A Comparative Demographic Study of Atypical Spitz Nevi and Malignant Melanoma

Dear Editor,

Spitz tumors are a subset of melanocytic neoplasms characterized by epithelioid or spindled melanocytes([1]). The benign nature of the "Spitz nevus" has since been clarified, but the debate regarding Spitzoidtumors (STs) is still ongoing. Spitzoid tumors encompass a wide spectrum of cutaneous lesions ranging from benign Spitz nevus (SN) to Spitzoid melanoma (SM), the latter displaying capacity for widespread metastasis and a potentially lethal outcome (2). The term atypical Spitz tumors (ASTs) refers to melanocytic tumors exhibiting the morphological features of SN, as well as some features associated with malignancy, but not sufficient to classify them as SMs. Currently, histopathology is the gold standard for the diagnosis of STs and cutaneous MM. However, the differential diagnosis between benign and malignant melanocytic lesions with spitzoid features remains challenging (3-6).

In order to facilitate the work of clinicians and pathologists, we attempted a comparative clinical and demographic study comparing ASTs and MMs of patients referred to two Italian institutes. Patient data were obtained from two different Italian dermatological centers (Melanoma Registry of the Instituto Dermopaticodell'Immacolata IDI-IRCCS Rome, Lazio and the Skin Cancer Unit of Dermatology, Hospital Sant'Orsola-Malpighi, University of Bologna), from January 2007 to December 2017. Histological reports presenting pre-operative queries of both "atypical Spitz nevi" or "malignant melanoma" and a final diagnosis confirming one of the queries were included in the study.

The chi-square test or Mann-Whitney U-test were applied to analyze differences between the groups for categorical variables such as sex, diagnosis, and continuous variables (age). The "anatomic site" variable was classified into three categories as follows: the limbs, trunk, and head/neck. A multivariate binary logistic model was used to investigate if the anatomic site was an independent predictor of MM. Age and sex were considered confounding factors.

A total of 504 patients (51.8% men; 48.2% women) met the inclusion study criteria (mean age 52 years, SD = 22.8) (Table 1). 373 were cases of MM and 131 were cases of AST. Mean age of MM cases and AST were 61.2 years old (SD = 17.6) and 25.8 years

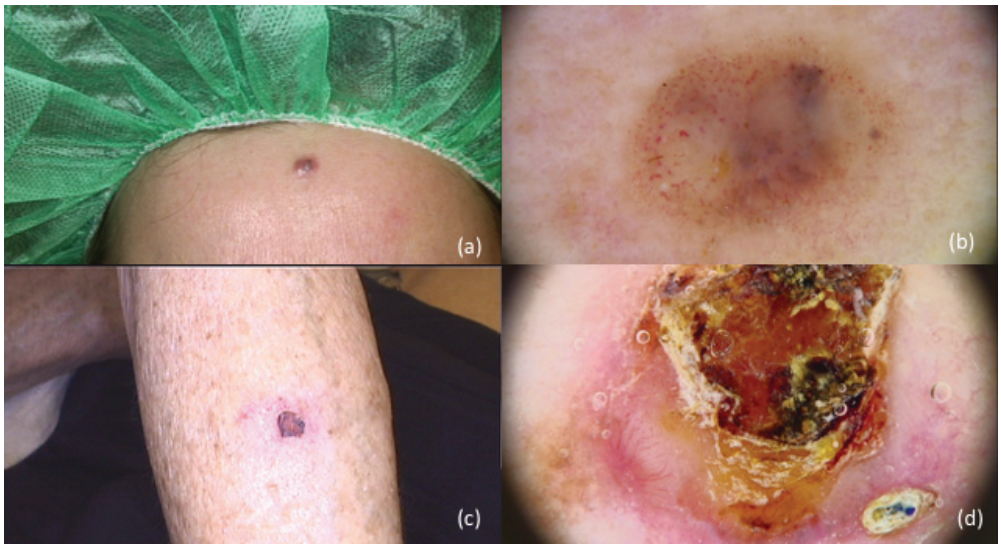

Figure 1. Clinical (a, c) and dermoscopic (b, d) presentations of nodular cutaneous melanomas.

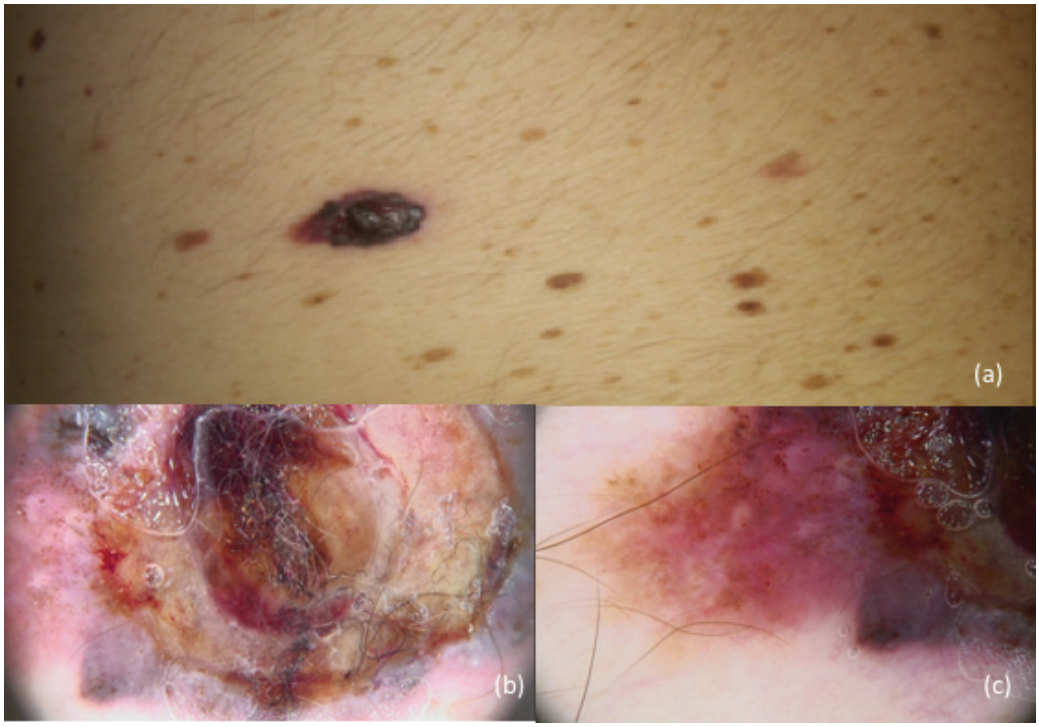

Figure 2. Clinical (a) and dermoscopic (b, c) presentations of a nodular cutaneous melanoma of the trunk.

Table 1. Demographic and clinical characteristics by type of melanocytic lesion

	All	Melanoma	AtypicalSpitzNevus	
	(N=504)	(N=373)	(N=131)	
Characteristics:	N (%)	N (%)	N (%)	*P* value[a]
Centre				
center A[b]	430 (85.3)	321 (86.1)	109 (83.2)	
center B[c]	74 (14.7)	52 (13.9)	22 (16.8)	0.43
Sex				
Men	261 (51.8)	217 (58.2)	44 (33.6)	
Women	243 (48.2)	156 (41.8)	87 (66.4)	<0.0001
Age, y				
mean (SD)	52.0 (22.8)	61.2 (17.6)	25.8 (13.8)	
median (IQR)	52 (36-71)	62 (47-76)	25 (15-35)	0.0001[d]
Anatomic site				
Head/neck	75 (14.9)	64 (17.2)	11 (8.4)	
Trunk	178 (35.3)	148 (39.7)	30 (22.9)	
Limbs	251 (49.8)	161 (43.1)	90 (68.7)	<0.0001

Abbreviation: SD, Standard Deviation; IQR, Interquartile Range.

a: $\chi 2$ test.

b: Instituto Dermopaticodell'Immacolata (IDI-IRCCS), Rome.

c: University hospital Sant'Orsola-Malpighi, Bologna.

d: Mann-Whitney U test.

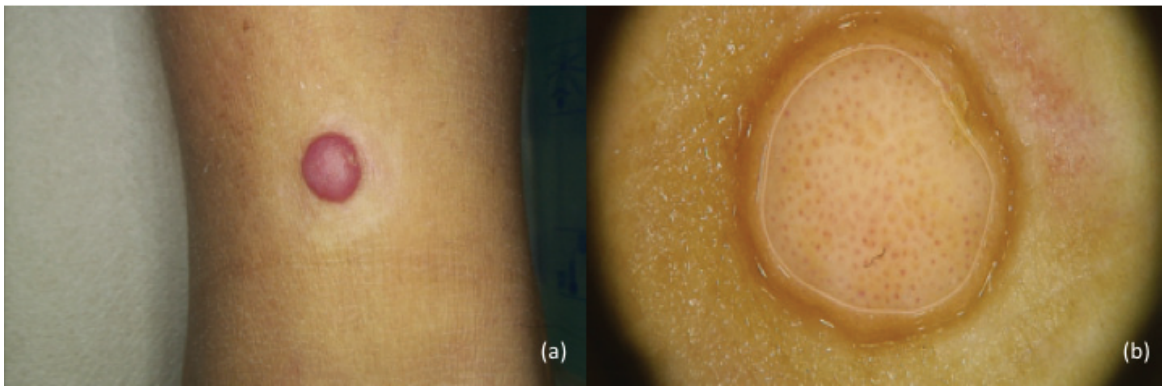

Figure 3. Clinical (a) and dermoscopic (b) presentations of a nodular amelanotic atypical Spitz tumor of the lower limb.

old (SD = 13.8), respectively. Subjects with MM were predominantly men (58.2% versus 33.6%) (*P*<0.0001) and older (median age 62 years versus 25 years) (*P*=0.0001) than subjects with AST. The most frequent anatomic site for MM was the trunk (39.7 %), while the lower limb was the most frequent anatomic site for AST (48.1 %) (*P*<0.0001). Table 2 shows the multivariable analysis used to assess if anatomic site was an independent predictor of cutaneous melanoma. Multivariate analysis confirmed an increased risk for MM in comparison with AST for both localization on the trunk (OR:2.78; 95 %CI: 1.74-4.45) (*P*<0.0001) and head/neck (OR:3.20; 95% CI: 1.60-6.38) (*P*=0.0001). After introducing age (model 1, OR: 2.11; 95% CI: 1.08-4.12) (*P*=0.003) and sex into the model, the only anatomic site that remained statistically significant was the trunk (model 2, OR: 2.03; 95% CI: 1.0.3-3.99) (*P*=0.04). The results show that if the lesion was located on the trunk, the probability of being a MM was two times higher than that of AST, independent of sex, age, or center. After stratifying for sex, the effect was stronger for women (OR: 2.72; 95% CI: 1.14-6.50). After stratifying for age, the effect was stronger for younger subjects (<40 years) (OR: 2. 59; 95% CI: 1.20-5.60) (*P*=0.02).

In this study, we focused on the clinical-epidemiological data in an attempt to improve the identification of nodular melanocytic lesions by providing clinicians with further information in order to reduce the rate of misdiagnosis and assist in providing critical clinical information to surgeons and pathologists. Consistently with the literature, ASTs were mainly found in young-adult patients (mean age was 25.8 years), in the female sex (66.4%), and were typically located on the lower limbs (48.1%) (3,7-10). MM were found to be slightly more common in male patients (58.2%) in the overall patient group; the mean age at the time of the diagnosis was 61.2 years old, and the majority of lesions were located on the trunk (39.7%). These data were similar to those reported by other authors (11-13). ASTs cases were mainly women and younger than MM cases, and were typically located on the lower limbs (Figure 3 and Figure 4). Nodules located on the trunk resulted in a two times greater risk of MM in comparison with AST.

In summary, distinguishing ASTs from MMs is often challenging, and histopathology remains the diagnostic gold standard for melanocytic neoplasms, but a specific clinical framework may help surgeons, pathologists, and clinicians to correctly diagnose and manage these lesions in children and adults.

Table 2. Association between patient characteristics and type of melanocytic lesion

	model 0		model 1		model 2	
	ORs (95%CI)[a]	*P* value	ORs (95%CI)[b]	*P* value	ORs (95%CI)[c]	*P* value
Anatomic site						
Limbs	1		1		1	
Trunk	2.78 (1.74-4.45)	<0.0001	2.11 (1.08-4.12)	0.03	2.03 (1.03-3.99)	0.04
Head/neck	3.20 (1.60-6.38)	0.001	1.94 (0.67-5.61)	0.22	1.81 (0.62-5.28)	0.27

Abbreviation: OR, Odds Ratio; CI, Confidence Interval.

a: ORs adjusted for center.

b: ORs adjusted for center and age.

c: ORs adjusted for center, age and sex.

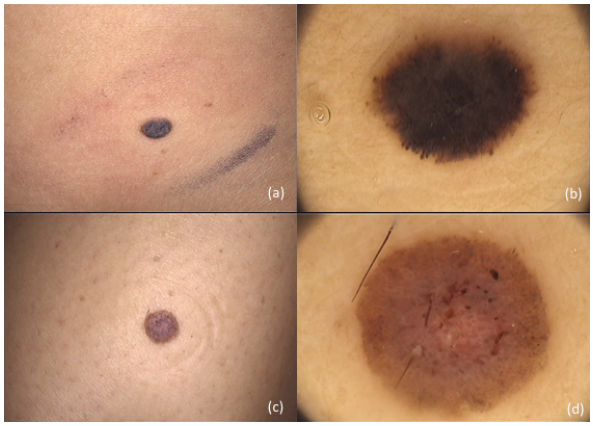

Figure 4. Clinical (a, c) and dermoscopic (b, d) presentations of atypical Spitz tumors of the lower limbs.

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