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Case study

A retrospective study of bevacizumab for treatment of brainstem glioma with malignant features ☆

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ABSTRACT

Brainstem glioma is impossible to resect completely, and patients with this type of glioma show a poor prognosis. Therefore, a more effective adjuvant therapy is required to prolong survival. Bevacizumab is an endothelial growth factor monoclonal antibody with strong anti-vascular effects, which may suppress tumor progression.

We performed a retrospective study of data from 6 patients with brainstem glioma showing malignant features who were treated with bevacizumab.

Tumor-associated lesions, as evaluated by T2 weighted or fluid-attenuated inversion-recovery magnetic resonance imaging, were reduced in all patients, although the timing of the start of bevacizumab administration and pretreatment were not uniform. Clinical symptoms improved in 4 patients and progression was inhibited in 2 patients. The Karnofsky performance status improved from 56.7 to 71.7 on average. The median reduction ratio of tumor-associated lesions was 76.3%, but tumor suppression did not last in any of the cases. Furthermore, 5 patients died of tumor progression, and 1 patient died of a complication of necrotizing colitis. The median progression-free survival after bevacizumab administration was 7 months. The median overall survival after diagnosis was 16.5 months.

Bevacizumab might be a potential therapeutic option for progressive brainstem gliomas with malignant features.

1. Introduction

The principle of treatment for glioma is surgical resection as much as possible and subsequent adjuvant therapies such as radiotherapy and chemotherapy. However, in most cases, it is impossible to resect brainstem glioma completely due to tumor localization. Furthermore, the efficacy of adjuvant therapies is limited in brainstem glioma. This type of glioma is rare and its histopathological diagnosis is not conclusive in all cases. Moreover, its clinical findings are insufficient for diagnosis, and the standard therapy for brainstem glioma has not been established. It is frequently diagnosed based on radiological findings. In such cases, adequate adjuvant therapies are prescribed on the basis of radiological diagnosis, but the resulting therapeutic response is not satisfactory. In general, patients with brainstem glioma show a poor prognosis, regardless of the tumor grade. Tumor invasion and peritumoral edema deteriorate the clinical course significantly. Although steroids have been administered to improve the clinical symptoms, their efficacy is limited. Therefore, more effective adjuvant therapy is required for brainstem glioma to prolong survival and avoid deterioration of clinical symptoms (see Figs. 1–6).

Bevacizumab is an anti-vascular endothelial growth factor (VEGF) monoclonal antibody, which has been shown to prolong progression-free survival (PFS) in patients with initial glioblastomas in a phase III randomized placebo-controlled trial (AVAglio study) [1]. The plurality of phase II trials suggests that bevacizumab might be a therapeutic option for patients with recurrent malignant gliomas [2,3,4]. This compound does not have a direct tumoricidal effect; however, its strong anti-vascular effect may suppress tumor progression and peritumoral edema. Since clinical trials to date have not studied patients with brainstem gliomas, the efficacy of bevacizumab in patients with brainstem gliomas is

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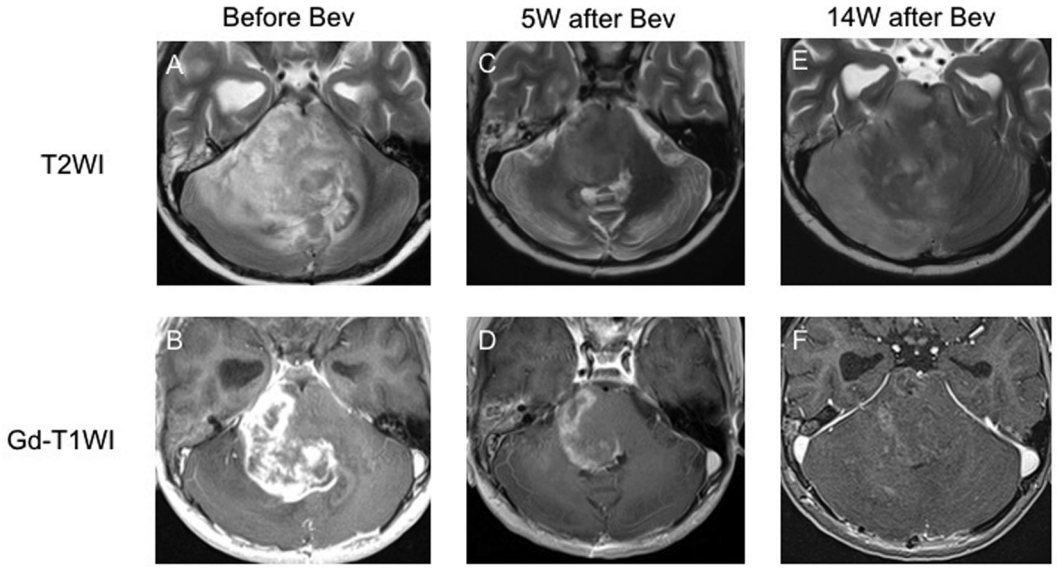

Fig. 1. Case 1. T2WI and post-contrast images at malignant progression (A, B), maximal response (C, D), and final examination (E, F). T2WI: T2 weighted image; Gd-T1WI: Gadolinium-enhanced T1 weighted image; Bev: bevacizumab.

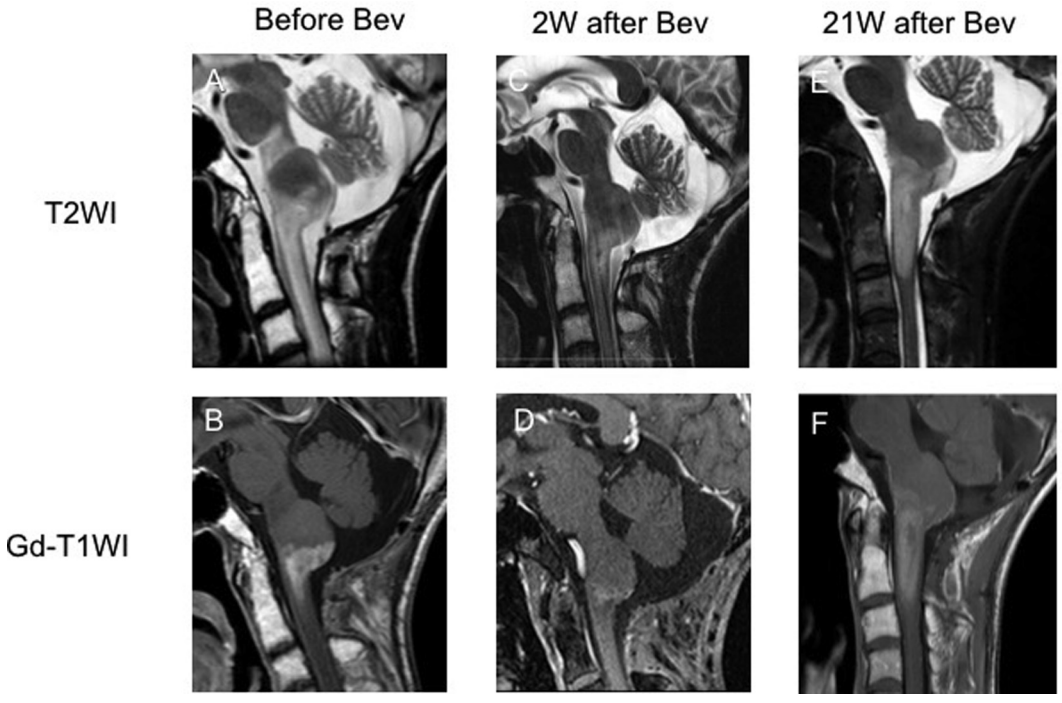

Fig. 2. Case 2. T2WI and post-contrast images at malignant progression (A, B), maximal response (C, D), and final examination (E, F). T2WI: T2 weighted image; Gd-T1WI: Gadolinium-enhanced T1 weighted image; Bev: bevacizumab.

unclear. Furthermore, case reports on brainstem glioma treated with bevacizumab are rare. Evidence of the tumor-suppressive effect of bevacizumab for brainstem glioma with malignant features could provide another therapeutic option for such tumors. Therefore, in this report, we present 6 cases of brainstem glioma showing malignant features that were treated with bevacizumab, and discuss its pharmacological effectiveness (see Tables 1 and 2).

2. Material and methods

We performed a retrospective review of the database of the Fujita Health University from June 2013 to March 2016. We obtained informed consent from all individual participants included in the study. We evaluated overall survival (OS), survival after bevacizumab administration, reduction ratio, PFS, and adverse events (AEs). The reduction ratio was measured as the sum of multiplication of the maximal diameters and orthogonal diameters in T2 weighted images (T2WIs) or fluid-attenuated inversion-recovery (FLAIR) high-intensity lesions in magnetic resonance imaging (MRI) scans (5-mm thick slices). PFS was defined as the time from the first bevacizumab administration to tumor progression according to modified McDonald criteria [1]. AEs were graded according to the Common Terminology Criteria for AEs v4.0 published by the National Cancer Institute.

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