VOLUME 25 · NUMBER 11 · APRIL 10 2007

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Melanoma in Children and Teenagers: An Analysis of Patients From the National Cancer Data Base

Julie R. Lange, Bryan E. Palis, David C. Chang, Seng-Jaw Soong, and Charles M. Balch

From the Department of Surgery, Johns Hopkins Medicine, Baltimore, MD; The National Cancer Data Base, American College of Surgeons, Chicago, IL; and the Biostatistics and Bioinformatics Unit, University of Alabama School of Medicine, Birmingham, AL.

Submitted August 18, 2006; accepted January 12, 2007.

Presented in part at the 6th World Melanoma Congress, September 6-10, 2005, Vancouver, British Columbia, Canada.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Address reprint requests to Julie R. Lange, MD, ScM, 600 N Wolfe St, Carnegie 681, Baltimore, MD 21287; e-mail: jlange@jhmi.edu.

0732-183X/07/2511-1363/$20.00

DOI: 10.1200/JCO.2006.08.8310

ABSTRACT

Purpose
This study examines the demographics, presentation, and outcomes of children and teenagers with melanoma using a US hospital-based oncology database.

Patients and Methods
Data from the National Cancer Data Base from 1985 through 2003 were examined for demographics, presentation, and survival of patients aged 1 to 19 years, as well as a comparison group of patients aged 20 to 24 years. Two-sided linear and Pearson χ^2 tests were calculated to examine associations. Proportions were compared using two-sided z tests. Five-year overall observed survival was evaluated using the Kaplan-Meier method and the log-rank test. Cox proportional hazards regression was used to estimate risk of mortality.

Results
Of 3,158 patients aged 1 to 19 years, 96.3% had cutaneous melanoma, 3.0% had ocular melanoma, and 0.7% had an unknown primary tumor. Cutaneous melanoma in patients aged 1 to 19 years was more common in girls (55.5%) and patients older than 10 years (90.5%). The demographics and presentation of cutaneous melanoma were age related; younger children were significantly more likely to be nonwhite and male and more likely to present with a head and neck primary tumors and with regional or distant metastases (linear χ^2, $P < .001$ for sex, race, and extent of disease). Poorer survival was associated with higher stage and younger age. In contrast to patients aged 20 to 24 years, survival was not related to thickness in patients aged 1 to 19 years with localized invasive melanoma.

Conclusion
Melanoma in children and teenagers differs from melanoma in young adults in demographics, presentation, and survival. Further investigation is warranted to elucidate possible biologic correlates of the unique aspects of melanoma in children and teenagers.

J Clin Oncol 25:1363-1368. © 2007 by American Society of Clinical Oncology

INTRODUCTION

Melanoma is a significant public health problem in the United States, with an estimated 62,190 new cases of invasive melanoma and 7,910 deaths attributable to melanoma in 2006.[1] Melanoma is uncommon in teenagers and rare in younger children. The Centers for Disease Control and Prevention estimated 475 new cases of melanoma in the United States in 2002 for persons ≤ 19 years of age and only 47 new cases in children less than 10 years old.[2] The incidence of melanoma grew rapidly in adults over the past several decades.[3] The incidence of melanoma in adolescents has also been reported to be increasing in both the United States and Sweden.[4,5] A recent report from the Surveillance, Epidemiology, and End Results (SEER) database confirms an increase in the incidence of melanoma in children of approximately 2.9% per year from 1973 to 2001.[6]

In adults, the demographics and presentation of melanoma are known to be age related; older melanoma patients are more likely to be male, have head and neck primary tumors, and lentigo maligna histology.[3,7-9] It is not well understood whether children with melanoma differ from adults in presentation or outcomes, and it is unclear whether older children differ substantially from younger children. Melanoma in children may differ from melanoma in adults in etiology, natural history, and prognosis. The National Cancer Data Base (NCDB), a large hospital-based cancer database maintained by the American College of Surgeons in collaboration with the American Cancer Society, collects data on incident cancer patients from tumor registries of hospitals approved by the American College of Surgeons

Commission on Cancer. The primary goal of this study is to describe the demographics and clinical presentation of children with melanoma; treatment and outcomes are described as well.

PATIENTS AND METHODS

The NCDB serves as a comprehensive clinical surveillance resource for cancer care in the United States. Data are submitted annually from the cancer registries of hospitals with cancer programs approved by the American College of Surgeons Commission on Cancer. The NCDB currently contains information on approximately 75% of newly diagnosed cancer patients in the United States from approximately 1,430 hospitals in 49 states. Of all patients with melanoma reported to the NCDB from 1985 through 2003, 0.7% were aged 1 to 19 years.

The NCDB was queried for analytic melanoma cases reported in persons 1 to 24 years old diagnosed between the years 1985 and 2003, and information on race/ethnicity, sex, type of melanoma, and anatomic site of cutaneous melanoma was obtained. The diagnosis was designated by the pathologist at the treating facility; there was no central pathology review. Data were abstracted according to histology using standard International Classification of Diseases–O2/3 melanoma codes (M8720-8790).

Pediatric patients were identified as being aged 1 to 19 years, and a comparison group of young adults was aged 20 to 24 years. Neonatal patients were excluded by omitting patients designated as age 0. For analysis of age-related parameters, the Centers for Disease Control and Prevention–defined age groups (1 to 4, 5 to 9, 10 to 14, 15 to 19, and 20 to 24 years) were used; for some analyses, ages 1 to 9 or 1 to 19 years were combined because of small numbers. Racial designations were reported as non-Hispanic white or nonwhite, which encompasses all other specific designations, including African American, Asian/Pacific Islander, and Native American. The American Joint Committee on Cancer staging system is not formally observed for children ≤ 15 years old, and therefore, a SEER general summary stage was used to classify cancer as in situ, localized invasive, regional, or distant disease. Treatment and outcomes were also examined. Sentinel node biopsy was reported beginning in 1998. Use of biologic therapies is reported, although the database does not specify type of biologic therapy such as interferon, vaccine therapy, or other biologic response modifier. Localized invasive melanomas were analyzed from patients diagnosed from 1985 through 2002 for uniformity of T-stage grouping. Primary tumors were grouped as ≤ 1.5 mm or more than 1.5 mm for one survival analysis.

Two-sided linear and Pearson χ^2 tests were calculated to examine significance of age, sex, race, site, T stage, and extent of disease associations. Proportions were compared using two-sided z tests. Outcomes were reported as observed overall survival rather than disease-specific survival because of the expectation of excellent overall survival in the absence of disease. Five-year overall observed survival was evaluated using the Kaplan-Meier method and log-rank test. Cox proportional hazards regression was used to estimate risk of mortality for patients with localized invasive melanoma aged 1 to 19 years and for those aged 20 to 24 years. Models included thickness, sex, and primary site. All calculations were performed using SPSS 14.0 (SPSS Inc, Chicago, IL).

RESULTS

Distribution of Melanoma Type and Sex

Of the 3,158 patients aged 1 to 19 years, 96.3% had cutaneous melanoma, with only a small minority of patients designated as having ocular melanoma (3.0%) or an unknown primary site (0.7%). Only one patient with mucosal melanoma was reported (Table 1). Overall, melanoma was more common in girls (55%) than in boys.

Demographics of Cutaneous Melanoma Patients

Among the children with melanoma aged 1 to 19 years, 3.8% were 1 to 4 years old, 5.7% were 5 to 9 years old, 17.3% were 10 to 14 years old, and 73.2% were 15 to 19 years old. Younger patients were more likely to be male. The percentage of girls increased with each age group, from 39.3% of patients aged 1 to 4 years to 56.8% of patients aged 15 to 19 years and 65.6% of young adults aged 20 to 24 years (linear χ^2, $P < .001$; Fig 1A; Table 2). Of patients with reported race, the percentage designated as nonwhite decreased with increasing age, from 17.7% of patients aged 1 to 4 years to 4.9% of patients aged 15 to 19 years and 4.2% of patients aged 20 to 24 years (linear χ^2, $P < .001$; Table 2).

Site of Cutaneous Melanoma

The anatomic distribution of primary cutaneous melanoma was associated with age and sex. Children aged 1 to 4 years had a higher percentage of head and neck primary tumors (38.5%) and a lower percentage of truncal primary tumors (18.8%); with increasing age into young adulthood, the percentage of head and neck primary tumors decreased to 12.4%, and the percentage of truncal primary tumors increased to 41.6% (linear χ^2, $P < .001$; Table 2; Fig 1B). Females at all ages except ages 1 to 4 years were significantly more likely to have lower extremity primary tumors than males ($P < .05$; Fig 1B). Females 10 years and older were significantly less likely to have head and neck primary tumors ($P < .001$; Fig 1B). The percentage of truncal primary tumors increased with age in both sexes to the same extent (Fig 1B).

Cutaneous Melanoma: Extent of Disease

Using reported TNM stage when available and reported general summary stage when TNM stage was not reported, 91.5% of patients had designated stage. Three fourths of children aged 1 to 19 years presented with localized disease, either in situ melanoma (13.4%) or localized invasive melanoma (62.3%). With increasing age, the percentage of patients with localized invasive melanoma increased from 48.0% in patients aged 1 to 4 years to 75.3% in patients aged 20 to 24 years, whereas the percentage of patients

Table 1. Type of Melanoma in Pediatric Patients Aged 1 to 19 Years

Type of Melanoma	1-4 Years		5-9 Years		10-14 Years		15-19 Years		Total	
	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%
Cutaneous	117	95.9	172	95.6	527	95.8	2,226	96.5	3,042	96.3
Ocular	1	0.8	7	3.9	19	3.5	68	2.9	95	3.0
Mucosal	0	0	0	0	0	0	1	0.1	1	< 0.1
Unknown primary	4	3.3	1	0.6	4	0.7	11	0.5	20	0.7
Total	122	100	180	100	550	100	2,306	100	3,158	100

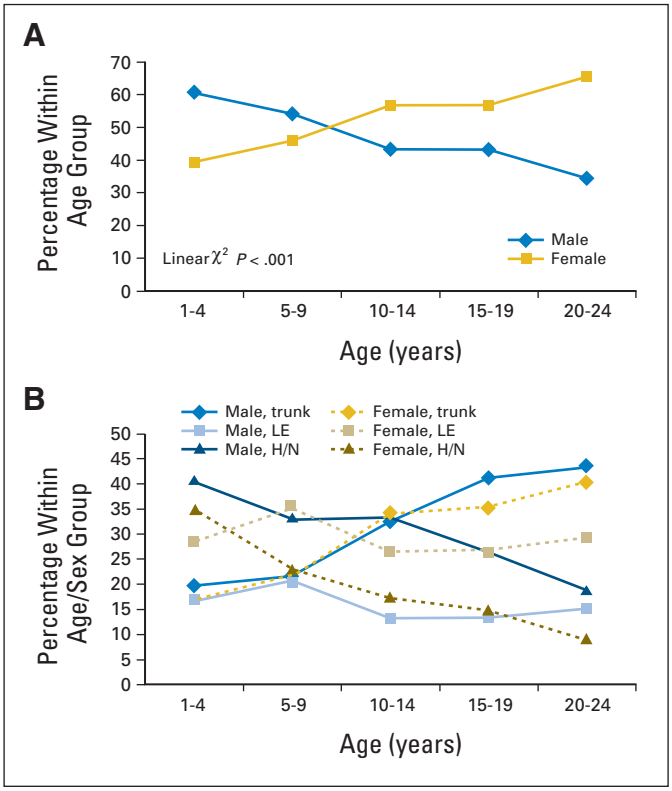

Fig 1. (A) Distribution of cutaneous melanoma patients by age and sex. (B) Distribution of cutaneous melanoma patients by age, sex, and primary site. Lower extremity (LE) sex comparison: two-sided *z* test, $P < .05$ for age groups 5 to 9, 10 to 14, 15 to 19, and 20 to 24 years. Head and neck (H/N) sex comparison: two-sided *z* test, $P < .001$ for age groups 10 to 14, 15 to 19, and 20 to 24 years.

with regional disease decreased from 25.5% in patients aged 1 to 4 years to 9.1% of patients aged 20 to 24 years. The percentage of patients presenting with distant disease decreased with age from 14.3% in patients aged 1 to 4 years to 3.0% in patients aged 20 to 24 years (Linear χ^2, $P < .001$; Table 2). Sex differences were also noted. Boys aged 10 years and older were significantly less likely to present with localized invasive disease and significantly more likely to present with regional disease (both $P < .01$, data not shown). Both sexes at ages 1 to 19 years were equally likely to present with distant disease, but young men aged 20 to 24 years were more likely to present with distant disease than were young women ($P < .001$, data not shown).

Localized Cutaneous Melanoma: Thickness Distribution

Of children aged 1 to 19 years with localized invasive melanoma, 71.7% had known T stage. For children with known T stage, most melanomas were ≤ 1.5 mm. Young adults and older teenagers were more likely to have thinner lesions than were children aged 1 to 14 years; localized invasive melanoma was ≤ 1.5 mm in 58.9% of patients aged 1 to 14 years, 69.5% of patients aged 15 to 19 years, and 74.0% of patients aged 20 to 24 years (Pearson χ^2, $P < .001$; Table 3).

Treatment

Surgery was part of the initial treatment for most patients with localized invasive melanoma (at least 87%) or regionally metastatic melanoma (at least 84%), and for most patients, surgery was the only treatment reported. From 1998 to 2003, in surgically treated patients with localized invasive melanoma, sentinel node biopsy was performed in 34.0% of patients aged 1 to 9 years, 43.2% of patients aged 10 to 19 years, and 36.2% of patients aged 20 to 24 years. Of children with regional metastases, at least 47.1% of patients younger than 10 years and 37.1% of patients aged 10 to 19 years received some form of biologic therapy. Few patients with localized invasive or regionally metastatic melanoma received radiation therapy or chemotherapy.

Outcomes

Median follow-up time was 59 months for patients aged 1 to 19 years with cutaneous melanoma. Overall 5-year observed survival was strongly associated with initial summary stage (98.7% ± 0.9% for in situ disease, 93.6% ± 0.9% for localized invasive disease, 68.0% ± 4.2% for regionally metastatic disease, and 11.8% ± 6.4% for distant disease; $P < .05$ for all comparisons; Fig 2) Survival analysis for all patients with cutaneous melanoma (excluding in situ) demonstrated that age groups of 10 to 14, 15 to 19, and 20 to 24 years had similar 5-year overall observed survival rates (88.0% ± 2.5%, 87.5% ± 1.3%, and 87.7% ± 0.8%, respectively). However, children aged 1 to 9 years had significantly poorer 5-year overall observed survival (77.0% ± 4.5%) compared with other age groups ($P < .05$, data not shown).

Females had significantly better overall survival than males, except in patients aged 1 to 9 years (Fig 3A). For patients with localized invasive cutaneous melanoma, a sex difference in observed survival was seen only in the comparison group of young adults aged 20 to 24 years (females had better survival than males) and not in any age group younger than 20 years (data not shown). For patients with regionally metastatic melanoma, patients aged 1 to 19 years had similar overall 5-year observed survival compared with patients aged 20 to 24 years; females had better survival than males in the group aged 20 to 24 years but not in the group aged 1 to 19 years (data not shown).

Observed overall 5-year survival for patients with localized invasive cutaneous melanoma was analyzed after grouping by ages 1 to 19 and 20 to 24 years and dichotomizing thickness as ≤ 1.5 mm or more than 1.5 mm. Pairwise comparison showed that patients aged 20 to 24 years with thinner melanoma had significantly better survival (96.8% ± 0.6%) than patients with thicker lesions (82.4% ± 2.0%). However in the group aged 1 to 19 years, observed survival was not significantly different between the thinner (94.3% ± 1.2%) and thicker (92.1% ± 2.0%) lesions. Also, for patients with thicker lesions, patients aged 1 to 19 years had a significantly better overall survival than patients aged 20 to 24 years, whereas for patients with thinner lesions, patients aged 1 to 19 years had significantly worse survival (Fig 3B). Multivariate Cox regression analysis for patients with localized invasive melanoma aged 1 to 19 years and aged 20 to 24 years factored by thickness, sex, and primary site demonstrated that the only significant factor was thickness in the patients aged 20 to 24 years (≤ 1.5 mm; hazard ratio = 0.171; 95% CI, 0.111 to 0.264).

DISCUSSION

As in adults, most reported cases of melanoma in children are cutaneous, with far fewer noncutaneous cases reported. Melanoma occurs far more frequently in older versus younger children.[4,10] The demographics, site distribution, stage, and outcomes of children and teenagers with melanoma differ from those of young adults, and younger children differ from older children as well. Our data are consistent

from 10.1200/JCO.2006.06.2116

Table 2. Characteristics of Cutaneous Melanoma Patients Aged 1 to 24 Years

Characteristic	1-4 Years		5-9 Years		10-14 Years		15-19 Years		20-24 Years	
	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%
Sex*										
Male	71	60.7	93	54.1	228	43.3	959	43.1	2,110	34.4
Female	46	39.3	79	45.9	299	56.7	1,265	56.9	4,031	65.6
Race†										
Non-Hispanic white	79	82.3	132	88.6	441	93.8	1,814	95.1	4,944	95.8
Nonwhite	17	17.7	17	11.4	29	6.2	94	4.9	219	4.2
Unknown	21	—	23	—	57	—	318	—	980	—
Primary tumor site‡										
Trunk	22	18.8	37	21.5	176	33.4	845	38.0	2,554	41.6
UE	15	12.8	32	18.6	96	18.2	412	18.5	1,113	18.1
LE	25	21.4	47	27.3	109	20.7	467	21.0	1,498	24.4
H/N	45	38.5	49	28.5	128	24.3	438	19.7	762	12.4
Other/NOS	10	8.5	7	4.1	18	3.4	64	2.8	216	3.5
Extent of disease§										
In situ	12	12.2	18	12.1	70	15.3	307	14.8	715	12.5
Localized	47	48.0	77	51.7	307	67.0	1,463	70.3	4,305	75.3
Regional	25	25.5	45	30.2	74	16.2	257	12.4	522	9.1
Distant	14	14.3	9	6.0	7	1.5	53	2.5	173	3.0
Unknown	19	—	23	—	69	—	146	—	428	—
Total	117	100	172	100	527	100	2,226	100	6,143	100

Abbreviations: UE, upper extremity; LE, lower extremity; H/N, head and neck; NOS, not otherwise specified.
*Four patients with unknown sex were excluded. Linear χ^2, $P < .001$.
†Race was unknown for 13.8% of patients; they were excluded from the analysis. Linear χ^2, $P < .001$.
‡Linear χ^2, $P < .001$ for trunk and H/N.
§Linear χ^2, $P < .001$.

with previous reports showing that the overall pediatric melanoma population is predominantly female.[6,11,12] However, our study shows that, in patients aged 1 to 9 years, there is a male predominance that is striking and most prominent in the youngest patients. The higher percentage of nonwhite patients in the younger children compared with older children and young adults has been described in SEER data and is seen in the current data set as well.[4,6]

In adults, the presentation of cutaneous melanoma is known to be associated with both age and sex.[3,7-9,13] The current study shows that children present with a different primary site distribution than young adults and that younger children are more likely to present with higher stage disease, similar to the SEER data.[6] In our data set, children less than 15 years old with localized invasive melanoma had thicker primary tumors compared with older teenagers and young adults. Girls older than age 4 had a higher percentage of lower extremity melanoma, and boys $\geq$ 10 years old had a higher percentage of head and neck melanomas. The percentage of boys and girls younger than 10 years old with regional metastases at presentation is similar, but with increasing age, this percentage decreases sooner and to a greater extent in girls than in boys and remains lower in females into young adulthood. The demographics, site distribution, and stage distribution of cutaneous melanoma in children changes with increasing age.

The mainstay of management of stage 0 through III cutaneous melanoma is surgery, which is reflected in the current data. Sentinel node biopsy has been integrated into surgical management of primary melanoma in children, as it has been in adults. In the literature, sentinel node biopsy in children seems to be associated with a 25% to 40% rate of node positivity, consistent with the observation in adults

Table 3. Breslow Thickness by Age in Patients With Localized Cutaneous Melanoma for Diagnosis Years 1985 to 2002*

Age (years)	Breslow Thickness								Unknown (No. of patients)†	All Patients (No.)
	$\leq$ 0.75 mm		0.76-1.5 mm		1.6-4 mm		$>$ 4 mm			
	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%		
1-9	28	45.9	8	13.1	19	31.1	6	9.8	41	102
10-14	62	36.5	38	22.4	56	32.9	14	8.2	76	246
15-19	310	38.1	255	31.4	217	26.7	31	3.8	296	1,109
20-24	1,134	44.0	773	30.0	598	23.2	73	2.8	864	3,442

*Overall Pearson χ^2, $P < .001$.
†Patients with unknown thickness were removed from the row percent calculations.

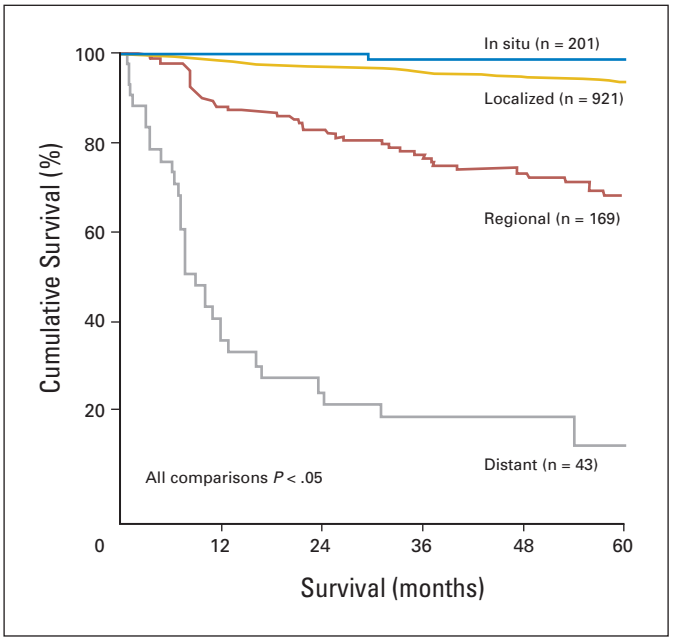

Fig 2. Observed survival curves of cutaneous melanoma by stage for patients aged 1 to 19 years.

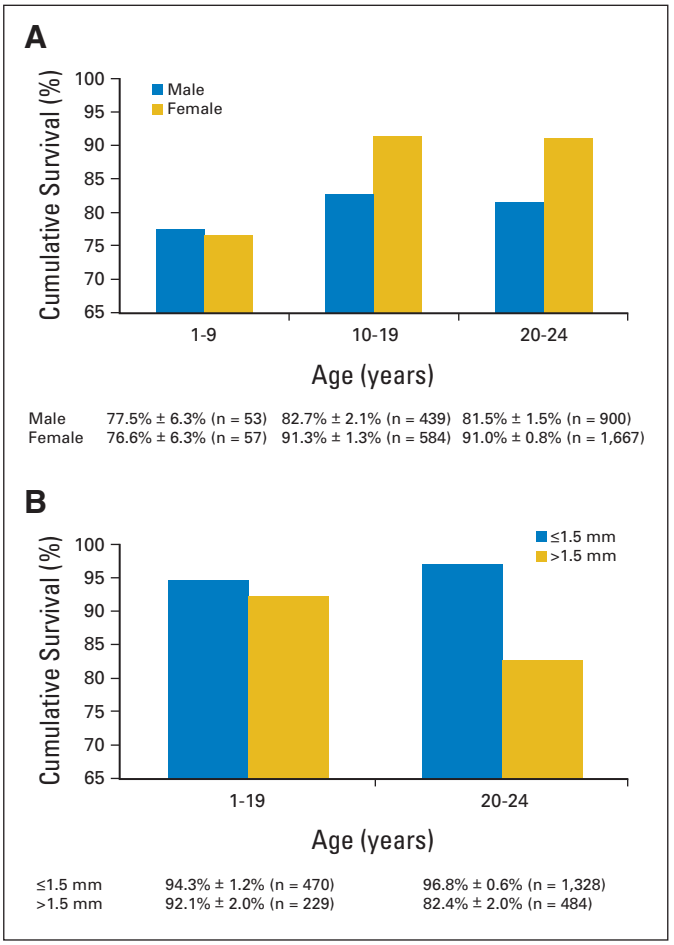

Fig 3. (A) Observed 5-year survival of patients with all stages (excluding in situ) of cutaneous melanoma by age and sex. Age comparison: $P < .05$ for ages 1 to 9 and 10 to 19 years and for ages 1 to 9 and 20 to 24 years. Sex comparison: $P < .001$ for ages 10 to 19 and 20 to 24 years. All other comparisons were not significant. (B) Observed 5-year survival of patients with localized cutaneous melanoma by thickness and age. Age comparison: $P < .05$ for thickness ≤ 1.5 mm, and $P < .01$ for thickness more than 1.5 mm. Thickness comparison: $P = .413$ for ages 1 to 19 years, and $P < .001$ for ages 20 to 24 years.

that younger adults have a higher chance of being node positive compared with older adults.[14-17] The use of high-dose interferon alfa-2b has been described in children with resected, high-risk melanoma and seems to be tolerated well.[18,19] The current study documents frequent use of biologic response modifiers in children and teenagers with regionally metastatic melanoma, although the use of these therapies remains controversial.

Survival of children with melanoma is clearly related to extent of disease. Observed overall survival of all stages together (excluding in situ disease) is significantly worse for children aged 1 to 9 years than for persons aged 10 to 24 years. In children less than 10 years old, overall observed survival is similar in males and in females, whereas males aged 10 to 24 years have worse outcomes than females, consistent with the findings in adults. This contrasts to the reported SEER data, where all children ≤ 19 years old are reported as a single group and show poorer survival for males.[6] Among the patients with localized invasive melanoma, it is notable that, in the group aged 1 to 19 years, survival was not associated with primary tumor thickness, and it was also notable that patients aged 1 to 19 years with thicker melanomas had far better survival compared with the young adults with thicker melanoma. This may suggest an inherently different biology and natural history in children with melanoma because tumor thickness is the single most important prognostic factor in all other age groups but does not seem to be a prognostic factor in children.

Among patients with invasive melanoma aged 1 to 9 years, there was a striking trend towards a higher percentage of patients with regional or distant disease at initial presentation, and younger patients diagnosed with localized invasive cutaneous melanoma are more likely to present with thicker tumors. Possible reasons include delayed diagnosis or age-related differences in biologic behavior that are not yet understood. The clinical and pathologic characteristics of melanoma in children can make diagnosis difficult.[20-23] Although the most common presentation of melanoma in children is a change in a mole, some melanocytic lesions in children have atypical appearance.[24,25] Because they may not clinically look like adult melanoma and because this rare diagnosis is sometimes not considered in young children, the diagnosis can be missed or delayed.[24-26] Some melanocytic lesions in childhood and adolescence are hard to classify pathologically as benign or malignant; it is possible that some malignant lesions are misclassified as benign and only recognized as malignant when they recur, and it is possible that some benign lesions are misclassified as malignant when they, in fact, have no malignant potential.

Registry data do not include whether individual patients may have had a delayed diagnosis or a false-positive diagnosis. The data presented here are hospital based and include only patients who have been given a diagnosis of melanoma; it is possible that this database over-represents patients with higher severity of disease. Cancer registry data have no information on whether any of the patients were originally diagnosed with an atypical lesion and subsequently diagnosed with metastases; in cancer registry data, such individuals would appear to be diagnosed with metastatic disease at initial presentation. This database also has no information on comorbidities, second

from 10.1200/JCO.2006.08.2116

neoplasms, family history, or many predisposing factors. However, we believe this to be by far the largest reported series on pediatric melanoma. It has sufficient detail on demographics, presentation, and outcomes to convincingly describe some of the unique features of melanoma in this population.

It is not well understood why the incidence of melanoma seems to be increasing in teenagers; given the consistency of the increase over many years and in reports from more than one country, it is probably not an artifact of more complete reporting to tumor registries. In adults, the risk of melanoma is epidemiologically strongly related to UV exposure, and there may be plausible mechanisms to account for UV as an etiologic agent.[27,28] The SEER data report that melanoma incidence in teenagers is higher in areas of the United States with greater sun exposure.[6] The use of artificial tanning facilities has been reported to be high in American teenagers, with as much as 47% of girls aged 17 to 18 years using tanning facilities at least three times.[29,30] UV exposure as an etiologic agent in young children seems less likely because most childhood exposure occurs in the teen years, and the youngest patients simply have not been alive long enough to have a plausible interval from exposure to diagnosis.

These data raise the possibility that melanoma, or at least some melanomas, may be biologically different in children compared with adults. In addition to the differences in demographics and presentation, perhaps more compelling is the apparent lack of prognostic value of tumor thickness in children with localized invasive melanoma. Melanoma in children and teenagers may have unique biologic features and a different natural history than melanoma in adults. Comparative genomic hybridization has shown that adult melanoma differs from benign nevi in the presence of frequent chromosomal aberrations; more research in the molecular genetics of pediatric melanoma is needed. A better understanding of the molecular and genetic aspects of this disease may help resolve the diagnostic dilemmas posed by cases that are pathologically ambiguous and may lead to targeted therapies for children with melanoma.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The authors indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: Julie R. Lange, Seng-Jaw Soong, Charles M. Balch
Administrative support: Bryan E. Palis, David C. Chang
Provision of study materials or patients: Bryan E. Palis
Collection and assembly of data: Julie R. Lange, Bryan E. Palis, David C. Chang
Data analysis and interpretation: Julie R. Lange, Bryan E. Palis, David C. Chang, Seng-Jaw Soong
Manuscript writing: Julie R. Lange, Bryan E. Palis, David C. Chang, Charles M. Balch
Final approval of manuscript: Julie R. Lange, Bryan E. Palis, David C. Chang, Seng-Jaw Soong, Charles M. Balch

REFERENCES

1. American Cancer Society: Cancer Facts and Figures 2006. Atlanta, GA, American Cancer Society, 2006
2. US Cancer Statistics Working Group: United States Cancer statistics: 1999-2002 incidence and mortality web-based report. http://www.cdc.gov/cancer/npcr/uscs/
3. Desmond RA, Soong SJ: Epidemiology of malignant melanoma. Surg Clin North Am 83:1-29, 2003
4. Hamre MR, Chuba P, Bakhshi S, et al: Cutaneous melanoma in childhood and adolescence. Pediatr Hematol Oncol 19:309-317, 2002
5. Karlsson P, Boeryd B, Sander B, et al: Increasing incidence of cutaneous malignant melanoma in children and adolescents 12-19 years of age in Sweden 1973-92. Acta Derm Venereol 78:289-292, 1998
6. 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 23:4735-4741, 2005
7. Elwood JM, Gallagher RP: Body site distribution of cutaneous malignant melanoma in relationship to patterns of sun exposure. Int J Cancer 78:276-280, 1998
8. Bulliard JL, Cox B: Cutaneous malignant melanoma in New Zealand: Trends by anatomical site, 1969-1993. Int J Epidemiol 29:416-423, 2000
9. Gillgren P, Mansson-Brahme E, Frisell J, et al: Epidemiological characteristics of cutaneous malignant melanoma of the head and neck: A population-based study. Acta Oncol 38:1069-1074, 1999
10. Whiteman D, Valery P, McWhirter W, et al: Incidence of cutaneous childhood melanoma in Queensland, Australia. Int J Cancer 63:765-768, 1995
11. Pappo AS: Melanoma in children and adolescents. Eur J Cancer 39:2651-2661, 2003
12. Conti EM, Cercato MC, Gatta G, et al: Childhood melanoma in Europe since 1978: A population-based survival study. Eur J Cancer 37:780-784, 2001
13. Stang A, Stabenow R, Eisinger B, et al: Site- and gender-specific time trend analyses of the incidence of skin melanomas in the former German democratic republic (GDR) including 19351 cases. Eur J Cancer 39:1610-1618, 2003
14. Toro J, Ranieri JM, Havlik RJ, et al: Sentinel lymph node biopsy in children and adolescents with malignant melanoma. J Pediatr Surg 38:1063-1065, 2003
15. Roaten JB, Partrick DA, Pearlman N, et al: Sentinel lymph node biopsy for melanoma and other melanocytic tumors in adolescents. J Pediatr Surg 40:232-235, 2005
16. Chao C, Martin RC II, Ross MI, et al: Correlation between prognostic factors and increasing age in melanoma. Ann Surg Oncol 11:259-264, 2004
17. Sondak VK, Taylor JM, Sabel MS, et al: Mitotic rate and younger age are predictors of sentinel lymph node positivity: Lessons learned from the generation of a probabilistic model. Ann Surg Oncol 11:247-258, 2004
18. Chao MM, Schwartz JL, Wechsler DS, et al: High-risk surgically resected pediatric melanoma and adjuvant interferon therapy. Pediatr Blood Cancer 44:441-448, 2005
19. Navid F, Furman WL, Fleming M, et al: The feasibility of adjuvant interferon alpha-2b in children with high-risk melanoma. Cancer 103:780-787, 2005
20. Wechsler J, Bastuji-Garin S, Spatz A, et al: Reliability of the histopathologic diagnosis of malignant melanoma in childhood. Arch Dermatol 138:625-628, 2002
21. Barnhill RL, Flotte TJ, Fleischli M, et al: Cutaneous melanoma and atypical spitz tumors in childhood. Cancer 76:1833-1845, 1995
22. Milton GW, Shaw HM, Thompson JF, et al: Cutaneous melanoma in childhood: Incidence and prognosis. Australas J Dermatol 38:S44-S48, 1997 (suppl 1)
23. Spatz A, Ruiter D, Hardmeier T, et al: Melanoma in childhood: An EORTC-MCG multicenter study on the clinico-pathological aspects. Int J Cancer 68:317-324, 1996
24. Saenz NC, Saenz-Badillos J, Busam K, et al: Childhood melanoma survival. Cancer 85:750-754, 1999
25. Boddie AW Jr, Smith JL Jr, McBride CM: Malignant melanoma in children and young adults: Effect of diagnostic criteria on staging and end results. South Med J 71:1074-1078, 1978
26. Melnik MK, Urdaneta LF, Al-Jurf AS, et al: Malignant melanoma in childhood and adolescence. Am Surg 52:142-147, 1986
27. Fears TR, Bird CC, Guerry D IV, et al: Average midrange ultraviolet radiation flux and time outdoors predict melanoma risk. Cancer Res 62:3992-3996, 2002
28. Gilchrest BA, Eller MS, Geller AC, et al: The pathogenesis of melanoma induced by ultraviolet radiation. N Engl J Med 340:1341-1348, 1999
29. Demko CA, Borawski EA, Debanne SM, et al: Use of indoor tanning facilities by white adolescents in the United States. Arch Pediatr Adolesc Med 157:854-860, 2003
30. Cokkinides VE, Weinstock MA, O'Connell MC, et al: Use of indoor tanning sunlamps by US youth, ages 11-18 years, and by their parent or guardian caregivers: Prevalence and correlates. Pediatrics 109:1124-1130, 2002