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Boswellia Serrata for Management of Radiation Necrosis after Stereotactic Radiosurgery for Benign Conditions and Brain Metastases

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Abstract
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Abstract

Objectives:

Radiation necrosis (RN) is the dose limiting side-effect of stereotactic radiosurgery (SRS) for both brain metastases as well as benign conditions. Oral corticosteroids continue to be the mainstay of management; however, they have multiple side effects and drug interactions. Boswellia serrata (BS) is an over-the-counter supplement used for its anti-inflammatory properties and has been recently shown to reduce cerebral edema after brain RT. We evaluated the response rates with BS in a series of patients with brain metastases or benign conditions who developed RN after SRS.

Methods:

We included patients who developed grade 1-3 RN after SRS and were treated with BS. Patients were prescribed over the counter BS 4.2-4.5g daily in divided doses. Follow-up MRI imaging was obtained every 2-3 months after starting BS. Response was assessed using Response Assessment in Neuro-Oncology (RANO) criteria. Primary endpoint was overall response rate defined as RANO CR or PR or decrease in edema volume on T2-FLAIR MRI to ⩾30% from baseline.

Results:

A total of 113 patients were included, of which 107 underwent SRS for brain metastases, 3 for arterio-venous malformations(AVM), 2 for vestibular schwannoma, 1 for meningioma and 1 for obsessive compulsive disorder(OCD). Patients had Grade 1-3 CTCAE v5.0 RN (G1=30.1%, G2=65.1%, and G3=4.8%).
For patients with brain metastases, median age was 62.8 years (range 36.9 – 50) and median RT dose was 24 Gy in 3 fractions. Median follow-up after starting BS was 7m and 91% patients had at least 1 follow up MRI available to evaluate response. The best response was complete response (CR) in 14% patients and partial response (PR) in 40.4% while 26.3% had stable disease (SD) and 10.5% had progressive disease, yielding an overall response rate of 59.6% (CR+PR) in eligible patients. Median time to best response was 3m (3-15m) and median duration of response was 8.5m (2-31m). Percentage of patients who had any response (CR or PR) at 3, 6, 9 and 12 months was 30.8%, 37.5%, 60.0% and 68.4%, respectively. At baseline, 56% patients presented with progressive neurologic symptoms of which 83% required steroid use, while only 44% of asymptomatic patients needed steroids. 18.9% patients on long-term steroids had a decreased steroid requirement after starting BS. No patients had any CTCAE grade 3 or higher toxicities. 12.3% had any adverse events of whom 7% had grade 1 and 5.3% had grade 2 gastrointestinal intolerance or diarrhea.
Among patients with benign conditions, 2 patients (28.6%) had a CR and 4 (57.1%) had a PR, with 1 patient having no available imaging for response assessment. Median age was 31.0 years (range 12 – 80). None of the patients had any adverse events. Specifically, 1 patient with OCD who underwent staged bilateral gamma knife ventral capsulotomy, developed early grade 2 RN (3 months post SRS) and subsequently steroid induced paranoid disorder (5 months post SRS). He was tapered off steroids and started on BS. He had a complete response with resolution of T2F edema and marked reduction in post-contrast enhancement 3 months after initiating BS, with no added toxicities.

Conclusion(s):

We observed response rates of 60% and 100% with the use of BS in our patients with RN after SRS for brain metastases and benign conditions respectively. It was safe with no significant additional side-effects or

increased risk of hemorrhage in patients with AVMs. More than one-third of patients with RN were able to avoid long-term steroid use. BS is an easily available over-the-counter drug that appears to be a safe and promising treatment option for RN and can potentially decrease steroid dependence in these patients. Further prospective studies comparing BS with placebo are warranted.