Wilms' Tumor Associated with Congenital Aniridia

Tadao KIRIYAMA and Yoriaki KAMIRYO
The Department of Urology, Yamaguchi University School of Medicine, Ube, Yamaguchi, Japan
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ABSTRACT

The third case of the aniridia-Wilms' tumor complex in Japan is reporetd herein. The patient received a radical nephrectomy and survived the period of risk. A radiotherapy and six series of chemotherapy treatments have been used for adjuvant therapy. It was learned from this case that even 6-month intervals are not frequent enough for Wilms' tumor examinations in children with nonfamiliar aniridia.

Aniridia is a very rare anomaly, with an estimated incidence of 1 in 50,000[15]. Similarly, Wilms' tumor, although one of the most commonly encountered malignant tumors in infants, is also rare. An intimate relationship between these uncommon conditions has been recently discovered. According to Miller and his associates[13], who first reported the association between the two conditions in 1964, in a group of 440 patients with Wilms' tumor six had aniridia, a prevalence of 1:73. Up to 1974, 24 cases of aniridia-Wilms' tumor syndrome have been reported in English language medical literature, but there have been only two cases reported in Japan.

CASE REPORT

S.E., YU-46-1074, a 29-month-old girl, was admitted to the urological ward of Yamaguchi University Medical School hospital on August 9, 1971, with an unusual abdominal mass and symptoms of painless gross hematuria which were first noticed 2 weeks prior to admission. She had been born after a normal and full-term pregnancy, and weighed 2,600 gm at birth. Neither of her parents had any congenital anomalies, but they were first cousins. She showed signs of delayed physical growth and slight mental retardation. Her father died in an automobile accident shortly after her birth. She had no siblings.

The patient had wide palpebral fissures and exophthalmos on both sides, and received two operations at the ages of 3 and 4 months for

the condition, which was diagnosed as bilateral congenital glaucoma. At the age of 20 months, she was admitted to the ophthalmological ward of this hospital with diagnoses of bilateral aniridia, bilateral glaucoma, bilateral congenital cataract of the posterior pole, bilateral coloboma, and bilateral horizontal nystagmus. She underwent surgery for the right cataract. At that time, no space-occupying lesions could not be detected in either of the kidneys by an intravenous urogram (IVP) performed by the urological out-patient service.

On admission to the urological ward, physical examination revealed a rather small and slow in movement, but well-nourished child. Her body temperature was 36.4°C, BP 110/60, and her pulse was 90 beats/minute. Bilateral exophthalmos was noted. There was white opacity in the left lens, which had not been operated upon, and bilateral absence of the iris. There was no abnormality of the ear-lobes on either side. Examination of the abdomen revealed a large, round, very hard mass with a well defined but nodular surface, which filled the left side of

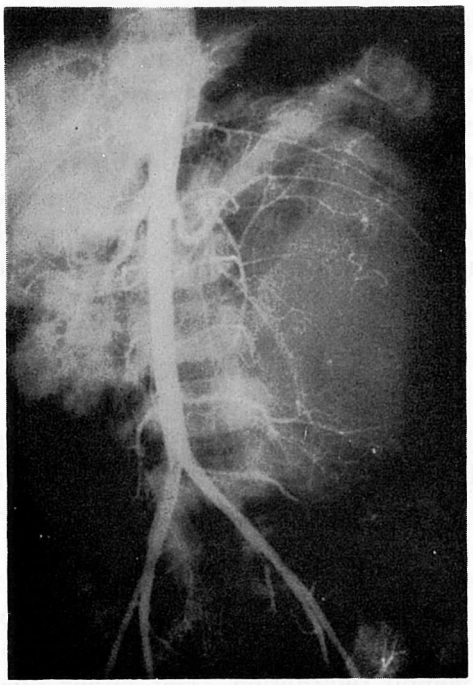

Fig. 1. Retrograde femoral aortogram. Elongated and irregular tumor vessels were shown especially in lower pole of left kidney with distortion of intrarenal branches by mass. Poorly vascularized mass was present in midportion.

her abdomen and extended to the midline. There was no enlargement of superficial lymph nodes anywhere. The external genitalia were normally developed. The remainder of the examination was unremarkable. The findings of the laboratory tests were all negative.

A chest roentgenogram revealed no abnormalities; no metastatic nodules were evident. An IVP revealed a lobular protuberance on the lateral margin of the enlarged contour of the kidney. There was also a displacement of all of the calices, which made them look as if they were grasping some round object, and a moderate dilatation of some of the calices. A retrograde aortography (Fig. 1) revealed finer, elongated, and displaced intra-renal branches with sparse distribution, which surrounded an avascular area in the middle of the kidney. "Pooling" of the contrast dye was noted. A radiographic survey revealed no radiolucent areas in the skeletal system.

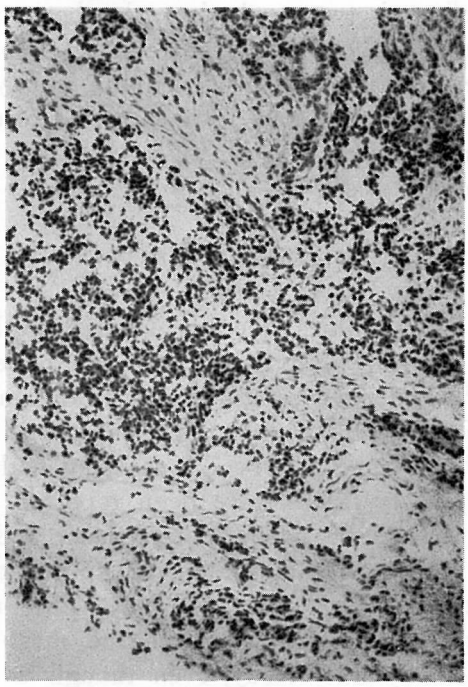

Fig. 2. Microscopic feature. Tumor elements consisted of masses of sarcomatous spindle-cells and columnar cells of embryonic character. Early tubules, simulating embryoid bodies, were found in some places to be enclosed within spindle-cell stroma. These newly formed tubules lacked basement membrane and varied in size. Mesenchymal cells, such as striated muscle, cartilage and bone were not found. Mitotic figures were frequent.

A bone marrow study produced normal results. No atypical cells were found. A chromosome study revealed a normal karyotype with a count of 46 chromosomes. Intra-ocular tension was 17 mmHg. in the right side and 24 mmHg. in the left side.

An transperitoneal nephrectomy was completed on August 19, 1971. The procedure revealed a large encapsulated left-sided retroperitoneal tumor with vascular congestion surrounding it. The tumor, which was confined to the left kidney and had displaced the bowel and intestine to the right, was removed in total with perirenal fat. The removed kidney measured 10 by 8 cm. and weighed 507 gm. All but a small part of the normal kidney at the upper pole had been replaced by an encapsulated gray-whitish tumor with central necrosis, which histologically proved to be Wilms' tumor (Fig. 2). Metastasis in the lymph nodes was negative.

Postoperatively, the child was treated with actinomycin-D, 12 mg. daily for 8 days, followed two weeks later by betatron therapy, with a total radiation dose of 4,000 rads. She received another five series of actinomycin-D therapy during the subsequent two years following the completion of the betatron therapy. Recently she returned to the urological ward. She was confirmed to be in good health without any signs of recurrence or metastasis.

DICCUSSION

Wilms' tumor has at times been considered to be associated with certain congenital anomalies, such as total hemihypertrophy, horseshoe kidney[2,5,9,10,11,14,16], and male pseudohermaphroditism[4,17,18]. In addition, sporadic cases of Wilms' tumor in patients with chronic infantile glomerulonephritis[16,17], nephrotic syndrome[17], agonadism[1], and duplication of the upper urinary tract[8] have been reported. In order to more fully define the relation between the neoplasm and these congenital defects, Miller et al[13]. made an intensive epidemiological study of a series of 440 cases of Wilms' tumor in 1964. The intimate connection between the neoplasm and aniridia was the most interesting among the results revealed by the study, even though a high frequency of Wilms' tumor was established in cases of hemihypertrophy, hypospadia, cryptorchism, horseshoe kidney and duplication of the upper urinary tract, and a suggested correlation was revealed in cases of pigmented or vascular nevi. The study revealed six aniridic children out of the 440 cases, an incidence of 1:73. Aniridia is a very rare anomaly with an expected at-birth incidence of 1:50,000[15]. In an additional study by

Fraumeni und Glass[7], out of 28 children with congenital aniridia, one had Wilms' tumor on admission and the neoplasm subsequently developed in six of the children.

The children with the aniridia-Wilms' tumor complex tended to be younger when their tumors were first diagnosed than the non-aniridic children with neoplasia[3]. Two thirds (64.9%) of aniridic children were found to have at least one parent with aniridia (familiar aniridia)[15], however a majority of the children with the aniridia-Wilms' tumor complex had no family history of the eye anomaly (non-familiar or sporadic aniridia)[12,13]. This suggests that the disorders are brought about either by gene mutation or by environmental effects on embryogenesis. If mutation is the cause, it might be speculated that either (a) the gene for aniridia interacts with that for Wilms' tumor or (b) a single aniridia gene has pleiotrophic effects.

Twenty-seven cases of this complex were collected from literature, our experience, and the two other cases in Japan. As summarized in Table 1, other concurrent anomalies, besides aniridia, can be seen among the cases. Cataract and glaucoma are usually known to be associated with aniridia[20]. The common and significant anomalies include small head circumference and microcephaly, mental retardation, retarded growth and development, deformed, especially recurved, pinna, undescended testis, and hypospadia. Skull or craniofacial anomalies, retarded bone age, dwarfism, renal aplasia or hypoplasia, pseudohermaphroditism, inguinal or umbilical hernia, dislocation of the hip, and hemangioma have been described as uncommon nonocular anomalies. When associated with genitourinary anomalies, unusual cancer risk is considered to be induced or enhanced in children with nonfamiliar aniridia by the teratogenic influences which affect the genitourinary tract.

Knowledge of the excessive incidence of certain congenital anomalies in children with Wilms' tumor may throw further light upon the etiology of these conditions, and may give clues to aid in the early diagnosis, of this disease which can lead to surgical removal of the affected kidney before metastases have occurred. In addition, it was learned from both Woodard and Levine's report[19] and our patient that even 6-month intervals are not frequent enough to obtain followup excretory urograms in children with nonfamiliar aniridia.

Table 1. Previously Reported Cases of Wilms' Tumor Associated with Aniridia

Authors	Case	Sex	Age	Cataracts	Microcephaly	Mental retardation	Detect of pinna	Genitourinary anomaly	Other defects
Brusa and Torriceili*1 (1953)	1	M	2½	+		+		cryptorchidism	
Miller et al[13] (1964)	2	M	2	+	+	+	−		piagiocephaly, inguinal hernias
	3	F	2	+	+	+	indented helix	cryptorchidism	craniofacial dysmorphism
	4	M	1	+	+	+	recurved		micrognathia
	5	M	3	+	−	+			
	6	M	1¼	+	+	−	recurved		exostosis (ilium)
	7	M	1	−	−	−		contralateral hypoplastic kidney	
Fontana et al.[6] (1965)	8	F	2½	+	−		recurved	contralateral bifid renal pelvis	
DiGeorge and Harley[3] (1965)	9	M	2¼	+		+		cryptorchidism with gonadoblastoma	
	10	M	2	−		+		small phallus	
	11	M	1½	+		+		cryptorchidism	
	12	M		−	−	+			
Schroeder and Cardle*2 (1965)	13	M	1¼	+	+	+		cryptorchidism	
Zimmerman and Font[20] (1966)	14		½	+	+	+			
Schweisguth et al.*1 (1967)	15	F	1½	−	+				
	16	F	1½	−	+	+		double renal artery	
	17	F	4½	+	−	−		hypoplastic kidney in pelvis with double artery	
	18	F	1	+	+				
Fraumeni and Glass[7] (1968)	19	F	3	+	−	−			
	20	M	1¾	−	+	+	recurved	cryptorchidism hypospadias	craniofacial dysmorphism and cerebral defect, extensive hemangiomata xanthomatous plaques inguinal and umbilical hernias
	21	F	1	+	−	−		contralateral aplastic kidney	congenital dislocation of hips
	22	M	1½	+	−	+	deformed		pyloric stenosis, inguinal and umbilical hernias, Meckels' diverticulum
	23	F	2	+	−	−	low set pointed		
Woodard and Levine[19] (1969)	24	F	1½	+	−	−	recurved		
Tajima et al.*3 (1971)	25	M	3	−	−	+		cryptorchidism hypospadias	disturbance of speech
Koyama*3 (1972)	26	M	2 1/12	+	−	−		cryptorchidism hypospadias	
Kiriyama and Kamiryo	27	F	2 5/12	+	−	+			

*1 : cited by Fraumeni et al.[7] *2 : cited by Miller.[12] *3 : written in Japanese.

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