Phenotypic Variability of Pigment Dispersion Syndrome in Children

Pigment dispersion syndrome (PDS) typically develops in young adults and is most commonly diagnosed in the third and fourth decades, although the mean age at onset remains unknown.1 The diagnostic triad of PDS consists of Krukenberg spindle on corneal endothelium, slitlike, radial, midperipheral iris transillumination defects, and dense, homogeneous trabecular meshwork pigmentation.1 Pigment dispersion syndrome is rarely seen before the midteenaged years. Grassi et al2 described atypical pigment dispersion in an 8-year-old boy. We describe an 11-year-old girl with bilateral PDS with elevated intraocular pressure (IOP) as well as two 12-year-old boys, one with a more severe phenotype and both parents affected (suggesting the probability of homozygosity or inheritance of a predisposing gene from each parent) and the other with a less severe phenotype and 1 parent affected (showing the phenotypic variability that can occur in this syndrome).

Report of Cases. Case 1. An 11-year-old girl (family 1, III:3) was found to have PDS during her routine ophthalmological checkup. Her maternal uncle and grandmother had pigmentary glaucoma (Figure 1, family 1). Her best-corrected visual acuity was 20/20 OU with −2.25 diopters (D) OD and −1.75 D OS. Her IOP was 28 mm Hg OD and 30 mm Hg OS. She had bilateral Krukenberg spindles and corneal thicknesses of 585 µm OD and 590 µm OS. The anterior chambers were deep and quiet. Iris transillumination defects were noted in both eyes. Gonioscopy revealed dense pigmentation of the trabecular meshwork with iris concavity in both eyes (Figure 2). The cup-disc ratio was 0.1 OU. She had no lattice degeneration. Humphrey visual fields (24-2) were normal in both eyes. Anterior segment optical coherence tomography showed a concave iris configuration in both eyes (Figure 3). Her mother had PDS and elevated IOP (Figure 1, family 1).

Case 2. A 12-year-old boy (family 2, II:1) was referred for elevated IOP. He had no history of trauma or surgery. On examination, his best-corrected visual acuity was 20/20 OU with −3.00 D OD and −3.75 D OS. He had a Krukenberg spindle in both eyes. Corneal pachymetry was 470 µm OD and 487 µm OS. Radial transillumination defects were noted in both eyes. His IOP was 26 mm Hg OD and 31 mm Hg OS. The angles were wide open with dense trabecular pigmentation. After pupillary dilation, moderate pigment dispersion was noted in the anterior chambers but the IOP remained the same. The lenses were clear with Zentmayer rings. The cup-disc ratios were 0.60 OD with a healthy neuroretinal rim and 0.65 OS with early thinning of the superotemporal rim. Humphrey visual fields (24-2) and multifocal visual evoked potential testing results were within normal limits. Optic coherence tomography showed possible focal thinning of the superotemporal quadrant in the left eye, while Heidelberg retinal topography showed borderline thinning of the rim superiorly in both eyes and results from scanning laser polarimetry with variable corneal compensation were within normal limits in both eyes. Argon laser peripheral iridotomy was performed in 1 eye, and after results were judged to be beneficial by a reduction in the IOP, argon laser peripheral iridotomy was performed in the fellow eye 1 year later (Figure 4). Both of the boy’s parents had PDS with normal IOP, with greater pigmentation in the father than in the mother (Figure 1, family 2).

Case 3. A 12-year-old boy (family 3, III:3) was found to have PDS during his routine checkup for refractive error. His father had PDS and elevated IOP. His paternal aunt, first cousin, and grandfather had pig-
mentary glaucoma (Figure 1, family 3). His best-corrected visual acuity was 20/15 OU with –2.25 D OD and –1.75 D OS. His IOP was 29 mm Hg OD and 27 mm Hg OS. The anterior chambers were deep and quiet. Slitlamp examination results were significant for Krukenberg spindles and iris transillumination defects greater in the right eye than in the left eye. Gonioscopy revealed a grade IV angle with moderate pigmentation of the trabecular meshwork in both eyes. The cup-disc ratio was 0.2 OU. Humphrey visual fields (24-2) were normal. Ultrasound biomicroscopy showed a concave iris configuration in both eyes on accommodation. Because of non-compliance with medical therapy, argon laser peripheral iridotomy was performed in the right eye and the IOP reduced to 12 mm Hg following the procedure.

Comment. In 1961, Stankovic described a family with 4 generations of pigmentary glaucoma. Men develop glaucoma about 3 times as often as women and at a younger mean age. Various articles have indicated that PDS can be familial with an autosomal dominant pattern of inheritance. Becker and Podos described a large family with PDS and pigmentary glaucoma over 3 generations, emphasizing that patients discovered to have PDS should be followed up closely for glaucoma and that members of their families should be examined.

The youngest described patient with PDS was an 8-year-old with atypical features of PDS. However, to our knowledge, our 11-year-old girl is the youngest with typical features of bilateral PDS and elevated IOP.

The gene for PDS was first reported to be located at chromosome 7q35-36. Further evidence narrowed this to 7q36 and also indicated a possible second locus on chromosome 18q, suggesting genetic heterogeneity.

Our patients (2 families) displayed autosomal dominant inheritance. Phenotypic evaluation revealed more severe clinical findings in individual II:1 from family 2, manifested by a full-blown picture of PDS and medically unmanageable IOP. Considering that both parents had PDS and that this patient had an early and severe phenotypic manifestation of PDS, we believe that he inherited a gene for the disease from each parent. The other possibilities include homozygous or heterozygous mutations in the same disease-causing gene or heterozygous mutations in 2 different PDS-causing genes. The alternative possibility includes variable expressivity of only 1 disease-causing gene inherited from either parent. The first and third patients had a less severe phenotypic manifestation with 1 parent being affected, suggesting a possible heterozygosity. Phenotypic variability is common in PDS and is associated with the severity of myopia.

To our knowledge, individual III:3 from family 1 is the youngest patient described with fully developed PDS and elevated IOP and individual II:1 from family 2 is the only one described with both parents affected, accounting for the more aggressive clinical manifestation. Genetic analysis of individual II:1 from family 2 did not reveal any mutations in the myocilin gene, and we are confirming other genes to clarify the severe phenotype.

We wish to emphasize the necessity of thorough family screening in all patients with PDS given the fact that this is an autosomal dominant disorder. Also, family screening will lead us to identify hitherto undiagnosed cases (as in individuals II:2 from family 1, I:1 from family 2, and
I:2 from family 2) and to provide treatment for them.

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Correction

Error in Figure and Omission of Clinical Trial Registration Number. In the Clinical Trials article by Heier et al titled “Ranibizumab Combined With Verteporfin Photodynamic Therapy in Neovascular Age-Related Macular Degeneration,” published in the November issue of the ARCHIVES (2006;124:1532-1542), Figure 3A contained an error. In the key, the boxes should have been reversed so that the white bars corresponded to “PDT Alone” and the blue bars to “Ranibizumab + PDT.” In addition, the Clinical Trial Registration number should have been listed in the abstract. It is NCT00056823. The ARCHIVES regrets the error.