

Clinical Features, Dermoscopic Patterns, and Histological Diagnostic Model for Melanocytic Tumors of Uncertain Malignant Potential (MELTUMP)

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ABSTRACT Cutaneous melanocytic lesions with atypical histological features can be difficult to categorize as benign or malignant. In the diagnosis of melanocytic lesions, the melanocytic tumor of uncertain malignant potential (MELTUMP) category has been widely used. Although one may favor a benign or malignant interpretation, a definitive diagnosis is not always possible, and long term clinical follow-up remains the only true evidence of biological behavior. We report 14 cases of MELTUMP with expert second opinion. Clinical pictures were available in 8 cases; dermoscopy was available in 5 cases. Accurate guidelines are delineated in the formulation of the diagnosis. We think that the histological diagnosis should be accompanied by a note in which the pathologist describes the histological pattern that has generated diagnostic uncertainty. Since the MELTUMP term does not exclude the malignant nature of the lesion, all microstaging attributes for melanoma should be added. Moreover, superficial atypical melanocytic proliferation of uncertain significance (SAMPUS) and MELTUMP categories should be included in the WHO classification of melanocytic tumors of the skin. The role of sentinel lymph node biopsy in MELTUMP has not yet been established. Recent studies have looked at concurrent tumor deposits in lymph nodes of MELTUMP, mostly of atypical Spitzoid lesions, and shown that these lesions rarely progress to overt malignancy. In our study, sentinel node metastasis was found in only one case. The follow-up period of this case and of the others has shown that the clinical outcome of MELTUMP tends to be favorable.

KEY WORDS: melanocytic tumors of uncertain malignant potential (MELTUMP); superficial atypical melanocytic proliferation of uncertain significance (SAMPUS); clinical management; dermoscopy; histology; second opinion; sentinel lymph node (SLN)

INTRODUCTION

Melanocytic tumors of uncertain malignant potential (MELTUMP) represent a highly select subset of melanocytic lesions that is difficult to classify cor-

rectly as benign or malignant, reflecting an inherent biologic problem. They probably represent a spectrum or group of one or more low-grade melanocytic



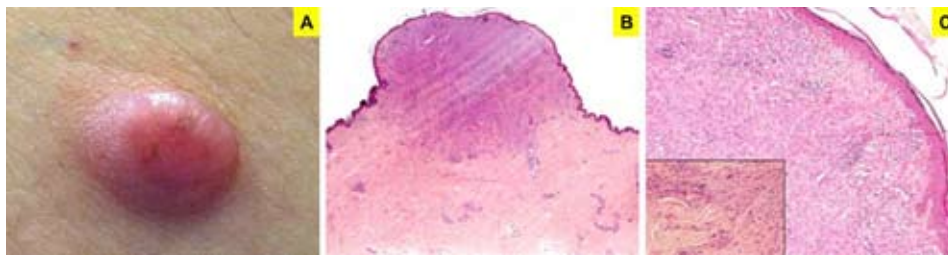


Figure 1. **A** (macroscopy): A pink papulo-nodular lesion with a smooth surface, focal pigmented areas on the top, and blurred margins. **B** and **C** (microscopy): Severely atypical combined melanocytic proliferation with Spitzoid features. While the lesion shows focally severe cytologic atypia, it is overall symmetrical with a plexiform/infiltrative architecture at the base, so it was considered to have uncertain malignant potential [case 1].

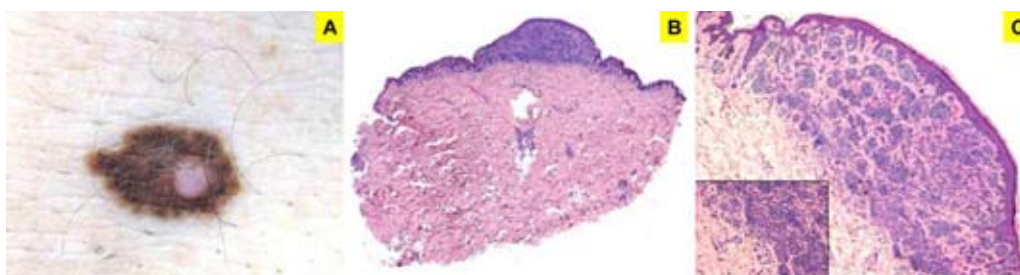


Figure 2. **A** (macroscopy): A pigmented oval asymmetric lesion with sharp borders and a pink raised eccentric area. **B** and **C** (microscopy): Lentiginous compound dysplastic nevus with severe atypia of both the intraepidermal and intradermal components. Focal malignant change within the superficial component of this lesion cannot be entirely excluded and it is therefore best considered to have uncertain malignant potential [case 3].

tumors with potential for lymph node involvement and, rarely, for distant metastasis (1-3). In the diagnosis of these lesions the second opinion is mandatory (2). We report the histological diagnostic model, according to expert second opinion, of 14 cases of MELTUMP, 8 of which are accompanied by clinical images and 5 by both clinical and dermoscopic pictures. All cases were reviewed by an expert consultant.

PATIENTS AND METHODS

Fourteen cases of MELTUMP were retrieved from the files of the Institute of Pathology, Rovereto Hospital. Inclusion criteria were as follows: a) histological cases of melanocytic tumors with uncertain classification (benignant vs. malignant) sent out for expert second opinion; b) samples completely excised (no shave, no punch, no partial biopsies); and c) follow-up period >3 years. Lesions were evaluated for tumor thickness, tumor infiltrating lymphocytes (TIL), and dermal mitotic figures/mm² (mitogenicity). Eight cases were accompanied by clinical images and five of them by both clinical and dermoscopic pictures.

RESULTS

The results are shown in Table 1. The median age of the 14 patients was 34.8 years (range: 14 to 68

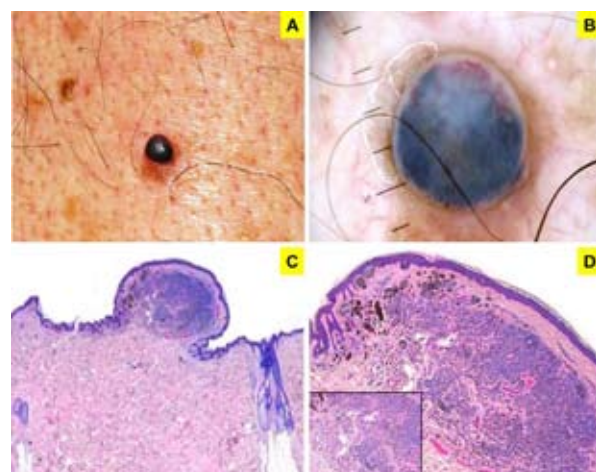


Figure 3. **A** (macroscopy): An asymmetric pigmented lesion with a flat light brown component, a raised blue-grayish area with smooth surface, and blurred margins. **B** (dermoscopy): The flat area has a regular reticular pattern, while the raised area has a bluish homogeneous pattern with focal bluish globules at the inferior pole and irregular vessels at the superior pole. **C** and **D** (microscopy): Atypical epithelioid cell compound melanocytic proliferation, most consistent with epithelioid cell/Schwannian transformation in a lentiginous compound nevus. The lesion is best regarded as having uncertain biological potential [case 4].

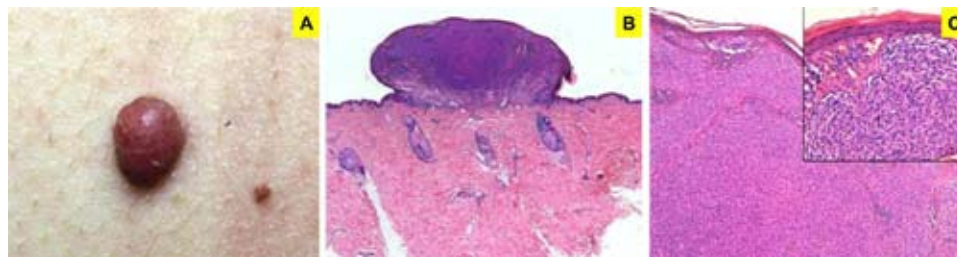


Figure 4. **A** (macroscopy): A polypoid reddish lesion with smooth surface and sharp borders. **B** and **C** (microscopy): Severely atypical compound Spitzoid melanocytic neoplasm. The lesion is dominated by a large expansive nodule devoid of maturation and containing numerous mitoses. Cytologically, the nodule is composed of cells with significant atypia but without features of fully-evolved melanoma, and there is a small cell component with more nevoid features at the perimeter. Overall, the lesion must at least be considered to represent a melanocytic tumor of uncertain malignant potential [case 7].

years), there were 9 male and 5 female patients, the average tumor thickness was 2.5 mm, and the median number of dermal mitosis/mm² was 1.3. Brisk tumor-infiltrating lymphocytes (TIL) were found in 5 cases, non-brisk TIL in 1 case, and 8 cases showed no TIL. No patients presented with ulceration. Eight lesions were found on the trunk, while 4 lesions were located on the extremities and 2 lesions were detected on the head. Clinical pictures were available in 8 cases (panel A in Figure 1, 2, 3, 4, 5, 6, 7; Figure

8). In these cases the median diameter of the lesion was 9.25 mm (range: 6 to 15 mm). The clinical features were suggestive of malignant melanoma in 6 of these 8 cases. Applying the ABCD rule, 4 lesions were Asymmetric, 3 lesions presented irregular Borders, 6 lesions had an uneven Color, and 3 lesions showed a Dimension more than 6 mm. Dermoscopy was available in 5 cases, 4 of which with images (panel B in Figure 3, 5, 6, 7). All cases showed some features of malignancy: atypical vascular pattern (2 cases), atypical

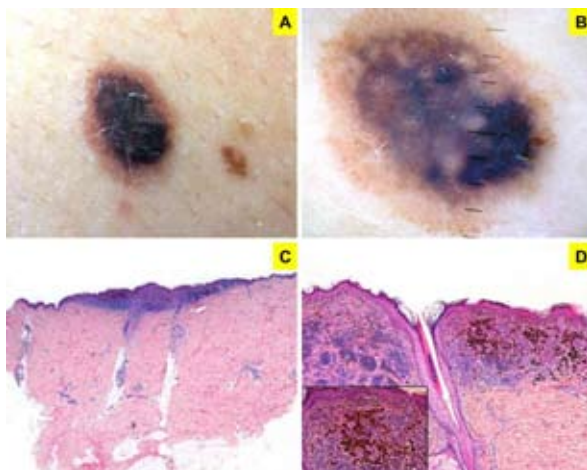


Figure 5. **A** (macroscopy): A slightly raised pigmented lesion with color variegation and sharp borders. **B** (dermoscopy): A multicomponent global pattern, peripheral globules, focal irregular striae, irregular hyperpigmented structureless areas in the center of the lesion, and blue-black blotch in close proximity of the striae. **C** and **D** (microscopy): Severely atypical compound melanocytic proliferation consistent with a melanocytic tumor of uncertain malignant potential. Worrisome features include its breadth and focal asymmetry zones of junctional confluence, occasional high-level pagetoid cells within the epidermis, and incomplete maturation by a focally coalescent and expansive dermal component involving enlarged epithelioid cells with marked nuclear atypia [case 12].

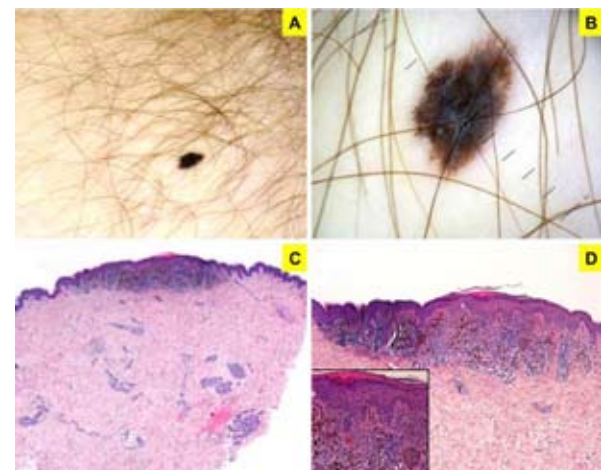


Figure 6. **A** (macroscopy): Asymmetric hyperchromic flat lesion with irregular borders. **B** (dermoscopy): A multicomponent global pattern, irregular pigmented striae on about three-quarters of the lesion, irregular pseudopodia in the remaining part, and whitish-blue irregular areas in the middle. **C** and **D** (microscopy): Compound pigmented melanocytic proliferation with severe atypia. The lesion shows some overlap with an epithelioid variant of a pigmented spindle cell nevus of Reed. However, there is disturbing cytological atypia, mitotic figures are easily found in the dermal component, and there is a focally brisk lymphoid infiltrate possibly representing an early inflammatory phase of regression, as observed in borderline lesions of uncertain biological potential [case 13].

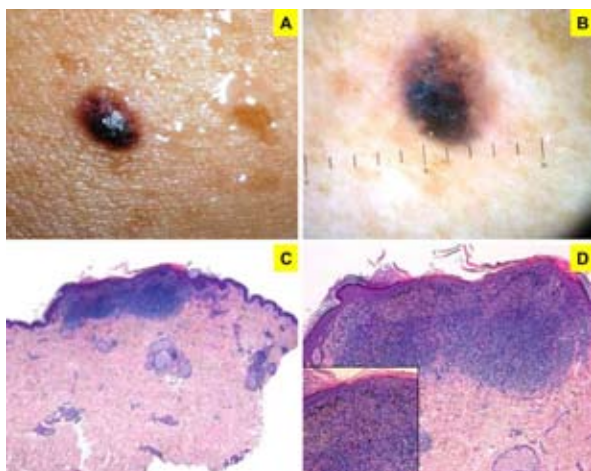


Figure 7. A (macroscopy): A pigmented, slightly raised oval lesion with color variegation and blurred irregular borders. B (dermoscopy): A multicomponent global pattern, irregular hyperpigmented structureless areas in the lower part and focal regression in the upper half, and follicular structures reminiscent of comedo-like openings and milia-like cysts in the middle. C and D (microscopy): Severely atypical compound melanocytic proliferation with halo-like lymphoid response. While the melanocytic proliferation is diffusely and severely atypical, only one small region borders on melanoma *in situ*, and several junctional nests at the perimeter appear nevoid. The lesion is best regarded as a melanocytic tumor of uncertain malignant potential [case 14].

pigment network (3 cases), gray-blue areas (1 case), irregular diffuse pigmentation (blotches) (1 case), and regression pattern (1 case). All cases were reviewed by an expert dermatopathologist (panel B in Figure 1, 2, 4; panel C in Figure 1, 2, 3, 4, 5, 6, 7; panel D in Figure 3, 5, 6, 7). The second opinion is reported in Table 1 as “assessment” and “comment/recommendation”. The TIL is reported in Table 1 as well. In all cases, vascular/lymphatic invasion and microscopic satellites were not observed. Thirteen patients underwent widened excision: in only a single case was a residual tumor found. Biopsy of the sentinel lymph node (SLN) was performed in 6 patients, one of which resulted positive. A regional lymphadenectomy was done, but no additional metastases were found. All patients were free of disease after a follow-up period of >3 years (range: 38 to 54 months).

DISCUSSION

The term “atypical” has been widely used for melanocytic lesions in which a degree of atypia is evident, a source of some concern to the pathologist but insufficient to merit a diagnosis of outright malignancy. In the World Health Organization (WHO) histological



Figure 8. Macroscopic appearance of the raised nodular polypoid grayish lesion of the left scalp with a smooth surface, later diagnosed as MELTUMP [case 6].

classification of melanocytic tumors, atypical or ambiguous lesions have been not considered (4). After the publication of the WHO histologic classification of melanocytic tumors, numerous reports described a subset of cases in which a specific and reproducible diagnosis is difficult or even impossible to establish (1,2,5). In the AFIP fascicle of the melanocytic tumors of the skin (6), Elder and Murphy divided these cases into two categories: the Superficial Atypical Melanocytic Proliferation of Uncertain Significance (SAMPUS), a non-tumorigenic group of junctional melanocytic lesions and melanocytic proliferations that are confined to the epidermis and papillary dermis without evidence of mitotic activity; and the MELANOCYTIC TUMORS OF UNCERTAIN MALIGNANT POTENTIAL (MELTUMP), a descriptive term for an ill-defined group of dermal melanocytic tumors that are often quite bulky and frequently exophytic, exhibiting one or several features indicative of possible malignancy but insufficient in number or degree to justify a diagnosis of malignancy. The MELTUMP category should include melanocytic proliferations that may generate uncertainty and which have been referred to in the past by various names: compound nevocellular nevi with dermal mitoses and atypia, Spitz nevi with atypical features (atypical Spitz tumors), pigmented spindle cell nevi with dermal atypia, dermal-based borderline melanocytic tumors, dysplastic nevi with dermal atypia, halo and inflamed nevi with atypia, desmoplastic nevi with unusual features, cellular blue nevi with atypia, some deep penetrating nevi, pigmented epithelioid melanocytomas, nevi lacking maturation, and any Spitz nevus in older individuals (3). MELTUMP is a provisional diagnosis; although a particular physician may favor a benign or malignant interpretation, a definitive diagnosis is not always

N ^o	SEX AGE (years)	SITE	CLINICAL FEATURES	DERMOSCOPY	ASSESSMENT	MITOGENICITY THICKNESS TIL	COMMENT / RECCOMANDATION	TREATMENT	FOLLOW-UP
1	M 19	Left side	Pink papulo-nodular lesion with smooth surface, focal pigmented areas on the top, blurred margins and sized 12x10 mm.		Severely atypical combined melanocytic proliferation with Spitzoid features (MELTUMP).	0 5 mm absent	While the lesion shows focally severe cytologic atypia it is overall symmetrical and shows a plexiform / infiltrative architecture at the base. Moreover, mitotic figures are infrequent. Spitzoid melanocytic proliferations are notoriously difficult to classify in adulthood, and even in a 19-year-old, I would consider this lesion to have uncertain malignant potential.	Re-excision (negative)	FD
2	M 38	Right elbow			Severely atypical compound epithelioid and spindle cell melanocytic proliferation.	0 1 mm absent	While the lesion has features of a Spitz tumor, the patient's age and the severe atypia are worrisome, and such lesions in adulthood are best regarded as melanocytic tumors of uncertain malignant potential (MELTUMP). Complete excision and dose clinical follow-up are recommended. Overall, prognosis tends to be favorable for such lesions.	Re-excision (negative) SLNB (negative)	FD
3	M 54	Trunk	Pigmented oval asymmetric lesion, with sharp borders and a pink raised eccentric area, sized 15x8 mm.		Lentiginous compound dysplastic nevus with severe atypia of both the intraepidermal and intradermal components.	0 0.9 mm absent	Focal malignant change within the superficial component of this lesion cannot be entirely excluded and it is therefore best considered to have uncertain malignant potential, particularly upon incomplete excision. HMB-45 and MIB-1 stains relatively negative in tumor cells.	Re-excision (negative) SLNB (negative)	FD
4	M 68	Back	Asymmetric pigmented lesion with a flat light brown component and a raised blue-grayish area with smooth surface, blurred margins and sized 6x5 mm.	The flat area shows a regular reticular pattern, while the raised area a bluish homogeneous pattern with focal bluish globules at the inferior pole and irregular vessels at the superior pole.	Atypical epithelioid cell compound melanocytic proliferation, most consistent with epithelioid cell / Schwannian transformation in a lentiginous compound nevus.	0 1.3 mm absent	The case is distinctly unusual, and given the patient's age, the process is best regarded as having uncertain biological potential. Close follow-up is recommended.	Re-excision (negative)	FD
5	M 28	Back			Severely atypical compound melanocytic proliferation.	0 2.1 mm absent	Although the lesion is overall symmetrical and shows a junctional nevic component along with a delicately infiltrative deep component, it also shares features with a superficial variant of a deep penetrating nevus, a lesion that is incompletely studied with regard to biological potential. Moreover, the extent of cytologic atypia exceeds that normally encountered in a deep penetrating nevus; therefore, the lesion is best classified as having uncertain biological potential. Re-excision is recommended in a manner to ensure against local persistence / recurrence. Overall, prognosis should be favorable.	Re-excision (positive)	FD



6	M 14	Left scalp	Raised nodular polypoid grayish lesion with smooth surface sized 12x10 mm.		Severely atypical nodular melanocytic proliferation arising in association with a lentiginous compound dysplastic nevus with special site (scalp) features.	2 / mm ² 9 mm absent	This is an extremely challenging lesion. Although the nodule displays profound architectural atypia and variable cytologic dysplasia, mitotic figures are difficult to identify. Nonetheless, such lesions are best classified in the provisional category of melanocytic tumor of uncertain malignant potential (MELTUMP). As such, complete excision is recommended in a manner to ensure against local persistence / recurrence, and close interval follow-up should be instituted.	Re-excision (negative) SLNB (positive) Regional lymphadenectomy (negative)	FD
7	F 17	Right side	Polypoid reddish lesion with smooth surface, sharp borders and sized 8x5 mm.	A lesion devoid of evident pigmentation, vascular pattern with irregular vessels (glomerular, linear and hairpin) throughout the lesion.	Severely atypical compound Spitzoid melanocytic neoplasm.	3 / mm ² 2.5 mm brisk	This is an extremely difficult lesion. The overall cytology is suggestive of origin in a Spitz nevus. The lesion is dominated by a large expansive nodule devoid of maturation and containing numerous mitoses. Cytologically, the nodule is composed of cells with significant atypia but without features of fully-evolved melanoma, and there is a small cell component with more nevoid features at the perimeter. Overall, the lesion must be considered to represent at least a melanocytic tumor of uncertain malignant potential, with Spitzoid malignant, invasive to a depth of approximately 2.5 mm, anatomic level IV not entirely excluded. In either case, it should be noted that such severely atypical Spitzoid tumors in children and young adults tend to have a more favorable prognosis that would be predicted for conventional melanoma, with long-term survival even in the presence of regional lymph node involvement. Such patients should be screened carefully and close follow-up should be instituted.	Re-excision (negative) SLNB (negative)	FD
8	M 37	Right back			Several atypical compound melanocytic proliferation with Spitzoid features and halo-like immune response.	2 / mm ² 2.5 mm brisk	Such lesions that do not fully qualify for a diagnosis of conventional melanoma are best considered in the provisional category of melanocytic tumor of uncertain malignant potential (MELTUMP). Such lesions generally do not have the same prognostic implications of melanoma, and even fully-evolved Spitzoid melanoma tends to have more indolent behavior in this age group.	Re-excision (negative) SLNB (negative)	FD
9	M 53	Right thigh			Junctional melanocytic proliferation with moderate atypia and many features of a more epithelioid variant of a pigmented spindle cell nevus of Reed; lesion in close (within 0.4 mm) to side margin.	5 / mm ² 0.9 mm absent	Although the lesion does not qualify for a diagnosis of melanoma, Spitzoid lesions in adults are notoriously difficult to classify. The lesion is best considered as having uncertain biologic potential. A complete excision to ensure against local persistence / recurrence is advised.		FD

10	F 28	Right thigh			Severely atypical compound melanocytic proliferation with Spitzoid features; margins appear negative. Dermal mitoses number 1 / mm ² and are confined primarily to the upper one-half of the lesion.	1 / mm ² 3.6 mm brisk	Although the lesion shows many features of an atypical Spitz tumor / nevus, Spitzoid melanocytic proliferations in adults are notoriously difficult to classify. Accordingly, the lesion is best considered as having uncertain malignant potential. Close interval follow-up is recommended. Overall, prognosis tends to be favorable for such lesions, in my experience.	Re-excision (negative) SLNB (negative)	FD
11	F 23	Left ear helix			Severely atypical compound melanocytic neoplasm most consistent with melanocytic tumor of uncertain malignant potential (MELTUMP).	4 / mm ² 4.5 mm absent	This unusual tumor, while diffusely atypical and mitotically active, is strikingly nevoid with respect to architecture, maturation and pigment distribution. Some of the features are "Spitzoid", including its relationship to the epidermis and <u>perme-</u> <u>ative</u> and sclerosing deep dermal component. I would recommend additional excision with a 2-cm margin, careful screening, and close interval follow-up. Prognosis is often quite favorable in young adults, such as is the case here.	Re-excision (negative)	FD
12	F 21	Left shoulder	Slightly raised pigmented lesion with color variegation and sharp borders, sized 9x6 mm.	Multicomponent global pattern, peripheral globules, focal irregular striae, irregular hyperpigmented structureless areas in the center of the lesion, blue-black blotch in close proximity of the striae.	Severely atypical compound melanocytic proliferation (melanocytic tumor of uncertain malignant potential; "MELTUMP").	0 0.6 mm Non-brisk	This is an extremely interesting and challenging lesion. Worrisome features include its breadth and focal asymmetry zones of junctional confluence and occasional high-level pagetoid cells within the epidermis, and incomplete maturation by a focally coalescent and expansive dermal component involving enlarged epithelioid cells with marked nuclear atypia. However, many of the junctional and intradermal nests are more nevoid in architecture and cytology, mitotic figures or apoptotic cells are not observed, and several regions within the dermis show features reminiscent of combined nevus (dysplastic and deep penetrating types). Moreover, many of the dermal elements fail to express HMB-45. Overall, I do not believe that the lesion has sufficient criteria for a designation of conventional melanoma, and thus prefer the MELTUMP category (as further described in the AFIP Fascicle, Melanocytic Tumors of the Skin, Third Series). This is not a definitive category, but rather a provisional one that requires substantial further genomic and epigenomic study to determine true biological significance. In my experience, however, most lesions with such hybrid histologic features do not behave as aggressively as melanoma, and complete excision is often curative. In addition to complete excision, careful screening and close interval follow-up are recommended for such proliferations.	Re-excision (negative)	FD

13	M 38	Left thigh	Asymmetric hypochromic flat lesion with irregular borders sized 6x4 mm.	Multicomponent global pattern, irregular pigmented striae on about three-quarters of the lesion, irregular pseudopodia in the remaining part, whitish-blue irregular areas in the middle.	Compound pigmented melanocytic proliferation with severe atypia (see comment).	1 / mm ² 0.4 mm brisk	The lesion shows some overlap with an epithelioid variant of a pigmented spindle cell nevus of Reed. Reassuring features include a perimeter defined by well-formed junctional nests, small size, symmetry, relative lack of high-level pagetoid spread, and foci consistent with maturation of the dermal component. However, there is disturbing cytological atypia, mitotic figures are easily found in the dermal component, and there is a focally brisk lymphoid infiltrate possibly representing an early inflammatory phase of regression and thus, I consider it to be a borderline lesion of uncertain biological potential. However, I favor that this lesion will behave in a banal manner, with cure upon complete excision. Close follow-up is advised.	Re-excision (negative)	FD
14	F 49	Right shoulder	Pigmented slightly raised oval lesion, with color variegation, blurred irregular borders, sized 6x4 mm.	Multicomponent global pattern, irregular hyperpigmented structureless areas in the lower part and focal regression in the upper half; in the middle follicular structures reminiscent of comedo-like openings and milia-like cysts.	Severely atypical compound melanocytic proliferation with halo-like lymphoid response.	0 0.5 mm brisk	This is a challenging lesion. While the melanocytic proliferation is diffusely and severely atypical, only one small region borders on melanoma <i>in situ</i> and several junctional nests at the perimeter appear nevoid. Moreover, in my experience, halo-like immune responses in overt melanomas are unusual. Nonetheless, the lesion is best regarded as a melanocytic tumor of uncertain malignant potential (MELTUMP), with an unusual melanoma (level III, 0.5 mm) difficult to fully exclude. Additional excision, careful screening, and close follow-up are recommended. Overall, I would anticipate a favorable prognosis.	Re-excision (negative)	FD

TIL: Tumor-infiltrating lymphocytes; FD: Free of Disease; SLNB: Sentinel Lymph Node Biopsy

possible at initial presentation, and long term (or perhaps life-long) clinical follow-up remains the only true evidence of biological behavior. These lesions often require expert consultation and, frequently, prompt aggressive management such as would accompany a melanoma diagnosis (7,8). Since the diagnosis of MELTUMP is provisional, accurate guidelines should be delineated in the formulation of the diagnostic report. Elder and Xu believe that the final diagnosis of MELTUMP should be accompanied in the report by a note in which the pathologist describes the histological findings that have generated diagnostic uncertainty (1). Since a MELTUMP category does not exclude the possibility of the malignant nature of the lesion, all microstaging attributes should be always reported. These parameters should be considered by a dermatologist in the management of the lesion and in the prognostic models. In our experience with

“second opinions”, we believe that the histological report of MELTUMP should include the “assessment” and the “comment/recommendation” sections. In the “assessment”, the histological characteristics of the lesion should be accurately reported. In the “comment/recommendation” section, the MELTUMP diagnosis should be accompanied by recommendations for the management of the lesion. There is little clinical data for MELTUMP: it may be associated with high rates of loco-regional involvement, including sentinel node metastasis. The rate of involvement reported varies from about 16% to 50% (9,10,11). In patients with MELTUMP who have undergone completion lymphadenectomy it is very unusual for the disease to re-occur, while in adults with melanoma and a positive sentinel node about 1/6 or 1/7 have further nodes showing melanoma after completion lymphadenectomy. Even patients with MELTUMP who had local or

nodal recurrence did not usually develop significant systemic disease, although there was an occasional report of death (9,12,13). Luo and colleagues reported that the mortality for adult atypical Spitzoid tumors is less than 5%; thus, sentinel lymph node positivity, which is 30-50%, is poorly predictive of outcome. In cases with metastatic SLN there may be a temptation to revise the diagnosis to malignant melanoma (14). Therefore, in a situation where a "melanocytic tumor of uncertain malignant potential" is found to be associated with regional lymph node metastases, Elder and Xu use the definition of "metastatic melanocytic tumor of uncertain malignant potential". The authors indicate that the biological potential of this metastatic tumor remains uncertain (1). Abraham *et al.* believe that the role of SNL biopsy in MELTUMP has not yet been established (9,12). Recent studies have looked at concurrent tumor deposits in lymph nodes of MELTUMP, mostly of atypical Spitzoid neoplasms, and show that these lesions rarely progress to overt malignancy (7). Since SNL biopsy is not currently the standard of care in these lesions and can potentially cause morbidity, especially with completion lymphadenectomy, the lymphatic invasion identified by immunohistochemical staining could provide a surrogate marker for sentinel lymph node positivity (7). In our study, only one case of SNL metastasis was found, but the patient was free of disease after 40 months of follow-up. In the documentation on these lesions, most MELTUMPs had been examined in consultation so the clinical features were not accurately described. Clinical pictures were available in 8 cases. The clinical features were suggestive of malignant melanoma in 6 of these 8 cases. Applying the ABCD rule, 4 lesions were considered asymmetric, 3 lesions presented with irregular borders, 6 lesions had an uneven color, and 3 lesions measured >6 mm. Dermoscopy has been increasingly regarded as a valuable aid in diagnosis of early melanoma. Of particular value in the diagnosis of melanoma is the presence of an irregular pigment network (uneven thickness of the lines, presence of broad lines at the periphery of the lesion), of black or brown dots irregularly distributed within the lesion, irregular lines at the lesion's periphery that are not clearly combined with the pigment network (streaks), a blue-whitish veil corresponding to infiltrates of melanophages below a thick epidermis with hypergranulosis, an atypical vascular pattern, and regression structures. Argenziano *et al.* have proposed a 7-point checklist for dermoscopic scoring in atypical melanocytic lesions: atypical pigment network, gray-blue areas, atypical vascular pattern, radial streaming (streaks), irregular diffuse pigmentation (blotches), irregular dots and globules, regression pattern (15).

This approach allows diagnosis of melanoma with a sensitivity of 95% and a specificity of 75%. In our cases, all 5 cases studied by dermoscopy showed some features of malignancy.

CONCLUSION

Cutaneous melanocytic lesions with atypical histological features can be difficult to categorize as benign or malignant, even by experienced pathologists. The MELTUMP category has been widely used in the diagnosis of melanocytic lesions, indicating that no histological criteria are infallible. This diagnosis is provisional and a definitive diagnosis is not always possible at initial presentation, and long term clinical follow-up remains the only way to understand its biological behavior. The diagnosis of MELTUMP requires expert consultation. In the diagnostic phase, an accurate description of the lesion and the microstaging attributes should be reported. Furthermore, the SAMPUS and MELTUMP categories should be included in the WHO classification of melanocytic tumors of the skin. The role of SNL biopsy in MELTUMP remains unestablished. In our experience, the clinical features and the dermoscopy were indicative of malignancy. In one case a metastatic SLN was found; however, follow-up in all our cases indicates that the clinical outcome of MELTUMP tends to be favorable.

References

1. Elder DE, Xu X. The approach to the patient with a difficult melanocytic lesion. *Pathology* 2004;36:428-34.
2. Pusiol T, Morichetti D, Pisciole F, Zorzi MG. Theory and practical application of superficial atypical melanocytic proliferations of uncertain significance (SAMPUS) and melanocytic tumors of uncertain malignant potential (MELTUMP) terminology: experience with second opinion consultation. *Pathologica* 2012;104:70-7.
3. Cerroni L, Barnhill R, Elder D, Gottlieb G, Heenan P, Kutzner H, *et al.* Melanocytic tumors of uncertain malignant potential: results of a tutorial held at the XXIX Symposium of the International Society of Dermatopathology in Graz, October 2008. *Am J Surg Pathol* 2010;34:314-26.
4. LeBoit PE, Burg G, Weedon D, Sarasin A. Melanocytic tumors. In: LeBoit PE, Burg G, Weedon D, Sarasin A, editors. *World Health Organization Classification of Tumors. Pathology & Genetics. Skin tumors*. Lyon: International Agency for Research on Cancer (IARC) press; 2006. pp. 49-50.
5. Barnhill RL, Cerroni L, Cook M, Elder DE, Kerl H, LeBoit PE, *et al.* State of the art, nomenclature, and

- points of consensus and controversy concerning benign melanocytic lesions: outcome of an international workshop. *Adv Anat Pathol* 2010;17:73-90.
6. Elder DE, Murphy GF. Management of uncertain melanocytic neoplasms: superficial atypical melanocytic proliferations of uncertain significance (SAMPUS) and melanocytic tumors of uncertain malignant potential (MELTUMP). In: Elder DE, Murphy GF, editors. *Atlas of Tumor Pathology (series 4). Melanocytic tumors of the Skin*. Washington, DC: American Registry of Pathology (ARP) in collaboration with Armed Forces Institute of Pathology (AFIP); 2010. pp. 264-8.
 7. McCormack CJ, Conyers RK, Scolyer RA, Kirkwood J, Speakman D, Wong N, *et al.* Atypical Spitzoid neoplasms: a review of potential markers of biological behavior including sentinel node biopsy. *Melanoma Res* 2014;24:437-47.
 8. Zembowicz A, Yang SE, Kafanas A, Lyle SR. Correlation between histologic assessment and fluorescence in situ hybridization using MelanoSITE in evaluation of histologically ambiguous melanocytic lesions. *Arch Pathol Lab Med* 2012;136:1571-9.
 9. Abraham RM, Ming ME, Elder DE, Xu X. An atypical melanocytic lesion without genomic abnormalities shows locoregional metastasis. *J Cutan Pathol* 2012;39:21-4.
 10. Cochran AJ, Binder S, Morton DL. The role of lymphatic mapping and sentinel node biopsy in the management of atypical and anomalous melanocytic lesions. *J Cutan Pathol* 2010;37:54-9.
 11. Lohmann CM, Coit DG, Brady MS, Berwick M, Busam KJ. Sentinel lymph node biopsy in patients with diagnostically controversial Spitzoid melanocytic tumors. *Am J Surg Pathol* 2002;26:47-55.
 12. Abraham RM, Karakousis G, Acs G, Ziober AF, Cerioni L, Mihm MC Jr, *et al.* Lymphatic invasion predicts aggressive behavior in melanocytic tumors of uncertain malignant potential (MELTUMP). *Am J Surg Pathol* 2013;37:669-75.
 13. Murali R, Sharma RN, Thompson JF, Stretch JR, Lee CS, McCarthy SW, *et al.* Sentinel lymph node biopsy in histologically ambiguous melanocytic tumors with Spitzoid features (so-called atypical Spitzoid tumors). *Ann Surg Oncol* 2008;15:302-9.
 14. Luo S, Sepehr A, Tsao H. Spitz nevi and other Spitzoid lesions part II. Natural history and management. *J Am Acad Dermatol* 2011;65:1087-92.
 15. Argenziano G, Giacomel J, Zalaudek I, Blum A, Braun RP, Cabo H, *et al.* A clinico-dermoscopic approach for skin cancer screening: recommendations involving a survey of the International Dermoscopy Society. *Dermatol Clin* 2013;31:525-34.