Bevacizumab-induced regression of anaplastic meningioma

Anaplastic meningiomas (World Health Organization grade III) are aggressive tumors, with a median overall survival time of 15 months [1]. Resection and focal radiotherapy are essential parts of the treatment. However, there is no established chemotherapy for patients without further surgical or radiotherapeutic options. After an initial report on successful therapy with hydroxyurea in progressive meningiomas, additional case series did not further substantiate this effect in low-grade and malignant meningioma [1]. More intensive chemotherapy on adriamycin base has been suggested to be associated with some benefit [2], but this anecdotal experience has never been explored systematically. Temozolomide, irinotecan and epidermal growth factor receptor inhibitors [3] have proven unsuccessful, while interferon-alpha-2B may stabilize recurrent meningiomas but does not induce meningioma regression. Recent developments include the application of a somatostatin preparation to patients with scintigraphy-proven somatostatin-receptor-positive relapsing meningioma showing partial responses in 25% of patients [4]. In the search for new treatments, it appears promising that meningiomas are often vascularized tumors and might therefore be amenable to antiangiogenic therapy. In particular, malignant meningiomas produce high levels of vascular endothelial growth factor (VEGF) [5]. On this base, it appears to be consequent to apply antiangiogenic therapy to otherwise untractable malignant meningioma. We here present the first patient with a substantial regression of an anaplastic meningioma upon therapy with the VEGF antibody bevacizumab.

At the beginning of 2008, the 52-year-old female patient developed a progressive psychomotoric syndrome and fluent aphasia. A large tumor in the trigonum of the left lateral ventricle (Figure 1A, A1) was subsequently completely resected. Histology revealed anaplastic meningioma with cytological signs of atypia, necrosis, vascularization and up to 39 mitotic figure per 10 high-power fields. The patient received postoperative adjuvant radiotherapy of the tumor region (60 Gy in 2 Gy daily fractions). Control magnetic resonance imagings (MRIs) 8 and 15 months after resection showed a tumor relapse with progressive lesions along the transventricular approach extending to the region medial of the trigonum (Figure 1A, A2 and A3). Repeat surgery and re-irradiation was regarded as inappropriate. Due to the lack of alternatives, experimental therapy with bevacizumab 10 mg/kg body weight every 2 weeks was started after obtaining written informed consent. Already at the first control MRI 6 weeks after start of bevacizumab, the contrast-enhancing tumor had regressed substantially showing a partial response (Figure 1B, B1–B6). Also, the hyperintense lesions on FLAIR and T2-weighted MRIs had slightly regressed in the sense of a minor response. Six months after the start of bevacizumab, MRI continues to show a partial response. Bevacizumab therapy was so far tolerated well without hypertension or any other side-effects and is intended to be applied until progression of the tumor. The patient gave written informed consent for publication of his case report.

This is the first report of a partial remission of an anaplastic meningioma induced by antiangiogenic therapy. The fact that the regression did not only include the contrast-enhancing T1 lesions but also the T2 hyperintensities in the center of the tumor (not only the peripheral edema zone) suggests a true tumor regression beyond mere vascular effects and pseudoresponse appears to be unlikely. Since anaplastic meningioma is a devastating disease without established chemotherapeutic option, the therapeutic success presented here is substantial. On the base of the presented case, bevacizumab therapy should be explored further in this indication.


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Figure 1. Magnetic resonance imaging (MRI) scans documenting the course of the anaplastic meningioma. (A) Development until the start of bevacizumab therapy. Preoperative MRI scans revealed a large intraventricular, contrast-enhancing tumor, which was localized in the left trigonum (A1). MRI scans 8 months after surgery showed some contrast enhancement along the transventricular approach (A2). Seven months later (15 months after surgery), MRI showed a clear enlargement of the contrast-enhancing structures on T1-weighted scans (A3), suggesting a recurrent tumor. (B) Response of recurrent tumor to bevacizumab therapy. Before bevacizumab therapy, a new contrast-enhancing lesion medial of the transventricular approach was observed (arrows, B1 axial contrast-enhanced T1 image, B2 coronal contrast-enhanced T1 image). Also, T2 hyperintensities in this area and lateral to it were observed (B3). Following three courses of bevacizumab, the contrast-enhancing area substantially decreased in size on T1-weighted axial (B4, arrow) and coronal scans (B5, arrow). On T2-weighted scans, a slight reduction of T2 hyperintensities was observed (B6, arrow). The insets show the enlarged tumor region on T2 images before therapy (B3) and after three courses of bevacizumab (B6). Particularly, the dorsal parts of the T2-hyperintense lesion (arrows) showed a mild regression. A subsequent MRI scan 3 months later revealed no change compared with the first control after initiation of bevacizumab (not shown).