Leukocoria and Vitreous Hemorrhage as the Initial Manifestation of Sickle Retinopathy in a 3-Year, 6-Month-Old Child With Sickle Trait (AS)

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ABSTRACT
The authors present the youngest reported child with proliferative sickle retinopathy. A 3-year, 6-month-old boy presented with leukocoria in the left eye, left esotropia, and dense free-floating white vitreous cells obscuring the fundus, suspicious for endophytic retinoblastoma. Ultrasonography depicted dense debris in the vitreous with no distinct calcific echo or retinal mass. Transcorneal, transzonular fine-needle aspiration biopsy of the vitreous confirmed the presence of dehemoglobinized vitreous red blood cells without tumor. The opposite eye showed peripheral retinal pigment epithelial proliferation and fibrosis with angiographic peripheral ischemia. Hemoglobin electrophoresis disclosed sickle trait (AS). The findings were classified as proliferative sickle cell retinopathy with vitreous hemorrhage in the left eye and non-proliferative sickle cell retinopathy in the right eye. Leukocoria generally raises warnings for retinoblastoma, but can also reflect chronic vitreous hemorrhage. [J Pediatr Ophthalmol Strabismus 2011;48:e58-e60.]

INTRODUCTION
Sickle cell disorders are relatively common, as are the other ocular sequelae of these disorders, including sickle retinopathy.¹,² However, children show a lower incidence of sickle retinopathy than adults.³⁻⁸ Proliferative sickle retinopathy is particularly uncommon in early childhood.¹,⁴,⁷,⁸ We could find no previously reported cases in patients younger than 7 years.³⁻⁸,¹² However, the presence of proliferative retinopathy and vitreous hemorrhage in this 3-year, 6-month-old patient with sickle trait (AS) shows that sickle trait may contribute to proliferative retinopathy at an early age.

CASE REPORT
A 3-year, 6-month-old African American boy presented with a history of painless left esotropia of 2 weeks’ duration and a poor red reflex. His prenatal and family history were unremarkable. Visual acuity was 20/32 in the right eye and light perception in the left eye. The pupils were normal without afferent defect. Leukocoria was noted in the left eye (Fig. A). There was a 12 prism diopter left esotropia with full motility in both eyes. In the patient’s left eye, there were 1+ white cells in the anterior chamber and 4+ dense, confluent white cells in the vitreous, coating the posterior capsule of the lens; there was no view of the fundus due to the vitreous opacity. B-scan ultrasonography of the left eye disclosed dense, partially mobile vitreous debris with no identifiable intraocular mass, stalk, or retinal detachment (Fig. B). There were no calcific echoes. Fundus examination of the right eye revealed diffuse retinal pigment epithelial alterations with fibrosis in the periphery for 360° and truncation of retinal arterioles in the inferior periphery (Fig. C). Fluorescein angiography of the right eye revealed patchy areas of hyperfluorescence inferiorly.
along with peripheral retinal arteriolar truncation (Fig. D). A preliminary diagnosis of bilateral ischemic retinopathy with proliferative retinopathy and vitreous hemorrhage in the left eye was made.

To definitively rule out retinoblastoma in the left eye, fine-needle aspiration biopsy through a clear-corneal approach into the aqueous, through the peripheral iris and zonule, and into the vitreous was performed to avoid subconjunctival seeding from the standard trans pars plana approach. Cryotherapy was applied to the corneal wound. Cytology revealed dehemoglobinized red blood cells, consistent with vitreous hemorrhage. No malignant cells were seen. Subsequent hemoglobin electrophoresis revealed sickle cell trait (AS). The patient underwent a vitrectomy and retinal photocoagulation in the left eye. This revealed fibrosis consistent with retinal neovascularization. On last examination at the 7-month follow-up, the patient was orthophoric with a corrected visual acuity of 20/32 in both eyes.

**DISCUSSION**

Sickle cell disorders are relatively common. Eight percent of African Americans are heterozygous for hemoglobin S, whereas 0.15% of African American children are homozygous for hemoglobin S. Erythrocytes containing hemoglobin S are prone to change from biconcave in shape to elongated crescents in reduced oxygen states. These sickled erythrocytes are rigid, disrupting blood flow in small caliber arterioles and capillaries and causing ischemia. The primary ocular finding is ischemic retinopathy; secondary proliferative retinopathy may progress to vision-threatening complications, such as vitreous hemorrhage or retinal detachment.

Sickle retinopathy is less frequent in children than in adults. An age-of-onset analysis of 786 patients with sickle disease (SS) revealed no children younger than 15 years of age with proliferative retinopathy. A similar analysis of 533 patients with sickle disease (SC) disease showed proliferative reti-
sickletype retinopathy in only 5 of 77 children younger than 14 years and none younger than 10 years.\textsuperscript{3} In children who do develop sickle retinopathy, pain crisis, male gender, and splenic sequestration have been identified as risk factors.\textsuperscript{4}

A Jamaican cohort study prospectively examined the incidence, prevalence, and natural history of proliferative sickle retinopathy in children.\textsuperscript{5,6} A total of 473 patients with SS and SC disease received annual eye examinations from age 5 to 25 years. The earliest age of onset of proliferative retinopathy in the study was 8 years. By age 26 years, proliferative retinopathy was present in 14% of patients with SS and 43% of those with SC; however, it was typically self-limiting.\textsuperscript{5} Thirty-six percent of eyes showed spontaneous resolution and only 2 patients developed retinal detachments. In all, proliferative sickle cell retinopathy was uncommon in children and vision loss was rare when it was present.\textsuperscript{5}

Other studies confirm the rarity of proliferative sickle retinopathy in children. The incidence of proliferative retinopathy in children younger than 21 years has been reported as 4 of 150 (3%),\textsuperscript{1} 2 of 37 (5%),\textsuperscript{7} and 7 of 263 (3%).\textsuperscript{8} Vitreous hemorrhage and retinal detachments were not reported in these studies, although they have been reported elsewhere in children as young as 11 years.\textsuperscript{4}

Regardless of age, proliferative sickle retinopathy is rare in patients with sickle trait (AS).\textsuperscript{9-11} Nagpal et al. described 7 patients with sickle trait (AS) and proliferative sickle retinopathy.\textsuperscript{9} These patients were all adults with systemic diseases, including diabetes, syphilis, tuberculosis, and sarcoidosis. The authors questioned whether the presence of systemic disease might have contributed to the development of proliferative retinopathy.\textsuperscript{9} An additional patient with sickle trait, proliferative retinopathy, and gestational diabetes was reported separately.\textsuperscript{10} Mild trauma in patients with sickle trait can also lead to latent proliferative retinopathy.\textsuperscript{11} In our case, a review of systems and the pediatrician’s evaluation failed to suggest any comorbid systemic diseases. The patient’s family history was negative for familial exudative vitreoretinopathy and there was no temporal dragging of the retinal vessels. There were also no historical or physical examination findings to suggest trauma. However, we cannot definitively exclude the possibility that additional conditions could have contributed to this patient’s proliferative retinopathy.

This case is unusual for several reasons. The patient is the youngest reported child with proliferative sickle retinopathy, presenting at 3 years and 6 months of age. A PubMed search was performed using the term “proliferative sickle cell retinopathy OR proliferative sickle retinopathy OR sickle retinopathy,” revealing 462 articles. We could identify no previously reported cases younger than 7 years.\textsuperscript{3-5,7,12} It demonstrates that proliferative sickle retinopathy can occur in patients with sickle trait (AS). Finally, it serves as a reminder that chronic vitreous hemorrhage can result in leukocoria and should be considered in the differential diagnosis of leukocoria in young children.

\textbf{REFERENCES}