Journal of Pediatric Surgery 49 (2014) 1500–1504

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Internal hemipelvectomy in the management of pelvic Ewing sarcoma – are outcomes better than with radiation therapy?☆

Anna Raciborska [a,*], Katarzyna Bilska [a], Magdalena Rychlowska-Pruszynska [a], Katarzyna Drabko [b], Radosław Chaber [c], Monika Pogorzała [d], Katarzyna Połczyńska [e], Jan Godziński [f], Carlos Rodriguez-Galindo [g], Wojciech Woźniak [a,1]

[a] Department of Surgical Oncology for Children and Youth, Institute of Mother and Child, Warsaw, Poland
[b] Department of Pediatric Hematology, Oncology and Transplantology, Medical University of Lublin, Lublin, Poland
[c] Department and Clinic of Pediatric Oncology, Hematology and Bone Marrow Transplantation, Wroclaw Medical University, Wroclaw, Poland
[d] Department of Pediatric Hematology and Oncology Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland
[e] Department of Pediatric Hematology and Oncology, Medical University of Gdansk, Gdansk, Poland
[f] Department of Paediatric Surgery Marciniak Hospital, Chair of Emergency Medicine, Medical University, Wroclaw, Poland
[g] Pediatric Oncology, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, Harvard Medical School, Boston, TX

ARTICLE INFO

Article history:
Received 4 December 2013
Received in revised form 10 March 2014
Accepted 25 April 2014

Key words:
Ewing sarcoma
Hemipelvectomy
Radiotherapy

ABSTRACT

Background: Pelvic Ewing sarcoma (ES) is commonly associated with a worse prognosis. Large size and location limit local control options to radiation therapy, and local recurrences are common. We evaluated the impact of hemipelvectomy and radiation on outcomes, including function.
Materials and methods: Thirty-nine patients (median age 13.5 years) with ES of the pelvis and sacral bones were treated during the period 2000–2012. Fifteen were treated with definitive radiotherapy (RT), 9 patients underwent hemipelvectomy alone, and 15 were treated with combined hemipelvectomy and RT.
Results: Twenty patients (51.2%) are alive with a median follow-up 3.2 years from diagnosis. Median time from diagnosis to relapse was 1.3 years. Three-year estimates of EFS and OS were 47% and 61%, respectively. Patients treated with surgery or surgery with RT had better outcome than patients treated with RT only (3-year OS 78% or 81% *vs.* 36%, respectively, $p = 0.00083$). The outcome of patients with pelvic ES treated with hemipelvectomy was not significantly different from the outcome of all patients with Ewing sarcoma treated on the national Polish protocol.
Conclusions: Internal hemipelvectomy offers good chances of cure for patients with pelvic ES, with a reasonable rate of complications and good function.

Ewing sarcoma is a malignant small round blue cell tumor of neuroectodermal origin; it is the second most common pediatric bone neoplasm, comprising 3% of all paediatric malignancies [1]. The pelvis is one of the most common sites; approximately 25% of the cases originate in the pelvic bones or sacrum [2]. This location is associated with adverse prognostic factors such as larger size and higher frequency of metastatic disease; the outcome for these patients has been considered to be worse, with higher cumulative incidence of local and distant relapse [2,1].

The integration of multimodal therapy in the management of ES has been a critical component in the improvement of the outcomes of patients with this neoplasm. Local control by means of surgery or radiation has shown to be necessary for cure. While both treatment modalities are considered to be effective, surgery alone or in combination with radiation therapy has traditionally been associated with improved local outcomes [2,1]. Pelvic ES is difficult to resect because of their proximity to critical structures, locoregional extension, and large size [3]. For these reasons, radiation therapy is commonly the primary local control modality [2,4]. Overall, long-term survival rates for patients with localized ES of the pelvis treated with RT only are approximately 50–70% [2,5,6,4]. A large proportion of failures in this group of patients occur owing to local relapse; the cumulative incidence of local failure can be in excess of 20% [1]. Therefore, better local control options should be explored.

Early pelvic-sparing procedures were associated with a high rate of local recurrence and morbidity [7]; however, in recent years the role and the range of surgical treatments have evolved. In the Polish Group

☆ This manuscript is dedicated to the memory of Professor Wojciech Wozniak, a long-time Head of the Department of Pediatric Oncology at The Mother and Child Institute in Warsaw; a great surgeon, a pioneer of orthopaedic surgery in children with bone tumors, and more importantly a wonderful man and friend.

* Corresponding author at: Department of Surgical Oncology for Children and Youth, Institute of Mother and Child, Warsaw, Poland, 01-211 Warszawa, ul. Kasprzaka 17a. Tel.: +48 22 3277205; fax: +48 22 6329851.
E-mail address: anna.raciborska@hoga.pl (A. Raciborska).

[1] Deceased.

http://dx.doi.org/10.1016/j.jpedsurg.2014.04.013
0022-3468/

for the Treatment of Children with Solid Tumors we explored the role of aggressive surgical intervention for patients with ES of the pelvis and we sought to evaluate the impact of the different local control modalities in disease control and functional outcomes.

1. Materials and methods

1.1. Patients

Between 2000 and 2012, 141 patients with ES were treated at institutions of the Polish Group for Paediatric Solid Tumours; among those, 39 had pelvic or sacral primaries. All patients had standard tumour imaging using CT, MRI, bone scan or PET, as clinically indicated. Demographic, treatment, and outcome data were collected. Informed consent was obtained from all patients or their guardians before treatment. Approval for this retrospective study was obtained from all the relevant Institutions in compliance with international regulations for protection of human research subjects.

1.2. Treatment

All patients were treated following the guidelines of the Euro-EWING regimen [8]. Treatment included induction therapy with vincristine, ifosfamide, doxorubicin, and etoposide (VIDE), followed by risk- and response-adapted adjuvant chemotherapy with vincristine, actinomycin D, and cyclophosphamide/ifosfamide (VAI/VAC) after local control. Local control was performed after 6 courses of VIDE. All patients were centrally reviewed, and those eligible for internal hemipelvectomy based on surgical criteria were offered surgery and reconstruction, which included allogenic bone graft, custom-made endoprosthesis, and non-absorbable mesh to restore the hip joint. Criteria for offering surgery included the following: 1) feasibility of conducting a radical surgery without significantly affecting function (free sacral bone foramen, free vessels and nerves, possibility to maintain good function of lower limbs and sphincters; 2) patients approval; 3) lack of disease progression. According to the Enneking classification of pelvic resection [9], 12 patients had type I, 4 patients type I/II, 1 patient type I/IIA, 5 patients type IIA/III, and 2 patients type III surgery. All surgeries were performed by W.W. at Mother and Child Institute in Warsaw. Patients that were not eligible for surgery were treated with definitive irradiation (54.4 Gy). Patients with microscopic residual disease, and those with completely resected large tumors with poor histologic response received postoperative irradiation (45–54 Gy). Patients with metastatic disease or poor histological response were offered consolidation with high-dose therapy (busulfan and melphalan regimen) and autologous hematopoietic stem cell transplant (aHSCT).

1.3. Statistical methods

Overall survival was defined as the time interval from the date of diagnosis to the date of death or last follow-up. Event-free survival was defined as the time interval from the date of diagnosis to the date of disease progression, recurrence, second malignancy, or death, or to the date of last follow-up for patients without events. Time to relapse (TTR) was defined as the time interval from the date of initial biopsy to the date of disease recurrence. Result distributions were estimated using the method of Kaplan-Meier. Factors were examined as predictors of OS using log-rank test. The multivariate Cox proportional hazards model was applied to evaluate multiple factors as a predictors of OS. $p \leq 0.05$ was regarded as significant. Statistical analysis was performed using STATA 10.0 for Windows.

2. Results

2.1. Patient characteristics and treatment

Clinical characteristics by local control modality are shown in Table 1. The median age at the time of diagnosis was 13.5 years (range 2.2–19.6 years). There were no significant differences in the clinical characteristics between patients >10 and ≤10 years. Primary tumors were located in the iliac bone in 24 patients, pubic bone in 5, ischium in 3, pubis and ischium in 3, and sacral bone in 4. The size of the tumor at the time of diagnosis did not appear to influence the surgical decision; 6 out of 10 (60%) patients with tumors <200 ml, and 18 out of 29 (62%) patients with tumors ≥200 ml underwent hemipelvectomy (Table 1). Response to chemotherapy was determined in 33 patients. Of the 30 patients whose tumors were <200 ml after induction chemotherapy, 20 (66.6%) underwent hemipelvectomy vs. 4 of 9 (44.4%) of patients whose tumors remained ≥200 ml.

Patients treated with radiation therapy only had a higher proportion of metastatic disease at diagnosis than patients treated with surgery or surgery and RT. Twenty-four patients underwent internal hemipelvectomy with the following reconstructions: allogenic bone graft in 14, custom-made endoprosthesis in 6, and nonabsorbable mesh to restore the hip-joint in 4. Four patients had microscopically incomplete resections and received postoperative radiation. There were no major perioperative complications; the median time to start postoperative treatment was 13.5 days (range 10–31 days). Late complications occurred in 8 patients; surgery-related infections in 2 and wound necrosis and/or dehiscence in 6. In one case, the complications led to external hemipelvectomy 2 years after primary treatment. There was one toxic death during aHSCT.

2.2. Follow-up and outcome

Outcome is depicted in Table 2. With a median follow-up of 3.2 years (range 0.4–9.5 years), 20 patients (55.8%) are alive. Median time from diagnosis to relapse was 1.3 years (range 0.5–2.5 years).

Table 1
Patients characteristic.

Pts. characteristic	Surgery only Number (%)	Surgery + RT Number (%)	RT only Number (%)	p value
Total number	9 (23.1%)	15 (38.45%)	15 (38.45%)	
Age				
≤10	4 (44.4%)	4 (26.7%)	2 (13.3%)	p = 0.098
>10	5 (55.6%)	11 (73.3%)	13 (86.7%)	
Primary tumor location				
Pelvic	9 (100%)	15 (100%)	11 (73.3%)	p = 0.017
Nonpelvic (sacrum)	0		4 (26.7%)	
Stage of disease				
Metastatic	3 (33.3%)	9 (60%)	12 (80%)	p = 0.026
Localized	6 (66.7%)	6 (40%)	3 (20%)	
Metastatic sites				
Lungs	3 (100%)	7 (77.8%)	6 (50%)	p = 0.0042
Others	0	2 (22.2%)	6 (50%)	
Primary chemotherapy				
VIDE regimen	9 (100%)	15 (100%)	15 (100%)	
Autologous stem cell transplant	4 (44.4%)	9 (60%)	5 (33.3%)	p = 0.416
Tumor volume before neoadiuvant CHT				
<200 ml	2 (22,2%)	4 (26.7%)	4 (26.7%)	p = 0.83
≥200 ml	7 (77.8%)	11 (73.3%)	11 (73.3%)	
Tumor volume after neoadiuvant CHT				
<200 ml	8 (88.9%)	12 (80%)	10 (66.7%)	p = 0.19
≥200 ml	1 (11.1%)	3 (20%)	5 (33.3%)	

RT, radiation therapy; VIDE, vincristine, ifosfamide, doxorubicin, etoposide.