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LETTER TO THE EDITOR

Bevacizumab in adult malignant brainstem gliomas

Shahzad Raza · Martin Donach

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To the Editor:

Torcuator et al. recently presented a case report in the Journal of Neuro-Oncology regarding an adult Brainstem glioma (BSG) treated with Bevacizumab and Irinotecan. The authors speak about clinical benefit and sustained radiographic response in an adult patient with diffuse BSG. They noted initial discordance between clinical improvement and increased enhancement on MRI, an enhancement which decreased in subsequent scans [1]. However, the report lacks clarity in terms of the neuro-radiographic characteristics on MRI which are correlated with high grade tumors, as well as the presence/absence of several other prognostic factors which may have an impact on clinical response and survival.

Unfortunately, the data concerning BSG in the pre-MRI era are mostly reported in neurosurgical series where both pediatric and adult patients are grouped together [2]. Several of the author's observations on the prognosis of the disease seem to stem from this. Recent studies in adults have shown that adult patients with BSGs tend to do better than children. Those patients who do better present without necrosis on MRI, low-grade histology and longer duration of symptoms (>4 months) prior to diagnosis. [2–5]. Table 1 presents a summary of the more important prognostic factors.

S. Raza (✉)
Department of Neuro-Oncology, New York University Langone Medical Center, New York, NY 10016, USA
e-mail: shahzad.raza@nyumc.org

S. Raza · M. Donach
Department of Radiation Oncology, New York University Langone Medical Center, New York, NY 10016, USA

Despite all these controversies, if, according to the authors, this patient had a high grade tumor on MRI and poor prognostic factors, then the response to bevacizumab and irinotecan can be considered truly impressive. But discordance between clinical and radiological responses in these tumors is not uncommon. The authors mention the importance of anti-edema effect of Bevacizumab. VEGF (Vascular Endothelial Growth Factor) inhibitors, as important determinants of capillary permeability, may be responsible for decreased enhancement (and vasogenic edema) which could result in transient improvement even in the absence of a substantial impact on the tumor burden [2, 6].

At our institution we have treated one adult affected by malignant infiltrative diffuse BSG who presented with shorter duration of symptoms (<3 months), cranial nerve deficits and heterogeneous contrast enhancement in the pons and medulla with a rim of necrosis (high grade using MRI).

This case of malignant BSG was treated with Bevacizumab and concomitant Temozolomide and radiation because the treatment protocol (later published by Narayana et al. [7]) was already open at our institution and preliminary results were proving Bevacizumab to be safe with radiation and Temozolomide in the upfront management of high grade gliomas. At 6-month follow up, contrast enhancement disappeared, marked reduction was observed in non-enhanced tumor volume and perfusion drop off. At 30-month follow up, the patient is alive and stable with no new neurological symptoms.

Nonetheless, given the enthusiasm for the use of Bevacizumab in adult BSGs, response should be interpreted in the context of prognostic factors if no biopsy is available for these tumors.

Table 1 Prognostic factors

Prognostic factors [2–4]	Prognostic significance
Demographics	
KPS > 70	Good
Race: Caucasian	Poor
Age > 40	Usually Poor
Need for steroids	Poor
Clinical Presentation	
Duration of symptoms ≤ 4 months	Poor
MRI findings[a]	
Heterogeneous contrast enhancement (T1) in pons and/or upper medulla[b]	Poor
Necrosis	Poor
Dorsal exophytic component	Good prognosis (surgical candidate)

[a] MRI has become the accepted standard for diagnosis of a brainstem glioma

[b] Definition of malignant Brainstem glioma

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