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# Likelihood of finding melanoma when removing a Spitzoid-looking lesion in patients aged 12 years or older

Aimilios Lallas, PhD,<sup>a</sup> Elvira Moscarella, MD,<sup>a</sup> Caterina Longo, PhD,<sup>a</sup> Athanassios Kyrgidis, PhD,<sup>a</sup> Yuka de Mestier, MD,<sup>b</sup> Gabrielle Vale, MD,<sup>c</sup> Stefania Guida, MD,<sup>d</sup> Giovanni Pellacani, PhD,<sup>d</sup> and Giuseppe Argenziano, PhD<sup>a</sup>

*Reggio Emilia and Modena, Italy; Tokyo, Japan; and Rio de Janeiro, Brazil*

**Background:** Dermoscopy improves the recognition of melanoma and Spitz nevus but occasionally melanoma may exhibit a symmetric pattern mimicking Spitz nevus.

**Objective:** We sought to investigate the likelihood of finding melanoma when excising a symmetric Spitzoid-looking lesion in patients aged 12 years or older.

**Methods:** This study included patients aged 12 years or older with symmetric, Spitzoid-looking lesions that were diagnosed histopathologically as Spitz nevus or melanoma. Demographic, clinical, and dermoscopic variables were included in the analysis. We used  $\chi^2$  for nonparametric comparisons. Crude odds ratios and 95% confidence intervals were calculated by univariate logistic regression.

**Results:** Of 384 included lesions, 333 (86.7%) were histopathologically diagnosed as Spitz nevus and 51 (13.3%) as melanoma. The risk of melanoma significantly increased with increasing age, being 50% or higher after the age of 50 years.

**Limitations:** Limitations are retrospective design, exclusion of patients younger than 12 years, lack of detailed histopathologic data, and limited sample size.

**Conclusion:** Our results confirm the observation that melanoma may be dermoscopically indistinguishable from Spitz nevi, strongly suggesting that the only safe strategy not to miss melanoma is to excise all Spitzoid-looking lesions in patients aged 12 years or older. (J Am Acad Dermatol 2015;72:47-53.)

**Key words:** dermoscopy; diagnosis; management; melanoma; Reed nevus; Spitz nevus.

After the initial description of Spitz nevus, the clarification of its biologic nature has been a source of controversy among clinicians and pathologists for several decades.<sup>1,2</sup> Today, Spitzoid tumors are considered a heterogeneous family of lesions that share similar clinical and histopathologic features, but differ significantly concerning their biologic behavior.<sup>3-5</sup> On the 2 opposite edges, Spitz nevi (or spindled and epithelioid cell nevi) are

associated with a completely benign physical course after sequential phases of fast growth, stabilization, and involution, whereas Spitzoid melanoma carries a prognosis not different from melanoma lacking Spitzoid features.<sup>6-9</sup>

Dermoscopy significantly improved the recognition of Spitz nevi, because they have been shown to exhibit a characteristic pattern of morphologic structures.<sup>10-12</sup> In detail, pigmented Spitz nevus

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From the Skin Cancer Unit, Arcispedale Santa Maria Nuova Istituto di Ricerca e Cura a Carattere Scientifico (IRCCS), Reggio Emilia<sup>a</sup>; Department of Dermatology, Faculty of Medicine, University of Tokyo<sup>b</sup>; University of the State of Rio de Janeiro<sup>c</sup>; and Department of Dermatology, University of Modena and Reggio Emilia, Modena.<sup>d</sup>

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Reprint requests: Aimilios Lallas, PhD, Skin Cancer Unit, Arcispedale Santa Maria Nuova IRCCS, Viale Risorgimento 80, 42100, Reggio Emilia, Italy. E-mail: [emlallas@gmail.com](mailto:emlallas@gmail.com).

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(Reed nevus) is dermoscopically typified by a starburst pattern, which consists of a central area of homogenous blue to black pigmentation and peripheral, radially, and symmetrically distributed dark-brown to black streaks or pseudopods. Globular, homogenous, reticular, and multicomponent patterns can also be found in pigmented Spitz nevi, but they are less common and less specific.<sup>12,13</sup> Dermoscopy of nonpigmented Spitz nevus usually reveals symmetrically distributed dotted vessels combined with the so-called “inverse network” or “reticular depigmentation.”<sup>14-16</sup> The latter criterion has been assessed as highly specific for the diagnosis of pigmented and nonpigmented Spitzoid lesions and corresponds, in the analytic terminology, to white crossing lines in between the vascular structures or the pigmented globules.<sup>16</sup>

From a morphologic point of view, a Spitzoid pattern by definition presupposes a symmetric arrangement of colors and structures. In contrast, asymmetrically distributed peripheral streaks, pseudopods, or globules are considered melanoma criteria, which are usually combined to each other forming the so-called “multicomponent pattern.”<sup>17-19</sup> However, the rule of symmetry has its limitations. Previous studies have shown that about 20% of Spitz nevi may exhibit an asymmetric and/or multicomponent pattern and, on the opposite, a certain proportion of melanomas may exhibit a symmetric Spitzoid pattern.<sup>11,12</sup> The aim of this study was to investigate the likelihood of finding melanoma when excising a symmetric Spitzoid-looking lesion in patients aged 12 years or older.

## METHODS

This was a retrospective study conducted at 2 specialized units for skin cancer diagnosis and management in Modena and Reggio Emilia, Italy. The databases of our centers were screened for eligible patients with excised Spitzoid-looking lesions. Because the management of Spitzoid-looking lesions varies significantly among different centers, a clarification of our standard procedure is required: routinely in our units, typical Spitzoid-looking lesions in patients younger than 12 years of age enter regular follow-up until stabilization. Instead, the

recognition of a Spitzoid-looking lesion in patients aged 12 years or older warrants excision, even if the dermoscopic morphology of the lesion is completely symmetric.

This study included only lesions fulfilling all of the 3 following criteria: (1) a clinical-dermoscopic diagnosis of Spitz nevus, (ie, typified either by a completely symmetric starburst or globular pattern, or by symmetrically distributed dotted vessels, combined or not with an inverse network); (2) patients aged 12 years or older—as mentioned above, Spitzoid-looking lesions in patients of this age group are routinely excised in our centers; and (3) a histopathologic diagnosis of Spitz nevus or melanoma. Based on the aforementioned inclusion criteria, Spitzoid lesions dermoscopically exhibiting an asymmetric distribution of colors or structures and lesions histopathologically diagnosed as atypical Spitz tumor were not included in the current study.

Patients' age and sex, along with the anatomic site of the tumor were recorded and 2 independent investigators evaluated the clinical and dermoscopic images of the included lesions. A third investigator was involved in case of disagreement. The clinical images were used to classify the tumors as flat/slightly elevated or nodular, and the dermoscopic ones to assess the presence of pigmentation. Lesions dermoscopically displaying pigmentation on less than 10% of their surface were classified as nonpigmented.

## Statistical analysis

Outcome dichotomous variable was set to definite histopathologic diagnosis of melanoma or Spitz nevus. Demographic, clinical, and dermoscopic variables were included in the analysis. Colinearity was assessed via a correlation matrix, using Spearman Rho correlation coefficient. Nonparametric Mann-Whitney U test was used to compare means. Pearson  $\chi^2$  was used for nonparametric cross-tabulation comparisons. Relative risks were calculated for dichotomous variables. Crude odds ratios and corresponding 95% confidence intervals were calculated by univariate logistic regression.

## CAPSULE SUMMARY

- Dermoscopy improves the recognition of melanoma and Spitz nevus but occasionally melanoma may exhibit a symmetric pattern mimicking Spitz nevus.
- The likelihood of finding melanoma when excising a symmetric Spitzoid-looking tumor in patients aged 12 years or older is 13.3%. The probability increases to 50% or higher after the age of 50 years.
- Our results highlight that the only safe strategy not to miss melanoma is to excise all Spitzoid-looking lesions in patients aged 12 years or older.

**Table I.** Clinical and dermoscopic characteristics: cross-tabulation by histologic diagnosis from 384 patients with excised Spitzoid-looking lesions

	Nevus (n = 333) N, (%)	Melanoma (n = 51) N, (%)	P value
Age, y (mean ± SD)	32.87 ± 10.91	44.78 ± 15.36	<.001*
Anatomic site			
Head/neck	9 (2.7%)	2 (3.9%)	.829 <sup>†</sup>
Thorax	21 (6.3%)	2 (3.9%)	
Abdomen	21 (6.3%)	3 (5.9%)	
Back	63 (18.9%)	7 (13.7%)	
Upper extremities	54 (16.2%)	10 (19.6%)	
Lower extremities	143 (42.9%)	23 (45.1%)	
Acral	13 (3.9%)	1 (2.0%)	
Buttock	9 (2.7%)	3 (5.9%)	
Clinical characteristics			
Nodular tumor	19 (5.7%)	9 (17.6%)	.006 <sup>†</sup>
Dermoscopic characteristics			
Presence of pigment	287 (86.2%)	44 (86.3%)	.986 <sup>†</sup>
Pattern			
Starburst	204 (61.3%)	36 (70.6%)	.430 <sup>†</sup>
Globular	82 (24.6%)	10 (19.6%)	
Dotted vessels	47 (14.1%)	5 (9.8%)	
Inverse network	52 (15.6%)	7 (13.7%)	.727 <sup>†</sup>

\*Mann-Whitney U.

<sup>†</sup>Pearson  $\chi^2$ .

Both false-positive and false-negative results were classified as failures. Assuming 20% failures among study lesions and 5% failures among remaining lesions, we would be able to reject the null hypothesis that the failure rates for each group of lesions are equal with probability (power) of 0.866. A Fisher exact  $\chi^2$  statistic was used to evaluate this null hypothesis.

The type I error probability associated with all tests in this study was set to 0.05. An alpha less than 0.10 was considered to signify a trend. All statistical calculations were made with software (SPSS 17.0, IBM Corp, Armonk, NY).

## RESULTS

Of 384 included patients, 131 were male and 253 female. Mean age was 33.87 ± 12.78 years for male patients and 34.75 ± 12.00 for female patients, ranging from 12 to 85 years (Mann-Whitney U test,  $P = .399$ ). In 51 patients (13.3%) the histopathologic diagnosis was melanoma and in 333 (86.7%) it was Spitz nevus. Of 51 melanomas, 19 were in situ and 33 were invasive with a mean Breslow thickness of 0.86 mm.

The most frequent body site of involvement was the lower extremities (166/384 lesions, 43.3%), followed by the back (70/384, 18.2%) and upper extremities (64/384, 16.7%). Analytic results of the anatomic site of the tumor development are presented in Table I. No significant difference was found

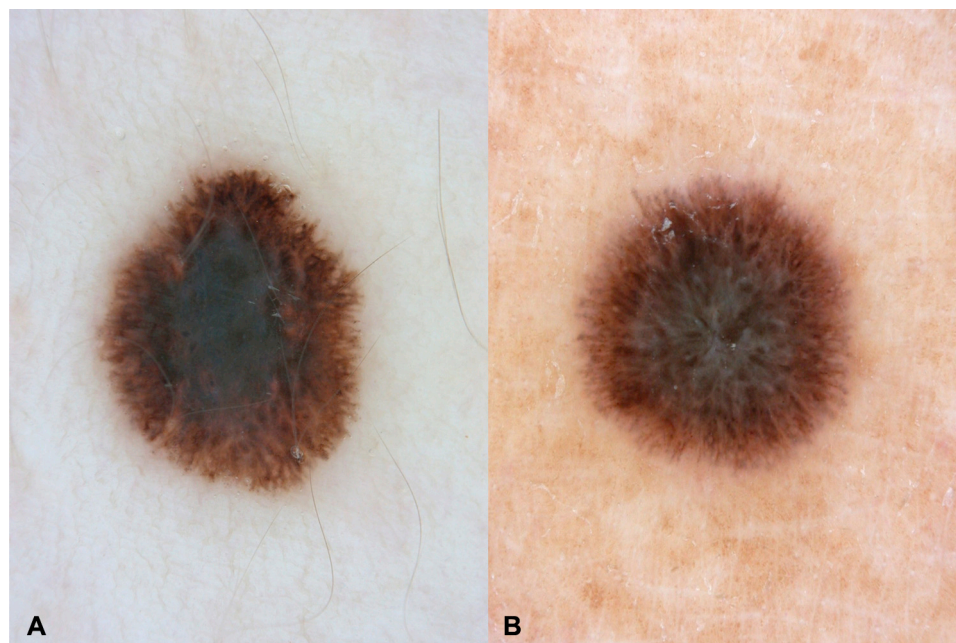
between nevi and melanoma concerning the tumor localization.

Both groups (nevi and melanoma) were characterized by a female predominance and the gender was not associated with a specific histopathologic diagnosis ( $\rho = -0.26$ ,  $P = .613$ ).

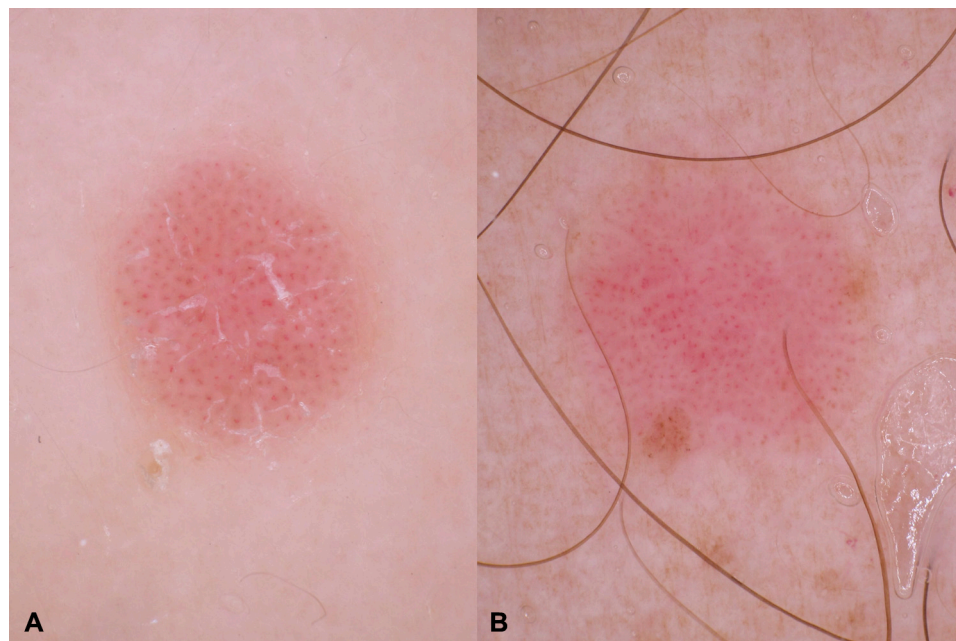
Based on the evaluation of the clinical images, 356 of 384 tumors were flat or slightly elevated (92.7%) and 28 were nodular (7.3%). Nine of 51 melanomas (17.6%) and 19 of 333 nevi (5.7%) were nodular (Pearson  $\chi^2$ ,  $P = .002$ ). The possibility of a nodular lesion being a melanoma was 32.1%, significantly higher compared with flat lesions (11.8%), posing a 3-fold higher risk of melanoma for nodular tumors (odds ratio 3.541, 95% confidence interval 1.505-8.335,  $P = .004$ ).

The analysis of the dermoscopic images revealed that 331 lesions were pigmented (86.2%), whereas 53 tumors (13.8%) were not pigmented (Figs 1-3). The pigmentation status did not differ between Spitz nevus and melanoma, with 287 of 333 nevi (86.2%) and 44 of 51 melanomas (86.3%) being pigmented. Acral Spitzoid-looking tumors were more frequently nonpigmented, comparing with all other anatomic sites (Pearson  $\chi^2$ ,  $P = .036$ ). No other correlation was observed between the pigmentation status and the anatomic site of the lesion.

Based on the dermoscopic analysis, the starburst was the most common pattern both for nevi and melanomas, followed by globular and the pattern of



**Fig 1.** Spitz nevus and melanoma. The stereotypical starburst pattern of a Spitz nevus (**A**), consisting of a structureless center and peripheral streaks, symmetrically and radially distributed. **B**, A melanoma exhibiting starburst pattern.

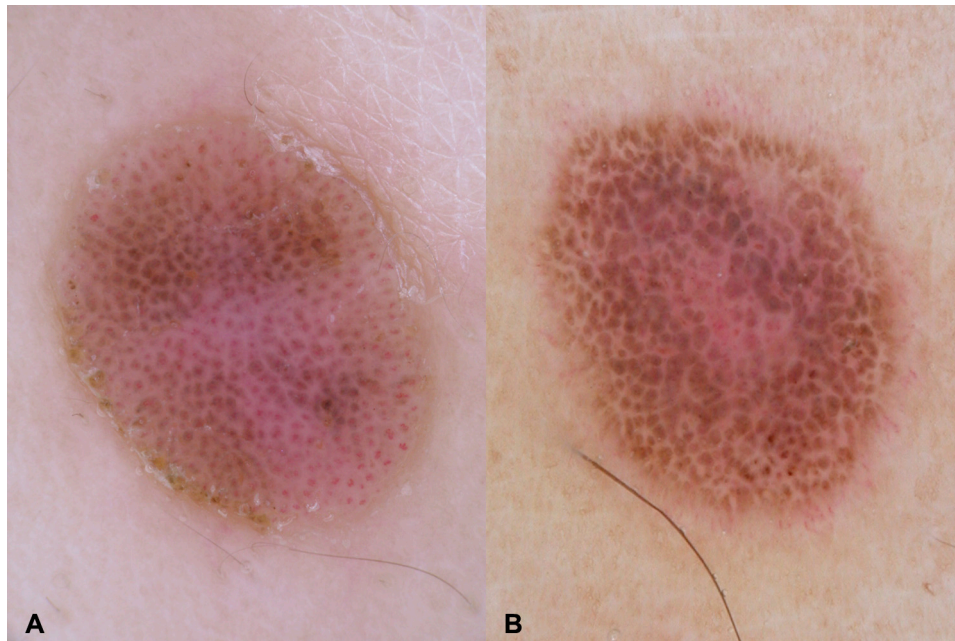


**Fig 2.** Spitz nevus and melanoma. Nonpigmented Spitz nevus (**A**) typically exhibits a symmetric pattern of dotted vessels in dermoscopy. Spitzoid amelanotic melanoma (**B**) can perfectly mimic this pattern.

symmetrically distributed dotted vessels (Table I). An inverse network was present in 52 of 333 nevi (15.6%) and in 7 of 51 melanomas (13.7%). No difference was observed between nevi and melanomas concerning the global dermoscopic pattern or the presence of inverse network. The presence of

inverse network was significantly associated with a pattern of dotted vessels or a globular pattern, compared with the starburst pattern.

As analytically shown in Table II, the odds for melanoma gradually increase with age, as demonstrated by the increasing odds ratios (some of them



**Fig 3.** Spitz nevus and melanoma. A partially pigmented Spitz nevus (A) and a melanoma (B), both dermoscopically typified by a pattern of globules and an inverse network.

trends) in the age groups from 21 to 70 years. Only 1 of 51 melanomas (2%) occurred in the age category of 12 to 20 years. This was a 0.78 mm-thick melanoma developing on the lower extremity of a 20-year-old male patient. Using age 12 to 20 years as a reference category, patients aged 21 to 30 years had a 4-fold higher risk for melanoma ( $P = .181$ , not significant), which increased to a 6-fold higher risk for ages 31 to 40 years ( $P = .096$ , trend) and 41 and 50 years ( $P = .095$ , trend). In patients older than 50 years, the risk of melanoma increased to a 20-fold higher risk in those aged 51 to 60 years ( $P = .006$ ) and a 132-fold higher risk from ages 61 to 70 years ( $P < .001$ ). Finally, only 2 tumors occurred in patients older than 70 years, both diagnosed as melanoma.

## DISCUSSION

According to our results, the likelihood of finding melanoma when excising a completely symmetric Spitzoid-looking lesion in patients aged 12 years or older is 13.3%, and this risk significantly increases with increasing age, becoming 50% or higher after the age of 50 years.

The epidemiologic characteristics of our patients are in agreement with pre-existing studies reporting a female predominance of Spitz nevi.<sup>7,20,21</sup> Notably, neither the gender nor the tumor localization was associated with a specific histopathologic diagnosis.

The morphologic similarity between Spitz nevus and melanoma poses significant difficulties in the clinical management of Spitzoid-looking tumors.<sup>22</sup>

This problem has not been sufficiently solved by dermoscopy, because, as confirmed by our findings, melanoma might display a completely symmetric dermoscopic pattern, perfectly mimicking a Spitz nevus.

To overcome this problem, some clinicians are prone to excise all Spitzoid-looking lesions, irrespectively of the patient age.<sup>9,22-24</sup> This approach eliminates the risk of missing melanoma, but results also in numerous unnecessary excisions of nevi, especially in children. Another approach, based on the evidence that melanoma is extremely rare before puberty,<sup>25</sup> is to monitor typical Spitz nevi in childhood until stabilization,<sup>26,27</sup> while excising Spitzoid-looking lesions after puberty, even if completely symmetric.<sup>28,29</sup> Although not based on appropriately designed studies, the most widely accepted age cut-off is 12 years.<sup>9</sup>

In contrast, the results of the current study highlight that the overall scenario changes completely in patients aged 12 years or older, with 13.3% of Spitzoid-looking lesions being melanomas. Furthermore, our findings suggest the age of 50 years as a threshold, after which the risk of melanoma is equal or higher than the possibility of a nevus, whereas after 70 years of age, a Spitzoid dermoscopic pattern is absolutely predictive of melanoma.

More than 1 of 3 Spitzoid-looking melanomas included in this study were in situ (37.3%), and the mean Breslow thickness of the invasive tumors was less than 1 mm (0.86 mm). This result can probably

**Table II.** Age group as a predictor of the histopathologic diagnosis of melanoma

Age group, y	P	OR	95% CI	
			Lower	Upper
11-20	Reference	Reference		
21-30	.181	4.151	0.516	33.408
31-40	.096	5.778	0.733	45.547
41-50	.095	6.000	0.734	49.041
51-60	.006*	20.533*	2.331*	180.864*
61-70	.000*	132.000*	12.290*	1417.776*

Univariate logistic regression with categorical variable coding.  
CI, Confidence interval; OR, odds ratio.

\*Statistically significant.

be explained by the study design. Specifically, advanced Spitzoid melanomas often develop dermoscopic characteristics that deviate the completely symmetric Spitzoid pattern, and were, effectively, excluded.

Notably, the benign-to-malignant ratio in our study was 6.5/1, highlighting that the procedure to excise all Spitzoid-looking tumors in patients aged 12 years or older results in an acceptable number of unnecessary interventions. Some investigators have proposed a different approach for nodular Spitz nevi, comparing with the classic flat, pigmented Reed nevi. According to the latter approach, nodular lesions are considered at higher risk for melanoma and should be excised irrespective of the patient age, whereas flat pigmented nevi could be monitored.<sup>30</sup> Although our study confirmed that nodular lesions are associated with a higher possibility of melanoma (32.1%), the risk of flat lesions remains considerable (11.8%). No other clinical or dermoscopic criterion was shown to predict the diagnosis of melanoma among Spitzoid-looking lesions.

Our study has some limitations. First, the retrospective design is subject to recall and observation bias. To address this problem, the evaluation was performed by 2 independent investigators, blinded to the histopathologic diagnosis, and a third investigator was involved in case of disagreement. Second, our study did not include patients younger than 12 years of age and, consequently, no conclusions can be drawn concerning the management of Spitzoid-looking lesions in this age group. Third, the assessment of the tumor's palpability based on a clinical image is subject to observation bias. To minimize this problem, the evaluation was performed by 2 independent investigators and a third investigator was involved in the event of disagreement. However, we still cannot rule out misclassifications between flat and nodular tumors. Fourth, because we did not evaluate the individual

histopathologic features of each tumor, no conclusions can be extracted concerning the histopathologic correlation of dermoscopic criteria. This would be an interesting topic for a study with an appropriate design. Fifth, although histopathologic examination is considered the gold standard for diagnosis of melanocytic tumors, the differentiation between Spitz nevus and melanoma might be very difficult even histopathologically in some cases. To minimize this bias, we included only cases with a definite histopathologic diagnosis. However, we still cannot rule out that some tumors were misdiagnosed. Finally, the small number of cases in our study did not allow modeling a classification and regression tree, which would probably require a multicenter study with a higher number of patients.

In conclusion, our results confirm the observation that melanoma may be dermoscopically indistinguishable from Spitz nevi, strongly suggesting that the only safe strategy not to miss melanoma is to excise all Spitzoid-looking lesions in patients aged 12 years or older.

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