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Comparison of Clinicopathological Findings of Spitz Nevus in Pediatric and Adult Patients

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What is already known on this topic?

- *A Spitz nevus is a benign skin tumor that is diagnostically challenging because of various histological subtypes.*

What this study adds on this topic?

- *This study reports the most common subtypes and localizations of Spitz nevus, both in adult and in pediatric patients.*

ABSTRACT

Objective: The aim of this study is to evaluate the demographic characteristics of patients diagnosed with Spitz nevus and to investigate potential distinctions in clinicopathological findings of Spitz nevi in relation to age and location of the lesion.

Materials and Methods: Clinical and histopathological findings of 32 patients who were diagnosed with Spitz nevus from our archives between 2010 and 2020 were obtained and evaluated retrospectively.

Results: A total of 32 patients were included, of whom 19 (59.4%) were female and 15 (40.6%) were under the age of 18 years. Most of the lesions (14, 43.7%) were located on the upper extremity, followed by the lower extremity and the head and neck. The most common histological subtype was the compound variant. In the pediatric age group, the majority of the lesions were located on the upper extremity, and the most common histological subtypes were pigmented and compound variant. In adults, the lesions were chiefly located on the lower extremitiy and the most common histological subtype was the desmoplastic variant.

Conclusion: In this study, it was found that the location of the lesions and histopathological subtypes of Spitz nevi may differ in children and adults. Further studies incorporating genetic data and involving larger cohorts of patients are needed in order to determine these differences between age groups more clearly. The small sample size is the main limitation of this study.

Keywords: Acral nevus, desmoplastic nevus, Spitz nevus, pagetoid features

INTRODUCTION

Spitz nevus is a benign neoplasm of epithelioid and/or spindle cells that may appear both in childhood and adulthood. Although these lesions have a benign nature, their clinical and histopathological features can pose challenges in distinguishing them from other benign or malignant skin tumors. Spitz nevus has many histopathological variants, including pigmented spindle cell nevus of Reed, desmoplastic, angiomatoid, halo Spitz, pagetoid, etc. Herein, we describe 32 cases of Spitz nevi and present their clinical and histopathologic characteristics to achieve a clinicopathological correlation.

MATERIALS AND METHODS

In this study, clinical data and histopathological findings of 32 patients with Spitz nevus or Reed nevus were retrieved from our institutional archives between 2010 and 2020 and evaluated retrospectively. The detailed histopathologic classification was made through the analysis of hematoxylin and eosin-stained slides, which had been considered representative

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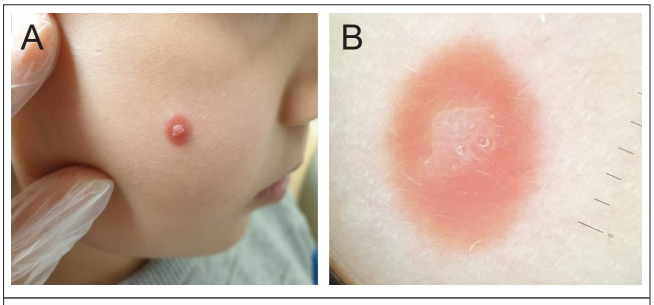

Figure 1. A pink nodular lesion on the right cheek of a 5-year-old girl with a whitish papular lesion in the middle.

of the lesion by the referring pathologists. Clinical data and dermoscopic images were obtained from the medical records in the dermatology department, and none of the collected lesions had been known to recur or metastasize. Some of the representative images of the lesions are shown in Figures 1-3. Informed consent was obtained from all patients. The age of the patients was classified as 18< and >18 years to compare pediatric and adult patients. The lesion location was classified into 3 groups, including head and neck, upper extremity, and lower extremity. No patients with trunk lesions were present in our cohort. The ethical approval was obtained from the Ethics Committee of Cerrahpaşa Medical Faculty (09/11/2020-157200).

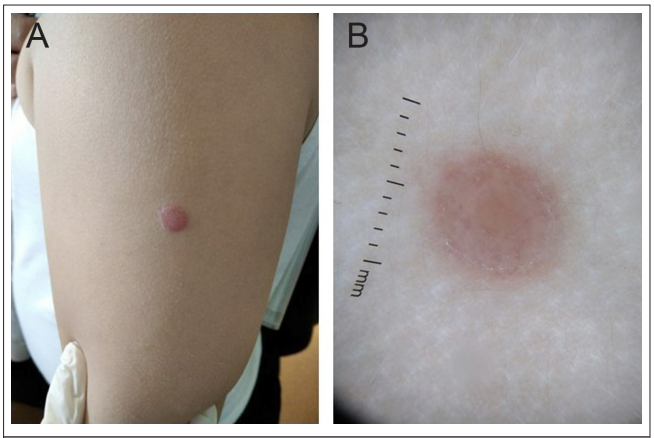

Figure 2. A pink nodular lesion on the lateral aspect of the left arm of a 10-year-old boy.

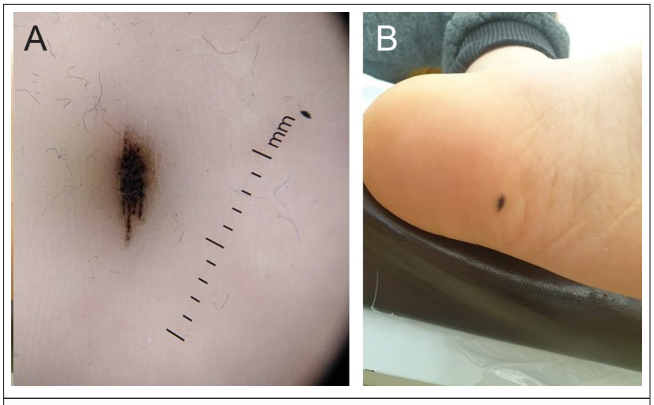

Figure 3. A black flat lesion on the left plantar surface.

Statistical Analysis

Statistical analysis was performed in the Statistical Package for Social Science Statistics software, version 21 (IBM Corp.; Armonk, NY, USA). Normal *Q–Q* controllable and detailed analysis (Shapiro–Wilk test) were examined. Results are median for non-distributed continuous as mean ± SD for normally continuous ranges, 25-75. The Mann–Whitney *U*-test was applied for comparisons between updates that were not normally distributed. Fisher's exact test (Fisher's exact test) was used for categorical comparisons. Results were considered statistically significant when the *P*-value < .05.

RESULTS

The demographic data of the patients are shown in Table 1. The total number of patients was 32, with 13 males (40.6%) and 19 females (59.4%). The mean age at diagnosis was 21.8 ± 14.9 (minimum–maximum: 1-53, IQR: 10-34.75). Of 32 cases, while 15 (47%) patients were younger than 18 years, 10 (31%) were under the age of 12 years. In 14 patients (43.7%), the lesion was located in the upper extremity, in 10 patients (31.2%) the lesion was located in the lower extremity, and in 8 patients (25%), the lesion was located on the head and neck. Histologically, among 32 cases, 9 were desmoplastic (28.1%); 10 were compound (31.3%); 7 were pigmented (21.9%); 2 were pagetoid (6.2%); 1 was intradermal (3.1%); 1 was junctional (3.1%); 1 was acral (3.1%); and 1 was a halo (3.1%) subtype (Figure 4-6). The location of each histological subtype is listed in Table 2. In patients younger than 18 years old, the lesions were mostly located on the upper extremity, and the most common histological subtypes were compound (n = 5, 33%) and pigmented (n = 5, 33%) variants. In patients older than 18 years old, the lesions were mostly located on the lower extremity, and the most common histological subtype was the desmoplastic subtype (n = 7, 41%), followed by the compound subtype (n = 5, 29%) (Table 3).

Table 1. Clinical and Histological Data of the Patients

Characteristics	**n = 32 (%)**
Sex, n (%)	
Female	19 (59.4)
Male	13 (40.6)
Age, years*	21.8 ± 14.9 (10-34.75)*
Female	26.8 ± 15.3 (13-40)*
Male	14.6 ± 11.2 (6-23.5)*
Localization, n (%)	
Upper extremity	14 (43.7)
Lower extremity	10 (31.2)
Head and neck	8 (25.0)
Histological subtype, n (%)	
Pigmented	7 (21.9)
Pagetoid	2 (6.3)
Desmoplastic	9 (28.1)
Compound	10 (31.3)
Junctional	1 (3.1)
Halo	1 (3.1)
Intradermal	1 (3.1)
Acral	1 (3.1)

*Values are presented as mean ± SD (IQR).

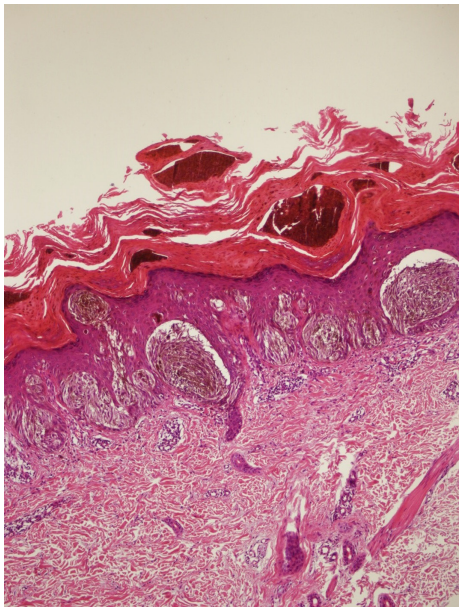

Figure 4. Intraepidermal Spitz nevus. Melanocytic nests are perpendicular to the epidermis (H&E, ´400).

DISCUSSION

Spitz nevus is a rare, benign proliferation of spindle and epithelioid melanocytes. It was first described by Sophie Spitz in 1948 as "juvenile melanoma," and afterward, it was thought to be restricted to the pediatric population.[1,2] Although they are usually seen in the pediatric age group, they can also be seen in adults.

Spitz nevi are usually characterized by solitary, red-reddish-brown, dome-shaped, papular, or nodular lesions but can sometimes be seen as multiple, hyperpigmented, and agminated lesions. Of the 30 patients in our study, clinically 23 (71.9%) of the lesions were non-pigmented and 9 (28.1%) were pigmented Spitz nevi. The diagnosis of Spitz nevi might be difficult both clinically and histologically. In the recent guidelines

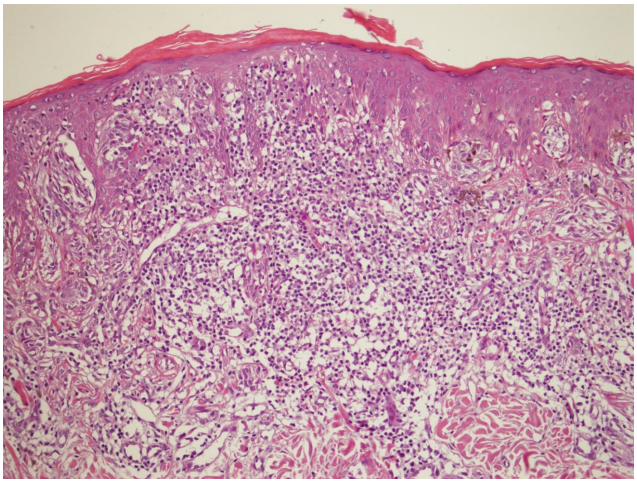

Figure 5. Spitz's nevus with inflammatory cell infiltration of its whole thickness (H&E, ´200).

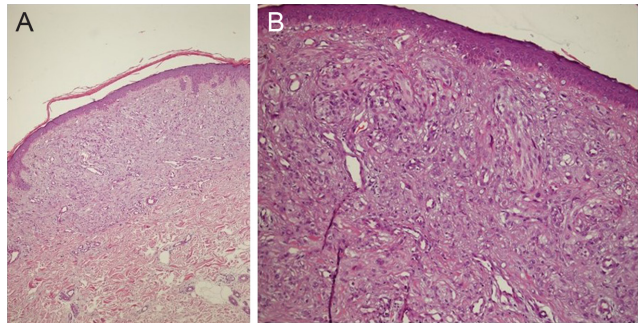

Figure 6. (A) Desmoplastic Spitz nevus. The epidermal and dermal proliferation of large epitheloid melanocytes within a desmoplastic stroma. (B) Spindled and epithelioid melanocytes are arranged as fascicles or single units between sclerotic collagen bundles (H&E, ´200).

of the International Dermoscopy Society published by Lallas et al,[3] it is recommended to manage the spitzoid lesions according to the patient's age, tumoral symmetry, nodularity, and dermoscopic patterns, and they offered to excise Spitz nevi or to follow up closely in patients over 12 years of age in this guideline. It was also recommended to excise the nodular and dermoscopically asymmetrical lesions. In our study, nodularity was the most important criterion for the excision of the lesion in patients, especially in the pediatric age group of those under 12 years of age.

Spitz nevi were reported to be more common in the first 2 decades of life.[4] In our study, most of the patients were older than 18 years (n = 17, 53%), and the mean age at diagnosis was 21.8 ± 14.9. In this study, 15 (47%) patients were in their first 2 decades, and most of the patients were adults. As reported in previous studies and in this study, we think Spitz nevi should not be considered restricted to childhood.

Spitz nevus is reported to be slightly more common in females.[4] In our study, similarly, most of the patients were female. In a previous study, which was conducted by Ersoy et al,[4] 30 patients with a diagnosis of Spitz nevus were evaluated, and the average age of diagnosis was 15.5 years, 56.7% of the patients were female, and this rate was similar to our study. In another retrospective study by Lott et al,[5] 65% of the patients were women among those with a diagnosis of Spitz nevus.

The localization of Spitz nevus may vary according to age. In previous studies, Spitz nevi were found to be more common on the face and ear in infants and children, while in adults,[6] Spitz nevi were commonly seen on the thighs, upper extremities, and trunk. In our study, in general, lesions were mostly located on the upper extremity, but as we compare the 2 age groups, in the pediatric age group, lesions were mostly located on the upper extremity (n = 9, 60%), followed by the ead and neck (n = 5, 33%), and in adults, lesions were mostly located on the lower extremity (47%), followed by the upper extremity. In a study conducted by Weedon and Little,[7] the most common location reported was the back. In the studies of Ersoy et al,[4] Lott et al,[5] and Scalvenzi et al,[8] the most common location was the lower extremity. In our study, there were no trunk lesions.

Histopathological criteria are important in distinguishing these nevi from other melanocytic or nonmelanocytic, benign,

Table 2. Localization of Spitz Nevi According to Histological Subtypes

		Localizations			
		Upper Extremity	**Lower Extremity**	**Head and Neck**	**Total**
Sub-type	Pigmented	3	3	1	7
		42.9%	42.9%	14.3%	100.0%
	Pagetoid	1	1	0	2
		50.0%	50.0%	0.0%	100.0%
	Desmoplastic	2	3	4	9
		22.2%	33.3%	444%	100.0%
	Compound	6	1	3	10
		60.0%	10.0%	30.0%	100.0%
	Junctional	0	1	0	1
		0.0%	100.0%	0.0%	100.0%
	Halo	1	0	0	1
		100.0%	0.0%	0.0%	100.0%
	Intradermal	1	0	0	1
		100.0%	0.0%	0.0%	100.0%
	Acral	0	1	0	1
		0.0%	100.0%	0.0%	100.0%
Total		14	10	8	32
		43.8%	31.3%	25.0%	100.0%

Table 3. Comparison of the Location and Histologic Subtypes of Spitz Nevi Between Children and Adults

	Children (n = 15)	**Adults (n = 17)**	***P****
Localization, n (%)			.123
Upper extremity	8 (53.3)	6 (35.3)	
Lower extremity	2 (13.3)	8 (47.1)	
Head and neck	5 (33.3)	3 (17.6)	
Histologic subtype, n (%)			.277
Pigmented	5 (33.3)	2 (11.8)	
Pagetoid	1 (6.7)	1 (5.9)	
Desmoplastic	2 (13.3)	7 (41.2)	
Compound	5 (33.3)	5 (29.4)	
Junctional	1 (6.7)	0 (0)	
Halo	0 (0)	1 (5.9)	
Intradermal	1 (6.7)	0 (0)	
Acral	0 (0)	1 (5.9)	

*P <.05 was considered statistically significant.

and malignant lesions, and the age of the patient may also affect the clinician's approach to spitzoid lesions. The most common histopathological subtype was the compound subtype, followed by the desmoplastic subtype and the pigmented Spitz nevus, respectively. As we compare the anatomical site predilections and histological subtype, compound Spitz nevi were more common on the upper extremity, and the desmoplastic Spitz nevi were more common in the head and neck, besides the upper extremity. The effect of ultraviolet light on desmoplastic skin lesions has been previously reported in patients with desmoplastic melanoma, and severe ultraviolet-induced mutations have been reported in these lesions.[9-11] In our study, we think that chronic sun damage may also play a role in the development of desmoplastic Spitz nevi since they are more common in adult patients and relatively more frequent in sun-exposed areas such as the head and face. In the study conducted by Ersoy et al,[4] the most common clinical type was pigmented Spitz nevus (70.4%), and the most common subtype was compound-type Spitz nevus (67.9%) histopathologically. In a study by Ferrara et al,[12] 83 cases with Spitz nevi were evaluated, and the most common clinical subtype was found to be pigmented Spitz nevus. In another study conducted by Berlingeri-Ramos et al[13] clinicopathological characteristics of 130 Spitz nevi, were evaluated, and the junctional subtype (42%) was found to be the most common histopathological type followed by

Table 4. Included Studies Evaluating the Characteristics of Spitz Nevus

	Median Age at Diagnosis (Years)	**Gender Distribution (F : M)**	**Location (Most Common)**	**Clinical Type (Most Common)**	**Histopathological Type (Most Common)**
Ersoy et al[4]	15.5 [3-49]	1.3 : 1	Lower extremity	Pigmented	Compound
Lott et al[5]	22 [1-61]	1.8 : 1	Lower extremity	–	Compound
Scalvenzi et al[8]	20.9 [1-58]	2.3 : 1	Lower and upper extremity	Pigmented	–
Weedon and Little[7]	[0.5-56]	1.3 : 1	Trunk	–	–
Ramos et al[13]	18.8 [0.5-78]	1.6 : 1	Lower extremity	Pigmented	Junctional
Requena et al[14]	21.3 [2-69]	1.7 : 1	Lower extremity	Pigmented	Compound
Cesinaro et al[15]	–	1.8 : 1	Lower extremity	–	Compound

compound subtype (38%) and the dermal subtype (20%). In a study of 349 cases by Requena et al,[14] the compound subtype (46%) was found to be the most common subtype, similar to our study, and junctional Spitz nevus (33%) constituted the second most common histopathological subtype. In a clinicopathologic study by Cesinaro et al,[15] 247 cases were included, and the most common subtype was a compound type. The included articles and results are summarized in Table 4. The limitations of our study include the limited number of patients and adjunctive genetic testings and the fact that it was a retrospective study.

Spitz nevi are rare benign melanocytic proliferations that can occur in all age groups. It should be kept in mind that Spitz nevi may have different appearances, and they are differentially diagnosed with many benign or malignant skin lesions based on their clinical appearance. They may also present with different histological involvement in age-compatible localizations. For sure, other factors, such as genetic mutations or other exogenous factors, may affect these results, and they should be investigated in a larger patient series.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by Ethics committee of Cerrahpaşa Medical Faculty (Approval number: 157200, date: 09/11/2020).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – T.K.U., S.N.Y.; Design – T.K.U., S.N.Y, A.M.Ö., B.E.; Supervision – T.K.U., S.N.Y, B.E.; Resources – T.K.U., S.N.Y, A.M.Ö., A.Ö.; Materials – T.K.U., S.N.Y, A.M.Ö.; Data Collection and/or Processing – T.K.U., S.N.Y, A.M.Ö.; Analysis and/or Interpretation –T.K.U., S.N.Y, A.Ö.; Literature Search –T.K.U., S.N.Y., A.Ö.; Writing – T.K.U., S.N.Y.; Critical Review – T.K.U. B.E.

Declaration of Interests: The authors have no conflict of interest to declare.

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