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ARTICLE

A 28-year single institution experience with primary skin malignancies in the pediatric population

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ABSTRACT

The aim of this study is to report our institution's experience with pediatric skin malignancies. A single institution retrospective review of pediatric patients with a primary skin malignancy from 1992 to 2020 was performed. Demographics, tumor characteristics and treatment outcomes were reviewed. Ninety-nine patients with 109 primary malignant skin lesions were reviewed. The most common lesion was malignant melanoma [MM] ($n = 50$, 45.9%). Compared to non-melanoma skin cancer (NMSC), MM were more likely to present on trunk or extremities (p=.01, OR = 3.2), and be misdiagnosed (p=.03, OR = 2.7). NMSC were more common in the head and neck region (p=.01, OR = 3.2), and were associated with a personal history of skin cancer (p=.0005, OR = 17.1) or a known risk factor (p=.04, OR = 2.5). Patients with MM were 12.4-times more likely to develop metastatic disease compared to NMSC (p<.0001). Increased Breslow's thickness also increased the odds of developing metastatic disease (p=.03, OR = 1.6 per 1-mm increase). Interval time between lesion recognition and diagnostic biopsy or surgical treatment did not impact overall survival. Malignant melanoma was the most common malignancy in our cohort, followed by basal cell carcinoma. Malignant melanoma was the most likely tumor to be misdiagnosed and/or metastasize. Treatment delays did not impact risk of metastasis, recurrence or survival rate, though some patients succumbed to disease. These results may be attributed to small sample size or the biology of melanoma in pediatric patients. Awareness of skin malignancies in the pediatric population is imperative to providers and the public, with low threshold for specialty consultation and excision when warranted.

Abbreviations: AK: actinic keratosis; BCC: basal cell carcinoma; CI: confidence interval; CMN: congenital melanocytic nevus; DFSP: dermatofibrosarcoma protuberans; FTSG: full thickness skin graft; HR: hazards ratio; IQR: interquartile range; LND: lymph node dissection; MM: malignant melanoma; MMS: Mohs micrographic surgery; NMSC: non-melanoma skin cancer; OR: odds ratio; RLND: regional lymph node dissection; SCC: squamous cell carcinoma; SD: standard deviation; SLNB: sentinel lynph node biopsy; SSI: surgical site infection; STSG: split thickness skin graft; WLE: wide local excision.

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Pediatric melanoma; pediatric skin cancer; basal cell carcinoma; squamous cell carcinoma; dermatofibrosarcoma protuberans

Introduction

Primary cutaneous malignancies are exceedingly rare in children and are associated with distinct epidemiologic, clinical and diagnostic characteristics compared to the adult population. This low incidence may contribute to under-recognition of malignant lesions. Furthermore, there is a natural reservation to perform a skin biopsy on a child. These factors contribute to potential diagnostic and treatment delays [1–5].

In this study, we sought to improve recognition of said lesions and streamline referral patterns. The purposes of this study were to identify risk factors associated with pediatric cutaneous malignancies and to assess the impact of delayed diagnosis and treatment.

Materials and methods

After approval by the Institutional Review Board (IRB#19-008294), all patients <18 years of age (at diagnostic biopsy) with histopathological diagnosis of a primary skin malignancy between January 1992 and January 2020 were retrospectively reviewed. Soft tissue malignancies with cutaneous extension, non-cutaneous melanomas, benign lesions such as Spitz nevi, melanocytic nevi, congenital melanocytic nevi and actinic keratoses were excluded.

Data including age, gender, personal or family history of skin cancer, known risk factors for developing malignant skin lesions were collected. Lesion characteristics, anatomic location, size, appearance and definitive treatment were reviewed. For malignant melanoma (MM); stage, subtype, Breslow's thickness and Clark's level were recorded. Preceding skin lesions, scars or previous trauma at the site of the primary skin malignancy were noted. The chronological details including age at lesion recognition (by parent/guardian, or physician) and diagnostic biopsy, time from lesion recognition to first physician evaluation, time between first physician evaluation and diagnostic biopsy, time between diagnostic biopsy and treatment, and time between outside institution physician evaluation and final diagnosis were collected.

Histopathology slides were reviewed by board-certified dermatopathologists at our institution in all cases. Initial clinical

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Table 1. Patient demographics and primary skin malignancies.

	n	%
Patients (lesions)	99 (109)	
Male	45	45.5
Female	54	54.5
Mean age at lesion recognition ± SD, years	10.1 ± 5.4	
Median age at lesion recognition (range), years	12 (0–17)	
Mean age at diagnostic biopsy ± SD, years	11.4 ± 5.0	
Median age at diagnostic biopsy (range), years	13 (0.9–17)	
Age groups (years)		
0–4	13	11.9
5–9	24	22.0
10–14	31	28.4
15–17	41	37.6
Personal history of primary skin cancer	5	5.1
Family history of primary skin cancer	27	27.3
Known risk factors	22	22.2
Gorlin syndrome	5	5.1
Congenital melanocytic nevus	5	5.1
History of sunburns/ultraviolet radiation exposure	4	4.0
Xeroderma pigmentosum	2	2
Radiation therapy history	2	2
Familial trichoepithelioma	1	1
Burn scar at lesion site	1	1
Familial atypical multiple mole melanoma syndrome	1	1
Immunosuppression	1	1
Types of diagnostic biopsy	109	
Excisional	65	59.6
Shave	21	19.3
Punch	15	13.8
Incisional	4	3.7
Unknown	4	3.7
Subgroup of the skin cancer	109	
Malignant melanoma	50	45.9
Basal cell carcinoma	28	25.7
Dermatofibrosarcoma protuberans (DFSPs)	20	18.4
Squamous cell carcinoma	6	5.5
Keratoacanthoma	1	0.9
Sweat gland cancer	2	1.8
Eccrine hidradenocarcinoma	1	0.9
Digital papillary adenocarcinoma	1	0.9
Langerhans cell histiocytosis	2	1.8
Sebaceous cell carcinoma	1	0.9
Site of lesions		
Head and neck	48	44.0
Extremities	36	33.0
Trunk	25	22.9

SD: standard deviation.

Table 2. Surgical treatment, reconstruction and clinical outcomes.

	n	%
Number of lesions	109	
Definitive surgical treatment		
Wide local excision	66	60.6
Mohs surgery	22	20.2
Excisional/punch biopsy without further procedure	20	18.4
Tumor debulking/partial excision	1	0.9
Wound closure technique		
Primary closure	92	84.4
STSG	7	6.4
FTSG	5	4.6
Wound matrix with skin graft		
Wound matrix with STSG	2	1.8
Wound matrix with FTSG	1	0.9
Pedicled flap		
Anterolateral thigh	1	0.9
Medial plantar artery	1	0.9
Lymph node procedures		
SLNB	37	33.9
Positive disease on SLNB	16	43.2
RLND	21	19.3
Chemotherapy	10	9.2
Malignant melanoma	8	7.3
DFSP	1	0.9
Sebaceous cell carcinoma	1	0.9
Radiation therapy	4	3.7
Malignant melanoma	2	1.8
Sebaceous cell carcinoma	1	0.9
Langerhans cell histiocytosis	1	0.9
Metastasis		
Including lymph nodes	22	20.2
Limited to lymph nodes	19	17.4
Recurrence	7	6.4
Malignant melanoma	4	3.7
Eccrine hidradenocarcinoma	1	0.9
DFSP	1	0.9
Sebaceous cell carcinoma	1	0.9
Death	5	4.6
Malignant melanoma	4	3.7
Eccrine hidradenocarcinoma	1	0.9
Postoperative complications	5	4.6
Wound dehiscence	2	1.8
Seroma	2	1.8
SSI	1	0.9
Median follow-up after diagnostic biopsy (IQR, months)	41.1 (85.6)	
Median follow-up after definitive surgery (IQR, months)	39 (76.3)	

STSG: split-thickness skin graft; FTSG: full thickness skin graft; DFSPs: dermatofibrosarcoma protuberans; SSI: surgical site infection; SLNB: sentinel lymph node biopsy; RLND: regional lymph node dissection; IQR: interquartile range.

diagnoses prior to biopsy were compared to the final pathologic diagnoses to determine clinical diagnostic accuracy. Inaccurate diagnoses were defined as any clinical or histopathological diagnosis which was discordant with the final histopathological diagnosis.

Descriptive statistics were performed to analyze characteristics of the lesion, patient and treatment modalities. Univariate logistic regression models were used to evaluate the associations between variables and outcomes that were assessed at the time of diagnosis/treatment. Characteristics of MM and non-melanoma skin cancer (NMSC) were also compared using a logistic regression model. Univariate analysis was performed to determine risk factors for metastasis among patients with melanoma. Pearson's chi-square, Student's *t*-test or Fisher's exact test were used to assess statistical significance for these associations. To identify risk factors for time-dependent outcomes, including recurrence and death, a time-to-event analysis using the Cox proportional-hazards models was performed. All analyses were performed using JMP Statistical Software (JMP®, Version <*14*>, SAS Institute Inc., Cary, NC, 1989–2019). An alpha error of 0.05 was used and values of $p < .05$ were considered statistically significant.

Results

Overall, 99 patients with 109 primary malignant skin lesions were included. Seventy-four (67.9%) lesions were referred to our institution by external providers following initial diagnostic biopsy. Patient demographics, lesions characteristics, diagnosis, treatment and reconstruction details, and clinical outcomes are summarized in Tables 1 and 2. Most common Fitzpatrick skin classification type was type II ($n = 32$). Most common malignancy was MM ($n = 50$) followed by basal cell carcinoma (BCC) ($n = 28$) and dermatofibrosarcoma protuberans (DFSPs) ($n = 20$).

Most common MM subtypes in this series were superficial spreading ($n = 16$) and spitzoid ($n = 15$). Patients who were aged 15 or older at the time of biopsy were more likely to have the superficial spreading subtype of MM compared to younger patients (p=.002, OR = 9.9, 95% CI [2.2, 45.0]). MM was most commonly diagnosed on the extremities ($n = 22$), followed by the head and neck region ($n = 16$) and trunk ($n = 12$). Mean Breslow's thickness of all MMs was 2.7 ± 3.1 mm. Breslow's thickness was found to significantly increase the odds of developing metastasis (p=.03, OR = 1.6 per 1-millimeter increase, 95% CI [1.1, 2.3]).

Table 3. Comparison of melanoma and non-melanoma cases.

Characteristic	Melanoma *n* (%)	Non-melanoma *n* (%)	*p* Value [95% CI]
Number of lesions	50	59	
Age at lesion recognition, mean ± SD (years)	10 ± 5.6	10.1 ± 5.3	.75 [−2.5, 1.8]
Age at diagnostic biopsy, mean ± SD (years)	11.7 ± 4.9	11.2 ± 5.0	.54 [−1.3, 2.5]
Lesion characteristics[a]			
Change in size/shape	33 (73.3)	30 (58.8)	.14 [0.8, 4.6]
Change in color	22 (48.9)	10 (19.6)	.003 [1.6, 9.5]*
Bleeding	7 (15.6)	4 (7.8)	.24 [0.6, 7.9]
Unknown	5 (10.0)	8 (13.6)	.57 [0.4, 4.6]
Site			.01 [0.2, 0.8]*
Head and neck, lesions	16 (32)	32 (54.2)	
Trunk/extremities	34 (68)	27 (45.8)	
Clinical misdiagnosis[a]	19 (41)	11 (20.8)	.03 [1.1, 6.5]*
Unknown	4 (8)	6 (10.2)	.70 [0.3, 4.9]
Metastatic lesion	19 (38)	3 (5.1)	<.0001 [3.1, 41.7]*
Sentinel lymph node biopsy	34 (68)	3 (5.1)	<.0001 [10.8, 146.2]*
Regional lymph node dissection	18 (36)	3 (5.1)	<.0001 [2.9, 38.4]*

CI: confidence interval; SD: standard deviation.
*Statistically significant value.
[a]Percentages were calculated after excluding the unknown patient data. Statistical significance between groups was tested using Fisher's exact test, Pearson's chi square or Student's *t*-test.

Children with MM presented with melanoma-in-situ ($n = 4$), stage I disease ($n = 8$), stage II disease ($n = 6$), stage III disease ($n = 14$) and stage IV ($n = 1$). Four recurrences and four deaths occurred in children with MM. Of the deceased, three had recurrences and one developed a new primary MM. Three received chemotherapy and one received radiation therapy.

Compared to MM, patients with NMSC were more likely to have a previous skin cancer (p=.0005, OR = 17.1) and a known risk factor (p=.04, OR = 2.5). Patients with MM were more likely to present with lesion color changes (p=.003, OR = 3.8). MM development was more likely on the trunk or extremities, whereas NMSC was more common on the head and neck region (p=.01, OR 3.2). MM was more likely to be inaccurately diagnosed on clinical exam (p=.03, OR = 2.7), and more likely to have metastasis (p<.0001, OR = 12.4) when compared to NMSC (Table 3).

Median interval between lesion recognition and the first physician evaluation was 1 month (range: $r = 0$, 214.3 months). Median interval from the first physician evaluation to diagnostic biopsy was 0 ($r = 0$, 126 months). Median interval between diagnostic biopsy and definitive treatment was 21 days ($r = 0$, 22.5 months). Of the 73 patients referred to our institution, median time from evaluation at another facility to evaluation at our institution was 3.2 months (0.2–127.7 months). Twenty of them were told to monitor the lesion without biopsy and nine (12.2%) were offered alternative treatments, such as cryotherapy and topical agents, including 5-fluorouracil, imiquimod and antibiotics.

In 30 (27.5%) of all cases and 23 (31.1%) of referred cases, there was a discrepancy between the clinical impression (pre-biopsy) and the final histopathological diagnosis. In these instances, providers most commonly attributed the lesions to be either benign vascular tumors ($n = 11$) such as pyogenic granulomas and hemangiomas, or Spitz nevi ($n = 5$). Of the patients with a discrepancy between the clinical impression and final diagnosis, the median time between first physician evaluation and diagnostic biopsy was 1.8 months (0–126 months). Eight of these patients (26.7%) developed metastases. However, there was no statistically significant difference in overall outcomes, including metastasis, recurrence or mortality when compared to those without this discrepancy.

Fifty-eight (78.4%) referred cases subsequently underwent surgical treatment, either lesion re-excision with wider margins or lymph node dissection (LND). Of the 36 frozen specimens reviewed in our cohort, seven (19.4%) were initially reported to have negative margins (either the lesion itself or sentinel node), but were later found to have disease involvement on permanent pathology. Five of them required LND, one required re-excision without recurrence.

Metastases were documented in 22 (20.2%) cases, of which 19 occurred in the regional lymph nodes, and three were distant metastases. Metastasis was most common in patients with MM ($n = 19$), followed by SCC ($n = 1$), sebaceous cell carcinoma ($n = 1$) and hidradenocarcinoma ($n = 1$). Most patients with metastatic disease had their original lesion on the extremities ($n = 10$, 45.5%), although anatomic location was not found to be significantly associated with metastasis. Patient age was not found to be a significant risk factor for recurrence, advanced stage of disease, metastasis or mortality when stratified by age groups (0–4; 5–9; 10–14; 15–17 years).

Among patients with metastatic disease, there was an average of a 5.4 month delay from initial evaluation to diagnostic biopsy. This delay was not found to be a statistically significant risk factor for metastasis or disease recurrence. In eight (36.4%) patients with metastases, the initial clinical impression was a benign lesion. Five patients (22.7%), four with MM and one with hidradenocarcinoma, who developed metastatic disease, succumbed to their disease. Metastasis was significantly associated with mortality (p<.0001, Figure 1(a)).

Overall, seven (6.4%) lesions recurred after definitive surgical treatment, of which four were MM, one sebaceous cell carcinoma, one hidradenocarcinoma and one DFSPs. Anatomic location of the lesion was not found to be associated with recurrence. All had undergone wide local excision, except for one who had undergone Mohs micrographic surgery. Surgical treatment type was also not found to be predictive of recurrence. Of the patients with disease recurrence, four succumbed to their disease (three MM and one hidradenocarcinoma). Recurrence was found to be a statistically significant risk factor for mortality (p<.0001, HR: 46.2; Figure 1(b)).

Discussion

This review identifies the commonly encountered cutaneous malignancies among pediatric patients and highlights the risk, albeit rare, for metastases and disease-specific death in this cohort

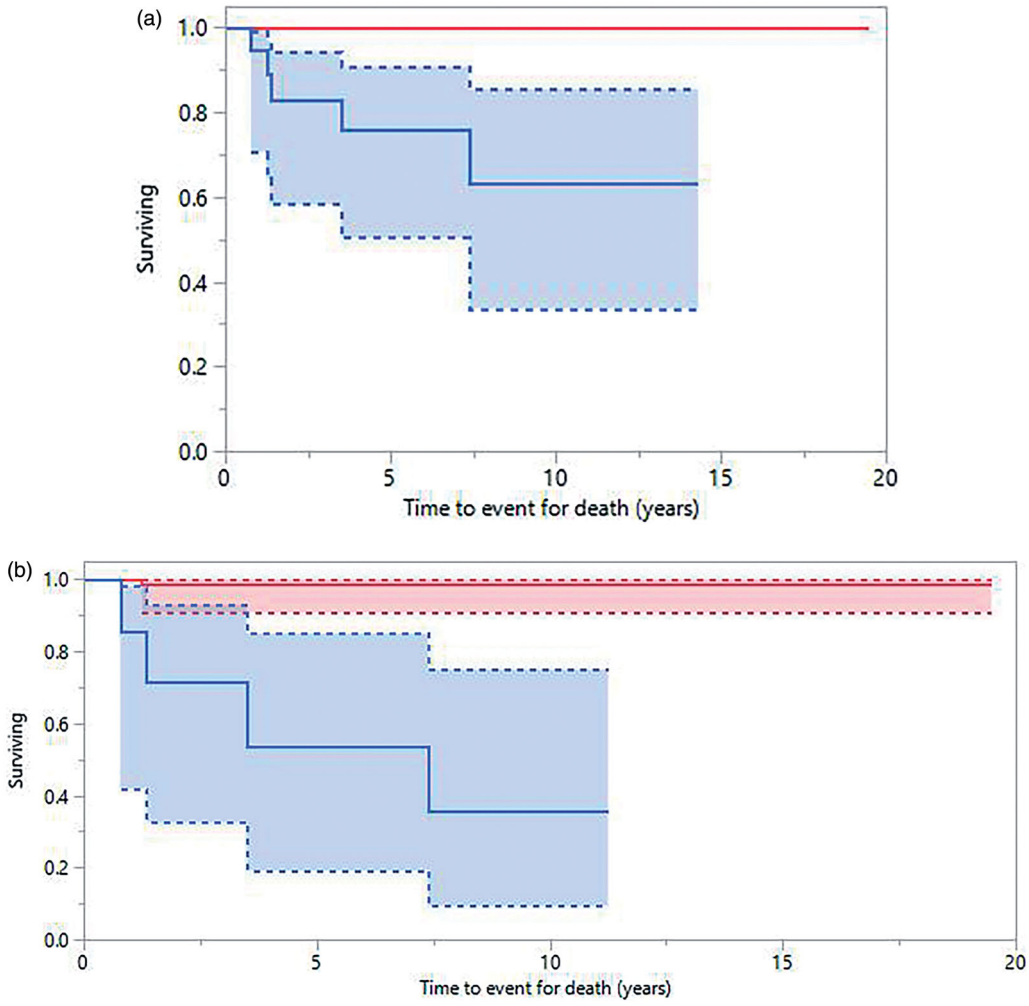

Figure 1. Kaplan–Meier's survival curves. (a) Kaplan–Meier's survival curve in which the death was considered the end point. Blue line represents patients with a metastatic lesion whereas the red line represents the patients without metastatic lesion. (b) Kaplan–Meier's survival curve in which the death was considered the end point. Blue line represents patients with recurrent lesion whereas the red line represents the patients without a recurrent lesion.

[1–15]. The most common pediatric cutaneous malignancy in our cohort was MM, followed by BCC and DFSP, respectively. Only 22.2% of patients in our series presented with a known risk factor, highlighting that the majority of lesions in this series were not associated with known risk factors.

A diagnosis of MM conferred 12.4-times-higher odds of developing metastasis when compared to other tumors. Every 1-mm increase in Breslow's thickness correlated with 1.6-times greater odds of developing metastasis, which was consistent with previous studies [12,16]. Additionally, when stratifying patients by age groups, patient age was not found to have a significant association with disease recurrence, advanced stage of disease, metastases or death. These findings are comparable to findings by others [1,2].

It is important to note that although a degree of statistical significance was lacking for several seemingly contributory variables within our study, practitioners are encouraged to have a heightened sense of awareness when evaluating pediatric skin lesions, particularly when risk factors are present [1,2,4,5,11,12]. This is particularly important since multiple prior studies have demonstrated that diagnostic unfamiliarity with pediatric cutaneous malignancies exists among providers [1–15]. Additionally, 27% of the referred patients were advised to monitor the lesion without biopsy. While these factors did not contribute to statistically significant negative outcomes in our series, our study sample size may not have sufficient power to show such significance.

Further, 27.5% of cases had discrepancies in the original clinical impression when compared to the final diagnosis. In these instances, providers most commonly attributed the lesions to be either benign vascular tumors or Spitz nevi. These results emphasize the importance of developing a broad differential diagnosis when clinically evaluating patients and the inherent challenges associated with timely and accurate diagnosis of cutaneous malignancies in children [4,12]. As such, the modified ABCD detection criteria in children should be followed for MM (amelanotic; bleeding; bump; color uniformity; de novo; any diameter) [1–5,11,12].

An additional consideration for timely diagnosis and treatment is accurate dermatopathology diagnoses. In 5.4% of the lesions referred to our institution, there was a discrepancy between the outside and our histopathology diagnosis. Furthermore, 19.4% of the frozen pathology specimens were later found to have positive margin involvement on permanent sectioning. While none of these patients developed recurrences, six patients ultimately required additional surgical intervention. These findings highlight the importance of involving expert dermatopathologists, and encourage close collaboration/communication with them while establishing a diagnosis [1–7,9–12,14,15,17,18].

While recommendations for performing biopsies on pediatric skin lesions remain unclear, experts suggest that diagnostic biopsies should be selectively reserved for lesions which exhibit a particularly unusual history or present with recognizably concerning features [12,14,15]. Despite limited evidence-based recommendations, if referral to a pediatric dermatologist is not feasible, the authors suggest performing a biopsy to rule out malignancy [12,14,15].

This study is not without limitations. Its retrospective nature may be associated with potential selection bias of the subjects with atypical lesions or more advanced disease. Second, as a referral center for MM, nearly three-quarters of the patients in this study received their first clinical evaluation and diagnostic biopsy at another center. However, all outside records and pathology reports were reviewed for diagnostic accuracy [1]. Additionally, although our inclusion criteria were well-established, it is possible that the overall number of pediatric skin malignancies was underrepresented if patients or parents/guardians elected not to pursue biopsy, or if a biopsy was never recommended. Furthermore, although delay from the time of initial lesion recognition to first diagnostic biopsy or surgical treatment did not negatively impact any outcome measure on statistical analysis, it is possible that our study may have been underpowered to accurately demonstrate such an association [1–15].

Pediatric primary cutaneous malignancies remain uncommon and unique from the adult population. Although diagnostic and treatment delays did not impact patient outcomes, this study highlights the intrinsic challenges associated with timely and accurate diagnosis of cutaneous malignancies in children.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

[1] 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(21):4735–4741.

[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(11):1363–1368.

[3] Ceballos PI, Ruiz-Maldonado R, Mihm MC. Melanoma in children. N Engl J Med. 1995;332(10):656–662.

[4] Huang JT, Coughlin CC, Hawryluk EB, et al. Risk factors and outcomes of nonmelanoma skin cancer in children and young adults. J Pediatr. 2019;211:152–158.

[5] Khosravi H, Schmidt B, Huang JT. Characteristics and outcomes of nonmelanoma skin cancer (NMSC) in children and young adults. J Am Acad Dermatol. 2015;73(5): 785–790.

[6] Dean PH, Bucevska M, Strahlendorf C, et al. Pediatric melanoma: a 35-year population-based review. Plast Reconstr Surg Glob Open. 2017;5(3):1–8.

[7] Hamre MR, Chuba P, Bakhshi S, et al. Cutaneous melanoma in childhood and adolescence. Pediatr Hematol Oncol. 2002;19(5):309–317.

[8] Friedman EB, Scolyer RA, Thompson JF. Management of pigmented skin lesions in childhood and adolescence. Aust J Gen Pract. 2019;48(8):539–544.

[9] Kalani N, Guidry JA, Farahi JM, et al. Pediatric melanoma: characterizing 256 cases from the Colorado Central Cancer Registry. Pediatr Dermatol. 2019;36(2):219–222.

[10] Waldman RA, Grant-Kels JM. Malignant skin tumors: kids are not just little people. Clin Dermatol. 2017;35(6): 517–529.

[11] Cordoro KM, Gupta D, Frieden IJ, et al. Pediatric melanoma: results of a large cohort study and proposal for modified ABCD detection criteria for children. J Am Acad Dermatol. 2013;68(6):913–925.

[12] Mitkov M, Chrest M, Diehl NN, et al. Pediatric melanomas often mimic benign skin lesions: a retrospective study. J Am Acad Dermatol. 2016;75(4):706–711.e4.

[13] Lowe GC, Brewer JD, Peters MS, et al. Incidence of melanoma in children: a population-based study in Olmsted County, Minnesota. Pediatr Dermatol. 2015;32(5):618–620.

[14] Cypel TKS, Somers GR, Pope E, et al. Predisposing factors and outcomes of malignant skin tumors in children. Plast Reconstr Surg. 2010;126(2):508–514.

[15] Al-Himdani S, Naderi N, Whitaker IS, et al. An 18-year study of malignant melanoma in childhood and adolescence. Plast Reconstr Surg Glob Open. 2019;7(8):1–6.

[16] Averbook BJ, Lee SJ, Delman KA, et al. Pediatric melanoma: analysis of an international registry. Cancer. 2013;119(22): 4012–4019.

[17] Elder DE, Piepkorn MW, Barnhill RL, et al. Pathologist characteristics associated with accuracy and reproducibility of melanocytic skin lesion interpretation. J Am Acad Dermatol. 2018;79(1):52–59.e5.

[18] Geller BM, Frederick PD, Knezevich SR, et al. Pathologists' use of second opinions in interpretation of melanocytic cutaneous lesions: policies, practices, and perceptions. Dermatol Surg. 2018;44(2):177–185.