

RESEARCH LETTERS

Oral Propranolol for Exudative Retinal Detachment in Diffuse Choroidal Hemangioma

The main abnormality of the uveal tract in patients with Sturge-Weber syndrome is diffuse choroidal hemangioma (DCH). Diffuse choroidal hemangioma can lead to a total retinal detachment and secondary neovascular glaucoma. Radiotherapy and photodynamic therapy are currently the preferred methods of treatment. Low-dose lens-sparing radiotherapy or proton beam irradiation can induce tumor regression

and resolution of subretinal fluid.¹ Short-term treatment success using photodynamic therapy has also been reported.²

The use of oral propranolol hydrochloride has been described for infantile orbital³ and periorbital hemangioma. Recently, Léauté-Labrèze et al³ observed that systemic propranolol could inhibit the growth of infantile hemangioma (IH) lesions in children. The response of IH to propranolol catapulted the use of this treatment to first-line status among physicians managing this disease.³⁻⁶

We report the use of oral propranolol for exudative retinal detachment in DCH associated with Sturge-Weber syndrome.

Report of a Case. A 58-year-old Hispanic woman had decreased visual acuity in the left eye for 3 years and in-

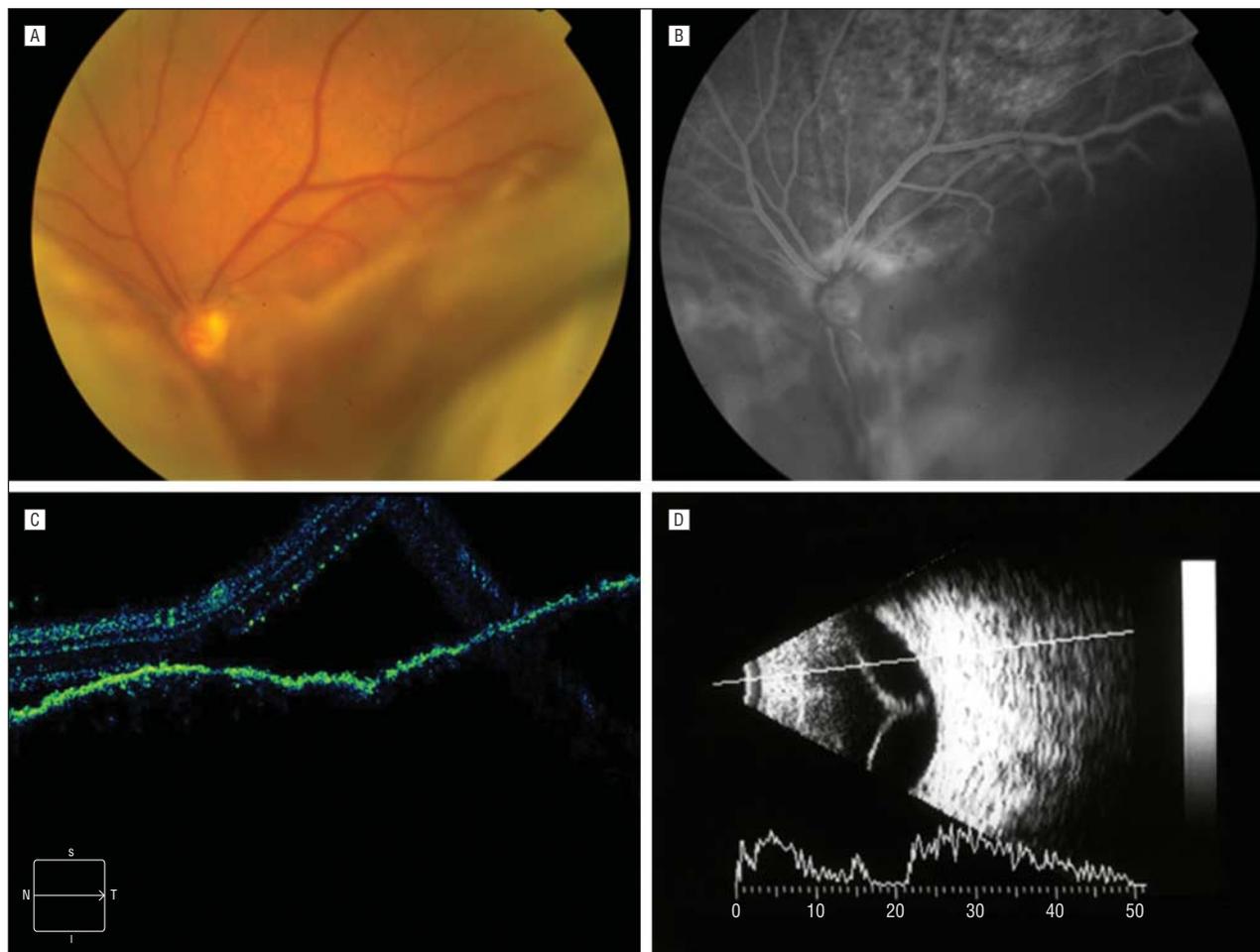


Figure 1. Initial fundus examination, fluorescein angiography, optical coherence tomography, and ultrasonography. A, Fundus examination shows inferior exudative retinal detachment with shifting fluid. B, Fluorescein angiography demonstrates early diffuse hyperfluorescence and late hypofluorescence. The late-phase fluorescein angiograph is shown. C, Optical coherence tomography demonstrates an exudative retinal detachment. S indicates superior; T, temporal; I, inferior; and N, nasal. D, B-scan ultrasonography confirms diffuse thickening of the choroid and an exudative retinal detachment with A-scan high internal reflectivity of the choroidal mass, corresponding with the diagnosis of a diffuse choroidal hemangioma.

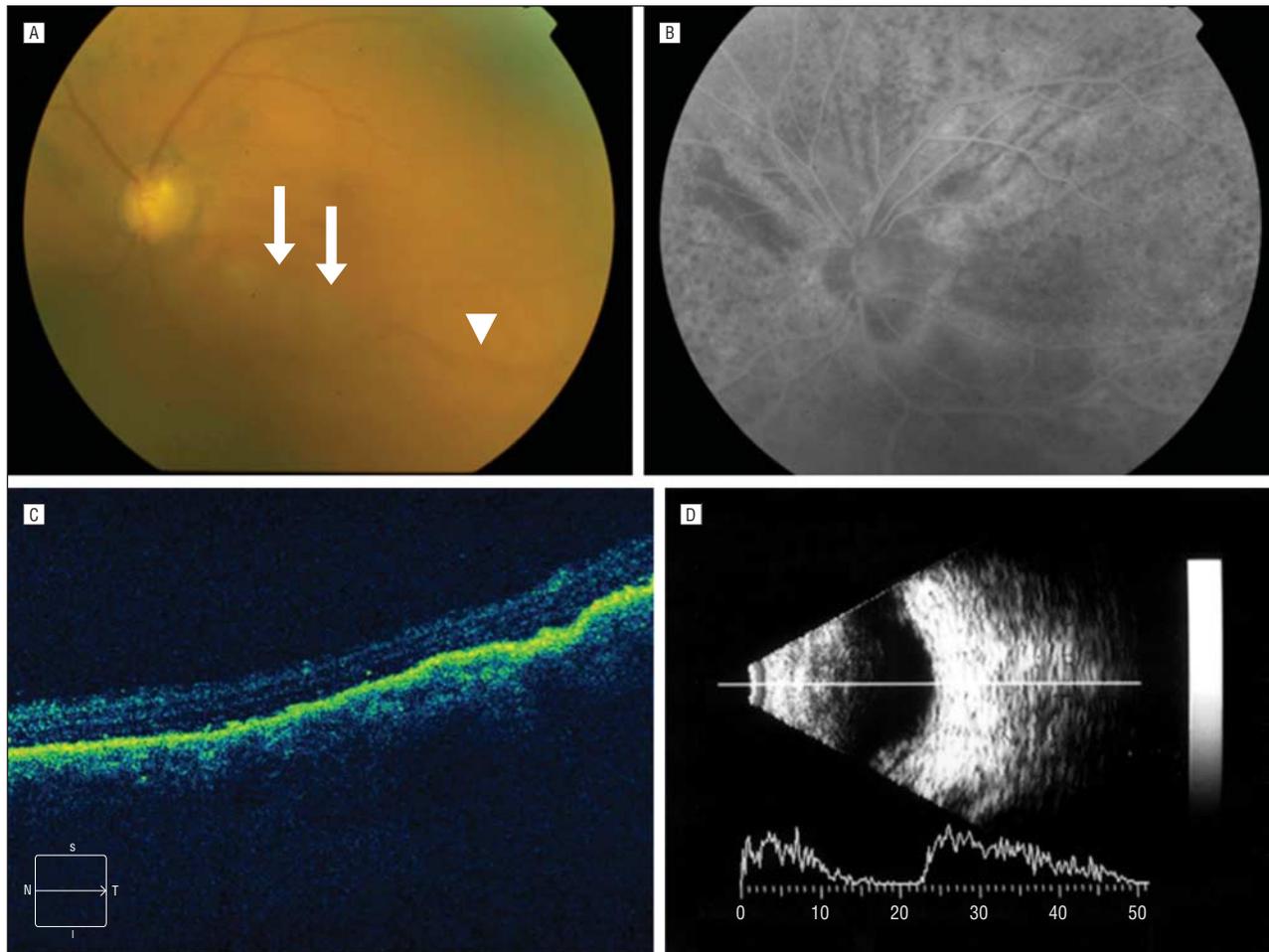


Figure 2. Fundus examination, fluorescein angiography, optical coherence tomography, and ultrasonography after treatment. A, Color photograph demonstrates that the retina is attached with a demarcation line (arrows). The inferotemporal vein is elevated and casting a shadow (arrowhead), suggesting the persistence of a small amount of subretinal fluid. B, Fluorescein angiography demonstrates mottled hyperfluorescence due to retinal pigment epithelium changes. No subretinal fluid is seen. Optical coherence tomography (C) and A- and B-scan ultrasonography (D) confirm that the retina is attached. S indicates superior; T, temporal; I, inferior; and N, nasal.

termittent episodes of pain and red eye. On examination, her best-corrected visual acuity was 20/20 OD and light perception OS. She had diffuse nevus flammeus involving the left upper eyelid, cheek, and nose, suggestive of Sturge-Weber syndrome. The anterior segment of the left eye demonstrated dilated and tortuous conjunctival vessels, clear cornea, shallow anterior chamber, and normal iris. The intraocular pressure was 27 mm Hg OS, and fundus examination showed exudative retinal detachment in the left eye (**Figure 1A**) with shifting fluid. Fluorescein angiography (**Figure 1B**) demonstrated early diffuse hyperfluorescence and late hypofluorescence, and optical coherence tomography (**Figure 1C**) confirmed the presence of subretinal fluid. B-scan ultrasonography confirmed diffuse thickening of the choroid and an exudative retinal detachment with A-scan high internal reflectivity of the choroidal mass (**Figure 1D**), corresponding with the diagnosis of a DCH.

An Nd:YAG-laser iridotomy was performed in the left eye, and treatment with oral propranolol hydrochloride (80 mg orally twice a day) was started. At 18 days after the initiation of propranolol treatment, the dosage was reduced to 40 mg twice a day because of secondary effects described by the patient as dizziness and weak-

ness. Six weeks after the initiation of propranolol treatment, best-corrected visual acuity was hand movements OS, intraocular pressure was 21 mm Hg OS, and the retina was attached, with complete reabsorption of subretinal fluid (**Figure 2A** and **B**) confirmed by optical coherence tomography (**Figure 2C**) and ultrasonography (**Figure 2D**).

Comment. Propranolol, a nonselective β -blocker, was serendipitously discovered to induce accelerated involution of a proliferating IH.³ The mechanism by which propranolol causes this dramatic effect is unclear. However, propranolol interferes with endothelial cells, vascular tone, angiogenesis, and apoptosis.⁵

Léauté-Labrèze and colleagues suggested a propranolol hydrochloride dosage of 2 mg/kg/d in children with IH. We treated our patient with a dosage usually used in adults for arterial hypertension. However, we reduced the dosage by half at day 18 because of secondary effects. Nevertheless, this lower dosage was still effective to allow for resolution of the exudative retinal detachment associated with DCH. The optimal dosage in adults for this indication is still unknown. It is possible that lower dosages may be effective and without adverse effects. In

addition, the duration of treatment to induce retinal reattachment is currently unknown. However, patients with IH have been treated for several months.

Hemangiomas consist histologically of cavernous and capillary vascular networks. The mechanism by which oral propranolol aids in the resolution of exudative retinal detachment in DCH associated with Sturge-Weber syndrome is unknown. It is possible that, similar to IH, there is vasoconstriction of the DCH due to decreased release of nitric oxide, blocking of proangiogenic signals including vascular endothelial growth factor and basic fibroblast growth factor, and apoptosis in proliferating endothelial cells with vascular tumor regression.⁵

To our knowledge, the benefits of propranolol therapy have not been reported in adult hemangioma or for DCH. This is the first reported case of propranolol treatment in an adult with exudative retinal detachment in DCH associated with Sturge-Weber syndrome.

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1. Schilling H, Sauerwein W, Lommatzsch A, et al. Long-term results after low dose ocular irradiation for choroidal haemangiomas. *Br J Ophthalmol.* 1997; 81(4):267-273.
2. Anand R. Photodynamic therapy for diffuse choroidal hemangioma associated with Sturge Weber syndrome. *Am J Ophthalmol.* 2003;136(4):758-760.
3. Léauté-Labrèze C, Dumas de la Roque E, Hubiche T, Boralevi F, Thambo JB, Taïeb A. Propranolol for severe hemangiomas of infancy. *N Engl J Med.* 2008; 358(24):2649-2651.
4. Siegfried EC, Keenan WJ, Al-Jureidini S. More on propranolol for hemangiomas of infancy. *N Engl J Med.* 2008;359(26):2846.
5. Storch CH, Hoeger PH. Propranolol for infantile haemangiomas: insights into the molecular mechanisms of action. *Br J Dermatol.* 2010;163(2):269-274.
6. Sans V, de la Roque ED, Berge J, et al. Propranolol for severe infantile hemangiomas: follow-up report. *Pediatrics.* 2009;124(3):e423-e431.

Oguchi Disease With Unusual Findings Associated With a Heterozygous Mutation in the SAG Gene

Oguchi disease is a type of congenital stationary night blindness with an autosomal recessive inheritance pattern. Two causative genes have been reported for Oguchi disease: the *SAG* and *GRK1* genes. Homozygous Oguchi disease is characterized by

a golden-yellow discoloration of the fundus that disappears after prolonged dark adaptation, called the Mizuo-Nakamura phenomenon. The International Society for Clinical Electrophysiology of Vision—protocol bright-flash electroretinograms (ERGs), performed after 30 minutes of dark adaptation, are typically electronegative with a severely reduced b-wave and milder reduction of the a-wave.^{1,2} After 3 to 4 hours of dark adaptation, both amplitudes recover to nearly normal, especially the a-wave.² However, the recovered rod function is rapidly lost after a short light exposure or a single bright white flash.^{2,3}

We describe a case of Oguchi disease with unusual findings caused by a putative heterozygous mutation in the *SAG* gene.

Report of a Case. A 40-year-old woman with visual acuity of 20/20 OU had fundus abnormalities and was referred to our institute. She had photophobia but did not report night blindness. There was no autosomal dominant family history. The retina had a golden-yellow appearance (**Figure, A**). The Mizuo-Nakamura phenomenon was observed after 30 minutes of dark adaptation (**Figure, B**). Sequencing of the *SAG* gene identified a heterozygous mutation of 1147del A at codon 309. No mutation was found in *GRK1*.

The International Society for Clinical Electrophysiology of Vision protocol was used to record the ERGs. The scotopic ERGs after 30 minutes of dark adaptation showed slightly reduced amplitude and delayed implicit time in b-wave (**Figure, C**). The bright-flash ERG (30 candelas-seconds/m²) had a positive configuration, although the b:a ratio was lower than normal (**Figure, C**). The photopic and flicker ERGs performed after 10 minutes of light adaptation were normal (**Figure, C**). To determine the extent of the rod function recovery, bright-flash ERGs were recorded 4 times at 30-second intervals after 30 minutes of dark adaptation. During the 4 stimuli, the waveform changed from the positive pattern to a negative configuration with a severely reduced b-wave and additional milder reduction of the a-wave, which is characteristic of homozygous Oguchi disease (**Figure, D**). To our knowledge, this phenomenon has never been reported in normal eyes, in eyes with the typical type of Oguchi disease, or in other cases of Oguchi disease with the same heterozygous *SAG* mutation (**Figure, D**). The superimposed ERGs elicited by the 4 consecutive flashes show the variation of rod function recovery (**Figure, E**).

Comment. To our knowledge, this is the first case of Oguchi disease with a distinct fundus appearance and mild electrophysiological abnormalities associated with a putative heterozygous *SAG* mutation. However, we cannot exclude the possibility that another mutation exists in the intron of another allele, which causes the mild phenotype in this patient.

The repetitive-flash ERG protocol was crucial for the diagnosis. It has been reported that double- or triple-flash stimulations after prolonged dark adaptation induce ERG alterations in typical patients with Oguchi disease.³ However, the use of a 30-second interval allowed us to follow the degree of rod function recovery.