Original Article

The Atypical Spitz Tumor of Uncertain Biologic Potential

A Series of 67 Patients From a Single Institution

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BACKGROUND: Atypical Spitz tumors (AST) are rare spitzoid melanocytic proliferations with an uncertain malignant potential. ASTs have overlapping features of both Spitz nevi and spitzoid melanoma, and consequently generate controversy with diagnosis and management. Sentinel lymph node biopsy (SLNB) has been proposed as a possible means to gain additional insight into the true biologic potential of these tumors; however, previous reports on the use of SLNB in ASTs have been limited by small numbers of patients and short durations of follow-up. **METHODS:** The authors extracted data from their institution's prospective melanoma database, collected between 1994 and 2007, for all patients with ASTs of uncertain biologic potential. They reviewed the clinical features of these patients, including the sentinel lymph node status, and the histological features of the tumors. **RESULTS:** A total of 67 patients with ASTs were identified, with a median age of 23.7 years. The mean depth was 2.4 mm. Of these, 57 had a SLNB performed, with 27 (47%) having a positive sentinel lymph node. SLNB-positive cases had a significantly lower mean age than SLNB-negative cases (17.9 vs 28.7 years; $P = .013$); however, no other significant differences were observed. All 27 patients with a positive SLNB were alive and disease free with median follow-up of 43.8 months. One patient who did not receive a SLNB developed recurrent disease with regional and distant metastases. **CONCLUSIONS:** ASTs do not appear to behave like conventional melanoma. There is a high incidence of microscopic lymph node deposits in SLNBs, but despite this finding, patients have a favorable prognosis. Our findings raise several questions regarding the malignant potential of ASTs, and the role of SLNB in their management. **Cancer 2009;115:631–41. © 2009 American Cancer Society.**

KEY WORDS: atypical Spitz tumor, Spitz nevus, melanoma, sentinel lymph node biopsy.

Although most spitzoid melanocytic proliferations can be identified as either benign Spitz nevus or spitzoid melanoma, a rare subset that is difficult to classify histologically also exists. These lesions contain intermediate histologic features seen in both benign Spitz nevi and malignant melanoma, and subsequently generate considerable uncertainty regarding their biological potential. These equivocal borderline lesions were previously designated as malignant spindle and epithelioid cell nevi, malignant Spitz nevi,

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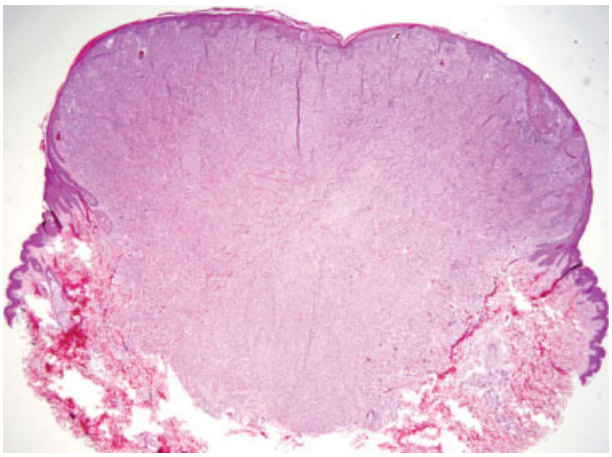

FIGURE 1. An atypical Spitz tumor of uncertain biologic potential from a 11-year-old girl is shown, with a Breslow depth of 7.9 mm with a negative sentinel lymph node biopsy. At scanning magnification, the lesion is symmetrical, being well circumscribed with a wedge-shaped silhouette, an expansile bulging growth pattern and pushing borders at the base.

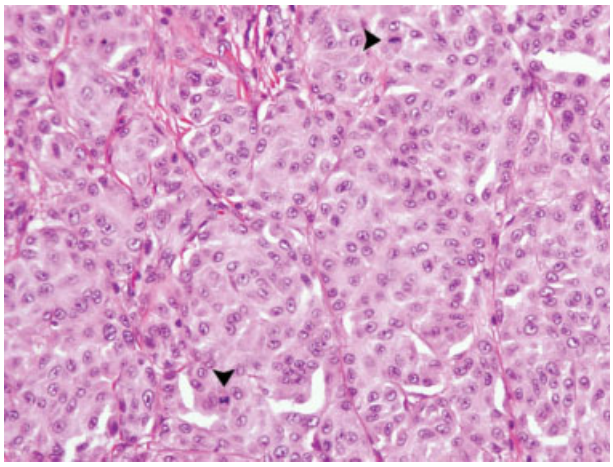

FIGURE 2. A section from the mid-dermis at high power in the same patient as in Figure 1 shows epithelioid melanocytes in a sheet-like growth pattern with deep mitoses present (arrowheads).

diagnostically controversial spitzoid melanocytic tumors, atypical epithelioid melanocytic proliferations of uncertain biologic potential, and atypical Spitz tumors.[1-4] We currently favor the term atypical Spitz tumor of uncertain biologic potential (AST) to describe such lesions (Figs. 1 and 2).

Previous attempts to characterize ASTs histologically have identified several features, including: large size (often >10 mm diameter), asymmetry, poor circumscription, ulceration, deep growth often into subcutaneous fat, greater degree of cytological atypia than seen in Spitz nevi with significant nuclear pleomorphism, aberrant or sheet-like dermal growth pattern with a high cellular density, lack of maturation with increasing depth, and the presence of deep dermal mitoses.[5] However, many of these features are also seen in spitzoid melanoma, and subsequently the diagnosis is based on the assessment of the severity and frequency of multiple histopathological factors with clinicopathological correlation. Given the lack of definitive diagnostic features, considerable disagreement exists with little consensus among expert dermatopathologists and clinicians regarding both diagnosis and clinical management.[6]

The difficulty and disagreement with diagnosis, and the resulting uncertain biologic behavior and clinical management, create considerable confusion for the patient and the treating physician. This is further complicated because often patients with AST are young, with a lower likelihood of developing melanoma. Although ASTs have generally been reported to have a good prognosis, there are well-documented cases of metastasis and death.[5,7] Because the malignant potential of ASTs remains uncertain, most clinicians and patients decide to treat more aggressively to avoid undertreating a potentially lethal lesion. ASTs are generally treated in a similar manner to melanoma, with a wide excision of the primary lesion, and in many cases a sentinel lymph node biopsy (SLNB).

The use of SLNB in atypical spitzoid melanocytic proliferations has been reported in a total of 78 patients.[4,8-16] Although it is unclear whether all of these reports have included lesions that would be classified as ASTs, they are all likely to be controversial and would generate differing opinions regarding their malignant potential. Of the 78 patients, 31 had a positive SLNB (39%). Although there are previous reports of atypical spitzoid melanocytic proliferations resulting in metastasis and death, all 31 patients with a positive SLNB were alive and disease free, with a mean follow-up of 29 months. These prior studies suggest a good prognosis even with a positive SLNB, but reported follow-up is relatively short, precluding definite conclusions.

At our institution, we have typically treated ASTs ≥1 mm in depth or 0.75 to 0.99 mm with other adverse

features, such as a high mitotic rate or ulceration, with wide local excision and SLNB. It was once thought that the SLNB status would provide useful information and insight that may help better assess the true biologic potential of these tumors and allow for better counseling and subsequent therapy.[17] Our objective was to describe our experience with ASTs, including the use of SLNB. This series, which is the largest with the most complete long-term follow-up reported to date, provides a unique opportunity to re-evaluate what a positive SLNB means in this context and to propose a therapeutic algorithm for management of these problematic lesions.

MATERIALS AND METHODS

Study approval was obtained from the institutional review board of the University of Michigan Medical School. We queried our prospectively collected melanoma database for all cases of spitzoid melanocytic proliferations between 1994 and 2007. The medical records were reviewed, and those with a diagnosis of an atypical Spitz tumor or spitzoid melanocytic proliferation of uncertain biologic potential were selected for analysis. The diagnosis was rendered by at least 1 of our 4 board-certified dermatopathologists, and each diagnosis was recorded. If a diagnosis was given by a dermatopathologist outside our institution who had recognized expertise in melanocytic pathology, their diagnosis was recorded as well. We extracted clinical parameters from the medical record, including: age, sex, family history of melanoma, history of immunosuppression, prior severe sunburns, history or presence of dysplastic nevi, lesion location, lesion color and shape, SLNB status if performed, complete lymph node dissection (CLND) status if performed, and any adjuvant therapy used. Histopathologic parameters recorded included: the lesion depth, Clark level, presence of nuclear pleomorphism, presence of deep dermal or marginal mitoses, incomplete maturation, and confluent or aberrant dermal growth pattern. In patients who had an SLNB performed, location, number of positive and negative nodes, status of hematoxylin and eosin (H&E) stained sections, S-100 and Melan-A immunostaining on the SLNB, and presence or absence of capsular nodal nevi were recorded. The positive SLNB slides were retrieved and reviewed by 1 board-certified dermatopathologist. Location of the tumor deposit (subcapsular, parenchymal, or both), size expressed in percentage of the lymph node surface area (<1%, 1%-10%, >10%), largest dimension of the largest deposit in millimeters (<0.2 mm, 0.2-2 mm, >2 mm), number of cells within the largest aggregate (<10, 10-50, >50 cells), cell morphology (epithelioid, spindle or both), presence of pigmentation, and presence and morphology of capsular nevi were recorded. Because mitotic figures within the SLN tumor deposit were rare, a formal mitotic count was not performed. To perform further analysis on the SLN characteristics, if the patient had more than 1 positive SLN, the most severe or largest variable was used. The SLNB technique and the method of SLN evaluation have been described previously.[18,19] If a CLND was performed, location and number of positive and negative nodes were recorded. Follow-up data were obtained from the medical record or by contacting the patient or the referring physician to obtain the most current disease status.

Statistical Analysis

The Wilcoxon rank sum test was used to assess the association between a continuous variable (such as age at diagnosis) and a 2-level categorical variable (such as SLNB status). The Kruskal-Wallis statistic was used to test the association between a continuous variable and a categorical variable with more than 2 levels. The chi-square and Fisher exact test were used to assess the association between categorical variables, as appropriate. The Spearman rank correlation coefficient was used to assess the association between continuous and ordered variables. Overall survival was defined as the time to either last follow-up or death from any cause. Time to recurrence was defined as time to recurrence of the atypical Spitz tumor, and subjects whose tumor did not recur were censored. Survival estimates were calculated using the Kaplan-Meier method. A P value of .05 or less is considered to be statistically significant, and all of the tests are 2-sided.

RESULTS

The clinical and histopathological features are summarized in Table 1. We identified 67 patients from January 1994 to August 2007 with a diagnosis of an AST. The median age of the patients was 23.7 years, ranging from 1.7 to 65 years. Forty-one patients were female, 26 were male. The most common location of the primary lesion was the

Table 1. Clinical and Pathologic Features of Patients With Atypical Spitz Tumors

	Total	Age ≤20 y	Age >20 y
Sex			
Female	41	17	24
Male	26	18	8
Color			
Pink/red	34	19	15
Brown/back	17	8	9
Other	5	2	3
Unknown	11	6	5
Lesion shape			
Raised	46	27	19
Flat	3	1	2
Unknown	18	7	11
Location			
Head and neck	19	12	7
Trunk	15	9	6
Arms	11	5	6
Legs	20	9	11
Feet	2	0	2
Breslow depth, mean mm	**2.4**	**2.6**	**2.1**
Clarks Level			
II	3	0	3
III	4	1	3
IV	33	16	17
V	2	2	0
Unknown	25	16	9
Pleomorphism			
Present	24	13	11
Absent	33	14	19
Unknown	10	8	2
Dermal mitoses			
Present	47	25	22
Absent	3	1	2
Unknown	17	9	8
Maturation with depth			
Present	35	19	16
Absent	26	11	15
Unknown	6	5	1
Aberrant growth pattern			
Present	28	15	13
Absent	39	20	19
Unknown	0	0	0

leg (30%), followed closely by the head and neck (28%), trunk (22%), arm (16%), and foot (3%). The majority of the lesions were amelanotic with a pink or red color (51%), and the primary lesion was raised in 69% of cases. The original lesion was congenital in 4 patients (6.0%).

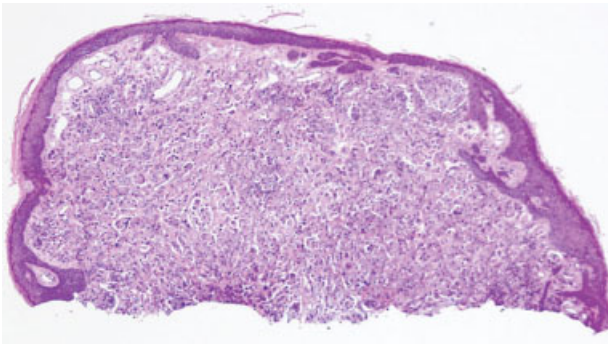

FIGURE 3. An atypical Spitz tumor of uncertain biologic potential from a different 11-year-old girl is shown, with a Breslow depth of 1.45 mm. The sentinel lymph node biopsy was positive, with <1% surface area involved. The lesion is well circumscribed and symmetrical, yet lacks maturation.

A positive family history of melanoma was present in 8 patients (12%); none was immunosuppressed. A history of prior blistering or peeling sunburn was reported in 43 (64%), and 41 (61%) had Fitzpatrick skin types I-III. The majority of patients had no history of dysplastic nevi (94%), nor clinical presence of dysplastic nevi (78%).

Fifty-nine of the 67 cases were reviewed by 2 or more UM dermatopathologists, with 25 reviewed by 2 dermatopathologists, 32 by 3, and 2 by 4. A concordant diagnosis was reached in 38 (64%). Of the 21 (36%) cases with discordance, the alternative diagnoses included atypical Spitz nevus in 35% and spitzoid melanoma in 65%. The depth ranged from 0.3 mm to 8 mm (mean, 2.4 mm). The Clark level was recorded for 42 patients; 33 were Clark level IV (49%). Nuclear pleomorphism was present in 24 (36%) cases, deep dermal or marginal mitoses were present in 47 (70%), lack of maturation with increasing depth in 35 (52%), and an aberrant dermal growth pattern in 28 (42%) (Figs. 1-6)

The clinical management is summarized in Figure 7. Six patients had primary lesions with a depth <1 mm, or 0.75 to 0.99 mm with no other adverse features, and were treated with wide local excision (WLE) alone, usually with a 1-cm margin. The remaining 61 patients had lesions that were considered to be suitable for SLNB counseling, with depth of ≥1 mm, or 0.75 to 0.99 mm with other adverse features such as the presence of ulceration, a high mitotic rate, or a young age.[19,20] Of these 61 patients, 57 underwent wide local excision and SLNB, whereas 4 received wide local excision alone. One of the 4 WLE-only group was an 18-month-old infant

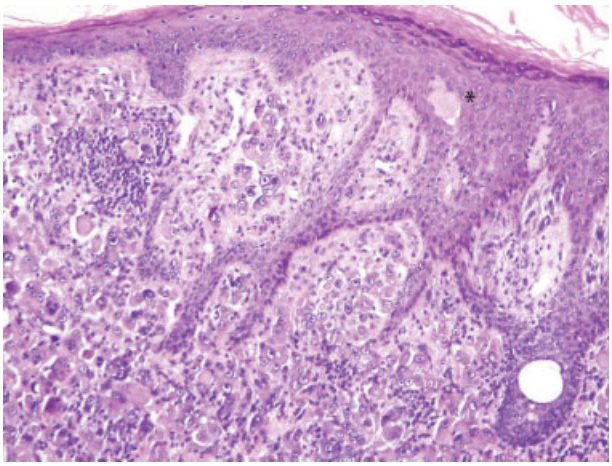

FIGURE 4. At high power, the junctional component from the same patient as in Figure 3 shows some features seen in typical Spitz nevi, with epidermal hyperplasia and Kamino bodies (asterisk)

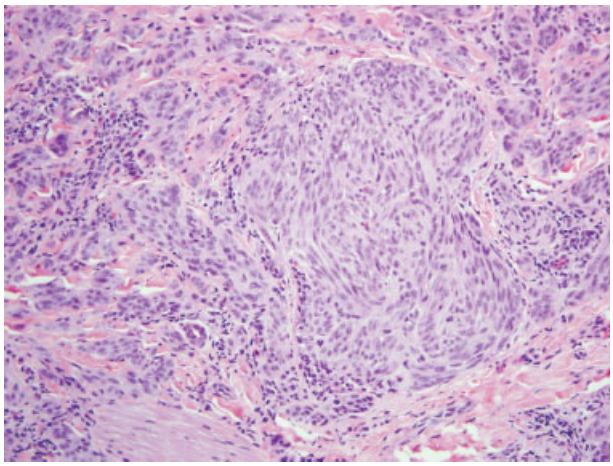

FIGURE 6. Spindle and epithelioid melanocytes in the deep dermis of the same patient as in Figure 5 show slight nuclear pleomorphism, a sheet-like growth pattern, and lack of maturation.

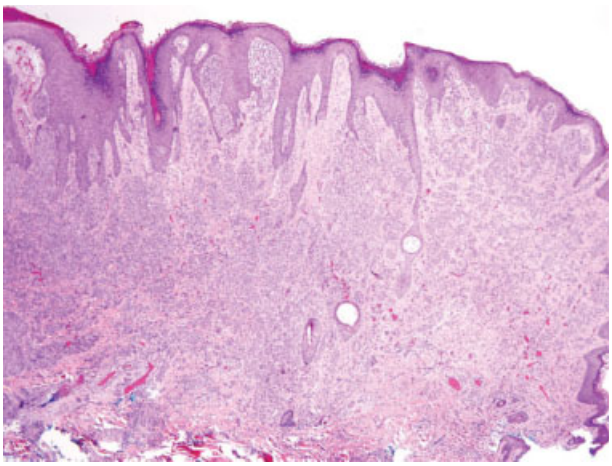

FIGURE 5. An atypical Spitz tumor of uncertain biologic potential from an 8-year-old boy is shown, with a Breslow depth of 3 mm. The sentinel lymph node biopsy was positive, with effacement of the lymph node. At scanning magnification, there are some Spitz nevus-like features, with good circumscription, epidermal hyperplasia, and mild dermal papillary edema.

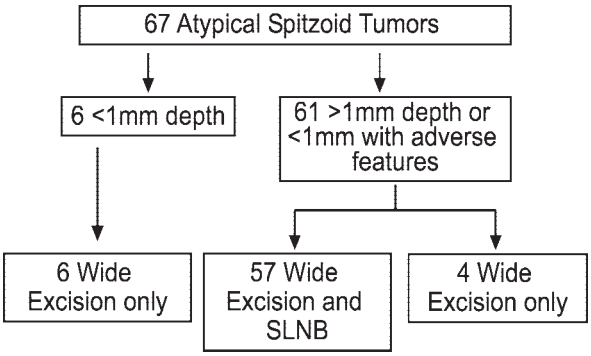

FIGURE 7. Clinical management of patients with atypical Spitz tumor of uncertain biologic potential is represented. Adverse features considered include: ulceration, high mitotic rate, and young age. SLNB indicates sentinel lymph node biopsy.

whose parents decided against performing a SLNB after discussion of the potential benefits and risks of the procedure. Of the remaining 3 WLE-only group, all were treated at a different institution, and 2 of these were lost to follow-up.

Figure 8 summarizes the SLNB findings. A positive SLNB was identified in 27 (47%) of 57 who received a SLNB. Of these 27, 17 had deposits present in 1 SLN, 7 had deposits in 2 SLNs, and 3 had deposits in 3 SLNs.

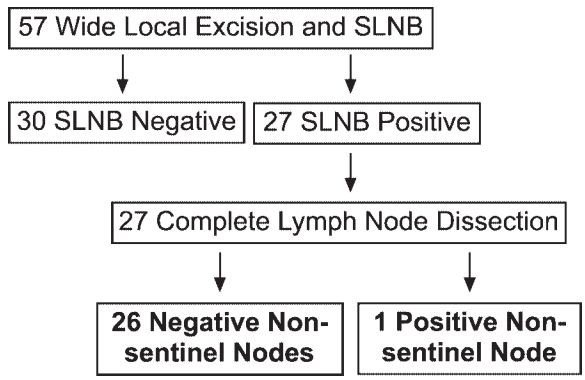

FIGURE 8. An overview is shown of the sentinel lymph node biopsy findings and subsequent lymph node dissection. SLNB indicates sentinel lymph node biopsy.

Table 2. Histological Features of Positive Sentinel Lymph Nodes

SLN Parameter	Frequency	Percentage (%)
Location within lymph node		
Subcapsular sinus	15	41%
Parenchymal	11	30%
Subcapsular and parenchymal	11	30%
Cell morphology		
Epithelioid	25	68%
Spindle	0	0%
Epithelioid and spindle	12	32%
Pigmentation		
Present	10	27%
Absent	27	73%
Surface area of lymph node involved		
<1%	31	84%
1%-10%	5	14%
>10%	1	3%
Size of largest tumor aggregate		
<0.2 mm	23	62%
0.2-2 mm	13	35%
>2 mm	1	3%
Only isolated tumor cells present		
Yes	7	19%
No	30	81%
Size of largest tumor aggregate (total number of cells)		
<10 cells	18	49%
10-50 cells	12	32%
>50 cells	7	19%
Capsular nevus		
Ordinary morphology	2	5%
Spitzoid morphology	1	3%
None	34	92%

SLN indicates sentinel lymph node.

Additional negative SLNs obtained at the time of SLNB, ranging from 1 to 4 in number, were removed in 17 patients (63%). All 27 with a positive SLNB underwent a CLND of the involved regional nodal basin. One (4%) patient had 1 additional non-sentinel lymph node deposits.

The microscopic SLN deposits were visible using H&E staining in 23 (85%) patients. Of the remaining 4 with a negative H&E but positive immunostaining, S-100 and Melan-A were both positive in 3, and Melan-A was positive alone in 1. Benign capsular nodal nevi were present in 8 (14%) patients. A total of 37 of the 40 positive SLNBs were available for histological review, and their findings are summarized in Table 2. SLN tumor deposits were more frequently located in the subcapsular sinus (41%) than the parenchyma (30%) or both locations (30%). Most of the SLN deposits had an epithelioid cell morphology (68%), and were not pigmented (73%). The majority of the SLN deposits had an atypical cytological appearance similar to the primary cutaneous lesion, with abundant cytoplasm and prominent nucleoli. Most of the SLN tumor deposits were small, with 84% involving $<1\%$ of the surface area of the SLN, 62% being <0.2 mm in size, and 49% containing <10 cells (Fig. 9). One patient had a SLN deposit involving greater than 10% of the lymph node surface area (Fig. 10). Only 3 of the positive SLNs contained nodal nevi, with 1 having a spitzoid morphological appearance. There were no significant associations found between the patient and primary tumor characteristics and the various positive SLN variables. A trend was observed with a younger age at diagnosis

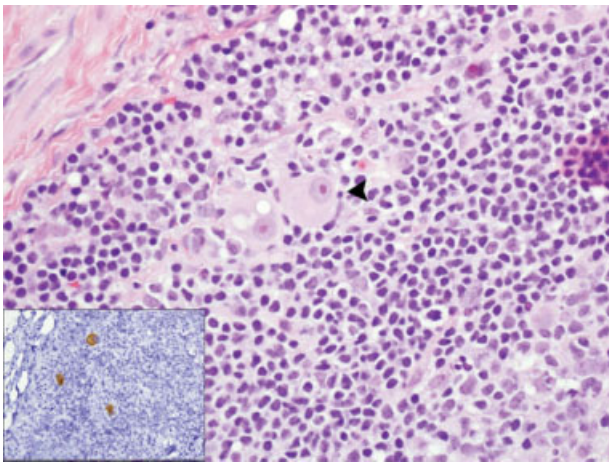

FIGURE 9. A few atypical epithelioid melanocytes within the parenchyma of the sentinel lymph node from the same patient as in Figure 3 are visible on hematoxylin and eosin (arrowhead) and with positive Melan-A immunostaining (inset).

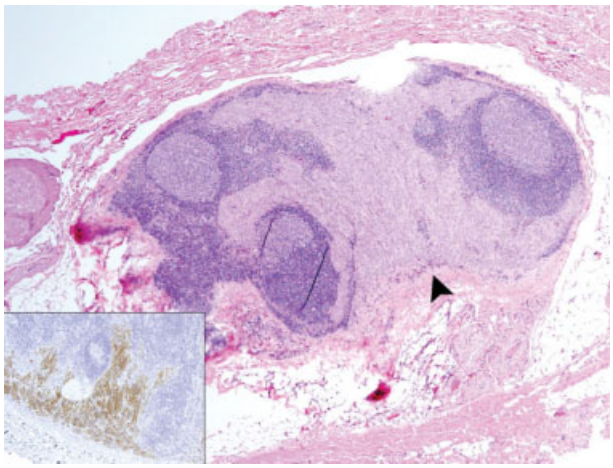

FIGURE 10. Spindle and epithelioid melanocytes involve >10% of the lymph node and partially efface the sentinel lymph node parenchyma (arrowhead), with Melan-A immunostain section (inset) from the same patient as in Figures 5 and 6.

being associated with an epithelioid and spindle cell morphology; however, this did not reach statistical significance ($P = .073$).

The differences between the SLNB-positive and -negative groups are summarized in Table 3. Seventeen (63%) of 27 patients with a positive SLNB were female; 10 (37%) were male. Seventeen (57%) of 30 patients with a negative SLNB were female; 13 (43%) were male. The depth of the positive SLNB group ranged from 1.1 to 8 mm (mean, 2.9 mm), whereas the negative SLNB group ranged from 0.8 to 5.5 mm (mean, 2.3 mm). No significant differences were seen between SLNB-positive and -negative cases in the frequency of nuclear pleomorphism (41% vs 33%), deep dermal mitoses (63% vs 80%), lack of maturation with increasing depth (48% vs 63%), and aberrant dermal growth pattern (41% vs 43%). Patient age was found to be the only significant difference between the 2 groups, with SLNB-positive cases having a mean age of 17.9 years (range, 2.9-50.1 years) and SLNB-negative cases 28.7 years (range, 2.3-65.3 years) ($P = .013$). Adjuvant therapy was administered to 24 (89%) of the 27 patients with a positive SLNB. Adjuvant interferon-α2b was used in 23, and an adjuvant vaccine was used in 1. One patient with a negative SLNB received adjuvant interferon-α2b at a different institution.

The Kaplan-Meier estimated median follow-ups were as follows: for the SLNB-positive group it was 43.8 months (range, 32.4-57.3 months), for the SLNB-negative group it was 28.6 months (range, 19.8-47.0 months), and for the WLE-only group it was 32.5 months (range, 7.1-57.0 months). All patients in the SLNB-positive and -negative groups were alive and disease free at the last point of follow-up. One patient who was a candidate for an SLNB but was treated with wide excision alone developed recurrent disease with regional and distant metastases, and died from disease. Seven of 9 treated with wide excision alone were alive and disease free, with 2 treated at an outside institution lost to follow-up.

The only case of recurrent disease occurred in a 46-year-old woman treated with WLE alone at a different institution. She was diagnosed with a Spitz nevus by 3 dermatopathologists at an outside facility. The lesion was excised, but extended to 1 peripheral margin, and close observation was recommended. She was seen at our institution 2 years after her excision, presenting with a palpable left inguinal lymph node metastasis. The original biopsy was reviewed and interpreted as an atypical Spitz tumor with a depth of 1.1 mm. She was treated with a CLND and adjuvant interferon. She subsequently developed brain and lung metastases and died from disease approximately 3 years after initial diagnosis.

DISCUSSION

In this analysis of ASTs, we observed a high incidence of positive SLNB (47%). Despite this high incidence, within the total cohort, only 1 case of recurrent disease was

Table 3. Analysis of Differences Between SLN-Positive and -Negative Cases

	Total	SLN+	SLN−	*P* Value*
Number	**57**	**27**	**30**	
Sex				.79
Female	34	17	17	
Male	23	10	13	
Age, y	**23.7**	**17.9**	**28.7**	**.013**†
Breslow depth, mean mm	**2.4**	**2.9**	**2.3**	**.13**†
Clark level				.076
III	3	0	3	
IV	31	14	17	
V	2	2	0	
Unknown	21	11	10	
Pleomorphism				>.99
Present	21	11	10	
Absent	27	13	10	
Unknown	9	3	6	
Dermal mitoses				.57
Present	41	17	24	
Absent	3	2	1	
Unknown	13	8	5	
Maturation with depth				.40
Present	32	13	19	
Absent	20	11	9	
Unknown	5	3	2	
Aberrant growth pattern				>.99
Present	24	11	13	
Absent	33	16	17	
Unknown	0	0	0	

SLN indicates sentinel lymph node.
All *P* values are calculated excluding the unknown category.
* Fisher exact test unless noted otherwise.
† Calculated using Wilcoxon rank sum test.

observed, which led to death from disease. SLNB was offered to patients with ASTs based on the initial hypothesis that it may provide further prognostic information regarding the malignant potential and classification of the lesion.[17] Initially, it was proposed that if metastatic disease was found in the SLNB, this provided evidence that the original, borderline lesion was indeed malignant; whereas a negative SLNB would favor a benign lesion.[17] However, our findings raise several questions regarding the malignant potential of ASTs, and the use of SLNB in their classification, prognosis, and subsequent clinical management.

The histologic interpretation of SLNB in melanocytic lesions can be challenging. In conventional melanoma, the presence of cytologically atypical melanocytes within the parenchyma or subcapsular sinuses of the lymph node is usually considered to represent metastatic disease. These cells have been shown to have chromosomal aberrations consistent with malignancy, supporting this interpretation.[21] In ASTs, the presence of melanocytes within the parenchyma or subcapsular sinuses of the lymph node has also been commonly interpreted as evidence for malignant metastasis. Although the pattern of lymph node metastatic deposits is well known for conventional melanomas, it remains to be fully characterized for ASTs. This has led some investigators to question the biologic significance of SLN involvement in AST, and whether they are biologically analogous to those from melanoma.[22,23] Some benign melanocytic proliferations, such as cellular blue nevi, have been shown to have benign lymph node deposits within the parenchyma or subcapsular sinuses.[24-27] In addition, whereas most benign nodal nevi are found in the capsule or trabeculae of the lymph node, there are rare reports of intraparenchymal nodal nevi.[26,27] Although the origin of benign nodal nevi is unknown, it is suggested that they may result from migration of benign melanocytes from cutaneous nevi.[28,29] It is also possible that they represent primary benign remnants or rests of development within the lymph node. On the basis of these observations, it is conceivable that parenchymal and subcapsular sinus lymph node deposits found in ASTs may represent a benign process, analogous to those deposits seen in cellular blue nevi. The high incidence of a positive SLNB and the excellent survival observed in our study would be consistent with this possibility.

Although previous studies of SLNB in controversial spitzoid melanocytic proliferations have reported no instances of systemic metastatic disease, even with a positive SLNB, they have been limited by short follow-up intervals (12-34 months).[4,13-16] Similarly, we also observed no disease recurrence in all patients who underwent an SLNB. In addition, the larger numbers and longer follow-up data in our study allow us to make some interesting comparisons to melanoma. In the Multicenter Selective Lymphadenectomy Trial (MSLT-1) the 5-year disease-free survival for SLNB-positive melanoma was 59%, and the 5-year melanoma-specific survival was 72.3%.[30] By comparison, all of our SLNB-positive ASTs patients are disease-free, with a median follow-up of 43.8 months (3.65 years). However, the mean age of the MSLT-1 patients was 49 years, compared with 17.9 years in our SLNB-positive group. As melanoma survival is

known to decrease with increasing age,[31] a comparison with a younger melanoma population maybe more meaningful. In patients aged 1 to 19 years from the National Cancer Database, the 5-year overall survival for patients with regional metastatic melanoma was 68%.[32] By comparison, ASTs appear to have a better prognosis than conventional melanoma, even in younger populations. This suggests that some ASTs may be benign or behave in a more indolent fashion when compared with melanoma. Longer follow-up of 5 to 10 years is still required to fully evaluate the frequency of late recurrence.

We found that a positive SLNB was significantly associated with decreasing age, which is similar to what has been described in conventional melanoma.[19,20,31] In conventional melanoma, decreasing age is associated with an improved prognosis, despite the increased incidence of positive SLNB.[19,20,31] It has been hypothesized that SLNB in younger patients detects a greater proportion of micrometastatic deposits that are clinically insignificant, possibly because of a more intact immune system that is able to eliminate micrometastatic deposits and prevent further metastasis from occurring.[31] The excellent outcomes in our study could be explained by a similar mechanism, whereby the intraparenchymal melanocytic deposits seen in ASTs are malignant metastases, but are biologically inconsequential. Alternatively, it remains possible that in some, the micrometastatic deposits are clinically significant, and the SLNB itself was therapeutic. We did observe 1 patient who developed regional and then distant metastases, which illustrates that some ASTs are lethal and are capable of both biologically significant lymphatic and hematogenous metastasis. Given that the only example of distant metastases in our series was in a patient who did not undergo an SLNB, the possibility that the SLNB itself may be of therapeutic benefit remains.

Given the dilemma in interpretation of both the histology of the primary cutaneous lesion and the SLNB, a diagnostic test that could determine the malignant potential with high sensitivity and specificity would be invaluable. Various methods have been investigated, including the Ki-67 proliferation index, p-53, *bcl*-2, fatty acid synthase expression, and loss of heterozygosity.[33-35] Comparative genomic hybridization (CGH) is a molecular technique that determines DNA copy number gains and losses. By using CGH, Bastian et al reported that 80% of Spitz nevi have no copy number gains, and 20% have a gain of chromosome 11p.[36] This corresponds to the site of the H-*RAS* gene, which is mutated in 67% of cases.[37] By comparison, melanoma often has multiple copy number changes, including gain of chromosome 1q, 2, 6p, 7, 8q, 17, and 20 and loss of chromosome 6q, 8p, 9, and 10.[38,39] Given these differences, CGH may be able to determine the malignant potential of a controversial lesion. As the CGH profile of spitzoid melanoma with a malignant clinical course is not yet known, it is not definitive whether CGH will accurately predict the clinical behavior of ASTs. However, this technique holds promise and warrants investigation in validation series with complete clinical information and follow-up.

On the basis of the current knowledge in the field, the optimal management strategy for ASTs remains challenging and controversial. On the basis of our interpretation of the best available evidence, we currently recommend that ASTs be excised most commonly with a 1-cm margin to ensure complete removal to prevent local recurrence. The decision as to whether to perform an SLNB is more difficult. We presently counsel patients and families regarding the potential risks and benefits of SLNB for ASTs with a depth of $\geq$1 mm, or 0.75 to 0.99 mm with other adverse features.[19,20] Although our results suggest that some SLNB deposits may be benign or clinically insignificant, a negative result is reassuring to patients and alleviates distress, and the possibility remains that SLNB itself may have therapeutic value.

If a positive SLNB shows a larger tumor burden with involvement of $>$1% of the lymph node surface area and/or with effacement of the lymph node architecture, we consider the lesion more likely to be malignant and counsel regarding CLND and adjuvant therapy. If the SLNB contains only a few microscopic deposits of intraparenchymal melanocytes with $<$1% lymph node surface area involvement, the question of proceeding with CLND and adjuvant therapy remains controversial. In our analysis, 59% of patients with a positive SLN had additional negative SLNs, and only 1 had a positive nonsentinel lymph node on CLND, suggesting that most patients do not have a large number of additional lymph nodes involved with tumor. In addition, CLND is associated with greater morbidity than SLNB.[40-42] Because benign spitzoid proliferations are more common in children and adolescents compared with adults, we use an age-based approach toward the management of a minimally

involved SLN. If the patient is $\leq$20 years and has <1% of the lymph node involved, we believe that closely observing the regional nodal basin clinically is a reasonable option after extensive counseling. In addition, serial ultrasound may be beneficial to monitor the nodal basin. If the patient is >20 years and has <1% of the lymph node involved, we discuss the option of observation, but maintain a lower threshold for considering a CLND, given the higher incidence of melanoma in this population.

In conclusion, ASTs do not appear to behave like conventional melanoma. There is a high incidence of microscopic intraparenchymal deposits in SLNs, but despite this finding, patients have a favorable prognosis. Although it seems likely that many of these SLN deposits may actually represent benign deposits or clinically insignificant malignant metastases, some of these deposits may be clinically significant malignant metastases, albeit from a more indolent melanoma variant. Although in many cases the SLN status does not help determine the true biologic potential of the lesion, a role for SLNB still exists, and it is possible that the SLNB is therapeutic for some patients who have malignant disease. Many questions remain unanswered, and future science, particularly at the molecular level, will certainly change the evolving management for AST.

Conflict of Interest Disclosures

The authors made no disclosures.

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