

## Case Report

# WAGR syndrome in a Nepalese male child

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## Abstract

WAGR syndrome which includes Wilms' tumor, aniridia, genitourinary anomalies and mental retardation is a rare, sporadic, genetic disorder characterized by *de nova* deletion in the distal band of 11p13 chromosome. Here, we report first case of WAGR from Nepal of a 5 year old male child with hypospadias, right Wilms' tumor and bilateral aniridia treated successfully by surgery and chemotherapy.

**Key words:** WAGR syndrome, Wilms' tumor, Hypospadias, Aniridia, Chemotherapy.

## Introduction

WAGR Syndrome is a multiple congenital anomaly gene deletion syndrome characterized by interstitial deletion of distal portion of chromosome 11p13. WAGR is an acronym for W-Wilms' tumor, A-aniridia, G-genital anomalies and R-mental retardation. Wilms tumor and male genital anomalies are caused by deletion of the WT1 tumor suppressor gene, and aniridia is caused by deletion of PAX6 ocular developmental gene. Mental retardation is thought to be due to deletion of multiple as yet unidentified genes in the region.<sup>(1)</sup> Till date no case of WAGR has been reported from Nepalese population. We hereby report a case of WAGR syndrome in a male child with complaints of passage of urine from ventral surface of penis, pain abdomen, abdominal mass and photophobia. On examination, the patient was found to have right Wilms' tumor, hypospadias and aniridia. Miller first described the association of aniridia, hemi hypertrophy and other congenital anomalies with Wilms' tumor. The syndrome subsequently became known as WAGR syndrome (contiguous gene syndrome).<sup>1</sup>

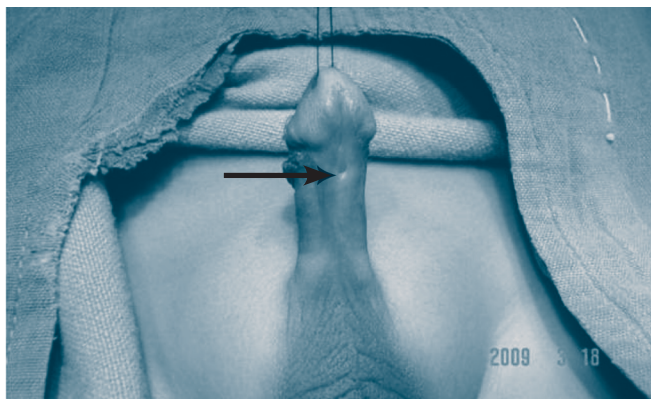
## Case Report

A five year old male child presented to our hospital with pain abdomen, lump on right side of abdomen, passage of urine from ventral surface of penis. Patient

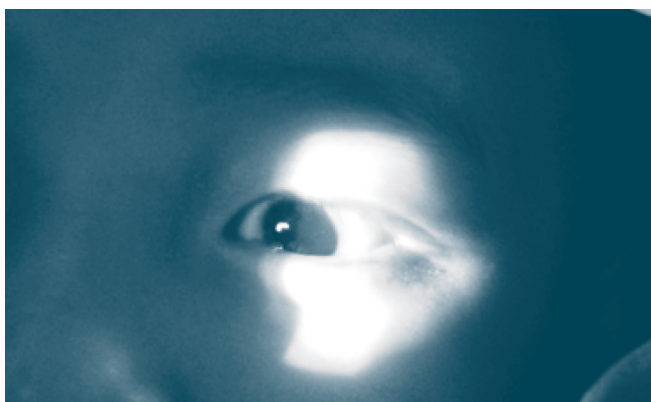
also complained of photophobia in sunlight. The patient was mentally sound and studied in class 1. There was no family history of aniridia or Wilms' tumor. Physical examination revealed right flank mass, hypospadias, but the scrotum was normal with bilateral testes. The penile examination revealed distal penile hypospadias with stenosed urethral orifice. Mother's family, gestational and birth history of the child was normal. Ophthalmic examination revealed bilateral aniridia with no other ocular abnormality. His chest X-ray and renal function tests were normal. Abdomen ultrasonography was suggestive of right Wilms' tumor.



**Figure 1. Abdominal mass: Right Wilms' tumor**

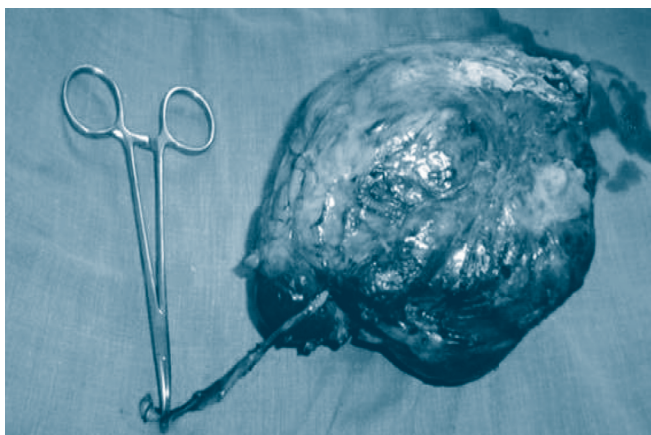


**Figure 2. Distal penile Hypospadias**



**Figure 3. Aniridia – Absence of Iris**

An abdominal CT scan revealed right Wilms' tumor of 8 x 9 cm with normal functioning left kidney. The patient underwent laparotomy with right nephroureterectomy. Histopathological report of kidney was consistent with stage II Wilms' tumor with favorable histological features. Postoperatively patient received chemotherapy. Chromosome analysis could not be done because of its unavailability in Nepal. The child is on regular follow up with Pediatric surgeon and ophthalmologist with regular monitoring of renal functions.



**Figure 4. Resected Right Wilms' tumor**

## Discussion

WAGR syndrome with clinical association of Wilms' tumor, aniridia, genitourinary anomalies, and mental retardation (WAGR) was first noted by Miller et al.<sup>(2)</sup> Patients invariably have a de novo deletion in the distal band of 11p13 as described by Riccardi et al.<sup>(3)</sup> and Franke et al.<sup>(4)</sup> WAGR syndrome is a contiguous gene deletion syndrome. Children with WAGR syndrome invariably have a germ line chromosome deletion at 11p of variable size and nature, but always affecting the WT1 and PAX6 genes, both on band 13(11p13).<sup>(5)</sup> Mutation in the WT1 gene is also thought to be responsible for genitourinary abnormalities.<sup>(6,7)</sup> The patient presenting to us met the diagnostic criteria for WAGR syndrome clinically and confirmed by histopathology. Cytogenetic study could not be done. Clinically, the boy presented with hypospadias, right Wilms' tumor and bilateral congenital aniridia. Our patient did not have mental retardation.

Children with WAGR syndrome generally present in the newborn period with sporadic aniridia. Approximately one third of patients with sporadic aniridia will have WAGR syndrome.<sup>(8)</sup> The combination of sporadic aniridia along with genitourinary anomalies should alert the clinician to the possibility of WAGR syndrome. Boys are often born with genital abnormalities, such as cryptorchidism or hypospadias but more rarely ambiguous genitalia. Our patient presented with both aniridia and hypospadias. One fifth of the patients with sporadic aniridia may develop a Wilms' tumor.<sup>(9)</sup> In patients with WAGR syndrome the risk for developing Wilms' tumor has been estimated to be up to 45%.<sup>(10)</sup> When associated with aniridia, a Wilms' tumor is diagnosed before the age of 5 years in 80% of cases.<sup>(9)</sup> Even our patient presented to us at the age of 5 years. Therefore, renal ultrasound is recommended every 3-6 months until approximately 5 years of age. Clinicians should maintain a high index of suspicion for Wilms' tumor in patients of any age with WAGR syndrome.<sup>(11)</sup> Physical examination (abdominal palpation) and laboratory testing for hematuria are recommended. Although the syndrome is not classically associated with nephropathies, increased rate of renal failure are reported. Hence, periodic evaluation of serum creatinine, blood urea nitrogen and urine for proteinuria should be done.<sup>(8)</sup> Our patient was diagnosed early due to presence of hypospadias and abdominal mass which raised a high suspicion of Wilms' tumor. The child underwent laparotomy with right nephroureterectomy and hypospadias surgery followed by chemotherapy

and is on regular follow up. Once WAGR syndrome has been suspected, a genetic study is recommended using G- banding, fluorescence in situ hybridization (FISH), and/or microsatellite analysis.<sup>(9)</sup> This could not be done in our case because of its unavailability in Nepal and due to financial constraints.

Recently the National Wilm's Tumor Study Group reviewed almost 8600 patients with Wilms' tumor enrolled between 1969 and 2000. Among them 64 (0.75%) had WAGR syndrome. Of 64 patients with WAGR syndrome, 14 developed renal failure. The cumulative risk of renal failure at 20 years were 52.8% and 1.4% for WAGR and non-WAGR patients respectively. Survival estimates for WAGR and non-WAGR patients were 95% and 92 % at 4 years, but 48% and 86% at 27 years from diagnosis respectively. Five late deaths in WAGR patients were from end-stage renal disease. Currently, little is known to explain the histopathology underlying WAGR associated renal failure, but nephropathy is associated with this apparent late manifestation of WT1 deletion.<sup>(9)</sup> Our patient had normal left kidney and is tumor free till date, off chemotherapy with preserved renal function. The child has maintained good visual acuity as the child does not have foveal hypoplasia, glaucoma or cataract. He is managed with dark glasses for aniridia leading to photophobia.

## Conclusion

Every infant or child who presents with genitourinary abnormalities and aniridia should be evaluated for Wilms' tumor. Timely intervention by Pediatric surgeon, ophthalmologist and oncologist is mandatory for good prognosis of the child. Parent counseling and integrated activity at school is important for quality life. Hence, this is the first ever reported Nepalese male child who presented with 3 components of the WAGR syndrome.

**Conflict of interest:** None declared

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