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Prognostic factors in primary nonmetastatic Ewing sarcoma of the rib in children and young adults

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Abstract

Background: The rarity of Ewing sarcoma of rib has resulted in paucity of data, particularly on the prognostic factors and pattern of relapses. We analyzed the recurrences in patients with primary nonmetastatic Ewing sarcoma of the rib and examined prognostic factors of poor outcome.

Methods: From January 2004 to January 2011, 37 patients were treated. After induction chemotherapy, complete (from costal cartilage to vertebra) or partial excision of involved rib with or without adjacent ribs was performed. Postoperative radiotherapy was administered for positive margins, poor response to chemotherapy, and large primary tumors with significant soft tissue component at presentation.

Results: Disease relapsed in 16 patients: at the local site (n = 5), both local and distant (n = 2), and distant site only (n = 9). The projected 5-year cause-specific, relapse-free survival and local control were 50%, 44%, and 72%. Poor response to chemotherapy (>5% residual tumor) and resection of adjacent lung parenchyma (a surrogate for tumor extension) were adverse prognostic factors for relapse-free survival in multivariate analysis.

Conclusion: Relapses occurred more often at distant sites and had a poor outcome. In this study, poor histologic response to chemotherapy ($P = .04$) and the infiltration of adjacent lung parenchyma ($P = .01$) are adverse prognostic factors.

Ewing sarcoma (ES) is the most common malignant tumor of the chest wall in children and adolescents. Approximately 6% to 16% of ES involve the chest wall [1-5]. It is also referred to as Askin-Rosai tumor. The presence of a specific translocation t(11;22)q(24;12) in ES, primitive neuroectodermal tumor, and the Askin-Rosai tumor led to grouping of these entities under the ES family of tumors. Rib is an uncommon site of primary ES. The rarity of ES of rib has resulted in limited published reports or clustering of data with other primary sites of the chest wall [6-12]. For similar reasons, there is limited information on

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the patterns of relapse and their outcome. Although surgery remains an important modality of treatment for ES of rib, the extent of surgery is not well defined [8,13-15]. The aim of this study was to analyze prognostic factors predicting poor outcome in patients with primary nonmetastatic ES of the rib and to examine the pattern of relapses.

1. Methods

We reviewed the records of patients with ES of the ribs treated between January 2004 and January 2011 at a single tertiary cancer center. Of the 45 patients identified from the hospital database, 37 patients with nonmetastatic disease were selected.

All patients had a comprehensive clinical evaluation and a core biopsy for confirmation of the diagnosis. Patients who underwent a surgical exploration elsewhere had their biopsied specimen reviewed at our center. Translocation studies were not performed routinely. Cytologic evaluation of pleural fluid was not performed in all patients who had pleural effusion. Each patient was discussed in the multidisciplinary tumor board meeting for planning of treatment strategies.

1.1. Radiology

A chest computed tomographic (CT) scan was performed for evaluation of the primary tumor, which included precise tumor localization and the presence of any pleural effusion or pulmonary metastases. Tumor characteristics were described using the French Society of Pediatric Oncology criteria [10]. A *large tumor* was defined as a neoplasm more than 8 cm in greatest dimension, and a smaller tumor, with greatest dimensions of less than 8 cm. Depending on the level of involved rib, tumors were classed in 2 groups: the upper ribs (1st to 4th) and the middle or lower ribs (5th-12th). The rib component in which the primary tumor occurred was classified into 3 groups: anterior, lateral, or posterior. A *posterior component* was defined as being the more posteriorly located segment of the ribs to the tangent line at the anterior edge of the spinal body.

Magnetic resonance imaging was performed in patients with posterior rib lesion for assessment of intraspinal extension. All patients underwent investigations to exclude the presence of metastatic disease including whole-body technetium bone scan, bone marrow aspiration, and biopsy. Whole-body positron emission tomography scan was also performed in some patients.

1.2. Chemotherapy

The institutional chemotherapy protocol included 2 courses of VIE couplet (vincristine, ifosfamide, and etoposide) followed by 2 courses of VAC couplet (vincristine, cyclophosphamide, and doxorubicin) administered every 3 weeks (see Table 1). Maintenance therapy after treatment of the primary tumor included 10 courses of alternating VAC and VIE couplets, with actinomycin D substituted for doxorubicin after a total dose of 360 mg/m^2. Vincristine was given weekly throughout between the chemotherapy pulses.

1.3. Surgery

A posterolateral thoracotomy was performed for accessing the primary tumor. For anterior lesions, incisions were

Table 1 Institutional chemotherapy protocol for ES.

CY	C1			C2			C3		C4	
WK	0	1	2	3	4	5	6	7	8	9
CT	VIE	V	V	VIE	V	V	VAC	V	VAC	V

Local treatment (surgery and/or radiotherapy) at week 10

CY	C5			C6			C7	
WK	11	12	13	14	15	16	17	18
CT	VCD	V	V	VCD	V	V	VCD	V

Radiotherapy along with concomitant chemotherapy

CY	C8			C9			C10			C11			C12		
WK	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
CT	VIE	V	X	VIE	V	X	VAC	V	X	VAC	V	X	VCD	V	X
CY	C13			C14			C15			C16			C17		
WK	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
CT	VCD	V	X	VAC	V	X	VAC	V	X	VCD	V	X	VCD	V	X

V, vincristine (1.5 mg/m^2); I, ifosfamide (2 gm/ m^2); E, etoposide (100 mg/ m^2); A, doxorubicin (60 mg/ m^2); C, cyclophosphamide (600 mg/ m^2); D, actinomycin D (1mg/ m^2); CY, cycle; WK, week; CT, chemotherapy.