Tumor Cells Detected in Retrieved Thrombus: Cancer-associated Stroke

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Abstract:
A 51-year-old man with a history of renal cell carcinoma presented with sudden aphasia, right hemiparesis, and dysesthesia. MRA showed left middle cerebral artery occlusion, and he was diagnosed with acute ischemic stroke and treated with intravenous recombinant tissue plasminogen activator and endovascular thrombectomy. The pathological diagnosis of the retrieved thrombus was consistent with the already-known pathological findings of the primary renal cell carcinoma. Therefore, a diagnosis of cerebral embolism caused by tumor cells was made. The pathological findings of the retrieved thrombus were important in determining the cause of ischemic stroke.

Key words: cerebral infarction, cancer, thrombectomy, thrombus

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Introduction
The pathophysiological mechanisms of stroke in patients with cancer include hypercoagulability, therapeutic or diagnostic interventions, and infection (1). However, in clinical practice, the precise diagnosis of whether stroke is caused by the cancer itself, by treatment for cancer, or by general causes of stroke remains still challenging. Tumor embolization can directly result in cerebral embolism, but there have been few reports of pathologically diagnosed tumor embolization in patients with ischemic stroke (2-5).

Case Report
A 51-year-old man with a history of primary renal cell carcinoma, pleural metastasis, and cancerous pleural effusion presented with sudden aphasia, right hemiparesis, and dysesthesia. He underwent left nephrectomy for primary renal cell carcinoma at 46 years old and subsequently received chemotherapy and radiotherapy for metastases to the adrenal gland, mediastinal lymph nodes, pleura, bone, and a carcinomatous pleural effusion. The baseline National Institutes of Health Stroke Scale (NIHSS) score was 7.

Diffusion-weighted magnetic resonance imaging (MRI) showed a hyperintense area in the left insular cortex and the left middle cerebral artery territory (Figure a). Magnetic resonance angiography (MRA) showed left middle cerebral artery occlusion (Figure b). The D-dimer level was 7.93 μg/dL. The diagnosis was acute ischemic stroke. He had diffusion-weighted imaging-fluid-attenuated inversion recovery mismatch, which indicated that the stroke had occurred within the past 4.5 hours (2), suggesting the presence of salvageable brain tissue.

He was treated with intravenous recombinant tissue-type plasminogen activator and endovascular thrombectomy. Using a Penumbra System (Penumbra, Alameda, USA) and Solitaire (Medtronic, Dublin, Ireland), a red and white combined ‘clot’ was retrieved. Successful recanalization (Thrombolysis in Cerebral Infarction Grade 2b) was achieved, and the NIHSS score improved to 1 after treatment. The time course for this patient was 102 minutes from the onset to door, 176 minutes from the onset to needle, and 257 minutes from the onset to recanalization.

The retrieved thrombus was 3 mm×1 mm×1 mm in size and consisted mainly of clotted tissue with fibrin precipita-
The histopathological examination of the retrieved thrombus showed degenerated tumor cells with clear cytoplasm (Figure c), resembling the previous findings of the renal cell carcinoma operated on five years earlier (Figure d). His 24-hour electrocardiogram, transthoracic echocardiogram, and carotid ultrasonography findings were normal. Chest CT showed pleural effusion due to the renal cell carcinoma metastasis. There was no mass lesion in the left atrium on CT. The final diagnosis was cerebral embolism due to tumor cells based on the pathological diagnosis of the retrieved thrombi and primary renal cell carcinoma.

Because the thrombi contained fibrin, subcutaneous heparin therapy was selected for secondary prevention, as for cancer-associated stroke. The patient was discharged home on the 15th day without assistance. He died two months after discharge from the hospital due to exacerbation of cancerous pleural effusion and respiratory failure associated with renal cell carcinoma. He and his family were able to achieve a satisfactory end of life.

**Discussion**

In the present case, the pathological findings of the mechanically retrieved thrombi were extremely important for determining the cause of ischemic stroke. This proved a major point, with tumor embolization from known cancer resulting in embolic stroke based on the pathologically confirmed findings of the retrieved thrombi.

There have been a few reports of mechanical tumor embolectomy performed for acute ischemic stroke in patients with cancer (3-8). The previous reports of tumor cells retrieved by endovascular thrombectomy for acute ischemic stroke are shown in Table. Those reports suggest that tumor cells can enter the bloodstream through direct invasion to the pulmonary vein or left heart, although there have been no autopsy reports to prove this. In the present case, body CT showed no evidence of gross pulmonary venous invasion, but there was pleural dissemination. The tumor cells invaded the intersegmental and interlobar veins within the lung. It appears that the tumor cells infiltrated microscopically into the subpleural small pulmonary veins in the pleu-
and then caused occlusion of the intracranial artery. Cells flowed into the left atrium from the pulmonary vein. Even in cases of subdiaphragmatic carcinoma, pleural disseminated lesions can cause cerebral embolism.

The stroke mechanism in the present patient was likely as follows: disseminated tumor cells infiltrated microscopically into the small intersegmental intrapulmonary vein and then extended to the larger interlobar vein and denatured to form thrombi. Thereafter, detached thrombi with collapsed tumor cells flowed into the left atrium from the pulmonary vein and then caused occlusion of the intracranial artery.

**Conclusions**

Prompt reperfusion therapy for cancer-associated stroke should be considered in some cases to maintain patients’ quality of life during their limited lifetime, even if their cancers are advanced, as long as each patient’s condition permits.

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

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