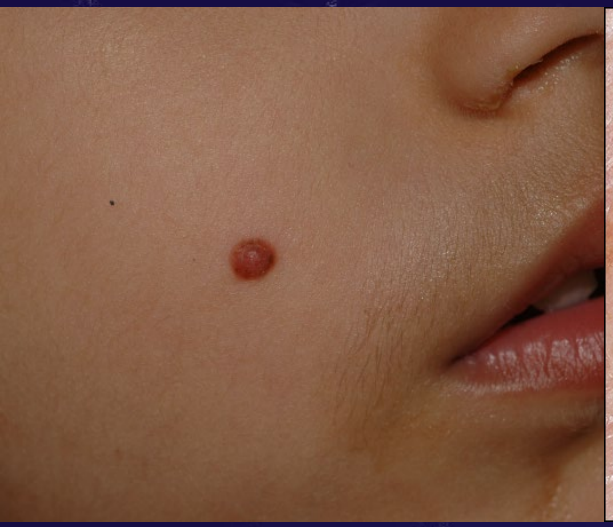
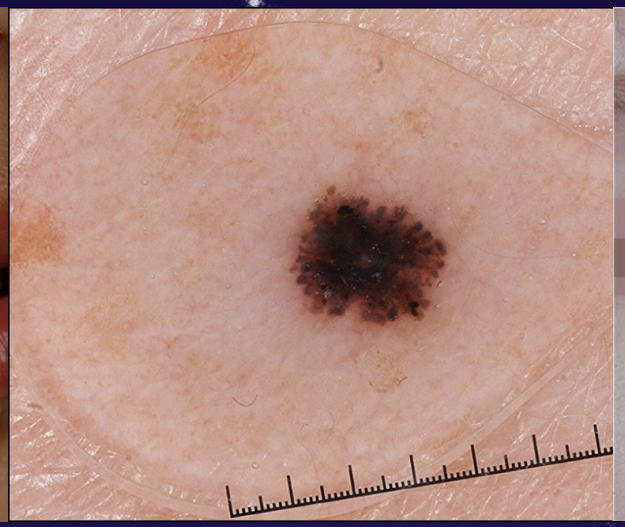
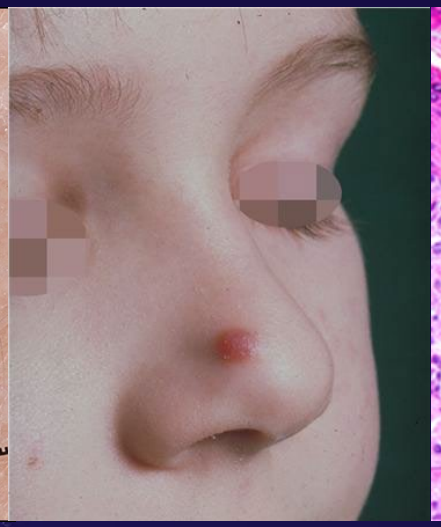
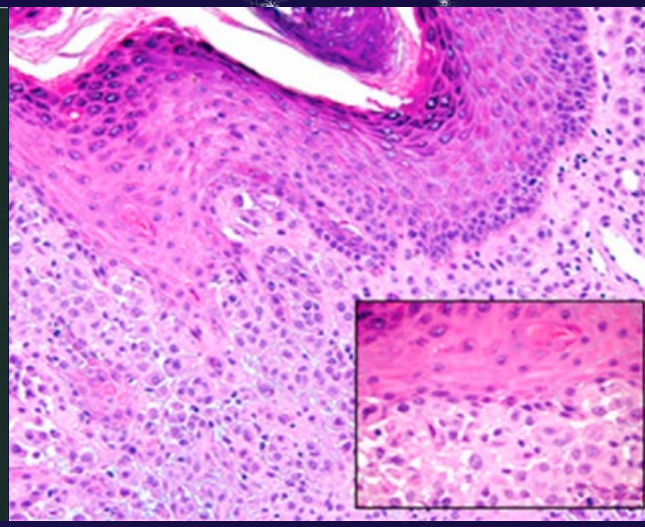





Nevus de Spitz Atípico

Shirley Ariza Maestre

Dermatóloga

Universidad Nacional de Colombia

Definición

" El termino diagnóstico 'Nevus de Spitz atípico' es usado para describir las lesiones que se salen de la apariencia típica del Nevus de Spitz y tienen un significado biológico incierto"

N. Spitz con atipia – N. Spitz Atípico
T. Spitz Atípico – T. Spitzoide de potencial maligno incierto

MELTUMPs (Tumores Melanociticos de Potencial Incierto):
1. Actividad Mitótica 2. Mitosis cerca a la base
3. Inflamación (VP significativo de las evaluaciones)

de Giorgi V, Sestini S, Massi D, Papi F, Lotti T. *Atypical Spitz tumour: a 'chameleon' lesion.* Clin Exp Dermatol. 2008 May;33:3

Clínica

Table I. Clinical features of classic Spitz nevi and atypical Spitz tumors

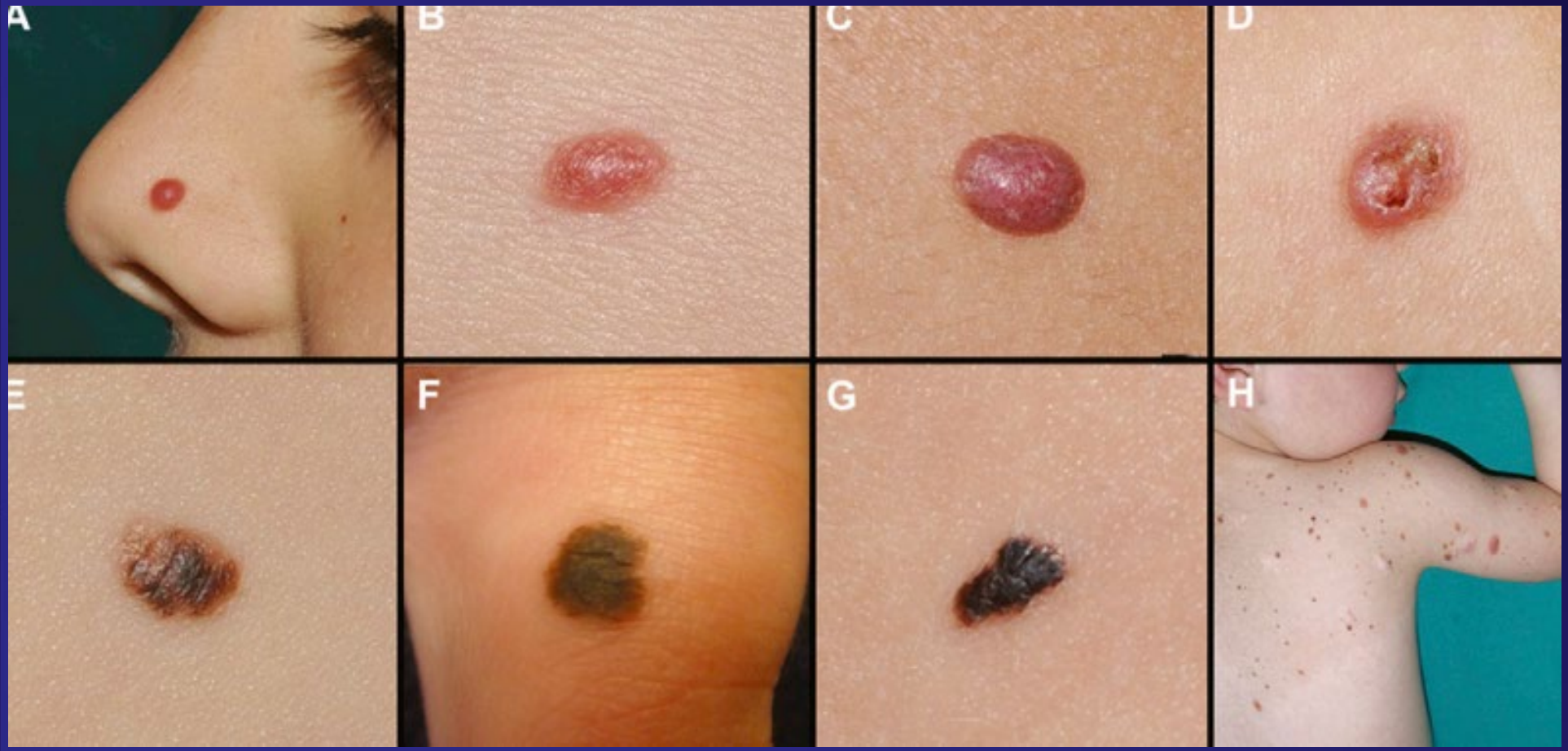
Clinical feature	Classic Spitz nevi	Atypical Spitz tumors
Age	<10 years old	10-20 years old
Location	Extremities, face, neck	Back 6%
Size	<5-6 mm in diameter	>1 cm in diameter
Shape	Symmetric, dome-shaped	Increasing asymmetry
Border	Well defined	Irregular
Surface	Smooth	Irregular, ulcerated
Color	Pink/reddish	Irregular

Cabeza y cuello 37%
Extremidades Inf. 28%

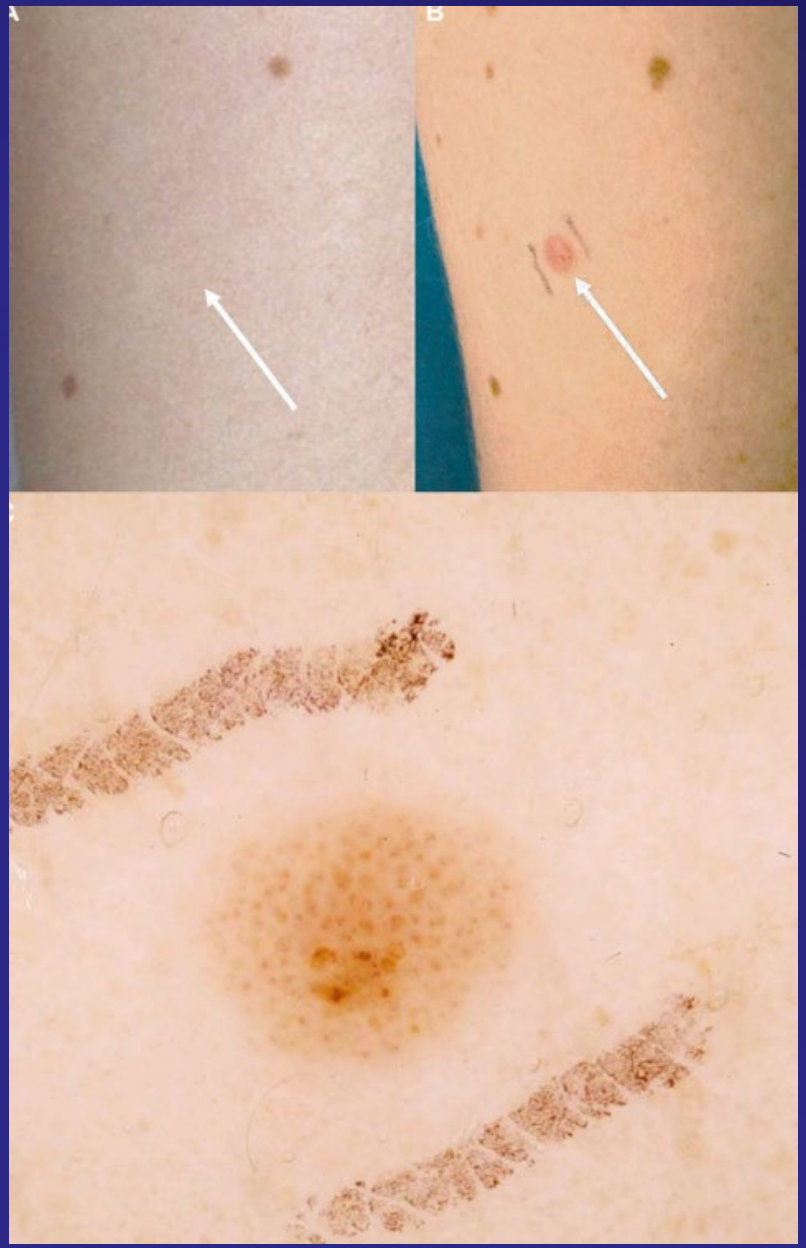
10% Pigmentados

Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions Part I. Background and diagnoses.* J Am Acad Dermatol 2011;65:6

Clínica



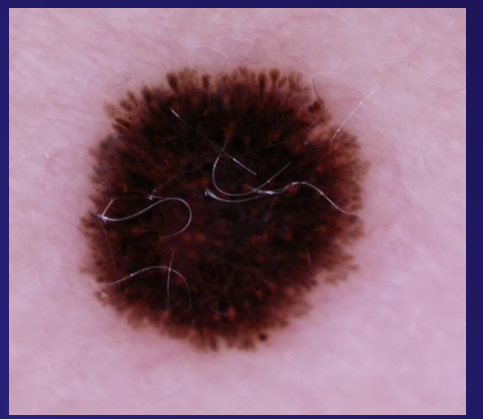
Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions Part I. Background and diagnoses.* J Am Acad Dermatol 2011;65:6



Clínica

Patrón vascular punteado
Pigmentación globular naranja

Reed: patrón "starburst" o "globular"



Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions Part I. Background and diagnoses.* J Am Acad Dermatol 2011;65:6

Histopatología

Table II. Histopathologic attributes of classic Spitz nevi and atypical Spitz tumors

Attribute	Classic Spitz nevus	Atypical Spitz tumors
Organization	Orderly, nondisruptive	Haphazard, infiltrative
	Symmetric	Asymmetric
	Sharply demarcated	Poorly circumscribed
	Intact, hyperplastic epidermis	Disrupted, ulcerated epidermis
	Aggregates of Kamino bodies	Absent or few Kamino bodies
	Junctional clefting	Lack of junctional clefting
	Lack of deep involvement	Subcutaneous involvement
	Limited pagetoid spread, lower epidermis	Prominent, single-cell pagetoid spread, beyond epidermal nests
	Diminished cellularity with depth	Confluence, dense cellularity
	Zonation: side-to-side uniformity	Lack of zonation
	Smaller nests with depth	Persistent, expansile deep nests
Proliferation	Mitoses $<2/mm^2$	Mitoses $\geq 2\text{-}6/mm^2$
Cytology	Spindled or epithelioid cell type	More heterogeneous cell types
	Ground glass or opaque cytoplasm	Granular, dusty cytoplasm
	Low nuclear to cytoplasmic ratio	High nuclear to cytoplasmic ratio
	Delicate, dispersed chromatin	Hyperchromatism
	Uniform nucleoli	Large, eosinophilic nucleoli

Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions Part I. Background and diagnoses.* J Am Acad Dermatol 2011;65:6

Histopatología

Inmunohistoqímica:

Ki-67: *Mayor porcentaje en núcleos Melanoma*

HMB45: *Superficial del Nevus de Spitz clásico vs profundo del Melanóma maligno.*

P16: *Nevus Spitz clásico> Tumor de Spitz Atípico> Melanoma*

P53/Bcl-2/Cdc-7: *Melanoma > Nevus de Spitz clásico.*

CD99: *Melanoma Maligno (difuso) > Nevus de Spitz clásico (focal)*

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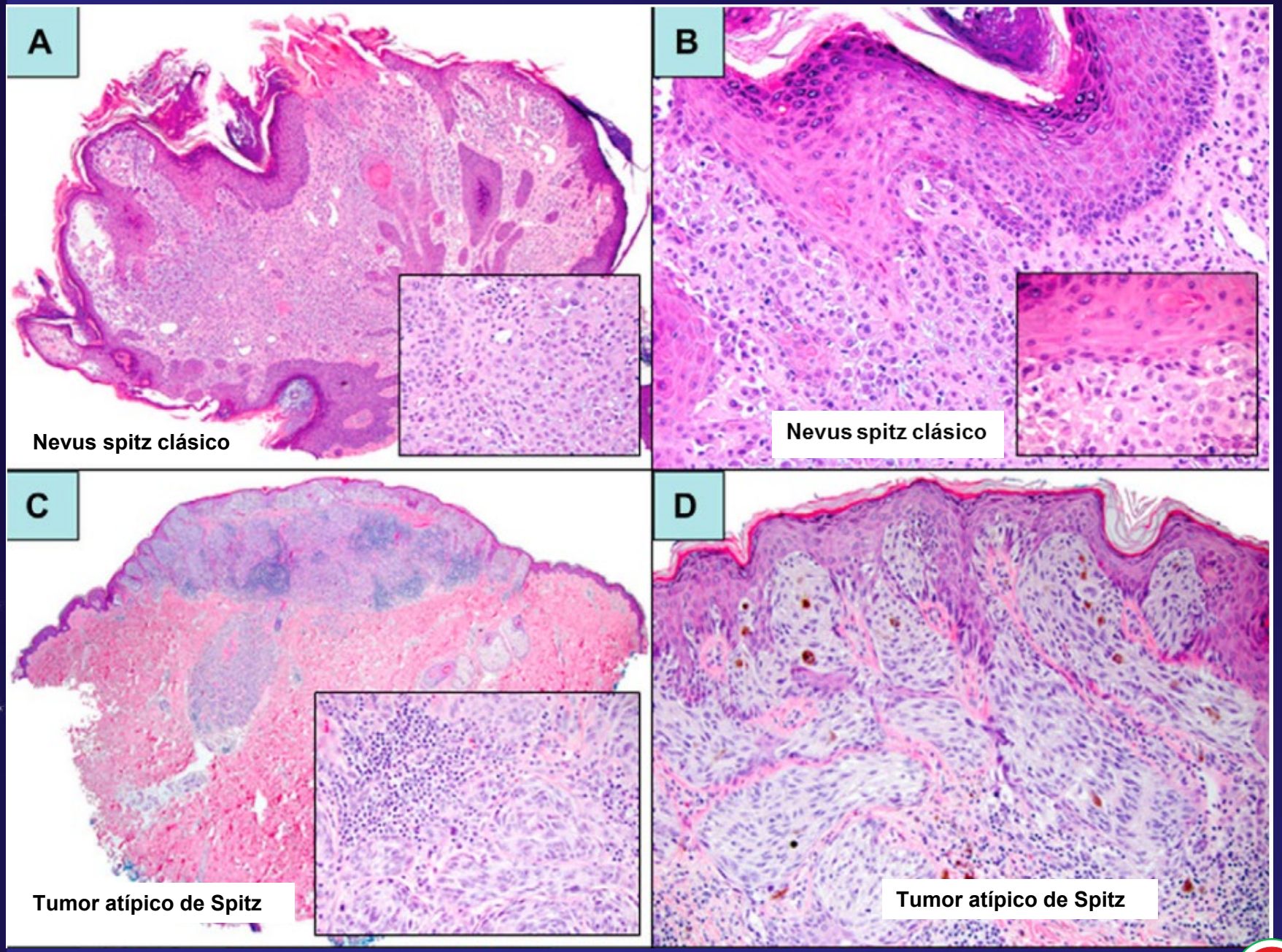
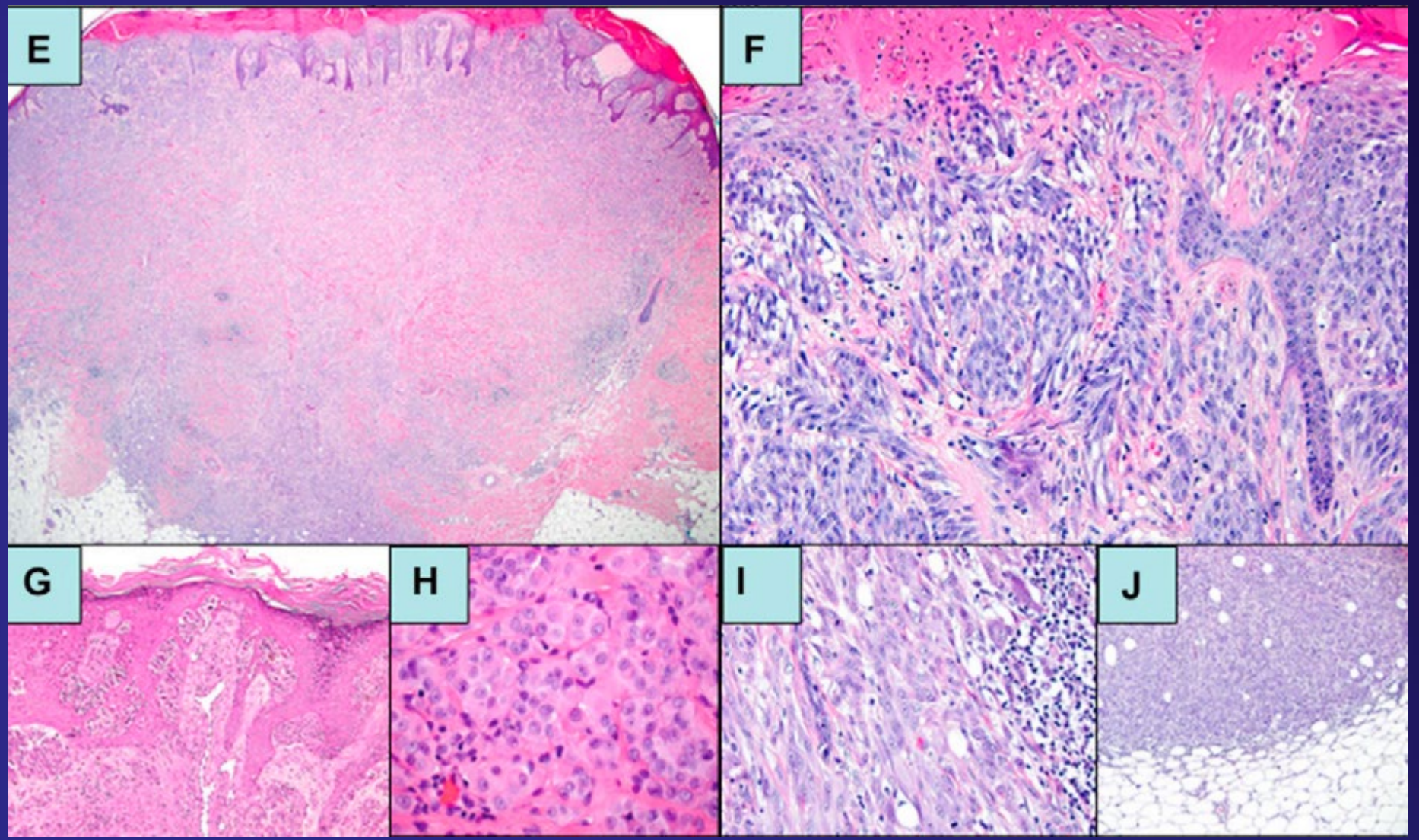


Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions Part I. Background and diagnoses.* J Am Acad Dermatol 2011;65:6

Melanoma spitzoide



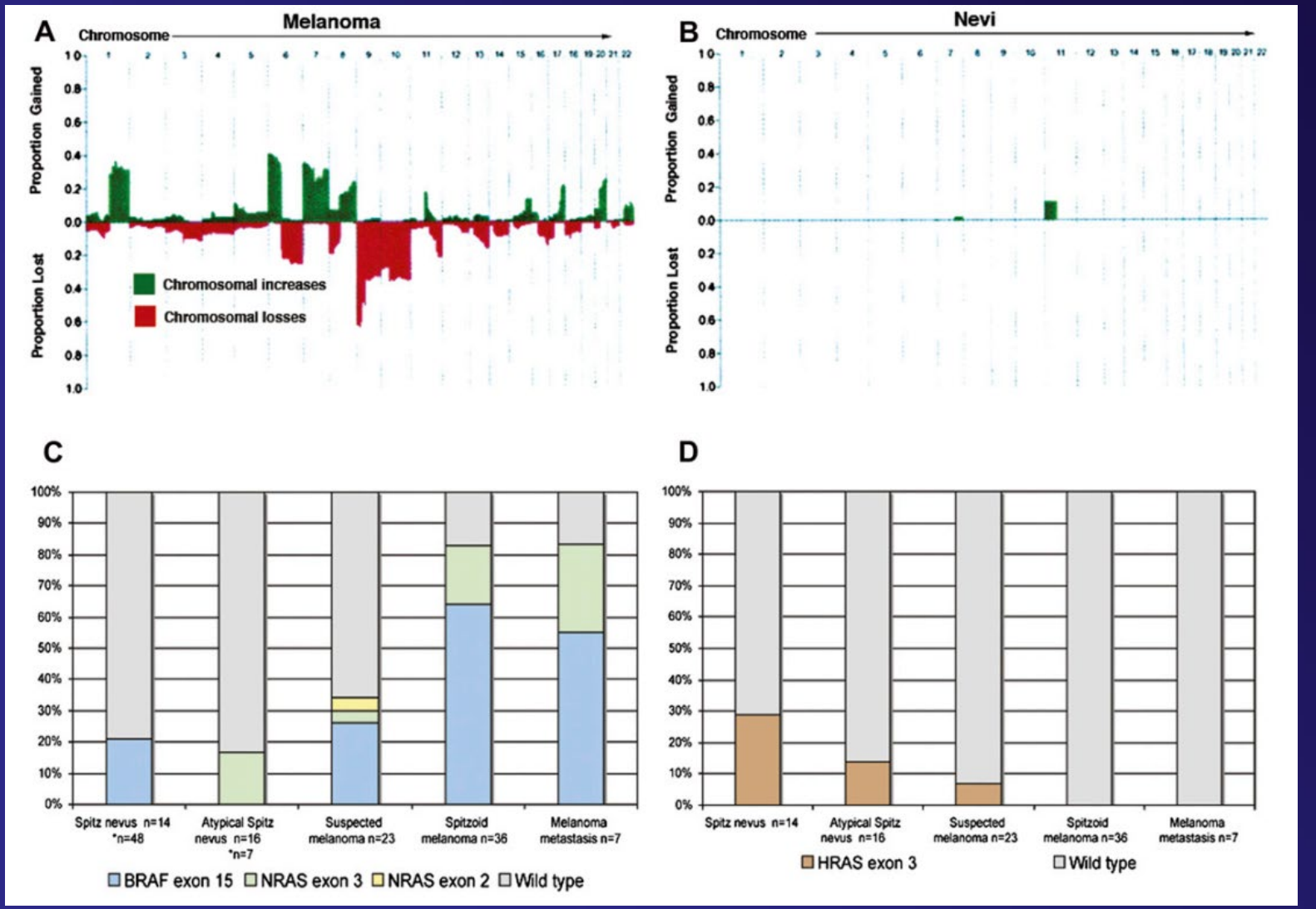
Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions Part I. Background and diagnoses.* J Am Acad Dermatol 2011;65:6

Análisis Molecular

- Hibridación genómica: *11p única para T de Spitz*
- *11p = HRAS*
- *Algunos Nevus de Spitz comparten anomalías cromosómicas con el melanoma*
- ***La utilidad del FISH para el Tto no ha sido establecida***

Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions Part I. Background and diagnoses.* J Am Acad Dermatol 2011;65:6

Hibridización genómica



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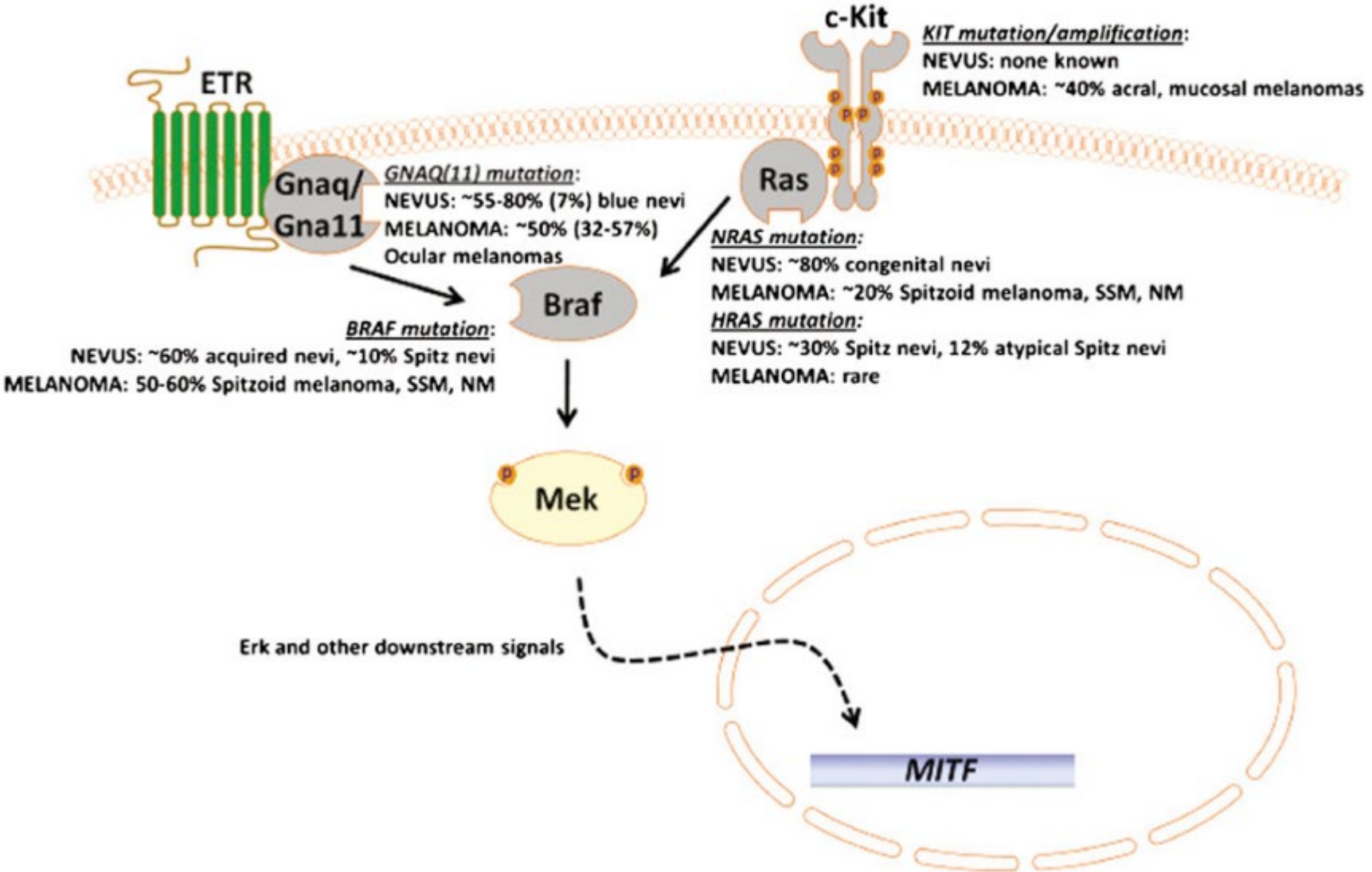

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Features of Spitz Nevi, Spitzoid Melanoma, and Atypical Spitz Tumor

	Spitz Nevus	Atypical Spitz Tumor	Spitzoid Melanoma
Clinical presentation	Typically younger patients (subset occur in adults) Small papule or nodule	Typically younger patients Papule or nodule	Typically older patients Large, changing lesion
Scanning magnification	Symmetrical Well circumscribed Epidermal acanthosis Well-formed nests, limited pagetoid scatter	Large, deep tumor May be asymmetrical	Asymmetrical Poorly nested Some architectural features of Spitz nevus (large nests with clefting, epidermal acanthosis)
High magnification	*Cytologic atypia:* Limited pleomorphism Lack of high-grade cytologic atypia *Junctional component:* Well nested, may be central pagetoid scatter *Dermal component:* Dermal maturation Few/no mitoses	*Cytologic atypia:* Most cases lack extreme pleomorphism, hyperchromasia, atypical mitoses *Junctional component:* Typically lacks findings of melanoma in situ May be ulceration *Dermal component:* Cellular, with spindled or epithelioid cells, often in fascicles Multiple dermal mitoses Some investigators allow for focal necrosis	*Cytologic atypia:* High-grade cytologic atypia *Junctional component:* Poor nesting, pagetoid scatter Consumption May be ulceration *Dermal component:* Lack of maturation Mitoses may be numerous, deep/marginal, or atypical May have tumor necrosis
Immunohistochemistry	p16 typically retained HMB-45 lost in deeper dermal component Low Ki-67 index	p16 loss in minority Intermediate Ki-67 index	p16 loss in minority Elevated Ki-67 proliferative index Deep HMB-45 expression in minority
Molecular	FISH: no aberration (or rare heterozygous loss of *CDKN2A*) CGH: isolated gains of 7p, 11q, tetraploidy Other: *HRAS*-activating mutations Tyrosine kinase fusions	FISH: aberrations overlap with spitzoid melanoma; homozygous 9p21 loss may herald aggressive course CGH: may have one or multiple chromosomal abnormalities Loss of 3 (associated with BAP1 inactivation) Other: Tyrosine kinase fusions BAP1 mutation	FISH: aberrations of 9p21, 6p25, 11q13, and 8q24 CGH: multiple chromosomal abnormalities Other: Tyrosine kinase fusions *BRAF, NRAS* mutations *HRAS* mutations rare
Prognosis	Benign	Typically indolent, but there are rare cases with widespread metastases, death	Malignant (may be slightly better outcome relative to conventional melanoma)

Abbreviations: CGH, comparative genomic hybridization; FISH, fluorescence in situ hybridization.

Harms KL, Lowe L, Fullen DR, Harms PW. *Atypical Spitz Tumors: A Diagnostic Challenge*
Arch Pathol Lab Med. 2015;139: 10

Tratamiento

Table I. Assessing risk of metastasis in atypical Spitz tumors

Presence of parameter	Score conferred
Age >10 years old	1
Diameter >10 mm	1
Subcutaneous fat involvement	2
Ulceration	2
Mitoses	
<5/mm^2	0
6-8/mm^2	2
>8/mm^2	5
Maximum no. of points	11
Risk categories	
Low	0-2
Intermediate	3-4
High	5-11

Adapted from Spatz et al.[1]

Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions. Part II. Natural history and management.* J Am Acad Dermatol 2011;65:6

Tratamiento

Table II. Sentinel lymph node status in atypical Spitz tumors

Study	No. of SLN-positive	Total no. of SLNs	Rate of positivity
Gow et al[3]	1	3	33%
Roaten et al[4]	2	3	67%
Gamblin et al[5]	3	10	30%
Lohmann et al[6]	5	10	50%
Urso et al[7]	4	12	33%
Magro et al[8]	5	14	36%
Cochran et al[9]	8	18	44%
Murali et al[10]	6	21	29%
Ghazi et al[11]	6	27	22%
Ludgate et al[12]*	27	57	47%
Total	67	175	38%

SLN, Sentinel lymph node.
*Includes patients from the 2003 University of Michigan series by Su et al.[13]

Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions. Part II. Natural history and management.* J Am Acad Dermatol 2011;65:6

Tratamiento

- Ausencia de consenso
- *Tumores de Spitz Atípicos tienen mayor similitud al melanoma y deberían ser tratados mas agresivamente que Nevus de Spitz Clásicos.*
- Resección local amplia (Margen min 1 cm Nivel 4)
- Biopsia de ganglio centinela?

  40% positivo - no modifica supervivencia

Luo S, Sepehr A, Tsao H. *Spitz nevi and other Spitzoid lesions. Part II. Natural history and management.* J Am Acad Dermatol 2011;65:6

Atypical Spitz tumours and sentinel lymph node biopsy: a systematic review

Aimilios Lallas, Athanassios Kyrgidis, Gerardo Ferrara, Harald Kittler, Zoe Apalla, Fabio Castagnetti, Caterina Longo, Elvira Moscarella, Simonetta Piana, Iris Zalaudek, Giuseppe Argenziano

In conclusion, existing data do not show any prognostic benefit of sentinel lymph node biopsy in patients with atypical Spitz tumours, although the lack of high-quality evidence must be taken into account when interpreting these findings. Additionally, sentinel lymph node biopsy, and the procedures after a possible positive result such as complete lymph node dissection, are associated with high rates of morbidity, especially in children. It might be prudent to use complete excision with clear margins and careful clinical follow-up as the initial treatment for patients with atypical Spitz tumours. FISH analysis could be useful to identify patients with more aggressive tumours, for which sentinel lymph node biopsy might have a therapeutic benefit.

Lancet Oncol. 2014 Apr;15:4

Gracias!