

## Propranolol Treatment of Cavernous Malformations with Symptomatic Hemorrhage

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- BACKGROUND: Cerebral cavernous malformations are more common than generally thought, affecting approximately 1 in every 250 adults. Most of these lesions are asymptomatic or have a relatively benign course, but a small minority behave aggressively and present with recurrent episodes of symptomatic hemorrhage. A safe and effective medical treatment option for the management of this latter group would be useful. Propranolol has recently been shown to be effective in the treatment of infantile hemangioma, a close pathologic counterpart of cavernous malformations. These results suggest a potential role for propranolol treatment in the management of patients with symptomatic cavernous malformations.
- METHODS: Low-dose propranolol (20 mg, three times daily) was used to treat 2 adult female patients in their mid- to late fifties, both of whom had symptomatic cavernous malformations and a history of repeated hemorrhage. Serial magnetic resonance imaging studies after the initiation of propranolol demonstrated regression of the lesions and no evidence of recurrent hemorrhage.
- CONCLUSIONS: Propranolol may offer a safe and effective treatment for patients who have cavernous malformations with symptomatic hemorrhage. Additional studies are needed to confirm these findings.

#### INTRODUCTION

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urgical resection is the primary mode of treatment for cerebral cavernous malformations (CCMs) in patients who present with recurrent symptomatic hemorrhage. Although surgery for superficial hemispheric lesions is typically well tolerated, the resection of deep lesions involving the brainstem and basal ganglia can be daunting and has been associated with high risk for new deficits. An effective medical treatment that reduces or eliminates the risks of hemorrhage in patients with deep symptomatic CCMs would be invaluable.

Recent reports have documented clinically significant benefit for treatment with the beta-blocker propranolol in the management of aggressive infantile hemangioma. <sup>2,3</sup> Pathologically, cavernous malformations are closely related to hemangiomas, and the terms cavernous malformation and cavernous hemangioma are often used interchangeably in the medical literature describing these lesions. <sup>4,5</sup> Propranolol is inexpensive and well tolerated in both children and adults.

We describe 2 adult patients with symptomatic CCMs, in whom the administration of low-dose oral propranolol appears to have ameliorated the risk of recurrent hemorrhage.

#### CASE 1

The patient is an adult woman with a well-documented history of familial CCMs. She is well known to the senior authors (J.M.Z. and R.F.S.), having previously undergone surgical resection of a symptomatic right posterior frontal lobe CCM in 1990 at 34 years of age. She made a good recovery from surgery and was subsequently enrolled in our prospective Natural History of Familial Cavernous Malformations study. In 1998 at age 42, a routine magnetic resonance imaging (MRI) scan was negative for any evidence of new lesions (Figure 1A); however, in 2008 at age 51, a repeat MRI demonstrated development of 2 asymptomatic de novo CCMs: the first in the left corona radiata and the second in the left occipital lobe (Figure 1B). Two years later, in October 2010 at age 54, the patient presented with complaints of new-onset numbness in the right lower extremity. An MRI scan revealed a 2.25-cm focus of acute and subacute hemorrhage in the left corona radiata lesion (Figure 1C). Imaging characteristics were consistent with gross

#### Key words

- Beta-blockers
- Cavernous malformations
- Cerebral cavernous malformations
- Hemorrhage
- Propranolol
- Symptomatic

### **Abbreviations and Acronyms**

**CCM**: Cerebral cavernous malformation MRI: Magnetic resonance imaging

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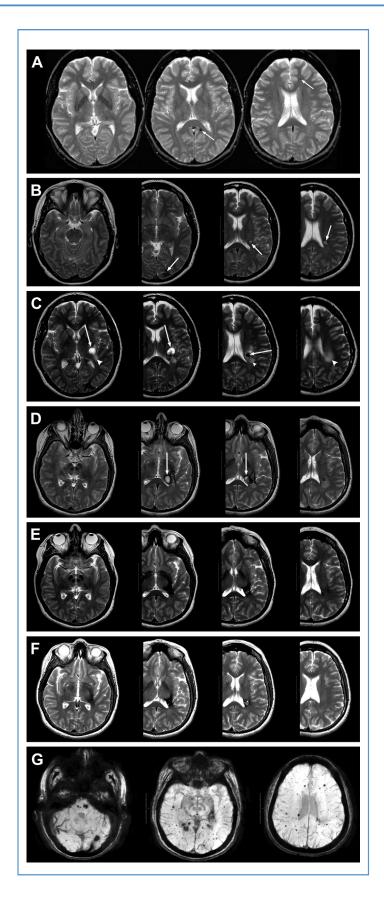
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