Long-term survival of a patient with carcinomatous meningitis caused by non-small cell lung cancer: The advantage of absence of primary tumor recurrence

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Abstract The prognosis of carcinomatous meningitis is very poor, although epidermal growth factor receptor-tyrosine kinase inhibitors have recently improved it. A 56-year-old woman was diagnosed with adenocarcinoma of the lung and underwent left lobectomy. Four years after the operation, she was diagnosed with carcinomatous meningitis. There was no recurrence of lung cancer at the time of initial carcinomatous meningitis diagnosis. Epidermal growth factor receptor-tyrosine kinase inhibitors were not used for this patient, because epidermal growth factor receptor mutations were not detected. She was treated by whole-brain radiation therapy and intrathecal chemotherapy, resulting in a very long-term survival of 889 days (29.6 months) from diagnosis of carcinomatous meningitis. We can expect long-term survival in patients with carcinomatous meningitis from non-small cell lung cancer, especially in patients without the primary tumor recurrence at the time of diagnosis, even without treatment with epidermal growth factor receptor-tyrosine kinase inhibitors.

Introduction

The prognosis of patients with carcinomatous meningitis (CM) is very poor, and the median survival is reported as 4–6 weeks without therapy and 2–3 months with any therapy,1 although epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors (TKI) such as erlotinib and gefitinib have recently prolonged survival in CM patients with mutations of the EGFR gene.2–4 Here, we report a patient who survived for 29.6 months from the diagnosis of CM despite being treated by only conventional radiation therapy and chemotherapy without EGFR-TKI.

Case report

A 56-year-old woman had a medical check-up in which an abnormal shadow was detected in the left lung on X-ray images. Chest computed tomography (CT) showed a left pulmonary tumor (Fig. 1a). She was diagnosed with left adenocarcinoma without an EGFR mutation (T2N0M0, stage I), and underwent left lobectomy followed by administration of tagaful/uracil for 3 months. Four years later, she was admitted to our hospital, Akita, Red Cross Hospital, Japan, because of chronic headache, nausea and diplopia. She was diagnosed with CM based on detection of adenocarcinoma cells in the cerebrospinal fluid. No recurrence of lung cancer was detected by whole-body CT and positron emission tomography. Mutational analysis using the peptide nucleic-acid-locked nucleic acid polymerase chain reaction clamp method revealed no mutations related to lung cancer including missense mutations in exons 18, 19 and 21, and deletions in exon 19 in the EGFR gene (LSI Medience Corporation, Tokyo, Japan). Therefore, we abandoned EGFR-TKI treatment for this patient. She was treated by whole-brain radiation therapy (total, 30 Gy) followed by intrathecal chemotherapy, resulting in a very long-term survival of 889 days (29.6 months) from diagnosis of carcinomatous meningitis. We also underwent ventriculoperitoneal shunting for hydrocephalus. Malignant cells in the cerebrospinal fluid temporarily disappeared after the methotrexate treatment. She complained of severe numbness of her left leg at 8 months from the diagnosis of CM. Lumbar magnetic resonance imaging revealed contrast-enhanced lesions in the cauda equina, suggesting dissemination of adenocarcinoma cells. She was treated by radiation therapy in her lumbar region (total, 40 Gy) followed by intrathecal administration of methotrexate (5 mg/week × 13 weeks) through an Ommaya reservoir drainage system. She also underwent ventriculoperitoneal shunting for hydrocephalus.
from acute respiratory failure at 29.6 months (889 days) from the diagnosis of CM.

Post-mortem examination showed adenocarcinoma cell invasion in the subarachnoid space of the left temporal region (Fig. 1c) and the dorsal roots of the lumbar spinal cord (Fig. 1d) with superficial parenchymal invasion and diffuse white matter degeneration in the cerebrum with loss of myelinated fibers and fibrillary gliosis. Pleural and peritoneal adenocarcinomatosis were also evident. Adenocarcinoma cells were positive for AE1/AE3, CK7, TTF-1 and Napsin A, but not for CK20, which is a specific marker of lung adenocarcinoma, thus showing the operated lung cancer as its origin.

Discussion

Several reports have recently described the effectiveness of EGFR-TKI in patients with CM originating from lung adenocarcinoma with EGFR mutations. The use of EGFR-TKI was proven to confer the survival benefit of patients with CM originating from non-small cell lung cancer (NSCLC) in some retrospective studies. In contrast with the long-term survival of this patient, Umemura et al. showed that the median survival time of patients with CM originating from NSCLC without EGFR mutations was 1.4 months, which was significantly shorter than that of patients with EGFR mutations. We speculate that the absence of recurrence of lung cancer for at least 15 months during treatment of CM contributed to the long-term survival of the present patient, because primary cancer generally becomes uncontrollable in CM patients with poor prognosis.

Some large-scale studies have shown that a good performance status, intrathecal chemotherapy, systemic chemotherapies such as EGFR-TKI use, whole-brain radiation therapy and ventriculoperitoneal shunt operation are significant predictors of a better survival in patients with CM originating from NSCLC. This patient had these factors for a favorable prognosis, except EGFR-TKI use. Park et al. suggested that patients with a good performance status and those with CM at the time of initial NSCLC diagnosis are appropriate candidates for aggressive treatment, such as intrathecal or systemic chemotherapy and whole-brain radiation therapy. Patients with CM without evidence of recurrence of the primary tumor at the time of the initial CM diagnosis might also be good candidates for aggressive treatment, and they are expected to survive longer even though they are not treated with EGFR-TKI. A large case...
study with CM patients without recurrence of the primary tumor is required to establish an appropriate treatment strategy.

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**References**