A female infant small for gestational age had unusual findings on examination of the eyes. Although the corneal diameters were appropriate (10 mm), the pupils were remarkably large (Figure). The pupil size did not change with light stimulation. No suggestion of iris tissue could be identified in either eye. The corneas and lenses were clear, and a red reflex was present and symmetric in appearance in each eye. Findings from funduscopic examination showed no abnormality, and the remainder of the physical examination results were unremarkable. There was no family history of similar findings. Results of a chromosomal analysis were normal (46, XX). A renal ultrasound examination showed no abnormalities. At age 1 month, the infant developed glaucoma.
Denouement and Discussion

Congenital Aniridia

Aniridia is a rare condition occurring in 1 in 64,000 to 1 in 96,000 live births. Actually, the term is a misnomer since iris tissue is not absent but is hypoplastic. The disorder is not a simple defect of iris tissue; other parts of the eye are affected as well, including the cornea, anterior chamber angle, lens, retina, and optic nerve. The abnormality is apparent at birth in most cases because of the abnormally large pupils, almost always bilaterally, and the presence of nystagmus.

GENETIC FORMS

Three genetic forms of aniridia have been described. Familial aniridia, designated AN 1, is an isolated ocular defect accounting for approximately two thirds of all cases and inherited in an autosomal dominant fashion. A microdeletion at band 13 on the short arm of chromosome 11 (11p13) is responsible for AN 1. Only the aniridia locus is affected; all neighboring genes are spared.

Sporadic nonfamilial aniridia (AN 2) comprises almost one third of congenital aniridia cases. The genetic defect is also a deletion or mutation of the same chromosome, 11p13, but the defect may also involve the contiguous Wilms tumor suppressor gene (WT 1). One fourth to one third of these patients will develop Wilms tumor, usually by age 3 years. The association of aniridia and Wilms tumor is known as Miller syndrome. In contrast to AN 2, only one case of Wilms tumor has been reported in children with AN 1.

Individuals with Wilms tumor and aniridia may have a more extensive deletion of chromosome 11p13, creating the WAGR contiguous gene syndrome, which includes Wilms tumor, aniridia, genitourinary anomalies, and mental retardation. Children with this syndrome have a rather characteristic appearance with a long, narrow face, prominent nose, and low-set, poorly lobulated ears. The palpebral fissures are short and downward slanted. Additional abnormalities may include growth failure, microcephaly, delayed closure of the anterior fontanel, and tracheomalacia.

The third form, AN 3, accounts for approximately 2% of cases of aniridia. Known as Gillespie syndrome, AN 3 is associated with mental retardation, cataracts, and cerebellar ataxia. This form of aniridia is an autosomal recessive disorder, with about one third of cases occurring sporadically.

ASSOCIATED EYE PROBLEMS AND MANAGEMENT

Individuals with aniridia usually have or develop additional ocular and visual problems. Glaucoma develops in up to 75% of cases, usually in the preadolescent or early adult years. Congenital or infantile glaucoma may occur. Cataracts develop in the first 2 decades of life in 50% to 85% of cases. Infants with AN 2 may have cataracts in the neonatal period. Superficial corneal opacification with or without vascularization may occur, occasionally resulting in a totally opaque cornea, which may demonstrate relentless progression by age 2 years. Corneal transplantation may be necessary.

Macular and optic nerve hypoplasia is common, resulting in poor vision and troublesome photophobia. Narrowed palpebral fissures with brow furrowing are characteristic, attributed to the voluntary grimace resulting from photophobia. A visual acuity of 20/100 or worse in the better eye is found in 86% of patients. Macular involvement produces nystagmus, which is almost always present. Retinal function approaches normal in some patients.

Infants with aniridia must be followed up closely to detect the development of glaucoma and other ocular complications to preserve as much sight as possible. Children with AN 2 must undergo regularly scheduled renal ultrasonography to detect the development of Wilms tumors.

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