

Original Article

Clinical and pathological features of pediatric melanocytic skin tumors: A retrospective study

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Abstract

Objective: To examine the clinical characteristics of patients diagnosed with melanocytic neoplasms in childhood.

Methods: The study included patients diagnosed with malignant melanoma and Spitzoid melanocytic tumors who were followed up and treated in our clinic between 2000 and 2024. The patients' data were analyzed retrospectively.

Results: Of the 36 patients included in the study, 52.8% were female and 47.2% were male. The mean age of the patients was 115.69 ± 47.4 months (range, 24–193). According to the localization of lesions, the most frequent site was the extremities, with 58.3% (n = 21). Pathology results revealed that 38.9% of the patients (n=14) were diagnosed with Spitz nevus, 36.1% (n=13) with malignant melanoma, 19.4% (n=7) with Spitz melanocytoma, and 5.6% (n=2) with Spitzoid melanoma. According to our findings, malignant cases were observed in older age groups (p = 0.017) In 66.7% (n=10) of the patients diagnosed with malignant or Spitzoid melanoma, surgical treatment alone was sufficient. Five patients received adjuvant chemotherapy, BRAF inhibitors (dabrafenib, trametinib, and vemurafenib), and immune checkpoint inhibitors (nivolumab). Histopathological examination showed Clark levels ranging from 4 to 5 and Breslow thickness between 5 and 12 mm. Two patients developed relapse, and one patient had refractory disease. Relapse sites were the kidney and liver. The refractory case was a patient diagnosed with a lesion in the anal region with positive surgical margins. Molecular analysis revealed BRAF V600E positivity in three patients and negativity in 2 patients. The mean follow-up period was 77.25 ± 48.11 (3–168) months. Two of the 15 patients diagnosed with malignant tumors died. The mean survival rate was 86.7%.

Conclusion: Skin tumors in childhood remain rare and challenging cases. Advances in molecular studies may contribute to the diagnostic process.

Keywords: Childhood, skin tumors, melanoma, Spitz.

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INTRODUCTION

Malignant skin tumors in childhood are very rare. The most common malignant skin tumor is malignant melanoma, accounting for 1–3% of all childhood cancers (1). The incidence of malignant melanoma increases with age. Below the age of 10, they are seen equally in boys and girls, whereas above the age of 10, they are more common in girls (2). In childhood, they may demonstrate different clinical behaviors before and after puberty. Prepubertal melanomas are classified as congenital, infantile, and childhood melanomas. Postpubertal melanomas generally resemble adult-type melanomas. Sun exposure, congenital melanocytic nevi, and a family history of malignant melanoma can be considered major risk factors. In most malignant melanoma, alterations in CDKN2A, KIT, and BRAF V600E can be observed (3). In children, Breslow thickness at diagnosis has been found to be greater compared to adults, and this has been associated with poor prognosis (4,5). Spitzoid melanocytic tumors are those most frequently confused with malignant melanoma. These tumors include Spitz nevi, Spitz melanocytoma, and Spitzoid melanomas (6). Spitz nevi are common benign lesions in childhood. In both children and adults, Spitz nevi constitute 1–2% of surgically excised nevi (7). Spitz melanocytomas are considered borderline lesions between Spitz nevi and Spitzoid melanomas in terms of malignancy potential. Spitzoid melanomas are malignant tumors capable of metastasizing to regional lymph nodes.

In this study, we aimed to examine the follow-up outcomes of patients monitored and treated in our clinic with a diagnosis of malignant melanoma and Spitzoid melanocytic tumors.

MATERIALS AND METHODS

Ethics committee approval was obtained from the relevant hospital ethics committee under protocol number 2025/821/15-12. The study included patients diagnosed with melanocytic tumors and followed up and treated in our clinic between 2000 and 2024. Age at diagnosis (months), sex, tumor localization, surgical margin, Clark level, Breslow thickness, metastatic sites, treatment protocols, survival times, and pathology results were retrospectively analyzed from patient records. The study included pediatric patients aged 0–18 years at the time of diagnosis. This study was designed as a descriptive retrospective study. No inferential statistical analyses were performed, and the results are presented descriptively.

Statistical Analysis

Statistical analyses were performed using SPSS v. 29.0 (IBM Corp., Armonk, NY, USA). The participants' demographic characteristics, ages, and tumor localizations were determined using descriptive statistics. Data were expressed as mean \pm standard deviation and median (minimum–maximum) values. Categorical data were compared using the chi-square test. Statistical significance was set at $p < 0.05$.

RESULTS

Of the 36 patients included in the study, 52.8% ($n=19$) were female and 47.2% ($n=17$) were male. The mean age of the patients was 115.69 ± 47.4 (24–193) months. According to localization, the most frequent site was the extremities at 58.3% ($n = 21$). Head and neck involvement was observed in 27.8% ($n = 10$) of the patients, while trunk involvement was rarer at a rate of 13.9% ($n = 5$) (Table 1). Since most patients were referred to our clinic with postoperative pathology results, we did not

have full access to initial clinical findings. According to pathology results, 38.9% of the patients (n = 14) were diagnosed with Spitz nevus, 36.1% (n = 13) with malignant melanoma, 19.4% (n = 7) with Spitz melanocytoma, and 5.6% (n = 2) with Spitzoid melanoma. Patients diagnosed with Spitz melanocytoma and Spitzoid or malignant melanoma underwent secondary surgery for wide excision based on their pathology results.

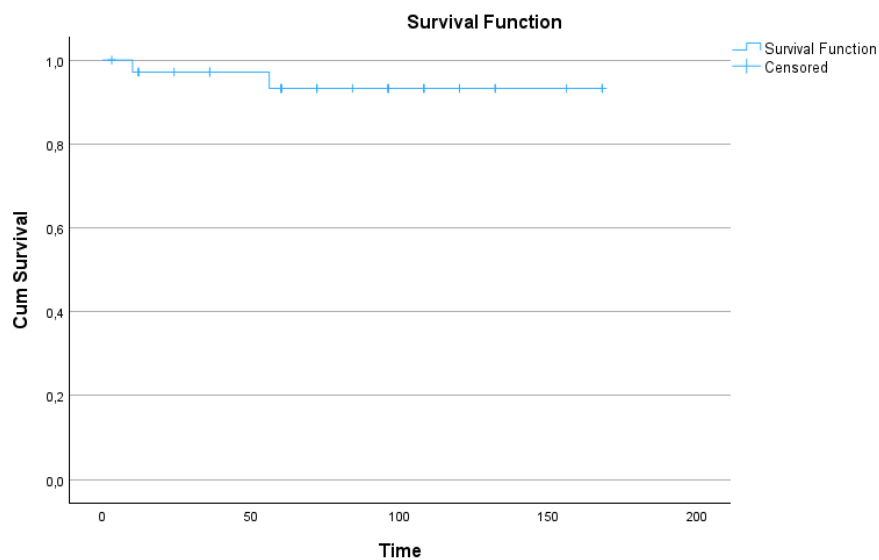
Table 1. Demographic characteristics of the patients

Characteristic	n=36 (%)
Age (months)	115.69 ± 47.4 (24–193)
Gender Female:	19 (52.8)
Male:	17 (47.2)
Diagnosis	
Spitz nevus	14 (38.9)
Spitz melanocytoma	7 (19.4)
Spitzoid melanoma	2 (5.6)
Malignant melanoma	13 (36.1)
Tumor Localization	
Head and neck	10 (27.8)
Trunk	5 (13.9)
Extremity	21 (58.3)

According to our findings, malignant cases occurred in older age groups, whereas Spitz melanocytomas were more common in younger age groups ($p = 0.017$). Regarding sex distribution, malignant melanoma and benign Spitz nevi were more frequent in girls, while atypical cases were significantly more common in boys. Breslow thickness measurements were available for 8 of the 13 patients diagnosed with malignant melanoma. Among these patients, 4 had a Breslow thickness of 1.5–4 mm and 4 had a thickness >4 mm. Both refractory or relapsed cases had a Breslow thickness >4 mm. One patient's result was unavailable. In 66.6% (n = 10) of the patients diagnosed with malignant or spitzoid melanoma, surgical treatment alone was sufficient. Five patients received adjuvant chemotherapy, interferon-alpha, BRAF inhibitors (dabrafenib, trametinib, and vemurafenib), and immune checkpoint inhibitors (nivolumab). Histopathological examination showed Clark levels ranging from 4 to 5 and Breslow thickness between 5 and 12 mm. Two patients experienced relapse, and one patient had refractory disease. The relapse sites were the kidney and liver. The refractory case was a patient diagnosed with a lesion in the anal region with positive surgical margins. This patient received nivolumab treatment but did not achieve a therapeutic response and died due to progressive disease. Molecular analysis showed BRAF V600E positivity in three patients and negativity in two patients (Table 2). The mean follow-up duration was 77.25 ± 48.11 months (range, 3–168 months). Among the 15 patients diagnosed with malignant tumors, two patients died, resulting in an overall survival rate of 86.7% (Figure 1).

Table 2. Characteristics of patients with malignant melanoma receiving post-surgical treatment

Age (months)	Sex	BRAF V600E	Localization	Clark level	Breslow thickness (mm)	Relapsed or refractory disease	Treatment	Final status
167	F	-	Head-neck	4	5	Absent	Interferon -alpha	In remission
53	F	-	Trunk	5	12	Present (refractory disease)	Nivolumab	Death
193	F	+	Head-neck			Present (kidney)	Chemotherapy, BRAF inhibitors	Death
163	F	+	Head-neck			Absent	BRAF inhibitors	In remission
189	M	-	Extremity	4	6	Present (liver)	Chemotherapy, checkpoint inhibitors	Ongoing treatment

**Figure 1.** Survival analysis of patients diagnosed with malignant skin tumors

DISCUSSION

In terms of differential features, we compared benign and atypical Spitzoid tumors with malignant or Spitzoid melanomas. Malignant melanoma in childhood is among the rare malignant tumors encountered in pediatric oncology practice. However, due to their risk of relapse and aggressive course, they require careful evaluation and a multidisciplinary approach. Malignant melanoma is often confused with benign lesions such as Spitz nevi. Childhood malignant melanoma shows no sex difference before adolescence, whereas they are more common in girls during adolescence. In terms of localization, they most frequently arise in the extremities (8). Head and neck localization

is considered a poor prognostic factor. It is known that Spitz nevi also occur more frequently in the extremities (9). In our study, the extremities represented the most common site of lesion localization. Spitz melanocytoma is evaluated as intermediate lesions between Spitz nevi and Spitzoid melanomas in terms of malignancy potential. According to the 2024 recommendations of the Children's Oncology Group, Spitz melanocytomas should be excised with a 1-3 mm margin (10). In our patients diagnosed with Spitz melanocytoma, secondary surgery was performed based on pathology results, and no relapses were observed in any case. Survival in malignant melanoma decreases with increasing age (11). Among our deceased patients, one was prepubertal and the other was postpubertal. Another prognostic factor is Breslow thickness greater than 1.5 mm (12). Among patients for whom Breslow thickness measurements were available, 50% had lesions thicker than 4 mm, and 2 of these patients experienced relapse. In children, malignant melanoma is generally diagnosed with greater thickness than in adults (13). This may be due to delayed diagnosis as a consequence of the rarity of the tumor. The use of molecular studies in differentiating Spitzoid tumors from malignant melanoma is increasing. Alterations such as HRAS mutations, BRAF mutations, and ALK fusions can be found in Spitzoid tumors, whereas malignant melanoma more frequently harbor BRAF or NRAS mutations (14,15). The most commonly detected alteration in malignant melanoma is the BRAF V600E mutation (16). Our study included patients from the year 2000 onward, and since these mutations were not routinely tested in our hospital at that time, data could not be obtained. BRAF V600E was detected in 3 of our patients. In one mutation-positive patient, a BRAF inhibitor and systemic chemotherapy were administered, but the patient showed progression and died. Spitz nevi are benign lesions that may be mistaken for malignant melanoma. They can cause concern among families and clinicians. They grow rapidly and then become stable. They may appear in a variety of colors, including pink, brown, black, and red (17,18). Among our cases in which malignancy was suspected and surgery or biopsy was performed, the most common pathology result was Spitz nevus. Spitz tumors and Spitzoid melanomas are more frequently observed at younger ages (19). Consistent with this finding, our study revealed that malignant melanoma occurred predominantly in older age groups, whereas benign and atypical tumors were more commonly observed in younger patients. Early diagnosis of malignant melanoma, negative tumor cells at surgical margins, Clark stage, increased Breslow thickness, and age are important prognostic factors (20). In our patient who developed melanoma in the anal region, clear surgical margins could not be achieved due to the tumor site, and despite repeated surgeries, survival was not improved. In the remaining two patients with relapse, metastasis to distant organs such as the kidney and liver demonstrated the importance of close monitoring not only in terms of tumor localization but also for systemic metastasis.

Limitations: This study has certain limitations. Its retrospective design, relatively small sample size, and limited follow-up restrict the generalizability of our findings. Furthermore, the lack of molecular analysis prevented confirmation of possible genetic alterations in our cases. Despite these limitations, our study contributes to the understanding of pediatric melanocytic tumors and highlights the importance of careful clinicopathological correlation.

CONCLUSION

Spitzoid melanocytic tumors and malignant melanoma in children remain diagnostically challenging entities with significant clinical implications. Accurate diagnosis requires a multidisciplinary approach, including clinical features, histopathology, immunohistochemistry, and, when possible, molecular testing.

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