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PROGRESSIVE DIFFUSE MENINGIOANGIOMATOSIS: RESPONSE TO BEVACIZUMAB TREATMENT

Meningioangiomas is an uncommon nonmalignant disorder characterized by a progressive focal lesion, typically presenting as seizure disorder.¹ Histologically, the lesion exhibits prominent cortical vasculature with associated perivascular mesenchymal cell proliferation. The standard treatment is surgical resection.^{1,2}

Here we describe a patient with diffuse meningioangiomas that caused permanent cortical blindness. He was treated with bevacizumab with resultant clinical stabilization and marked radiographic improvement.

Level of evidence. This single observational study without controls provides Class IV evidence.

Case report. A 67-year-old man with a history of hyperlipidemia, benign prostatic hypertrophy, and smoking noticed visual impairment. This was initially attributed to cataracts but cataract surgery did not result in clinical improvement. His visual impairment progressed over the following month to light perception only.

Six months later, he was admitted. On admission, he had severe visual impairment and mild hearing loss. The rest of the neurologic examination was intact. MRI demonstrated diffuse bilateral occipital T2/fluid-attenuated inversion recovery (FLAIR) hyperintensity with gyral enhancement on postgadolinium T1 sequences. Blood workup for collagen vascular disease was negative. CSF studies showed normal cell count, mildly elevated protein (89 mg/dL), negative cytology, and negative PCR for JC virus. EEG showed diffuse slowing. Stereotactic brain biopsy revealed mildly atypical astrocytes and staining for JC virus was negative.

The patient was readmitted 6 months later, at which time MRI showed progressive gyral enhancement and T2/FLAIR hyperintensity that affected both occipital lobes and the right temporal lobe (figure, C and D). The CSF study was remarkable for mildly elevated protein (60 mg/dL), negative cytology, and lack of monoclonality on flow cytometry. Very long chain fatty acid and aryl sulfatase assays were negative.

An open brain biopsy was performed, with a resultant diagnosis of meningioangiomas (figure, A and B). Characteristic histopathologic features were a cellular proliferation, including a predominant epithelial membrane antigen (EMA)-negative spindle cell population with occasional EMA-positive meningothelial nests, involving the leptomeninges and perivascular zone of the penetrating cortical arteries. Scattered atypical neuronal perikarya (ganglion cells) were present, and the proliferation index was low. Immunohistochemistry confirmed the presence of dysplastic neurons, which were positive for NeuN, neurofilament protein, and synaptophysin. Glial fibrillary acid protein staining showed marked reactive astrogliosis. Immunostaining for p53 protein and mutant IDH1 R132H protein were both negative. PCR for 6 BRAF codon v600 mutations, BK virus, and JC virus assays were also negative. Neurofibromatosis type 2 (NF2) mutation was not assessed.

A year and a half after presentation, bevacizumab treatment (5 mg/kg every 2 weeks) was started following MRI that revealed progressive disease. Two months later, follow-up MRI demonstrated marked improvement, with only a trace of residual contrast enhancement and substantial reduction in T2/FLAIR hyperintensity (figure, E and F). Since starting treatment with bevacizumab, the patient has remained blind and has been clinically stable for 9 months.

Discussion. Meningioangiomas is an uncommon nonmalignant disease that affects the cortex and overlying leptomeninges. It is a congenital disorder and appears more often in children, but several cases have been described in adults.^{3,4} Meningioangiomas may arise in patients with NF2. It can also occur in the setting of a meningioma.⁴ Sporadic cases are typically solitary and symptomatic, while NF2-associated meningioangiomas is often multifocal and asymptomatic.⁵ The primary histopathologic features are leptomeningeal and perivascular mesenchymal cell proliferation and the presence of dysplastic neurons. Immunohistochemistry is of limited diagnostic value.²

About 174 cases of meningioangiomas have been described in the past. By far the most common symptom is seizures; however, a few cases with focal neurologic manifestations have been described.⁴ The

(A) Hematoxylin & eosin staining shows a cellular proliferation composed of spindle cells with occasional meningothelial nests involving the leptomeninges and perivascular space of the penetrating arteries. Atypical neurons and reactive astrogliosis are present in the parenchyma. (B) Immunohistochemical staining for NeuN shows dysplastic neurons. (C, D) T2 fluid-attenuated inversion recovery (FLAIR) and T1 with contrast MRI sequences at the time of second biopsy show hyperintensity in the occipital and temporal lobes and gyriform enhancement bilaterally. (E, F) T2 FLAIR and T1 with contrast MRI 2 months after starting treatment with bevacizumab demonstrate significant improvement in the enhancement and FLAIR signal abnormality.

most common radiographic characteristic of meningioangiomas is gyriform enhancement, but solid and cystic imaging patterns are also described.² Bilateral occipital cortical involvement with associated progressive cortical blindness, similar to our case, has been reported only once previously.⁵

The only known treatment for meningioangiomas is surgical resection; however, in this unique case, surgical resection was not feasible because of the extensive, diffuse nature of the disease.² Since one of the primary histopathologic features of meningioangiomas is meningovascular proliferation, we hypothesized that antiangiogenic therapy, such as bevacizumab, a recombinant humanized monoclonal antibody that blocks angiogenesis by inhibiting vascular endothelial growth factor A, might be beneficial. Bevacizumab has been approved for treatment of glioblastoma, in which it induces a high rate of radiologic response secondary to normalization of permeable tumor vessels.⁶

Bevacizumab has also been associated with improvement in hearing in NF2-associated vestibular schwannomas.⁷ We postulate that in our patient bevacizumab produced a similar effect that resulted in radiologic response and clinical stability.

Treatment with bevacizumab might be beneficial in patients with symptomatic meningioangiomas for whom surgical resection is not an option.

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