

A rare case of WAGR syndrome with Peter anomaly

Rohit S. Adyanthaya, Michael X. Repka

Wilmer Ophthalmological Institute, the Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Abstract

We report a case of the WAGR syndrome associated with the Peter anomaly. A 6-day-old baby boy was found to have bilateral corneal opacities, 360 degrees of iris hypoplasia and cataracts. Physical examination revealed bilateral undescended testicles. Family history was unremarkable and genetic testing revealed a deletion 11p11.2-13 indicating WAGR syndrome. A Wilms tumor developed and was removed at age 2 years. There was moderate developmental delay. The occurrence of WAGR syndrome with Peter anomaly has been reported in three other patients to our knowledge.

Introduction

WAGR syndrome is a disorder characterized by microdeletions of the short arm of chromosome 11 at band p13 and is clinically associated with Wilms tumor, aniridia, genitourinary anomalies and mental retardation (W-A-G-R). Deletions of neighboring genes, the *PAX6* ocular development gene and the Wilms tumor gene (*WT1*), result in aniridia and Wilms tumor, respectively. Peter anomaly is an anterior segment dysgenesis in which there is abnormal development of the anterior chamber.

Case Report

A 6-day-old infant boy was evaluated for bilateral corneal opacities. His prenatal history was uneventful with spontaneous vaginal delivery at 36 weeks gestation. The right eye had a central white corneal opacity, which extended to the limbus from 4 o'clock to 7 o'clock. There were 360 degrees of iris hypoplasia with iris vessels visible. There was an area of irido-corneal adhesion inferiorly. The anterior chamber was shallow. The horizontal and vertical corneal diameters were 8.8 mm. There was a nuclear cataract visible behind the corneal opacification. The left eye had denser central corneal opacification. There were 360 degrees of iris hypoplasia with a vascular ring at the poorly formed pupillary margin. The anterior

chamber was noted to be shallow, especially inferiorly with an area of irido-corneal adhesions. A dense nuclear and cortical cataract was noted. The corneal diameters were 9.0 mm vertical and 10.5 mm horizontal. The intraocular pressure measured with a handheld applanation tonometer (Tono-pen: Bio-Rad, Santa Ana, CA, USA) varied from 18 to 22 mm of Hg in both eyes. B-scan ocular echography found bilateral lenticular opacities and attached retinas. Systemic examination revealed bilateral undescended testicles. Abdominal sonography showed normal kidneys. Family history was unremarkable. Genetic testing revealed a deletion on chromosome 11p11.2-13. Bilateral (non-simultaneous) penetrating keratoplasties with lensectomy were performed. A second corneal graft was performed in each eye after about one year. Glaucoma developed in the right eye, with subsequent retinal detachment, and corneal graft failure. The graft in the left eye remained clear at 6 years of age. In addition, quarterly sonograms of the abdomen were conducted. A computed tomography (CT) scan of the abdomen and pelvis at age 2 years demonstrated a 2.0×1.8×2.4 cm mass in the mid pole of the left kidney leading to the diagnosis of Wilms tumor, which was successfully excised.

The pathology was consistent with a stage I Wilms tumor, and was negative for tumor-specific loss of heterozygosity. Furthermore, over time, he was noted to have moderate developmental delay with learning disability and attention deficit hyperactivity disorder (ADHD).

Discussion

The occurrence of WAGR syndrome with Peter anomaly has been reported in three other patients to our knowledge. These were a 2-month-old boy with the Peter anomaly and deletion of 11p13 who did not have Wilms tumor,¹ a 6-day-old boy with the Peter anomaly and a Wilms tumor (chromosomal analysis was not performed)² and a 1-month-old boy with deletion on chromosome 11p13-15.1 with an anomalous anterior segment and microphthalmos with bilateral Wilms tumors developing at the age of 3 years.³ Our case of Peters anomaly plus Wilms tumor presents further evidence of an association of WAGR syndrome and Peter anomaly.

WAGR syndrome (OMIM 194072) was first described by Miller, *et al.*⁴ and is an extensively studied *contiguous gene syndrome*. Children with WAGR syndrome invariably have a germline chromosomal deletion at 11p of variable size, but always affecting *WT1* and *PAX6* genes, both on band 13 (11p13).⁵

Aniridia occurs sporadically or as an autosomal dominant inherited condition. One-third

Correspondence: Rohit Adyanthaya, Stony Brook University, HSC L-2, Rm 152, Stony Brook, New York 11768, USA.
E-mail: rohitedoctor@gmail.com

Key words: WAGR syndrome, Peter anomaly.

Received for publication: 9 April 2011.
Accepted for publication: 31 July 2011.

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

©Copyright R.S. Adyanthaya and M.X. Repka., 2011
Licensee PAGEPress, Italy
Eye Reports 2011; 1:e4
doi:10.4081/eye.2011.e4

of patients with sporadic aniridia will be found to have WAGR syndrome.⁶ The *PAX6* gene, involved in ocular embryogenesis, has been identified as a candidate gene for aniridia. Therefore, it is reasonable that ocular anomalies other than aniridia might result from a deletion in the *PAX6* gene.

The second gene in this region is the *WT1* gene (Wilms tumor gene). Individuals who have a deletion in this gene have an increased risk for developing Wilms tumor as well as having abnormal genitalia. Their risk of having Wilms tumor is around 45-57%.^{7,8} 90% of Wilms tumors present by the age of 4 years and 98% by the age of 7 years. Screening for Wilms tumor includes ultrasound every three months during this period. There is also approximately a 40% chance of renal problems, including renal failure in late adolescence in children with WAGR and Wilms tumor.⁹ The associated genitourinary findings include cryptorchidism present in nearly 60% of the cases,⁸ hypospadias, micropenis and other urinary tract abnormalities (also caused by *WT1* gene deletions).

Peter anomaly is an anterior segment dysgenesis in which abnormal cleavage of the anterior chamber occurs. Mutations may involve the *PAX6* gene.^{9,10} with reported cases of Peter anomaly and aniridia.^{11,12} though Churchill, *et al.* found no such association.¹³ Peter plus syndrome is characterized by genitourinary abnormalities, syndactyly, brachycephaly, and cardiac, neural, and hearing abnormalities. Since the *PAX6* gene is also involved in the development of the central nervous system, a wide variety of neurological, behavioral, and psychiatric abnormalities can also be present.⁸

References

1. Hanson IM, Fletcher JM, Jordan T, et al. Mutations at the *PAX6* locus are found in

- heterogeneous anterior segment malformations including Peters' anomaly. *Nat Genet* 1994;6:168-73.
2. Eiferman RA. Association of Wilms' tumor with Peters' anomaly. *Ann Ophthalmol* 1984;16:933-4.
 3. Kawase E, Tanaka K, Honna T, Azuma N. A case of atypical WAGR syndrome with anterior segment anomaly and microphthalmos. *Arch Ophthalmol* 2001;119:1855-6.
 4. Miller RW, Fraumeni JF Jr, Manning MD. Association of Wilms tumor with aniridia, hemihypertrophy and other congenital malformations. *N Engl J Med* 1964;270:922-7.
 5. Crolla JA, Cawdery JE, Oley CA, et al. A FISH approach to defining the extent and possible clinical significance of deletions at the WAGR locus. *J Med Genet* 1997;34:207-12.
 6. Ivanov I, Shuper A, Shohad M, et al. Aniridia: recent achievements in clinical practice. *Eur J Pediatr* 1995;154:795-800.
 7. Muto R, Yamamori S, Ohashi H, Osawa M. Prediction by FISH analysis of the occurrence of Wilms tumor in aniridia patients. *Am J Med Genet* 2002;108:285-9.
 8. Fischbach BV, Trout KL, Lewis J, et al. WAGR syndrome: a clinical review of 54 cases. *Pediatrics* 2005;116:984-8.
 9. Breslow NE, Collins AJ, Ritchey ML, et al. End stage renal disease in patients with Wilms tumor: results from the National Wilms Tumor Study Group and the United States Renal Data System. *J Urol* 2005;174:1972-5.
 9. Azuma N, Yamaguchi Y, Handa H, et al. Missense mutation in the alternative splice region of the PAX6 gene in eye anomalies. *Am J Hum Genet* 1999;65:656-63.
 10. Sawada M, Sato M, Hikoya A, et al. A case of aniridia with unilateral Peters anomaly. *J AAPOS* 2011;15:104-6.
 11. Mayer UM. Peters' anomaly and combination with other malformations (series of 16 patients). *Ophthalmic Paediatr Genet* 1992;13:131-5.
 12. Koster R, van Balen AT. Congenital corneal opacity (Peters' anomaly) combined with buphthalmos and aniridia. *Ophthalmic Paediatr Genet* 1985;6:241-6.
 13. Churchill AJ, Booth AP, Anwar R, Markham AF. PAX 6 is normal in most cases of Peters' anomaly. *Eye (Lond)* 1998;12:299-303.

Non-commercial use only