Cancer-related Stroke due to Mural Thrombus in the Extracranial Carotid Artery

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Abstract

A 41-year-old man was admitted to our hospital because of a cancer-related stroke (CRS) caused by a thrombus of the extracranial carotid artery. He had undergone neoadjuvant radiochemotherapy for metastatic colorectal adenocarcinoma. The serum D-dimer values were within the normal range. We treated him with intravenous unfractionated heparin followed by warfarin. There were no recurrent stroke events over six months. The leading cause of a CRS is an embolism caused by hypercoagulopathy, mainly represented by non-bacterial thrombotic endocarditis. However, it was unusual that, in the current case, a thrombus of the extracranial carotid artery was formed with no significant residual stenosis, thus resulting in an artery-to-artery embolism.

Key words: acute stroke, cancer, carotid ultrasound, chemotherapy


Introduction

Cancer is often associated with a hypercoagulable state, particularly in the case of a mucinous carcinoma of the pancreas, lung and gastrointestinal tract (1, 2). Cerebrovascular complications reportedly occur in 15% of cancer patients (3). It has recently been reported that the main mechanism of a cancer-related stroke (CRS) other than the conventional stroke etiology is an embolism related to hypercoagulopathy (1, 4, 5), including non-bacterial thrombotic endocarditis and a paradoxical embolism related to deep venous thrombosis. In contrast, cases of CRS due to a large vessel thrombus have only rarely been reported. In most of them, cisplatin-based chemotherapy as well as cancer itself contributed to the thrombus formation (2, 6-10). We herein report a patient presenting with ischemic stroke due to a thrombus of the extracranial carotid artery complicating metastatic colorectal adenocarcinoma.

Case Report

A 41-year-old man was admitted to our hospital because of transient drooling, slurred speech and weakness in the left limbs 40 minutes after the onset of symptoms. He had undergone neoadjuvant therapy, including radiation and S-1 administration, for metastatic colorectal adenocarcinoma for over 1.5 months. He had no cardiovascular risk factors, except for being a former smoker. A neurological examination on presentation revealed a slight disturbance of consciousness and left inferior quadrantanopia. On laboratory tests, the complete blood count showed leukopenia (white blood cell count: 3,300/μL), while blood chemistry results, including homocysteine levels, were normal. Antinuclear antibody, SS-A, SS-B, anti-DNA and antiphospholipid antibodies were negative. Coagulation test results, including thrombin-antithrombin complex and D-dimer levels, were within the normal range. Positron emission tomography with fluorine-18 2-deoxy-2-fluoro-D-glucose integrated with computed tomography of the whole body showed a primary colorectal tumor [maximum standardized uptake value (SUVmax) of 10.2], a liver metastatic lesion (SUVmax of 4.2) and obturator lymphnode metastasis (SUVmax of 2.4). On brain magnetic resonance imaging, diffusion-weighted imaging (DWI) showed acute cerebral infarctions in the right middle cerebral artery (MCA) territory (Figure A) and distal occlusion in the horizontal portion of the right MCA (Figure B). Carotid ultrasonography demonstrated an ulcerated thrombus...
that extended 1.9 cm from the right carotid bifurcation to the ipsilateral internal carotid artery (Figure C). Transthoracic echocardiography and venous ultrasonography of the lower limbs identified no sources of the embolism. We diagnosed his condition as involving an artery-to-artery embolism based on the presence of the ulcerated thrombus in the extracranial carotid artery, and treated him with intravenous unfractionated heparin followed by warfarin. Follow-up magnetic resonance angiography a month after the symptom onset showed that the right MCA remained occluded. Follow-up carotid ultrasonography showed rapid shrinkage of the thrombus nine days after the symptom onset (Figure D), resulting in no residual atherosclerotic stenosis two months after the symptom onset (Figure E). The modified Rankin Scale score at the time of discharge was 0. There were no recurrent ischemic or hemorrhagic stroke events over six months.

Discussion

In patients with cancer, a hypercoagulable state is exacerbated by the cancer itself and factors associated with the treatment of cancer, including indwelling chatheters, surgery and chemotherapeutic agents, resulting in venous and arterial thromboses. Since a CRS in patients without the conventional stroke etiology is characterized by the elevation of D-dimer levels and the presence of microembolic signals detected by transcranial Doppler, its etiological mechanism is mainly regarded as an embolism caused by hypercoagulopathy (1, 4, 5). In contrast, cases of a CRS that produces a thrombus in a large vessel have rarely been reported, and in most of them, cisplatin-based chemotherapy was administered (2, 6-10). Thrombus formation is assumed to be due to vascular toxicity associated with cisplatin, including induced endothelial damage and increased platelet aggregation (11), as well as hypercoagulopathy due to cancer itself. Thus, it was unusual that an ischemic stroke was caused by a thrombus of the extracranial carotid artery in our patient with a metastatic colorectal adenocarcinoma receiving neoadjuvant chemotherapy with S-1 monotherapy.

The so-called Virchow’s triad, the three elements of thrombosis, comprises endothelial damage, abnormal blood flow and hypercoagulability. In line with this, it follows that thrombus formation in a CRS is primarily due to hypercoagulopathy, and is infrequently modified by endothelial damage associated with chemotherapy. The carotid bifurcation, which is the region of flow division and low shear stress, is one of the most common sites of atherosclerotic plaque (12). In the current case, although disruption of the endothelium and fibrous cap was not directly demonstrated by imaging techniques, endothelial damage associated with either one or both of atherosclerotic changes and S-1 mono-
therapy, in addition to a hypercoagulable state due to the cancer itself, might become a trigger for the formation of a thrombus at the carotid bifurcation.

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

References


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