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Retrospective study of the surgical management and outcome of nonrhabdomyosarcoma soft tissue sarcomas of the groin and axilla in children

Gideon Karplus^a, Matthew J. Krasin^b, Carlos Rodriguez-Galindo^c, Beth McCarville^b, Jesse Jenkins^d, Bhaskar Rao^{a,e}, George Spyridis^a, and Sheri L. Spunt^{c,¶}

^a Department of Surgery, St. Jude Children's Research Hospital, Memphis, TN 38105, USA

^b Department of Radiological Sciences, St. Jude Children's Research Hospital, Memphis, TN 38105, USA

^c Department of Oncology, St. Jude Children's Research Hospital, Memphis, TN 38105, USA and Department of Pediatrics, University of Tennessee School of Medicine, Memphis, TN 38105, USA

^d Department of Pathology, St. Jude Children's Research Hospital, Memphis, TN 38105, USA

^e Department of International Outreach, St. Jude Children's Research Hospital, Memphis, TN 38105, USA

Abstract

Background/Purpose—The incidence of pediatric NRSTSs of the groin and axilla is unknown, and the optimal surgical approach to these patients is unclear.

Methods—We conducted a retrospective study of patients treated at St. Jude Children's Research Hospital from January 1962 to March 2007 for NRSTSs of the groin and axilla. Demographic variables, tumor pathology, clinical management, and outcome were reviewed.

Results—Of the 300 patients treated for NRSTSs, only 10 had tumors of the axilla or groin (6 of whom had synovial sarcoma). Surgical interventions included wide resection of the tumor ($n=7$), marginal resection ($n=1$), subtotal resection ($n=1$), and biopsy only ($n=1$). Six patients underwent lymph node sampling; all were negative for tumor. Short- and long-term surgical complications were rare. Four patients received adjuvant chemotherapy ($n=3$) and/or radiotherapy ($n=2$). At a median follow-up of 8.5 years, 7 of the 10 were surviving free of disease. Two of these patients died of tumor progression (1 with metastases at diagnosis and 1 with an unresectable tumor at diagnosis) and one patient who was free of NRSTS died of secondary breast carcinoma.

Conclusions—Pediatric NRSTSs of the axilla and groin are rare, but outcomes are similar to those of other patients with NRSTS. Wide local excision of the tumor with preservation of good limb function should be the surgical goal, and may be sufficient therapy in some cases.

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[¶]Corresponding author. Sheri L. Spunt, MD, Department of Oncology, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105. Tel.: 901-595-3984; fax: 901-521-9005; sheri.spunt@stjude.org..

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*The author was affiliated with St. Jude at the time of the study. His current affiliation is the Department of Pediatric Surgery, Rambam Medical Center, Haifa, Israel, 31096.

Keywords

Soft tissue sarcoma; groin; axilla; child

Soft tissue sarcomas (STSs) are a heterogeneous group of neoplasms that arise from primitive mesenchymal cells throughout the body. According to population-based data from the Surveillance Epidemiology and End Result (SEER) program, STSs account for approximately 7% of all cancer cases in children and adolescents under the age of 20 years, with 900 cases reported annually in the U.S.[1] Traditionally, pediatric STSs are divided into rhabdomyosarcoma (RMSs), which accounts for about 40% of cases in the U.S., and nonrhabdomyosarcoma soft tissue sarcomas (NRSTSs).[2] NRSTSs, which represent a biologically and clinically heterogeneous group of tumors, account for approximately 4% of all childhood malignancies, annually affecting 500 children and adolescents under the age of 20 years in the U.S.[1] The most common NRSTSs in children are dermatofibrosarcoma protuberans, synovial sarcoma, sarcoma not otherwise specified, malignant fibrous histiocytoma, and fibrosarcoma.[3]

The approach to treatment of NRSTSs in children is based largely on findings from adult studies because few prospective pediatric studies have been conducted.[4-9] Surgery is a mainstay of treatment, as relatively few patients with gross residual disease are curable.[10] Radiotherapy contributes to local tumor control in patients with microscopic residual disease after surgery[11] and in those with initially unresectable primary tumors.[12] The use of chemotherapy is controversial, as its benefits are small and its toxicity significant.[13] The prognosis of childhood NRSTS varies greatly, depending primarily on the tumor size and grade, the extent of disease at diagnosis, and the extent of surgical resection achievable.[4-6, 14-17]

According to the guidelines used for the treatment of rhabdomyosarcoma, tumors of the axilla and groin are considered to originate in the extremity rather than in the trunk wall.[18] Extremity tumors account for approximately half of childhood NRSTSs.[14, 17] Although most patients with non-metastatic extremity NRSTSs fare well, those with tumors that are both large (> 5 cm) and high-grade (American Joint Committee on Cancer stage III) have a 5-year survival of approximately 50% due to the development of distant metastatic disease. Those with unresectable tumors, regardless of tumor size or grade, also have a 5-year survival of approximately 50%.[16] Surgery, with or without radiation therapy, has helped achieve excellent local control and functional results in extremity STSs. Local recurrence rates for patients with primary disease are about 15%, [19] and only about 5% of patients require amputation.[20]

The importance of complete resection of NRSTSs is well established. In NRSTSs of the axilla and groin, the surgeon is faced with the added challenge of preserving the functionality of the limb without increasing the risk of local tumor recurrence. We describe in this paper our experience with childhood NRSTSs of the axilla and groin area to illustrate the challenges posed by tumors in these anatomic sites and to define the optimal approach to the surgical management of these patients.

Methods

We conducted a retrospective review of the medical records of all patients treated at the St. Jude Children's Research Hospital, Memphis, TN, for NRSTSs of the groin and axilla from January 1962 to March 2007. The charts were reviewed for demographic variables, tumor pathology, clinical management, and outcome. This study was approved by the St. Jude

Institutional Review Board and conformed to the ethical principles and regulatory policies of St. Jude, the Department of Health and Human Services (DHHS), and the Food and Drug Administration (FDA).

The tumors were staged according to the tumor-node-metastasis (TNM) system of the American Joint Committee on Cancer.[21] Tumor grade was assigned according to the Pediatric Oncology Group grading system for childhood NRSTS.[22]

Results

During a 45-year period from January 1962 and March 2007, 300 patients were treated for NRSTSs at St. Jude. Only 11 (3.6%) had NRSTSs of the axilla or groin. One of these patients had a malignant peripheral nerve sheath tumor at age 29.9 years after treatment of Hodgkin's lymphoma at age 15.4 years and osteosarcoma at age 24.6 years, and was excluded from this analysis. The clinical features, treatment, and outcomes of the remaining 10 patients are shown in Table 1. There were 4 boys and 6 girls aged 6.0-16.2 years (median 13.6 years), and 9 patients were Caucasian. The length of follow-up of survivors was 4.3-36.9 years (median 8.4 years).

All patients presented with a mass or swelling of the involved site. The groin was the most common site ($n = 7$). The most common histologic subtype was synovial sarcoma ($n = 6$). Seven of the 10 patients (70%) presented with a T1 tumor (<5 cm in diameter). The tumor was low grade (POG grade 1 or 2) in 6 patients and high grade (POG grade 3) in 4 patients.

Surgical treatment consisted of wide excision of the tumor ($n = 7$), marginal excision ($n=1$), and subtotal resection of the tumor ($n = 1$). One patient with an unresectable tumor underwent a biopsy without any further therapy. Six patients underwent lymph node sampling (none by sentinel lymph node mapping); none of the sampled lymph nodes contained tumor. Three patients received multiagent chemotherapy and 2 received radiotherapy (1 after wide excision, 1 after marginal excision).

Seven of the 10 patients (70%) survived. The tumor had been completely resected in all of the survivors. One patient with a large, unresectable tumor at initial presentation received no therapy and died of local and distant tumor progression. A second patient with metastatic disease at initial presentation underwent a subtotal resection and no further therapy and died of distant metastatic disease. The final patient who died succumbed to metastatic breast cancer that was diagnosed 12.1 years after the diagnosis of synovial sarcoma of the groin treated successfully with wide excision and chemotherapy. She was not known to have Li-Fraumeni syndrome (constitutional p53 gene mutation). The 7 survivors had no significant long-term complications. Two patients had mild lymphedema which, in one, completely resolved after 6 months. One patient had wound breakdown that required a skin graft.

Discussion

In this retrospective study of children with NRSTSs of the axilla and groin, we document the rarity of tumors in these anatomic sites. Only 4% of our pediatric patients with NRSTSs had tumors arising in the axilla or groin, despite the fact that extremity sites account for approximately 50% of pediatric NRSTS cases. Two of the 10 patients (20%) in our series died of disease progression. These patients had high-risk features (metastases at initial diagnosis or > 5 cm, high-grade tumor). These findings are consistent with published data about survival outcomes in childhood NRSTS,[7-9, 14-17] although our small patient population prevents us from drawing any firm conclusions about the survival of patients with axillary and groin NRSTS.

As in NRSTS at other anatomic sites, adequate surgical resection appeared to play an important role in local tumor control and cure. Six of our 7 survivors underwent wide local excision; the remaining survivor underwent marginal excision followed by adjuvant radiotherapy. Several recent studies in adults suggest that wide excision alone may be sufficient for cure of STS.[23, 24] This approach has not been previously tested in pediatric NRSTS, although ongoing studies by the Children's Oncology Group and the European Sarcoma Study Group are addressing which patients with NRSTSs can be managed with surgery alone. Our small series supports the idea that surgery alone may be sufficient therapy for selected patients, as four of our survivors were cured with wide excision alone.

To preserve limb function and viability, the surgeon is sometimes reluctant to extend the margins of the resection to the desired distance from tumor tissue. Adult series of groin NRSTS surgery have demonstrated that in selected cases when the femoral nerve is involved it can be sacrificed.[25] Postoperatively, patients need a knee brace, but the residual function is in most cases very good. Femoral vein involvement can be managed by partial resection and repair when feasible, although vein ligation was usually well tolerated in adult series. When the femoral artery is involved and careful dissection cannot free the vessel, ligation and bypass are preferred. If the tumor has invaded and occluded the vessel, an adequate collateral circulation often exists, and the patient may tolerate femoral artery ligation without a bypass. None of our patients required such extensive maneuvers to achieve the desired tumor-free margins. Preservation of functionality is an important goal, particularly in the pediatric patient population. Carefully weighing the risks of aggressive surgical approaches to achieve wide margins against the long-term toxicity of high-dose radiotherapy that will be required after a marginal excision will help determine the optimal approach to local tumor control.

In our series, none of the 9 patients who underwent lymph node sampling were found to have nodal metastases. This finding is consistent with data from studies in adults that document the rarity of regional nodal involvement except in certain histologic subtypes such as epithelioid sarcoma and clear cell sarcoma.[26] Sentinel lymph node biopsies or blind lymph node sampling is justified in epithelioid sarcoma and clear cell sarcoma; the yield otherwise is so low that the procedures is contraindicated. Because lymph node dissection may result in potentially permanent lymphedema and associated complications, we advocate restricting lymph node dissection to patients with grossly involved nodes.

Our small case series prevents an assessment of the efficacy of chemotherapy in patients with axillary and groin NRSTSs. There is ongoing debate about the role of chemotherapy for NRSTSs.[13] A few studies have shown a modest survival benefit for patients receiving chemotherapy, though the magnitude of this benefit is quite small. The most active agents used are ifosfamide and doxorubicin; however, the rate of tumor response following neoadjuvant treatment with these agents is only 25–40%.[4, 5] These drugs also carry significant long-term risks, including renal insufficiency, cardiomyopathy, infertility, and induction of secondary malignancies. Because of its limited efficacy and serious toxicity, chemotherapy is generally considered only for high-risk patients: those with > 5 cm, high-grade tumors (where chemotherapy may decrease the risk of distant metastasis), those with unresectable tumors (where chemotherapy may induce a response that permits surgical resection), and perhaps those with metastatic disease (where chemotherapy may provide some palliative benefit). Recent data in adults suggest that neoadjuvant combined chemotherapy and radiotherapy may be superior to either modality alone in inducing a tumor response in unresectable NRSTSs.[12] Preoperative treatment may also permit the use of a smaller dose and field of radiotherapy, although it increases the risk of postoperative wound complications.

This study has a number of important limitations, namely that it is a retrospective analysis of a small number of patients treated at a single institution over a long time period during which therapy evolved considerably. Consequently, it is difficult to make any definitive clinical recommendations on the basis of this study. However, our preliminary findings suggest that NRSTS of the axilla and groin are sufficiently similar to other NRSTS of the extremities that future studies should categorize these anatomic locations as extremity sites. Our limited experience suggests that lymph node sampling is not necessary in most of these patients, although judicious use of this procedure is warranted in patients with lymphadenopathy and in those with certain histologic subtypes such as epithelioid sarcoma and clear cell sarcoma.[26] Adequate local control, either via wide local excision or marginal excision with adjuvant radiotherapy, is critical to successful treatment of NRSTS at all anatomic sites.[10, 11, 23] Our small series of patients with axillary and groin NRSTS confirmed the importance of local tumor control and documented a favorable outcome for those with low-risk tumors (i.e., resected low-grade and resected high-grade tumors < 5 cm in maximal diameter), most of whom were treated with surgery alone. Further clinical trials are needed to confirm our study's findings, to clarify risk factors for treatment failure, and to more clearly define the indications for adjuvant therapy.

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Table 1

Clinical features, treatment, and outcome of 10 patients with nonhabdomyosarcoma soft tissue sarcomas of the axilla and groin

Pt #	Age	Sex	Race	Site	Histology	Grade	TNM Classification	Surgery	RT	Chemo	Recurrence	Status
1	14.5	M	W	L groin	Synovial	2	T1aN0M0	GTR -	None	VC	None	NED, 36.9 yrs
2	14.9	M	W	R axilla	Synovial	2	T2bN0M0	Biopsy	None	None	Local, distant (lung)	DOD, 2.7 yrs
3	7.9	F	W	R groin	Fibrosarcoma	2	T1bN0M0	GTR -	None	None	None	NED, 28.2 yrs
4	16.2	M	W	L axilla	MPNST	3	T2bN0M1	STR	None	None	Distant (bone)	DOD, 0.1 yrs
5	15.1	F	W	L groin	Synovial	3	T1aN0M0	GTR -	None	VACA	None	DOS [*] , 13.7 yrs
6	6.0	F	W	R groin	Synovial	3	T1aN0M0	GTR -	None	None	None	NED, 12.4 yrs
7	14.5	F	W	R groin	Synovial	3	T1bN0M0	GTR -	56 Gy	VID	None	NED, 8.4 yrs
8	12.6	M	W	R groin	DFSP	1	T1aN0M0	GTR -	None	None	None	NED, 4.3 yrs
9	8.8	F	W	R axilla	Angiomatoid fibrous histiocytoma	1	T1aN0M0	GTR -	None	None	None	NED, 9.9 yrs
10	11.8	F	B	L groin	Synovial	2	T2bNxM0	GTR +	50.4 Gy ^{**}	None	None	NED, 7.8 yrs

DFSP: dermatofibrosarcoma protuberans; DOD: dead of disease; DOS: dead of second malignant neoplasm; GTR -: gross total resection, microscopic margins negative; GTR +: gross total resection, microscopic margins positive; MPNST: malignant peripheral nerve sheath tumor; NED: no evidence of disease; STR: subtotal resection; VACA: vincristine, doxorubicin, cyclophosphamide, and actinomycin D; VC: vincristine and cyclophosphamide; VID: vincristine, ifosfamide, and doxorubicin

* Patient developed breast carcinoma 12.1 years after NRSTS diagnosis and died of breast cancer progression

** Patient also received brachytherapy boost of 25.6 Gy