

Atypical Spitz Nevus in a Teenager, Melanocytic Proliferation of Difficult Diagnosis

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Abstract

The atypical Spitz nevus is a lesion of frequent occurrence in children, which is classified within the spectrum of "Spitzoid" injuries, which is characterized by a significant deviation on the findings of conventional Spitz nevus but without meeting the diagnostic criteria malignant melanoma.

The prognosis is uncertain and only after the study and monitoring of a sufficient number of patients, may obtain truly objective information for management.

We report the case of a teenager with a gluteal injury diagnosed with atypical Spitz nevus.

Keywords: Spitz nevus; Spitzoid proliferations; Atypical spitz nevus.

Introduction

The Spitz nevus, named after Sophia Spitz, who first described it in 1948 as "Juvenile melanoma" in her historic article entitled Melanomas of childhood. But Darier and Civatte, in 1910, described an unusual (Spitzoid) melanocytic tumor developing rapidly on the nose of a young child, and they were completely thwarted in their efforts to decipher whether the lesion was benign or malignant.

This benign melanocytic proliferation is also known as "large spindle and/or epithelioid cell nevus" to reflect its histological features.

Spitz nevi occur most often during the first two decades of life. However, they can arise at any age [1]. Rarely, it may be congenital or emerge in a congenital nevus.

They occur predominantly in the white population. Spitz nevi occur anywhere in the body; the cheeks and ears are favored sites in children while the limbs and trunk are the most common in adults [1,2].

Typically, the lesion is a solitary, pink, red or slightly pigmented nodule, usually of less than 1 cm in size.

Generally, pigmentation of Spitz nevus is more common in adolescence and adulthood. Occasionally, multiple Spitz nevi could exist either agminated or widely disseminated. Although most Spitz nevi are diagnosed with confidence and can be differentiated easily from melanoma, equivocal lesions are among the most problematic entities in diagnostic dermatopathology.

Clinical case

Female teenage of 17 years old, who consults for nodular lesión, 2-month of evolution, located in right buttock. The were not subjective symptoms and the lesión not changed with the passage of time.

As personal background she regards great sun exposure in recent years, at least six months in the year and two stories of sunburn.

On physical examination there is a nodular lesion, defined edges and net boundaries, 8 mm major axis, smooth, not eroded surface, which sits on right buttock.

The lesion with good margins of resection is removed and the surgical specimen is referred for histopathological study with the diagnosis of "Angioma".

One losangic skin fragment is received, on which sits a well defined, regular edges and net limits, unpigmented or ulcerated 8 mm major axes, pink nodular lesion.

Histologically, epidermal lining is thin and it forms a Collarte in the base of the lesion (Figure 1). An unencapsulated tumor, formed by epithelioid melanocytic cells, seated in dermis is observed. There are giant tumoral cells (Figure 2). The nuclei are irregular, and there is obvious hypertrophic nucleoli. Mitosis is observed in small numbers but even in the deep portion of the lesion (Figure 3, arrow).

Immunohistochemistry: S100 and Melan A positive. HMB45 negative. Cell proliferation index <5% (Figures 4 A to D).

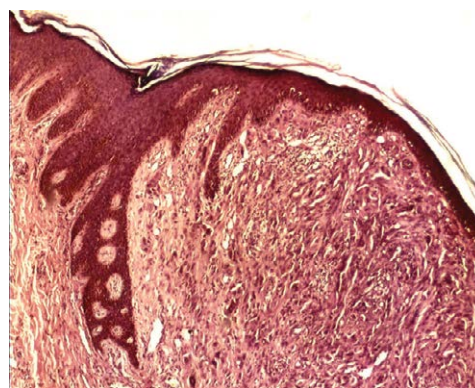


Figure 1: Thin epidermal lining that forms a Collarte in the base of the lesion (HE4X).

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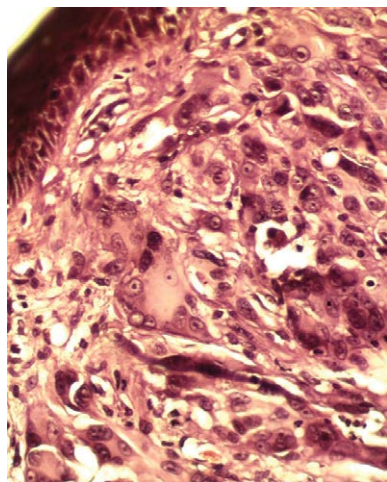


Figure 2: An unencapsulated tumor, formed by epithelioid melanocytic cells, seated in dermis is observed. There are giant tumoral cells (HE 20X).

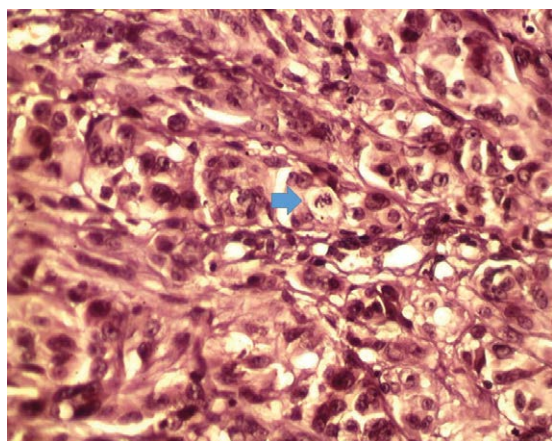


Figure 3: The nuclei are irregular, and there is obvious hypertrophic nucleoli. Mitosis is observed in small numbers but even in the deep portion of the lesion (HE 40X, arrow).

Final diagnosis: atypical Spitz intradermal nevus of epithelioid cells (Score 1).

Comments

The diagnosis of Spitz nevus requires examination of the whole lesion and careful assessment of a range of architectural and cytological features. Most Spitz nevi are compound lesions, but some are entirely junctional or intradermal.

The architectural features include: Symmetry, sharp lateral demarcation, zonation, maturation (diminution with depth in cell size, cellularity, loss of pigmentation and loss of proliferative activity), and regular pattern of epidermal hyperplasia.

The epidermal component tends to be arranged in a vertically oriented nests that usually not extending beyond the dermal component.

The architecture of the deep dermal part of the Spitz nevi is infiltrating rather than pushing [2].

Pagetoid melanocytosis, if present, is generally only focal, relatively

slight and usually limited to the lower half of the epidermis. An additional diagnostic clue is the Kamino bodies; an amorphous, PAS-positive, eosinophilic globules found at, or immediately subjacent to, the dermoepidermal junction in 60% of cases where they often aggregate in clumps. The finding of artifactual semilunar clefts separating the nests from the overlying epidermis is a useful diagnostic feature in Spitz nevi with junctional activity.

The most important common denominator is the large size of the melanocytes; these may be epithelioid and/or spindled with abundant amphophilic cytoplasm. In early childhood, the Spitz nevi are often composed wholly or largely of epithelioid cells with scarce or absent melanin pigment, while those in adults are significantly more likely to be intradermal, composed largely of spindle cells and are often pigmented [2,3]. The nuclei are large, with pale, delicate chromatin pattern and uniform nucleoli. Mitoses are absent in about half of the cases. Atypical mitoses, dermal mitotic rate more than two mitoses in square millimeter or mitoses within the lower half of the lesion should be interpreted with great caution.

Melanin pigment is often scarce or absent; when present, there are no substantial variations in degree or quality of pigmentation between areas at the same level of the lesion.

Multinucleated epithelioid giant melanocytes may be present and numerous in some cases.

Histopathological variants of Spitz nevi include: desmoplastic, halo, angiomatoid, pagetoid, hyalinizing, combined, plexiform, tubular, polypoidal and dysplastic [2,4].

A subset of Spitz nevi poses substantial diagnostic difficulty, even among experts, due to inadequate guidelines for the dichotomous distinction from malignant melanoma. "Atypical Spitz nevi" considered by most of the dermatopathologists as distinct lesions with borderline behavior residing between Spitz nevi and malignant melanoma [3].

These lesions may display architectural and cytological atypia to a degree beyond what is accepted in a benign Spitz nevus, but the atypical features are not sufficient for a histological diagnosis of melanoma. Others believe its "nondiagnosis" and stressing that the lesions must be signed out either Spitz nevus, melanoma, or "I don't know" when it must be subjected for another opinion from a respected colleague [5].

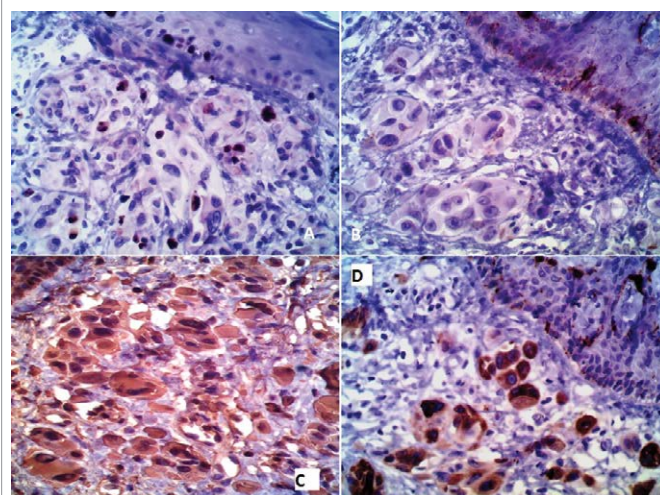


Figure 4: Immunohistochemistry. A. Ki67 5%. B. HMB45 negative. Positive internal control. C. positive S100. D. positive Melan-A (40X).

Lesions reported to have features of atypical Spitz nevus have spread to regional lymph nodes without subsequent disease progression, but some metastasized to distant organs and resulted in death [2,5,6]. Therefore, it has been recommended that such atypical Spitz tumors should be categorized into risk categories for aggressive behavior. Spatz et al. have attempted to develop a scoring system for risk stratification based on age of the patient age, diameter of the lesion, involvement of subcutaneous fat, ulceration and mitotic activity. This permits grading of the lesions into low, intermediate and high risk categories (Table 1) [7].

Spitzoid melanoma is a subtype of melanoma that clinically and histopathologically resembles Spitz nevus. While Spitz nevus can be usually be confidently diagnosed by experienced dermatopathologists, the current histological criteria do not allow distinguishing Spitz nevus from spitzoid melanomas in all cases. However, the features, which assist in this differential diagnosis from the literatures, are summarized in (Table 2).

Ancillary immunohistochemical stains studied in the literature including HMB-45, Ki67, Mart-1, fatty acid synthetase, MIB-1, cyclin D-1 and p-53 are rarely helpful in the real life cases [2,3,6].

Recent progress in molecular characterization of melanocytic proliferations holds some promise for development of molecular diagnostic tests. Mutations in the BRAF gene (53-80%) and N-RAS gene (~10%) that lead to activation of the mitogen-activated protein kinase (MAPK) pathway play a role in the pathogenesis of many conventional melanomas [9].

Similarly, a high rate of activating mutations in B-RAF is found in benign melanocytic nevi (70-90%), suggesting a role for B-RAF in both benign and malignant melanocytic tumors [6-9]. In contrast, activating hot spot mutations in B-RAF or N-RAS are not found in Spitz nevi.

Unfortunately, this features is not helpful in differential diagnosis between Spitz nevus and spitzoid melanoma as a recent study demonstrated only one mutation in B-RAF (of 33 cases) and no mutations in N-RAS in spitzoid melanoma [9].

The most useful currently available molecular diagnostic test appears to be comparative genomic hybridization (CGH) which shows normal chromosomal complement or gains of chromosome 11p in Spitz nevus, which contrasts with complex chromosomal aberrations

Criteria	Spitz nevus	Atypical/Malignant
Size	<10 mm	>10 mm
Involvement of subcutaneous fat	Absent	Present
Symmetry	Present	Absent
Atraumatic ulceration	Absent	Present
Circumscription	Sharp	Poor
Pagetoid melanocytosis	Focal, and in lower half of epidermis	Over a large zone and in the upper half of the epidermis
Cellular density	Low	High
Zonation and maturation	Present	Absent
Kamino bodies	Present with aggregates	Few or non
Mitotic rate	< 2/ mm ²	> 2-6/ mm ²
Deep/ marginal mitoses	Absent	Present
Atypical Mitoses	Rare	Common
Ki-67 expression	< 10%	> 10%
Nuclear/cytoplasmic ratio	Low	High
Nuclear membrane	Regular	Irregular
Cytoplasm	Ground glass	Granular
Hyperchromasia	Few or absent	Present
Large nucleoli	Absent	Present

Table 2: Features which assist the differential diagnosis from Spitz nevus and atypical/malignant [8].

seen in melanoma [10]. However, CGH is expensive and has limited sensitivity.

There is no consensus concerning management of Spitz nevi. The lack of consensus in the medical literature reflects to some extent the lack of certainty in the histological differentiation of Spitz nevi from melanomas. These lesions are at the top of malpractice claims for misdiagnosed lesions in surgical pathology. Generally speaking, atypical Spitz nevi and spitzoid melanoma need inter-expert dermatopathologists consultation before a report is issued. Ideally, all Spitz nevi should be completely excised for further histopathological study and all the cases should be followed up clinically. To date, for frankly atypical spitzoid melanocytic neoplasms it is not possible to predict the biological behavior with certainty. The grading system for risk stratification and mutation analysis can providing useful but not definitive information for the management of atypical nevi, though, the safest course of action for these lesions is undoubtedly to perform local treatment as for a melanoma of equivalent depth with interpretation of a positive sentinel lymph node biopsy as evidence of a malignant potential of the tumor [4].

Conclusions

1. Given the difficulty in diagnosing these lesions, a histological evaluation of the entire lesion should be performed.
2. The relapse rate reaches 7-16% when the lesion is removed incompletely.
3. All Spitz tumors should be resected with clear margins.
4. Margins of 1 cm are recommended for atypical lesions, as in this case.
5. Patients with these lesions should be followed every 6-12 months and this group of lesions may also raise the embodiment of sentinel node biopsy.

References

1. Casso EM, Grin-Jorgensen CM, Grant-Kels JM (1993) Spitz nevi. *J Am Acad Dermatol* 9: 667-668.

Variable	Score
Age of patient (yr)	
0-10	0
11-17	1
Diameter of lesion (mm)	
0-10.0	0
>10.0 mm	1
Fat involvement	
Absent	0
Present	2
Ulceration	
Absent	0
Present	2
Mitotic activity (per mm ²)	
0-5	0
6-8	2
>8	5
Total	11

Scores of 0, 1, and 2 indicate low risk; 3 and 4 intermediate risk; and 5 through 11 high risk.

Table 1: Grading system for atypical spitz tumors.

2. Mooi, Wolter J (2002) Spitz nevus and its histologic simulators. *Adv Anat Pathol* 4: 209-221.
3. Kapur P, Selim MA, Roy LC, Yegappan M, Weinberg AG et al. (2005) Spitz nevi and atypical Spitz nevi/tumors: a histological and immunohistochemical analysis. *Modern pathology* 18: 197-204.
4. Dahlstrom JE, Scolyer RA, Thompson JF, Jain S (2004) Spitz naevus: diagnostic problems and their management implications. *Pathology* 36: 452-457.
5. Mones JM, Ackerman AB (2004) "Atypical" Spitz's nevus, "malignant" Spitz's nevus, and "metastasizing" Spitz's nevus: A critique in historical perspective of three concepts flawed fatally. *Am J Dermatopathol* 26: 310-333.
6. Raymond L Barnhill (2006) The spitzoid lesion: rethinking Spitz tumors, atypical variations, "Spitzoid melanoma" and risk assessment. *Modern pathology* 19: S21-S33.
7. Spatz A, Calonje E, Handfield-Jones S, Barnhill RL (1999) Spitz tumors in children: a grading system for risk stratification. *Arch Dermatol* 135:282-285.
8. Tawara M, Flotte TJ (2006) Case 2: Large spindle and/or epithelioid cell nevus (Spitz nevus). In: *Cases in Dermatopathology. Common Problems in Diagnosis of Pigmented Lesions*. Knowledge Books and Software, Brisbane, QLD 6: 7-16.
9. Lee DA, Cohen JA, Twaddell WS, Palacios G, Gill M, Levit E, et al. (2006) Are all melanomas the same? Spitzoid melanoma is a distinct subtype of melanoma. *Cancer* 106: 907-913.
10. Bastian BC, Wesselman U, Pinkel D, Leboit PE (1999) Molecular cytogenetic analysis of Spitz nevi shows clear differences to melanoma. *J Invest Dermatol* 113: 1065-1069.