Recovery from Carcinomatous Meningitis by Erlotinib

Gen Ohara^a Katsunori Kagohashi^a Koichi Kurishima^a
Mio Kawaguchi^a Hidetsugu Nakayama^b Hiroaki Satoh^a

^aDivision of Respiratory Medicine, Mito Medical Center, University of Tsukuba, Mito,

^bDepartment of Radiology, Tokyo Medical University, Japan

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A 66-year-old woman presented with a 1-month history of gradually increasing cough. On admission, physical examination was unremarkable. The serum level of carcinoembryonic antigen was elevated to 156.7 ng/ml (normal: <5.0 ng/ml). The chest computed tomography (CT) scan demonstrated a 3.5 × 2.5 cm left lung mass with several pulmonary nodules up to 1 cm in diameter in both lungs. Examination of a transbronchial biopsy revealed the tumor to be lung adenocarcinoma, having an in-frame deletion between codons 745 and 750 on exon 19 of the epidermal growth factor receptor (EGFR) gene. The diagnosis of clinical T2bN2M1a stage IV was confirmed. As the patient did not desire hospitalization any more, she received outpatient chemotherapy using modified doses of amrubicin. She received 7 courses of the chemotherapy, and the response was evaluated as partial response. She was in good condition for 8 months since the initiation of chemotherapy, but then she developed headache, nausea, and gait disturbance. Magnetic resonance imaging (MRI) of the head showed multiple brain metastases, with an intensive signal of the leptomeninges. As second-line therapy, the patient received 150 mg/day erlotinib therapy. Within 2 weeks, all her symptoms dramatically disappeared. A grade 1 (National Cancer Institute common toxicity criteria (NCI-CTC) version 2.0) skin rash was observed, but was tolerable. A follow-up MRI 1 month later showed decreases in both the size and number of brain metastases and the disappearance of the intensive signal of the leptomeninges. On the chest CT scan, the pulmonary metastases in both lungs had disappeared. The patient is currently doing well and is now, 4 months after the initiation of erlotinib, able to work.

Carcinomatous meningitis is considered to be one of the oncology emergencies requiring immediate treatment [1].

Treatment options include whole-brain irradiation, systemic chemotherapy, and intrathecal chemotherapy such as methotrexate [2]. Despite these measures, the prognosis is poor with a median survival of 2–3 months, and focal neurologic dysfunctions do not improve in most cases [1]. The benefit of EGFR tyrosine kinase inhibitors (TKIs) in the treatment of carcinomatous meningitis in patients with non-small-cell lung cancer (NSCLC) has recently attracted attention, although all publications were only case reports or case series [3–10]. Erlotinib is widely used in patients with advanced NSCLC and its clinical utility is now highly evaluated [5]; there are reports observing that erlotinib was effective in carcinomatous meningitis after the failure of gefitinib treatment [4, 6]. It is well known that the serum concentration of erlotinib is several times higher than that of gefitinib [6]. It is not likely that gefitinib, when administered at 250 mg/day, can achieve adequate levels in the central nervous system (CNS); therefore, higher doses of gefitinib may be necessary. Very recently, 2 research groups determined the concentrations of erlotinib in plasma and the cerebrospinal fluid (CSF) and confirmed that there was a measurable penetration of erlotinib into the CSF [9, 10]. This observation suggests that erlotinib may be a therapeutic option for patients with carcinomatous meningitis developing during gefitinib treatment. As the patient had a rapid onset of symptoms, she received erlotinib rather than gefitinib in order to achieve adequate therapeutic concentrations within the CNS.

In summary, we report on a rare case of NSCLC-related carcinomatous meningitis successfully treated with erlotinib.

Disclosure Statement

There is no potential conflict of interest related to the article or the research described.

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