To our knowledge, diffuse infiltrating retinoblastoma with central nervous system spread at the initial visit has not been previously reported.

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**Figure 2.** Results from B-scan ultrasonography, repeated lumbar puncture, fundus photography, and histopathological examination. A, B-scan ultrasonogram of the right eye showing vitreous clumps and a thickened retina (arrow). TGC indicates time gain control. B, Repeated lumbar puncture showing round, multinucleated cells in the cerebrospinal fluid (hematoxylin-eosin, original magnification ×20). C, Fundus photograph of the right eye showing resolution of disc swelling after treatment. D, Photomicrograph of the enucleated globe showing diffuse infiltration of retinal layers (arrow) with tumor cells (hematoxylin-eosin, original magnification ×20). V indicates vitreous.

**Topical Timolol for Periocular Hemangioma: Report of Further Study**

Childhood superficial capillary hemangiomas of the eyelid may lead to amblyopia or anisometropia.1,2 Although benign, such tumors can cause irreversible visual loss if not treated promptly. Treatment options for infantile hemangioma include both systemic
and intralesional corticosteroids, interferon alfa, laser, embolization, immunomodulators, surgery, and, most recently, propranolol. Guo and Ni first reported successful outcomes for a 4-month-old infant with superficial capillary hemangioma of the eyelid using topical timolol maleate application. We now report a series of 7 children in whom significant reductions of periocular and facial capillary hemangiomas occurred following topical application of timolol maleate, 0.5%, solution.

Report of Cases. We treated 7 children with superficial periocular hemangiomas without previous intervention. This study was approved by the institutional review board of our institution. All parents were instructed to apply and gently spread 2 to 3 drops of timolol maleate, 0.5%, solution (liquid) topically onto the surface of the hemangioma using a fingertip twice daily. In all 7 children, the tumors decreased in size and volume and faded in color. Response times ranged from 4 to 8 weeks following timolol treatment. All children continued receiving topical timolol until their last office visits, ranging from 1 to 6 months. Among these 7 children, the reduction in hemangioma size and volume varied from 55% to 95% with follow-up for 1 to 6 months after treatment. All 7 patients showed a fade in hemangioma color from bright red to light pink or normal skin tone following timolol application. All patients were monitored by their pediatricians during the course of treatment. We also checked the patients’ heart rates before and after timolol application during their office visits. All mothers were instructed to check pulse rates at home. No significant changes in heart rate and no local or systemic adverse effects were observed or reported in any children. Two illustrative cases are presented in Figure 1 and Figure 2.

Comment. All currently available treatment modalities are associated with adverse local or systemic effects. Intralesional corticosteroids are associated with disfiguring eyelid changes, elevated intraocular pressure, and central retinal artery occlusion, while oral steroids cause increased risk of hypertension, adrenal cortical insufficiency, delay of growth, immunosuppression, gastrointestinal bleeding, and behavioral changes. Surgical excision is associated with potential hemorrhage. Immunomodulators may cause myelosuppression, hepatotoxic effects, and neurotoxic effects.

Recently, propranolol, a β-blocker, was reported to successfully treat severe hemangiomas in infants when administered orally. However, use of oral propranolol is associated with systemic adverse effects, including bronchospasm, heart block, hypotension, severe bradycardia, congestive heart failure, and hypoglycemia. Children treated with oral propranolol must be monitored closely and frequently by the pediatrician.

Our findings suggest that application of topical timolol, another β-blocker, provides a safe and effective alternative treatment for superficial periocular hemangiomas and may have fewer systemic effects. While the mechanism(s) by which timolol reduces hemangiomas is unclear, β-blockade–mediated vasoconstriction, decreased vascular endothelial growth factor expression, and
endothelial cell apoptosis may all be contributory. Further studies on the use of topical β-blockers for the treatment of infantile hemangiomas, including close monitoring for potential adverse effects, are ongoing at our institution.

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Financial Disclosure: Dr Guo has filed a patent for the use of topical β-blockers in cutaneous hemangioma.

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