Journal of Pediatric Surgery (2006) **41**, 1641–1644

ELSEVIER

Journal of Pediatric Surgery

www.elsevier.com/locate/jpedsurg

Bilateral Wilms' tumor with anaplasia: lessons from the National Wilms' Tumor Study

Thomas E. Hamilton[a,*], Daniel M. Green[b], Elizabeth J. Perlman[c], Pedram Argani[d], Paul Grundy[e,f], Michael L. Ritchey[g], Robert C. Shamberger[h]

[a]*Division of Pediatric Surgery, Maine Medical Center, Portland, ME 04102, USA*
[b]*Department of Pediatrics, Roswell Park Cancer Institute, Buffalo, NY, USA*
[c]*Department of Pathology, Children's Memorial Hospital, Chicago, IL, USA*
[d]*Division of Surgical Pathology, Department of Pathology, The Johns Hopkins Hospital, Baltimore, MD, USA*
[e]*Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada*
[f]*Department of Oncology, University of Alberta, Edmonton, Alberta, Canada*
[g]*Division of Urology, University of Texas Houston Medical School, Houston TX, USA*
[h]*Department of Surgery, Children's Hospital, Boston, MA, USA*

Index words:
Wilms;
Bilateral;
Anaplasia;
Discordance

Abstract

Purpose: The purpose of this study was to evaluate whether initial diagnostic technique influenced the ability to identify anaplastic histology, to determine the time interval to diagnosis of anaplasia, and to delineate the incidence of discordant pathology in bilateral Wilms' tumor. We hypothesized that delay in diagnosis of anaplasia could affect time to appropriate surgery and intensive multimodality therapy.

Methods: One hundred eight-nine children were enrolled in the fourth National Wilms' Tumor Study with synchronous bilateral tumors, 27 of whom were eventually shown to have anaplastic histology. Initial diagnostic technique, time interval to diagnosis of anaplasia, and the incidence of discordant pathology were determined.

Results: Anaplasia was identified in 0 of 7 tumors by core needle biopsy, 3 of 9 tumors by open wedge biopsy, and in 7 of 9 cases by partial or complete nephrectomy. The mean duration of first chemotherapy regimen (DD or EE) was 20, 39, and 36 weeks, respectively, before anaplasia was identified at second surgery. Discordant pathology between bilateral tumors was identified on final tissue diagnosis in 20 patients. Only 4 patients had anaplastic tumors in both kidneys.

Conclusions: Core needle biopsy did not identify anaplasia in 7 of 7 children. Open biopsy or partial/complete nephrectomy identified anaplasia at initial diagnostic procedure in 10 of 18 children. Twenty of 24 patients at final tissue diagnosis had discordant pathology between the 2 kidneys. Earlier interval incisional biopsy or resection may identify anaplastic histology and limit the duration of chemotherapy targeted to favorable histology for children with bilateral Wilms' tumor and anaplasia.

The National Wilms' Tumor Study Group (NWTSG) has completed 5 studies of multimodality management of children with Wilms' tumor. The identification of prognostic factors including tumor stage and histology has produced

* Corresponding author. Tel.: +1 207 772 4444; fax: +1 207 772 7725.
E-mail address: hamilt@mmc.org (T.E. Hamilton).

0022-3468/$ – see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.jpedsurg.2006.05.053

highly effective treatment regimens with the most intensive regimens reserved for aggressive disease. Children with bilateral lesions pose a unique clinical challenge because of the need for parenchymal sparing to avoid renal failure. Despite the overall good survival with bilateral Wilms' tumor, those with anaplastic histology do poorly [1]. We hypothesized that initial diagnostic technique affected the ability to identify anaplastic histology which could result in significant delay of appropriate surgery and intensive multimodality therapy. We also set out to determine the incidence of discordant pathology to emphasize the importance of performing bilateral biopsies.

1. Materials and methods

The authors reviewed the charts of 189 children with bilateral (stage V) tumors who were enrolled in the fourth National Wilms' Tumor Study (NWTS-4). Of these, the only children included in this analysis had anaplastic histology. Operative reports, pathologic reports, surgical check lists, and complete medical records were reviewed by 3 of the authors (RCS, MLR, TEH). Central pathology review was performed and included assignment of histology and local stage. Factors analyzed included initial diagnostic technique, time interval to diagnosis of anaplasia, and frequency of discordant histology between kidneys.

2. Results

Twenty-seven (14%) of 189 children with bilateral tumors had anaplasia in at least 1 kidney diagnosed sometime in the clinical course of their disease. There were 15 girls and 12 boys with an average age at presentation of 43 months. None had rhabdoid tumor or clear cell sarcoma of the kidney.

Table 1 Discordance in pathology grouped by initial surgical management

NWTS no.	Sex	Age at dx months	Survival	Cause of death	Right	Left	Discordant
Needle							
8581	F	22	Alive		Diffuse anaplasia	Necrotic	Yes
7766	F	28	Alive		PLNR	Diffuse anaplasia	Yes
9285	M	57	Dead	tumor	Diffuse anaplasia	Diffuse anaplasia	No
7243	M	82	Dead	tumor	Diffuse anaplasia	Diffuse anaplasia	No
7108	M	27	Alive		favorable	Diffuse anaplasia	Yes
7943	F	56	Dead	tumor	favorable	Diffuse anaplasia	Yes
8193	F	21	Alive		Nodules no biopsy	Focal anaplasia	NA
No biopsy							
6824	M	63	Dead	Tumor	Necrotic	Diffuse anaplasia	Yes
6004	M	23	Dead	Tumor	Diffuse anaplasia		NA
Open biopsy							
7284	F	33	Dead	Tumor	Favorable	Diffuse anaplasia	Yes
7018	M	24	Alive	NA	Diffuse anaplasia	Favorable	Yes
6344	F	7	Alive	NA	Diffuse anaplasia	Favorable	Yes
8284	F	45	Alive	NA	No central review avail	Diffuse anaplasia	NA
8304	F	44	Alive	NA	Necrotic	Diffuse anaplasia	Yes
7665	M	42	Alive	NA	Diffuse anaplasia	Necrotic	Yes
7971	F	20	Dead	Tumor	Favorable	Diffuse anaplasia	Yes
7770	M	24	Alive	NA	Necrotic	Diffuse anaplasia	Yes
7833	F	38	Alive	NA	Diffuse anaplasia	Favorable	Yes
Partial/complete nephrectomy							
7109	F	40	Dead	Tumor	Diffuse anaplasia	Favorable	Yes
9092	M	57	Alive	NA	Focal anaplasia	Favorable	Yes
8953	F	60	Alive	NA	Diffuse anaplasia	Diffuse anaplasia	No
8519	M	40	Dead	Tumor	Favorable	Diffuse anaplasia	Yes
6339	M	39	Dead	Tumor	Favorable	Diffuse anaplasia	Yes
8633	F	72	Dead	Tumor	Diffuse anaplasia	favorable	Yes
6937	F	63	Alive	NA	Favorable	Diffuse anaplasia	Yes
7557	F	25	Dead	Tumor	Diffuse anaplasia	Diffuse anaplasia	No
7690	M	106	Dead	Tumor	Diffuse anaplasia	Favorable	Yes
	15 F, 12 M	43 m (mean)	14 alive, 13 dead				20/24

F indicates female; M, male; PLNR, perilobar nephrogenic rest; NA, not available.