Acute arterial thrombosis related to 5-fluorouracil and cisplatin combination chemotherapy regimen in an elderly patient

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In recent years, the vascular toxicity of cancer chemotherapy drugs has become more widely appreciated. Thrombosis is a well-known form of vascular toxicity of chemotherapy drugs and a frequent complication of cancer. The majority of thromboses occur in venous system; the incidence of arterial clots is much lower. This report describes a patient who developed distal acute arterial ischemia of the left leg after first cycle of combined 5-fluorouracil (5-FU) and cisplatin chemotherapy regimen for recurrent squamous-cell carcinoma of the oral cavity. [Turk J Cancer 2002;32(2):66-68]

Key words: Arterial thrombosis, cisplatin, 5-fluorouracil

In recent years, the vascular toxicity of cancer chemotherapy drugs has become more widely appreciated. They have been related mainly to three forms of vascular toxicity: 1) Vascular ischemia involving cerebral, myocardial, or extremity arterial vessels; 2) Veno-occlusive disease of hepatic vessels or in rare instances, of pulmonary vessels; 3) Venous or arterial thrombosis (1-3). Distal arterial ischemia is a rare complication induced by chemotherapy, and may be associated with preexistent organic changes.

Recently, we observed a patient who developed distal acute arterial ischemia of the left leg after first cycle of combined 5-fluorouracil (5-FU) and cisplatin chemotherapy regimen for recurrent squamous-cell carcinoma of the oral cavity.

Case Report

A 64-year old woman was first admitted with a mass in the left inferior gingivo-labial sulcus. Alveolo-mandibular segment resection along with left radical neck dissection was performed disclosing the diagnosis of squamous-cell carcinoma (T2N0M0). While she was followed without any problem after surgery, four years later, she presented with a mass in the left parotis region.
Magnetic resonance imaging showed a 5x6x6 cm lesion rooting from the level of left parotid gland surrounding the left internal carotid artery. Biopsy of the lesion was consistent with squamous-cell carcinoma. Laboratory examinations; including complete blood count, electrolytes, liver function tests, and lipid profile were all within normal ranges. Electrocardiogram was normal. Past medical history was unremarkable except for the presence of obesity (Body Mass Index: 39.06). She was given neoadjuvant 5-FU and cisplatin regimen (cisplatin 20 mg/m² i.v. infusion over 4-6 hours for 5 days and 5-FU 600 mg/m² continuous i.v. infusion over 24 hours for 5 days). Five days after completion of first cycle; she complained of sudden pain, coldness and erythema on the dorsum and sole of the left foot. Digital subtraction angiography showed thrombosis of arteries of the distal left leg. In spite of anticoagulant and vasodilator therapy, ischemia gradually worsened necessitating left infrapopliteal amputation.

Discussion

5-FU has been used as an antineoplastic agent for the treatment of a variety of solid tumors since the late 1950s. In a retrospective review, 9% of patients with head and neck or gastrointestinal cancer who were treated with infusional 5-FU based chemotherapy regimens experienced thrombotic vascular events occurring concurrently with treatment or several months following the completion of therapy and consisted mainly of cardiac arrhythmias, myocardial infarction, sudden death, and thromboembolism (4). 5-FU may cause nonlethal injury to benign endothelium, an unspecific toxicity that seems to be different from the antitumor effect of 5-FU. Such injury, with the possible accompaniment of thrombogenicity, could be one of the pathophysiologic mechanisms behind the vascular toxicity of it (5).

Cisplatin is an effective and widely used antineoplastic agent in the treatment of solid tumors, especially germ cell cancer. Some cisplatin combinations have been related to cerebral vascular strokes or to myocardial infarction, sometimes preceded by Raynaud’s phenomenon; but relationship between cisplatin-based chemotherapy and large-vessel ischemic events is not clear yet (6). In a retrospective analysis, no association between chemotherapy and short-term vascular events was found (7). However, substantial impact on cardiovascular risk factors was identified in 25% of patients after chemotherapy, including grossly elevated serum cholesterol levels with or without obesity and severe arterial hypertension (8). In a recent report, four cases of distal ischemic changes related to combination chemotherapy with cisplatin and gemcitabine have also been described (9).

In conclusion; we suggest that 5-FU and cisplatin combination chemotherapy regimen should be used with great caution in elderly patients even without having preexisting cardiovascular risk factors and these patients must be monitorized closely for the signs of ischemic changes by appropriate studies and in the presence of arterial spasms, anticoagulant and vasodilator therapy should be instituted.
References


