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Case Report

Mapping angiography and transarterial technetium macroaggregated albumin particle simulation of recurrent atypical intracranial meningioma: feasibility for potential vascular brachytherapy ☆

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ABSTRACT

Atypical meningioma (AM) (WHO-II) has a recurrence rate of 28% after gross total resection (GTR) with limited salvage options. Transarterial therapies may provide treatment opportunities in AM patients who exhausted standard-of-care therapy. In cases where favorable tumor vasculature and particle simulation demonstrate acceptable target dose, Yttrium-90 trans-arterial radioemobilization (TARE) could theoretically provide salvage therapy. A 67-year-old man presented with recurrent AM post gross total resection with adjuvant radiotherapy in 2012, 2014, and 2016. The patient was deemed a poor candidate for additional therapies. Tumor vasculature mapping was performed to determine TARE candidacy. Super-selective angiography and contrast-enhanced cone-beam computed tomography angiosomes demonstrated predominant pial collaterals and minor supply from a middle meningeal artery branch. Particle simulation was performed by infusing 0.3 mCi of 99mTc-macroaggregated albumin (99mTc-MAA). SPECT/CT-MRI fusion demonstrated conformal activity solely within the tumor volume perfused by the middle meningeal artery branch with a lung shunt fraction of 54.7%. The patient subsequently received off-label Nivolumab (PD-1 inhibitor). Mapping angiography for AM using 99mTc-MAA is feasible. It may identify candidates for TARE and potential AM patients with favorable blood supply. The potential for conformal intracranial vascular brachytherapy is intriguing, however, altered arterial supply in recurrent tumors is challenging.

☆ Declaration of Competing Interest: Beau Toskich is an advisors to Boston Scientific.

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Introduction

Meningioma is the most common primary intracranial tumor. According to the World Health Organization (WHO), meningioma is classified into 3 groups: WHO grade I (benign), II (atypical), and III (anaplastic) with grade II prevalence and recurrence rates reported at 5%-34% and 20%-50%, respectively [1,2]. Recurrent atypical meningiomas (AM) are particularly aggressive. Conventional treatment includes repeat resection, external beam radiotherapy, and systemic therapy with a median survival of approximately 34.6 months and a 5-year survival of 36% [3,4]. There is no consensus on the optimal treatment strategy for this patient population, and each therapy has unique limitations.

The deficiencies of available treatments for recurrent AM have driven the need for exploring new therapies. Ablative transarterial radioembolization (TARE) with Yttrium-90 (90Y) containing microspheres has emerged as a safe and effective therapy for unresectable hepatocellular carcinoma (HCC) and is one of several locoregional therapies recommended by the American Association for the Study of Liver Disease [5]. The hypervascular nature of most HCC allows for preferential transarterial deposition of radioactive microspheres into the tumor vascular bed, delivering high dose brachytherapy while effectively sparing adjacent structures. TARE for HCC has demonstrated ablative capabilities with complete pathologic necrosis rates of greater than 50% at >190 Gy in segmental applications for tumors ≤3 cm [6,7]. Segmental ablative TARE for lesions ≤5 cm has shown comparable outcomes to establish definitive therapies in patients with preserved liver function [8]. Patient selection for ablative TARE in the treatment of HCC is predicated on favorable arterial supply to tumor and an expendable volume of liver within the targeted angiosome. TARE candidacy has been conventionally determined via mapping angiography with the use of potential treatment vessel contrast-enhanced cone beam computed tomography (CT) and transarterial administration of Technetium-99m macro aggregated albumin (99mTc-MAA) SPECT-CT scintigraphy. As previously discussed by Salem et al in 2006, meningiomas that are safely accessed angiographically could potentially be considered for TARE [9]. Herein presented is a feasibility report on the mapping angiography and transarterial 99mTc-MAA particle simulation of recurrent AM.

Case report

This report was performed in accordance with institutional review board guidelines. A 67-year-old right-handed man with history of left frontotemporal AM presented with local recurrence per MRI. He previously underwent gross total resection with adjuvant radiotherapy in 2012, 2014, and repeat gross total resection in 2016. A multidisciplinary team deemed the patient a poor candidate for additional surgery or radiotherapy. Given the hypervascular nature of AM, tumor vasculature mapping angiography was performed to determine TARE candidacy. Superselective angiography and concurrent cone beam CT acquisition of both intra- and extracranial AM angiosomes demonstrated extensive truncation of middle meningeal branches due to previous resection, predominant recruitment of pial tumor supply, and focal tumor supply originating from a distal left middle meningeal artery branch (Fig. 1). There was no extracranial enhancement identified from either selected blood vessel. Particle simulation was performed by infusing 1 cc of a 0.3 mCi of 99Tc- MAA saline suspension via the middle meningeal artery branch (use of this agent was off-label). The patient tolerated the procedure well. Subsequent SPECT-CT/MRI fusion demonstrated conformal activity solely within the volume of middle meningeal artery perfused tumor (Fig. 2). No activity was identified within the recurrent tumor located along the brain interface confirming its supply from the intracranial vasculature rather than the middle meningeal artery. The lung shunt fraction was 54.7%. Given the large volume of pial tumor supply, the patient was treated with off-label Nivolumab (Ono Pharmaceutical) therapy and expired 7 months after treatment. Consent for publication was obtained form the patient's next of kin.

Discussion

Resection, external beam radiotherapy, and systemic therapy represent the current standard of care for AM. Unfortunately, there are limitations to all 3 modalities with high rates of recurrence. Preoperative meningioma embolization is routinely practiced and there is some evidence to support the pursuit for definitive transarterial embolic therapy in select patients [10]. Although meningiomas and HCC are histopathologically different tumors, both are typically radiosensitive and hypervascular. Therefore the concept of transarterial brachytherapy for recurrent AM refractory to standard treatment is intriguing.[11,12], therefore, the concept of transarterial brachytherapy for recurrent AM refractory to standard treatment is intriguing. An established advantage of brachytherapy over stereotactic radiosurgery lies in its highly conformal energy deposition with zero entry dose. This property could allow for treatment of tumors adjacent to critical structures which have already received the maximum external beam radiation dose with ablative intent.

The other limitation to TARE is pulmonary radiation dose occurring as a result of arteriovenous shunting within the tumor. Mariani et al performed planar scintigraphic analysis of pulmonary shunts in meningiomas via transarterial injection of 99mTc-MAA with a calibrated diameter of 25–50 microns demonstrating shunt rates of less than 5% in 9 of 11 tumors (range 0%–86%), but recurrent AM was not included in the study [13]. While the lung shunt in this report was sizeable at 54.7%, the small target tumor volume (13 cc) would permit up to an 1800 Gy (1.06 Gigabecquerel) Medical Internal Radiation Dose administration and remain within the glass microsphere manufacturer recommendations for a single session lung dose (30 Gy). This report incorporates conventional angiography with the added data of contrast-enhanced cone beam CT and SPECT-CT/MRI fusions to improve the understanding of recurrent AM blood supply and its intratumoral particle dynamics [14]. While a volume of potentially treatable

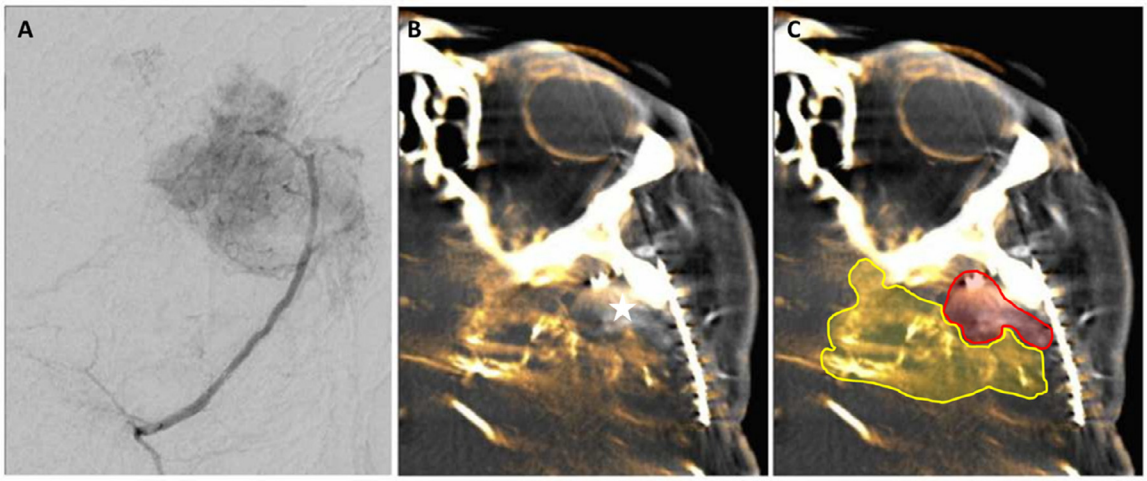

Fig. 1 – Selective angiography of the left middle meningeal artery (A) demonstrates truncation due to previous resection and focal supply to intracranial AM (Asterisk). Contrast enhanced cone beam CT (B) fusion of the intracranial (orange tint) and middle meningeal (asterisk and white tint). Pial angiosomes within the middle cranial fossa (yellow highlighted region) and meningeal supply to the tumor (red highlighted region) (C).

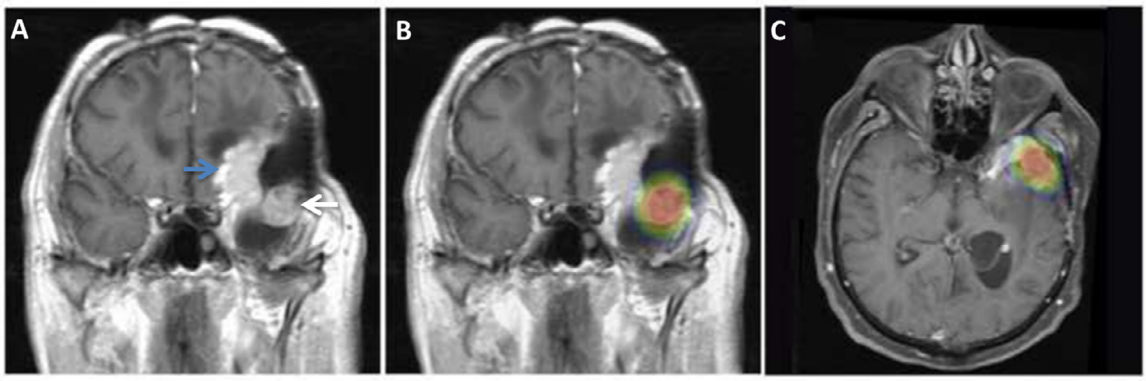

Fig. 2 – SPECT-CT/MRI Coronal native (A), coronal fused (B), and axial fused (C) images demonstrate 99mTc-MAA activity solely within the tumor perfused by the middle meningeal artery. Note the highly conformal deposition of sphere activity simulating brachytherapy (white arrows) and absence of uptake within the pial supplied tumor (blue arrows).

tumor was identified, the recruitment of pial collaterals and the truncations of meningeal supply to heavily pretreated AM identified in this case may represent the main limitation to transarterial therapies in this disease population. As such, while TARE candidacy of an untreated meningioma was not evaluated, native vascular supply may provide more favorable conduit for brachytherapy. Although tumors should not be routinely engaged unless complete therapy can be offered, vascular truncation may not limit the transarterial delivery of molecular agents or the partial treatment of tumor, perhaps as a means of antigen presentation to augment the effects of immunotherapy [15]. If pial blood supply should be targeted for TARE, the eloquence of a potential treatment angiosome would need to be assessed prior to treatment. This could be potentially accomplished with contrast-enhanced cone beam CT fused with functional neuroimaging. Nevertheless, the complexity of blood supply identified in this case highlights the added value of mapping angiography and 99mTc-MAA simulation. Other limitations to this report include a single case analysis and the current lack of a more accurate treatment surrogate for glass microspheres. The 99mTc-MAA particles used in this report ranged from 10 to 100 microns while the Mariani et al study [13] used more precisely calibrated aggregates and suggested that treatment of meningiomas could be considered with particles of equal or greater size (glass and resin 90Y microspheres range from 20-30 microns to 20-60 microns, respectively).

Mapping angiography and particle simulation of recurrent atypical intracranial meningioma for potential vascular brachytherapy is feasible. The concept of radioembolization is intriguing in this hypervascular tumor. Altered arterial supply in heavily pretreated tumors may present a disadvantage to transarterial therapies. A better understanding of angioarchitecture and the application of multimodality imaging to

asses flow patterns and functional significance may allow for more effective targeted therapies for an otherwise untreatable disease.

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