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Efficacy of Bevacizumab for the Treatment of Radionecrosis After Stereotactic Brain Radiotherapy: Results of a Retrospective Multicentric Study

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Abstract

Objectives:

Widespread use of stereotactic radiotherapy (SRT) in the treatment of brain metastases has led to an increased incidence of radionecrosis (RN). Based on its pathophysiology, BV (BV), a VEGF antagonist, has been used in the treatment of RN in prospective and retrospective studies with a limited number of patients. In this multicenter retrospective study, it was aimed to examine the efficacy of BV for RN developing after SRT for brain metastasis.

Methods:

A total of 39 patients from 10 centers who developed RN after SRT for brain metastases and were treated with BV were analyzed retrospectively. Presence of neurological symptoms and MR findings were used to define symptomatic RN. Clinical response to BV treatment was classified as complete (not requiring additional treatment), partial (needing steroids or repeat BV), and unresponsive (requiring surgery). Demographic, clinical and treatment-related parameters, the effects of BV dose and number of courses on the development of clinical response and neurological deficit were examined.

Results:

The median age of patients was 55 (range, 38-79 years), 29.7% had a Karnofsky performance score < 90 and 59% of the patients were male. The most frequent primary diagnosis was lung cancer in 59% and breast cancer in 25.6% of patients. The median diameter of metastases undergoing SRT was 20 mm (2-45.6 mm), and 64.1% were located in the frontal and parietal lobes. Stereotactic radiotherapy was administered in 1 (41%), 3 (48.7%) or 5 (10.3%) fractions (median dose 24 Gy, dose range: 11-30 Gy). Whole-brain RT (WBRT) with a median dose of 30Gy was applied to 41% of the patients and 25.6% of the patients were reirradiated with SRT (median dose 24.5 Gy, dose range: 13-30 Gy). The total median BED3 dose (Sum dose of WBRT and 2nd series SRT) in lesions which developed RN was found to be 148 Gy (range 51.3-346 Gy). The time from the last SRT to the development of RN was 11.5 months (Range: 4-39 months). Neurological deficit was observed in 25.6% of the patients with radiological RN, and other patients had only intracranial pressure symptoms. BV doses were 5 mg/m2 every 2 weeks in 20.5% of the patients, 7.5 mg/m2 every 3 weeks in 35.9% of the patients and other patients were treated with different protocols. The median total number of cycles was 4.5 (range: 1-26). Patients (69.2%) treated with BV for RN received steroids as first line treatment. BV was used as first line treatment in 30.8% of patients. Neurological symptoms regressed in 76.9% of patients after treatment with BV (46.1% complete response, 30.8% partial response). Three out of 9 patients who did not respond to the BV underwent surgery. No additional treatment was applied to the others.

Conclusion(s):

The use of BV in the treatment of RN after SRT for brain metastases caused clinical improvement in neurological symptoms at a rate of 76.9%, and the results are similar to the rates in the literature. The use of

Cureus ${\rm BV}$ as the first choice in the treatment of RN needs to be investigated in prospective studies.