

Adding Bevacizumab to Chemotherapy Effectively Control Radioresistant Brain Metastases in ALK-Positive Lung Adenocarcinoma

To the Editor:

Whole brain irradiation (WBI) is the standard of treatment for brain metastases in anaplastic lymphoma kinase (ALK)-positive lung cancer. However, it is difficult to treat such tumor that is refractory on WBI. Here, we presented a case effectively control of intracranial metastases by bevacizumab and chemotherapy.

CASE PRESENTATION

A 58-year-old never-smoking female presented with 2 weeks of persistent dizziness, headache, and unsteady gait. Computed tomography (CT) of chest on September 3, 2013 showed a 3.1×2.7 cm spiculated mass over left lower lung (LLL) that invaded to pleura and pericardium with ipsilateral hilar lymphadenopathy (Fig. 1A). Magnetic resonance imaging (MRI) of brain revealed multiple enhanced intracranial lesions with perifocal edema (Fig. 1B and C). The result of bronchoscopic biopsy proved lung adenocarcinoma. No activating epidermal growth factor receptor (EGFR) mutation was identified by Scorpions ARMS. The immunohistochemistry staining for ALK showed strongly positive by Ventana autostainer system.

The patient started chemotherapy with triweekly pemetrexed

(500 mg/m²) and cisplatin (60 mg/m²) after 2 weeks of WBI completed on October 18, 2013. After two courses of chemotherapy administered, she suffered from acute left lower leg weakness with focal myoclonic jerks on November 23. Magnetic resonance imaging of brain demonstrated enlarged all intracranial metastases with significant peri-tumor edema (Fig. 1E and F). On the other hand, computed tomography of chest revealed primary lung tumor regressed (Fig. 1D). To control intracranial metastases, we administered bevacizumab (5 mg/kg) on day 1 with pemetrexed and cisplatin on day 2 every 3 weeks to normalize tumor vasculature and improve drug delivery. The follow-up imaging showed regression of intracranial tumors with decreased peripheral enhancement and edema (Fig. 1H and J), as well as primary lung tumor continuing shrank (Fig. 1G). Her symptoms resolved completely. The

patient has continued on treatment for 8 months more without any neurologic adverse effects.

DISCUSSION

Intracranial metastasis is frequent in ALK-positive lung cancer patients, either for those untreated or on crizotinib treatment.¹ Most of ALK-positive lung cancer with brain metastasis response well to WBI.² For patients with progressive central nervous system (CNS) metastasis on crizotinib or radiotherapy, several next-generation ALK inhibitors showed a promising activity for CNS penetration and intracranial disease control.³ However, in the area lacks of reimbursement of crizotinib and no available new ALK inhibitors, it is very difficult to treat an ALK-positive, radioresistant brain metastasis patients. Bevacizumab, a humanized anti-vascular endothelial growth factor (VEGF) antibody, previously had

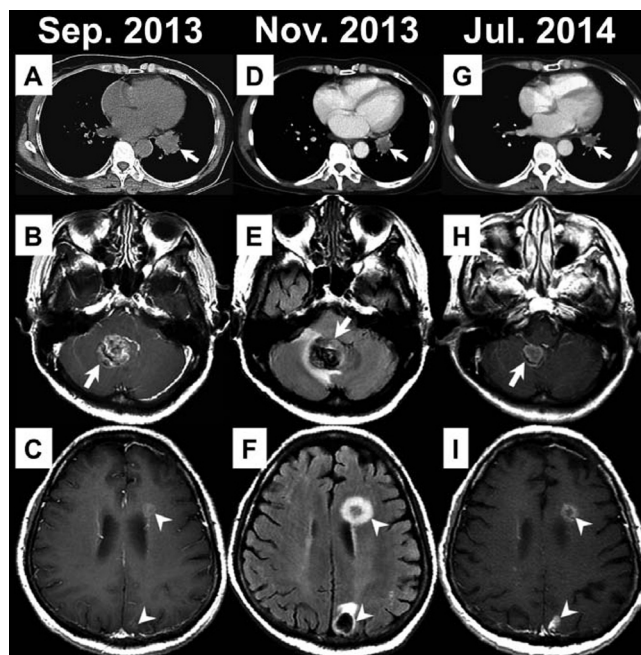


FIGURE 1. Representative image series from initial diagnosis (A–C), intracranial progression (D–F), and disease regression (G–I). A, A spiculated Left lower lung (LLL) mass in nonenhanced CT. B and C, T1 postgadolinium showed multiple intracranial metastases over right vermis, left posterior temporal, and frontal area. D, Left lower lung (LLL) tumor regressed after pemetrexed/cisplatin treatment. E and F, T2 FLAIR showed enlarged brain metastases with significant perifocal edema. G–I, Regression of primary tumor as well as intracranial metastases after adding bevacizumab to pemetrexed/cisplatin. CT, computed tomography.

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shown a great antitumor activity and good safety profiles for non-small-lung cancer patients, even for those with CNS metastasis.⁴ Several preclinical studies indicated bevacizumab lead to tumor vessels normalization and reduced interstitial fluid pressure that increased the delivery of cytotoxic chemotherapy. Lu et al.⁵ presented promising CNS response of BEEP (bevacizumab, etoposide, cisplatin) regimen for breast cancer patients with brain metastases refractory to WBI. Nine of 12 evaluable patients (75%) achieved CNS response, including six patients (50%) had greater than or equal to 80% CNS tumor volumetric reduction. In this case, on the basis of pemetrexed and cisplatin effectively controlled extracranial lesions, we added bevacizumab to increase CNS control successfully. The efficacy

of bevacizumab-contained regimen for ALK-positive-radioresistant brain metastasis is worthy to study in further prospective trials.

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