythemia, disseminated intravascular coagulation, or autoimmune diseases (1).

Moreover, the presence of abdominal aortic aneurysms, cardiac disease, or neurological abnormalities such as limb paralysis is highly associated with the development of aortic thrombosis (2).

On the other hand, arterial thrombosis has rarely been reported in cancer patients. However, chemotherapy is also recognized to be an independent risk factor for thrombosis and may cause damage to the vascular endothelium, disequilibrium between procoagulant and anticoagulant molecules, tumor/endothelial apoptosis, cytokine activation, and increased tissue factor activity (5). In a previous report, the actual incidence of thromboemboli was 12.1%, of which 10.1% were venous events, and 2.2% were arterial events. Furthermore, there were fewer thromboemboli cases in the
oxaliplatin group (oxaliplation + epirubicine + fluorouracil, or capecitabine) than in the cisplatin group (cisplatin + epirubicine + fluorouracil, or capecitabine). Cisplatin is most frequently associated with vascular events (6). On the other hand, no cases of S-1-associated arterial thrombosis have been reported to date.

Although the exact mechanism remains unclear, we speculate the following according to Virchow’s triad of thrombogenesis, i.e., an increased ability of cells to adhere to damaged internal vessel walls, a reduced blood flow, and an increased tendency to clot. First, a histological examination of the blood vessels after cisplatin infusion showed damage characterized by intimal edema with pyknosis of endothelial cells, thrombus formation, and detachment of the intimal layer (7). Cisplatin-based chemotherapy constituted a strong stimulus for the formation of arterial thrombosis. Second, due to the increased age of the patient, a slight risk of thrombosis must be considered. She had been a smoker, and some minor calcifications were detected in the aortic wall on staging CT. However, there were no clinical signs of systemic atherosclerosis and no other vascular risk factors. Therefore, there was no reason to consider a reduced aortic blood flow as the cause. Third, it is thought that cisplatin may enhance the activity, but not the expression, of tissue factor in human blood monocytes (8).

Furthermore, cisplatin can induce platelet activation and elevate von Willebrand factor, which can cause endothelial injury and potentiate arterial thrombosis (9). In our patient, the von Willebrand factor level was slightly increased; however, the previous level was not measured.

Therefore, cisplatin-based chemotherapy might lead to an increased clotting tendency in the blood due to humoral factors. Combination chemotherapy with S-1 and cisplatin is widely used for advanced gastric cancer, and its clinical efficacy is well documented. Moreover, restaging on chest and abdominal CT revealed regression of the metastases. Hence, we decided to continue the current chemotherapy using warfarin.

This case is unique because arterial thrombosis presented without any other predisposing factor, which suggests that cisplatin chemotherapy played a role in the thrombosis development. Chemotherapy is being continued even after thrombus resolution.

The authors state that they have no Conflict of Interest (COI).

References