Journal of Pediatric Surgery (2013) **48**, 1249–1253

ELSEVIER

Journal of Pediatric Surgery

www.elsevier.com/locate/jpedsurg

Complications in the surgical treatment of pediatric melanoma

Paul E. Palmer III[a], Carla L. Warneke[b], Andrea A. Hayes-Jordan[a,c,d], Cynthia E. Herzog[c], Dennis P.M. Hughes[c], Kevin P. Lally[a,c,d], Mary T. Austin[a,c,d,*]

[a]*Department of Pediatric Surgery, The University of Texas Medical School at Houston, Houston, TX, USA*
[b]*Department of Biostatistics, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*
[c]*Department of Pediatrics, Children's Cancer Hospital at the University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*
[d]*Department of Surgical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA*

Received 17 February 2013; accepted 8 March 2013

Key words:
Pediatric melanoma;
Surgery;
Complications

Abstract

Purpose: The purpose of this study was to characterize the complications associated with surgical treatment of pediatric melanoma.

Methods: We retrospectively reviewed all pediatric patients who received surgical treatment for melanoma at our institution between 1992 and 2010. We compared complications between three groups: wide local excision only (WLE), WLE and sentinel lymph node biopsy (SLNB), and WLE and completion lymph node dissection (CLND).

Results: One hundred twenty-five patients were identified: 37 patients received WLE only, 47 received WLE and SLNB, and 41 patients had WLE and CLND. Complication rates differed between the three groups: 19% in WLE, 11% in WLE + SLNB, and 39% in WLE + CLND ($P = .006$). The risk of complications was significantly lower among patients having WLE + SLNB versus WLE + CLND (OR 0.19, 95% CI 0.06–0.57, $P = .0032$). Lymphedema was a common complication with a higher incidence in the CLND group compared to the SLNB group (19.5% vs. 2.1%, $P = .01$). Complications were more frequent in inguinal compared to axillary dissections (52.0% vs. 17.1%, $P = .006$).

Conclusions: In the surgical treatment of pediatric melanoma, the addition of a completion lymph node dissection significantly increases complication risk. Thus, it is critical to determine which patients truly benefit from this procedure.

While melanoma is the 8th most commonly diagnosed cancer in the United States, it is relatively rare in the pediatric population comprising 0.7% of all melanoma diagnoses [1,2]. Melanoma is diagnosed 300–420 times a year in the United States in patients less than 20 years of age [3]. The most recent report from the Surveillance, Epidemiology and End Results (SEER) database showed an increase in the incidence of pediatric melanoma diagnosis of 2.9% per year from 1973 to 2001 [3]. Despite this rise in incidence, there is a paucity of literature on the treatment of melanoma in the pediatric population.

* Corresponding author. The University of Texas M.D. Anderson Cancer Center, 1400 Pressler, Unit 1406, Houston, TX 77030–1439. Tel.: +1 713 794 4408; fax: +1 713 794 5720.
E-mail address: MAustin@mdanderson.org (M.T. Austin).

0022-3468/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jpedsurg.2013.03.018

Approaches to the surgical treatment of pediatric melanoma have mostly been adopted from the surgical management guidelines used in the adult population [4]. Sentinel lymph node biopsy (SLNB) was introduced in 1992 to enhance the diagnosis and staging of early-stage melanoma [5]. SLNB incorporates preoperative lymphoscintigraphy followed by injection of blue dye into the skin surrounding the primary tumor or scar and use of a gamma probe intraoperatively to determine the lymph node(s) at risk for melanoma spread [5,6]. Sentinel lymph node biopsy has been shown to be accurate and effective for staging melanoma in both adult and pediatric populations and has been widely adopted [5–9]. In the adult population, SLNB has led to a selected use of completion lymph node dissection (CLND), and hence, an overall decrease in morbidity [10].

Many studies have examined the complications associated with the surgical treatment of adult melanoma patients [10–15]. To our knowledge, there has been no study that specifically evaluates complications related to the surgical treatment of pediatric melanoma. The goal of our study is to determine the incidence and characterize the complications which occur in the surgical treatment of pediatric melanoma.

1. Methods

A retrospective review of all patients less than 18 years of age who received surgical treatment for melanoma at The University of Texas MD Anderson Cancer Center (MDACC) between March 1992 and December 2010 was performed. In each case, the diagnosis of melanoma was confirmed by an MDACC dermatopathologist. Patients lacking follow-up data, presenting with stage IV disease or receiving their final lymph node dissections at other institutions were excluded from the study.

Surgical procedures performed included wide local excision (WLE), WLE + SLNB, and WLE + CLND. The type of surgical procedure was determined by standard melanoma treatment guidelines described by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology [16]. The NCCN guidelines recommend WLE only for patients with melanoma in situ or tumors ≤ 0.75 mm thick and WLE + SLNB for all patients with tumors >1.0 mm thick. [16] For lesions 0.76–1.0 mm, SLNB may be considered in the appropriate clinical context including lesions with a high mitotic rate ($>1/mm^2$) and/or the presence of ulceration. [16] For WLE, the size of the margin (the amount of normal skin surrounding the primary lesion or scar) removed was based on the thickness of the primary tumor [16]. The sentinel node basin was determined using preoperative lymphoscintigraphy and classified as axillary, inguinal (including superficial and deep), and cervical. One patient drained to both the axillary and inguinal nodal regions and was included in the CLND group, but excluded from the surgical site analysis.

Complications examined included lymphedema, wound infection, skin graft failure, seroma, epidermolysis, lymphocele, dehiscence, hematoma and cellulitis. Patients were diagnosed with lymphedema secondary to surgical treatment if they presented with moderate to severe lymphedema as determined by physical examination on at least two occasions >6 months after surgery.

Data collected included age, sex, self-determined ethnicity, primary tumor site, surgery type, surgical location, complications, tumor stage, Breslow depth, and Clark level.

Patient demographic and clinical characteristics were summarized using medians with minimum and maximum values for continuous variables and using counts and percentages for categorical variables. Associations between variables were assessed using the Fisher's exact test or Kruskal-Wallis test as appropriate. In addition, univariate logistical regression models were used to evaluate potential predictors of post-surgical complications. No adjustments were made for multiple comparisons. All reported P values are two sided at a significance level of 5%. Analyses were performed with SAS for Windows (release 9.2; SAS Institute Inc., Cary, NC). This study was approved under protocol DR09-0428 by the institutional review board at MDACC.

2. Results

There were 125 patients less than 18 years of age who received surgical treatment at MDACC for melanoma from March 1992 through December 2010. Patient demographic data is shown in Table 1. The median age was 13.8 years (range 1.9–17.9 years) with 52.0% (n = 65) males.

Tumor characteristics are shown in Table 2. The primary site of melanoma for the entire cohort was as follows: extremities (n = 52, 41.6%), trunk (n = 30, 24.0%), head and neck (n = 31, 24.8%), and mucosal (n = 2, 1.6%). Clark level ranged from 1 to 5 and was most frequently level 4 (43.7%). The median Breslow depth was 1.3 mm (range 0–12mm).

Surgical procedures included 37 WLE only, 47 WLE + SLNB, and 41 WLE + CLND. Of the patients receiving CLND, 11 had CLND without a prior positive SLNB. Indications for CLND without a positive SLNB included metastasis identified via fine-needle aspiration (n = 3), inability to identify the sentinel lymph node (n = 3), clinically palpable lymph node(s) (n = 2), inability to perform accurate SLNB secondary to previous primary site excision (n = 2), and delayed SLNB owing to pregnancy (n = 1). The Breslow depth varied between groups with a median depth of 0.34 mm (range 0–9.0mm) in WLE, 1.30 mm (range 0.3–6.55 mm) in WLE + SLNB, and 2.60 mm (range 0.7–12 mm) in WLE + CLND ($P < .0001$).

Table 1 Patient demographics.

Median Age, yr (range)	13.8 (1.9–17.9)
Sex: [n (%)]	
Male	65 (52.0)
Female	60 (48.0)
Ethnicity: [n (%)]	
White	109 (87.2)
Self-identified Latino	10 (8.0)
African-American	2 (1.6)
Asian	2 (1.6)
Indian	1 (0.8)
Arabic	1 (0.8)
Median Breslow depth, mm (range)	1.3 (0–12)
Primary location: [n (%)]	
Extremities	52 (41.6)
Trunk	40 (32.0)
Head and neck	31 (24.8)
Mucosal	2 (1.6)

Twenty-eight patients (22.4%) experienced post-surgical complications with 5 patients (4%) having more than one complication. Complications included wound infection (n = 11, 8.8%), lymphedema (n = 9, 7.2%), seroma (n = 4, 3.2%), and other wound related complications (n = 9, 7.2%). The complication rates varied based on the surgical procedure: 19% in WLE, 11% in WLE + SLNB, and 39% in WLE + CLND ($P = .006$). The risk of complications was significantly lower among those having a WLE + SLNB versus those having a WLE + CLND (OR 0.19, 95% CI 0.06–0.57, $P = .0032$). There was a trend toward a lower risk of complications among patients having a WLE only versus a WLE + CLND (OR 0.36, 95% CI 0.13–1.03, $P = .056$). Lymphedema was a common complication with a higher incidence in the CLND group compared to the SLNB group (19.5% vs. 2.1%, $P = .01$).

The site of lymph node dissection was associated with the risk of complications for both SLNB and CLND. Complications occurred in 52% of inguinal dissections, 17.1% of axillary dissections, and no complications occurred in patients undergoing cervical node dissections ($P < .0001$). Lymphedema occurred more frequently in inguinal dissections (32%) compared to axillary dissections (2.44%) and cervical dissections (0) ($P = .0002$). There was no difference in the risk of wound infection between the surgical sites with wound infections occurring in 14.6% of axillary, 8% of inguinal, and no cervical dissections ($P = .2$). There was one patient who had both axillary and inguinal dissections and developed an inguinal wound infection; however, this patient was not included in analysis of site dissections.

3. Discussion

In 2000, Neville and colleagues showed SLNB to be safe in the pediatric population [6]. Gow and colleagues demonstrated the accuracy of SLNB in the pediatric population [9]. SLNB has also proven useful in the staging and treatment of other pediatric malignancies including sarcomas, carcinomas, acinic cell cancer, rhabdomyosarcoma, non-rhabdomyosarcoma soft tissue sarcomas, breast cancer, Ewing sarcoma, fibrosarcoma and malignant schwannoma [6,9,17].

Table 2 Disease Characteristics and Complications.

	WLE (n = 37)	WLE + SLNB (n = 47)	WLE + CLND (n = 41)	p-value
Median age, years	14.8 (4.6-17.9)	13.5 (3.5-17.1)	13.8 (1.9-17.8)	
<10 years (n)	4	13	12	0.0964
≥10 years (n)	33	34	29	
Gender (n)				
Male	18	26	21	0.8543
Female	19	21	20	
Site (n)				
Extremities	11	21	20	0.1245
Trunk	13	18	9	
Head & Neck	11	8	12	
Mucosal	2	0	0	
Median Breslow Depth, mm (range) Complications (n)	0.34 (0–9.0)	1.30 (0.3-6.55)	2.60 (0.7-12.0)	<0.0001
Total Patients with Complications *	7	5	16	0.0060
Lymphedema	0	1	8	0.0109
Infection	2	2	7	0.1018
Other	5	3	5	0.5388

WLE – wide local excision, WLE + SLNB – wide local excision + sentinel lymph node biopsy, WLE + CLND – wide local excision + completion lymph node dissection.

* Some patients experienced more than one complication.

SLNB has been evaluated extensively in the adult population and serves an instrumental role in staging and prognosis of this disease. Although melanoma survival correlates directly with primary tumor thickness, positive SLNB is the strongest prognostic determinant in early-stage adult melanoma [4,8,18–22]. In addition, patients who undergo SLNB for intermediate-stage melanoma have a greater 5-year disease-free survival rate compared to patients who are managed with nodal observation [8]. Thus, SLNB has proven to be valuable in its ability to provide key prognostic information in management of melanoma. Morton and colleagues also showed that melanoma-specific death was attributed to 26.2% of patients who underwent immediate lymphadenectomy compared to 48.7% of patients who delayed lymphadenectomy until clinically evident metastasis were present [8]. These data support the treatment guidelines recommended by the NCCN, which include a recommendation that patients with intermediate stage melanoma should receive SLNB and if positive, an immediate CLND should be performed [16].

Another key advantage to SLNB is that it decreases the need for CLND in patients with early-stage disease, which thereby decreases the incidence of complications associated with CLND in these patients [5,10,23]. Wrightson and colleagues found that in adults, SLNB followed by CLND was associated with complications in 23.2% of cases, whereas, complications occurred in 4.6% of patients receiving SLNB [10]. These complication rates are somewhat lower than the complication rates found in our study (39% in CLND and 10.4% in SLNB).

Previous literature has also shown that the site of lymph node dissection impacts the risk of complications related to the procedure [10,15]. Inguinal dissections are associated with a significantly higher risk of complications compared to axillary and cervical dissections [10,11]. Faries and colleagues showed that the location of nodal dissection is the most significant predictor of postoperative lymphedema with inguinal dissections having the highest rate at 26.6% [11]. It is also important to note that patients undergoing inguinal CLND with surgical complications also have a median total cost 48% higher than patients without complications [12]. While wound infection is most often manageable and self-limited, lymphedema proves much more difficult and may result in long-term morbidity [12,24]. Our study found only 1 case of lymphedema in the SLNB group (2.4%) compared to 8 cases in the CLND group (19.5%) which is similar to reports in adults. Lymphedema has also been shown to be significantly higher in delayed CLND compared to immediate CLND following a positive SLNB, and therefore, CLND should immediately follow a positive SLNB, as opposed to delaying CLND until clinical recurrence is evident [11,16].

To date, the surgical treatment of pediatric melanoma has been founded on evidence-based principles that guide the treatment of adult melanoma. In our study, we showed similar complication rates and distribution of complications compared to those found in the adult studies with lymphedema occurring most often in patients undergoing CLND and patients receiving dissection to the inguinal nodal region. In the future, a greater understanding of the biologic differences between pediatric and adult melanoma is necessary to guide future treatment of pediatric patients with this disease.

References

[1] CDC: NPCR: United States CA Statistics. 7/14/2012. http://apps.nccd.cdc.gov/uscs/toptencancers.aspx.

[2] Lange JR, Palis BE, Chang DC, et al. Melanoma in children and teenagers: an analysis of patients from the National Cancer data base. J Clin Oncol 2007;25:1363-8.

[3] Strouse JJ, Fears TR, Tucker MA, et al. Pediatric melanoma: risk factor and survival analysis of the Surveillance, Epidemiology and End Results database. J Clin Oncol 2005;23:4735-41.

[4] Moore-Olufemi S, Herzog C, Warneke C, et al. Outcomes in pediatric melanoma-comparing prepubertal to adolescent pediatric patients. Ann Surg 2011;253:1211-5.

[5] Morton DL, Wen DR, Wong JH, et al. Technical details of intraoperative lymphatic mapping for early stage melanoma. Arch Surg 1992;127:392-9.

[6] Neville HL, Andrassy RJ, Lally KP, et al. Lymphatic mapping with sentinel node biopsy in pediatric patients. J Pediatr Surg 2000;35:961-4.

[7] Morton DL, Thompson JF, Essner R, et al. Validation of the accuracy of intraoperative lymphatic mapping and sentinel lymphadenectomy for early-stage melanoma: a multicenter trial. Multicenter selective lymphadenectomy trial group. Ann Surg 1999;230:452-63.

[8] Morton DL, Thompson JF, Cochran AJ, et al. Sentinel-node biopsy or nodal observation in melanoma. N Engl J Med 2006;355:1307-17.

[9] Gow KW, Rapkin LB, Olson TA, et al. Sentinel lymph node biopsy in the pediatric population. J Pediatr Surg 2008;43:2193-8.

[10] Wrightson WR, Wong SL, Edwards MJ, et al. Complications associated with sentinel lymph node biopsy for melanoma. Ann Surg Oncol 2003;10:676-80.

[11] Faries MB, Thompson JF, Cochran A, et al. The impact on morbidity and length of stay of early versus delayed complete lymphadenectomy in melanoma: results of the Multicenter Selective Lymphadenectomy Trial. Ann Surg Oncol 2010;17:3324-9.

[12] Chang SB, Askew RL, Xing Y, et al. Prospective assessment of postoperative complications and associated costs following inguinal lymph node dissection (ILND) in melanoma patients. Ann Surg Oncol 2010;17:2764-72.

[13] De Vries M, Hoekstra HJ, Hoekstra-Weebers JE. Quality of life after axillary or groin sentinel lymph node biopsy, with or without completion lymph node dissection, in patients with cutaneous melanoma. Ann Surg Oncol 2009;16:2840-7.

[14] Delman KA, Kooby DA, Ogan K, et al. Feasibility of a novel approach to inguinal lymphadenectomy: minimally invasive groin dissection for melanoma. Ann Surg Oncol 2010;17:731-7.

[15] Sarnaik AA, Puleo CA, Zager JS, et al. Limiting the morbidity of inguinal lymphadenectomy for metastatic melanoma. Cancer Control 2009;16:240-7.

[16] National Comprehensive Cancer Network: Clinical Practice Guidelines in Oncology: Melanoma. http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf.

[17] Kayton ML, Delgado R, Busam K, et al. Experience with 31 sentinel lymph node biopsies for sarcomas and carcinomas in pediatric patients. Cancer 2008;112:2052-9.

[18] Balch CM, Soong SJ, Gershenwald JE, et al. Prognostic factors analysis of 17,600 melanoma patients: validation of the American Joint Committee on Cancer melanoma staging system. J Clin Oncol 2001;19:3622-34.
[19] Sahin S, Rao B, Kopf AW, et al. Predicting ten-year survival of patients with primary cutaneous melanoma: corroboration of a prognostic model. Cancer 1997;80:1426-31.
[20] Haddad FF, Stall A, Messina J, et al. The progression of melanoma nodal metastasis is dependent on tumor thickness of the primary lesion. Ann Surg Oncol 1999;6:144-9.
[21] Leiter U, Buettner PG, Eigentler TK, et al. Prognosti factors of thin cutaneous melanoma: an analysis of the central malignant melanoma registry of the German Dermatological Society. J Clin Oncol 2004;22: 3660-7.
[22] Morton DL, Wanek L, Nizze JA, et al. Improved long-term survival after lymphadenectomy of melanoma metastatic to regional nodes. Analysis of prognostic factors in 1134 patients from the John Wayne Cancer Clinic. Ann Surg 1991;214:491-9.
[23] Wong SL. The role of sentinel lymph node biopsy in the management of thin melanoma. Am J Surg 2005;190:196-9.
[24] Baas PC, Schraffordt KH, Hoekstra HJ, et al. Groin dissection in the treatment of lower-extremity melanoma. Short-term and long-term morbidity. Arch Surg 1992;127:281-6.