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Short Communication

The Efficacy of a Single Low-dose Targeted Bevacizumab Infusion on Brain Radiation Necrosis

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We read with great interest the recent publication by Dashti., *et al*. [1] entitled " Single low-dose targeted bevacizumab infusion in adult patients with steroid-refractory radiation necrosis of the brain: a phase II open-label prospective clinical trial". We are intrigued to find how effective and safe they found intra-arterial single low-dose targeted bevacizumab infusion to be in the management of radiation-induced brain necrosis.

To begin with, the nationwide use of radiosurgery increased significantly during the early 2000s. Unfortunately, the most common consequence of radiosurgery is genuine recurrence; we surgically remove these lesions, and in 50% of cases, we do not find a tumor [2]. This disorder is called radiation necrosis, and it is a self-perpetuating localized noncancerous inflammatory process associated with the loss of healthy tissue caused by high doses of radiation treatment [3]. These lesions may manifest and act similarly to regrowing tumors [2,3].

In addition, prevention is the most effective treatment option. Since it's hard to predict who may get radiation necrosis, prophylaxis is difficult. Steroids are the preferred medical treatment, although long-term use has harmful effects [4]. Aspirin, anticoagulants, vitamin E, pentoxifylline and hyperbaric oxygen are reported [5]. Bevacizumab is the only drug proven to work randomly [6]. Published study recommends 5 - 10 mg/kg body weight every 2 - 4 weeks of bevacizumab [7-10]. Dashti., *et al*. [1] reported new low-dose bevacizumab outcomes.

Is there a target lesion selection for a single low dose (2.5 mg/kg) of bevacizumab? Dashti., *et al*. [1] identified eight examples of benign lesions; arteriovenous malformation (80%, 8/10), as well as two cases of brain metastases and atypical meningioma (20%, 2/10). Two incidences of recurrence after a single low dosage were reported: arteriovenous malformation and atypical meningioma. While Sanborn., *et al*. [10] claimed a better prognosis in a typical meningioma case with a regimen of 10 mg/kg Q 2 weeks, Levin., *et al*. [8] found a significant improvement in thirteen instances treated with 7.5 mg/kg Q 3 weeks × 4. Included in the research by Levin., *et al*. [8] were cases of anaplastic astrocytoma (3/13), astrocytoma (1/13), oligodendroglioma (3/13), malignant schwannoma (1/13), hemangiopericytoma (1/13), pituitary adenoma (1/13), squamous cell carcinoma (1/13) and nasopharyngeal carcinoma (2/13) Liu., *et al*. [9] reported four instances of pediatric pontine glioma. With a dose of 10 mg/kg Q 2 weeks, only one instance experienced a poor result. We hypothesize that various pathologies react differently to radiation therapy and, therefore, to bevacizumab treatment for radiation necrosis. Prospective studies with large populations should study the confounding variables that contribute to the variability of response.

In conclusion, Dashti., *et al*.'s [1] research has some limitations: ten patients are modest sample size for a phase II study, which is fewer than 50; 12-month follow-up; and uncontrolled trials lack randomization, making them quasi-experimental. Dashti., *et al*. [1] underlined that the provided dose was single and modest, which may be the future effective and safe dose, but the current study cannot identify the optimal dosage and number of bevacizumab cycles for radiation necrosis.

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