Brain tumor dispersal is the major cause behind the extreme difficulty of treatment and the inevitable recurrence of malignant gliomas. Determining the mechanism underlying the invasion of brain tumor cells will suggest rational therapeutic strategies. Importantly, acquisition of a highly aggressive invasive phenotype is being observed in patients with recurrent malignant gliomas treated with antiangiogenesis therapy and is considered to be responsible for the therapy failure. Although the cause for this tumor behavior remains elusive, it has been hypothesized that the tumor microenvironment may be one major influence in the invasive development. In this regard, we have recently described the recruitment of Tie2-expressing monocytes (TEMs) into the tumor/normal brain interface upon anti-VEGF therapies in preclinical models and in human surgical specimens, and reported that this specific myeloid population is responsible for the heightened invasive properties of brain tumor stem cells. Here we investigated changes in the cytokine milieu of these tumors and identified increased expression of Angiopoietin 2 (Ang2), a Tie2 ligand, after therapies targeting either VEGF (bevacizumab, aflibercept) or VEGFR (DC101), but no after standard chemotherapy. In vitro and in vivo models were combined to decipher the role of Ang2, and we observed that expression of Ang2 functioned as a potent chemoattractant of TEMs. Moreover, we observed that Ang2 stimulates the tissue remodeling properties of TEMs, further enhancing the pro-invasive properties of this tumor recruited population. Of interest, modulation of molecules blocking the Ang/Tie2 axes in a preclinical model jeopardizes the tumor recruitment of TEMs and drastically resulted in a complete abolition of the heightened invasion induced by antiangiogenesis therapy. These results might have important implications in the clinical scenario since decrease of the invasive tumor pattern could potentially render recurrent tumors amenable to surgical removal ultimately prolonging the survival of patients with malignant gliomas.