Sistema di Accreditamento ECM – Regione Piemonte

Lesioni melanocitarie borderline: criteri di diagnostica differenziale

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Lesioni melanocitarie borderline:
definizione

The **borderline melanocytic tumor (BTM)** is a morphologically and biologically indeterminate melanocytic proliferation manifesting worrisome architectural features and cytologic atypia exceeding that encountered in melanocytic nevi yet insufficient to warrant designation as melanoma.

The criteria that define the BMT are not well defined nor is the concept widely recognized.

Un **tumore melanocitico "borderline"** (TMB) è una proliferazione melanocitica morfologicamente e biologicamente indeterminata che presenta caratteri architetturali preoccupanti e atipie citologiche superiori a quelle che si riscontrano nei nevi ma ancora insufficienti per giustificare una diagnosi di melanoma. I criteri che definiscono la TMB non sono ben definiti e il concetto di TMB non è ampiamente riconosciuto.

Magro CM, Crowson AN, Mihm MC Jr, Gupta K, Walker MJ, Solomon G. The dermal-based borderline melanocytic tumor: a categorical approach. J Am Acad Dermatol. 2010 Mar;62(3):469-79.

Neoplasia melanocitica

Benigna
Atipica
Displastica
"Borderline"
Maligna
- in situ/non tumorigenica (HGP)
- invasiva/non tumorigenica (HGP)
- invasiva/tumorigenica (VGP)
- metastatica

Reed RJ, Ichinose H, Clark WH Jr, Mihm MC Jr. Common and uncommon melanocytic nevi and borderline melanomas. Semin Oncol. 1975 Jun;2(2):119-47.

State of the art, nomenclature, and points of consensus and controversy concerning benign melanocytic lesions: outcome of an international workshop. Barnhill RL, Cerroni L, Cook M, Elder DE, Kerl H, LeBoit PE, McCarthy SW, Mihm MC, Mooi WJ, Piepkorn MW, Prieto VG, Scolyer RA. **Adv Anat Pathol. 2010 Mar;17(2):73-90.**

Areas of controversy:

- including nevi with halo reactions, traumatized nevi, "dysplastic" nevi, and nevi from particular anatomic sites;
- malignant transformation associated with congenital nevi;
- atypical spitzoid neoplasms;
- particular melanocytic cellular phenotypes
- blue nevi, combined nevi, and other controversial lesions such as deep penetrating nevus and pigmented epithelioid melanocytoma.

The Group recommended the description of ambiguous or "borderline" lesions as tumors with indeterminate or uncertain biologic/malignant potential.

Abbreviations:

ASN	**A**typical **S**pitz **N**evus
AST	**A**typical **S**pitz **T**umor
B-DPN	**B**ordreline melanocytic proliferation arising in association with a **D**eep **P**enetrating **N**evus
BMT	**B**orderline **M**elanocytic **T**umor
BNMT	**B**orderline **N**evoid **M**elanocytic **T**umor
FAMMM	**F**amilial **A**typical **M**ultiple **M**ole **M**elanoma
MANIAC	**M**elanocytic **A**cral **N**evus with **I**ntraepidermal **A**scent of **C**ells
MelTUMP	**Mel**anocytic **T**umors of **U**ncertain **M**alignant **P**otential
PEM	**P**igmented **E**pithelioid **M**elanocytoma
PASNT	**P**ediatric **A**typical **S**pitz **N**evus/**T**umors
SNAFs	**S**pitz **N**evi with **A**typical **F**eature**s**
SPARK's	Nevi with cytologic characteristic of **Sp**itz and **Ar**chitectural features of Clar**k's**/dysplastic nevus

Borderline melanocytic tumors: variants

Superficial variant of borderline melanocytic tumors:

- superficial atypical Spitz tumor;
- de novo intraepidermal epithelioid melanocytic dysplasia.

Dermal variant of borderline melanocytic tumors:

- atypical proliferative nodules in congenital nevus;
- atypical Spitz tumor;
- atypical cellular blue nevus;
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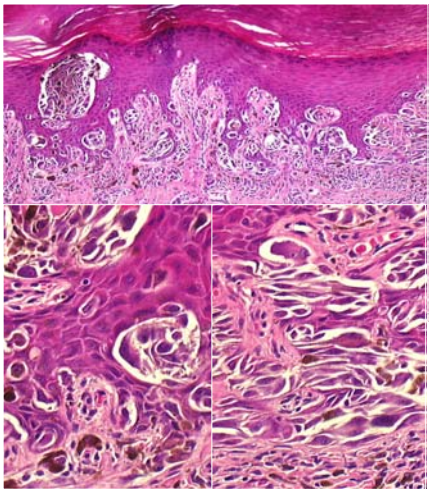
Superficial atypical Spitz tumor



- Younger female patients and common occurrence on the thigh.
- These lesions overlap with higher-grade dysplastic nevi and de novo intraepidermal epithelioid melanocytic dysplasia.
- Transition into malignant melanoma of superficial spreading type arising in a background of the superficial atypical Spitz tumor.

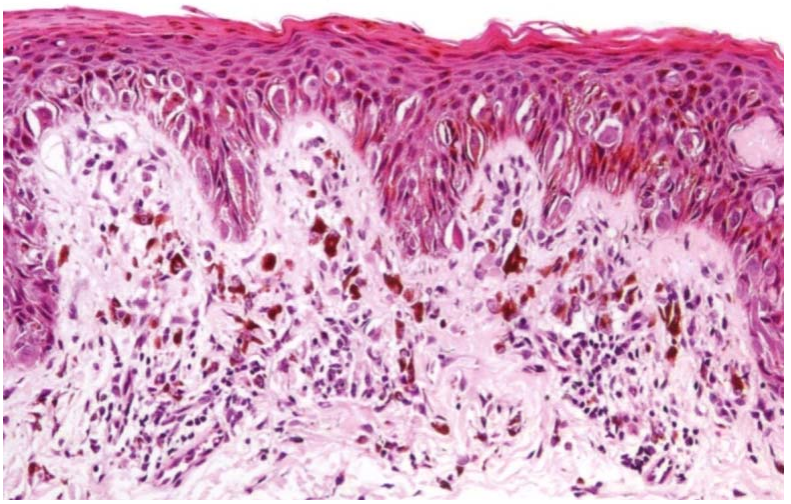
Magro CM, Yaniv S, Mihm MC. The superficial atypical Spitz tumor and malignant melanoma of superficial spreading type arising in association with the superficial atypical Spitz tumor: A distinct form of dysplastic Spitzoid nevomelanocytic proliferation. J Am Acad Dermatol 2009;60(5):814-23.

Tumore di Spitz atipico superficiale

diagnosi differenziali

- Nevo di Spitz pagetoide
- Nevo di Spitz tipo placca
- Nevo di Spitz acrale superficiale
- Nevo di Spitz lichenoide superficiale
- Nevo displastico, varietà pagetoide

Nevo di Spitz pagetoide

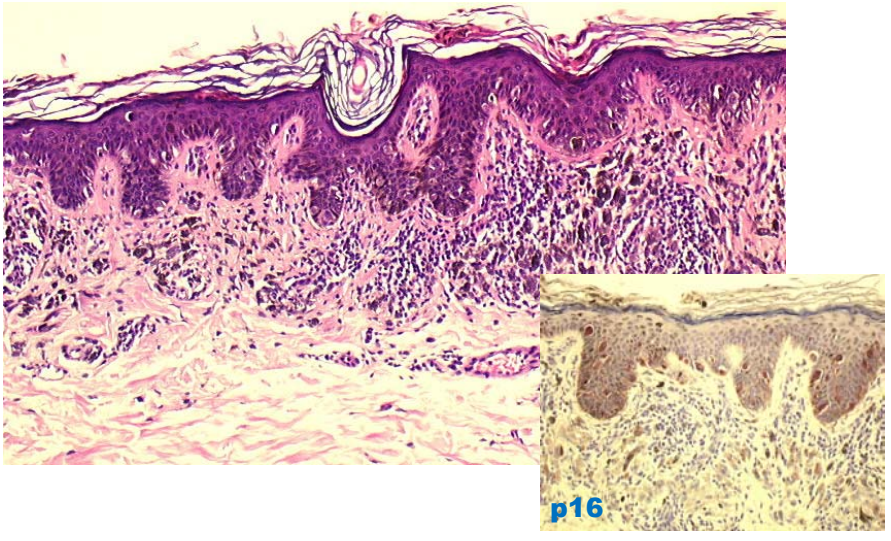


Busam KJ, Barnhill RL. Pagetoid Spitz nevus. Intraepidermal Spitz tumor with prominent pagetoid spread. Am J Surg Pathol. 1995 Sep;19(9):1061-7

Pagetoid Spitz	SSM
usually < 6mm	usually > 6 mm
symmetrical	asymmetric
ovoid perpendicular nests	variably oriented nests
pagetoid spread prominent	often prominent
spindle & epithelioid cells	usually epithelioid cells
cells uniform side to side	greater variability
scant melanin	fine dusty melanin
Kamino bodies	no Kamino bodies
maturation in dermis	little or no maturation

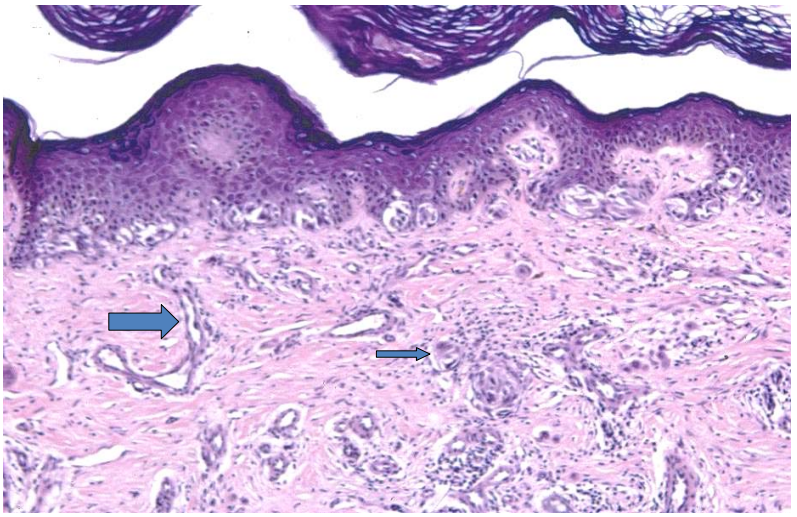
Xu X and Elder DE Pratical approaches to problematic melanocytic lesions. Personal course.

Nevo displastico pagetoide



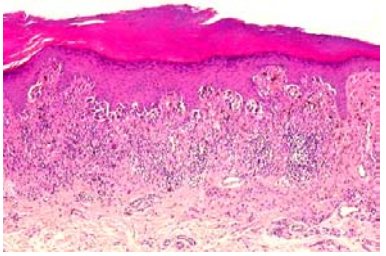
Coras B, Landthaler M, Stolz W, Vogt T. Dysplastic melanocytic nevi of the lower leg: sex- and site-specific histopathology. Am J Dermatopathol. 2010 Aug;32(6):599-602.

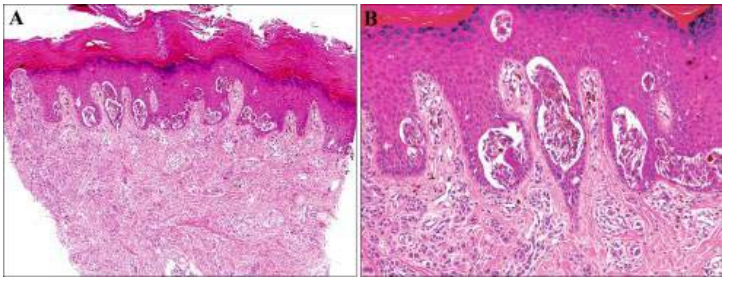
Plaque-like Spitz nevus



Crowson AN, Magro CM, Mihm MC. The melanocytic proliferations. A comprehensive textbook of pigmented lesions. Pag. 162-3 Wiley-Liss, 2001

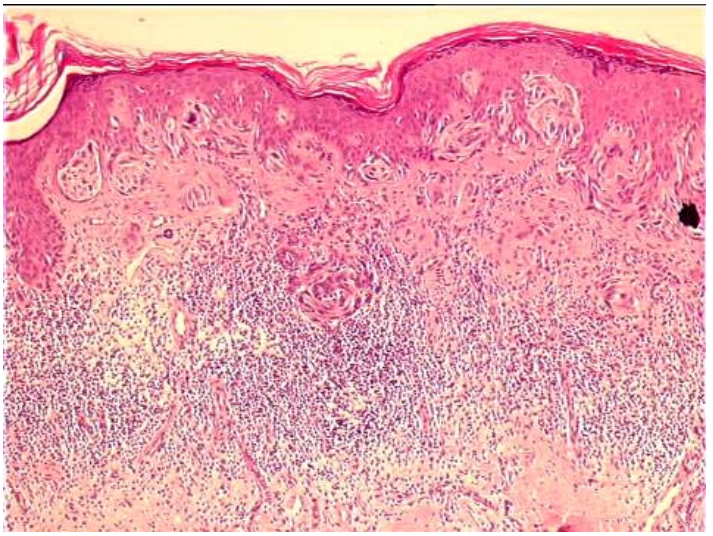
Nevo di Spitz acrale





Jang YH, Lee JY, Kim MR, Kim SC, Kim YC.Acral pigmented spitz nevus that clinically mimicked acral lentiginous malignant melanoma. Ann Dermatol. 2011 May;23(2):246-9. Epub 2011 May 27.

Nevo di Spitz lichenoide o alonato



Crowson AN, Magro CM, Mihm MC. The melanocytic proliferations. A comprehensive textbook of pigmented lesions. Pag. 133-5 Wiley-Liss, 2001

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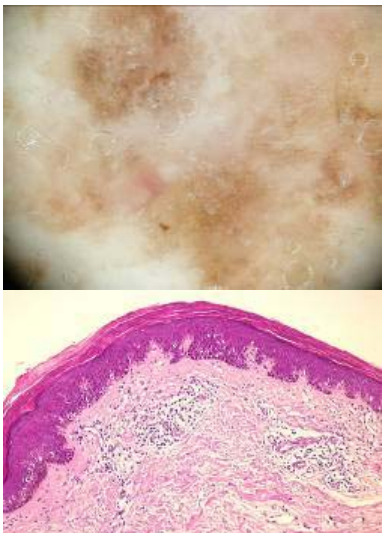
Displasia melanocitica intraepiteliale epitelioide

- Proliferazione intraepidermica di melanociti con atipie
- 2/3 dei pazienti hanno una familiarità per nevi displastici e/o melanoma
- Macule piatte, brunastre con bordi tondeggianti o irregolari, clinicamente simili ad un nevo displastico
- Sono localizzate prevalentemente su cute esposta ma anche su tronco, braccia e gambe.

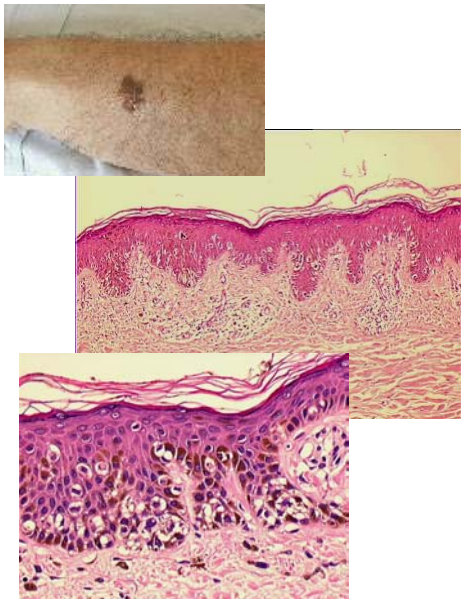


Crowson AN, Magro CM and Mihm MC Jr. Journal of the American Academy of Dermatology, 2004

Superficial variant of borderline melanocytic tumors:
differential diagnoses

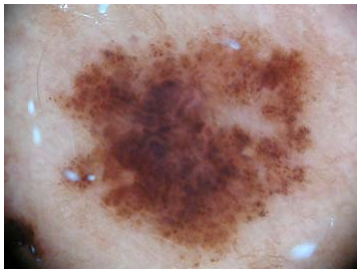
In situ pagetoid melanoma
Dysplastic type in situ melanoma
Acral lentiginous in situ melanoma
Lentigo maligna

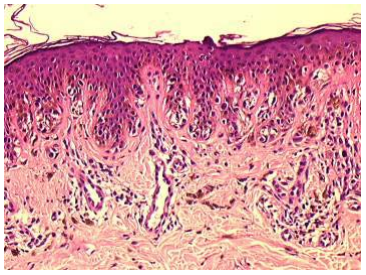
Melanoma in situ, “pagetoide”



- Proliferazione di melanociti con ampio citoplasma chiaro con crescita “aggressiva” nei confronti dell’epidermide ma sono confinati in essa.
- I melanociti maligni infiltrano gli sproni epiteliali a nidi con margini irregolari o a cellule singole e si estendono sino agli strati più superficiali dell’epidermide.
- Gli sproni epiteliali infiltrati appaiono aumentati di dimensioni ed espansi.

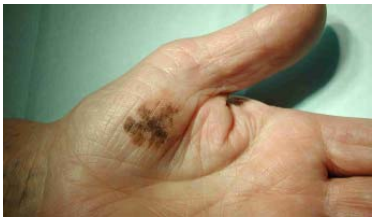
Melanoma in situ, tipo nevo displastico

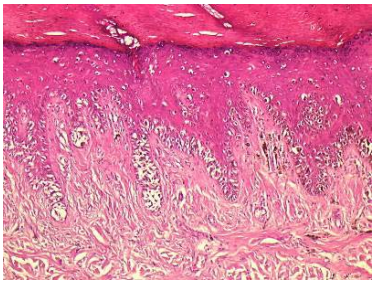




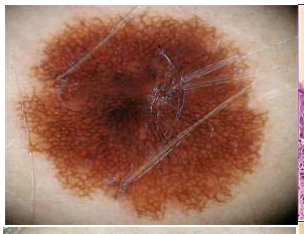
Proliferazione intraepiteliale di melanociti atipici con aspetto lentigginoso, a cellule singole e a nidi, con infiltrazione dell’epidermide (crescita aggressiva). Si associata fibroplasia, neogenesi vascolare e infiltrato infiammatosio dermico; l’infiltrato, nel melanoma in situ non prende contatto con l’epidermide e la neoplasia.

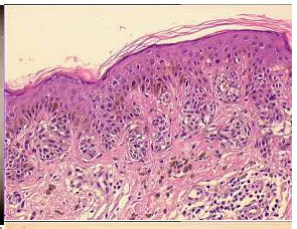
Melanoma in situ, acrale lentigginoso



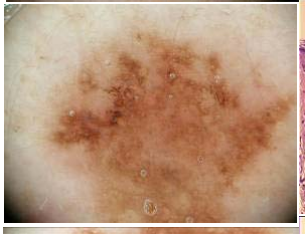


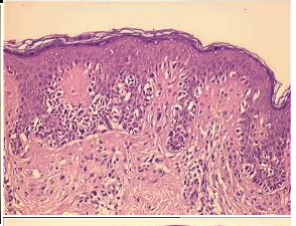
Proliferazione prevalentemente giunzionale e parabasale di melanociti atipici con aspetti “dendritici” isolati o a nidi confluenti. Eliminazione transepidermica di pigmento melanico. Acantosi dell’epidermide e infiltrato infiammatorio dermico.



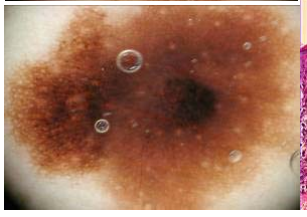


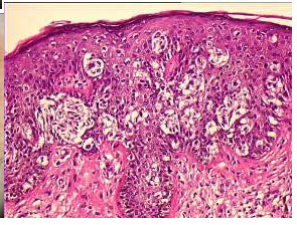
Nevo giunzionale / composto





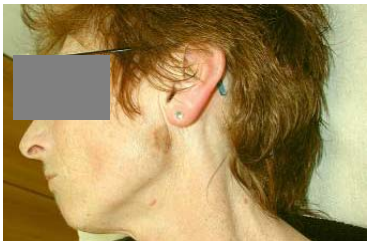
Nevo displastico

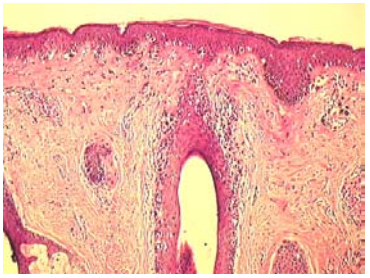




Melanoma in situ / in fase di crescita orizzontale

Lentigo maligna

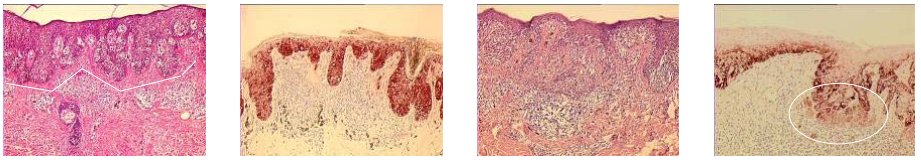




- Lesione piatta irregolarmente pigmentata che interessa la cute della faccia di pazienti anziani.
- Caratterizzata da una proliferazione di melanociti atipici lungo la giunzione dermo epidermica in una cute atrofica.
- Presenza di nidi giunzionali di cellule fusate che si estendono lungo gli annessi.
- Quando compare invasione spesso si dimostra un aspetto simil pagetoide con associato infiltrato infiammatorio dermico.
- Nel derma è presente elastosi.

Fase di crescita radiale/orizzontale

- Melanoma in situ, intraepidermico, limitato al di sopra della membrana basale dell'epidermide.
- Melanoma invasivo, inizialmente infiltrante il derma papillare



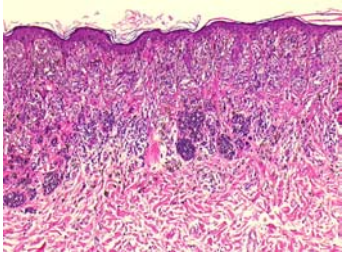
None of 161 patients showed metastases at a mean follow-up of 13.7 years

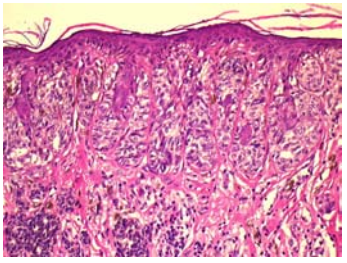
Guerry D 4th, Synnestvedt M, Elder DE, Schultz D. Lessons from tumor progression: the invasive radial growth phase of melanoma is common, incapable of metastasis, and indolent. J Invest Dermatol. 1993 Mar;100(3):342S-345S.

Diagnosi differenziali (HGP)

- Nevo giunzionale/composto (acrale, della cute dei genitali, della cintura, ecc.)
- Nevo displastico
- Nevo pigmentato a cellule fusate (nevo di Reed)
- Nevo a cellule epitelioidi e fusate, giunzionale/superficiale e varianti
- Nevo persistente (c.d. ricorrente o pseudomelanoma di Ackerman)

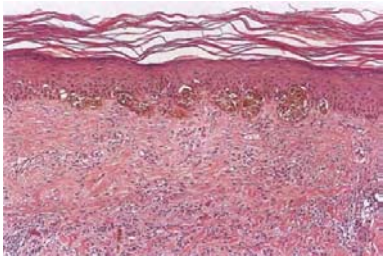
Nevo “attivato”





Sotto l’influenza della luce solare o di altri fattori (PUVA, gravidanza, uso di ormoni, pazienti HIV positivi ed immunodepressi, ecc) i nevi possono diventare più scuri ed acquisire caratteri istopatologici che simulano un nevo displastico.

Nevo persistente



- Lesione pigmentata che insorge in sede di incompleta asportazione di un nevo
- Può simulare clinicamente ed istologicamente un melanoma
- Dimensione variabile, ma spesso di pochi mm; margini irregolari
- Forma spesso asimmetrica; lesioni multiple
- Melanociti con atipie e architettura lentigginosa in corrispondenza della cicatrice; residui di nevo in profondità.

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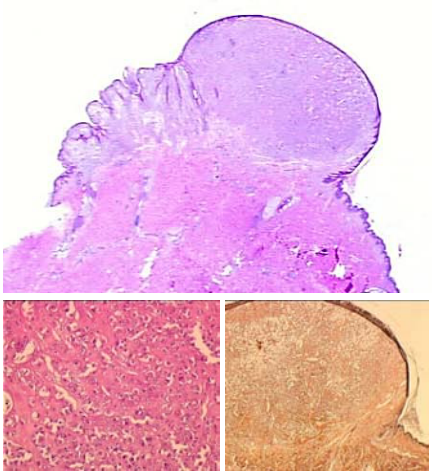
Nodulo di proliferazione dermico in nevo congenito



- I noduli possono presenti nel derma superficiale o profondo
- Noduli spesso ipercellulati con cellule epitelioidi, fusate o piccole, ben delimitati, scarsamente pigmentati
- Vari gradi di atipia ma uniformi con reticolo ben rappresentato, mitosi rare o assenti.

de Vooght A, Vanwijck R, Gosseye S, Bayet B. Pseudo-tumoral proliferative nodule in a giant congenital naevus. *Br J Plast Surg. 2003 Mar;56(2):164-7.*

Lowes MA, Norris D, Whitfeld M. Benign melanocytic proliferative nodule within a congenital naevus. Australas *J Dermatol. 2000 May;41(2):109-11.*

van Houten AH, van Dijk MC, Schuttelaar ML. Proliferative nodules in a giant congenital melanocytic nevus-case report and review of the literature. J Cutan Pathol. 2010 Jul;37(7):764-76.

Cellular and proliferative dermal nodules in congenital nevi

- **Cellular nodules**: no evidence of proliferation in the form of mitotic activity
- **Cellular and proliferative nodules**: when mitotic activity or other evidence of proliferation (e.g. Ki-67 reactivity) and minimal cytologic atypia is present.
- **Melanocytic tumors of uncertain malignant potential**: when mitotic activity and cytologic atypia is present.

Elder DE, Murphy GF. Melanocytic tumors of the skin. AFIP Atlas of Tumor Pathology, Series 4. ARP Press, 2010; pag.146-7

Features helpful in differentiating cellular nodules and melanoma forming in congenital nevi*

	Cellular Nodule	Melanoma
Clinical features		
Rapid growth	Present	May be insidious
Age of onset	Neonatal period	Childhood and adulthood
Architecture		
Diameter	Usually < 5mm	Often > 5mm
Blending with adjacent nevus cells	Gradual transition present	Abrupt demarcation
Focality	May be multifocal	Unifocal
Ulceration	Absent	May be present
Expansile/destructive growth	Absent	Present
Cytology		
High-grade atypia	Absent	Present
Mitoses	Absent or few	Often many
Necrosis	Absent	Often present

*Lesions with intermediate features are best regarded as atypical proliferative nodules and warrant complete excision and close follow-up.

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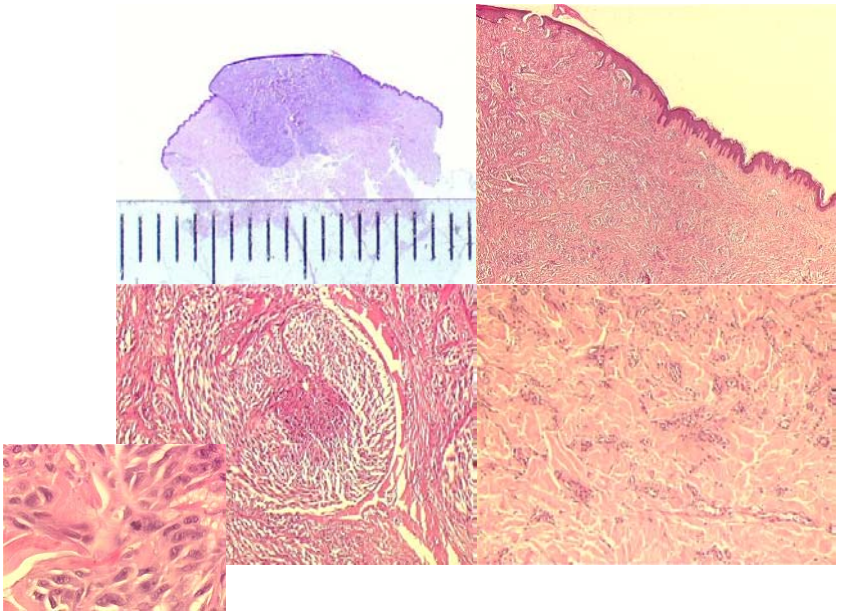
Tumore di Spitz atipico

(Barnhill et al., 1999)

- Un subset di proliferazioni melanocitiche spitzoidi con caratteri istologici “preoccupanti” e con evoluzione biologica indeterminata
  - architettura simile al melanoma in VGP
  - citologia simile al nevo di Spitz convenzionale
  - metastasi, quando presenti, tendono ad essere confinate ai linfonodi regionali
- Spesso più grandi dei nevi di Spitz usuali: >2mm
- Aspetto clinico altrimenti simile al comune nevo di Spitz

Tumore di Spitz atipico



Tumore di Spitz atipico

- **Spitz classico**
- Dimensione: <1 cm
- Simmetrico
- Ben demarcato
- Nidi regolari
- Estensione profonda assente
- Nodulo espansivo assente

- **Spitz atipico**
- Dimensione: >1 cm
- Asimmetrico
- Non ben demarcato
- Nidi irregolari
- Estensione profonda presente
- Nodulo espansivo talora presente

Barnhill RL, Argenyi ZB, From L, Glass LF, Maize JC, Mihm MC Jr, Rabkin MS, Ronan SG, White WL, Piepkorn M. Atypical Spitz nevi/tumors: lack of consensus for diagnosis, discrimination from melanoma, and prediction of outcome. Hum Pathol. 1999 May;30(5):513-20.

SLNB in Spitzoid Tumors

Study	Dx	N+/N	Age	Survival
MSK 2002	"controversial"	5/10	21	100%
Michigan '03	Atypical Spitzoid	8/18	16	100%
Michigan '04	MM/MELTUMP	12/14	8.5	100%
Colorado '05	MM/aSpitz	8/20	8-20	100%
Pittsburgh '06	atypical Spitz	3/10	"< 17	100%
Florence IT '06	atypical Spitz	4/12	23	100%

Differing Interpretations:

metastatic potential may be under-diagnosed"

"SLNB aids in confirming a diagnosis of melanoma"

"Long-term follow-up needed before SLNB can become a standard of care in pediatric melanoma or as a diagnostic tool to distinguish the atypical Spitz nevus from melanoma."

Xu X and Elder DE Pratical approaches to problematic melanocytic lesions. Personal course.

Features helpful in differentiating Spitz tumor and nodular melanoma°

	Spitz Tumor	Nodular Melanoma
Architecture		
*Diameter	Usually < 10mm	Usuallly > 10 mm
*Symmetry	Usually present	Often absent
*Lateral borders	Sharply demarcated	Often poorly demarcated
*Irregular nesting	Uncommon	Common
*Ulceration	Absent	Often present
*Deep estension (into fat)	Uncommon	Common in thick tumors
*Espansile nodule	Uncommon	Common
*Cellularity	Variable, nested	Dense, sheet-like, cohesive
Epidermal hyperplasia	Present	Minimal or absent
Junctional proliferation	Discontinuous	Often continuous
Junctional nest orientation	Perpendicular to epidermis	Random
Pagetoid spread	Inconspicuous or absent	Often apparent
Pigment distribution	Little or no pigment	Patchy, asymmetric
Nesting pattern at base	Small, uniform	Larger, variable
Nuclear pleomorphism	Mild or moderate	May be severe
Cytology		
*Mitoses in lower third	Absent	Often present
*Maturation/zonation	Present	Generally absent
*Deep border	Infiltrating	Rounded, pushing, fascicular
Kamino bodies	Single and confluent	Inconspicuous or absent
Chromatin pattern	Delicate, evently dispersed	Coarse, clumped
Necrosis	Absent	Often present

°Nodular melanoma lack radial growth phase at the periphery, which if diagnostic of melanoma, rules out Spitz tumor. Item marked with an* are elements of Barnhill (1995,1999) and Spatz (1999) grading system for atypical Spitz tumors.

Elder DE, Murphy GF. Melanocytic tumors of the skin. AFIP Atlas of Tumor Pathology, Series 4. ARP Press, 2010.

Tumore di Spitz atipico: grading

- Età superiore a 10 anni (1 punto)
- Tumore di diametro > 10 mm (1 punto)
- Estensione al tessuto adiposo, ulcerazione o mitosi da 6 a 8 per mm^2 (2 punti per ciascuno)
- Mitosi superiori 8 per mm^2 (5 punti)

0-2 punti: basso rischio

3-4 punti: rischio intermedio

5-11 punti: rischio elevato

- Spatz A. et al. Spitz tumors in children: a grading system for risk stratification. Arch Dermatol 1999; 135:282
- Barnhill RL, Argenyi ZB, From L, Glass LF, Maize JC, Mihm MC Jr, Rabkin MS, Ronan SG, White WL, Piepkorn M. Atypical Spitz nevi/tumors: lack of consensus for diagnosis, discrimination from melanoma, and prediction of outcome. Hum Pathol. 1999 May;30(5):513-20
- Barnhill RL, Flotte TJ, Fleischli M, Perez-Atayde A. Cutaneous melanoma and atypical Spitz tumors in childhood. Cancer. 1995 Nov 15;76(10):1833-45

Borderline melanocytic tumors: variants

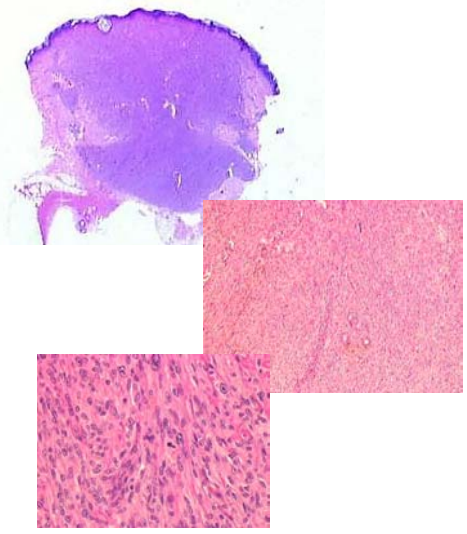
Superficial variant of borderline melanocytic tumors:

- superficial atypical Spitz tumor;
- de novo intraepidermal epithelioid melanocytic dysplasia

Dermal variant of borderline melanocytic tumors:

- atypical proliferative nodules in congenital nevus;
- atypical Spitz tumor;
- **atypical cellular blue nevus:**
- borderline melanocytic tumor arising in a deep penetrating nevus;
- pigmented epithelioid melanocytoma;
- paraganglioma-like dermal melanocytic tumor;
- squamomelanocytic tumor.

Atypical cellular blue nevus



- Clinicopathologic features intermediate between typical cellular blue nevus (CBN) and the rare malignant blue nevus (MBN)/malignant melanoma arising in a CBN.
- Architectural atypia (infiltrative margin and/or asymmetry) and/or cytologic atypia (hypercellularity, nuclear pleomorphism, hyperchromasia, mitotic figures, and/or necrosis).
- Histologic features of ACBN are also those of MBN. Because of these intermediate clinicopathologic features, ACBN warrant close scrutiny and long-term follow-up.

Tran TA, Carlson JA, Basaca PC, Mihm MC. Cellular blue nevus with atypia (atypical cellular blue nevus): a clinicopathologic study of nine cases. J Cutan Pathol. 1998 May;25(5):252-8.

Atypical cellular blue nevus

Pathology features

- Size greater than 3cm
- Increased cellularity
- Cellular polymorphism (focal areas of atypia in background of cellular blue nevus)
- Increased mitotic activity (but less than 2 mitoses/square mm and no atypical mitoses)
- Areas of necrosis

Murali R, McCarthy SW, and Scolyer RA.Â Blue Nevi and Related Lesions: A Review Highlighting Atypical and Newly Described Variants, Distinguishing Features and Diagnostic Pitfalls. Adv Anat Pathol 2009;16:365-82.

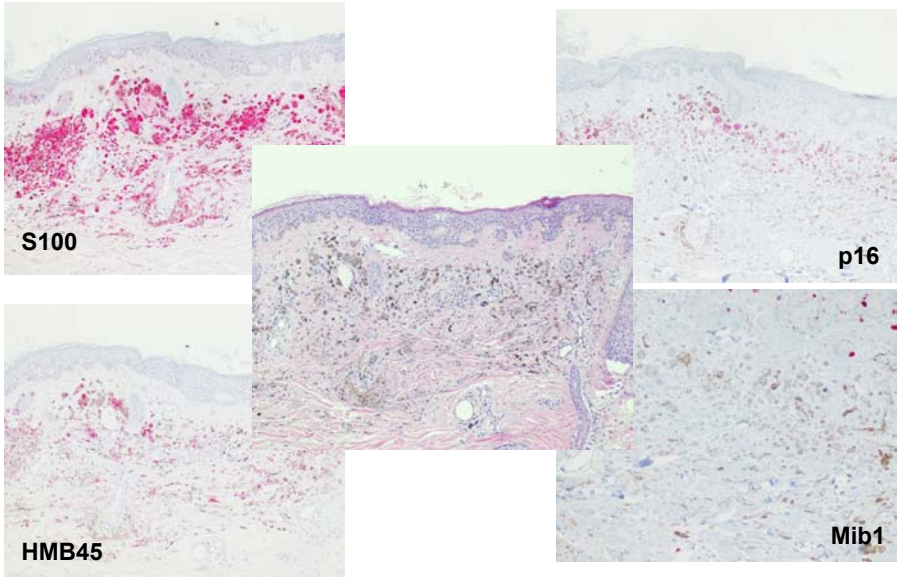
Atypical cellular blue nevus

Differential diagnoses

	Cellular blue nevus	Atypical cellular blue nevus	Malignant blue nevus	Pigmented epithelioid melanocytoma
Cytologic atypia	Rare to occasional	Intermediate	Severe	Variable
Mitotic activity	Rare	Usually <3/mm^2	High, usually >3/mm^2	Low, none to<3/mm^2
Atypical mitosis	Absent	Absent	Present	Absent
Necrosis	Absent	Rare	Often	Rare
Ulceration	Rare	Rare	Sometimes	Sometimes
Lymphovascular invasion	Absent	Absent	Sometimes	Rare
Epidermal hyperplasia	Absent	Absent	Absent	Frequent
Pigmentation	Variable	Variable	Variable	Heavy
Border	Usually well ciircumscribed	Usually well ciircumscribed	Often infiltrative	Usually infiltrative
Immunohistochemistry	HMB45+	HMB45+	HMB45+	HMB45+

Artur Zembowicz, Pushkar A. Phadke. Blue Nevi and Variants: An Update. Archives of Pathology & Laboratory Medicine: March 2011, Vol. 135, No. 3, pp. 327-336.

Epithelioid blue nevus



Borderline melanocytic tumors: variants

Superficial variant of borderline melanocytic tumors:

- superficial atypical Spitz tumor;
- de novo intraepidermal epithelioid melanocytic dysplasia
- *(intraepidermal/horizontal growth phase (HGP) melanoma)*

Dermal variant of borderline melanocytic tumors:

- atypical proliferative nodules in congenital nevus;
- atypical Spitz tumor;
- atypical cellular blue nevus:
- **borderline melanocytic tumor arising in a deep penetrating nevus**;
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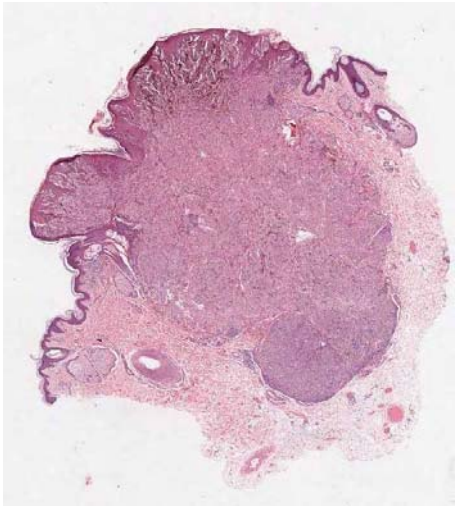
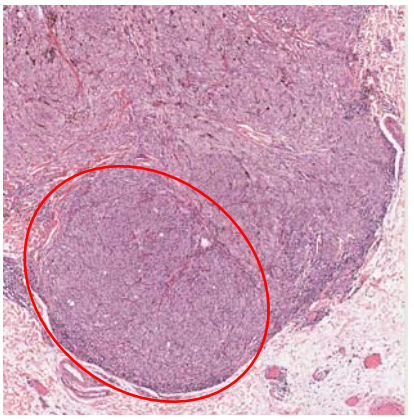
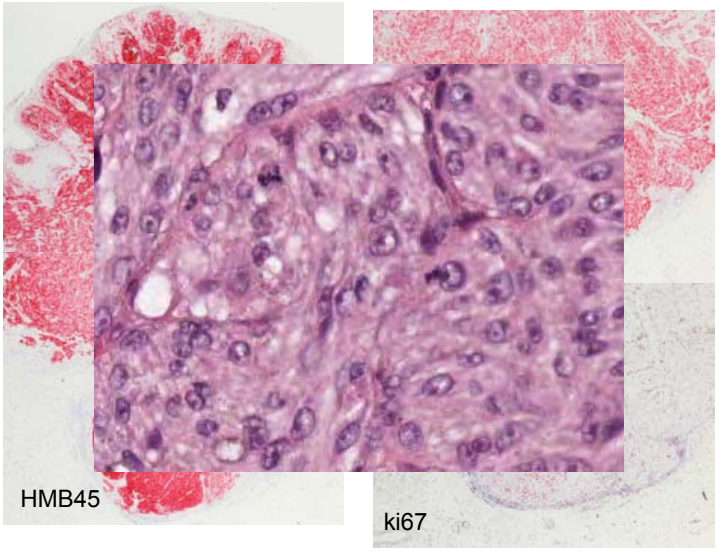
Borderline melanocytic tumor arising in a deep penetrating nevus





Borderline melanocytic tumor arising in a deep penetrating nevus



Borderline melanocytic tumor arising in a deep penetrating nevus

- Background melanocytic proliferation exhibiting all of the typical features of a deep penetrating nevus (DPN) in which were present additional features not encountered in the classic DPN.
- Cellular proliferative areas arranged to the long axis of the epidermis, in contradistinction to the dominant orderly vertical orientation seen in the typical DPN, or a nodular expansile growth at the base.
- Such foci also manifested enhanced cytologic atypia with cellular enlargement and increased mitotic activity, including marginal mitoses
- 4 of 7 patients had positive sentinel lymph nodes.
- All patients except one are alive and well without any clinical evidence of recurrent disease at a mean follow-up period of 4 years.

Magro CM, Crowson AN, Mihm MC Jr, Gupta K, Walker MJ, Solomon G. The dermal-based borderline melanocytic tumor: a categorical approach. J Am Acad Dermatol. 2010 Mar;62(3):469-79.

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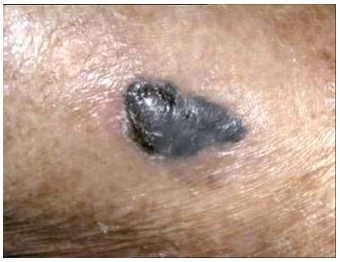
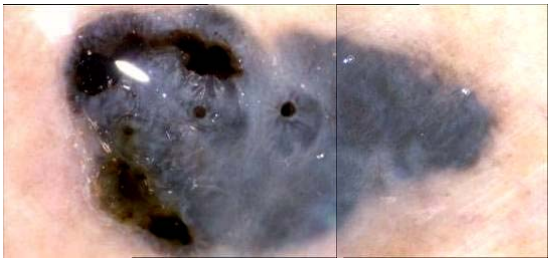
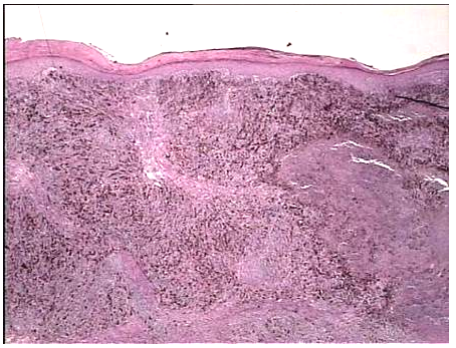
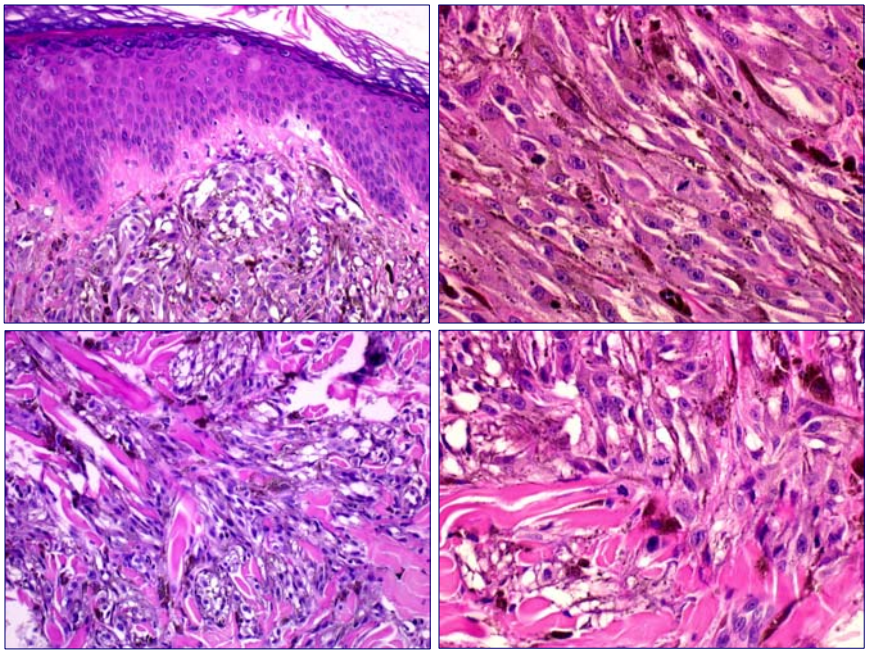
Melanocitoma epitelioide pigmentato



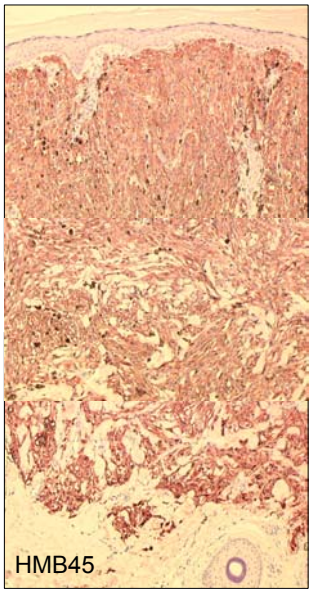


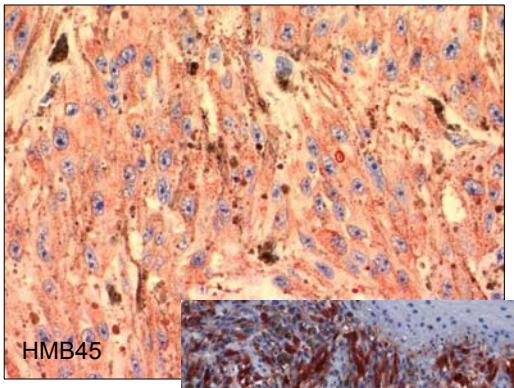
Crowson AN, Magro CM, Mihm MC Jr. Malignant melanoma with prominent pigment synthesis: "animal type" melanoma--a clinical and histological study of six cases with a consideration of other melanocytic neoplasms with prominent pigment synthesis. Hum Pathol. 1999;30(5):543-50.

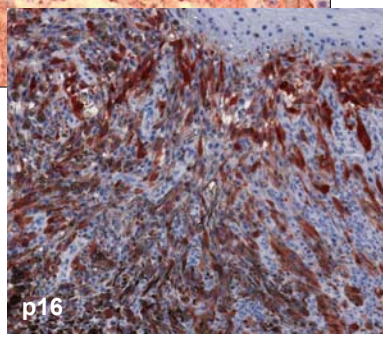




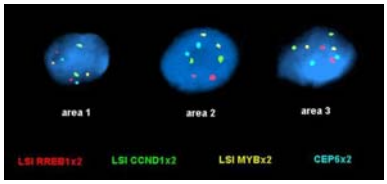
Immunoreattività



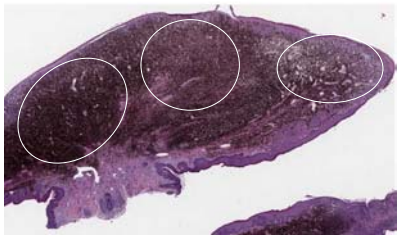




FISH test: negativo



- **10.00** *CCND1** gain (positive ≥38%)
- **32.00** *RREB1/CEP6*** *% gain* (positive >55%)
- **30.00** % loss of *MYB* against CEP6*** (positive ≥40%)
- **15.33** RREB1 **** gain (positive ≥29%)



Cut off secondo Gerami, 2009

* Probe for the CCND1 gene (located at 11q13)

** Probe for the RREB1 gene (located at 6p25)

*** Probe for the MYB gene (located at 6q23-q23)

**** Centromeric probe (CEP6) for the ploidy level of chromosome 6

Melanocitoma epitelioide pigmentato

Caratteri Generali	Letteratura
Età/sesso	Media 28 anni (7 mesi – 85 anni)/ M = 49% - F = 51%
Sede	Estremità 43-44%, tronco 27-30%, testa e collo 24-25%, genitali 2-5%
Dimensioni	2-10 mm
Ulcerazione	Solitamente assente
Regressione	Assente
TIL	Solitamente assente o non brisk
Invasione vasi/nervi	Assente
Invasione annessi	Spesso presente
Livello	La maggior parte 4°livello
Spessore	Media 3.3 mm (1.4-10.5 mm)
Mitosi	Rare (< 3 per mm^2)
Linfonodo sentinella	Positivo nel 41-47% dei casi
Sopravvivenza	90-98% (follow up tra 0.5-17 anni); giovani prognosi migliore
Metastasi a distanza	Rare (9%) (2 casi con metastasi epatica e 1 in transit)

- Il melanocitoma epitelioide pigmentato è una neoplasia melanocitica *borderline* o un melanoma a basso grado
- Applicare analisi di genetica molecolare (FISH) in tutti i casi istologicamente diagnosticati o sospetti oltre alla colorazione immunocitochimica con siero anti p16
- Segnalare al clinico e genetista il paziente da tenere sotto controllo e da valutare per un possibile complesso di Carney
- Chiedere una seconda opinione istopatologica

PEM Differential Diagnosis

- Cellular blue nevus
- Malignant blue nevus
- Deep penetrating nevus
- Pigmented spindle cell nevus
- Pigmented epithelioid variant of Spitz nevus
- Regressed melanoma with prominent melanophages

Xu X and Elder DE Pratical approaches to problematic melanocytic lesions. Personal course.

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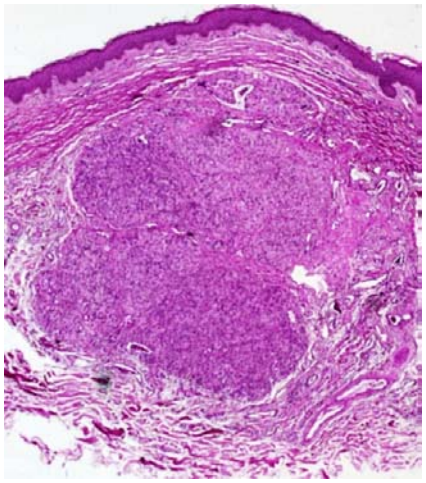
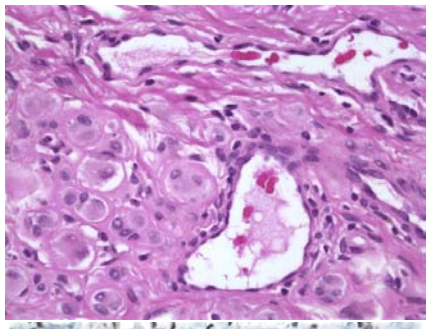
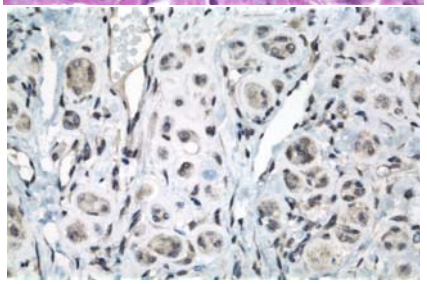
Paraganglioma-like dermal melanocytic tumor







Paraganglioma-like dermal melanocytic tumor

- A tumor composed of cells disposed in nests surrounding by o rich network of branching proliferative capillaries.
- A rare dermal melanocytic lesion, unusual in children that should be carefully diagnosed by histopathologic observation, immunohistochemistry (vimentin, S-100, Melan A +++; Ki67<1% in neoplastic cells; endothelial cells with an unusual high proliferation rate)
- No local reccurrences, nodal metastasis and excellent prognosis reported in already described cases.
- Actually classified by AFIP (Elder DE, Murphy GF, 2010) as “melanocytic tumor of uncertain malignant potential”

Cimpean AM, Ceauşu R, Raica M. Paraganglioma-like dermal melanocytic tumor: a case report with particular features. Int J Clin Exp Pathol. 2009 Nov 20;3(2):222-5.
Sarma DP, Teruya B, Wang B. Paraganglioma-like dermal melanocytic tumor: a case report. Cases J. 2008 Jul 18;1(1):48.
Deyrup AT, Althof P, Zhou M, Morgan M, Solomon AR, Bridge JA, Weiss SW. Paraganglioma-like dermal melanocytic tumor: a unique entity distinct from cellular blue nevus, clear cell sarcoma, and cutaneous melanoma. Am J Surg Pathol. 2004 Dec;28(12):1579-86.

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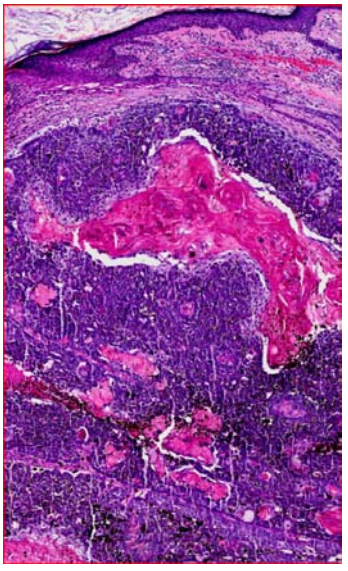
Tumore squamo-melanocitico dermico

- Neoplasia molto rara*
- Noduli rosso-nerastri del viso (> 1 cm)
- Età: 44-87 anni
- 3 M e 2 F
- In un caso è stata documentata una lentigo maligna come precursore
- Follow up dei casi descritti (media 3.5 anni) senza ripresa o metastasi
- Nodulo dermico senza connessione con l'epidermide; commistione tra carcinoma spinocellulare e melanoma.

*Pool SE et al Human Pathol 30, 525, 1999



Take home message

- La maggior parte delle lesioni pigmentate possono essere facilmente diagnosticate, tuttavia esiste un piccolo sottogruppo di lesioni problematiche.
- Una buona qualità del preparato è il presupposto fondamentale per una diagnosi corretta.
- Le notizie cliniche (dermatoscopia) sono spesso indispensabili.
- Le neoplasie melanocitiche superficiali (non tumorigeniche) possono recidivare localmente mentre quelle dermiche (tumorigeniche) possono potenzialmente sviluppare metastasi.
- Segnalare nel referto istopatologico, dove necessario, l'indicazione all'esame del linfonodo sentinella.
- Nei casi più difficili è importante richiedere una seconda opinione.

ANATOMIA PATOLOGICA

Casa di Cura San Pio X - Milano

Dr. Stefania Rao
Dr. Annamaria Ferrari
Dr. Cristina Campidelli
Dr. Federica Cetti Serbelloni
Sig.ra Loredana Alasio

I.R.C.C.S. Policlinico San Donato, Milano

Dr. Barbara Rubino
Dr. Barbara Bruni
Dr. Antonella Festa
Dr. Iasi Gabriela
Dr. Sara Leoncini
Dr. Anna Carini

…. e tutto il personale tecnico e amministrativo dei due laboratori

Grazie per l'attenzione!

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