International Journal of Recent Trends in Science And Technology, ISSN 2277-2812 E-ISSN 2249-8109, Volume 9, Issue 2, 2013 pp 267-269

WAGR Syndrome – A Case Report

Rakhee B. Khatiwala[1*], Vaishali Pawar[2], Deokrishna M. Sindal[3]

{[1]Resident, [2]Senior resident, [3]Professor and HOD}

Department of Ophthalmology, Krishna Institute of Medical Sciences Deemed University, Karad, Maharashtra, INDIA.

[*]Corresponding Address:

rakhee.bk@gmail.com

Case Report

Abstract: WAGR syndrome is a rare, sporadic genetic disorder characterized by W-Wilm's tumour, A-Aniridia, G-Genito-urinary anomalies and R-Mental Retardation due to de novo deletion in the distal band of 11p13 chromosome. It is a contiguous gene deletion syndrome. The syndrome is usually recognized by sporadic aniridia present at birth, often followed by the development of Wilm's tumour in early childhood, but possible at any age. Here we report a case of 4 years old female child having bilateral aniridia, abdominal mass and mental retardation.

Keywords: Wilm's Tumour, Aniridia, Genito-urinary anomalies, Mental Retardation.

Introduction

The WAGR syndrome is a rare, sporadic and multiple congenital anomaly–mental retardation syndrome caused by the interstitial deletion of the distal portion of chromosome 11p13. The abnormalities are related to the contiguous loss of the neighbouring genes. The deletion of one copy of the *PAX6* gene is responsible for aniridia. *PAX6* plays a role in CNS development as well and may be responsible for the mental retardation seen in a reported 75% of children with WAGR syndrome. The constitutional loss of one allele of the Wilm's tumour gene (*WT1*) results in GU anomalies.

Case Report

A four years old female child was brought to our hospital by her parents for complaints of a mass in right sided abdomen and bilateral searching eye movements. There is past history of showing to an Ophthalmologist when the patient was about 6 months old and the record showed that she had Corneal oedema in both eyes and was prescribed some eyedrops for the same. No other record of the follow-up was found.

There was no family history of aniridia or renal tumour.

Examination

On Ocular examination there was Facial dysmorphism andVisual acquity- follows light upto 2 meters in both eyes.

On anterior segment examination

There were jerky nystagmoid movements with normal Extra-ocular muscle movements, Aniridia with a small iris tag present at 6 o' clock, diffuse multiple lenticular opacities present in both eyes. Rest of the anterior segment was within normal limits.

On Fundus examination

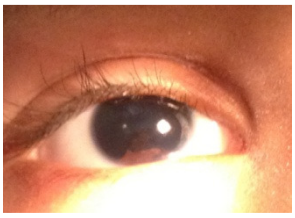
The media was slightly hazy due to lenticular opacities.

Optic disc was focused with -10D on Direct Ophthalmoscope and revealed slightly pale optic disc with normal cup:dics ratio and healthy neuro-retinal rim. Blood vessles of the fundus were normal. General visual fundus showed tesselated appearance and absent foveal reflex in both eyes.

Intra-ocular pressure with Schiotz Tonometer was 17.3mm of Hg in both eyes and was taken under sedation.

On Cycloplegic Refraction following readings were noted:

-8.50 ⊕ -8.00 (R.E.) -8.00 ⊕ -8.00 (L.E.)



On general physical examination there was a palpable mass located in the right sided flank, which was immobile on respiration. External genitalia appeared normal.

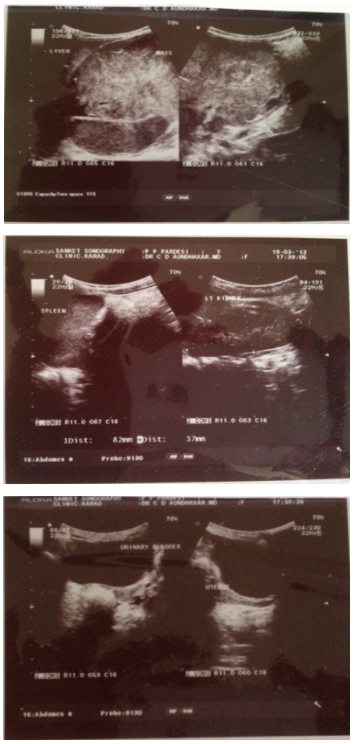
There was a delay in the language and gross-motor development.

Investigations

Routine blood and urine investigations were within the normal limits. Ultrasound of abdomen showed a large, solid and well encapsulated mass in the Right Renal fossa of about 124*82*86mm with smooth outline. Internal nodular architecture noted with multiple fibrous septae. Few scattered degenerative areas noted. Mild to moderate intra-lesional vascularity seen. No evidence of local infiltration or calcification seen. Right Renal vein was normal with no evidence of thrombosis. Histo-pathological examination which was in favour of features suggesting of Wilm's Tumour.

Treatment

-10D spectacles were prescibed for the High Myopia and the patient was advised to use Contact lens for the aniridia to prevent photophobia.
Right Radical Nephrectomy was performed.



Discussion

WAGR syndrome characterised by Wilm's tumour, Aniridia, Genito-urinary anomalies, and Mental Retardation was first described by Miller et al[1]. The discovery that WAGR syndrome is caused by deletion of band 11p13 led to identification of the *WT1* tumor-suppressor gene[2,3] and the *PAX6* ocular developmental gene[4] in the region. As late-onset nephropathy is now recognized as a long-term complication of the WAGR syndrome[5] individuals with sporadic aniridia and nephropathy should be considered highly likely to have the syndrome.The patient reported here met the criteria of WAGR syndrome. She presented with bilateral aniridia since birth, right sided Wilm's tumour and mental retardation Most individuals with the WAGR syndrome will have moderate to severe visual impairment, due to the pan ocular effects of deletion of one copy of the *PAX6* aniridia gene. The aniridia, or iris hypoplasia, per se can cause photophobia. However, significant visual loss occurs due to a combination of any or all of the following: foveal hypoplasia, optic nerve hypoplasia, cataract, corneal pannus, subluxation of the lens, secondary glaucoma, nystagmus[6]. The patient reported here had high myopia, cataract and nystagmus. For high myopia, we prescribed spectacles to prevent amblyopia and divergent squint. Contact lens was advised for aniridia. Since the lenticular opacities were not much advanced, cataract extraction surgery was not advised. Aniridia is found in about 1 in 50,000 persons and is bilateral in 98% of all patients, regardless of the mode of transmission. Aniridia is dominantly transmitted in two-thirds of the patients and sporadically transmitted in the rest and are considered to represent new mutations[7]. One-fifth patients having sporadic aniridia may develop Wilm's tumour[7]. So it recommended that all infants with sporadic aniridia be evaluated carefully for the WAGR syndrome. In WAGR syndrome, the risk of developing Wilm's tumour is about 45%[8] and when associated with aniridia, Wilm's tumour is diagnosed before the age of 5 years in about 80%[9] of the cases. So renal ultrasound is recommended every 3-6months until the age of about 5 years[7,10] and after that a thorough physical examination every 6 months until age of 8 years[11] and after that 6-12 monthly check up[12]. The case reported here presented with an abdominal mass, searching eye movements and developmental delay at the age of 4 years and no prior investigations were carried out. Genital anomalies are usually present in males, presenting typically as cryptorchidism, hypospadias, small penis, and/or hypoplastic scrotum. While there are no reports of female external genital anomalies, a variety of internal genital anomalies, including streak gonads, uterine malformation (hypoplastic vs. unicornuate), and absent uterus and ovaries have been observed in female[12,13.] In our case, the patient's external genitalia appeared normal. The range of cognitive impairment is quite wide, from normal functioning in a few individuals to more severe mental retardation in the majority[12]. The cognitive function of patients with WAGR syndrome is highly variable. The appearance of retardation is correlated with the amount and position of genetic material lost from chromosome 11. Cognitive testing must be performed carefully and is more difficult to evaluate in children with vision loss. In our case, the patient had a delay in language and gross-motor movement.

References

1. Miller RW, Fraumeni JF, Manning MD. Association of Wilm's tumour with aniridia, hemihypertrophy and other congenital malformations. N Engl J Med 1964; 270:922-7.
2. Call KM, Glaser T, Ito CY et al. Isolation and characterization of a zinc finger polypeptide gene at the human chromosome 11 Wilms' tumor locus. Cell 1990; 60: 509–20.
3. Gessler M, Poustka A, Cavanee W, Neve RL, Orkin SH, Bruns GAP. Homozygous deletions in Wilms' tumours of a zincfinger gene identified by chromosome jumping. Nature 1990; 343: 774–8.

4. Ton CC, Hirvonen H, Miwa H, et al. Positional cloning and characterization of a paired box- and homeobox containing gene from the aniridia region. Cell 1991; 67: 1059–1074.
5. Breslow NE, Takashima JR, Ritchey ML, Strong LC, Green DM . Renal failure in the Denys-Drash and Wilms' tumouraniridia syndromes. Cancer Res 2000; 60: 4030–32.
6. Traboulsi EI, Zhu D, Maumenee IH Aniridia. In: Genetic Diseases of the Eye (Oxford Monographs on Medical Genetics No.36), Traboulsi EI, ed. New York: Oxford University Press, 1998; 99–114.
7. Scott EO, Denise H, Laura PS. Abnormalities of pupil and iris In: Behrman RE, Kleigman RM, Jensen HB editors. Nelson Textbook of paediatrics, 18th edition Philadelphia:WB Saunders Co., 2007:2576.
8. Muto R, Yamamori S, Ahashi H, Osawa M. Prediction by FISH analysis of occurence of Wilm's tumour in aniridia patients. Am J Med Genet 2002; 108:285-9.
9. Pinna A, Carta A, Mannazzu MC, Dore S, Balata A, Carta F, WAGR syndrome with deletion of chromosome 11p11.2.13. J.AAPOS 2004; 8:396-7.
10. Fischbach BV, Trout KL, Lewis J, Luis CA, Sika M. WAGR syndrome: A clinical review of 54 cases, Paediatrics 2005; 116:984-8.
11. Clericuzio CL. Clinical phenotypes and Wilm's tumour. Med Paediat Oncol 1993; 21:182-7.
12. Schinzel A Catalogue of Unbalanced Chromosome Aberrations in Man, 2nd ed. New York: Walter de Gruyter, 2001; 485–90.
13. Andersen RS, Geertinger HW, Larsen M et al. Aniridia, cataract and gonadoblastoma in a mentally retarded girl with deletion of chromosome 11. Ophthalmologica 1978; 176: 171–7.

