Intra-arterial and Intra-venous Delivery of Bevacizumab Have Synergistic Effects in Recurrent Glioblastoma Treatment: Impact on Symptom Control, Steroid Dose and MRI Tumor Volume

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Introduction

Current salvage therapy for recurring high grade gliomas, glioblastoma multiforme (GBM) and anaplastic astrocytoma has little impact on the dismal prognosis after failure of first line therapy. Insufficient delivery across the blood brain barrier (BBB) by intravenous administration seemingly is one of the impeding factors in employing an effective treatment regimen. Bevacizumab (BV), a humanized monoclonal antibody targeting VEGF-A, leads to symptom improvement primarily by reducing peritumoral edema around these highly vascular tumors.

Methods

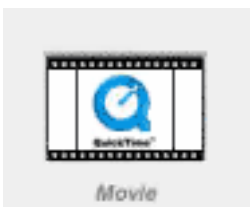
Seventeen patients demonstrating treatment failures, increase of over 25% under standard chemotherapy, were assigned in nonrandomized fashion to one of three treatment arms:

A. 12 patients, intra-arterial (IA) Bevacizumab single dose (15mg/kg) followed by biweekly intra -venous (IV) bevacizumab (10mg/kg)

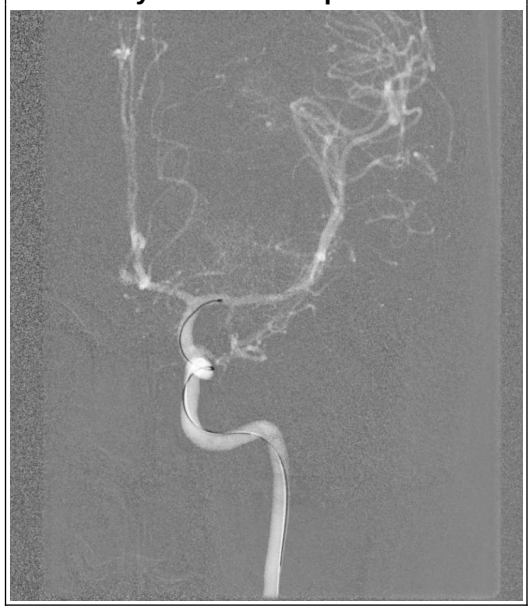
B. 2 patients, IA Bevacizumab, single dose (15mg/kg)

C. 3 patients, repeat IA bevacizumab (15mg/kg). BBB disruption with Mannitol was used in each super-selective intra-arterial BV infusion

Infusion of mannitol followed by bevacizumab into the left MCA



Visualization of left internal carotid artery and catheter placement



Results

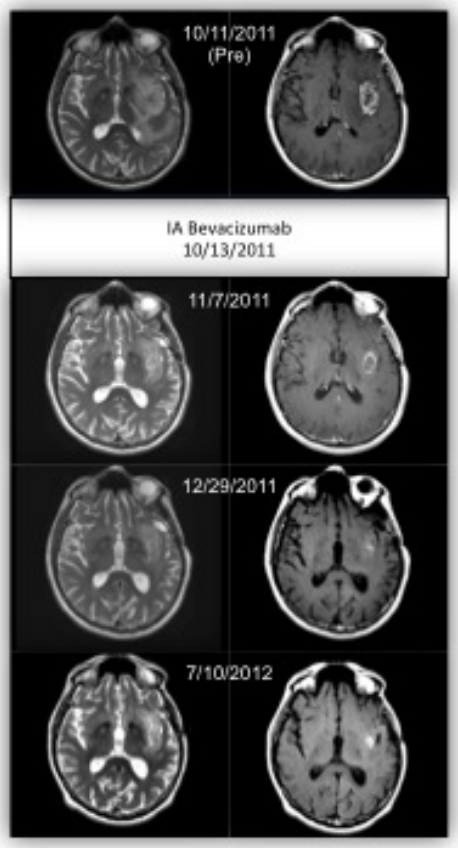
Clinical response and symptom improvement were observed in four group A patients (33.3%). One patient described vision improvement in group C. The mean Karnofsky performance score after treatment was 77±11, with the best score seen in arm C, 80±0. A decrease in dexamethasone dose was possible in two IA+IV patients and in one single dose IA patient, only three patients in arm A requiring increasing steroid levels for symptom control.

According to the RANO MRI criteria, ten patients (83.3%) in group A showed a decrease in tumor volume while all patients with single IA BV demonstrated stable disease. However, progression of disease was noted at two months in two out of three group C patients (66.6%). In terms of toxicity, pulmonary vessel thrombosis, truncal rash and transient groin hematoma were identified in three patients of arm A.

Conclusions

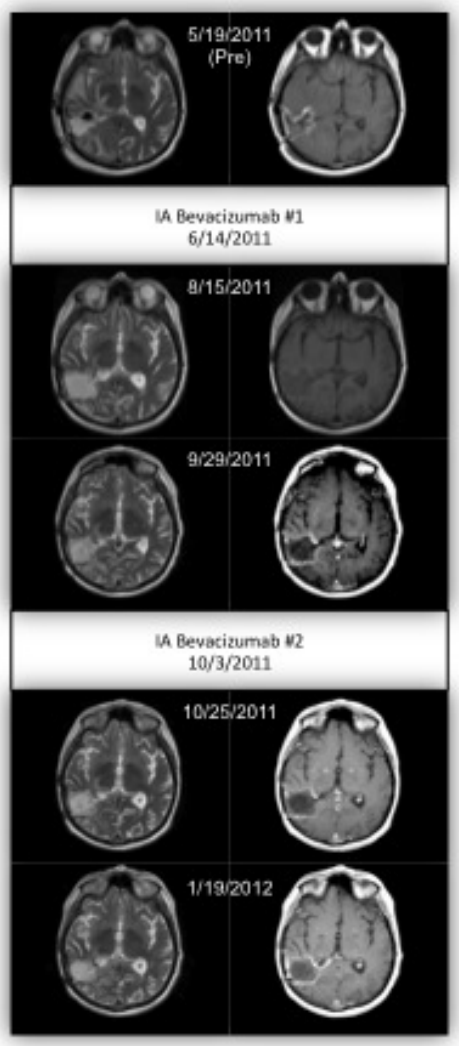
Intra-arterial combined with intra-venous delivery of bevacizumab is an effective treatment method for recurrent GBM leading to symptom alleviation, stable steroid dosage and imagistic tumor response.

MRI series in a patient recieving IA followed by IV bevacizumab



T2 (left side); T1 (right side)

MRI series in a patient recieving only IA bevacizumab



T2 (left side); T1 (right side)

References

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(2) Chang et al., Lancet Neurology, 2012;13(5):e196-204
(3) Boockvar et al., World Neurosurg. 2012;77(1):130-4