

Sentinel Lymph Node Biopsy for Patients with Problematic Spitzoid Melanocytic Lesions

A Report on 18 Patients

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BACKGROUND. Spindle and/or epithelioid melanocytic proliferations that display overlapping histopathologic features of Spitz nevus and Spitz-like melanoma are diagnostically difficult and controversial melanocytic tumors. There are reports of such lesions metastasizing to regional lymph nodes, with a few widely disseminating, resulting in death.

METHODS. The authors reviewed clinical and histopathologic data on all patients with atypical or borderline spitzoid melanocytic proliferations who underwent sentinel lymph node biopsy (SLNB). They examined how frequently histologically problematic or borderline spitzoid melanocytic lesions metastasized to sentinel lymph nodes (SLNs) and which clinical or histologic features, if any, predisposed patients to a higher risk lesion.

RESULTS. Six male patients and 12 female patients, ages 5–32 years (mean, 16 years), had tumors ranging in size from 1.2 mm to 7.9 mm (mean, 3.5 mm) in thickness. Atypical histologic features that were present most frequently included incomplete maturation (18 of 18 patients), deep dermal mitoses (16 of 18 patients), nuclear pleomorphism (10 of 18 patients), and focal sheet-like growth (10 of 18 patients). Eight of 18 patients (44%) had SLN metastasis and were offered adjuvant treatment. One of eight patients with SLN positive results who underwent regional lymphadenectomy had one additional involved lymph node. All 18 patients were alive and well with no evidence of recurrent or metastatic disease after a follow-up of 3–42 months (mean, 12 months).

CONCLUSIONS. Histologically atypical or borderline spitzoid, melanocytic tumors are diagnostically challenging and controversial melanocytic lesions, some of which represent unrecognized melanomas. SLNB aids in confirming a diagnosis of melanoma and identifies patients who may benefit from early therapeutic lymph node dissection and/or adjuvant therapy. *Cancer* 2003;97:499–507.

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KEYWORDS: Spitz nevus, atypical Spitz tumor, spitzoid melanoma, sentinel lymph node.

In a landmark study on *melanomas in childhood*,¹ Sophie Spitz observed that only 1 of 13 patients with *juvenile melanoma* had a malignant and fatal course. In her analysis, she concluded that the presence of giant cells in nearly half of the benign tumors, now eponymously called Spitz nevus, was a histologic finding that helped to distinguish them from melanoma. Since then, many have studied the histology of spindle and epithelioid melanocytic proliferations to uncover features that may help to differentiate benign Spitz nevus from melanoma with Spitz-like features. Although significant

progress has been made in defining histologic criteria for Spitz nevus and Spitz-like melanoma, the diagnosis of atypical spindle and epithelioid melanocytic proliferations remains a contentious area in dermatopathology with repercussions that extend to patient management.²

Although most spindle and epithelioid melanocytic proliferations readily are classifiable histologically as Spitz nevus or melanoma with Spitz-like features,^{1,3-5} there is a subset of problematic and diagnostically challenging melanocytic lesions variably designated as *atypical Spitz tumor*, *atypical Spitz nevus*, Spitz-like lesion in the *borderline category of indeterminate malignant potential*, and *diagnostically controversial spitzoid melanocytic tumors*, that defy classification into either category even by the most experienced dermatopathologists.^{2,6-10} These lesions simultaneously exhibit some histomorphologic features of classic Spitz nevus and Spitz-like melanoma, making diagnostic assignment to either Spitz nevus or Spitz-like melanoma difficult, controversial, and sometimes erroneous.

The biologic behavior of these problematic atypical spitzoid melanocytic lesions has not been elucidated clearly. Experts often regard these lesions as having an indeterminate malignant potential, yet there is excellent documentation of histologically atypical or controversial, spitzoid, melanocytic lesions metastasizing to regional lymph nodes,^{8,11-13} some with wide dissemination and fatal outcome.^{2,7,14,15} It is reasonable to conclude, in retrospect, that these lesions are classified better as melanomas.

For these reasons, at our institution, we proceed cautiously and conservatively when faced with melanocytic lesions classified as atypical Spitz tumor, borderline epithelioid melanocytic proliferation, or atypical epithelioid melanocytic proliferation of unknown biologic potential for which a consensus in diagnosis among experts cannot be reached. We recommend intraoperative lymphatic mapping (IOLM) and sentinel lymph node biopsy (SLNB) to patients with tumors that exceed 1 mm in Breslow depth or < 1 mm in Breslow depth with adverse histologic features, such as ulceration. Defining the sentinel lymph node (SLN) status provides valuable information that better defines the biologic potential of these diagnostically challenging lesions.^{8,16} This report on our institutional experience with SLNB for patients with problematic atypical spitzoid melanocytic lesions is the largest series to date.

MATERIALS AND METHODS

After obtaining approval from the University of Michigan Institutional Review Board, we queried the mel-

anoma and pathology data bases at the University of Michigan Medical Center for patients with atypical spitzoid melanocytic proliferations that fell within any of several designations (including atypical Spitz tumor, markedly atypical Spitz nevus, atypical epithelioid melanocytic proliferation of uncertain biologic potential, or borderline epithelioid melanocytic neoplasm) who underwent IOLM and SLNB. Also included were patients who were diagnosed with melanoma with spitzoid features for whom there was a discordance in diagnosis among expert dermatopathologists and patients in whom the diagnosis of melanoma could not be excluded. Clinical data and histopathologic material from primary lesions, SLNs, and regional lymphadenectomy specimens (when applicable) were retrospectively reviewed.

The clinical data extracted included patient age, gender, location of the primary lesion, number of SLNs obtained, and site of lymphadenectomy, if applicable. Histologic parameters of the primary lesion that were assessed included the presence or absence of Kamino bodies; tumor thickness measured in millimeters (Breslow depth); Clark level; presence or absence of ulceration; mitotic rate (including deep and/or atypical mitoses); and atypical or disturbing growth pattern, such as incomplete maturation/zonation or focal, confluent, or sheet-like growth. At least one and frequently all three board-certified dermatopathologists (L.D.S., D.R.F., and L.L.) evaluated the histopathologic material. Because of the borderline nature of many of the primary lesions, a consensus in diagnosis frequently could not be achieved. The differing opinions were recorded.

The procedure for IOLM and SLNB used in our institution is similar to that previously described.¹⁷⁻¹⁹ A combination of immediate preoperative lymphoscintigraphy with unfiltered ^{99m}Tc-sulfur colloid and intraoperative lymphatic mapping using both a γ detector and vital blue dye (Lymphazurin 1%; Hirsch Industries, Richmond, VA) was used to identify the SLN in all patients. The protocol for evaluating SLNs at our institution was as follows: SLNs were sectioned serially at a thickness of 2-3 mm, fixed in formalin, and embedded in paraffin. Two serial, 5- μ m sections from each SLN tissue block were stained with hematoxylin and eosin (H&E) for routine histologic examination. For blocks in which obvious metastatic tumor was not identified in routine sections, immunohistochemical stains were performed on every SLN tissue block. One serial section from each SLN block was immunostained for S100 protein (1:1000 dilution; Dako, Carpinteria, CA), Melan-A (1:12:5 dilution; Dako), and HMB-45 (1:100 dilution; Dako). In blocks in which only small foci suspicious for tumor were

TABLE 1
Clinical and Pathologic Data for Patients with Problematic Spitzoid Melanocytic Lesions

Patient	Age (yrs)	Gender	Site of primary tumor	Histologic diagnoses ^b	Breslow depth (cm)/Clark level	Atypical histologic features noted in tumor ^a				Sentinel lymph nodes			Follow-up and duration (months)		
						NP	DM ^c	NM	FCG	Kamino bodies present	Site	No. positive		Capsular nevi present	Other positive lymph nodes in lymphadenectomy
1	10	F	R eyebrow	AS	3.3/V	—	3	X	X	No	R preauric	1 of 3	No	0 of 47	AW (5)
2	17	F	Sacrum	SN(2),AS,SM	1.3/IV	X	2	X	—	Few	L groin	1 of 2	No	0 of 14	AW (2)
3	24	F	L shoulder	AS,SM(3)	1.5/IV	X	4	X	—	No	L axilla	2 of 5	No	0 of 11	AW (17)
4	8	M	R ear	AS(3)	3.6/V	X	1	X	X	Few	R neck	1 of 2	Yes	0 of 44	AW (7)
5	12	M	R ankle	AS(3)	4.0/IV	—	1	X	X	No	R groin	2 of 11	No	1 of 13	AW (7)
6	5	F	L calf	AS(2)	3.0/IV	X	2	X	—	No	L groin	2 of 2	No	0 of 14	AW (8)
7	29	F	Back	AS	2.2/IV	X	—	X	—	No	R axilla	1 of 3	Yes	0 of 13	AW (8)
8	8	M	R thigh	AS(3)	3.5/IV	X	4	X	X	Many	R groin	1 of 2	No	0 of 10	AW (14)
9	32	M	R thigh	AS(2)	4.5/IV	—	1	X	—	No	R groin	0 of 2	No	—	AW (36)
10	24	F	R leg	AS, SM	1.2/IV	—	1	X	—	Many	R groin	0 of 1	No	—	AW (11)
11	22	M	Back	AS(3)	3.6/IV	X	1	X	X	No	R axilla	0 of 4	No	—	AW (10)
12	21	M	L arm	AS,SM(2)	2.5/IV	X	1	X	X	No	L axilla	0 of 1	Yes	—	AW (7)
13	16	F	L buttock	AS,SM(2)	6.5/IV	—	5	X	—	Few	L groin	0 of 4	No	—	AW (7)
14	16	F	L thigh	AS,SM	1.3/IV	X	—	X	—	No	L groin	0 of 1	No	—	AW (7)
15	13	F	L ear	AS(2)	7.0/IV	—	2	X	X	No	L neck	0 of 1	No	—	AW (19)
16	31	F	L arm	AS(2)	2.5/IV	—	2	X	X	Many	L axilla	0 of 3	No	—	AW (3)
17	12	F	R arm	AS,SM(2)	2.9/IV	X	1	X	X	Many	R axilla	0 of 3	Yes	—	AW (5)
18	11	F	L flank	AS,SM(2)	7.9/IV	—	4	X	X	Few	L axilla	0 of 2	No	—	AW (4)

NP: nuclear pleomorphism; DM: dermal mitoses; NM: incomplete or no maturation/zonation of dermal melanocytes; FCG: focal confluent (sheet-like) growth in dermis; SN: Spitz nevus; F: female; M: male; R: right; L: left; AS: atypical Spitz tumor/atypical epithelioid melanocytic proliferation of uncertain biologic potential; SM: Spitz-like melanoma; AW: alive and well with no evidence of disease.

^a Atypical histologic features (marked with X) were noted in tumors.

^b Histologic diagnoses at biopsy by staff and consultants: numbers in parentheses indicate the number of consultants who reached the same diagnoses (if greater than one).

^c If deep (DM) were present, then the numbers of mitoses per mm² in the lower one-third of the tumor are indicated.

present in H&E-stained sections, all three immunostains were obtained to confirm the impression of metastatic involvement.

RESULTS

The clinical findings are summarized in Table 1. We identified 18 patients from January 1998 to December 2001. Twelve patients were female, and 6 patients were male. Their ages at the time of diagnosis ranged from 5 years to 32 years (mean age, 16 years). The majority of lesions were found on the extremities (9 of 18 lesions), whereas 6 lesions were located on the trunk, and 3 lesions were located in the head and neck region.

Pertinent histopathologic features also are included in Table 1. All tumors were spindle and/or epithelioid melanocytic proliferations and displayed at least two other features commonly seen in conventional Spitz nevus: epidermal hyperplasia, symmetrical growth, circumscribed margins, papillary dermal edema, or Kamino bodies. The most prominent atypical histologic features were as follows. In all tumors (18 of 18 tumors), there was incomplete or no matu-

ration/zonation of dermal melanocytes, identified as a failure of dermal melanocytes to completely disperse as single cells that insinuate themselves between collagen bundles and a failure to diminish in size with dermal descent. In 16 of 18 tumors, mitotic activity was noted in the lower one-third of the tumor, ranging from 1 mitoses per mm² to 5 mitoses per mm². There were no atypical division figures. We noted variability in nuclear size and shape (nuclear pleomorphism) in 10 of 18 tumors. An aberrant dermal growth pattern that was characterized by focal sheet-like growth was present in 10 of 18 tumors. None of the tumors were ulcerated. In addition, no tumor demonstrated upward, pagetoid scattering of melanocytes. Variable numbers of eosinophilic Kamino bodies were identified in three lymph node positive primary tumors and in five lymph node negative primary tumors.

At the time of presentation, a histologic diagnosis of atypical epithelioid melanocytic proliferation of uncertain biologic potential or atypical Spitz tumor of uncertain biologic potential was rendered in 10 of 18 patients. Figures 1 and 2 illustrate the histologic features of one such patient (Patient 8). Figure 3 demon-

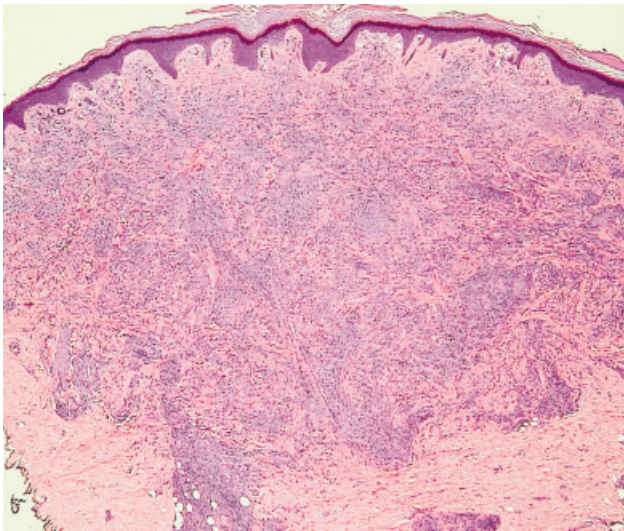


FIGURE 1. On scanning magnification, an atypical Spitz tumor from Patient 8 has slight epidermal hyperplasia and a circumscribed, wedge-shaped, and symmetrical silhouette.

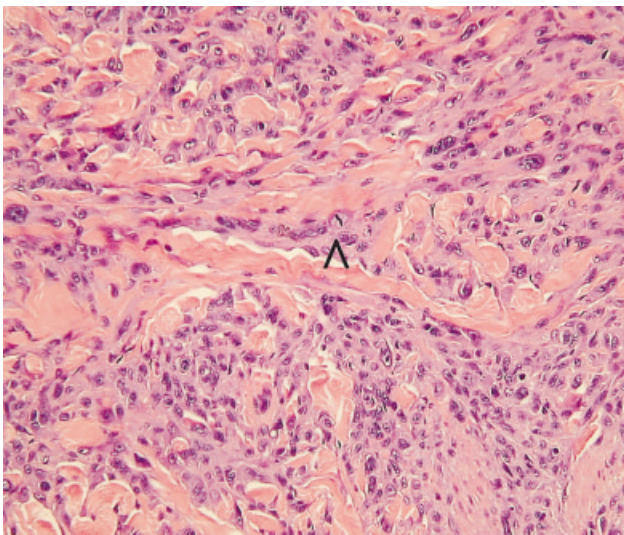


FIGURE 2. In a section of deep dermis from Patient 8, at high magnification, spindle and epithelioid melanocytes do not mature with descent into the dermis and display focal sheet-like growth, moderate nuclear pleomorphism, and division figures (arrowhead).

strates the SLN metastasis identified in this patient. In 8 of 10 patients, the lesions were reviewed by at least 1 other dermatopathologist who concurred with the diagnosis. The remaining eight patients had slightly more varied diagnoses, and concordance could not be reached among the dermatopathologists at our institution. These lesions were interpreted as melanoma with Spitzoid features by at least one dermatopathologist; however, atypical, epithelioid, melanocytic proliferation/atypical Spitz tumor of uncertain biologic

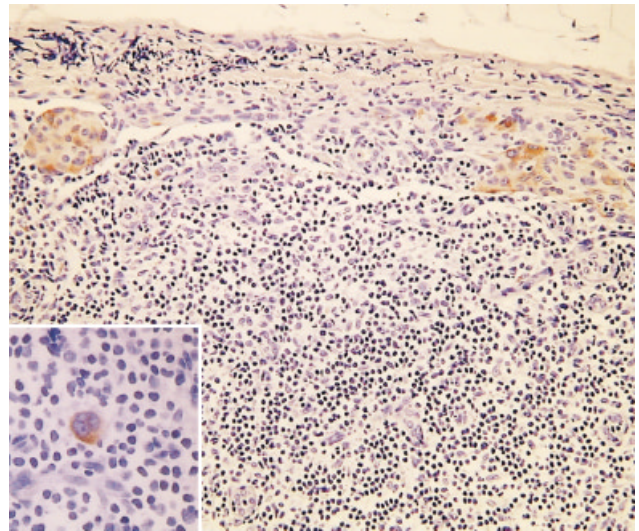


FIGURE 3. HMB-45-immunostained sections from Patient 8 show tumor cells lodged in the subcapsular sinus with a few scattered singly in the parenchyma (inset).

potential was favored by at least one other dermatopathologist. There was only one patient for whom a diagnosis of benign Spitz nevus was proposed (Patient 2). This lesion was classified as *Spitz nevus* by two highly experienced melanoma consultants outside of our institution. At our institution, one dermatopathologist favored melanoma, and another favored atypical Spitz tumor. Figures 4 and 5 demonstrate the Spitz-like and atypical features of this lesion. SLN metastasis was identified subsequently in this patient (Fig. 6).

SLN metastasis was identified in 8 of 18 patients (44%). In all eight patients with positive lymph nodes, tumor cells were found in the subcapsular sinuses and lymph node parenchyma. None of the 8 patients with positive lymph nodes had large metastases that partially or totally replaced the lymph node. Metastatic foci varied in size from 0.1 mm to 1.0 mm (Table 2). Immunostaining was required in all eight tumors, because the metastatic foci either were not detected in the H&E-stained sections (in 2 of 8 patients) or were few or small in size, requiring immunophenotypic distinction from sinus histiocytes or macrophage aggregates. Nonspitzoid, capsular nevi were found in 2 of 8 patients with positive lymph nodes and in 2 of 10 patients with negative lymph nodes (Table 1).

The mean age of patients with positive lymph nodes was 14 years (range, 5–29 years). The mean age of patients with negative lymph nodes was 23 years (range, 11–32 years). The mean Breslow depth for patients with positive lymph nodes was 2.85 mm (range, 1.3–4.0 mm). The mean Breslow depth for patients

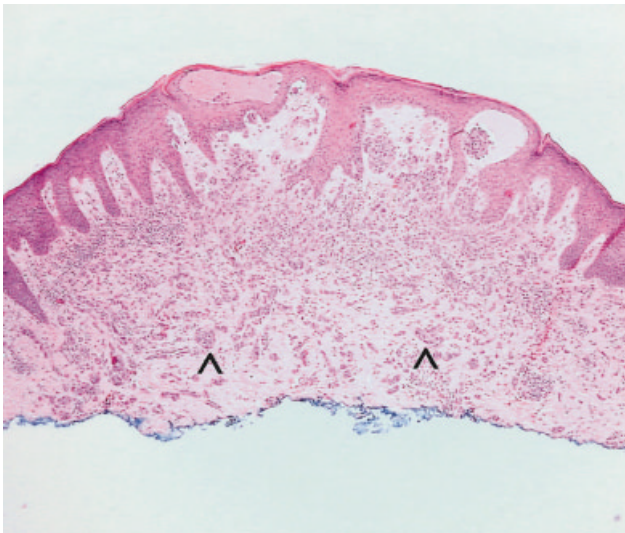


FIGURE 4. A controversial Spitz tumor (approximately 4 mm in greatest dimension) on scanning magnification from Patient 2 shows some histologic features of a classic Spitz nevus, including epidermal hyperplasia; a circumscribed, symmetrical, and somewhat wedge-shaped silhouette; and papillary dermal edema. An atypical finding (arrowheads) is the presence of nested melanocytes in the deep dermis intermingled with more dispersed melanocytes (*incomplete maturation/zonation*).

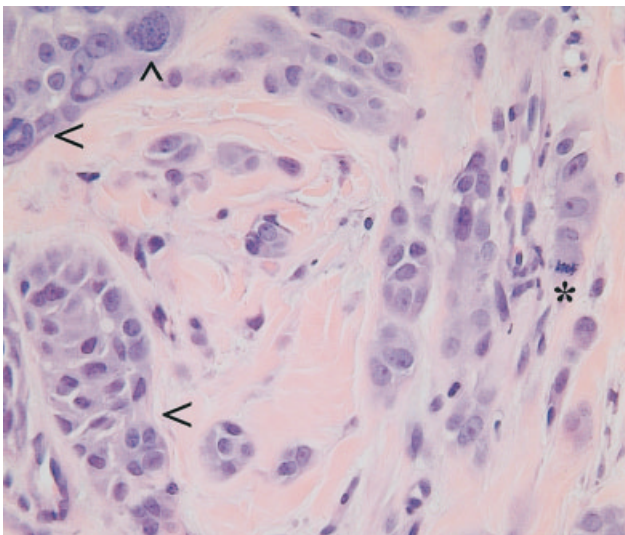


FIGURE 5. The controversial Spitz tumor from Patient 2 at high magnification displayed division figures in deep dermis (asterisk), nuclear pleomorphism (upward arrowhead), and large nests intermingled with more dispersed melanocytes (leftward arrowheads), indicating incomplete maturation/zonation.

with negative lymph nodes was 3.99 mm (range, 1.2–7.9 mm). The age, gender, site of the primary tumor, histologic diagnosis, and atypical histologic features observed did not appear to predict or predispose patients to lymph node metastasis. The histologic diag-

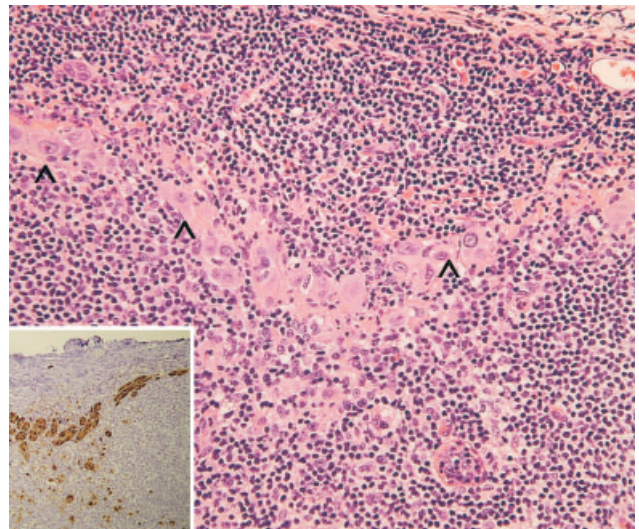


FIGURE 6. Atypical epithelioid melanocytes from Patient 2 are found in the substance of a sentinel lymph node in hematoxylin and eosin-stained sections (arrowheads) and in Melan-A and S100-immunostained sections (inset).

TABLE 2
Histologic Findings in Patients with Positive Sentinel Lymph Nodes

Patient	Size range (in mm) of metastatic deposit(s)	Immunostaining results			
		Routine H&E sections ^a	S100 ^b	Melan-A ^b	HMB-45 ^b
1	0.1–0.2	+	+	+	NR
2	0.5–0.9	+	+	+	+
3	0.3–1.0	+	+	+	+
4	0.1–0.2	—	+	+	—
5	0.1–0.8	+	+	+	—
6	0.3–1.0	+	+	+	+
7	0.1–0.2	—	NR	+	—
8	0.1–0.8	+	+	+	+

H&E: hematoxylin and eosin; NR: tumor not represented (indeterminate for immunostaining).

^a +: Tumor detected in H&E sections;—: tumor not detected in H&E sections.

^b +: Tumor positive for immunostaining;—: tumor negative for immunostaining.

nosis rendered in six of eight patients with positive lymph nodes was atypical Spitz tumor/atypical epithelioid melanocytic proliferation of uncertain biologic potential. In the other two patients, a consensus in diagnosis could not be reached, and melanoma was favored by at least one dermatopathologist. In five of eight patients with positive lymph nodes, one SLN contained tumor, whereas in three of eight patients with positive lymph nodes, two SLNs were involved. All patients with a positive SLN underwent therapeutic lymph node dissection (TLND). One additional non-SLN in one patient (13%) (Patient 5) was positive for metastatic melanoma.

All eight patients with positive lymph nodes were

offered adjuvant treatment. Two patients received investigational melanoma vaccines at other institutions, and six patients received interferon- α 2b. All patients were without evidence of recurrent disease, in remission, at 3–42 months of follow-up (mean, 12 months).

DISCUSSION

The concept that spindle and epithelioid, melanocytic proliferations display morphologic features in a histologic continuum, with benign Spitz nevus at one end and Spitz-like melanoma at the other, has been accepted by many investigators.^{6,7,20} The reports of widely metastasizing disease from lesions not histologically discernible from banal Spitz nevi^{21–23} support this concept of a phenotypic continuum and underscore the point that the accurate diagnosis of melanoma with Spitzoid features can be problematic, even for the most experienced dermatopathologist.

The stereotypic benign Spitz nevus^{20,24,25} is domed shaped, symmetrical in silhouette, laterally well marginated, and consists of large spindle and epithelioid melanocytes uniformly arrayed as nests along the junction of hyperplastic epidermis. Artifactual clefts may form around junctional nests. Eosinophilic Kamino bodies commonly are deposited along the dermoepidermal interface. Dermal melanocytes mature with descent into the dermis and lack significant pleomorphism and deep mitotic activity. A melanocytic lesion with this appearance is recognized readily as a benign Spitz nevus, as are other tumors that deviate only slightly from this stylized depiction.

At the other end of the histologic continuum are spindle and epithelioid melanocytic proliferations that retain some histologic attributes of Spitz nevus, but the preponderance of features are those of conventional melanoma. Piepkorn cites as worrisome findings high-grade nuclear atypia, high mitotic rate with deep dermal mitoses or atypical mitoses, no or only focal maturation at the base, deep penetration into lower dermis or subcutis, ulceration, and large lesional size.²⁰ Other authors have cited similar criteria, as well as other criteria, for the diagnosis of Spitz-like melanoma, such as marked pagetoid spread,²⁶ single-cell epidermal invasion below parakeratosis,²⁷ asymmetry,⁵ destruction of collagen,³ substantial and/or deep melanization,²¹ and variability of cellular features between adjacent cell groups.⁴ Reed proposed that confluent or expansile, nodular aggregates of atypical Spitz-like cells in the dermis represent a *vertical growth phase* or possess a competence for metastasis and are regarded best as minimal deviation melanoma, Spitz-like type.⁹ Dermatopathologists generally agree that no single histologic finding is diagnostic in and of itself for Spitz nevus or Spitz-like

melanoma. Rather, the diagnosis depends on the assessment of multiple histomorphologic features and often requires clinical correlation.^{3,28–30} If a spindle and epithelioid melanocytic tumor demonstrates many or most of the above-cited atypical or worrisome histologic features, then it is recognizable as Spitz-like melanoma.

Spindle and epithelioid melanocytic proliferations that fall in the central portion of the histologic continuum, variously termed *atypical Spitz nevus*, *atypical Spitz tumor*,^{6,7,20} *diagnostically controversial Spitzoid melanocytic tumors*,⁸ and Spitz-like lesion in the *borderline category of indeterminate malignant potential*,⁹ defy classification as Spitz nevus or Spitz-like melanoma.^{2,6–9} These melanocytic lesions deviate substantially from the stylized depiction of Spitz nevus, retaining some attributes of classic Spitz nevus but also exhibiting a few or several findings for melanoma. All 18 patients in this study had spindle and/or epithelioid melanocytes and at least 2 other features of classic Spitz nevus. The most notable atypical histologic features were incomplete maturation, deep dermal mitoses, nuclear pleomorphism, and focal sheet-like growth.

Histologic criteria for the diagnosis of atypical Spitz tumors have been proposed,^{7,30} but the tumors nevertheless cause diagnostic controversy when they are evaluated by dermatopathologists because of interobserver variation in the interpretation and in the application of criteria.² The obvious concern is the accurate diagnosis of lesions that are melanoma. At a minimum, lesions that are potentially *higher risk*, *borderline*, or of *indeterminate biologic potential* need to be identified. In the current study, we were able to achieve some consensus in recognizing an atypical Spitz tumor/atypical, epithelioid, melanocytic proliferation of uncertain biologic potential. This diagnosis was rendered in 10 of 18 patients. In the other eight patients, one or more dermatopathologist favored a diagnosis of melanoma. The most striking example of discordance in diagnosis was for Patient 2 (Fig. 4), for whom the diagnoses ranged from wholly benign to malignant, all of which were rendered by highly experienced dermatopathologists with expertise in pigmented lesions.

In light of the controversy surrounding the histologic diagnosis of problematic atypical spitzoid melanocytic lesions and, as discussed above, the likelihood that some represent melanomas, ancillary diagnostic techniques that may be better at discriminating benign lesions from malignant melanocytic lesions are needed greatly. Immunohistochemical staining with Ki-67,^{31–34} Ki-67 and *bcl-2*,³⁵ and proliferating cell nuclear antigen^{36,37} has shown some promise in discrim-

inating melanoma from benign nevi, including Spitz nevi. In situ hybridization to detect expression of melastatin,³⁸ a melanocyte specific gene that is expressed in melanoma at levels inversely proportional to metastatic rates, is useful in predicting metastasis and disease free survival in adult patients with melanoma³⁹ and may be useful in predicting which atypical spitzoid lesion may be malignant. DNA in situ hybridization using a chromosome-1 centromere probe on routinely processed paraffin sections reportedly showed a clear difference in the number of aberrant (aneuploid) nuclei between Spitz nevi and melanoma.⁴⁰ When it was applied to five problematic Spitz tumors that initially were misdiagnosed as Spitz nevi and that metastasized later, the technique retrospectively identified three of five tumors as melanoma.⁴⁰ Recently, Bastian et al., employing the technique of comparative genomic hybridization, observed no chromosomal aberrations in 13 of 17 Spitz nevi and found gains in the p arm of chromosome 11 or chromosome 7q21-qter in the remaining 4 Spitz nevi.⁴¹ Because melanoma reportedly shows frequent deletions of chromosomes 9p, 10q, 6q, 8p and gains of chromosomes 7, 8, 6p, and 1q, this technique may be applied to diagnostically difficult and controversial spitzoid lesions to determine which tumors have cytogenetic findings of melanoma or Spitz nevus.⁴¹ Although these techniques are promising, they require further testing. Currently, no single technique has been found that unequivocally discriminates among these borderline lesions; and, clearly, light microscopy alone has its limitations.

We are in strong agreement with the proposal by Kelley and Cockerell that, in select patients, SLNB is a useful adjunct in the management of histologically difficult melanocytic lesions that measure ≥ 1.0 mm in thickness.¹⁶ The most powerful predictor of overall survival for melanoma is the status of the regional lymph nodes. IOLM and SLNB are procedures with low morbidity and are highly accurate for staging the entire regional lymph node basin, sparing patients with negative SLNB results the morbidity of undergoing TLND. In addition, patients with positive SLNB results are candidates for early intervention with potentially lifesaving TLND and adjuvant therapy, such as interferon- α 2b. In keeping with criteria for the diagnosis of metastatic melanoma in SLNs,⁴² if atypical melanocytic cells are identified in the parenchyma or subcapsular sinuses of the SLN(s), then the atypical or controversial, spitzoid, melanocytic lesion should be reclassified as melanoma.^{8,13} Although a negative SLNB result does not exclude melanoma, it offers some reassurance to patients that their tumor may be confined to the skin. In this way, results of SLNB may

identify high-risk patients who require closer surveillance and who may benefit from additional therapy. In the current study, 8 of 18 patients (44%) with atypical spitzoid melanocytic lesions were reclassified as melanoma based on positive SLNB results. These results were comparable to those observed in another study in which 5 of 10 (50%) diagnostically controversial spitzoid tumors metastasized to SLNs.⁸

The presence of a positive SLN(s) supports a diagnosis of melanoma in these problematic spitzoid melanocytic lesions. Because it is recognized that certain benign tumors, such as cellular blue nevi, may be found in regional lymph node parenchyma and subcapsular sinuses,⁴³⁻⁴⁵ some investigators have argued that finding metastatic deposits of Spitz-like tumor in an SLN is not sine que non evidence of metastatic melanoma. It has been suggested that these deposits in the parenchyma and subcapsular sinuses of the lymph node may represent *lymph node Spitz nevi* and not metastatic melanoma.⁴⁶ Investigators have made some strides in an attempt to clarify this contentious issue. Cytogenetic analyses of limited numbers of atypical or controversial Spitz tumors that metastasize to lymph nodes have documented cytogenetic abnormalities more in keeping with melanoma and not seen in Spitz nevus. Smith et al. performed cytogenetic analysis on an atypical Spitz tumor from the right cheek of a girl age 18 months that metastasized to an ipsilateral lymph node in the submandibular area.¹² Karyotypes of both the primary tumor and the metastatic tumor deposit yielded an abnormal chromosome 6, with deletion of a portion of the normal long arm of chromosome 6 and replacement by chromosomal material of unknown origin: findings most consistent with melanoma.¹² De Wit et al. performed DNA in situ hybridization using a chromosome-1 centromere probe on 15 Spitz nevi, 15 typical melanomas, and 5 problematic Spitz tumors that were classified initially as Spitz nevus and that later metastasized or displayed a malignant phenotype on recurrence.⁴⁰ In three of five problematic Spitz tumors and in many of the typical melanomas, those authors demonstrated supernumerary aberrations of chromosome 1 suggestive of aneuploidy, whereas Spitz nevi were euploid.⁴⁰ When these findings are coupled with reports of atypical, controversial, or problematic Spitz tumors disseminating with a lethal outcome,^{2,7,14,15,26,47-49} it is completely reasonable and tenable to regard an atypical Spitz tumor found in the lymph node parenchyma as biologically malignant.

The high frequency of metastasis observed in our study (44%) and in another study (50%)⁸ is disturbing but not unexpected. For melanoma measuring 2-4 mm in tumor thickness, occult metastatic disease

ranges from approximately 40% to 50%.⁵⁰ The rate of positivity for SLNB increases as the tumor thickness increases from < 5% for melanoma measuring < 1 mm thick to 30–50% for tumors measuring > 4.0 mm thick. The tumors in this study had a mean Breslow depth of 3.5 mm (range, 1.2–7.9 mm) with a metastatic rate of 44%. These results are very compatible with what is known about the behavior of melanoma. Because of our limited follow-up period (mean, 12 months), little can be said at this time regarding the biologic significance of a positive SLN in this subset of patients. We are in complete agreement with Lohmann et al. that long-term follow-up of these patients is necessary before we know where these lesions fall within the spectrum of conventional melanoma.⁸

What should not be missed from this discussion is acknowledgement of our patients' ages (mean, 16 years) and a clear-cut understanding that SLN metastases were identified in young children. The mean age of patients with positive SLNs was 14 years, including 1 child age 5 years, 2 children age 8 years, 1 child age 10 years, and one child age 12 years. It has been a long regarded axiom that melanoma in children is exceedingly rare. Accordingly, dermatopathologists are cautious in rendering a diagnosis of melanoma in children and adolescents. It is of paramount importance to recognize that atypical borderline melanocytic proliferations do occur in this subset of patients and that some of these lesions, in fact, are melanomas.

In summary, atypical spitzoid melanocytic proliferations are diagnostically challenging and controversial melanocytic lesions. For lesions that measure > 1 mm in Breslow depth for which a consensus in diagnosis cannot be reached among expert dermatopathologists and in which it is felt that the biologic potential of the lesion is uncertain and/or melanoma cannot be excluded, SLNB should be considered as a useful adjunct in patient management because of the diagnostic and prognostic information it provides. The utility of SLNB for patients with problematic spitzoid melanocytic lesions ultimately may have its greatest clinical relevance when it comes to the management of younger patients. A younger age alone should not dissuade physicians from evaluating SLNs in the context of a problematic or diagnostically challenging spitzoid lesion, because some of these lesions, in fact, are melanomas. It is unclear whether this class of tumors is a homogenous population that behaves like conventional melanoma or behaves differently. Unraveling the biologic nature of atypical spitzoid melanocytic lesions will require long-term surveillance of patients and further study with new molecular diagnostic techniques. Until such results are available, atypical spitzoid melanocytic lesions that

metastasize to SLNs are best regarded as melanomas. Results of SLNB can clarify the diagnosis and aid in selectively directing therapy and management.

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