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CLINICAL INVESTIGATION **Sarcoma**

CHEST WALL EWING SARCOMA FAMILY OF TUMORS: LONG-TERM OUTCOMES

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Purpose: To review the 40-year University of Florida experience treating Ewing sarcoma family of tumors of the chest wall.

Methods and Materials: Thirty-nine patients were treated from 1966 to 2006. Of the patients, 22 were treated with radiotherapy (RT) alone, and 17 patients were treated with surgery with or without RT. Of 9 patients with metastatic disease, 8 were treated with RT alone. The risk profiles of each group were otherwise similar. The median age was 16.6 years, and the most frequent primary site was the rib (n = 17). The median potential follow-up was 19.2 years.

Results: The 5-year actuarial overall survival (OS), cause-specific survival (CSS), and local control (LC) rates were 34%, 34%, and 72%, respectively. For the nonmetastatic subset (n = 30), the 5-year OS, CSS, and LC rates were 44%, 44%, and 79%, respectively. LC was not statistically significantly different between patients treated with RT alone (61%) vs. surgery + RT (75%). None of the 4 patients treated with surgery alone experienced local failure. No patient or treatment variable was significantly associated with local failure. Of the patients, 26% experienced Common Toxicity Criteria (CTC) Grade 3+ toxicity, including 2 pulmonary deaths. Modern intensive systemic therapy helped increase the 5-year CSS from 7% to 49% in patients treated after 1984 (p = 0.03).

Conclusions: This is the largest single-institution series describing the treatment of chest wall Ewing tumors. Despite improvements in survival, obtaining local control is challenging and often accompanied by morbidity. Effort should be focused on identifying tumors amenable to combined-modality local therapy and to improving RT techniques. **© 2011 Elsevier Inc.**

Ewing family of tumors, Ewing's sarcoma, Chest wall, Rib, Askin, Radiation therapy.

INTRODUCTION

Ewing sarcoma family of tumors is a rare malignancy primarily affecting adolescents and young adults, with approximately 200 cases diagnosed annually in the United States (1). Only 6% to 11% of primaries involve the chest wall (2, 3). The adjacent pleural cavity allows undiagnosed chest wall lesions to grow larger than tumors in the extremity sites. Radiotherapy (RT) has been the mainstay of treatment for Ewing tumors for more than 75 years (4). These tumors often approach or invade the adjacent lung, heart, kidney, brachial plexus, and spine. Yet, even if these structures are uninvolved, their proximity to the tumor often makes local management challenging. The low incidence of this disease means that published outcome data are scarce, particularly regarding long-term disease control and late toxicity from treatment (3, 5). These data are an essential component of informed decision making when comparing the therapeutic ratio of different local-control modalities. In the ongoing trial European Ewing Tumor Working Initiative of National Groups Ewing Tumor Studies 1999 (EURO-E.W.I.N.G. 99), tracking radiation-associated toxicity is a high priority, and each participating center must document the late effects in detail (5). For similar reasons, this retrospective review describes the University of Florida experience in treating Ewing tumors of the chest wall and contributes information on long-term disease control in the context of toxicity.

METHODS AND MATERIALS

Patients

Thirty-nine patients were treated for primary Ewing tumors of the chest wall at our institution between 1966 and 2006. As outlined in previous publications, patients were treated according to institutional and cooperative group guidelines according to era (6). Most patients (67%) were treated after 1984. The relevant medical records were

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reviewed in accordance with an Institutional Review Board–approved protocol. For this review, we also included patients with peripheral neuroectodermal tumors (PNET), which is a histopathologic diagnosis included in the collective Ewing sarcoma family of tumors.

The median patient age was 16.6 years (range, 4.8–41.1 years). Most patients were male (62%), and all patients were of white ethnicity. The most common complaint at presentation was local pain (82%), followed by concern regarding a mass (46%). The median time between the onset of symptoms and diagnosis was 6 months (range, 0–91 months). No specific disease subsite was associated with a disproportionate treatment delay.

Patient characteristics stratified by stage are shown in Table 1. Sixteen patients had tumors arising from the rib (most commonly the 6th, 11th, or 12th rib). In 9 of the 16 patients, the tumor involved the left side. The specific chest wall subsites included were selected to reproduce the population reported on by Schuck *et al.* in the European Intergroup Cooperative Ewing's Sarcoma Study (EICESS) (5). The median tumor diameter was 10 cm (range, 4–20 cm), and the median volume was 284 cm^3 (range, 25–2,356 cm^3). The largest tumors were the rib primaries. Seven patients had radiographic evidence of a pleural effusion and 19 patients had radiographic evidence of pleural infiltration. As part of the metastatic workup, 3 (8%) patients had only a chest X-ray before treatment. All other patients had an X-ray followed by either a thoracic computed tomography (CT) scan (79%) or tomogram (13%). Nine patients had visual or cytologic evidence of metastases at the time of diagnosis: lung, 4 patients; bone, 3 patients; lung and bone, 1 patient; and bone and bone marrow, 1 patient. We included these patients in this series because long-term survival or even cure can be achieved in certain patients with gross metastatic disease at diagnosis (2). A total of 74% of patients underwent CT or magnetic resonance imaging (MRI) workup of the primary tumor.

Therapy

Treatment characteristics are detailed in Table 2. Definitive RT (for gross disease) was used in 22 patients either once daily (36%)

Table 1. Population and treatment characteristics

	All patients				Nonmetastatic patients			
	Total	RT alone (n = 22)	Surgery + RT (n = 13)	Surgery alone (n = 4)	Total	RT alone (n = 14)	Surgery + RT (n = 12)	Surgery alone (n = 4)
Sex								
Male	24	17	6	1	16	10	5	1
Female	15	5	7	3	13	4	7	3
Age (y)								
Mean, range	16.6 (4.8–41.1)	15.3 (4.8–34.1)	19.4 (5.1–41.1)	14.4 (7.6–20.5)	16.1 (4.8–41.1)	13.6 (4.8–34.1)	19.7 (5.1–41.1)	14.4 (7.6–20.5)
Site								
Rib	16	9	5	2	13	7	4	2
Scapula	9	7	1	1	6	4	1	1
Axilla	1	0	1	0	1	0	1	0
Thoracic spine	6	4	2	0	5	3	2	0
Clavicle	3	0	3	0	3	0	3	0
Sternum	1	1	0	0	0	0	0	0
Chest wall NOS	3	1	1	1	2	0	1	1
Diameter								
>8 cm	24	14	8	2	15	6	7	2
Volume*								
≥420 cc	11	6	3	2	6	2	2	2
Soft-tissue component	38	21	13	4	30	14	12	4
Pleural effusion	7	5	2	0	4	2	2	0
Pleural infiltration	19	11	5	3	15	8	4	3
Hemithorax RT	7	4	3	0	6	3	3	0
TBI	11	6	5	0	9	4	5	0
Etop ± Ifos	17	9	5	3	12	5	4	3
Intensive therapy†								
Yes	23	11	8	4	18	7	7	4
No	16	11	5	0	12	7	5	0
Treatment era								
1965–1983	13	9	4	0	10	6	4	0
1984–2007	26	13	9	4	20	8	8	4

Abbreviations: NOS = not otherwise specified; RT = radiotherapy; TBI = total-boday irradiation.
* Information not available for 16 patients.
† Intensive therapy = HR-2, HR-3, HR-4, HR-5, or AEWS0031.