Pediatric Melanoma—Diagnosis, Management, and Anticipated Outcomes

Jennifer H. Aldrink, MD[a,*], Stephanie F. Polites, MD[b], Mary Austin, MD[c]

KEYWORDS

• Melanoma • Sentinel lymph node • Pediatric • Skin lesion

KEY POINTS

- Pediatric melanoma is the most common skin cancer in children and often presents with atypical findings including **A**melanosis, **B**leeding or **B**ump, **C**olor uniformity, **D**e novo or any **D**iameter, and **E**volution.
- Few pediatric-specific studies exist, and children have been excluded from most melanoma clinical trials; therefore, management is based on adult National Comprehensive Cancer Network guidelines.
- Survival for children with melanoma generally is favorable; however, disease stage strongly correlates with survival, with distant metastases portending a poor prognosis.

INTRODUCTION

Melanoma is one of the most common adult malignancies. In 2020, approximately 100,350 new cases of melanoma will be diagnosed in the United States, representing 5.6% of all adult cancer incidence, with an estimated 6850 melanoma-related deaths.[1] Of the adolescent and young adult age group (15–29 years), melanoma represents 8% of, or 7160, cases of new cancer diagnoses. Although only 0.4% of melanoma diagnoses and 0.1% of deaths from melanoma occur in patients under age 20 years, approximately 500 new diagnoses of melanoma are made in this youngest age group in the United States annually.[1] The incidence varies by race and ethnicity, with the highest incidence in the white population, at 6.68 per million in persons less than

[a] Division of Pediatric Surgery, Department of Surgery, Nationwide Children's Hospital, The Ohio State University College of Medicine, 700 Children's Drive, Faculty Office Building Suite 6B.1, Columbus, OH 43205, USA; [b] Division of Pediatric Surgery, Department of Surgery, Mayo Clinic, 200 1st Street Southwest, Rochester, MN 55905, USA; [c] Department of Surgical Oncology, Division of Surgery, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA
* Corresponding author.
E-mail address: Jennifer.Aldrink@nationwidechildrens.org

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19 years old.[2] The incidence of melanoma increases with age and is exceedingly rare in children less than 5 years old (0.87 per million children).[3] Although reports prior to 2008 suggested that the incidence of melanoma in children was increasing,[4] more recent studies show a declining incidence in both children and young adults.[2,3,5] This decline may be due in part to the increased use of sun protective clothing and sunscreen as well as the adoption of more strict indoor tanning regulations.[6]

The majority of childhood and adolescent melanoma occurs sporadically, with most attributed to UV pathophysiology exposure, especially in adolescents. Familial cases account for only 1% of melanoma in children,[7,8] but approximately 25% of pediatric patients have a preexisting condition known to be associated with melanoma.[9,10] The strongest risk factor for melanoma in adolescents is the presence of more than 100 nevi with a diameter greater than 2 mm.[11] Other less common predisposing conditions include dysplastic nevus syndrome, congenital melanocytic nevi, xeroderma pigmentosa, immunodeficiency, prior malignancy, and radiation therapy (**Box 1**).

DIAGNOSIS

In children and adolescents, a diagnosis of melanoma often is not considered due to its rarity and atypical presentation. Concerning features in a skin lesion include rapid growth, bleeding, and itching.[12] It has been shown that up to 60% of melanoma diagnoses in children under age 10 years and 40% of diagnoses in children ages 11 years to 19 years do not meet traditional asymmetry, border irregularity, color variegation, diameter greater than 6 mm, and evolution (ABCDE) criteria.[13] Thus, modified ABCDE criteria have been proposed to be used in addition to the traditional criteria to help identify suspicious skin lesions in children and adolescents. These criteria include amelanotic, bleeding or bump, color uniformity, de novo and any diameter, and evolution.[13] It is common for pediatric melanoma to be amelanotic, and amelanotic lesions more often are misdiagnosed as warts, pyogenic granulomas, or other benign skin lesions (**Fig. 1**). A recent study from the University of Michigan found approximately 80% of melanomas in prepubertal children and 25% in adolescents were amelanotic and that the lack of pigmentation was associated with a median delay in diagnosis of 9 months.[12]

Presentation patterns can vary by age, gender, and ethnicity. Melanoma of infancy presents almost exclusively either as malignant transformation of a congenital melanocytic nevus or via placental transmission with multiple cutaneous or visceral metastatic deposits.[14,15] Younger children are more likely to be male with a higher incidence of nonwhite ethnicity than seen in the adult population.[13,16] Tumors in young

Box 1
Preexisting conditions associated with pediatric melanoma

- Congenital melanocytic nevus
- Transplacental transmission
- Xeroderma pigmentosa and other genetic disorders that affect tumor suppressor genes
- Dysplastic nevi and dysplastic nevus syndrome
- Immunosuppression
- Sun-sensitive phenotype (facial freckling, inability to tan)
- Family history of melanoma

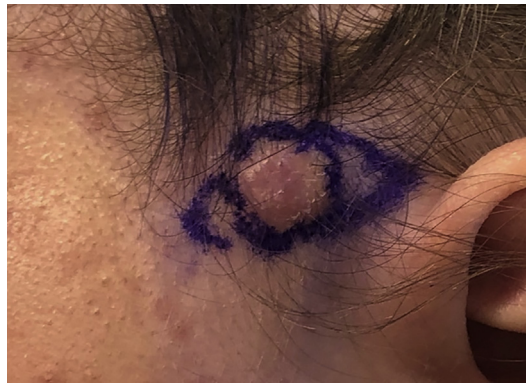

Fig. 1. Photograph of an amelanotic spitzoid melanoma in a 14-year-old girl.

children are thicker, and between 25% to 58% may present with regional nodal metastases.[17–19] In this younger age group, the role of UV exposure in children is uncertain because melanoma is more likely to arise from an existing congenital melanocytic nevus or dysplastic nevus. The clinical presentation of melanoma in adolescence mimics that of adults, with most tumors arising in previously healthy skin. Males tend to present with tumors of the face and trunk, whereas females more commonly present with extremity tumors.[4,18] According to the Surveillance, Epidemiology, and End Results (SEER) database, 85% of patients with melanoma under age 18 years are white, 5% Hispanic, and 2% Asian/Pacific Islander.[18]

There are 3 main categories of pediatric melanoma: conventional melanoma, melanoma arising in a congenital nevus, and spitzoid melanoma. Conventional melanoma genetically is similar to adult melanoma and demonstrates genomic characteristics secondary to UV damage, including an increased rate of single nucleotide variations.[20] In contrast, melanoma arising in congenital nevi demonstrates a much lower frequency of UV-related mutations.[9] There remains some debate among dermatopathologists regarding the distinction between atypical Spitz nevus, melanocytic tumors of uncertain malignant potential, and spitzoid melanoma.[21–23] In 1 study, 35% of spitzoid tumors initially were misdiagnosed as Spitz nevus and, on later review, were determined to be melanoma with epithelioid or spindle cells.[22] There is no single method to differentiate an atypical Spitz nevus from a melanoma; however, comparative genomic hybridization identifying chromosome copy number loss or gain often is helpful in that melanoma often has a variety of chromosomal aberrations compared with most Spitz nevi, which demonstrate a normal karyotype.[24] For this reason, it is essential that lesions concerning for melanoma be reviewed by a dermatopathologist with experience in diagnosing pediatric melanoma. If a lesion is determined to be a benign Spitz nevus or atypical Spitz nevus, excision with negative margins is indicated; however, spitzoid melanoma should be managed as melanoma per National Comprehensive Cancer Network (NCCN) guidelines.[25]

SURGICAL MANAGEMENT

The mainstay of treatment of pediatric cutaneous melanoma is cure by surgical resection. This process includes full-thickness biopsy for diagnosis, wide local excision (WLE) with margins based on lesion depth, and selective use of sentinel lymph node biopsy (SLNB) and completion lymph node dissection (CLND). Given the lack

of pediatric-specific clinical trials guiding surgical management, adult guidelines are applied to children with some modifications based on expected differences in cosmetic and functional outcomes in younger patients.

Biopsy and Wide Local Excision

Suspicious lesions should undergo diagnostic evaluation either by punch biopsy or surgical biopsy. Surgical biopsy may be incisional or excisional but if the latter approach is used, margins should be less than 3 mm to maintain lymphatics for potential SLNB. The need for WLE should be considered when choosing the incision for initial surgical biopsy. After confirmation of diagnosis by a dermatopathologist experienced in pediatric melanoma, WLE is performed to the depth of the muscular fascia. Deeper resections involving fascia or muscle are not performed because these have not been shown to be beneficial in adult patients.[26]

Surgical margins for WLE of melanoma in pediatric patients utilize NCCN guidelines based on Breslow thickness of the lesion (**Table 1**).[25] Specifically, a 1.0-cm margin is recommended for lesions less than or equal to 1.0 mm in depth and a 2.0-cm margin for lesions greater than or equal to 2.0-mm deep. Although patients with lesions greater than or equal to 2.0 mm who underwent excision with 1.0-cm margins experienced worse disease-free survival (DFS) and melanoma-specific survival (MSS), no survival advantage has been shown for margins greater than 2.0 cm in several multicenter prospective randomized controlled trials.[27–29]

The clinical trials that informed the NCCN guidelines excluded pediatric patients. Retrospective cohort studies suggest children have lower risk of local recurrence compared with adults and have identified trends toward decreased recurrence in young children compared with adolescents.[30,31] With this in mind, smaller margins should be considered when form or function would be substantially compromised using standard NCCN recommendations. When smaller margins are used, it is important to obtain final pathology results prior to performing any major reconstruction.

Regional Lymph Nodes

Regional lymph nodes are the first site of metastases for melanoma, and lymph node metastases occur more frequently in pediatric patients than adults.[30,32] Because clinical examination and imaging studies do not detect microscopic metastases, SLNB is utilized in select patients for staging and prognostic purposes. Selection of pediatric patients with melanoma to undergo SLNB is based on adult guidelines. SLNB is not indicated in patients with lesions less than 0.8-mm thick without concerning features, such as ulceration, lymphovascular invasion, or greater than or equal to 2 mitoses per

Table 1
Recommended surgical margins for wide local excision of melanoma based on Breslow thickness

Melanoma Thickness	Wide Local Excision Margin
Melanoma in situ	0.5–1.0 cm
≤1.0 mm	1.0 cm
>1.0 mm–2.0 mm	1.0–2.0 cm
>2 mm	2.0 cm

Data from Fleming MD, Galan A, Gastman B, et al. *NCCN Guidelines Version 3.2020 Cutaneous Melanoma NCCN Evidence Blocks TM Continue NCCN Guidelines Panel Disclosures*.; 2020. www.nccn.org/patients. Accessed August 20, 2020.

millimeter.[2] It is utilized selectively after a discussion of risks and benefits with the patient and family for those with lesions between 0.8-mm and 1.0-mm deep.[33] For those with lesions greater than or equal to 1.0 mm in depth, it always should be performed, because more than 1 in 3 patients have a positive sentinel lymph node.[34]

The risk of complications after SLNB is less than 5% and the most frequent complication is seroma. CLND carries greater morbidity, with 1 in 4 adult patients developing lymphedema.[35] Approximately half of pediatric patients who undergo WLE with CLND experienced complications as opposed to 11% of those who underwent WLE with SLNB.[36] The highest postoperative morbidity is associated with inguinal node dissection followed by axillary location.[37] Current NCCN guidelines acknowledge that lymph node dissections should be anatomically complete; however, there is not consensus on the definition of a complete dissection or the number of nodes that should be excised.[25]

CLND should be used judiciously in pediatric patients, balancing the risk of morbidity with the risk of recurrence over their longer life expectancies compared with adults. This procedure is performed routinely for clinically or radiographically positive nodes and selectively utilized for occult metastases identified by SLNB.[33] This paradigm shift is based on the findings of 2 adult clinical trials in which patients with a positive sentinel node who were observed with routine clinical examinations and ultrasounds had a higher rate of regional nodal recurrence but without decreased survival compared with those who underwent immediate CLND.[35,38]

These data must be interpreted with caution in pediatric melanoma, because enrolled adults had significantly shorter life expectancies than children and access to frequent, high-quality surveillance at experienced centers. A discussion of risks and benefits of CLND and access to follow-up is recommended for pediatric patients with a positive SLNB. CLND also should be considered strongly for patients who cannot return regularly for follow-up evaluations and ultrasound surveillance of the affected nodal basin. Additionally, patients with high-risk features, including extracapsular extension, primary tumor microsatellitosis, greater than 3 involved sentinel nodes, greater than 2 involved nodal basis, or immunosuppression, should be offered CLND, because these patients were excluded in the adult trials.[39–49]

In a recent study, Parikh and colleagues[50] used propensity score matched analyses of SEER data and showed no difference in MSS between children and adolescents who underwent SLNB and/or lymphadenectomy versus those who did not undergo lymph node sampling. They noted worse overall survival (OS) in patients with positive lymph nodes, however, compared with those with either no lymph nodes sampled or negative lymph nodes. The prognostic impact of lymph node status on survival may be age related. Lorimer and colleagues[51] found that in children ages 1 year to 10 years, there was no difference in OS based on lymph node positivity; however, adolescents with node-positive disease were at higher risk of death compared with adolescents with node-negative disease (hazard ratio [HR] 4.82; 95% CI, 3.38–6.87). Most studies to date have shown that regional disease is associated with worse survival compared with localized disease[17,18,51–56]

MEDICAL MANAGEMENT

Pediatric patients with stages III and IV melanoma are considered for additional therapy (**Table 2**). Immune and targeted therapies comprise contemporary adjuvant and systemic treatment (**Table 3**). The safety and efficacy of these therapies largely are extrapolated from clinical trials that excluded pediatric patients. For completely resected stage III melanoma, the 2020 NCCN guidelines recommend considering

Table 2
American Joint Committee on Cancer clinical staging for melanoma

Stage	T	N	M
0	Tis	N0	M0
IA	T1a	N0	M0
IB	T1b	N0	M0
	T2a	N0	M0
IIA	T2b	N0	M0
	T3a	N0	M0
IIB	T3b	N0	M0
	T4a	N0	M0
IIC	T4b	N0	M0
III[a]	Any T/Tis	≥N1	M0
IV	Any T	Any N	M1

T Category	Thickness	Ulceration
TX[b]	N/A	N/A
T0	N/A	N/A
Tis	N/A	N/A
T1a	<0.8 mm	Not present
T1b	<0.8 mm	Present
	0.8–1.0 mm	Present or not present
T2a	>1.0–2.0 mm	Not present
T2b	>1.0–2.0 mm	Present
T3a	>2.0–4.0 mm	Not present
T3b	>2.0–4.0 mm	Present
T4a	>4.0 mm	Not present
T4b	>4.0 mm	Present

Abbreviations: N/A, not applicable; Tis, melanoma in situ.
[a] There is 1 clinical stage group for stage III melanoma. Stages IIIA, IIIB, IIIC, and IIID are pathologic stages based on the extent of lymph node involvement and clinical versus occult presentation.
[b] Thickness cannot be assessed due to inadequate tissue.

systemic adjuvant therapy given the reported benefits in DFS with contemporary agents.[25] It is not yet known if this will translate to improved OS; it should be noted that these trials included patients who underwent CLND after a positive SLNB, and those who received adjuvant therapy for occult nodal disease had at least 1 lymph node metastasis greater than 1 mm.

Interferon Alfa-2b

Adjuvant therapy with high-dose interferon alfa-2b utilized for node positivity or a deep lesion greater than 4.0 mm. Three adult clinical trials demonstrated improved DFS with inconclusive results on OS.[57–60] The approved regimen includes 1 month of intravenous induction therapy followed by 11 months of subcutaneous maintenance therapy, although with significant toxicities the 12-month course commonly is abandoned prior to completion. The addition of polyethylene glycol (PEG) formulation of interferon has improved efficacy whereas low-dose or intermediate-dose therapy is not efficacious and no longer recommended.[57,61,62] Several retrospective pediatric studies support the results of adult studies and showed improved tolerance compared with adults,

Table 3
Systemic therapies for advanced melanoma

Drug Name	Mechanism of Action/Target	Application in Melanoma
Interferon alfa-2b	Multifunctional immunoregulatory cytokine, stimulates B cells, activates NK cells	Stage III
Talimogene laherparepvec	Modified virus induces tumor cell lysis, granulocyte-monocyte colony stimulating factor expression	Unresectable subcutaneous or nodal disease
Melphalan	Alkylating agent inhibits DNA and RNA synthesis	Regionally advanced melanoma used in isolated limb perfusion/ infusion
Dacarbazine	Methylation of guanine in DNA strands, preventing cell division	Metastatic
Ipilimumab	Monoclonal antibody against CTLA-4	Nodal recurrence or metastatic with prior anti–PD-1 exposure
Nivolumab	Monoclonal antibody against PD-1	Stage III, unresectable or metastatic
Pembrolizumab	Monoclonal antibody against PD-1	Stage III, unresectable or metastatic
Vemurafenib	BRAF inhibitor	BRAF V600E mutation–positive, unresectable or metastatic
Dabrafenib	BRAF inhibitor	BRAF V600E mutation–positive, unresectable or metastatic
Selumetinib	Selective MEK1 and MEK2 inhibitor (downstream of BRAF/MAPK/ERK pathway)	BRAF-activating mutation–positive
Trametinib	Selective MEK1 and MEK2 inhibitor (downstream of BRAF/MAPK/ERK pathway)	BRAF V600E–mutated, metastatic
Dabrafenib/ trametinib	Combination therapy	BRAF V600E/K–mutated Stage III, unresectable or metastatic
Imatinib	Targeted c-kit inhibitor	c-kit mutated or amplified

with the exception of a higher rate of neutropenia in children.[63–66] A phase II clinical trial of PEG–interferon alfa-2b in pediatric patients is ongoing (NCT005539591).[67]

Immune Checkpoint Inhibitors

Immune checkpoint inhibitors reduce the immune response to cancer cells including ipilimumab, a monoclonal antibody that binds the T-cell receptor antigen CTLA-4. It has been shown to improve survival in adult patients with resected stage III and unresectable melanoma.[68,69] Side effects are dose dependent and occur in up to 60% of patients. NCCN does not recommend ipilimumab for adjuvant therapy of resected stage III melanoma at this time due to better tolerated and more efficacious alternatives.[25] Following a phase I study that found ipilimumab to be safe in adolescents with unresectable disease, a phase II study evaluating it as a single agent or in

combination with nivolumab in pediatric patients with recurrent or refractory solid tumors, including melanoma is in process (NCT02304458).[70]

Other immune checkpoint inhibitors target the programmed death (PD)-1 protein expressed by T cells to prevent binding of tumor PD ligand protein. Nivolumab and pembrolizumab are 2 such therapies that are effective for both resected stage III and metastatic disease and now are the preferred immune checkpoint inhibitors for melanoma.[25] The former was better tolerated than ipilimumab when compared directly.[71] Although PD-1 expression in tumor cells was assessed in the clinical trials, patients with minimal expression responded as well and this should not be considered a contraindication. Pembrolizumab is being evaluated in children with melanoma and other malignancies in a phase 1 to phase 2 trial, with results expected in 2022.[72] A report of compassionate use in a pediatric patient with recurrent metastatic disease demonstrated remission at 1 year although the medication was discontinued due to adverse events.[73]

BRAF-Targeted Therapy

The signaling kinase BRAF is a target of therapy for melanoma with an activating mutation (BRAF V600).[74] Approximately half of patients with metastatic disease harbor this mutation and inhibitors of BRAF and downstream MEK have been developed. Tumors without BRAF mutations do not respond. BRAF inhibitors vemurafenib and dabrafenib have shorter response time and improved survival compared with chemotherapy; however, BRAF inhibitors have a high rate of relapse within 6 months , and vemurafenib has an approximately 20% risk of hyperproliferative cutaneous adverse events, including squamous cell carcinoma and, therefore, is not recommended as adjuvant monotherapy.[75–78] Although MEK inhibitor (trametinib, cobimetinib, and binimetinib) monotherapy also is more effective than chemotherapy for those with BRAF mutations, response rates are lower than BRAF inhibitors.[79]

For resected stage III disease, combination dabrafenib/trametinib therapy was Food and Drug Administration approved after it was shown to have improved DFS and decreased risk of developing metastatic disease.[80] The combination is better tolerated than BRAF inhibitor monotherapy. Clinical trials of BRAF and MEK inhibitors in pediatric patients are challenged by low enrollment, highlighting the importance of including this population in larger adult studies. A phase I study of vemurafenib in adolescents could not identify a safe and effective dose. Phase I studies of trametinib alone and in combination with dabrafenib for other pediatric malignancies, including gliomas, have shown it to be safe in children.[81–84]

Second-Line Systemic Therapies

Pediatric case series with dacarbazine, paclitaxel and temozolomide suggested improved response in children compared with adults, although exclusion of children from larger clinical trials has limited further investigation of chemotherapy in this population.[85–88] At least 2 children have been treated with systemic interleukin 2 for melanoma but literature is insufficient to conclude pediatric efficacy.[89–91]

OUTCOMES

Although studies evaluating long-term survival of children and adolescents with melanoma are limited, several reports have demonstrated improved survival over the past 40 years.[18,50,51] Five-year and 10-year OS rates for all stages range from 88.9% to 94.7% and 80.9% to 88%, respectively.[17,51,92–94] Studies lack consistency in reporting, but most report favorable outcomes with disease-specific survival rates greater

than 80% at 5 years.[18,92,95] Similar to adults, the strongest predictor of survival for children and adolescents with melanoma is stage of disease at presentation. In 2007, Lange and colleagues[17] reported the following 5-year OS by stage using data from the SEER program: 97.8% for in situ, 93.6% for localized melanoma, 68% for melanoma with regional metastases, and 11.8% for distant metastatic disease. More recent studies have confirmed the importance of stage as a strong predictor of survival in children and adolescents with melanoma.[50,51,92,93] Fortunately, most patients present with either localized (77%) or regional disease (15%), with only 1% presenting with distant metastases.[50] A significant limitation to both SEER and the National Cancer Database (NCDB) is a failure to collect all of the variables included in the American Joint Committee on Cancer (AJCC) staging for melanoma.[96]

It is not surprising that health disparities play a role in both disease presentation and outcomes for children and adolescents with melanoma. Using Texas Cancer Registry data, Hamilton and colleagues[97] demonstrated that Hispanic race/ethnicity was independently associated with increased odds of presenting with advanced disease (HR 3.5; 95% CI, 1.4–8.8) and Hispanics were 3 times more likely to die from melanoma than non-Hispanic whites. In a SEER study of pediatric and adult melanoma patients, black race was independently associated with increased risk of death (HR 1.84; 95% CI, 1.64–2.04) after controlling for age, sex, primary site, stage, type of therapy, and year of diagnosis.[51]

The data are conflicting regarding the prognostic importance of age, gender, primary site, histology, tumor thickness, mitoses per square millimeter, and lymph node status. Several studies have shown that younger children ($\leq$10 years age) are more likely to present with thicker lesions[17,18,51,92] and nodal disease compared with adolescents and adults.[17,18,50,52,98] Survival results vary, however, with Lange and colleagues[17] reporting a poorer 5-year OS rate for children ages 1 year to 9 years (77.0% $\pm$ 4.5%) compared with older age groups, whereas other studies either show no significant difference in survival by age[52,92] or improved survival for children less than or equal to 10 years of age at diagnosis.[18,51] Using the NCDB, Lorimer and colleagues[51] found that both children ages 1 year to 10 years and adolescents ages 11 years to 20 years had improved OS compared with adults greater than 20 years old (HR 0.11; 95% CI, 0.06–0.21, and HR 0.22; 95% CI, 0.19–0.26, respectively).

Several studies report favorable outcomes for females compared with males[18,50,51]; however, other studies found no significant differences in survival between genders.[92,93] Head and neck primary sites have been associated with worse prognosis compared with other sites.[18,51,94] In a recent study using SEER program data, Shi and colleagues[94] showed that pediatric and adolescent patients with head and neck melanoma had an increased risk of mortality (HR 1.6; 95% CI, 1.3–2.1) compared with those with non–head and neck melanoma after adjusting for gender, age, and race/ethnicity. In addition, nodular histology may portend a worse prognosis.[18,50,93]

There is debate about the role of tumor thickness and mitoses per square millimeter in prognosis of pediatric and adolescent melanoma. Lange and colleagues[17] reported that tumor thickness was not associated with OS, using a cutoff of greater than or equal to 1.5 mm to define thick melanoma. Several other studies have demonstrated the importance of Breslow thickness as a prognostic factor in pediatric and adolescent melanoma, including Averbook and colleagues,[92] who found that both OS and DFS were independently associated with tumor thickness greater than 1.0 mm in patients less than or equal to 20 years of age at diagnosis.[93] In the most recent version of the AJCC melanoma staging, mitotic rate greater than or equal to 1/mm^2 replaces level of invasion as the primary criterion for defining T1b melanomas[96]; however, the significance of mitotic rate for pediatric and adolescent melanoma remains

unknown. In a recent study from the Melanoma Institute Australia, mitotic rate greater than or equal to 1/mm^2 was found to be the only factor independently associated with worse relapse-free survival and MSS for children less than or equal to 19 years old after adjusting for gender, age, Breslow thickness, primary tumor site, histology, and lymph node status.[95]

Data also are limited on time to recurrence for pediatric patients and adolescents with melanoma. In a report from the Melanoma Institute Australia, the time between diagnosis of the primary melanoma and first recurrence ranged from 3 months to 13 years, with 5 patients (31%) experiencing a recurrence more than 5 years after diagnosis.[95] This emphasizes the importance of long-term follow-up, including regular comprehensive skin examinations by a physician with expertise in pediatric melanoma.

SUMMARY

Although rare, melanoma is the most common skin cancer in children and adolescents, with approximately 500 new diagnoses per year in the United States in persons less than 20 years of age. It often presents in an atypical fashion with modified ABCDE criteria. The mainstay of treatment is surgical resection. All suspicious skin lesions should undergo punch biopsy, incisional biopsy, or excisional biopsy. SLNB is indicated for all T1b and above lesions as well as those 0.8-mm to 1-mm thickness with concerning features (mitoses >2/mm^2, ulceration, or lymphovascular invasion). There has been a paradigm shift in the management of positive SLNB based on 2 large multi-institutional clinical trials in adults that demonstrated increased regional recurrence but no difference in OS for SLNB-positive patients who were managed with nodal observation versus those who underwent immediate CLND. The results of these trials have been applied to pediatric and adolescent patients; however, it is critical that patients undergoing observation be followed with regular ultrasounds performed in a center with experience in nodal surveillance by ultrasound. Targeted therapies and immunotherapy have changed the landscape for melanoma patients with advanced disease; and, although most clinical trials to date have excluded children, several have demonstrated safety and efficacy of these newer treatment modalities in adolescent patients. Survival generally is favorable in pediatric melanoma, with the exception of those with distant metastases, but even this is rapidly evolving field of immunotherapy.

DISCLOSURE

The authors have nothing to disclose.

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