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Clinical and Histopathology Features of Spitz Nevus: In 22 Cases

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Abstract

Background: Spitz Nevus is an infrequent acquired melanocytic nevus. There is still a challenge for dermatopathologists in distinguishing spitz nevus from malignant melanoma particularly in adults since there is no immunohistochemistry or molecular markers which differentiate Spitz Nevus from melanoma.
Objectives: The aim of this study is to make clear what clinico-histopathological features of Spitz Nevus are in order to reduce malpractice due to misdiagnosis.
Methods: In the present study, a series of twenty two patients have been reviewed who were diagnosed with Spitz Nevous based on proved histopathology features between the years 2009 - 2013. The patients were evaluated for demographic parameters like age, sex, clinical differential diagnosis, cutaneous location of tumor, tumor diameter, subtype, symmetry, maturation, upper clefting of melanocytic nest, shoulder phenomena, epidermal hyperplasia, type, kamino body, mitotic rate , inflammatory infiltration, pagetoid spread and regression.
Results: In our study, 45% of patients were younger than 10 years old. The average age of patients was 14 ± 11.37. Male to female ratio was 1.44. The commonest location was head and neck. Spitz nevus was the first clinical differential diagnosis in 20% of patients. The commonest variant type was conventional type and then polypoid and desmoplastic types. The mean size of nevi was 0.81 ± 0.59 mm. About 59% of nevi shows epithelioid cytologic features. Other histologic parameters from the most to the least frequency were symmetry (100%), maturation (100%), epidermal hyperplasia (77.3%), kamino body (68.2%), subtype (compound 68%), mitotic rate (63.6%), clefting (59%), inflammatory infiltration (54.5%), pagetoid spread (18.2%), shoulder (37.5%) and regression (9.1%).
Conclusions: We tried to hifhlight some clinical and histopathological features which are distinguishing Spitz nevus from other melanocytic nevi even malignant melanoma.

Keywords: Spitz Nevus, Clinical Findings, Histopathologic Findings

1. Background

Spitz nevus (Epithelioid and spindle-cell nevus) is an uncommon, benign, melanocytic nevus that is usually acquired and has histologic features that overlap with those of melanoma. Spitz nevi were previously diagnosed as melanomas due to their similar appearance under a microscope, until it was found that they did not show malignant behavior (1, 2). They tend to grow very rapidly, reaching a size of approximately 1 cm within 6 months and thereafter remaining static, which may be worrisome to patients. These lesions are more common in the younger population, with 70% of cases diagnosed during the first two decades of life. Although both sexes are affected equally, fair skinned individuals are most frequently affected. The cause of the Spitz nevus is currently unknown (3). Some cases of Spitz nevi have a unique aberration of genes on chromosome 11p which is not observed in melanomas. On physical examination, the Spitz nevus appears as a symmetric, well-circumscribed, smooth-surfaced or warty, firm, < 1 cm, dome-shaped papule or nodule. The Spitz nevus is usually a solitary lesion but may rarely be in clusters or present as eruptive widespread lesions. Spitz nevi are uniform in color and may be pink, red, red-brown, tan, blue-black, or even non-pigmented. They are most commonly located on the face, neck, and legs, although the upper extremities and trunk may be affected. Palms, soles, and mucous membranes are usually spared. A biopsy should be performed to determine malignant potential. However still, most histopathological criteria remain poorly predictive in cases that overlap with melanoma (4). There are several histologic variants of spitz nevi like compound, junctional and intradermal spitz nevi. Microscopic appearance of spitz nevus is very alternative but really composed of clusters (nests) and bundles (fascicles) of epithelioid and/or spindle-shaped melanocytes with neuclear enlargement at the dermo-epidermal junction and/or in the der-

mis associated with artifactual clefts around intraepidermal nests. Also, there is epidermal hyperplasia and hypergranulosis. Eosinophilic (Kamino) bodies may be seen in the superficial dermis. They rarely contain cytoplasmic melanin pigment. Maturation of cells within deeper parts of the lesions (cells atrophy and become smaller) and splay between collagen bundles (5). Occasional mitotic illustration may be seen, but are usually located in the superficial dermal component (2, 6, 7) and intradermal pagetoid melanocytes in the central portion of the lesion which is frequent.

2. Objectives

The current study aims to make clear some important clinical and histopathological features which differentiate Spitz nevus from other melanocytic nevi.

3. Methods

This is a descriptive and retrospective study of the surgical specimens from 22 patients with a diagnosis of Spitz nevus. The study was conducted at the pathological anatomy service of the Razi hospital; Tehran Medical University in 2009 to 2013. All patients signed concept form and they were given ethical approval for patient privacy.

Who participated in this study? Demographic and clinical data were obtained from patients' histories. Cases were excluded from the study when their histological preparations did not allow analysis and had no paraffin blocks or had no proper clinical history. The cases whose historical preparations did not allow analysis, or had no paraffin or proper clinical history were excluded from the study. Clinical variables were studied through gathering information from medical charts about the services of the hospital. We prepared a questionnaire for each patient with the following variables: patient age at diagnosis; gender, size of nevus (in millimeters), localization of the lesion, clinical diagnosis and clinical evolution.

Histological analysis was based on the classic histopathological criteria which are considered for classic Spitz nevus like lesions symmetry, epidermal hyperplasia, Kamino corpuscles, pagetoid dissemination, and dermal component maturation, presence of mitoses, clefting, inflammatory infiltration, pagetoid spread, shoulder and regression. Slides with 5 μm sections were prepared from paraffin blocks then stained with Hematoxylin and Eosin. All histological preparations were evaluated by two dermatopathologist. Cohen's Kappa value (inter-rater agreement) between two observers was 0.89 which is generally satisfactory. Diagnosis of spitz nevus has been confirmed by histopathological parameters like epidermal hyperplasia and ulceration, Kamino corpuscles, pagetoid dissemination, dermal component maturation, presence of mitoses, clefting, inflammatory infiltration, pagetoid spread, and shoulder and regression. Statistical analysis was carried out through SPSS software (version 16.0). Mean and standard deviation were quantitative data applied in this study. The amount of P-value was calculated less than 0.005 which indicated statistical significance.

4. Results

Epidemiological and demographic data are shown in Figures 1 and 2, and histopathologic criteria are shown in Figure 3.

Twenty patients diagnosed with Spitz nevus were included in current study. The age range of patients was 1.5 to 46 years old. Our study shows about 45% of patients were younger than 10 years old. The mean age of all patients was 14 $\pm$ 11.37 that for men was 9.96 $\pm$ 9 and for women was 20 $\pm$ 12.24 (P = 0.369). Male to female ratio was 1.44. The commonest locations were head and neck (54.5%), (Figure 1).

Figure 1. Distribution of Spitz Nevus Location

The first differential diagnosis for about 20% of patients was spitz nevus. Clinical differential diagnosis is performed for about 59.1% spitz nevus while it is not done for about 40.9% of them. The largest diameter of nevi was 25 mm and the smallest was 3 mm.The mean size of nevi was 0.81 $\pm$ 0.59 mm. The histologic types of nevi were compound, dermal and epidermal (Figure 2). Compound type was common in trunk and in men (P < 0.193), dermal type was common in trunk and in women (P < 0.220), epidermal type was common in trunk, lower extremity and 100% in men (P < 0.00).

Intraepidermal, hyalanized, reed, pagetoid, angiomatoid, tubular, plexiform, hallo, dysplastic and combined (Figure 3). The commonest variant type were conventional, polypoid, desmoplastic.

The commonest cytologic type was epithelioid (59.1%) and then spindle cell type (40.9%). Reactive epidermal hyperplasia has been noted in 77.3% which is more common in compound type (P < 0.020). Other histologic parameters from the most to the least frequent were symmetry (100%), maturation (100%), kamino body (68.2%), mitosis

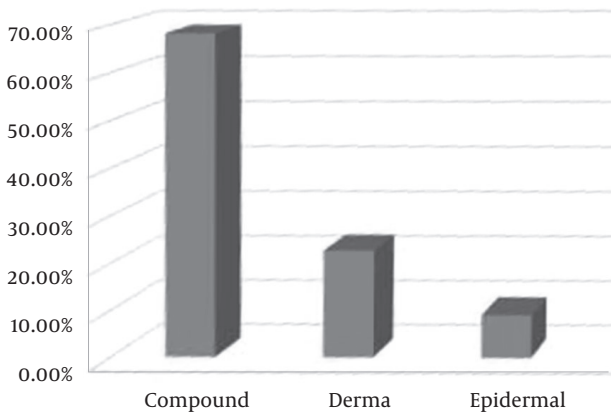

Figure 2. Frequency of Spitz Nevus Types

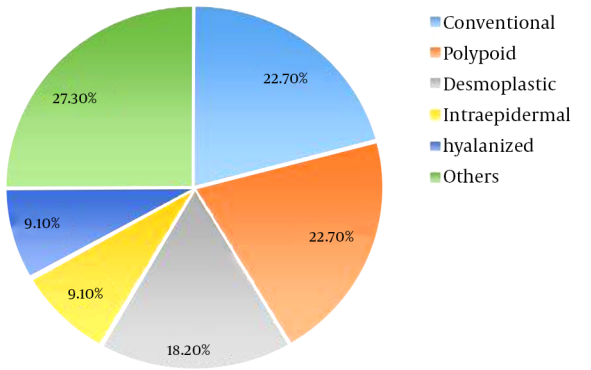

Figure 3. Histologic Frequency of Spitz Nevus

(63.6%), clefting (59%), inflammatory infiltration (54.5%), pagetoid spread (18.2%), shoulder (37.5%) and regression (9.1%).Ulceration was only in one case (4.5%). Melanocytic atypia was seen in six cases (27.2%).

5. Discussion

Spitz nevus is a clinically and histologically distinct variant of melanocytic nevus composed of spindled and/or epithelioid melanocytes (in the configuration of a benign tumor). Synonyms include Spitz's nevus, Spitz tumor, and spindle and epithelioid cell nevus.

The clinical diagnosis of Spitz nevi is variable but in the series of Requena (5), clinical findings of Spitz nevi occurred similar to the findings in our study.

In our study, 54.5% of patients were younger than 10 years old. More patients were in their first decade of life with SN prevalence decreasing gradually with patient's age (P = 0.192). Cesinaro et al. (8) noticed clear predominance age of spitz nevus in patients older than 20 years old (66%). Vollmer (9) noticed that patient age provides critical clinical information, because spitz nevus occurs mostly in children and he used mathematical formula for differential diagnosis between spitz nevus and malignant melanoma based on patient age (10).

The prevalence of lesions in head and neck was 54.5%, inferior extremities 18.2% and superior extremity and trunk were 13.6% each one. Fabrizi (11), Gantner (3) and Cesinaro et al. (8) reported that inferior extremity is the commonest location of spitz nevi. Requena et al. (5) reported commonest location of spitz nevi in men is in trunk and in women is inferior extremity. Symmetry and circumscription are also important criteria of benignity which help in the differential diagnosis with melanoma. According to some authors, it is found in 80% - 90% of the lesions, which is consistent with our findings (78 and 81%).(6.12) In our study, all (100%) nevi were symmetric and showed full dermal maturation like other studies except for Kernen and Ackerman study (12) who reported that dermal maturation was mostly absent.

Spitz nevus was one of the clinical differential diagnoses for 22 cases that for 20% of them was the first diagnosis. Requena et al. (5) reported that spitz nevus was the first clinical diagnosis.

Bogdanov-Berezovsky et al. (13) reported the commonest histologic types of spitz nevi were compound (72.7%) and then epidermal (15%) and dermal (12.3%) which are the same in our results.

The predominant cell type in our series of cases was epithelioid which was observed in all age groups ($P < 0.02$). In the series of Cesinaro, the lesions were mainly composed of epithelioid and spindle cells, whereas Requena described spindle cells as the most frequent cell type.

In melanomas, it is common to find atrophy of the epidermis is more common, while in Spitz nevi hyperplasia of the epidermis is frequent. In our series, prevalence of epidermal hyperplasia overlying of nevi was 77.3% which is more in compound type ($P < 0.03$). These results are similar to Requena study (5).

In our study, the roof cleft in melanocytic nest and shouldering phenomena was evident in 59.1% and 37.5% respectively but it has not been reported in other study.

Kamino bodies are frequently seen in Spitz nevus lesions with junctional component, especially if the cell density of the lesion is high (14). They were initially described in Spitz nevi and considered pathognomonic. Its occurrence was later also reported in melanomas (15). The presence of Kamino bodies in our cases, was 31.8% in nevi which are close to Requena results (5) but it was a little different

from others (6).

In our study, inflammatory infiltration was 54.5% predominantly lymphoid cells in nevi which are close to Requena results (5) but it was a little different from others (6). The inflammatory infiltrate which was present in 75% of cases, is consistent with the literature (5, 8). Plasma cells may be present in melanomas, but are not commonly found in Spitz nevi.

Spitz nevi may present mitotic figures, ranging from 10% to 58% in the different series (8).

The mitotic rate (one to two numbers in 10 HPF) was 63.6% which was 58% in Weedon study (16) but in Requena study (5) was 23%. They were all located in melanocytes of the basal layer. The location of the mitoses is an important criterion for differentiating Spitz nevus from spitzoid melanoma. In melanoma, mitoses are located in deeper portions (dermis) or grouped in a specific area of the lesion.

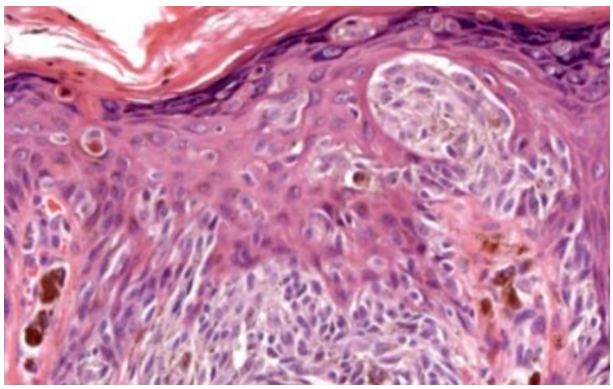

Figure 4. Compound spitz Nevus With Epithelioid Cell Type and Complete Nevic Cell Maturation

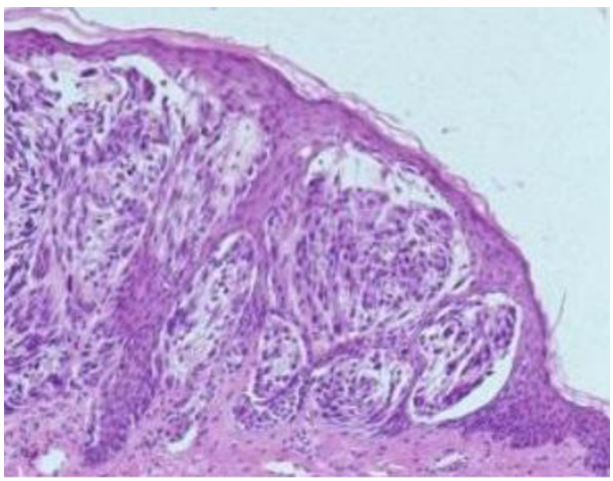

Figure 5. Conventional Spitz Nevus With Epidermal Hyperplasia, Shouldering and Kamino Body Phenomena

Maturation of melanocytes is an important benignity criterion in the diagnosis of melanocytic lesions and is usually present in Spitz nevi. Some series of cases report maturation in 72% - 86.6% (5, 8). In our study, such feature was observed in 100%.

Pagetoid spread of melanocytes to the upper layers of the epidermis is a frequent finding in melanomas. It may also be present in Spitz nevi, being generally restricted to the central portion of the lesion, and ranging from 13% - 63% in different studies (5, 8, 17). In the present study, we found 18.2% similarity to Requena study (5) but similarity to Weedon and Little (16) was reported less.

In our report, regression rate of spitz nevi during the time was only 10% which was not exactly detected in any studies.

In our study, however, we did not observe a correlation between age and clinical presentation and histopathologic findings ($P < 0.23$, $P < 0.12$, respectively).

5.1. Conclusion

The clinicohistopathologic features of Spitz nevi are highlighted: a, SN is more frequent in children but it may occur in adults; b, symmetry and circumscription are important criteria for SN; c, pagetoid spread are present in low intensities; d, maturation of melanocytes are regular and dominant; e, Kamino bodies are not essential; f, low mitotic rates may be present in the melanocytes located near the basal layer of the epidermis ; g, inflammatory infiltration and roof cleft with shouldering phenomena are present in varying intensities; epidermal hyperplasia overlying of nevi are regular and dominant. These cytologic and histologic features of Spitz nevi are helpful for the differential diagnosis with melanomas, but these criteria have not made definitive signs for this differentiation.

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Footnotes

Authors' Contribution: Mahtab Rahbar, has made substantial contributions to conception and design of the manuscript; Keykhosro Mardanpour, has been involved

in doing all surgical procedure, gathering data and drafting the manuscript, participated in the sequence alignment; Sourena Mardanpour, has made substantial contributions to acquisition of data from literature and writing the manuscript.

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