Spinal Infarction Related to the Adjuvant Chemotherapy for Surgically Resected Non-small Cell Lung Cancer: Report of a Case

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Received August 21, 2012; accepted February 12, 2013

We report the development of spinal infarction during adjuvant chemotherapy with tegafur, gimeracil and oteracil (TS-1) after surgery for lung adenocarcinoma. A 69-year-old female had a left upper lobectomy for pulmonary adenocarcinoma, T2aN0M0. Six weeks after the surgery, tegafur, gimeracil and oteracil were administered orally as adjuvant chemotherapy for 1 year. After 10 months of adjuvant chemotherapy, the patient suddenly showed signs of numbness and weakness in both lower limbs. The patient did not have a previous medical history, and was receiving only tegafur, gimeracil and oteracil with the stomach medication. Neurological findings showed muscle weakness, numbness and a loss of tendon reflex in both lower limbs, as well as bladder and rectal disturbance. Blood tests, brain magnetic resonance imaging and chest computed tomography showed no signs of abnormalities or metastasis. Magnetic resonance imaging of the spine showed a hyperintense lesion between the Th12 and L1 spinal levels by T2-weighted image. A spinal fluid test indicated no abnormalities, and cytological diagnosis was class II. Anti-aquaporin 4, anti-ganglioside and anti-neuronal autoantibodies were all negative. These results indicated that the patient had a spinal infarction, rather than myelitis or paraneoplastic neurological syndrome. The patient was treated with heparin and steroid pulse treatment followed by rehabilitation, and recovered sufficiently to be able to walk using a cane after 2 months. The development of spinal infarction during anti-cancer chemotherapy has not been previously reported. In this case, an association of spinal infarction with the use of adjuvant chemotherapy was strongly indicated due to the lack of abnormalities in coagulability, atherosclerotic lesions and aortic disease.

Key words: spinal infarction – adjuvant chemotherapy – TS-1

CASE REPORT

A 69-year-old female had a left upper lobectomy with a radical mediastinal lymph node dissection for pulmonary adenocarcinoma and the pathological TNM classification was T2aN0M0. Six weeks after the surgery, 120 mg of tegafur, gimeracil and oteracil (TS-1) was orally administered as adjuvant chemotherapy for 1 year (administration for 14 days followed by withdrawal for 7 days). After 10 months of adjuvant chemotherapy, the patient suddenly showed signs of numbness and weakness in both lower limbs, and was transferred to our hospital by ambulance for a thorough examination. The patient did not have a previous medical history such as hypertension, diabetes mellitus and vascular disease, and was receiving only TS-1 and stomach medication.

Neurological findings showed muscle weakness, numbness and a loss of tendon reflex in both lower limbs, as well as bladder and rectal disturbance. Blood tests showed no abnormalities such as coagulability or tumor markers, or collagen disease markers. A brain magnetic resonance imaging (MRI)
showed no signs of bleeding, infarction or metastasis; furthermore, no relapse was detected by chest CT. A spinal MRI showed a hyperintense lesion between the Th12 and L1 spinal levels by T2-weighted image (Fig. 1); furthermore, no enhancement by gadolinium-enhanced T1-weighted image was demonstrated. A spinal fluid test indicated no abnormalities such as contained cells, protein, glucose or IgG. Cytological diagnosis was class II. Anti-aquaporin 4, anti-ganglioside and anti-neuronal autoantibodies were all negative. These results indicated that the patient had a spinal infarction, rather than myelitis or paraneoplastic neurological syndrome. The patient was treated with heparin and steroid pulse treatment followed by rehabilitation. The patient recovered sufficiently to be able to walk using a cane in the second month after the development of the disease.

**DISCUSSION**

Spinal infarction is a spinal disorder caused by the occlusion of the spinal arteries. Spinal arteries have developed collateral circulation; therefore, the frequency of developing spinal infarction is low, being about one one-hundredth of that in the brain (1). Spinal infarction is largely caused by dissociation of the ascending aorta and complications after aortic surgery, and known to occur suddenly. It is believed that spinal infarction is most likely to have occurred in the case described in this study based on the neurological findings and sudden onset of symptoms; furthermore, it was confirmed by MRI results. Myelitis could also be predicted from the MRI results; however, this was dismissed since there were no abnormalities in the spinal fluid test as well as the absence of the anti-aquaporin 4 antibody. Paraneoplastic neurological syndrome could also be predicted because of the appearance of symptoms after surgery for lung cancer; however, this was also dismissed since there were no neurological abnormalities in the spinal fluid as well as the absence of the anti-neuronal autoantibodies.

TS-1 is an oral fluoropyrimidine-based anti-cancer drug. TS-1 has shown to be effective against digestive cancers, lung cancer and breast cancer. The main side effects are myelosuppression and digestive symptoms, such as loss of appetite and nausea (2). Fluoropyrimidine is also known to be the contributing factors to neurotoxicity. In our facility, after obtaining permission from the IRB, patients under the age of 80 years with stage I (T1b) and II non-small cell lung cancer who have undergone complete resection of lung cancer are generally treated with TS-1 for 1 year (administration for 14 days followed by withdrawal for 7 days), after a consent form is signed by the patients.

There has been a report regarding the development of spinal infarction by manipulation during hepatic arterial infusion chemotherapy with fluoropyrimidine (3); however, the development of spinal infarction during chemotherapy has not been reported.

In the case of stroke, there have been reports that a stroke can be triggered by cisplatin; however, the risk of developing a stroke by adjuvant chemotherapy is not increased (4). Fluoropyrimidine has also the risk of ischemic stroke, although the absolute risk is very low on the basis of presumably indirect effects on vascular endothelium.

We reported that spinal infarction developed during adjuvant chemotherapy after surgery with TS-1 for lung adenocarcinoma. In this case, the cause of spinal infarction could not be identified; however, an association of spinal infarction with the use of adjuvant chemotherapy was strongly indicated due to a lack of abnormality in coagulability as well as a lack of atherosclerotic lesion and aortic disease.

**Conflict of interest statement**

None declared.

**References**