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50 Years Ago in *The Journal of Pediatrics*

Understanding the Molecular Basis of 11p13 Deletion

Haicken BN, Miller DR. Simultaneous occurrence of congenital aniridia, hamartoma and Wilms' tumor. J Pediatr 1971;78:497-502

Haicken and Miller reported a 17-month-old female infant with aniridia, Wilms' tumor, microcephaly, spina bifida with meningocele, and lipoma. This child had features associated with Wilms' tumor–aniridia syndrome and represented the first occurrence of sacral lipoma and meningocele with this condition. This case represented the 25th case reported in which aniridia occurred in association with Wilms' tumor and the third reported case in which a hamartoma occurred in association with Wilms' tumor–aniridia, suggesting a link between this disorder and disorders of growth control. It had been proposed by Miller et al that a mutagenic agent could be responsible for both aniridia and Wilms' tumor.[1]

Subsequent studies demonstrated a de novo 11p13 deletion resulting in a contiguous gene deletion syndrome in patients with Wilms' tumor–aniridia genitourinary anomalies and mental retardation syndrome (WAGR). Although the size of the 11p13 deletion may vary among different patients, *PAX6* and *WT1* are critical genes in this genomic region.[2] *PAX6* encodes a transcriptional factor that is responsible for lens placode development. *WT1* encodes a zinc finger binding protein acting as a transcriptional activator or repressor and is responsible for normal genitourinary development.

The phenotypic spectrum of WAGR syndrome includes 50% risk for Wilms' tumor in addition to elevated risk for movement disorders, scoliosis, obesity, obstructive sleep apnea, polydactyly, diaphragmatic hernia, behavior, auditory processing deficits, and psychiatric problems. End-stage renal disease is associated with WAGR and includes focal segmental glomerulosclerosis. Early diagnosis of WAGR is extremely important, as WAGR-associated Wilms' tumor is associated with a more favorable histology prognosis as compared with isolated Wilms' tumor.

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