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ADULT WILMS' TUMOR

Role of combined modality treatment

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Abstract

Adults Wilms' tumor, unlike its pediatric counterpart, is extremely rare and highly lethal. Less than 200 cases have been reported in the world literature and a large proportion of these may not have been true Wilms' tumors. We report 3 cases seen at our institution who were treated with a multimodality approach, all three remaining alive without evidence of active disease at 6 years, 2.25 years and 8 months respectively from diagnosis. We also review results of multimodality management, emphasizing the poor outcome for stage III and IV tumors in spite of multiagent chemotherapy. Alternative drugs, such as cisplatinum may have a role in management. Finally, we propose that prophylactic pulmonary irradiation may have a place in advanced stages of adult Wilms' tumor.

Key words: Kidney neoplasms, adult Wilms' tumor, pulmonary irradiation.

Wilm's tumor is the commonest pediatric genitourinary malignancy in the USA with an incidence of 7.8 per million population from ages 0 through 14 (1). It is, however, extremely rare in adults. Consequently, while several cooperative trials have been carried out for pediatric Wilms' tumor (2–4) resulting in refined therapeutic guidelines, such guidelines for adult Wilms' tumor do not exist.

We report 3 cases seen at our institution, summarize the recent literature and analyze the results of multimodality managment of adult Wilms' tumor, in particular emphasizing the role of pulmonary irradiaiton.

Case reports

Case 1. K. K., a 17-year-old white female was seen by her physician in December 1981 with a 1-month history of a painless left upper quadrant mass without hematuria. Physical examination revealed a firm, nontender mass extending across the midline. Initial laboratory studies were unremarkable. Abdominal CT showed a large retroperitoneal mass. Intravenous pyelography (IVP) revealed this to be located at the inferior pole of the left kidney. At exploratory laparotomy, these findings were confirmed. Left nephrectomy was performed and a 1 200 g mass was removed. However, due to tumor rupture, spillage occurred throughout the peritoneal cavity. The initial pathologic diagnosis was leiomyosarcoma with capsular penetration and renal vein invasion, but no nodal metastasis were identified. Postoperatively she received 50.4 Gy in the tumor bed. Subsequent review of the slides by the National Wilms' Tumor Study (NWTS) pathologists resulted in a revision of the diagnosis to favorable histology Wilms' tumor (3). In light of the new histologic information, she was classified as having stage III Wilms' tumor and received adjuvant doxorubicin (Adria), actinomycin-D (Act-D), and vincristine (VCR) as per protocol DD of the National Wilms' Tumor Study (NWTS) Group 3 (4). As of December 1987, she remained free of recurrence or complications.

Case 2. M. T., a 21-year-old white male presented with a one-week history of hematuria in September 1985. Physical examination revealed a large left upper quadrant mass demonstrated to be intrarenal in location on IVP and measured 10×10 cm on CT. Plain radiograph and CT of the chest were unremarkable. Left radical nephrectomy and node dissection was carried out. The tumor extended into the renal vein. Histologic evaluation revealed the clear cell bone metastasising (unfavorable histology) variant of Wilms' tumor (3) with positive lymph nodes and the

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patient was thus staged as stage III. Postoperative adjuvant therapy consisted of 40 Gy in the left renal bed and triple drug chemotherapy consisting of doxorubicin, vincristine and actinomycin-D as per NWTS guidelines.

In December 1985, metastasis to the right humerus and left inguinal nodes were noted. The left hemipelvis and right humerus were treated to 30 Gy. The chemotherapy regimen was changed to an alternating non cross-resistant regimen of etoposide/cyclophosphamide and doxorubicin/cisplatinum. A clinical complete response was achieved with this combined modality approach.

In June 1987, right sacro-iliac metastases as well as a solitary pulmonary nodule were identified. The right hemipelvis was treated to 30 Gy and the right lung to 18 Gy with a boost to the nodule to 34 Gy. A complete radiographic response of the pulmonary nodule was documented and as of December 1987 the patient remained stable without evidence of disease progression at any site.

Case 3. F. B., a 22-year-old white male presented in April 1987 with a 2-week history of nausea, emesis, lower abdominal pain, fever and weight loss. Physical examination revealed a right upper quadrant mass. Initial evaluation included an abdominal CT which demonstrated a large right renal mass. Right radical nephrectomy and partial hepatectomy were performed because of direct tumor extension into the liver. Multiple peritoneal metastases were noted in the pelvic cul-de-sac. Lymph nodes were free of tumor. Histology revealed Wilms' tumor. Postsurgical chest CT revealed a noncalcified peripheral nodule in the left lung. The patient was staged as having stage IV disease. Postoperatively, he was commenced on doxorubicin, actinomycin-D and vincristine and received 12 Gy in the entire thorax and the lung nodule was boosted to 24 Gy. He then received 24 Gy in the whole abdomen, the left kidney being blocked after 15 Gy. The right hemiabdomen was boosted to 38.4 Gy. As of December 1987, the patient was disease-free.

Results in the literature

In 1980, Kilton et al. (5) reviewed the world literature on adult Wilms' tumor and identified 192 cases. Of these cases, 35 conformed to the diagnostic criteria set by them. The experience of the NWTS with a group of 31 adult Wilms' tumor was reported by Byrd et al. (6) in 1982. We carried out an exhaustive literature search for additional patients reported in the 1980s and identified 20 patients (7–16) and 3 more cases are now reported by us (Table 1).

Of the 23 cases evaluated, 3 were stage I, 1 was stage II, 9 were stage III, 9 were stage IV and staging information was unavailable for 1 patient. The age range was 17–84 with a median of 23 years. An almost equal male to female ratio was observed.

With the exception of 2 patients who died in the immediate postoperative period and a third patient whose therapeutic details were not reported, all patients received chemotherapy. Combination chemotherapy consisting of actinomycin-D and vincristine with or without doxorubicin was the most commonly used initial regimen. Of these 20 patients, 16 also received some form of radiation therapy as part of their adjuvant treatment. Prophylactic thoracic radiation was employed in only 1 patient.

The survival status of 2 patients was not reported. Of the remaining 21, 12 are known to have died, with an overall survival of 9/21, with a follow-up range of 1–72 months and mean follow-up of 19 months.

Of the 4 patients with stage I or II disease, 2 have remained alive without disease, 1 died from pulmonary metastases and the fourth is alive with liver metastases.

Follow-up data is available for 6 patients with stage III disease; 1 died postoperatively and only 1 of the remaining 5 has remained disease-free. Lung metastases developed in 4, 1 of whom is currently alive and in complete remission. None of these patients received prophylactic thoracic irradiation but of the 3 patients whose lungs were irradiated after pulmonary metastases appeared, 1 experienced a complete response. The overall survival for stage III therefore is 2/6 and disease-free survival is 1/6. The pulmonary failure rate in spite of chemotherapy and in the absence of thoracic irradiation is 4/5.

Of the 9 patients with stage IV disease, long-term follow-up data is available for 7 patients, 6 of whom are known to have died, with an overall survival of 1/7. All but 1 presented with lung metastases and 6 received thoracic irradiation. Complete response was experienced by 5 of 6. One of our stage IV patients is now disease-free at 8 months but has not been included as a long-term follow-up data point because of short follow-up.

Discussion

Unlike the pediatric experience where a large proportion of patients present with early stage disease, advanced stage (III or IV) was observed in over 80% of patients in this review. Advanced stage disease was observed in 44% of Kilton's (5) series and 54% of Byrd's (6) series. This may partially account for the significantly poorer survival of adult Wilms' tumor. However, even when corrected for stage, the outlook for adult Wilms' tumor remains grim (Table 2) and many authors have speculated that treating these patients along NWTS guidelines might improve survival.

Almost all patients reported by Byrd and reviewed by us have received therapy similar to that recommended by NWTS without any obvious survival impact for advanced stage disease. Consideration should, therefore, be given to alternative, more aggressive strategies. Our experience with cisplatinum in a single patient has been encouraging.

Table 1

Adult Wilms' tumor. Natural history

Case No.	Ref No.	Age	Sex	Stage	Survival status	Survival (months)	Initial radiotherapy (Gy)			Initial chemotherapy				Outcome
							Tumor bed	Abdomen	Thorax	Act-D	VCR	Adria	Other	
1	12	20	F	?	Dead	1	–	–	–	–	–	–	–	Cardiac arrest post-op
2	11	29	M	I	Alive	24	40	–	–	×	×	–	–	DFS
3	13	46	F	I	Alive	36	–	–	–	×	×	–	–	DFS
4	16	23	F	I	Alive	15	–	–	–	×	×	–	–	Alive with liver mets
5	16	45	M	II	Dead	41	–	–	–	×	×	×	–	Lung mets at 27 mo.
6	12	21	M	III	?	?	10	–	10	×	×	–	–	Unknown
7	12	28	F	III	?	?	–	–	–	×	×	×	–	Unknown
8	12	27	F	III	Dead	24	35	–	–	×	×	–	–	Liver/lung mets at 24 mo
9	13	32	F	III	Alive	?	P	P	–	P	P	P	?	Unknown
10	15	34	M	III	Dead	15	41	30	–	×	×	×	–	Lung mets at 12 mo. NR to XRT
11	16	23	F	III	Dead	23	DU	–	–	×	×	×	–	Lung mets at 7 mo. NR to XRT or chemo
12	16	84	F	III	Dead	1	–	–	–	–	–	–	–	Post-op pneumonia
13	*	17	F	III	Alive	72	50	–	–	×	×	×	–	DFS
14	*	21	M	III	Alive	27	40	–	– 12	×	×	×	–	CR to lung mets from XRT. Stable with mets
15	*	22	M	IV	Alive	6	44	24	24 (boost)	×	×	×	–	CR to lung met. Disease free at 8 mo.
16	7	19	F	IV	Alive	24	–	DU	DU	×	×	×	–	DFS
17	7	19	F	IV	Dead	3	30	30	–	×	×	×	–	Died of GI bleed during chemotherapy
18	7	18	M	IV	Dead	3	48	–	–	–	–	–	×	Dead of disease
19	8	63	M	IV	Dead	17	32	22	–	×	×	×	–	Lung mets at 10 mo. CR with XRT & chemo. Progressed
20	9	20	M	IV	Alive	?	28	–	14	×	×	×	–	CR. No. long-term follow-up
21	10	25	M	IV	Dead	10	20	–	DU	×	×	×	–	Progression of lung mets. New liver mets
22	14	26	M	IV	Dead	13	?	?	?	?	?	?	?	Dead of disease
23	15	22	M	IV	Dead	14	22	–	15	×	–	–	–	Lung mets CR to XRT later recurrence

DFS = Disease-free survival
CR = Complete reponse
NR = No response
* = Case reports in current paper
P = Planned
DU = Dose unknown

Table 2

Wilms' tumor. Survival by stage

Stage	Pediatric*	Adult**	Kilton's series	Byrd's series
I	90%	3/3	12/14+	5/9
II	80%	0/1		4/5
III	75%	2/6	2/6	1/6
IV	70%	1/7	0/5	1/9

* Preliminary results of NWTS-3
** Composite data from present review. Although the overall survival in this series is 9/21, 3 patients have been excluded from this table because of very short follow-up (less than 8 months).
+ For stage I and II combined.

Pulmonary irradiation may have a role in stage III and IV disease. This is borne out by the fact that 4/5 stage III patients with long-term follow-up developed pulmonary metastases and of the 3 patients who then received lung irradiation, 1 experienced a complete response. Of stage IV patients, 8/9 presented with lung metastases and 6/8 received pulmonary irradiation with a complete response rate of 5/6. Since a large proportion of advanced stage patients probably harbor subclinical disease in their lungs, prophylactic thoracic irradiation deserves more consideration in the future.

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REFERENCES

1. Young JL, Miller RW. Incidence of malignant tumors in U.S. children. J Pediatr 1975; 86: 254.
2. D'Angio GJ, Evans AE, Breslow ME, et al. The treatment of Wilms' tumor: Results of the National Wilms' Tumor Study. Cancer 1976; 38: 633.
3. D'Angio GJ, Evans AE, Breslow ME, et al. The treatment of Wilms' tumor: Results of the second National Wilms' Tumor Study. Cancer 1981; 47: 2302.
4. D'Angio GJ, Evans AE, Breslow ME, et al. Results of the third National Wilms' Tumor Study (NWTS-3). A preliminary report. Proc AACR 1984; 25: 183.
5. Kilton L, Mathews MJ, Cohen MH. Adults Wilms' tumor: A report of prolonged survival and review of literature. J Urol 1980; 124: 1.
6. Byrd RL, Evans AE, D'Angio GJ. Adult Wilms' tumor: Effect of combined therapy on survival. J Urol 1982; 127: 648.
7. Babian RJ, Skinner DG, Waisman J. Wilms' tumor in the adult patient. Cancer 1980; 45: 1713.
8. Abadir R. Wilms' tumors in adults: J Surg Oncol 1981; 16: 175.
9. Scully RE, Mark EJ, McNeely BU. Case records of the Massachusetts General Hospital case 32–1981. NEJM 1981; 305: 331.
10. Vorstman B, Rothwell D. Wilms' tumor in adult patient. Urology 1982; 20: 628.
11. Denes FT, Nahas WC, Alfer V. Adult Wilms' tumor treatment with surgery, radiotherpay and chemotherapy. Urology 1982; 19: 187.
12. Kumar R, Amparo EG, David R, Fagan CJ, Morettin LB. Adult Wilms' tumor: Clinical and radiographic features. Urol Radiol 1984; 6: 164.
13. Roth DR, Wright J, Cawood CD, Pranke DW. Nephroblastoma in adults. J Urol 1984; 132: 108.
14. Yatsuzuka H, Nakamura N, Aizawa S. Wilms' tumor in an adult with multiple osteoblastic metastases. Surg Neurol 1984; 21: 515.
15. Chung TS, Reyes CV, Stefani SS. Wilms' tumor in adults. Urology 1984; 24: 215.
16. Bailey LE, Durkee CT, Werner AL, Finlay KK. Wilms' tumors in adults. Am Surg 1987; 53:149.