The Spectrum of Spitz Nevi

A Clinicopathologic Study of 83 Cases

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Objective: To achieve a clinicopathologic classification of Spitz nevi by comparing their clinical, dermoscopic, and histopathologic features.

Design: Eighty-three cases were independently reviewed by 3 histopathologists and preliminarily classified into classic or desmoplastic Spitz nevus (CDSN, n=11), pigmented Spitz nevus (PSN, n=14), Reed nevus (RN, n=16), or atypical Spitz nevus (ASN, n=14); the remaining 28 cases were then placed into an intermediate category (pigmented Spitz-Reed nevus, PSRN) because a unanimous diagnosis of either PSN or RN was not reached.

Setting: University of Naples, Naples Institute of the Federico II University of Graz, Graz, Austria (Drs Soyer and Ackerman); Department of Dermatology, Medical University of Graz, Graz, Austria (Drs Soyer and Zalaudek); and the Pathology Institute of the Federico II University of Naples, Naples (Drs Staibano and De Rosa).

Results: Overlapping clinical, dermoscopic, and histopathologic findings were observed among PSN, RN, and PSRN, thereby justifying their inclusion into the single PSRN diagnostic category. Asymmetry was the most frequent indicator of histopathologic ASN (79%; n=11); in only 4 cases did dermoscopic asymmetry show no histopathologic counterpart, and in those cases the discrepancy was probably the result of an artifact of the gross sampling technique carried out with no attention to the dermoscopic features.

Conclusions: Among Spitz nevi, histopathologic distinction between PSN and RN is difficult, not reproducible, and may be clinically useless. A simple clinicopathologic classification of these neoplasms might therefore be structured as CDSN, PSRN, and ASN. Asymmetry should be assessed using both dermoscopic and histopathologic analysis, and reliability in histopathologic diagnosis may be enhanced by the simultaneous evaluation of the corresponding dermoscopic images.

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In 1948, Sophie Spitz2 described a series of “melanomas of childhood” as lesions fulfilling the biologic as well as the histopathologic criteria of malignancy. Indeed, just 1 year later, Arthur C. Allen2 in included juvenile melanomas in the category of the benign melanocytic lesions. The lesion was originally thought to occur largely in children, but it is now well recognized that more than half of Spitz nevus cases are detected in patients older than 14 years, and about one fourth of the cases occur in patients older than 30 years.6 A Spitz nevus usually presents as a solitary lesion on the lower extremities or the face. In its classic clinical appearance it is pink-red because of the scarcity of melanin; however, tan, brown, and even black pigmented Spitz nevus (PSN) are common as well.

In 1975, Reed et all described a deeply pigmented melanocytic lesion, found mostly in young adults on the lower extremities. Although some authors continue to use the nosologic peculiarity Reed nevus (RN), others regard the RN as a variant of PSN. The clinicopathologic distinction between PSN and RN is highly controversial even among expert dermatologists and histopathologists. The terms spindle-cell nevus and epitheloid cell nevus, introduced by Kernen and Ackerman in 1960, have been largely adopted in recent years as unifying diagnostic categories.

In the last 20 years, dermoscopy, a term coined by Friedman et al in 1991 and also known as dermatoscopy, epiluminescence microscopy, and skin surface microscopy, has been increasingly used as a noninvasive diagnostic technique for the in vivo observation of pigmented skin lesions. Dermoscopy allows a cutaneous lesion to be inspected using a handheld lens, hand-
A junctional, compound, or dermal melanocytic neoplasm associated with conspicuous epidermal hyperkeratosis or acanthosis and with little or no pigment deposition was classified as a classic or desmoplastic Spitz nevus (CDSN). Cytomorphologically, the CDSN was characterized by melanocytes with large nuclei, prominent nucleoli, and abundant ground-glass cytoplasm with polygonal (epithelioid) and often also cigar-shaped (spindle) outlines. Ancillary features include Kamino bodies, edema, teleangiectasias, and fibrosis of the papillary dermis. Extensive dermal desmoplasia encircling single melanocytes is seen in the desmoplastic variant.

**Pigmented Spitz Nevus**

The PSN is a junctional or compound neoplasm composed of heavily pigmented, highly cohesive spindle and/or epithelioid melanocytes, parallel and perpendicular to the skin surface, with artifactual clefts at the interface between the nests of melanocytes and the hyperplastic epidermis. It is also characterized by cytologic features akin to the spindle- and epithelioid-cell component of the CDSN as well as by ancillary features of the CDSN.

**Atypical Spitz Nevus**

An (almost) exclusively junctional neoplasm, the RN is composed of heavily pigmented, monomorphic, small to medium-sized spindle melanocytes, mainly arranged parallel to the skin surface. Typically, the RN is structured without sharp demarcation between the nests of melanocytes and the overlying epidermis, with the latter showing little or no hyperkeratosis-acanthosis. Ancillary findings can include a bandlike dermal infiltration of melanophages.

**Pigmented Spitz-Reed Nevus**

A further provisional category was introduced after the histopathologic study: pigmented Spitz-Reed nevus (PSRN). This category included lesions that had been diagnosed as either PSN or RN by each histopathologist but without unanimous agreement. The lack of unanimity was probably owing to the presence of largely overlapping microscopic features. The PSRN category was adopted only a posteriori to compensate for the strict requirement from the beginning of the study that the histopathologists arrive at a definitive diagnosis in every case. Cases were discarded if any other diagnostic discrepancy was raised.
Table 1. Clinical Characteristics of 83 Cases of Spitz Nevus by Provisional Histopathologic Type*

| Characteristic          | CDSN  
| (n = 11) | PSN  
| (n = 14) | RN  
| (n = 16) | PSRN  
| (n = 28) | ASN  
| (n = 14) |
|------------------------|--------|--------|--------|--------|--------|
| Patient age, range (mean), y | 5-50 (19.3) | 2-48 (21.6) | 1-58 (22.0) | 4-55 (22.2) | 8-34 (17.3) |
| Sex ratio, M:F          | 3:8    | 5:9    | 6:10   | 8:20   | 3:11   |
| Lesion site, No.        |        |        |        |        |        |
| Head or neck            | 0      | 1      | 0      | 1      | 1      |
| Trunk                   | 2      | 1      | 4      | 5      | 1      |
| Limbs                   | 9      | 12     | 12     | 22     | 12     |
| Size, range (mean), mm  | 5-9 (7.0) | 4-8 (5.4) | 3-6 (4.6) | 3-7 (4.8) | 4-9 (6.1) |
| Color, No.              |        |        |        |        |        |
| Pink-red                | 5      | 0      | 0      | 0      | 1      |
| Brown                   | 6      | 5      | 5      | 7      | 9      |
| Black                   | 0      | 0      | 11     | 21     | 4      |

Abbreviations: ASN, atypical Spitz nevus; CDSN, classic or desmoplastic Spitz nevus; PSN, pigmented Spitz nevus; PSRN, pigmented Spitz-Reed nevus; RN, Reed nevus.
*See the “Methods” section for a definition of these nevus types.

Table 2. Dermoscopic Patterns of 83 Cases of Spitz Nevus by Provisional Histopathologic Type*

<table>
<thead>
<tr>
<th>Dermoscopic Pattern</th>
<th>CDSN</th>
<th>PSN</th>
<th>RN</th>
<th>PSRN</th>
<th>ASN</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starburst</td>
<td>0</td>
<td>8</td>
<td>9</td>
<td>16</td>
<td>2</td>
<td>35</td>
</tr>
<tr>
<td>Globular</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Atypical and/or multicomponent</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Homogeneous</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Reticular, classic</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Reticular, superficial</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Hypopigmented</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>14</td>
<td>16</td>
<td>28</td>
<td>14</td>
<td>83</td>
</tr>
</tbody>
</table>

Abbreviations: ASN, atypical Spitz nevus; CDSN, classic or desmoplastic Spitz nevus; PSN, pigmented Spitz nevus; PSRN, pigmented Spitz-Reed nevus; RN, Reed nevus.
*See the “Methods” section for a definition of these nevus types.

(mean age, 20.9 years). The most common lesion sites were the limbs (81%; n = 67), followed by the trunk (14%; n = 12). Only 3 cases (5%) occurred on the face. Most neoplasms were described as brown (39%; n = 32) or black (54.2%; n = 45). Only 6 lesions (7%) were pink-red. Their sizes ranged from 3 to 9 mm (mean size, 5.4 mm).

Based on the given criteria, all 3 histopathologists unanimously agreed on the diagnoses in 11 cases (13%) as CDSN; 14 cases (17%) as PSN; 16 cases (19%) as RN; and 14 cases (17%) as ASN. The remaining 28 cases (34%) received a diagnosis of either PSN or RN by each histopathologist without unanimous agreement. These cases were thus placed into the PSRN category.

Table 1 summarizes the clinical features of the 83 cases classified according to the histopathologic diagnosis: PSN, RN, and PSRN were diagnosed at almost the same mean age (mean age range, 21.6-22.2 years); patients with ASN were significantly younger at the time of diagnosis (mean age, 17.3 years). Lesions diagnosed as PSN, RN, and PSRN were usually smaller and more often black than lesions in the other histopathologic categories.

Table 2 details the distribution of the 83 lesions according to the dermoscopic pattern and the histopathologic diagnosis. A great variability was observed in the dermoscopic appearance of Spitz nevi. Remarkably, however, the starburst, globular, and atypical patterns accounted for 66 (80%) of the 83 cases, thus representing the major dermoscopic patterns of Spitz nevi.

Cases of PSN, RN, and PSRN basically showed a similar distribution of dermoscopic patterns. In particular, the starburst pattern, previously reported as highly characteristic of RN,23,30 was present in 9 (56%) of 16 cases of RN but also in 8 (57%) of 14 cases of PSN and in 16 (57%) of 28 cases of PSRN. Figures 1, 2, 3, and 4 illustrate the dermoscopic-pathologic correlations in cases of RN and PSN, with both lesions showing a starburst pattern on dermoscopy. Because of the largely overlapping clinical, dermoscopic, and histopathologic features among PSN, RN, and PSRN, we propose the denomination PSRN as a unifying diagnostic category for all of these cases.

The association between dermoscopic and histopathologic atypia was remarkable but not absolute. Asymme-
try was by far the most common histopathologic feature of ASN (11/14; 79%) followed by the presence of deep dermal mitotic figures (n=3).

More than half (8/15; 53%) of the lesions showing an atypical and/or multicomponent dermoscopic pattern were found to be histopathologically atypical as well. Figure 5 and Figure 6 illustrate a case of a Spitz nevus showing dermoscopic and histopathologic features, respectively, of atypia. Among the lesions showing dermoscopic atypia with no histopathologic counterpart (7/15), 3 lesions showed a dermoscopic image characterized by a diffuse bluish pigmentation suggestive of a regression structure or a blue-whitish veil. In these cases histopathologic analysis revealed that the bluish pigmentation was simply due to a bandlike infiltrate of melanophages.

More interestingly, in 4 cases, dermoscopic atypia was due to a striking asymmetry that was not represented on histopathologic sections. This finding might point toward an underestimated limitation of histopathologic examination, namely, gross sampling carried out with no special attention to the clinical (dermoscopic) features of a given pigmented lesion. It has been already demonstrated that dermoscopy can turn
histopathologists’ attention to the suggestive area in melanocytic lesions; therefore, the histopathologic diagnosis can be radically different when dermoscopic information is not taken into account. **Figure 7** and **Figure 8** display dermoscopic and histopathologic images, respectively, of a Spitz nevus in which a poor gross sampling technique presumably led to discrepancies between dermoscopic and histopathologic features.

**COMMENT**

In recent years, dermoscopy has become the conceptual and practical link between the macrocosm of clinical dermatology and the microcosm of histopathology, allowing the clinician to visualize structures that are not discernible by the naked eye. The present study provides an example of how dermoscopy can integrate the clinical and histopathologic data about melanocytic skin neoplasms.

Our starting point was the adoption of a provisional histopathologic classification, which clearly demonstrated the great difficulties in distinguishing PSN from RN because of frequent overlapping histopathologic findings between these 2 entities. Moreover, PSN and RN, as well as their intermediate provisional counterpart, PSRN, showed basically the same dermoscopic features; in fact, the 3 major dermoscopic patterns—starburst, globular, and atypical—accounted for most cases included in this study (66/83; 80%), with no preferential distribution among cases of PSN, RN, and PSRN. Indeed, even the starburst pattern, previously considered to be typical of RN, was observed in 56% of cases (n=8) classified by histopathologists as clear-cut PSN.

As a corollary, the growth sequence reported by Pizzichetta et al in a case of PSN—the progressive transformation of a globular pattern into a starburst and, in turn, into a homogeneous one—underscores the observation that there is no close correlation between dermoscopic patterns and the histopathologic categories of PSN and RN. In our opinion, these data suggest that, in most cases, a clinicopathologic distinction between PSN and RN cannot be adequately supported. We therefore propose the following clinicopathologic classification of Spitz nevi.

1. **CDSN**: A subdivision of this category into 2 separate entities is justified on the basis of the previous histopathologic data. However, further studies on larger series are needed to elucidate the dermoscopic correlates of these types of melanocytic neoplasms.

2. **PSRN**: This category includes the provisional entities PSN, RN, and PSRN of the present study. A further subclassification of this category is difficult to apply, necessarily subjective, and clinically useless.
3. ASN, Either Epithelioid or Spindle-Cell Type: We retain this category because our review of data from the literature on cases of metastasizing spitzoid neoplasms demonstrates that the presence of even 1 atypical feature can be associated with an aggressive clinical course (data not shown).

The occurrence of an atypical (multicomponent) dermoscopic pattern in Spitz nevi is well recognized, as is the occurrence of melanomas with dermoscopic features of Spitz nevi.23 There are some theoretical and practical reasons why the dermoscopic-pathologic correlation of this group of lesions is often problematic. First, some concepts introduced in the literature have been confusing, and among these is the relationship between the so-called Spitz nevus with atypia and metastasis27 and the classic spitzoid melanoma. Moreover, the histopathologic features of lesions with spitzoid features are often not definitive, creating substantial diagnostic interobserver disagreement.23 Finally, when dermoscopy clearly reveals features of a Spitz nevus, sometimes the histopathologic analysis of the same lesion supports a diagnosis of a melanoma. Remarkably, the “spitzoid melanoma” does not have a distinctive dermoscopic counterpart. These diagnostic problems have led to the common practice in recent years of surgically removing all lesions in adults that show dermoscopic features akin to Spitz nevi.

The occurrence of dermoscopically unexpected histopathologic atypia can be easily explained: histopathologic analysis examines lesions at higher magnification and, most importantly, in their deeper portions. Certain histopathologic criteria of atypia (dermal sheets of melanocytes, absence of maturation, pleomorphic nuclei, mitotic figures, and asymmetrical features in the deeper portions of a given lesion) will never be seen under dermoscopy. On the other hand, it is more difficult to explain the absence of histopathologic atypia in dermoscopically atypical lesions.

In the present study, we found 7 lesions determined to be atypical (multicomponent) by dermoscopy that were devoid of histopathologic features of atypia. Among these lesions, we found that a potential source of dermoscopic overestimation was a bandlike dermal infiltrate of melanophages, a common ancillary feature of pigmented spindle-cell nevi. In fact, in 3 cases, this feature was responsible for a diffuse bluish pigmentation of the lesion, a worrisome dermoscopic feature that suggests the presence of either regression30,31,34 or a blue-whitish veil.23,30,31 In addition, and even more interestingly, 4 cases showed a striking dermoscopic asymmetry, which was not adequately represented on histologic sections. This was presumably due to the gross sampling technique, which had been carried out without consideration of the clinical (dermoscopic) features of the lesion. The various methods of gross sampling44,48 of cutaneous neoplasms, among them the “rule of halves,”44 do not all take into account the clinical features of the lesion. It is probably impractical for a histopathologist to review the dermoscopic features every time a melanocytic lesion is submitted to histologic examination; however, at least in selected cases, it would be important to minimize sampling errors by customizing the gross sampling technique to the dermoscopic picture of the same lesion. In these cases, the first cut made according to the rule of halves might be guided by the most representative dermoscopic features.

In cases in which melanoma is difficult to diagnose, the attention of the histopathologist should be directed to the areas of highest diagnostic relevance by means of dermoscopy.32 Data from the present study suggest that asymmetry is an important indicator of histopathologic atypia in Spitz nevi and that this feature deserves special attention in a setting of dermoscopic-pathologic correlation.

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REFERENCES

22. Kemen JA, Ackerman LV. Spindle cell nevus and epithelioid cell nevus (so-called

News and Notes

The Certifying Examination of the American Board of Dermatology (ABD) will be held at the Crowne Plaza Hotel, Chicago O’Hare, in Rosemont, Ill, on August 13 and 14, 2006. The deadline for receipt of applications is March 1, 2006. The recertification examination of the ABD will be administered online from May 1 to June 15, 2006. The deadline for receipt of applications for the recertification examination is December 15, 2005. The examination for subspecialty certification in Dermatopathology will be administered September 19, 2006, at the testing center of the American Board of Pathology in Tampa, Fla. The deadline for receipt of applications is May 1, 2006. (Dermatologists must submit applications to the ABD and pathologists to the American Board of Pathology.) The examination for subspecialty certification in Pediatric Dermatology will be administered on October 23, 2006. Location to be determined. The In-Training Examination for Dermatology residents (administered online at dermatology residency training centers in the United States and Canada) will be held on April 6, 2006. Deadline for receipt of applications is February 1, 2006.

For further information about these examinations, contact Antoinette F. Hood, MD, American Board of Dermatology, Henry Ford Health System, One Ford Place, Detroit, MI 48202-3450 (phone: 313-874-1088; fax: 313-872-3221; e-mail: abderm@hfhs.org), or check the ABD Web site at www.abderm.org.