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Imaging

The effect of bevacizumab (Avastin) on neuroimaging of brain metastases

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Abstract

Background: Bevacizumab is FDA approved to treat colon cancer and is currently used off label for metastatic breast, kidney, and lung cancers. Bevacizumab is a monoclonal antibody that binds to, and inactivates, VEGF and is believed to be antiangiogenic.

Case Description: The authors report the case of a 54-year-old woman with metastatic infiltrating ductal breast carcinoma who developed left occipital and right parietal intraaxial contrast-enhancing masses on surveillance magnetic resonance imaging (MRI). After surgical resection, she was placed on bevacizumab for control of systemic disease. Six months later, a nonenhancing right occipital lesion was detected on MRI. After stopping bevacizumab therapy, the patient underwent microsurgical resection of the lesion. Histopathologic examination was consistent with metastatic breast cancer indistinguishable from her previously resected enhancing brain metastasis. Six weeks after stopping bevacizumab therapy and 3 weeks after microsurgical resection, a new contrast-enhancing mass was noted on magnetic resonance in the right temporal lobe.

Conclusion: This case is unique in that we have neuroimaging on prebevacizumab, concurrent bevacizumab, and postbevacizumab brain metastases in the same patient with a single cancer primary, thus, assuring that alterations in neuroimaging characteristics are consistent with bevacizumab effect. As an internal control, it provides strong support for the premise that bevacizumab therapy can confound the diagnosis of brain metastases because of its effect on tumor enhancement.

Keywords: Brain neoplasms; Breast neoplasms; Drug therapy; Immunization, passive; Magnetic resonance imaging; Neoplasm metastasis

1. Introduction

Angiogenesis, the process whereby new blood vessels are formed, plays a pivotal role in the development, growth, and metastasis of malignant tumors [4,6]. Several growth factors have been identified as possible regulators of angiogenesis [5]. One of these growth factors, VEGF, a cytokine that is present in various human tumors and a potent inducer of vascular permeability, is considered to play an important role in tumor angiogenesis [1-3,9]. Bevacizumab (Avastin) is a monoclonal antibody that binds to, and inactivates, VEGF. Approved by the FDA as first-line therapy for metastatic colon cancer in 2004, bevacizumab is being used off label for a number of cancers, including metastatic breast, kidney, and lung cancers, and many of these patients eventually develop metastatic brain tumors. We report an internal controlled study where a patient developed separate metastatic brain tumors from the same primary cancer before, during, and after bevacizumab treatment, which allowed us to infer the effect of bevacizumab on the neuroimaging characteristics of metastatic brain tumors while controlling for the individual patient and primary tumor biology.

2. Case report

A 54-year-old woman with a history of metastatic infiltrating ductal breast carcinoma treated with bilateral

Abbreviations: DCE-MRI, dynamic contrast-enhancing MRI; FDA, Food and Drug Administration; FLAIR, fluid attentuated inversion recovery; VEGF, vascular endothelial growth factor.

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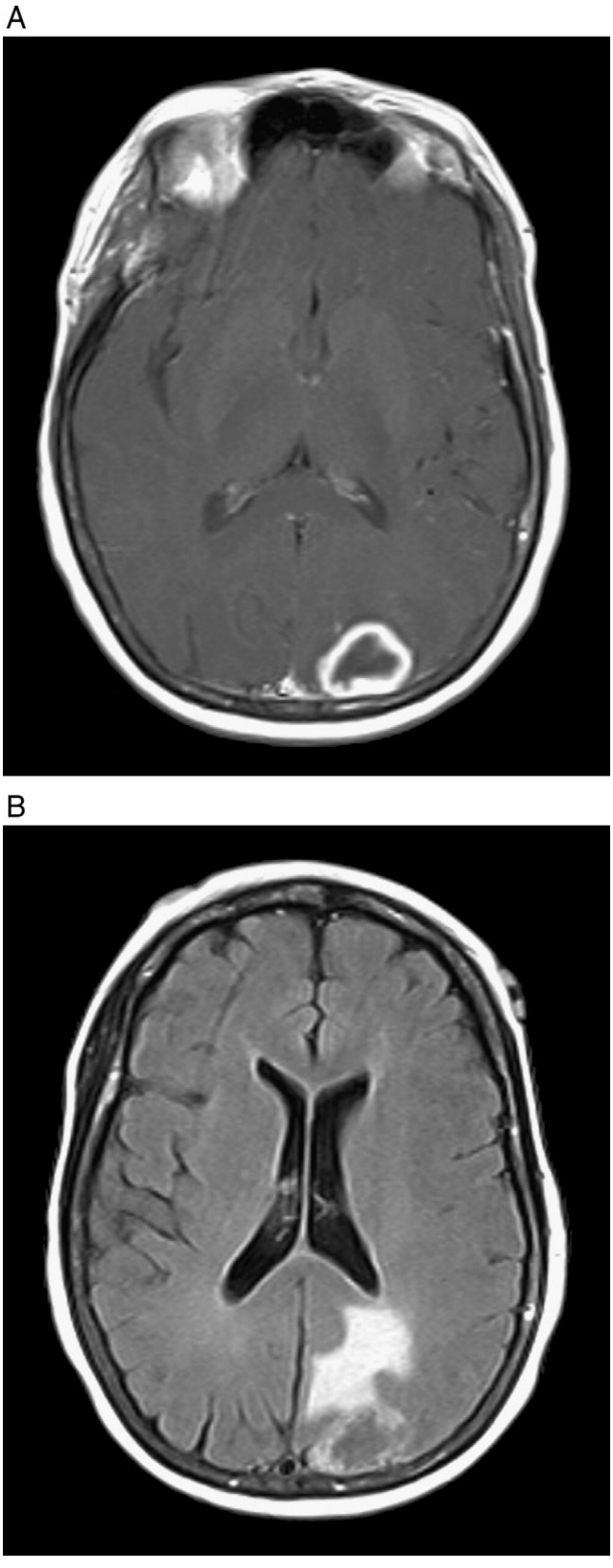
mastectomies, chemotherapy, and radiation was found to have a left occipital and right parietal contrast-enhancing masses with surrounding vasogenic edema on surveillance magnetic resonance imaging (MRI) (Fig. 1). She underwent left occipital and right parietal craniotomies for microsurgical resection of these lesions, followed by stereotactic radiosurgery to the resection beds. After the procedures, she was placed on bevacizumab for control of her systemic disease. After 6 months of treatment on bevacizumab, a right parietal nonenhancing lesion without surrounding edema was detected on a routine screening MRI (Fig. 2). Based on the nonenhancing character of the new lesion and the absence of surrounding edema, nonneoplastic processes such as granuloma, inflammation, and previous hemorrhage were considered in the differential diagnosis, although a metastatic lesion could not be ruled out considering the patient was on an antiangiogenic agent.



3. Results

Histopathologic examination of the nonenhancing right parietal lesion after surgical resection was consistent with metastatic breast cancer and was no different in appearance histologically from her previously resected enhancing metastatic brain tumors. Six weeks after stopping bevacizumab therapy and 3 weeks after microsurgical resection, multiple new contrast-enhancing lesions developed on follow-up MRI (Fig. 3). She was subsequently treated with whole-brain radiotherapy.

4. Discussion

Throughout her course, this patient served as her own internal control for assessing the potential effects of bevacizumab on the neuroimaging characteristics of metastatic tumors. Before bevacizumab treatment, her metastatic brain tumors showed typical neuroimaging findings of contrast enhancement and surrounding vasogenic edema (Fig. 1A, B). The tumor that developed while on bevacizumab treatment failed to enhance with contrast and demonstrated no surrounding edema or inflammatory response (Fig. 2C, D). Typical neuroimaging findings were restored in lesions that arose after bevacizumab was discontinued (Fig. 3A, B). Given the internal control of the same patient and presumably the same primary tumor biology, the timing of bevacizumab use, and the formation of tumors before, during, and after bevacizumab use, the

Fig. 1. A: Postcontrast axial T1-weighted (T1W) image at the level of the atria of the lateral ventricles shows an irregular, well-demarcated, rim-enhancing mass in the left occipital lobe at the gray/white matter junction. Low signal intensity in the center suggests central necrosis. B: Axial FLAIR image at the level of the body of the lateral ventricles shows mild to moderate vasogenic edema adjacent to the mass in the left occipital lobe.

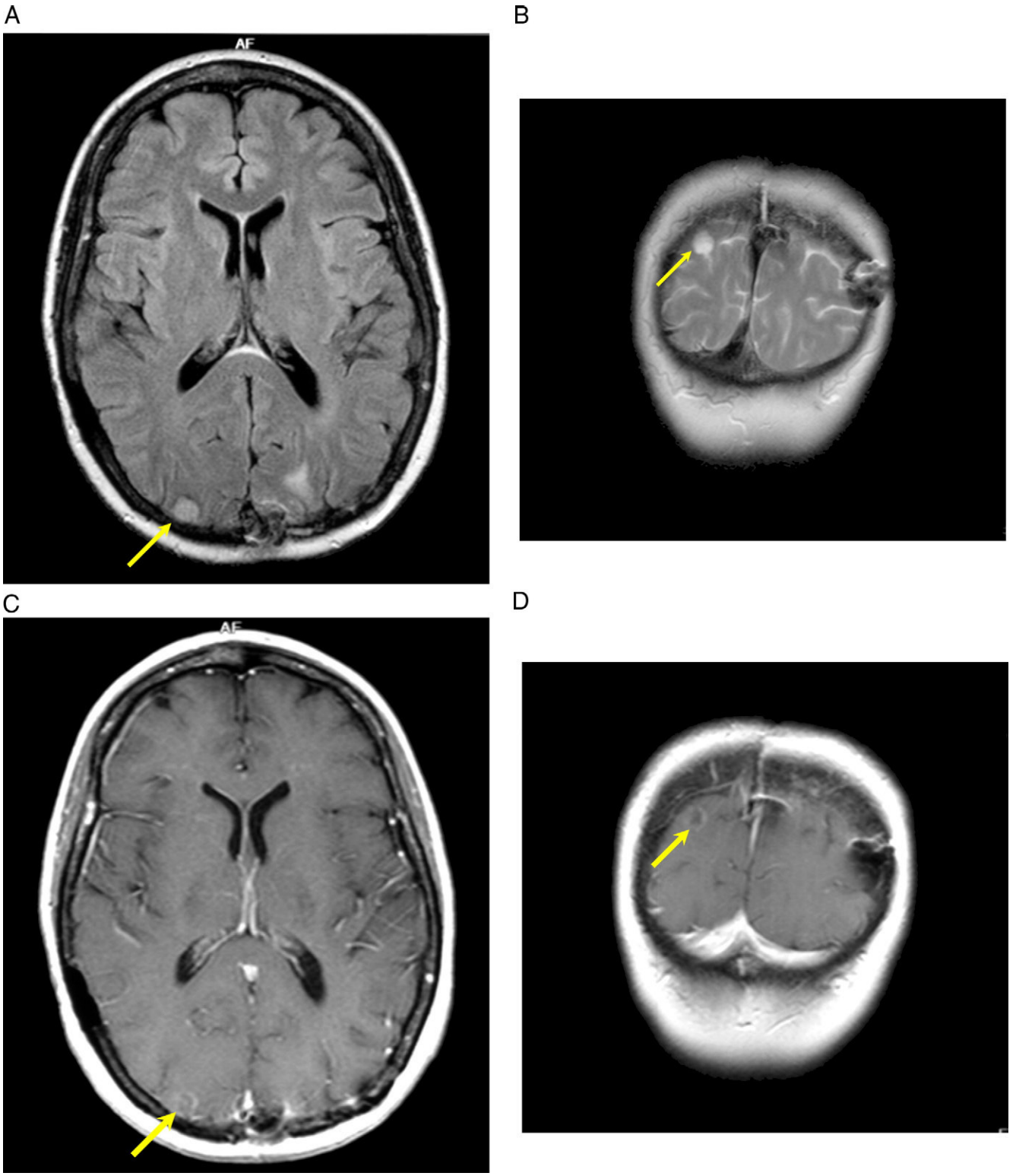


Fig. 2. A: Axial FLAIR image at the level of the roof of the third ventricle shows a hyperintense lesion in the right parietal cortex with no surrounding vasogenic edema. The lesion was surgically resected. Histopathologic examination showed the lesion to be consistent with metastatic breast carcinoma. B: Coronal T2-weighted MRI at the level of the torcula shows a hyperintense lesion. C: Postcontrast axial T1W image at the level of the roof of the third ventricle shows no clear contrast-enhancing lesion. An isointense area with subtle hazy marginal enhancement is seen in the left parietal cortex, the imaging features of which are atypical for a metastatic lesion. D: Postcontrast coronal T1W image at the level of the torcula shows no clear contrast-enhancing lesion. A lesion with subtle hazy marginal enhancement is seen.

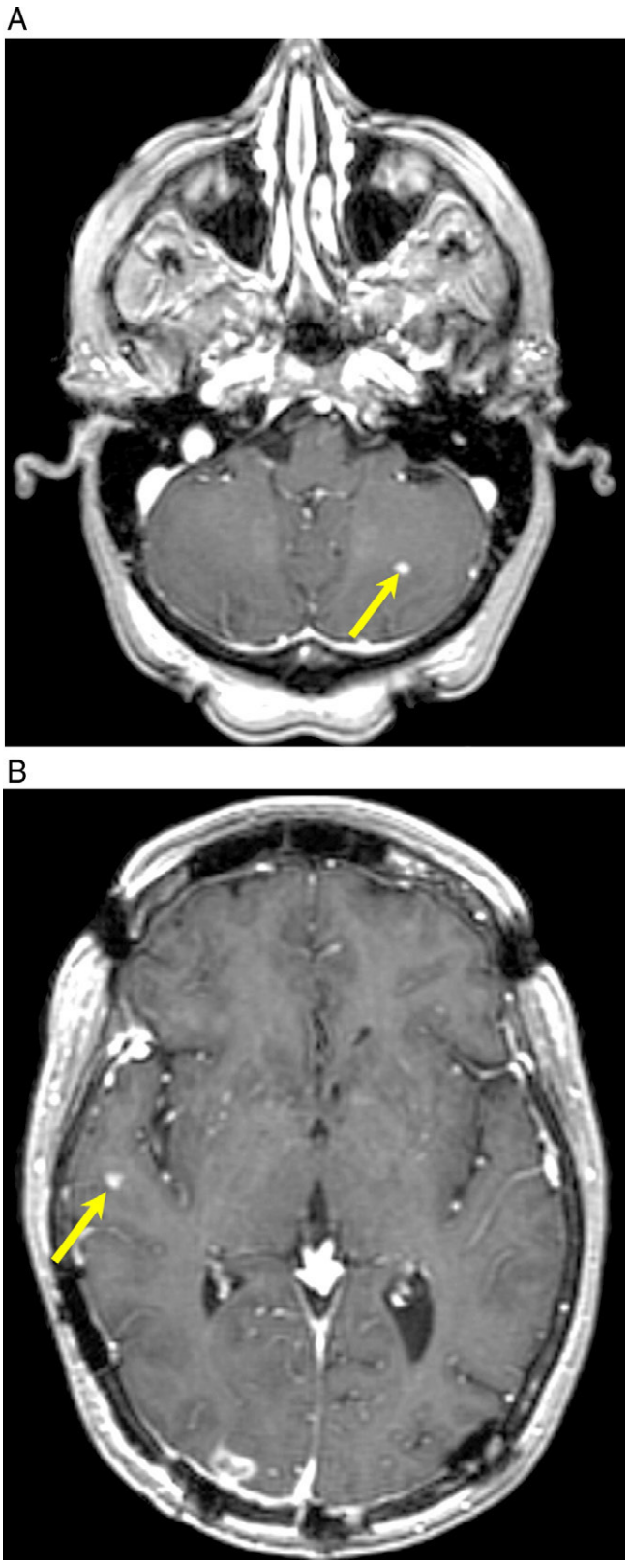


Fig. 3. A: Postcontrast axial T1W image at the level of the inferior cerebellar peduncles shows a contrast-enhancing tumor in the left cerebellar hemisphere. B: Postcontrast axial T1W image at the level of the atria of the lateral ventricles shows a contrast-enhancing lesion in the right temporal lobe as well as the prior resection cavity in the right occipital lobe.

varying imaging findings were almost certainly solely due to bevacizumab effect.

Contrast enhancement is routinely used to detect metastatic lesions in the brain, to monitor response to chemotherapy, and to distinguish metastatic tumors from other potential brain mass lesions. In a recent study in patients with recurrent high-grade gliomas, bevacizumab treatment resulted in shrinkage of contrast-enhancing tumor, with reductions evident in as little as 2 weeks after initiation of therapy [7]. These findings are consistent DCE-MRI studies, which have shown decreased uptake of contrast in bevacizumab-treated tumors elsewhere in the body [8,10].

It is important for clinicians to recognize that bevacizumab may alter typical patterns of blood-brain barrier breakdown and permeability of surrounding tumor vasculature seen with cerebral metastases. Further study is warranted to assess the generalizability of this observation, the relation of specific histology to the phenomenon, as well as the specific biologic mechanisms involved.

4.1. Conclusions

Bevacizumab-treated patients may pose a challenge for detecting and interpreting brain metastases on neuroimaging. This caution could potentially apply to future applications with newer drugs such as small molecule inhibitors of neoangiogenesis.

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