Walker–Warburg Syndrome:
Congenital Neurodysplasia and Bilateral Retinal Folds

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Abstract. A 2-month-old girl with a history of congenital hydrocephalus presented due to “wandering eyes.” Initial eye examination at age 2 months showed response to light and a prominent retinal fold that extended through the macula and made contact with the posterior and inferior temporal lens capsule in each eye. Combined with the patient’s neurologic findings, the results of the ocular examination led to the diagnosis of Walker–Warburg syndrome. During 5 years of follow-up, the patient developed progressive cataracts in both eyes but maintained ambulatory vision in the left eye. Walker–Warburg syndrome should be included in the differential diagnosis for pediatric patients with a history of prominent retinal folds. [Ophthalmic Surg Lasers Imaging 2004;35:256-258.]

INTRODUCTION

Originally described in 1942,1 Walker–Warburg syndrome is a rare autosomal recessive condition with characteristic neurodysplasia that results from a failure of neuronal migration between the sixth and ninth weeks of gestation.2 Walker–Warburg syndrome may present with a spectrum of eye and brain anomalies, including Peter’s anomaly; persistent fetal vasculature; retinal folds, dysplasia, and detachment; optic nerve coloboma; and prominent anergic cortical architecture with glial–mesenchymal proliferation in the leptomeninges leading to obliteration of the subarachnoid space and hydrocephalus. Central nervous system manifestations may include hydrocephalus, brain argyria, cerebellar hypoplasia, occipital encephalocoele, and Dandy–Walker malformation.2,3 Ocular findings may include iridocorneal malformations, retinal dysplasia, retinal folds, microphthalmos, and buphthalmos.4,5

Figure 1. RetCam (Massie Laboratories, Inc., Pleasanton, CA) photographs taken during examination under anesthesia at age 2 months demonstrating bilateral retinal fold in (A) the right eye and (B) the left eye.
We describe a patient in whom the ophthalmological and neurological features led to the diagnosis of Walker–Warburg syndrome.

**CASE REPORT**

An infant born at full term with shoulder dystocia, microcephaly, and hydrocephalus presented at age 2 months to an ophthalmologist due to “wandering eyes” noted by her mother. Her first eye examination at 2 months of age demonstrated response to light in each eye, partial leukocoria bilaterally, and bilateral prominent retinal folds (Fig. 1). In each eye, the retinal fold extended through the macula and toward the inferotemporal quadrant, and made contact with the posterior and inferior temporal lens capsule. The vitreous cavity was clear. During 5 years of follow-up, the patient developed ambulatory vision and progressive cataracts in both eyes (Fig. 2). The cataract in the right eye progressed to involve the visual axis. Visual acuity has remained ambulatory in the left eye (with more
precise visual acuity testing limited by the patient’s neurological status); the patient can ambulate independently to find toys using the left eye.

**DISCUSSION**

The differential diagnosis of retinal folds includes retinopathy of prematurity, toxocariasis, familial exudative vitreoretinopathy, persistent fetal vasculature (also known as persistent hyperplastic primary vitreous), incontinentia pigmenti, and Norrie’s disease (Table). Retinopathy of prematurity can usually be ruled out by the birth history and typical retinal features. In the newborn with retinopathy of prematurity, there is usually bilateral and symmetric disease in the anterior retina, which may include a neovascular ridge, avascular retina, tractional retinal detachments, or vitreoretinal interface changes (consistent with the previous existence of a ridge with neovascularization).

The remaining differential diagnosis of retinal folds is made up of rare diseases. Toxocariasis usually presents unilaterally and may present with a retinal fold associated with a peripheral granuloma. Familial exudative vitreoretinopathy may present with peripheral retinal neovascularization and macular dragging, and may appear clinically similar to retinopathy of prematurity, but without a history of premature birth. Tractional retinal detachments in familial exudative vitreoretinopathy may be localized or diffuse and, if tangential, macular dragging or retinal folds may occur.6,7 Persistent fetal vasculature is a congenital, nonhereditary malformation of the eye that follows failure of the embryological primary vitreous and hyaloid membrane vasculature to regress. It is usually unilateral without systemic findings.

Incontinentia pigmenti is an X-linked dominant condition that is fatal in males. It is a multisystem disorder with many ocular manifestations such as retinal ischemia, hemorrhage, exudation, tractional detachments, optic atrophy, foveal hypoplasia, microphthalmos, nystagmus, myopia, and retinal folds.8 The diagnosis is easily confirmed by a skin biopsy.8 Norrie’s disease, or congenital progressive oculo-acoustico-cerebral degeneration, is a rare X-linked recessive syndrome of retinal malformation, deafness, and mental retardation.9

It is important to consider the diagnosis of Walker-Warburg syndrome in pediatric patients who present with bilateral retinal folds and hydrocephalus, brain argyria, cerebellar hypoplasia, Dandy-Walker malformation, and occipital encephalocele.

**REFERENCES**