



**XXV Congreso de la SEAP y División Española de la Academia
Internacional de Patología
Zaragoza, mayo 2011**

Lesiones de Partes Blandas Superficiales

Tumores fibroblásticos y miofibroblásticos

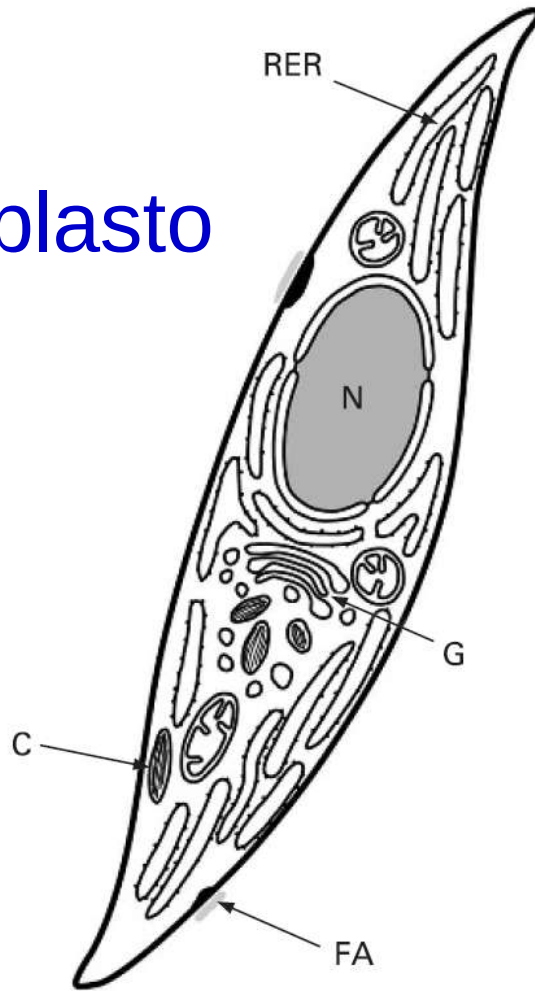
Carlos Monteagudo
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- Los miofibroblastos se reconocieron originalmente mediante microscopía electrónica
- Comparten con los fibroblastos
 - RER prominente
 - Golgi con gránulos de secreción de colágeno
 - Ausencia de membrana basal*
- Pero se distinguen de ellos por:
 - Miofilamentos periféricos
 - Fibronexus (con fibronectina; no con m. basal)
 - Uniones intercelulares tipo gap

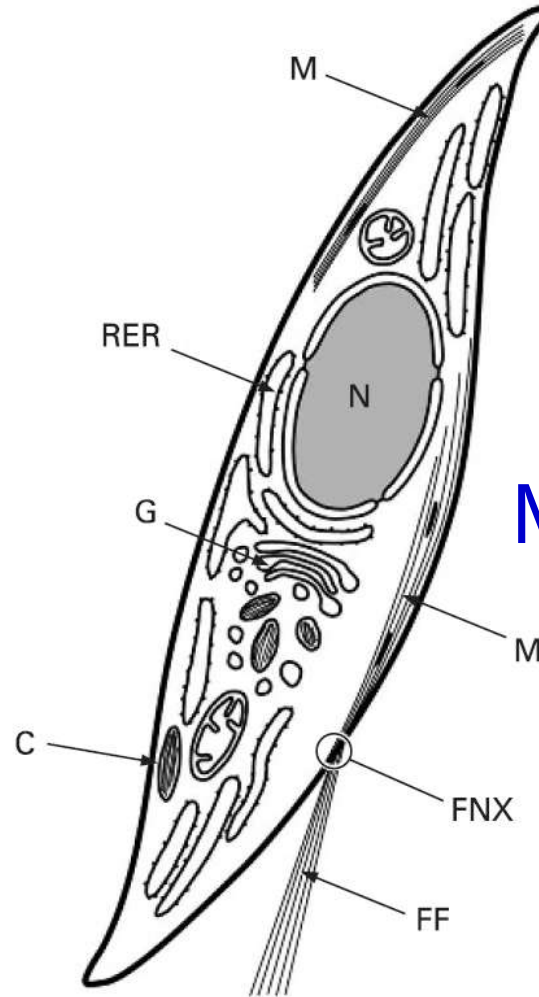
The myofibroblast and its tumours

B Eyden,¹ S S Banerjee,¹ P Shenjere,¹ C Fisher²

Fibroblasto

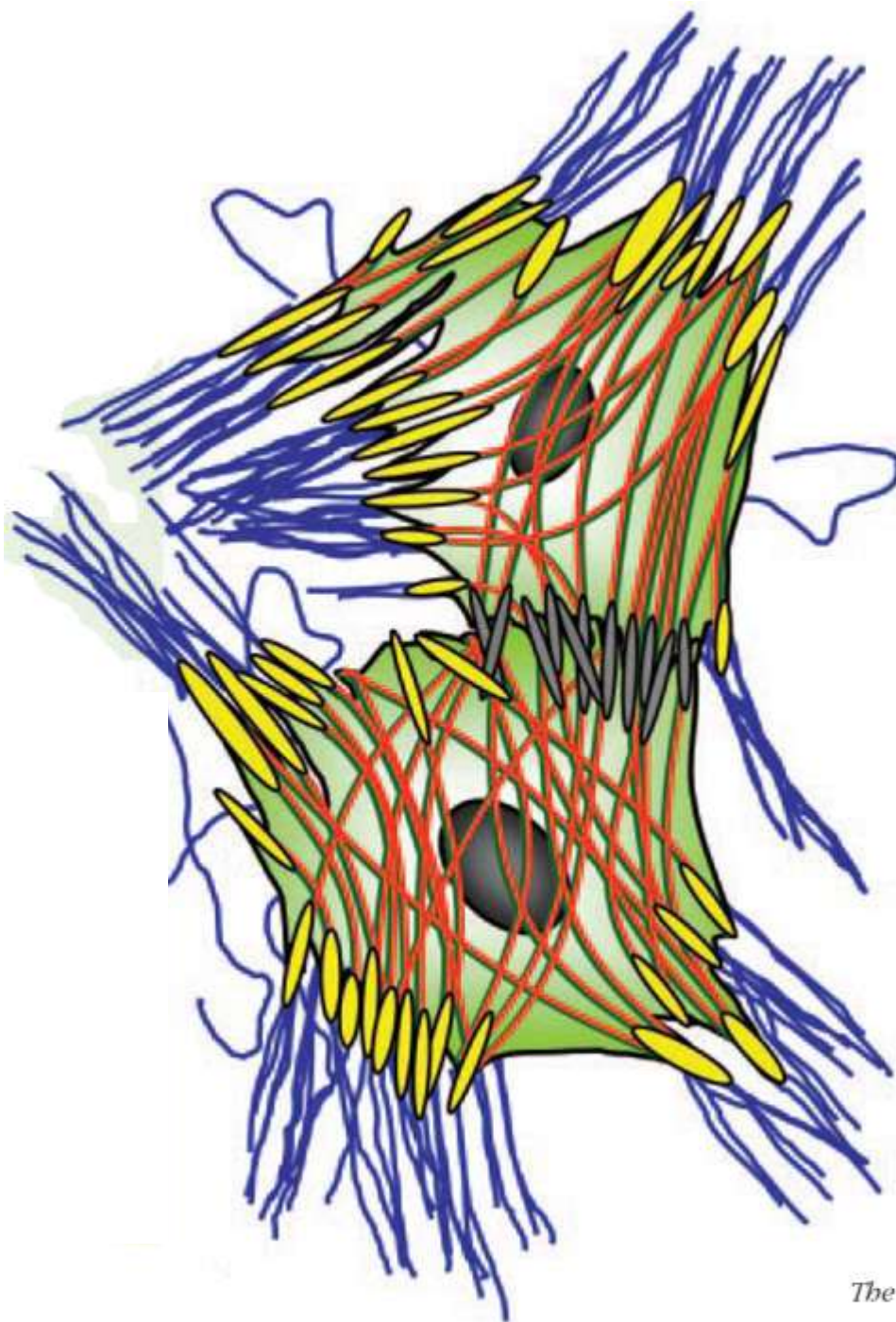


Miofibroblasto



- Además, los miofibroblastos se distinguen de los fibroblastos por:
 - la expresión de fibras de estrés de AML- α
 - la expresión del extradominio-A (ED-A) de la fibronectina (que requiere la presencia de TGF- β y de tensión mecánica)
 - la síntesis aumentada de varias proteínas de matriz extracelular y factores de crecimiento

Miofibroblastos

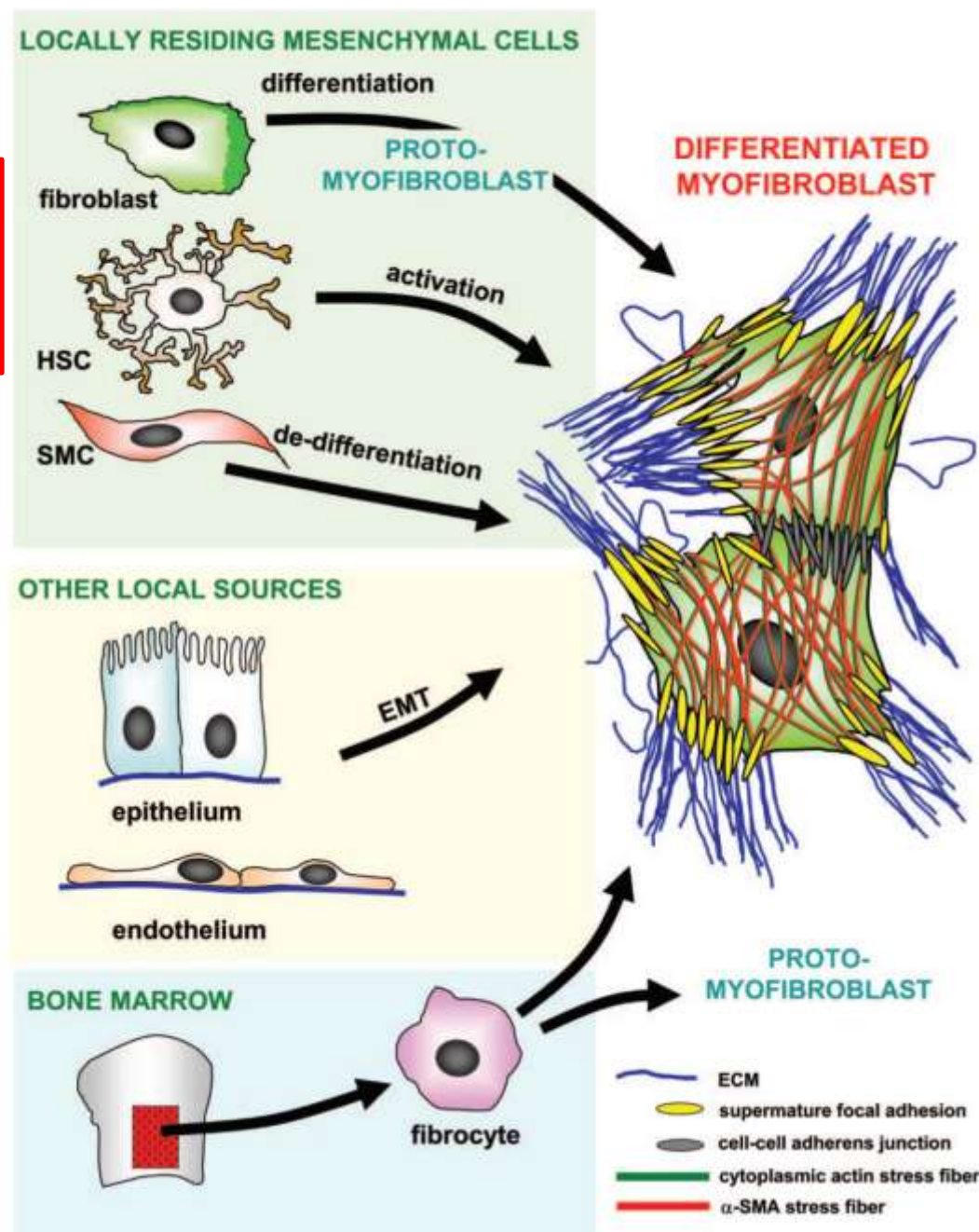


- ECM
- supermature focal adhesion
- cell-cell adherens junction
- cytoplasmic actin stress fiber
- α -SMA stress fiber

- Los miofibroblastos producen la contracción a consecuencia de:
 - contactos intercelulares
 - conexiones entre los microfilamentos contráctiles y la matriz extracelular (fibronexus)
 - las fuerzas de tracción
- La característica esencial de los miofibroblastos es el establecimiento de una red de fibras de estrés rica en AML- α

Pero los miofibroblastos no solo se generan a partir de fibroblastos...

MYOFIBROBLAST PROGENITORS



The Myofibroblast

One Function, Multiple Origins

Boris Hinz,^{*} Sem H. Phan,[†] Victor J. Thannickal,[‡] Andrea Galli,[§] Marie-Luce Bochaton-Piallat,[¶] and Giulio Gabbiani[¶]



La diferenciación miofibroblástica en los tumores
NO siempre cumple los requisitos aceptados para
los miofibroblastos ¿normales?,
como la presencia de fibronexus

Además, con frecuencia, la población tumoral no
es únicamente miofibroblástica

Table 3 Benign tumours and tumour-like lesions reported as showing myofibroblastic differentiation

(A) Prominent myofibroblastic differentiation

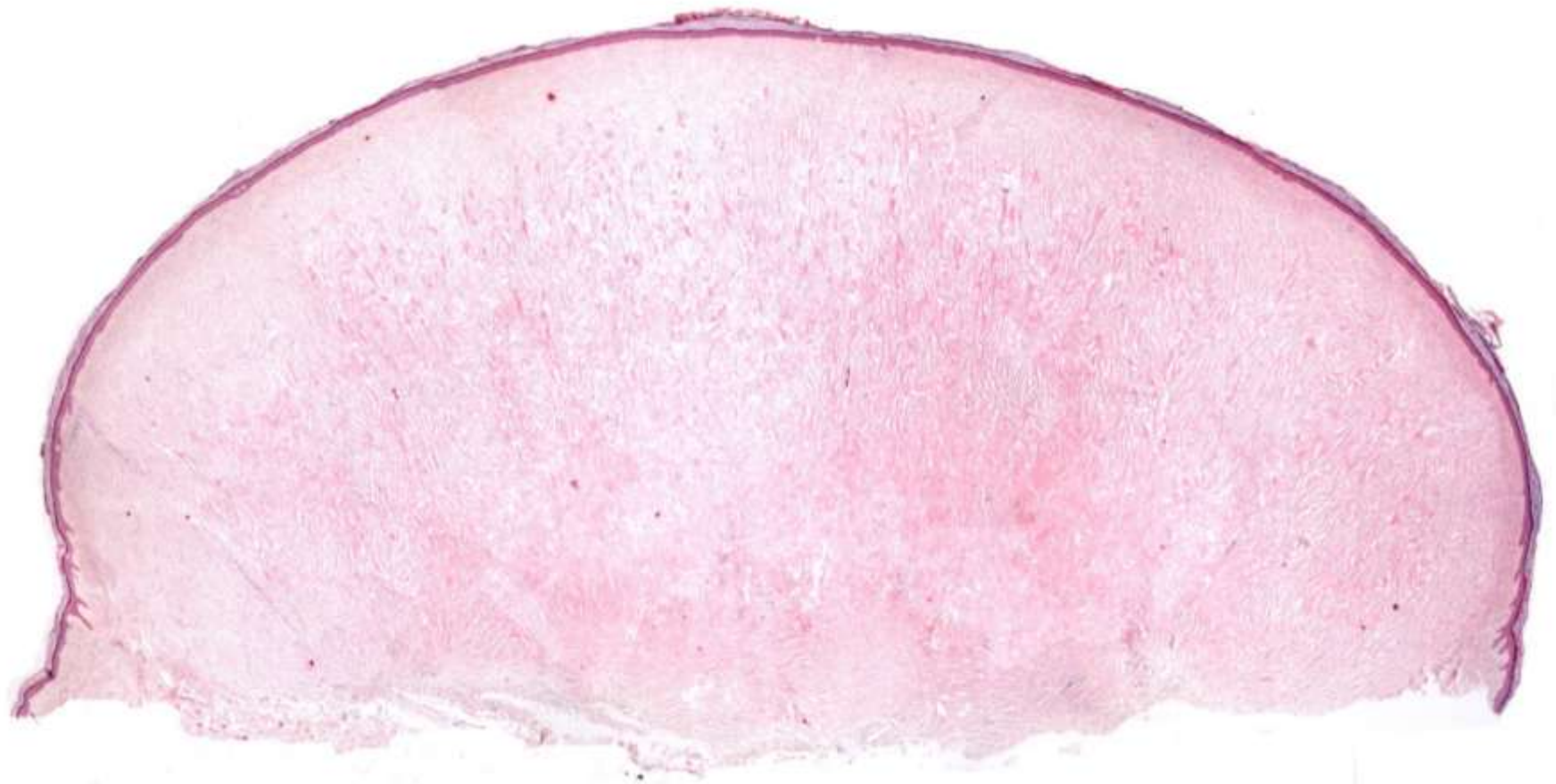
- ▶ Nodular fasciitis and related lesions (intravascular and cranial fasciitis)
- ▶ Proliferative fasciitis and myositis
- ▶ Myofibroma/myofibromatosis
- ▶ Fibromatosis
- ▶ Proliferative funiculitis
- ▶ Inflammatory pseudotumours
- ▶ Postoperative spindle cell nodule
- ▶ Myositis ossificans
- ▶ Fibroma of tendon sheath
- ▶ Dermatomyofibroma

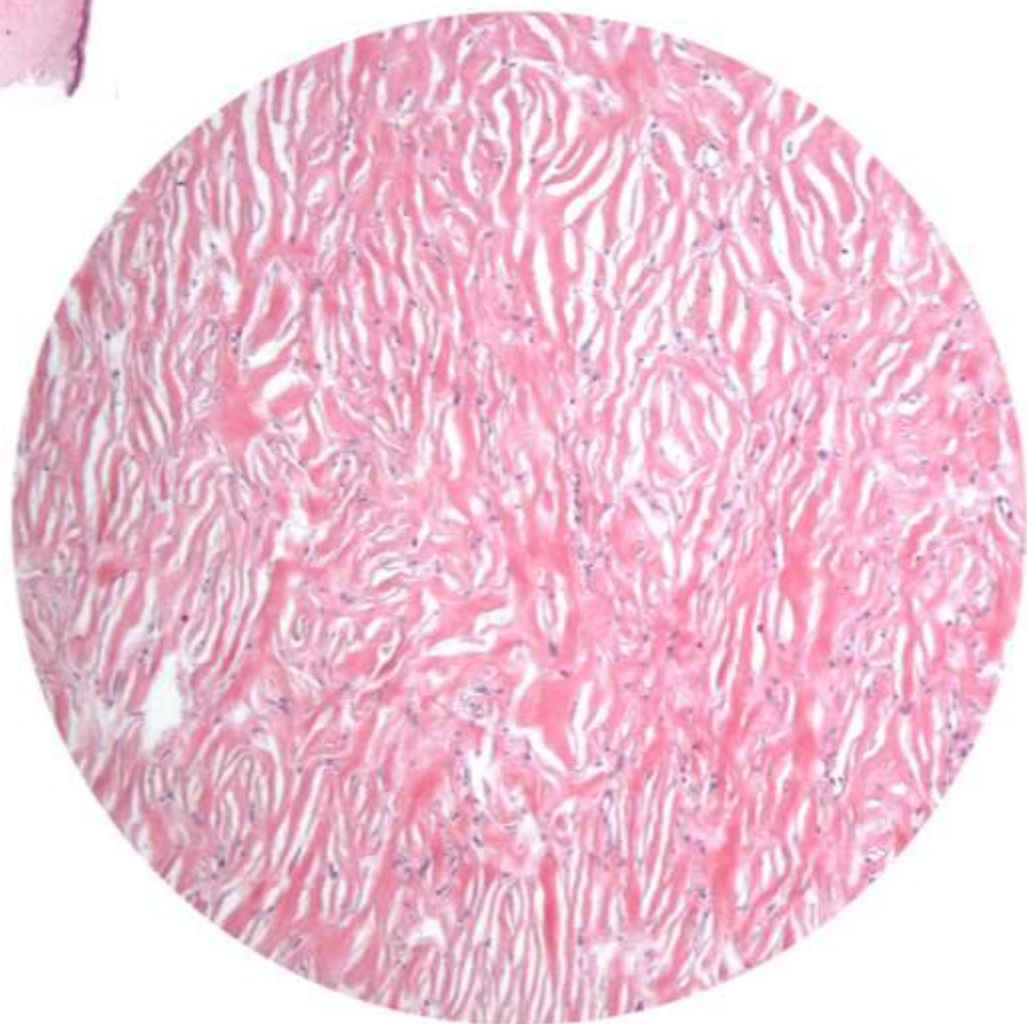
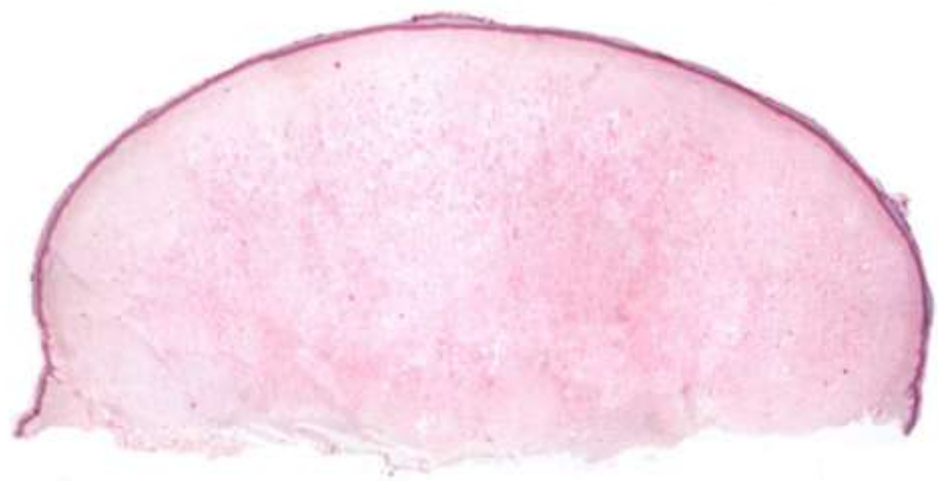
(B) Modest (incomplete) myofibroblastic differentiation

- ▶ Benign fibrous histiocytoma
- ▶ Desmoplastic fibroblastoma
- ▶ Fibrous hamartoma of infancy
- ▶ Nasopharyngeal angiofibroma
- ▶ Calcifying aponeurotic fibroma
- ▶ Calcifying fibrous tumour
- ▶ Aggressive angiomyxoma
- ▶ Ischaemic fasciitis
- ▶ Elastofibroma

Lesiones llamadas “fibrohistiocíticas” no son objeto de esta presentación

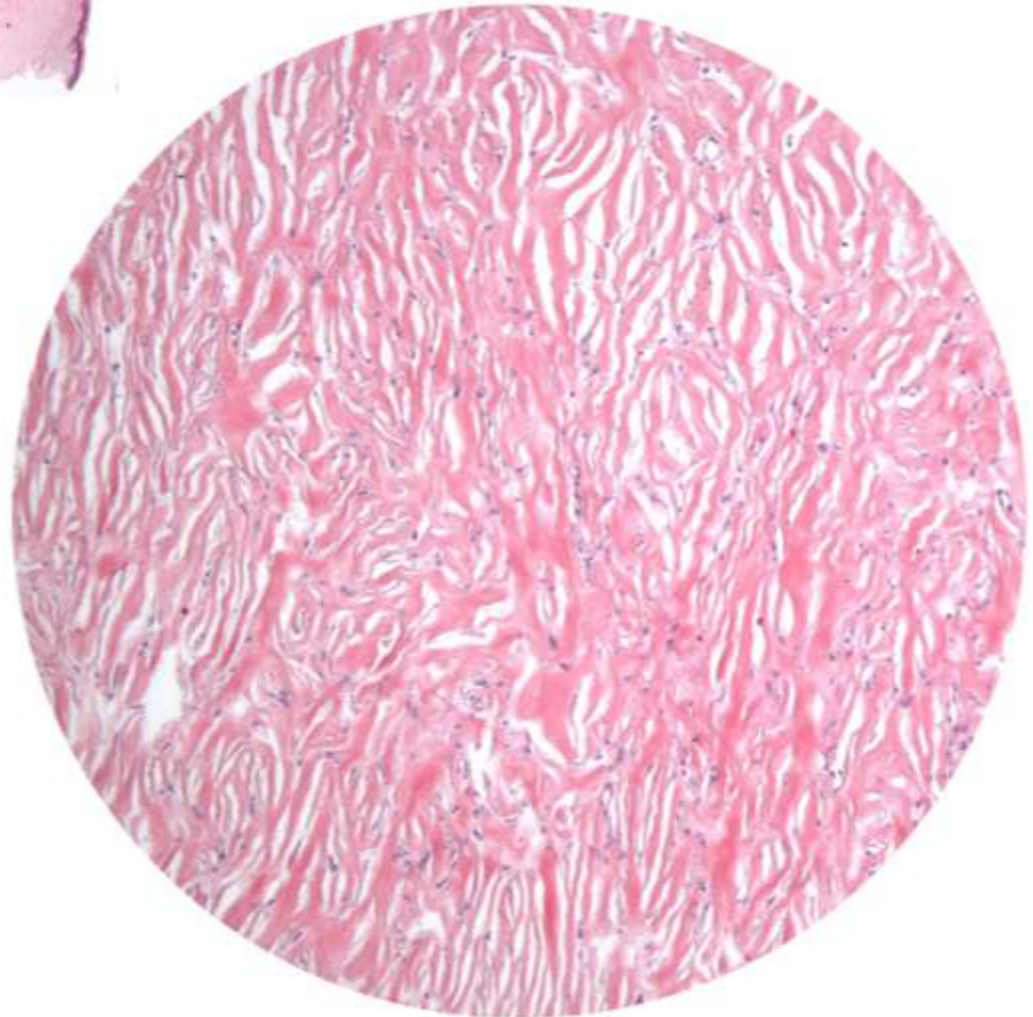
- **Dermatofibroma**
- **Tumor fibrohistiocítico plexiforme**
- **Fibroxantoma atípico**
- **Dermatofibrosarcoma protuberans***
- **Sarcoma pleomórfico**
- **Mixofibrosarcoma***







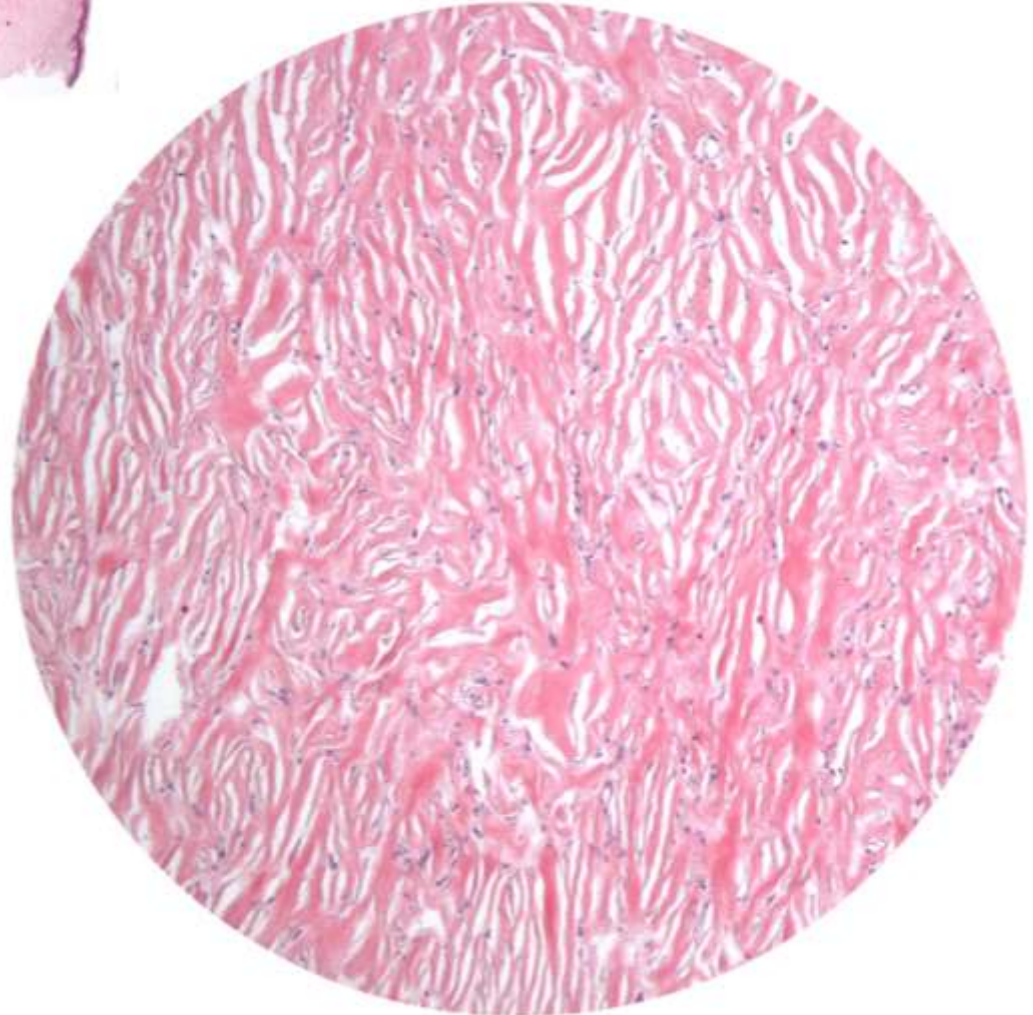
**Fibroma
esclerótico**





Fibroma Esclerótico

CD34+
+/- S. Cowden



Am J Surg Pathol 22;1998:557-563

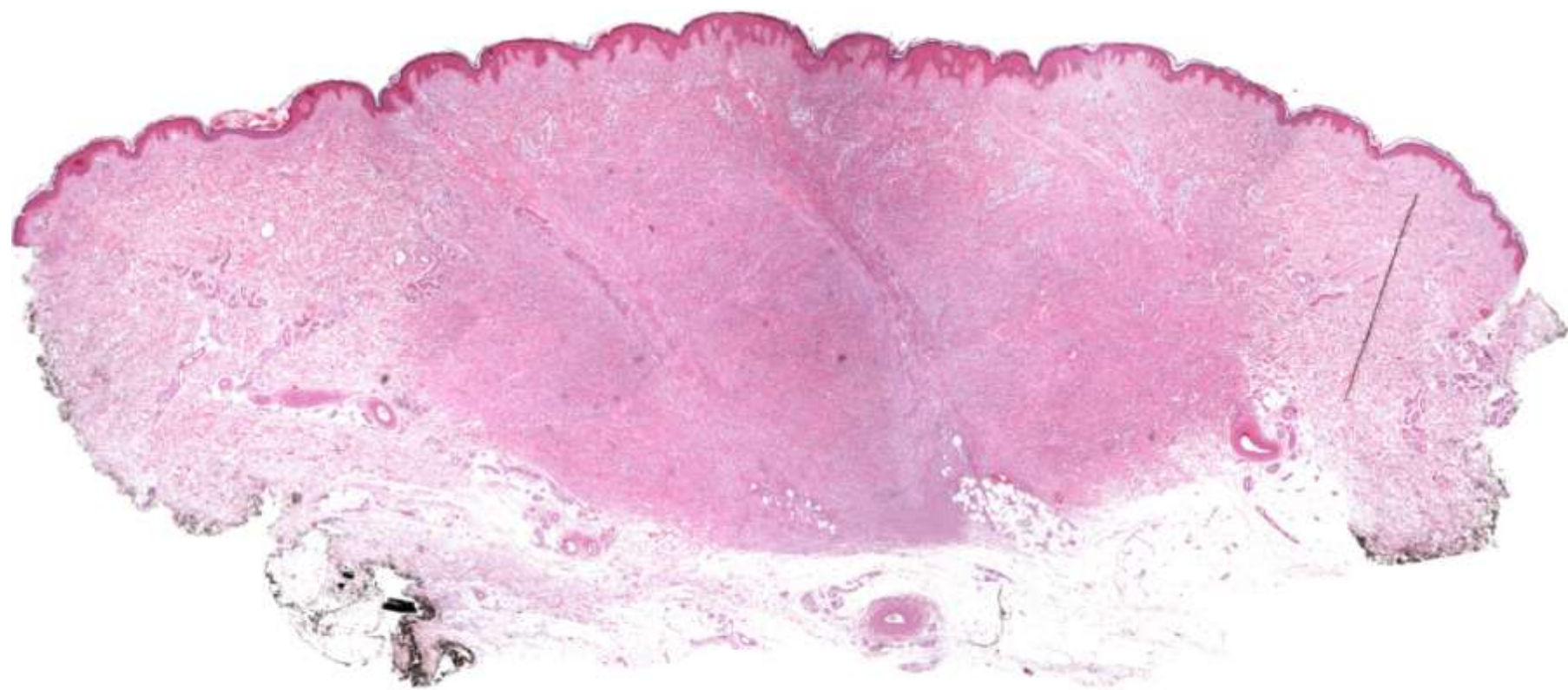
Giant Cell Collagenoma: A Benign Dermal Tumor With Distinctive Multinucleate Cells. (CD34-)

Rudolph, P.; Schubert, C; Harms, D.; Parwaresch, R

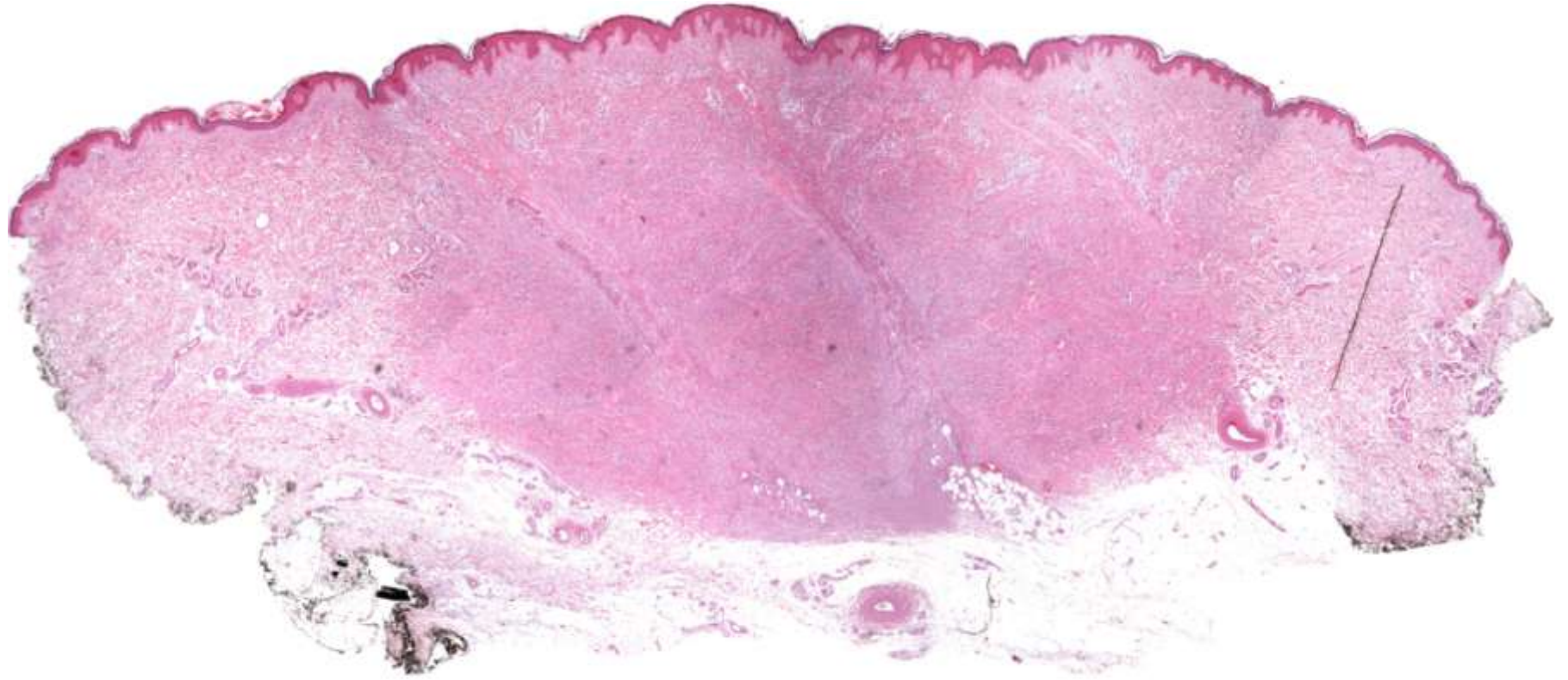
The American Journal of Dermatopathology 18(6): 620-624, 1996

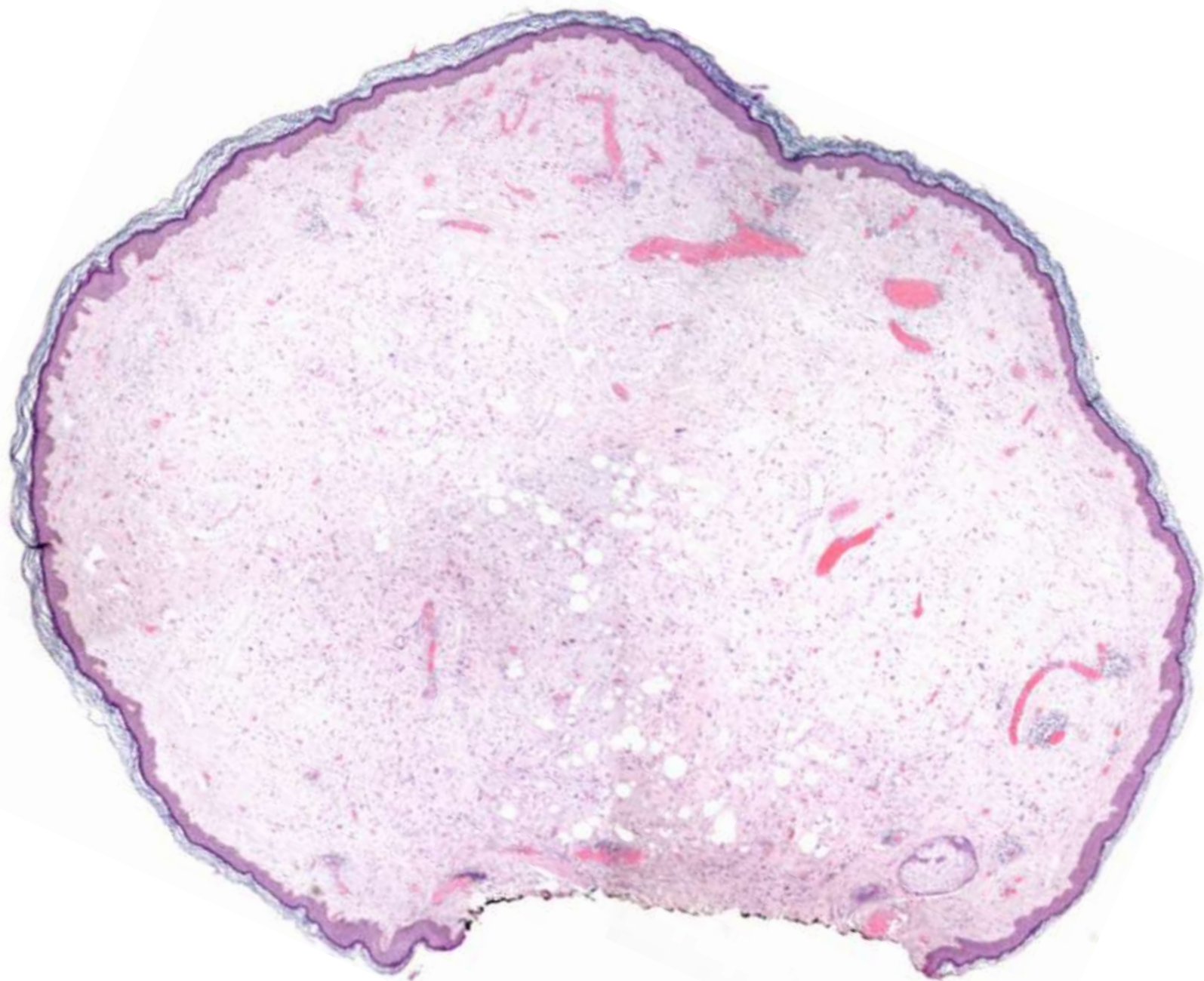
Solitary Sclerotic Fibroma of the Skin: A Sclerotic Dermatofibroma?

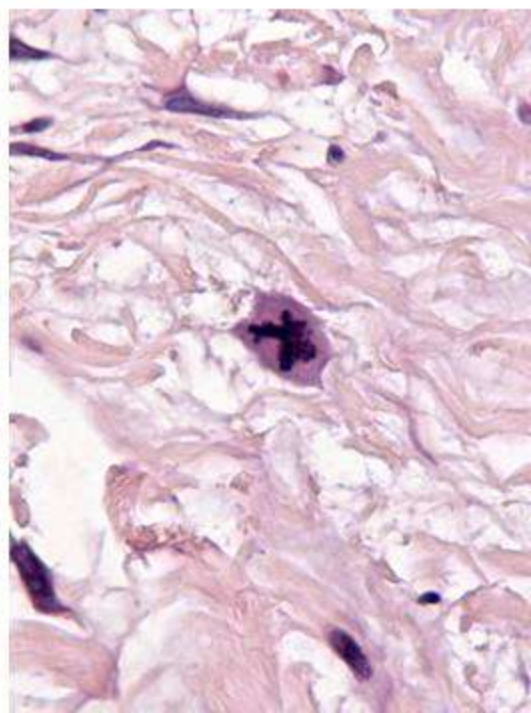
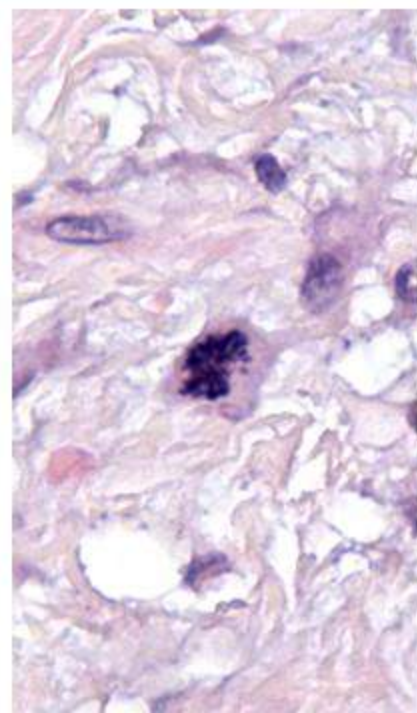
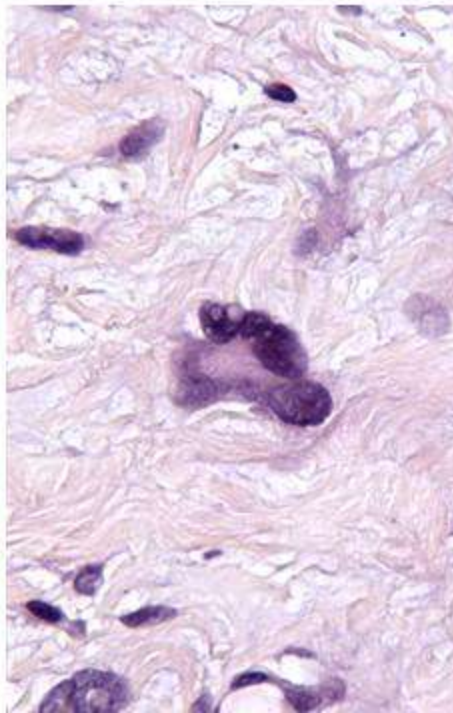
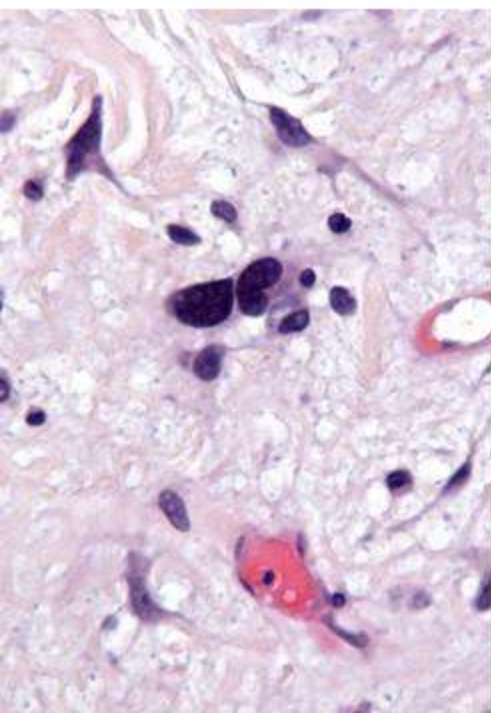
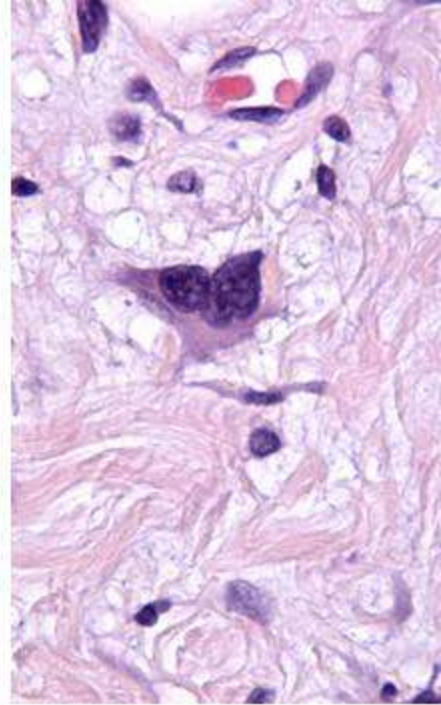
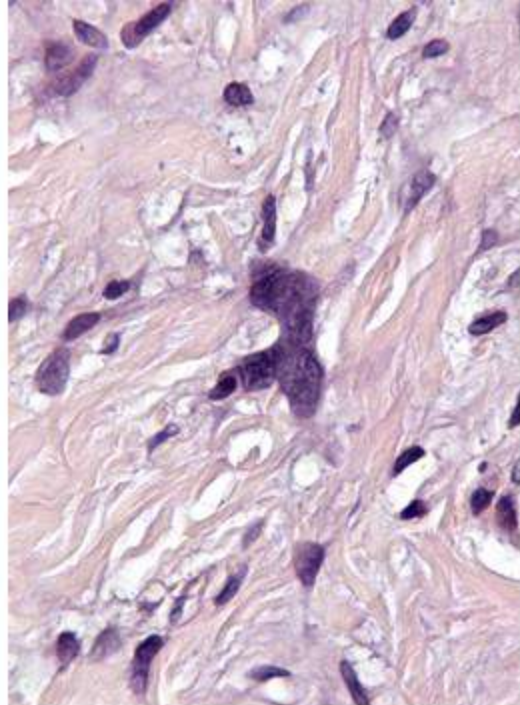
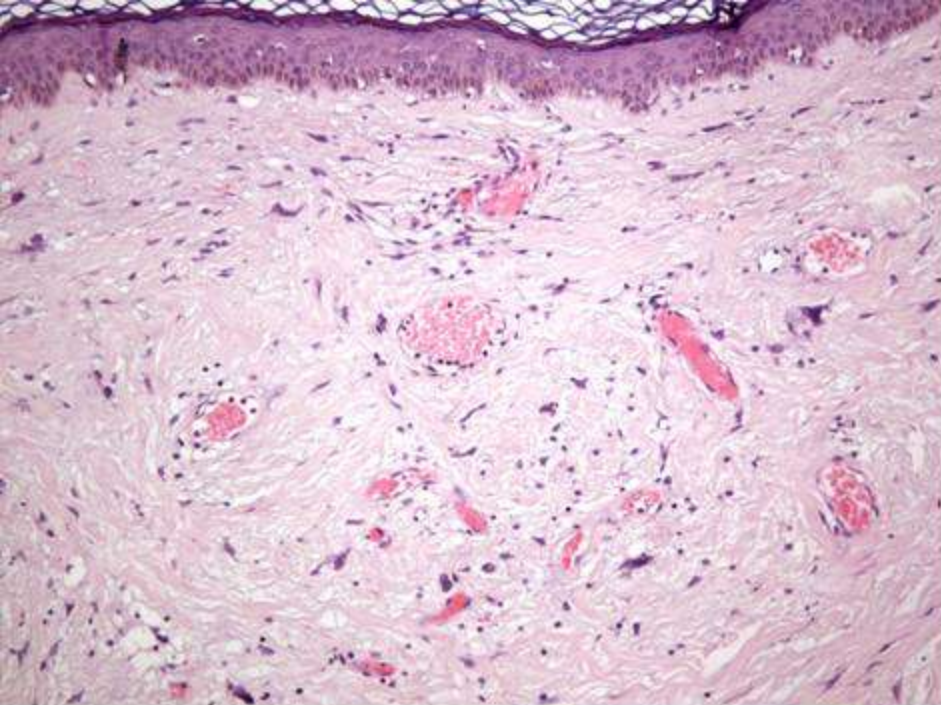
Ramon M. Pujol, M.D., Fernando de Castro, M.D.,
Arnold L. Schroeter, M.D., and W.P. Daniel Su, M.D.

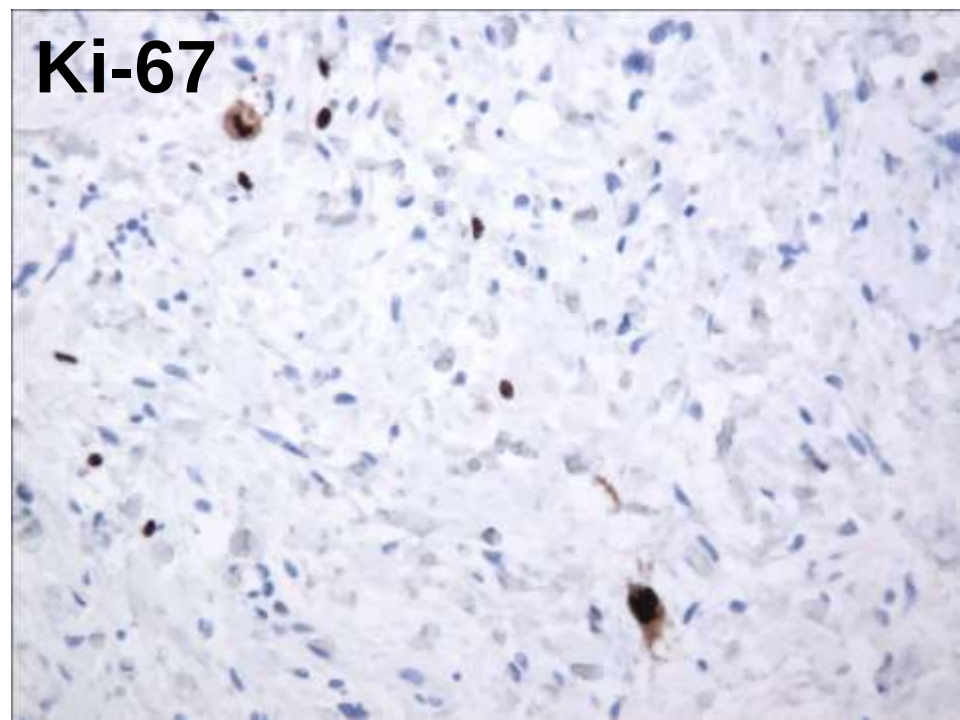
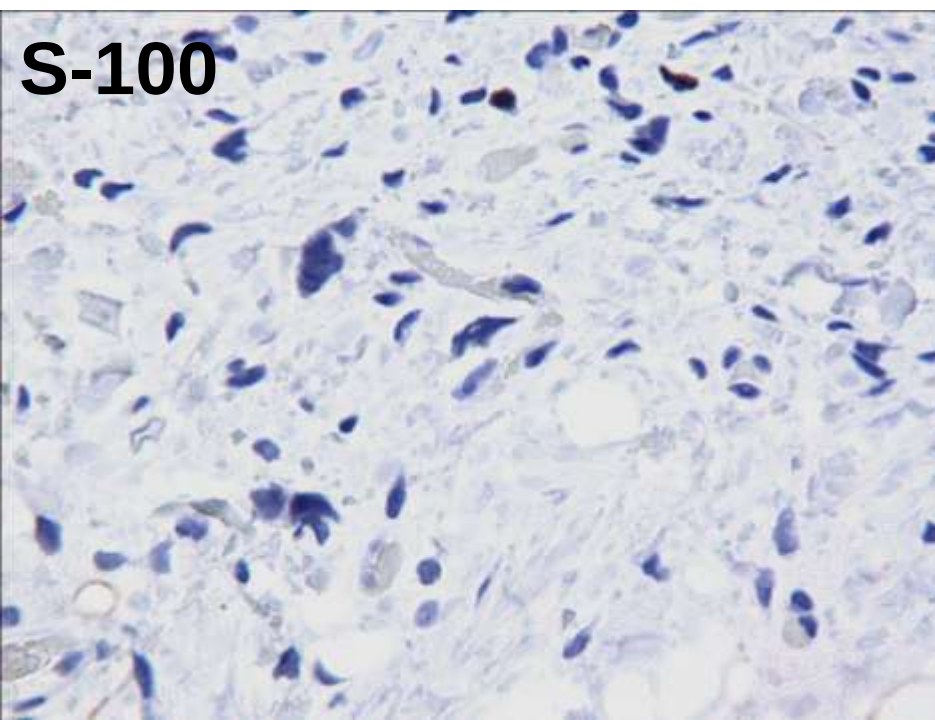
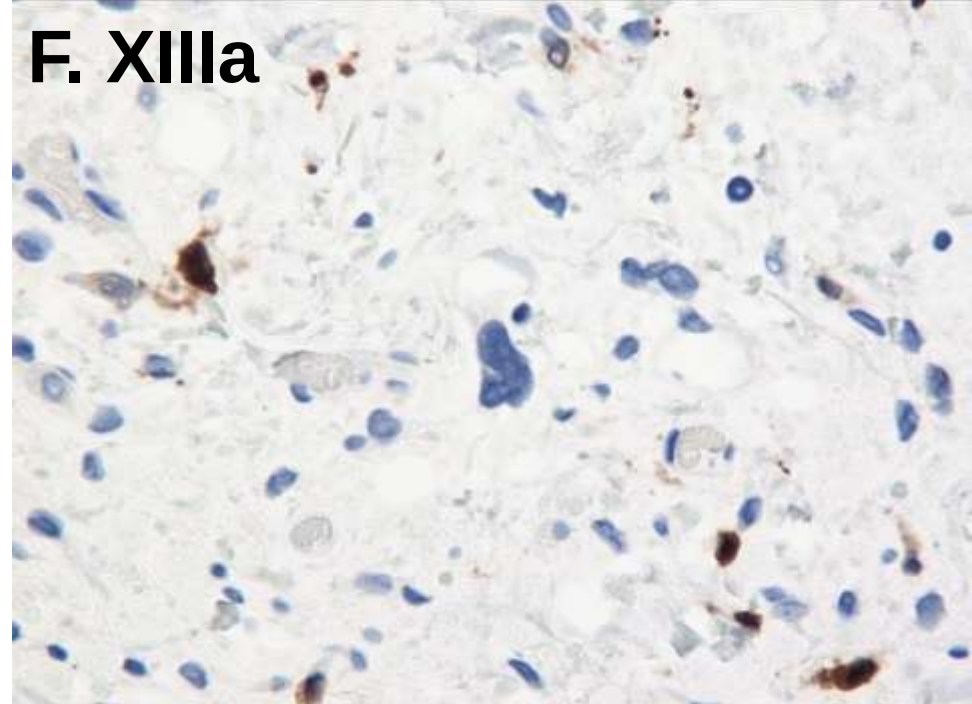
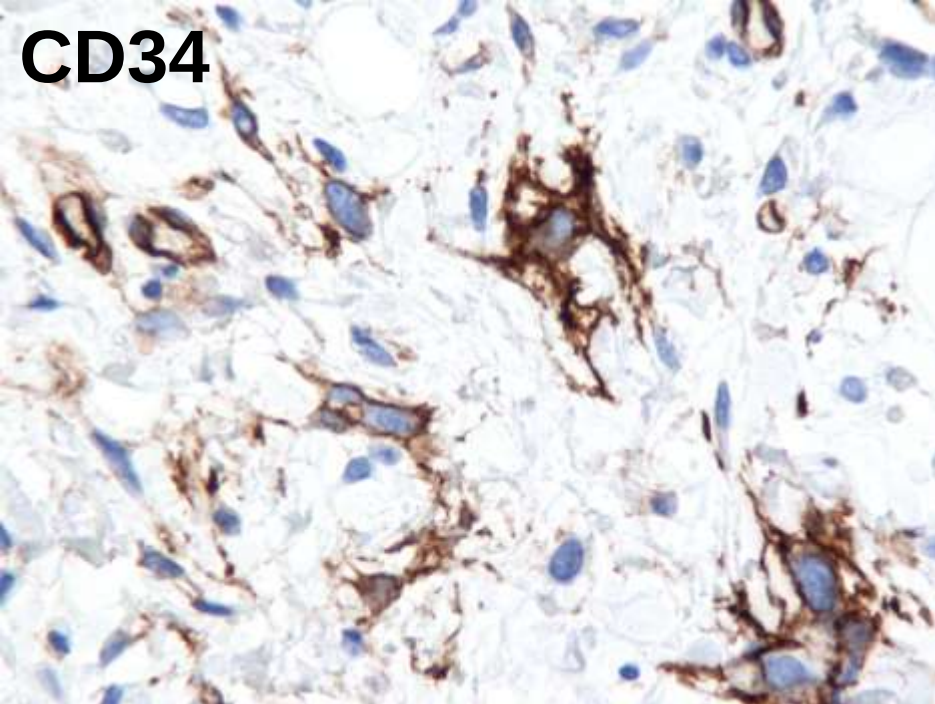


Dermatofibroma esclerótico









Fibroma pleomórfico

- Polipoide o hemisférico, no ulcerado, color piel, de 5 a 15 mm, en extremidades, y menos en tronco y cara
- Adultos: edad media 50 años
- Células fusiformes o irregulares dispersas entre abundantes fibras colágenas
- Núcleos pleomórficos, hiperocrómicos, con nucleolo pequeño, y citoplasma escaso y de límites mal definidos. Algunos núcleos lobulados o múltiples
- Escasas mitosis típicas. En 2 casos de la serie original, una mitosis atípica

Fibroma pleomórfico

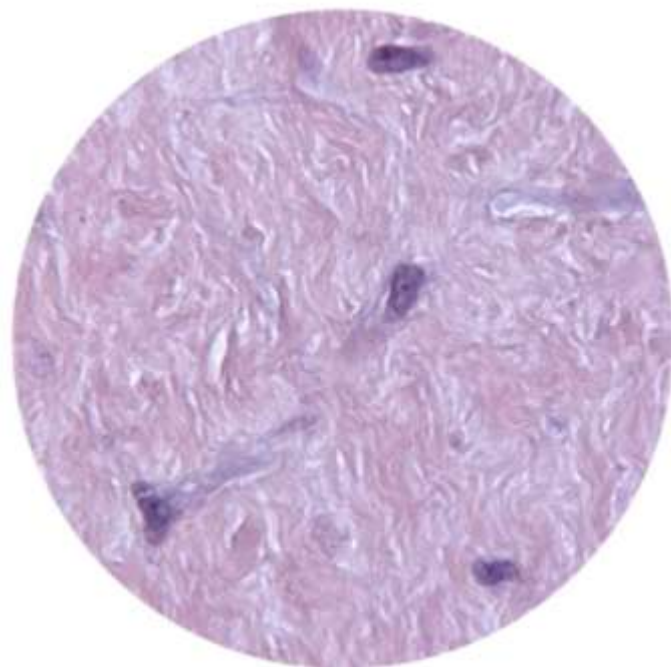
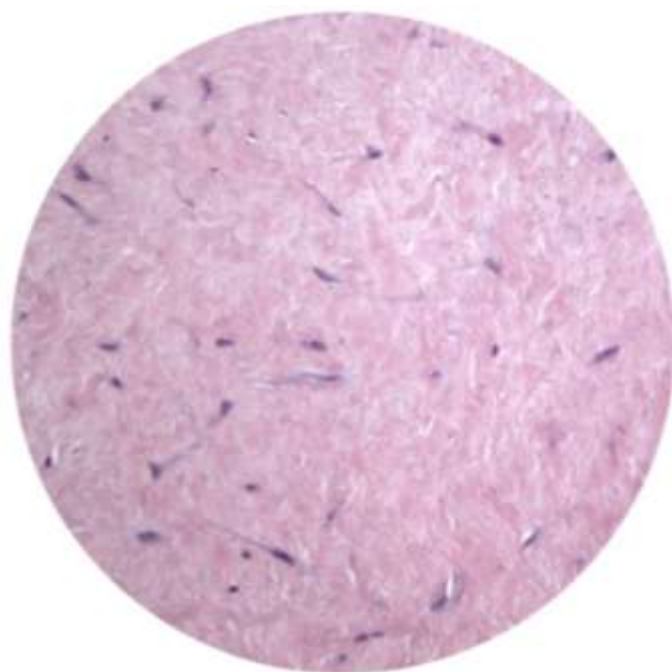
- Ocasionalmente patrón mixoide, localización subungueal, o características de fibroma esclerótico
- 1/2 casos: escaso componente linfocitario
- Las células pleomórficas son positivas para vimentina, siempre negativas para S-100 y citoqueratinas, y muy variable positividad para actina músculo específica, CD34, y CD99
- La evolución es benigna. Las recidivas son raras

Fibroma pleomórfico

Diagnóstico diferencial

- **El fibroxantoma atípico:** tiene más celularidad y más numerosas mitosis, típicas y atípicas, además de localizarse generalmente en la cabeza en personas mayores
- **El dermatofibroma “atípico”:** es más celular y fascicular, y suele tener algunas células espumosas y/o con hemosiderina, hiperplasia epidérmica, y mínima presencia de mucina
- **El fibroblastoma de células gigantes:** se caracteriza por la presencia de espacios pseudovasculares limitados por las células gigantes, y la fusión génica COL1A1-PDGFB

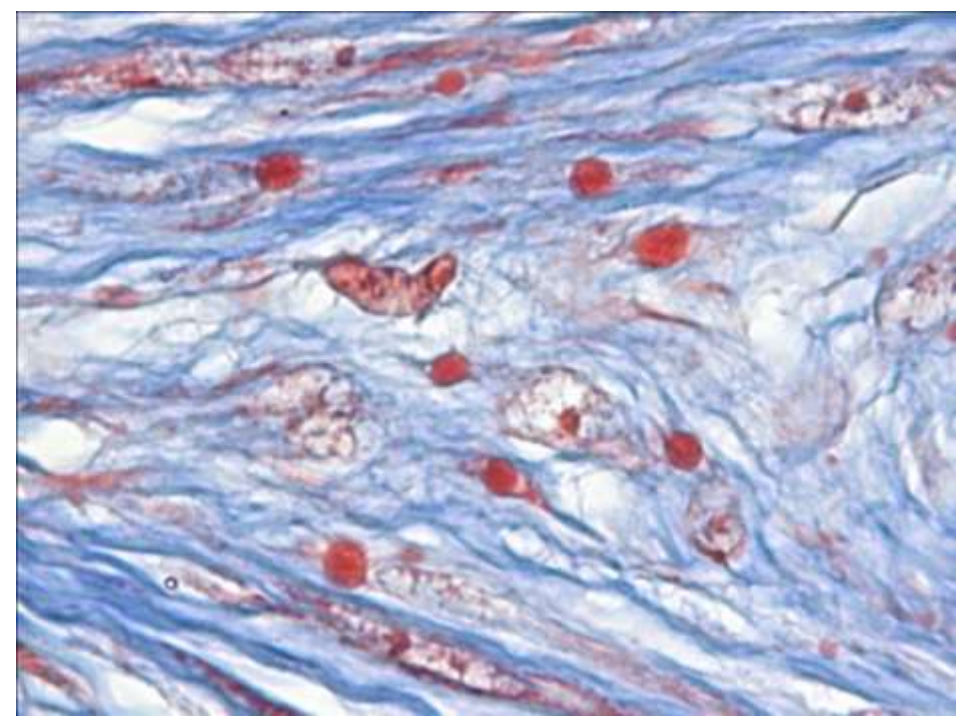
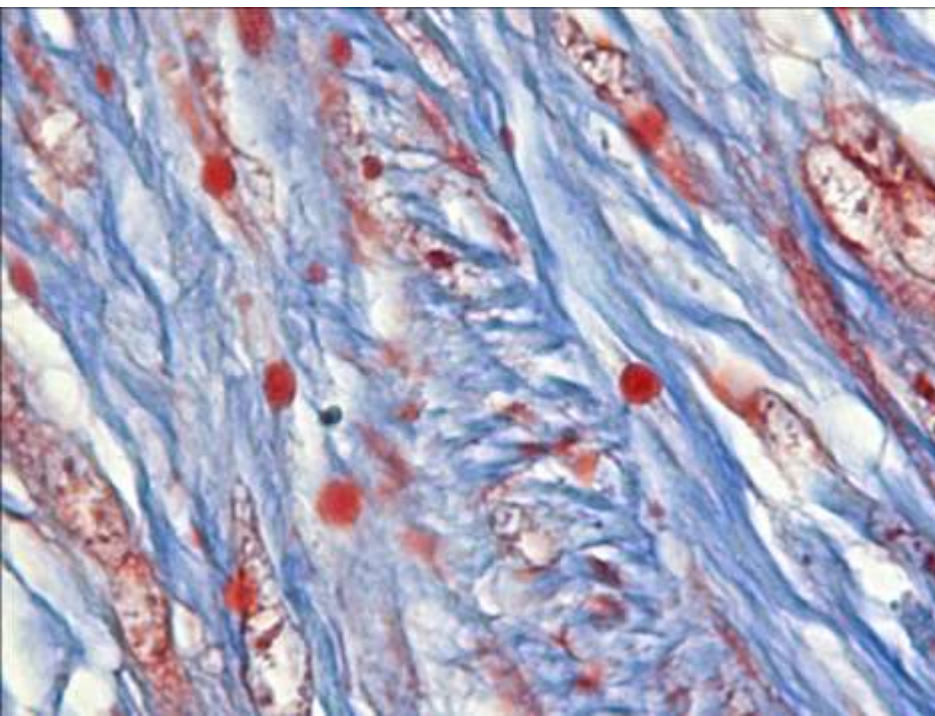
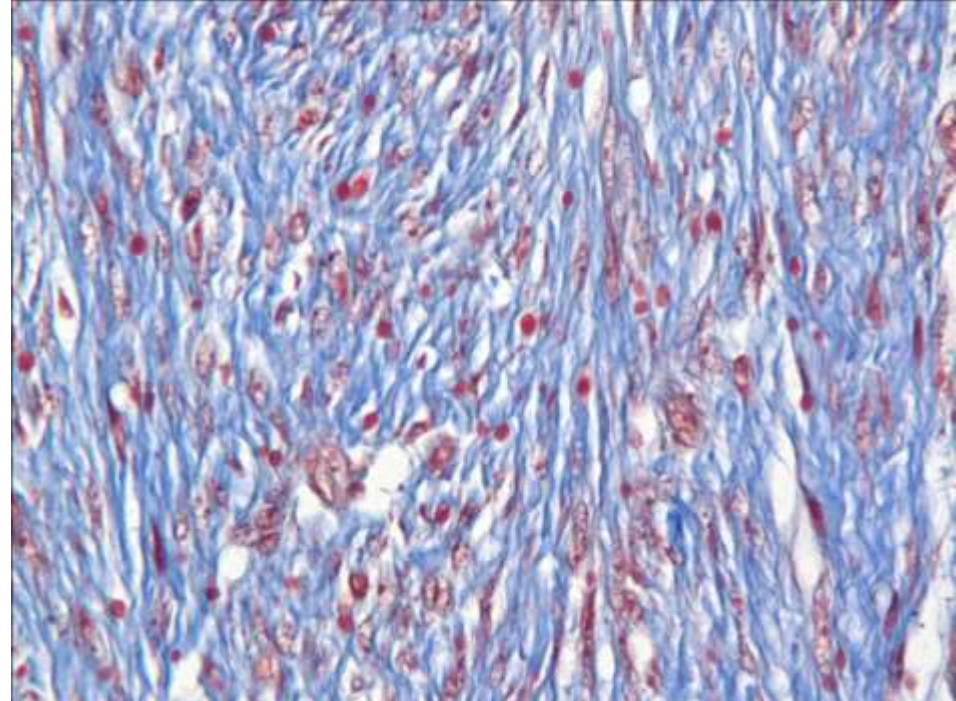
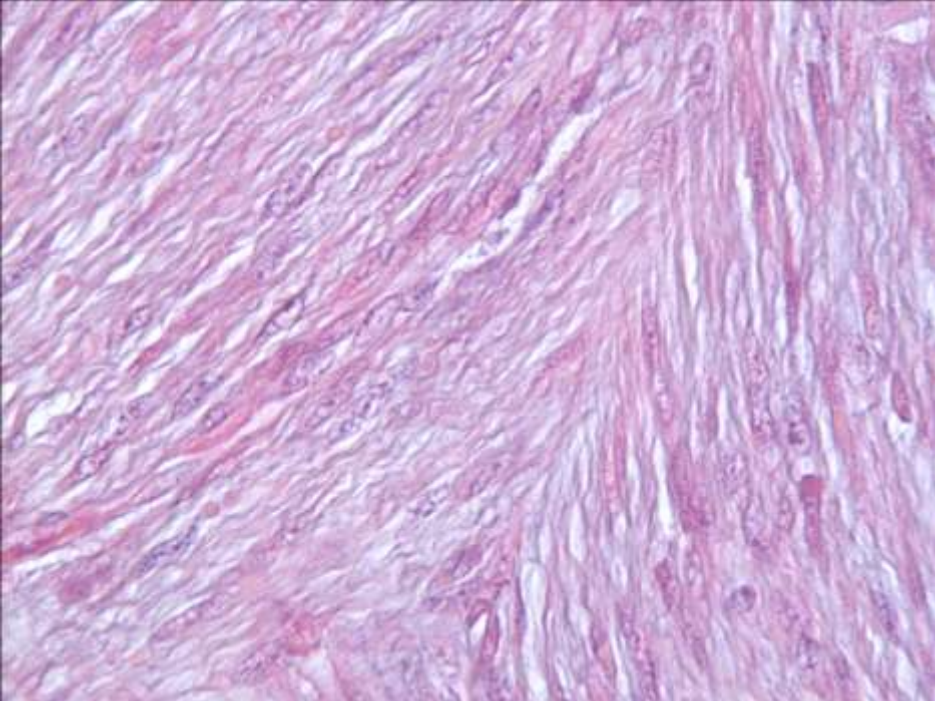




Fibroblastoma desmoplásico

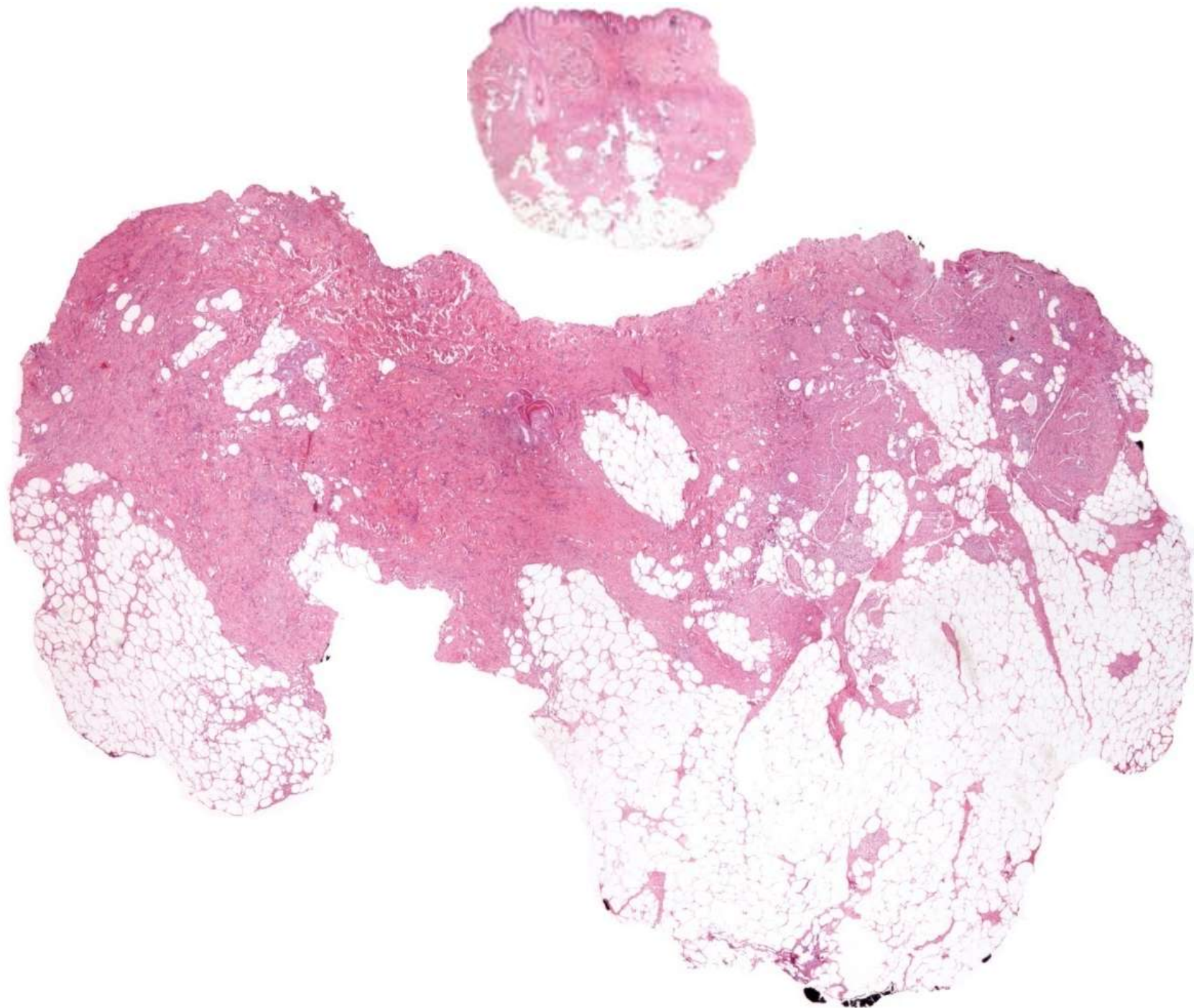
- Cuello, brazo, antebrazo, muslo, hombro, pie
- Tumor bien delimitado, subcutáneo o intramuscular
- Células fusiformes o estrelladas con nucleolo prominente y citoplasma anfófilo
- Fondo colágeno denso o fibromixoide
- Menos celularidad donde más colágeno
- NO mitosis ni necrosis
- Pocos vasos
- No recidiva
- **D. Diferencial:**
 - Fascitis nodular: más celular y menos fibrosa
 - Sarcoma fibromixoide de bajo grado:
 - Células más pequeñas
 - Más celular en algunas áreas
 - Doble componente fibroso y mixoide
 - Patrón arremolinado

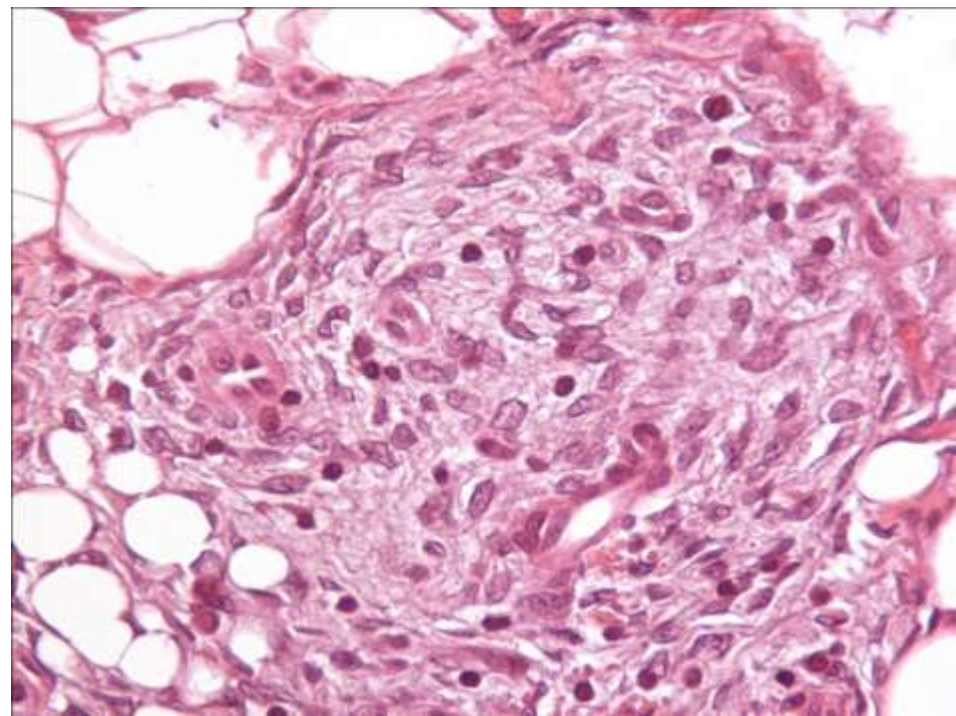
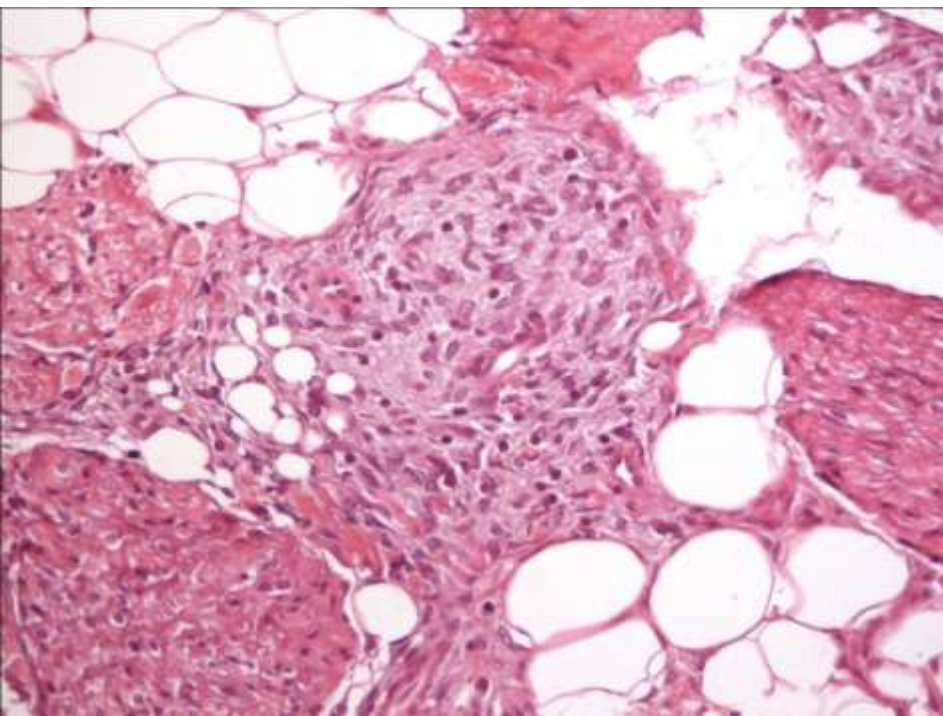
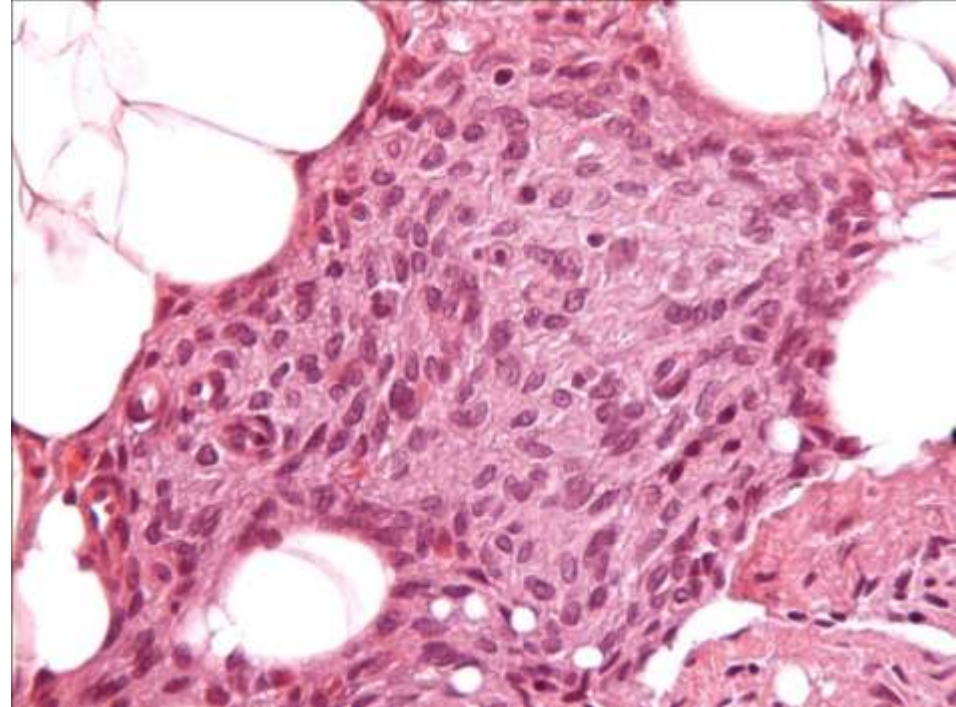
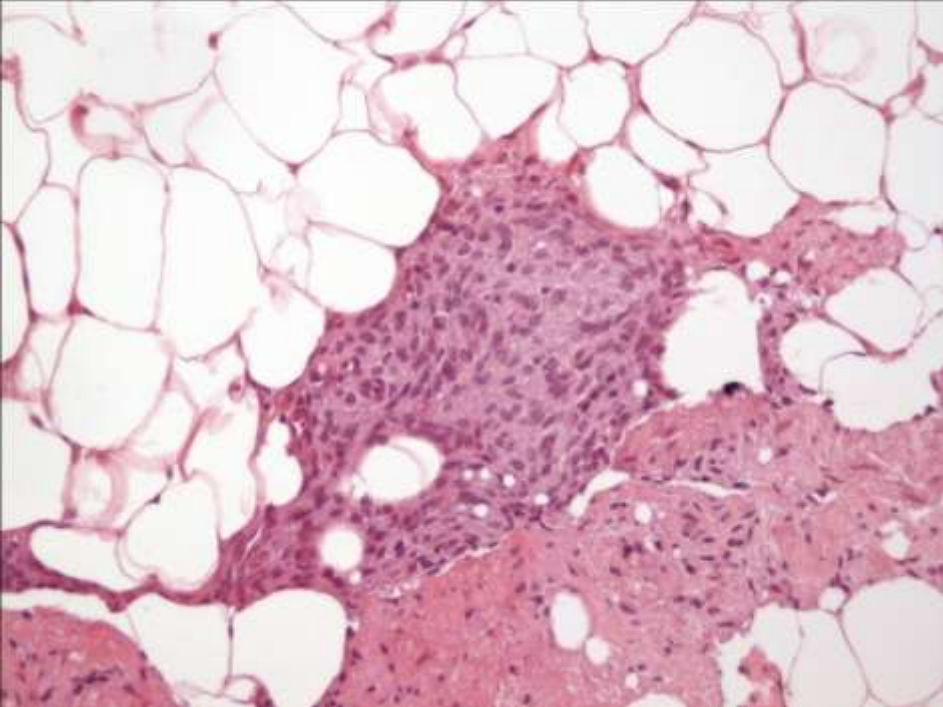




Fibroma/fibromatosis digital infantil

- Niños pequeños
- Nódulo hemisférico, superficie lisa
- Dedos manos y pies: distal, dorsal o dorso-lateral
- Generalmente solitario*
- Proliferación fusocelular en fascículos, arremolinados, cortos o estoriformes perianexiales
- Células miofibroblásticas con muy escasas mitosis
- Inclusiones paranucleares eosinófilas (1,5-24 μm) en la mayoría de casos (constituidas por agregados de actina*)
- Esporádico (aunque en el síndrome de displasia digitocutánea hay lesiones similares que NO tienen las inclusiones)
- Inmunohistoquímica: AML- α +, calponina+ y desmina+. No significativa inmunotinción nuclear para catenina- β
- Recidiva frecuente (60-75%). Pero se recomienda resección limitada. Posible regresión espontánea
- D. Diferencial:
 - Fibromatosis desmoide: profunda, catenina- β nuclear
 - Fibromatosis palmar o plantar*
 - Fibroma aponeurótico calcificante*

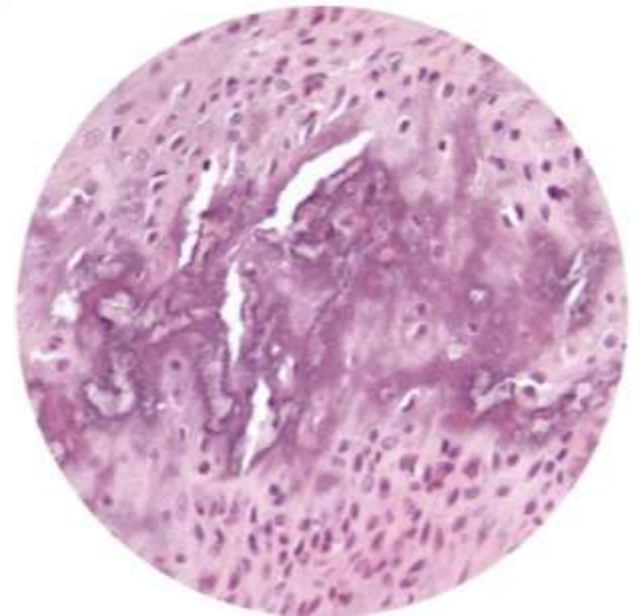
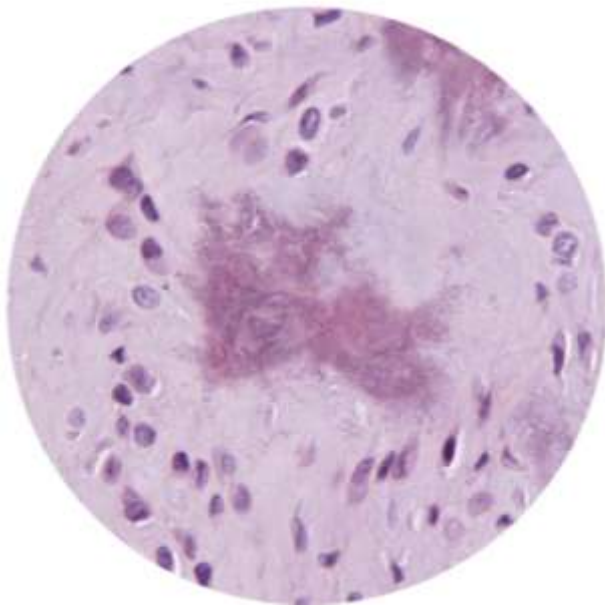
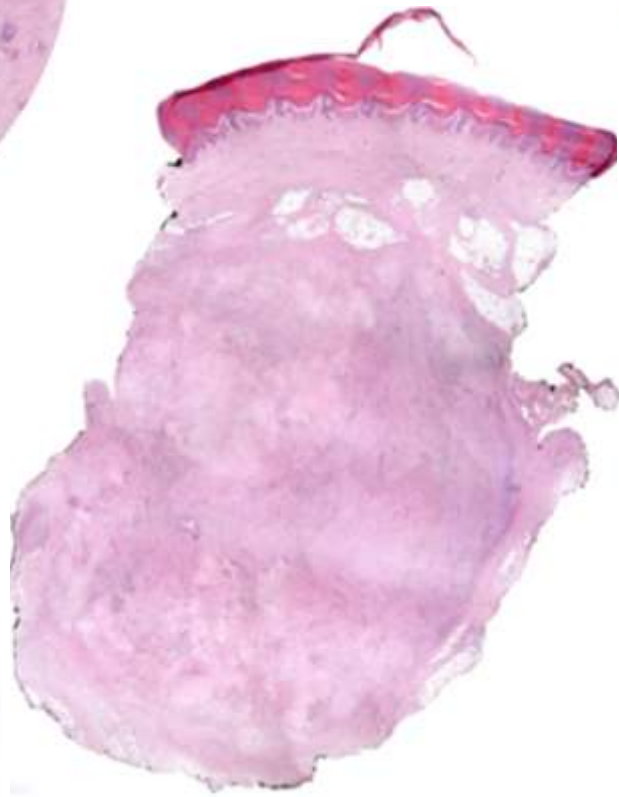
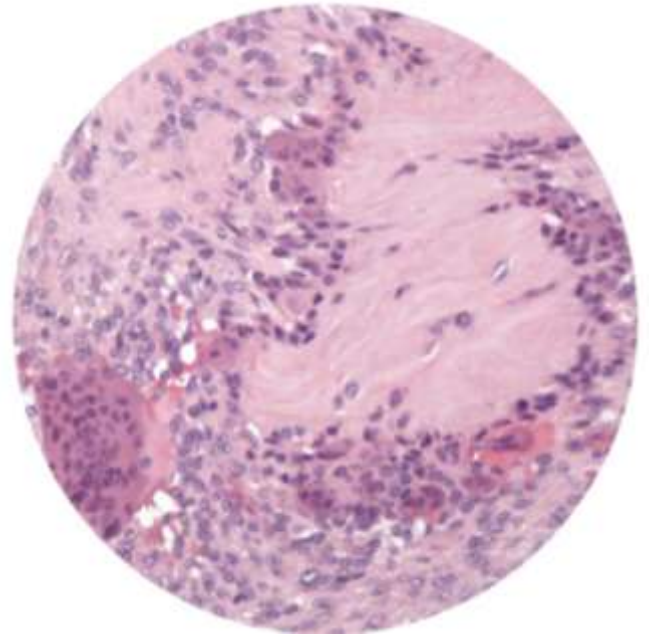
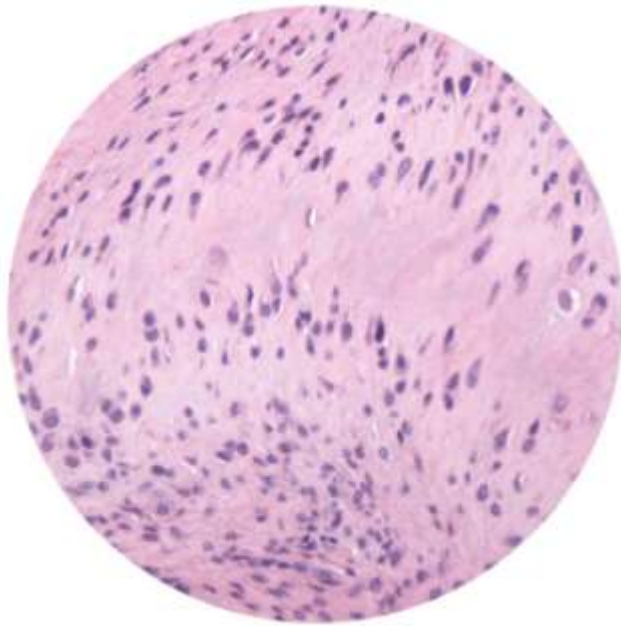




Hamartoma fibroso infancia

- Niños < 2 años
- Masa pequeña (<5 cm), superficial, crecimiento rápido
- Células fusiformes o estrelladas. Rara atipia celular
- Patrón TRIFÁSICO y organoide
 - Fascículos fibroblásticos bien diferenciados
 - Tejido adiposo maduro
 - Zonas inmaduras mesenquimales mixoides de células redondas o estrelladas
- NO mitosis ni necrosis
- Inmunohistoquímica: CD34+, variable actina muscular específica y desmina
- D. Diferencial:
 - Lipofibromatosis: No áreas inmaduras
 - Miofibroma/miofibromatosis: Zonación: periférica mioide, y central hemangiopericitoide (a veces necrosis)
 - Fibroma aponeurótico calcificante: distal, calcificaciones rodeadas por empalizada cels epitelioides



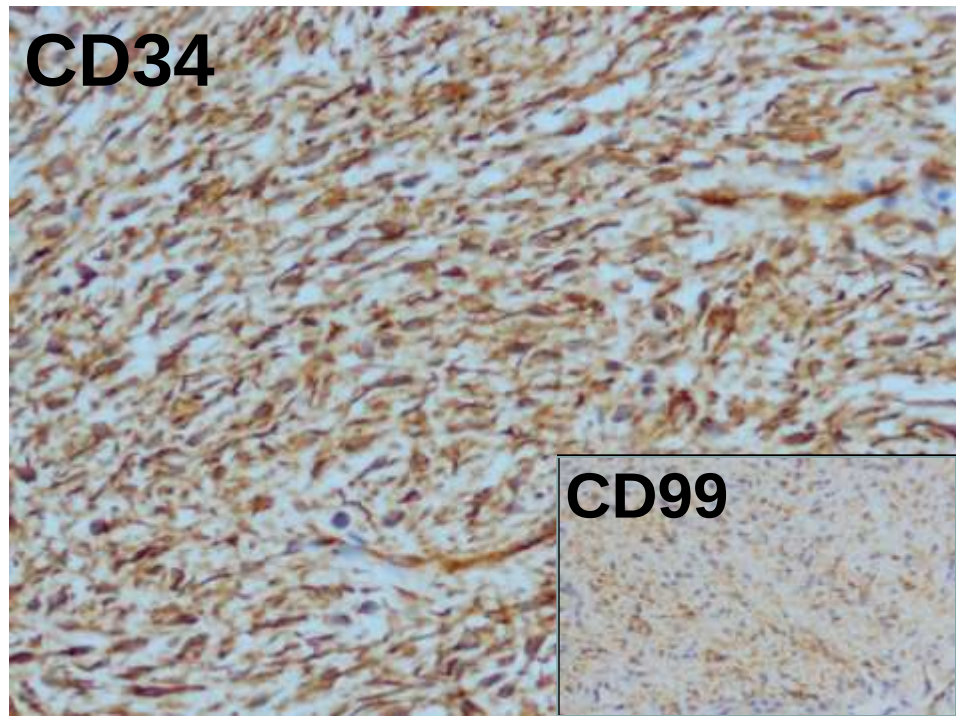
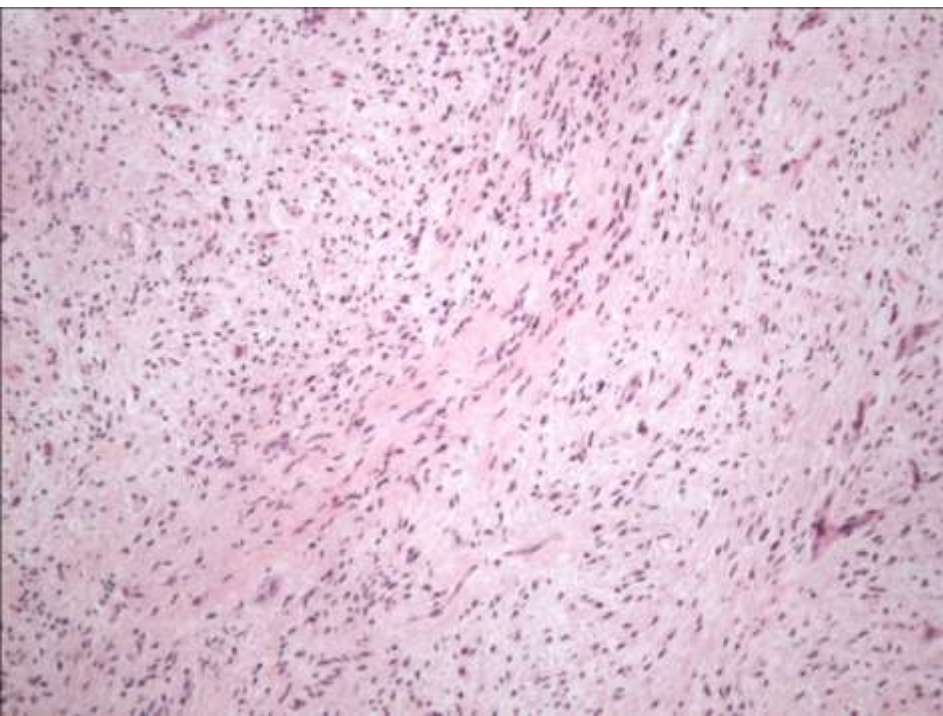
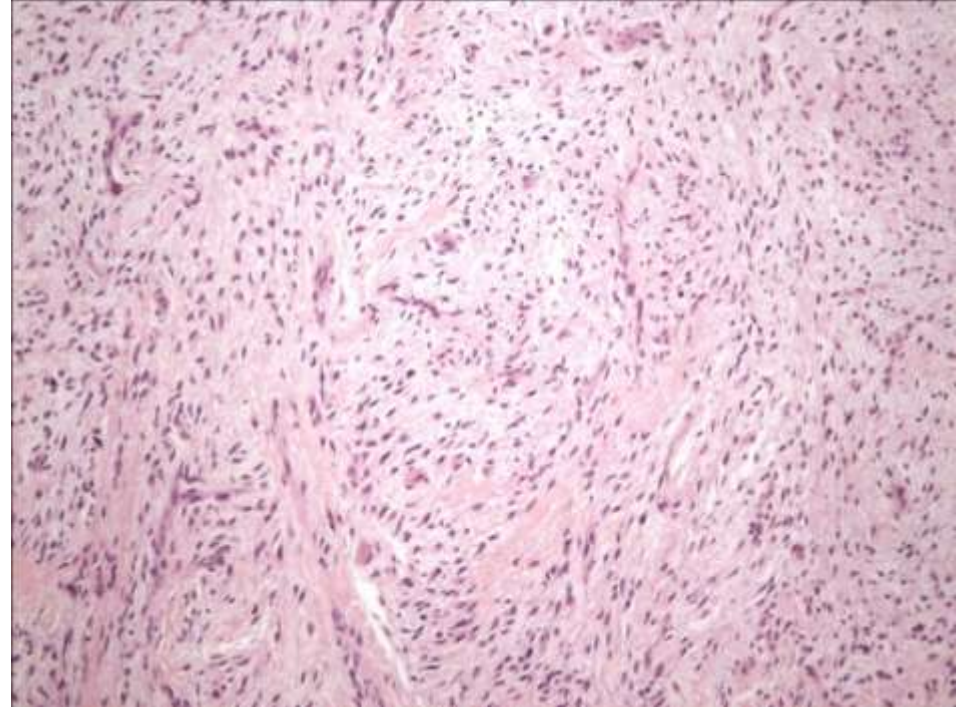
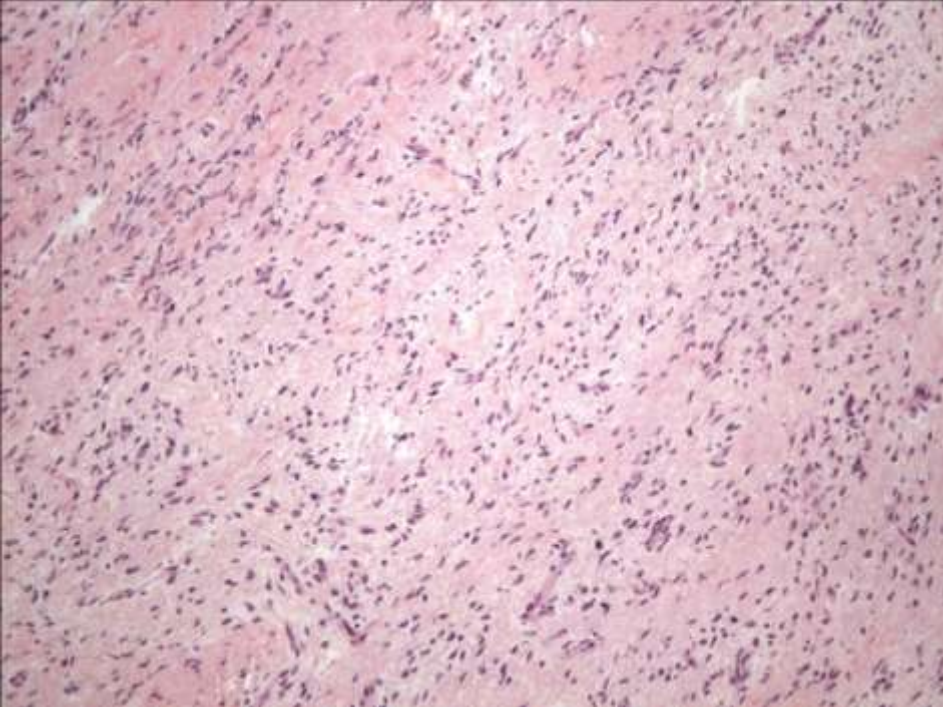


Fibroma aponeurótico calcificante

- Palmas y plantas
- Varones. Niños y adolescentes
- Masa indolora mal delimitada (<3 cm), crecimiento lento e infiltrativo
- Células fusiformes + empalizadas de cels epitelioides alrededor de espacios fibrocondrales, que tienden a calcificarse
- Puede haber células gigantes multinucleadas tipo osteoclasto
- Recidivas frecuentes (50%), pero se recomienda resección limitada
- D. Diferencial:
 - Condroma de partes blandas: más edad, predominio condral
 - Sarcoma sinovial monofásico: más celular y atípico, y expresión de marcadores epiteliales. T(X-18): fusión génica SS18-SSX1/2/4; SS18L1-SSX1)

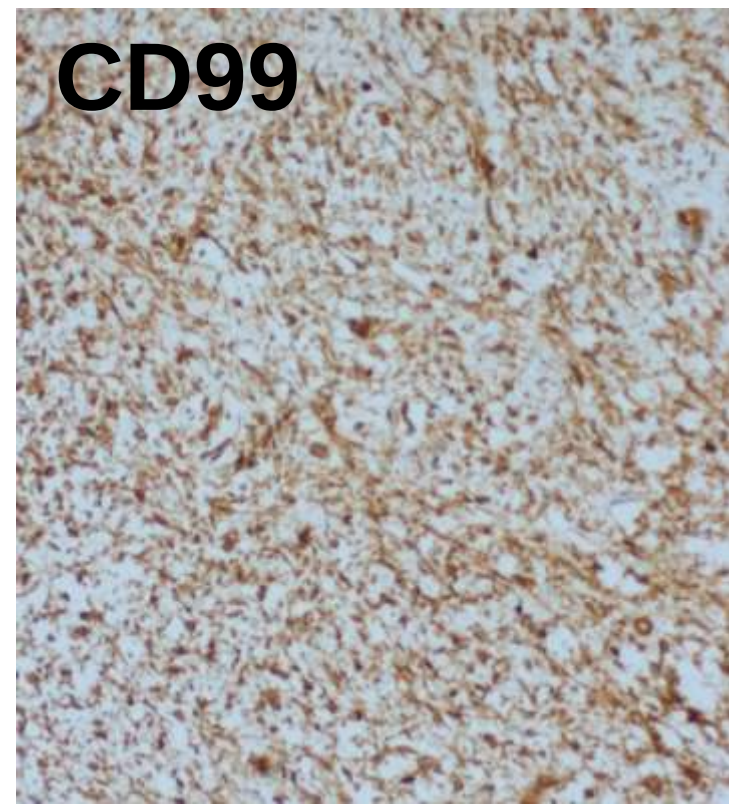
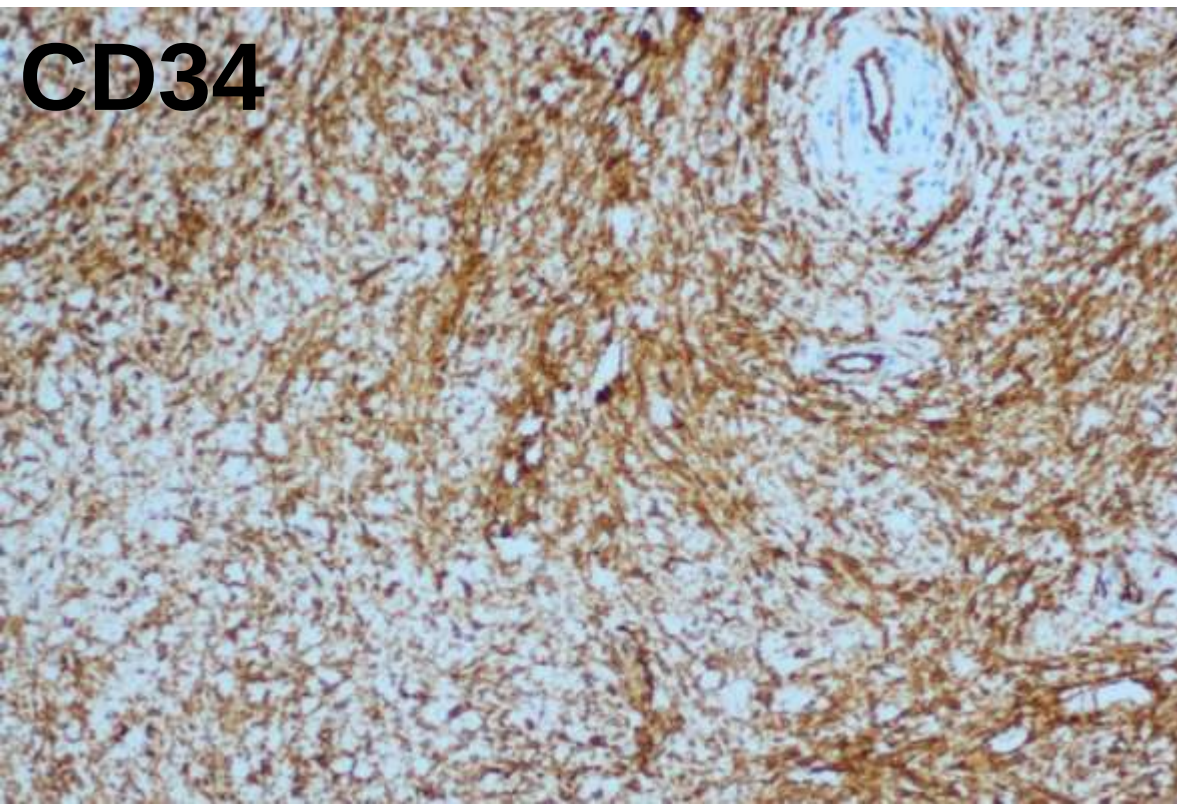
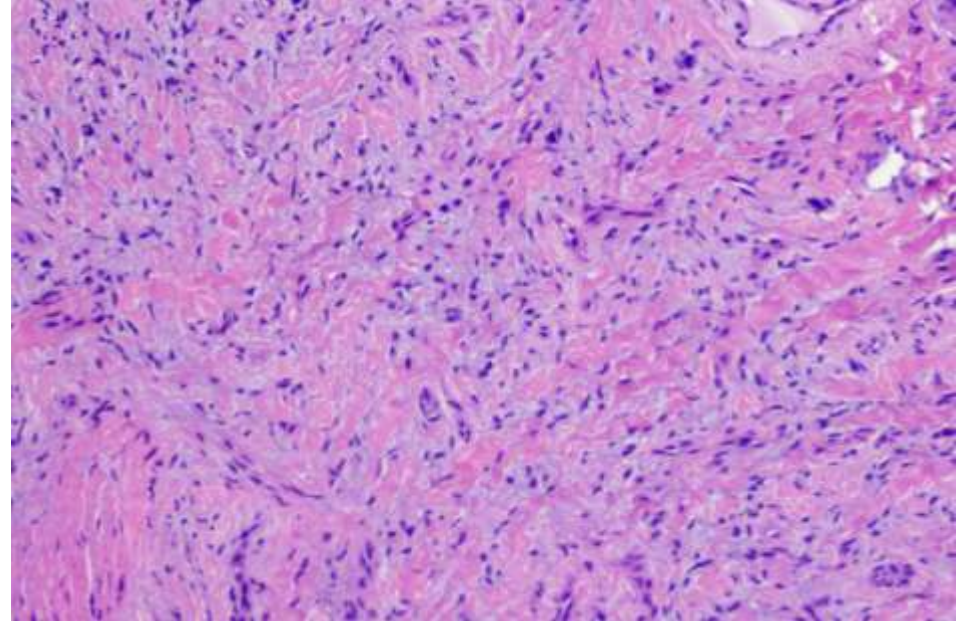








5º dedo del pie



Fibromixoma acral superficial

- Dedos manos o pies. Predilección lecho ungueal. Raro en talón
- Adultos (hombres > mujeres)
- Células fusiformes o estrelladas. Rara atipia celular
- Patrón arremolinado o fascicular
- Matriz mixoide y colágena
- Aumento de microvascularización. Dispersos mastocitos.
- Asociación mal definida con papilomavirus
- **Positividad: CD34, CD99 y EMA**
- Negativas: actina muscular, desmina, S-100
- Excepcional recidiva

Fibromixoma acral superficial

- **D. Diferencial:**
 - **Angiomixoma superficial:** No acral, +/-componente epitelial, CD34-/+
 - **DFSP:** no suele afectar dedos-subungueal; infiltración subcutánea característica; patrón estoriforme; Fusión génica COL1A1-PDGFB
 - **Perineuroma periungueal:** CD34 no + difuso; EMA+
 - **Fibroqueratoma digital:** colágeno perpendicular a epidermis, EMA-, CD34-/+
 - **Sarcoma fibromixoide bajo grado:** NO acral; translocación-fusión génica típica
 - **Sarcoma mixoinflamatorio acral:** células Reed-Sternberg-like, inflamación, atipia celular

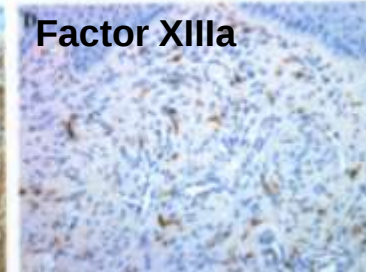
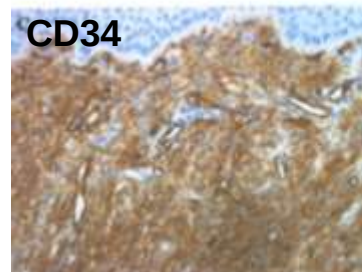
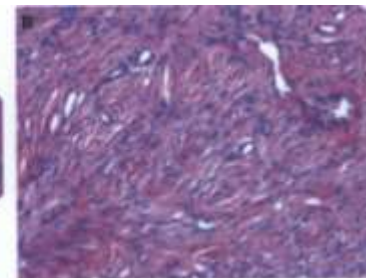
Cellular digital fibromas: distinctive CD34-positive lesions that may mimic dermatofibrosarcoma protuberans

Background: Digital fibromas are common benign acral tumors typically reported as angiofibromas (AFs) or acquired digital fibrokeratomas (ADFs). Cellular variants are not well recognized.

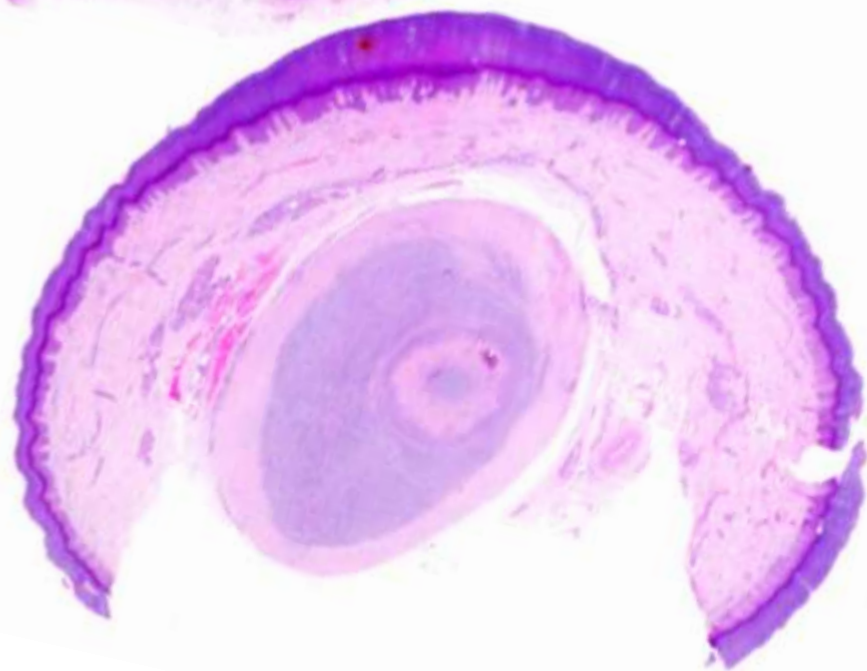
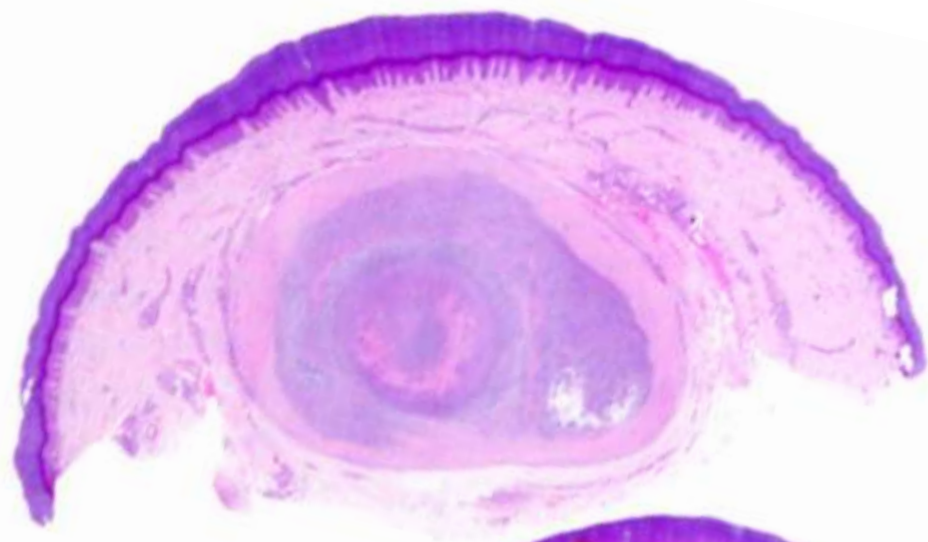
Methods: We collected 14 acral fibrocytic lesions showing a spindle cell morphology from our files, and evaluated CD34, Factor XIIIa, epithelial membrane antigen (EMA), and S100 protein staining of these lesions. We compared the histologic and immunohistochemical

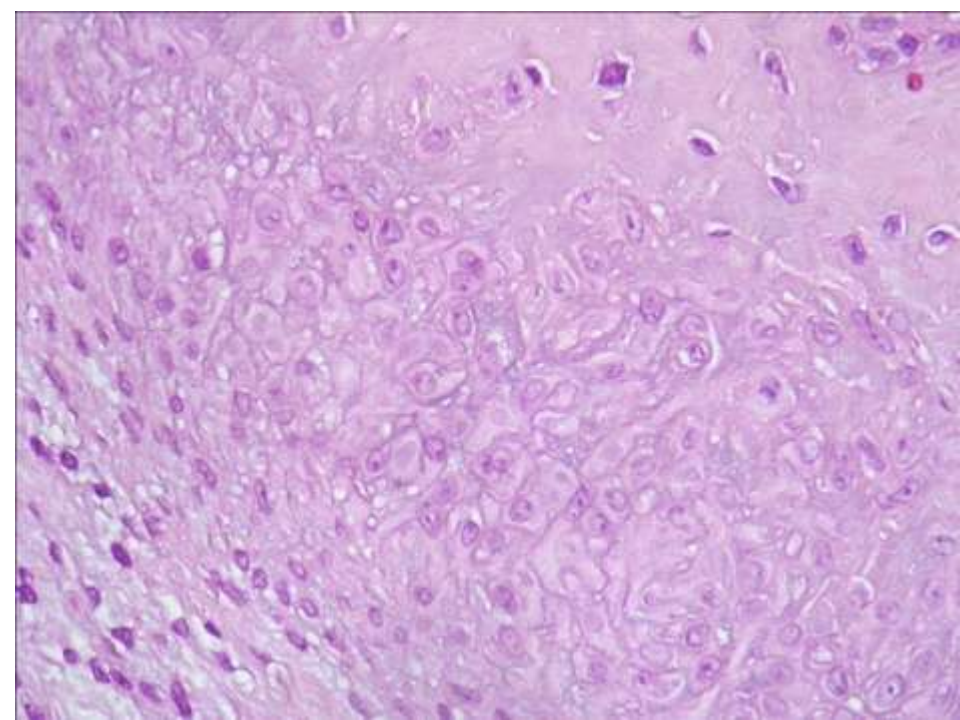
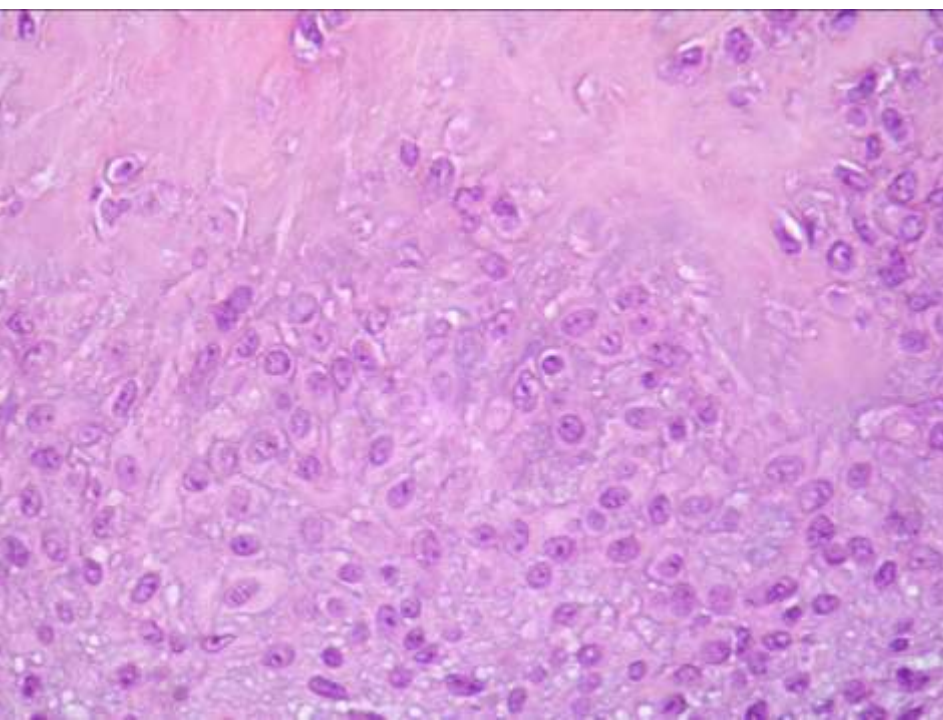
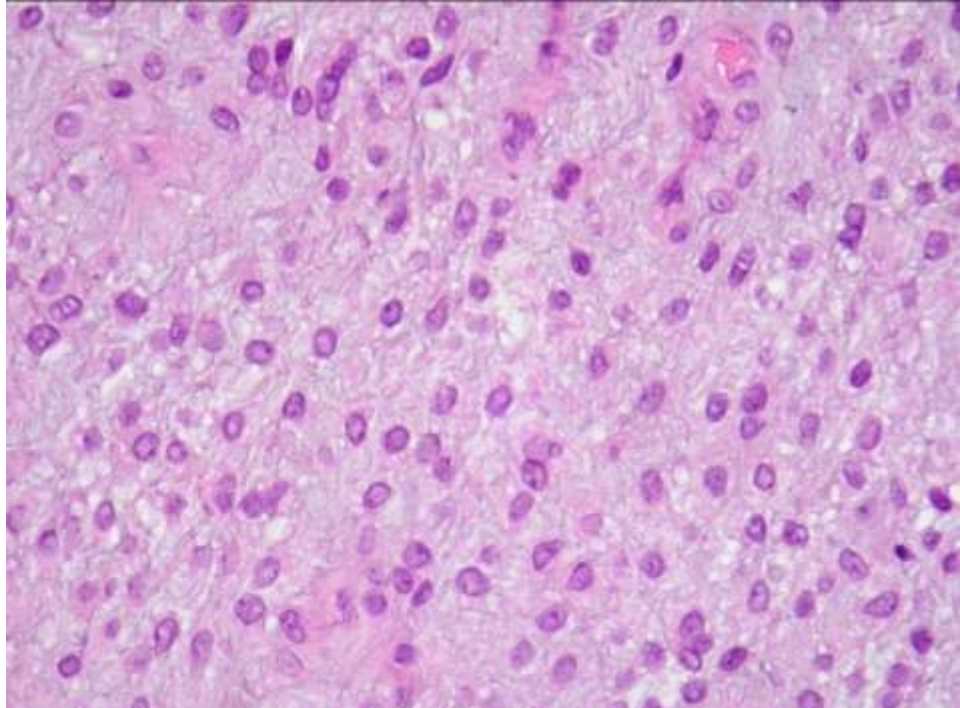
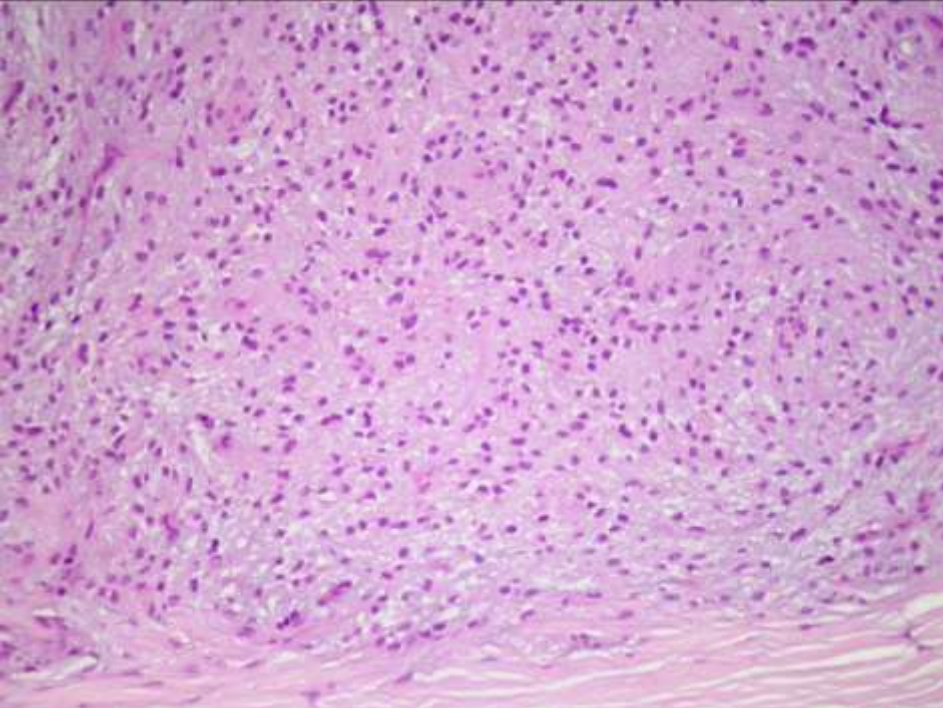
Jennifer M. McNiff, Antonio Subtil, Shawn E. Cowper, Rossitza Lazova and Earl J. Glusac

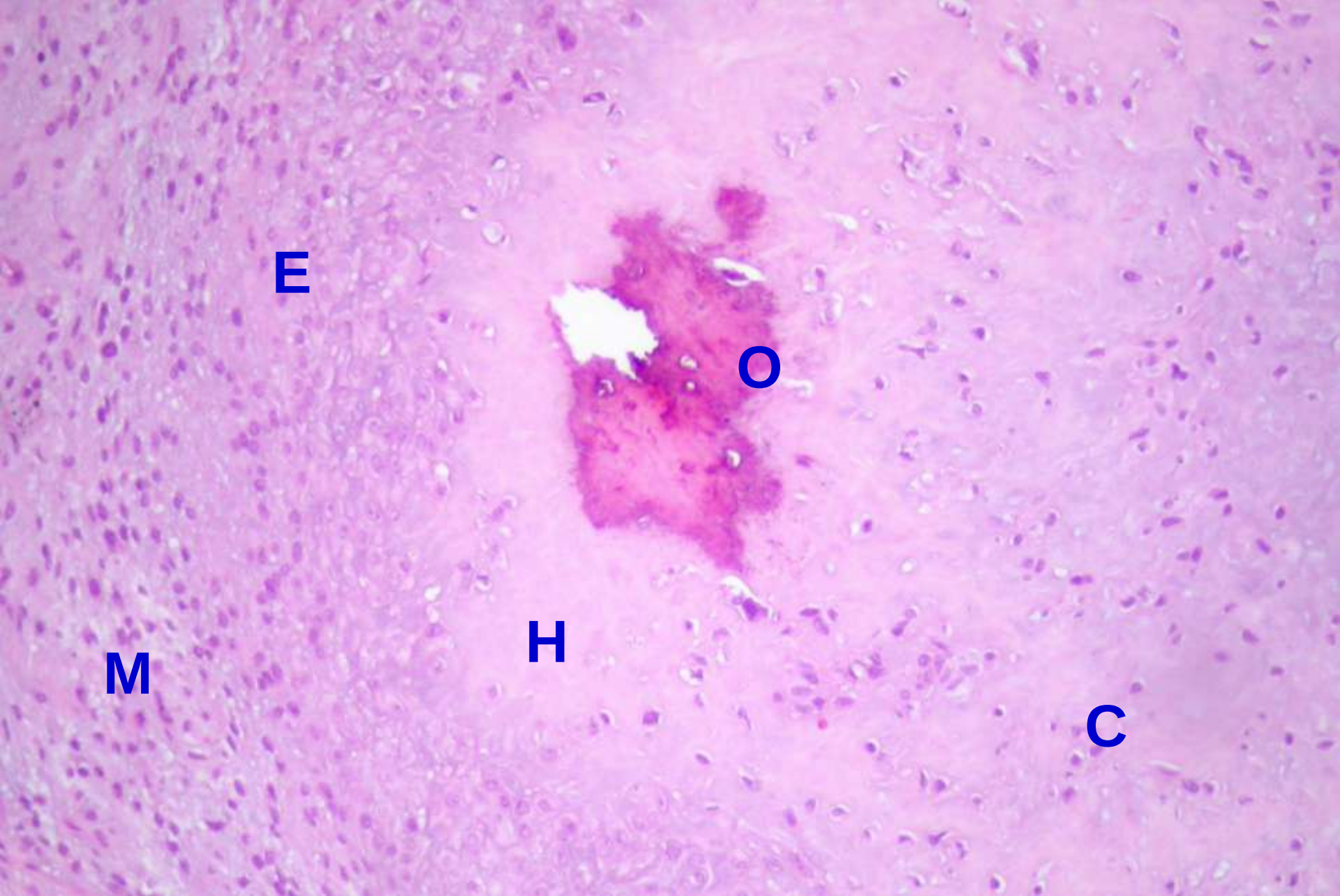
Departments of Dermatology and Pathology,
Yale University School of Medicine, New
Haven, CT, USA



(EMA -)







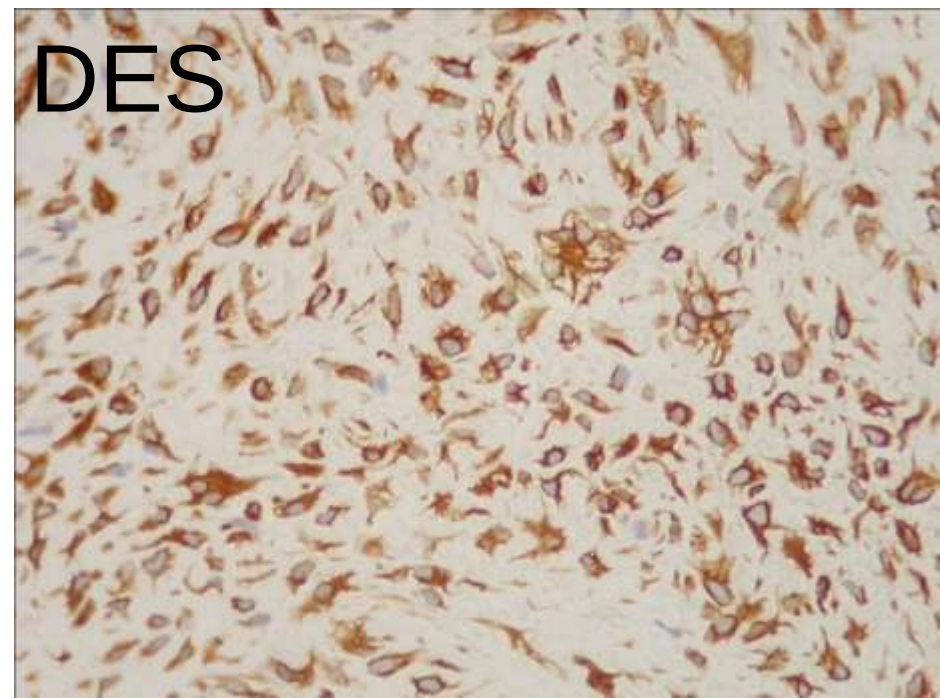
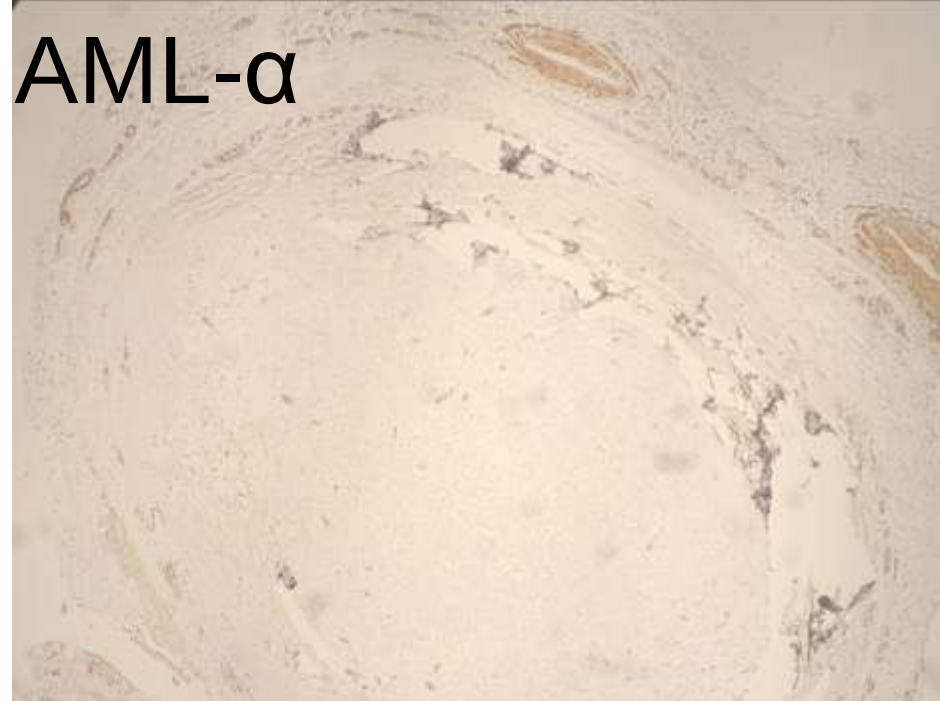
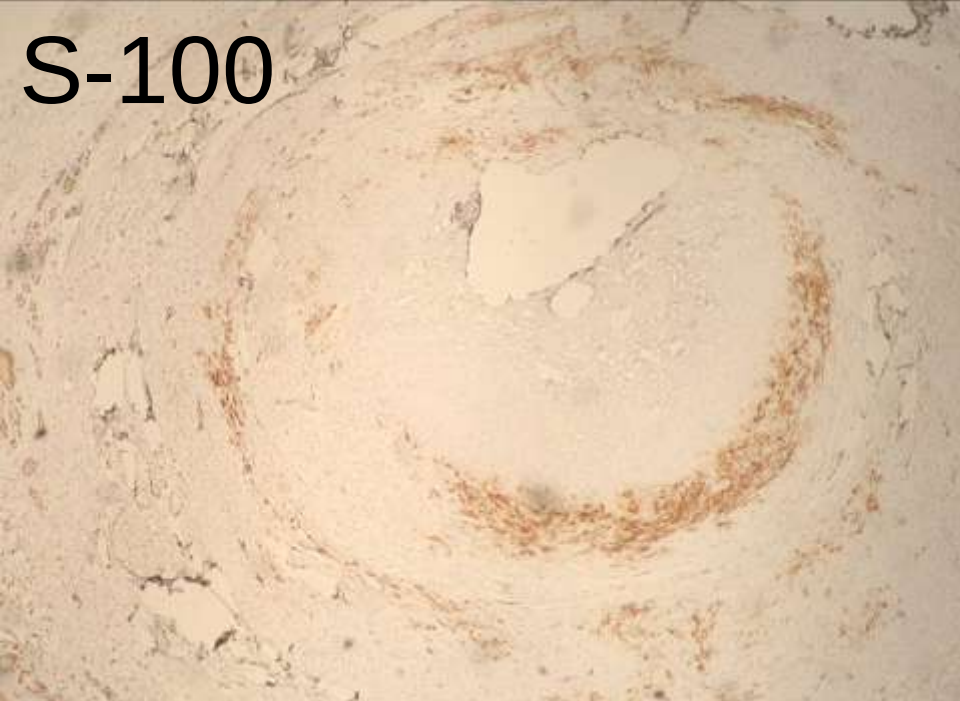
E

O

H

M

C



Tumor fibromixioide osificante

Tumor fibromixioide osificante

Clínica

- **Neoplasia (mesenquimal) rara**
- **Subcutánea**
- **Extremidades frecuentemente**
- **Indolora**
- **Crecimiento lento**
- **Adultos (hombres > mujeres)**
- **Recidiva (25%)**
- **(Metástasis: casos muy atípicos*)**

Tumor fibromixioide osificante

Histopatología

- **Generalmente encapsulado (cápsula muy gruesa)**
- **Lobulado y mixoide**
- **Rica vascularización**
- **Células núcleos redondos u ovales de límites mal definidos, o bien poligonales**
- **Áreas hialinas, a veces condroides**
- **Focal hueso laminar (63% casos)**

Tumor fibromixioide osificante

Inmunohistoquímica

- Positiva
 - Vimentina
- Variable y FOCAL:
 - S-100
 - Actina músculo liso
 - GFAP
 - Desmina
 - CD10
- Generalmente NEGATIVA
 - Citoqueratina, EMA, neurofilamentos

Ossifying Fibromyxoid Tumor of Soft Parts

A Clinicopathologic Study of 70 Cases With Emphasis on Atypical and Malignant Variants

Andrew L. Folpe, M.D., and Sharon W. Weiss, M.D.

Ossifying Fibromyxoid Tumor of Soft Parts— A Clinicopathologic and Immunohistochemical Study of 104 Cases With Long-term Follow-up and a Critical Review of the Literature

Markku Miettinen, MD, Val Finnell, MD, and John F. Fetsch, MD

Abstract: Ossifying fibromyxoid tumor (OFT) is a unique soft tissue tumor of uncertain histogenesis. The majority of reported cases (approximately 220) have pursued a benign clinical course. However, recent literature has emphasized the existence of

Key Words: ossifying fibromyxoid tumor, immunohistochemistry, differential diagnosis, low-grade fibromyxoid sarcoma, mixed tumor, S100 protein

(*Am J Surg Pathol* 2008;32:996–1005)

Tumor fibromixioide osificante

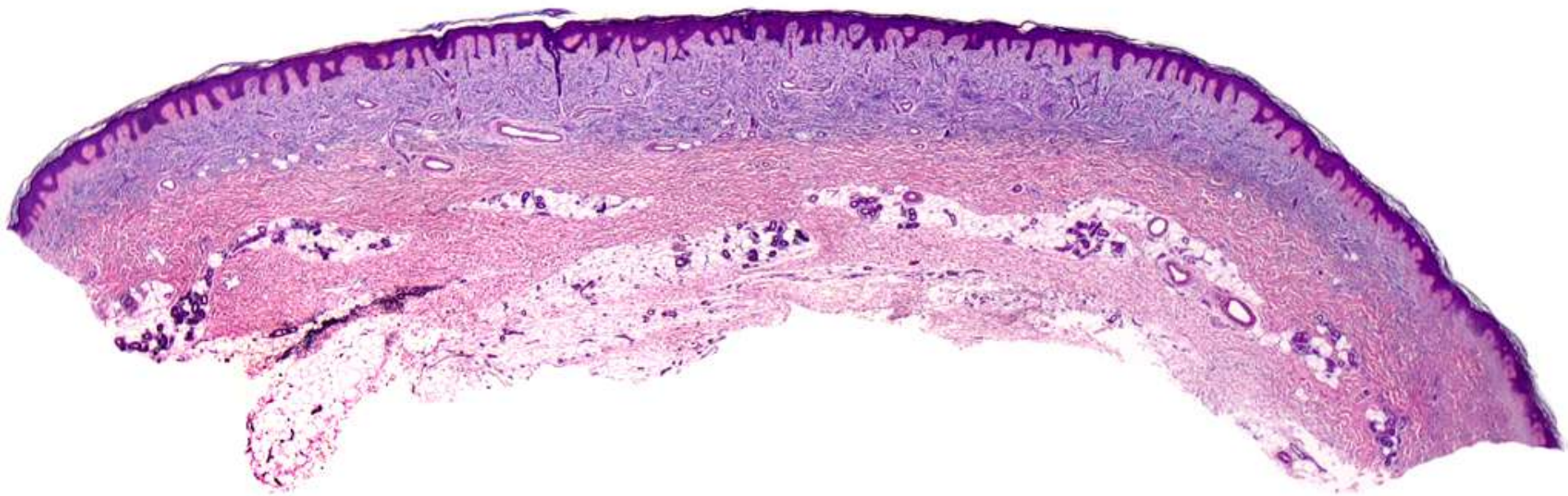
¿Criterios malignidad?

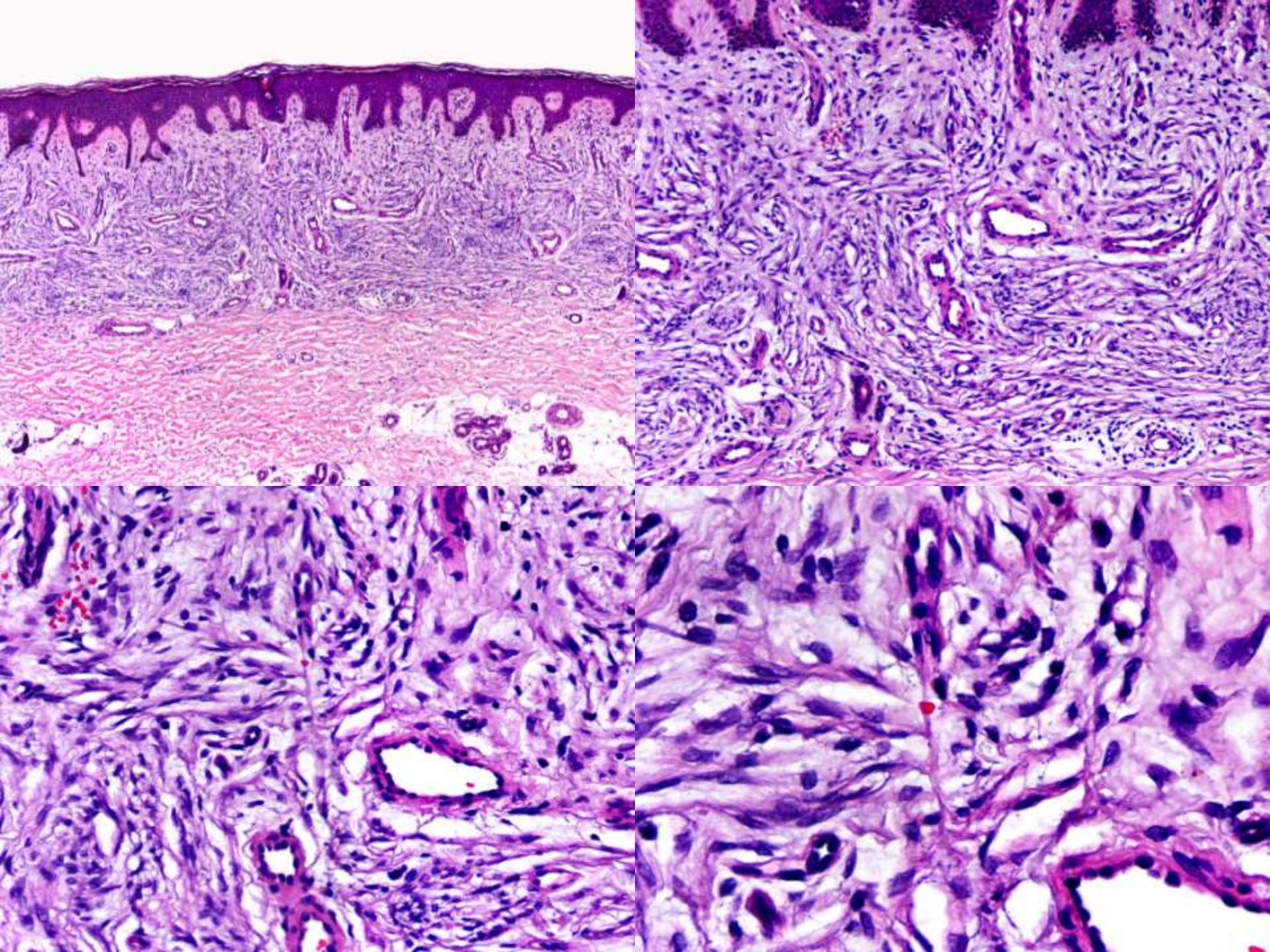
- **Alta celularidad**
- **Atipia celular prominente**
- **(Mitosis: >2 mitosis/50 campos)**
discutido – es frecuente, y parece asociarse más con la recidiva local

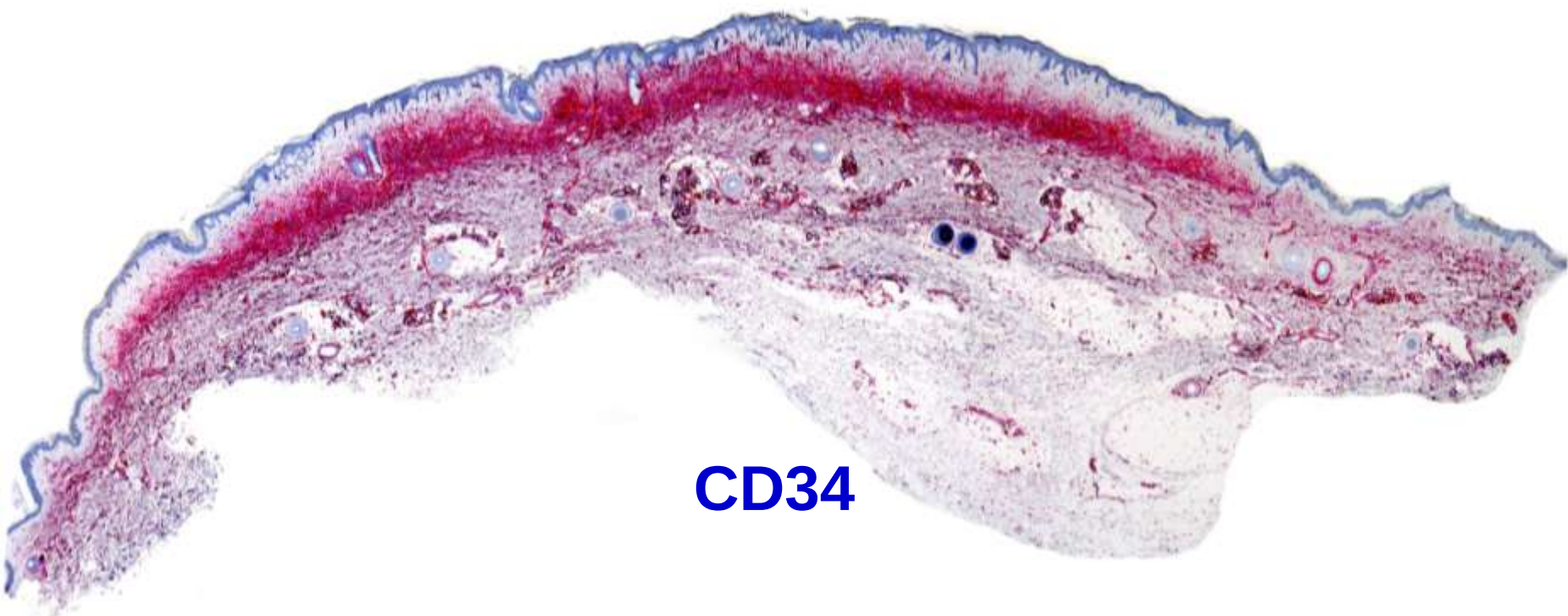
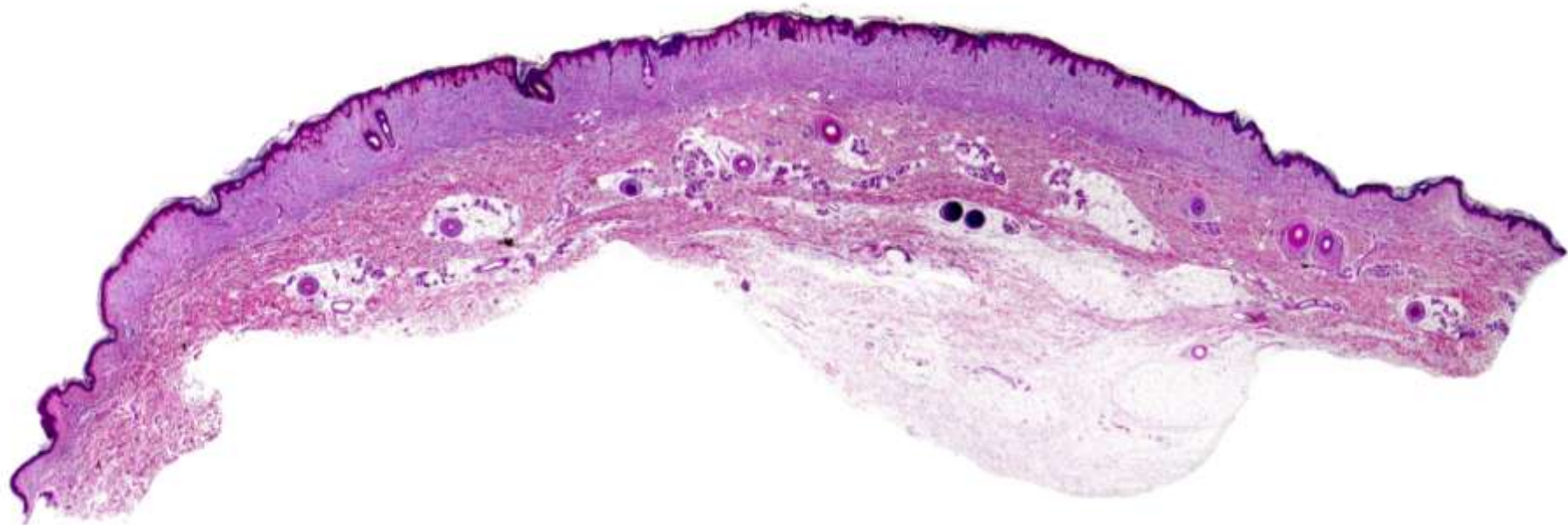
Tumor fibromixioide osificante

Diagnóstico diferencial

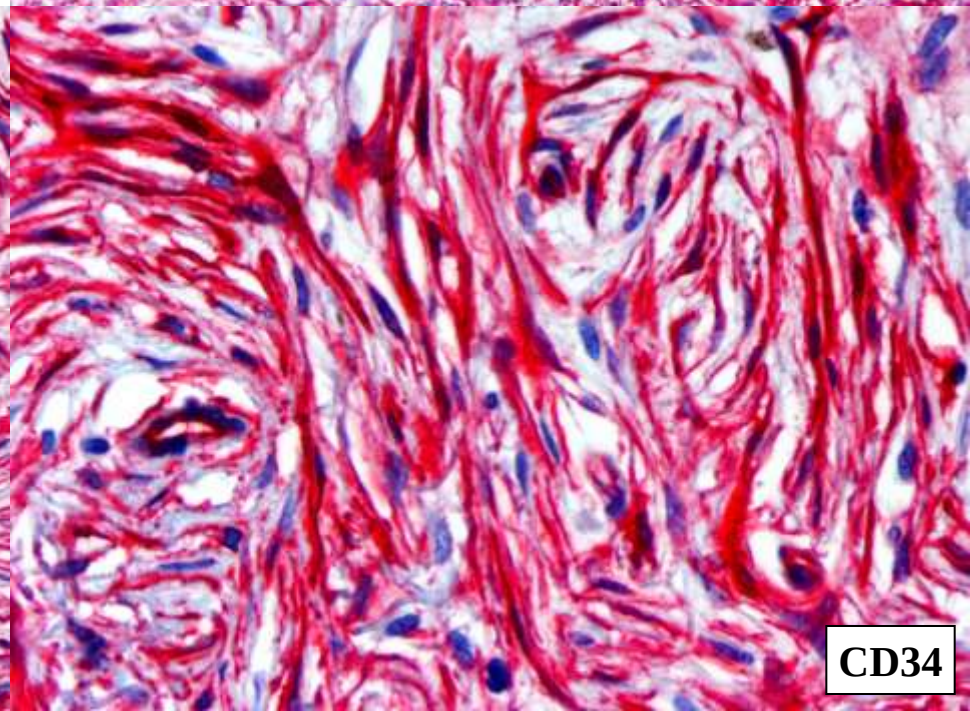
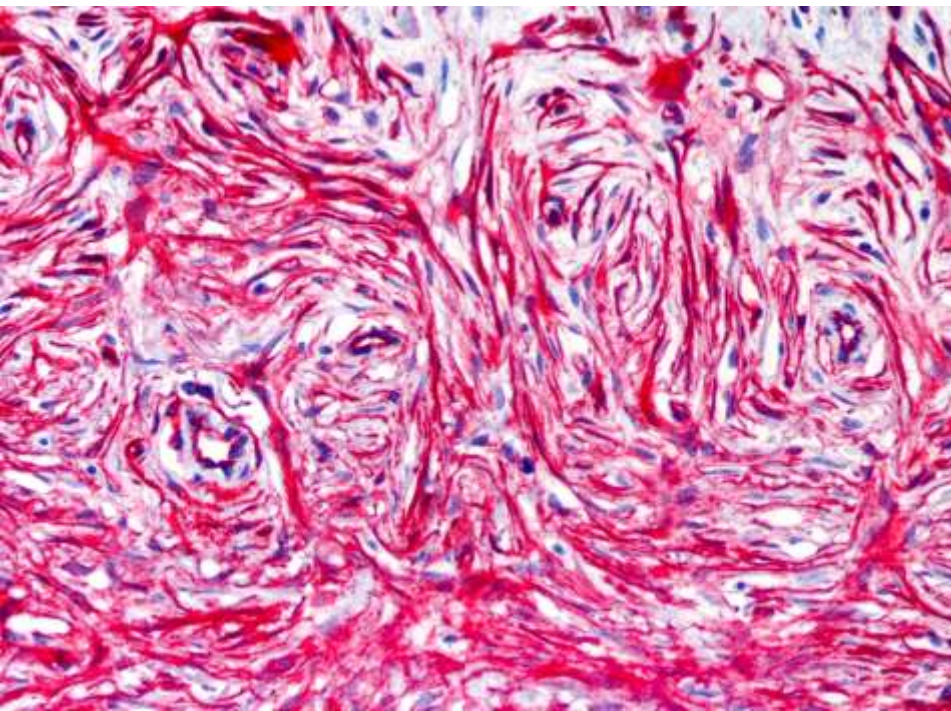
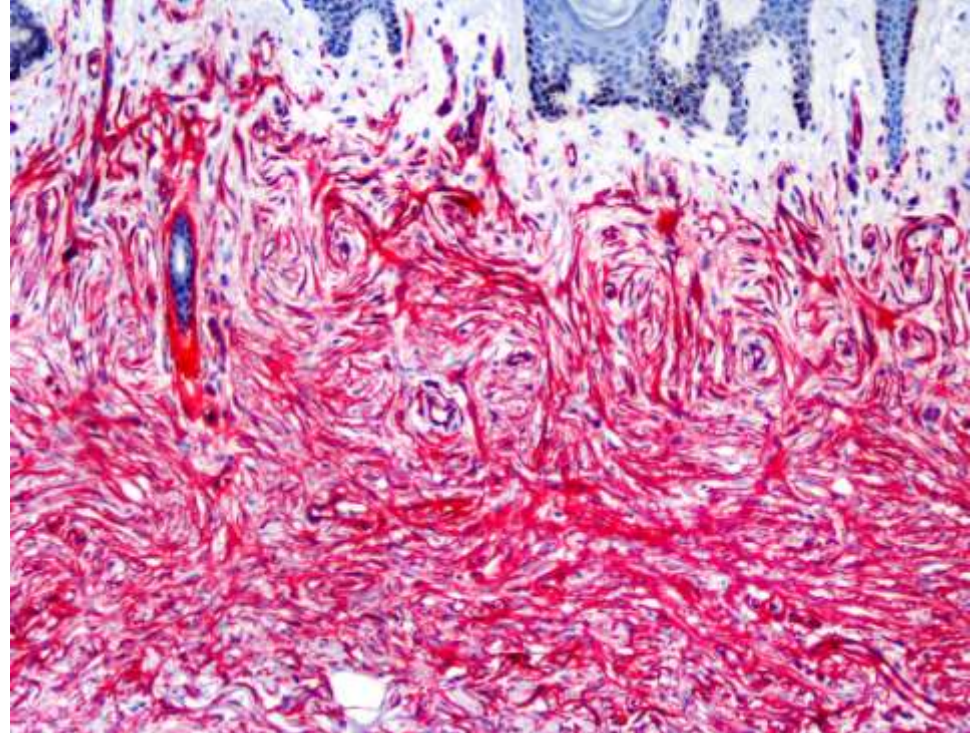
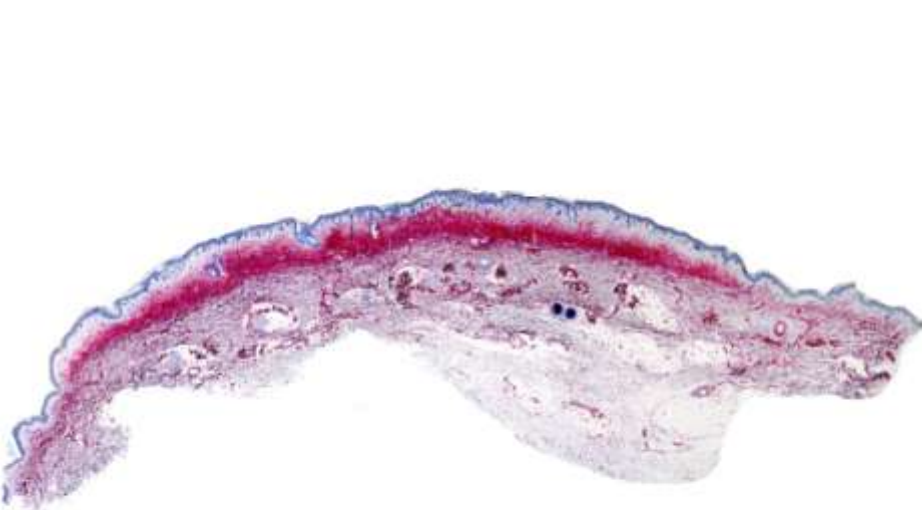
- **Schwannoma**
 - Cels fusiformes, S-100 generalizada, colágeno IV
- **Condrosarcoma mixoide extraesquelético**
 - Más grandes, profundos, t(9;22)
- **Tumor mixto cutáneo**
 - Cels epiteliales (citoqueratina constante)
- **Mixoma vaina nerviosa**
 - S-100 +, no encapsulado ni osificación
- **Cordoma**
 - Células multinucleadas, vacuolizadas, CK y EMA+



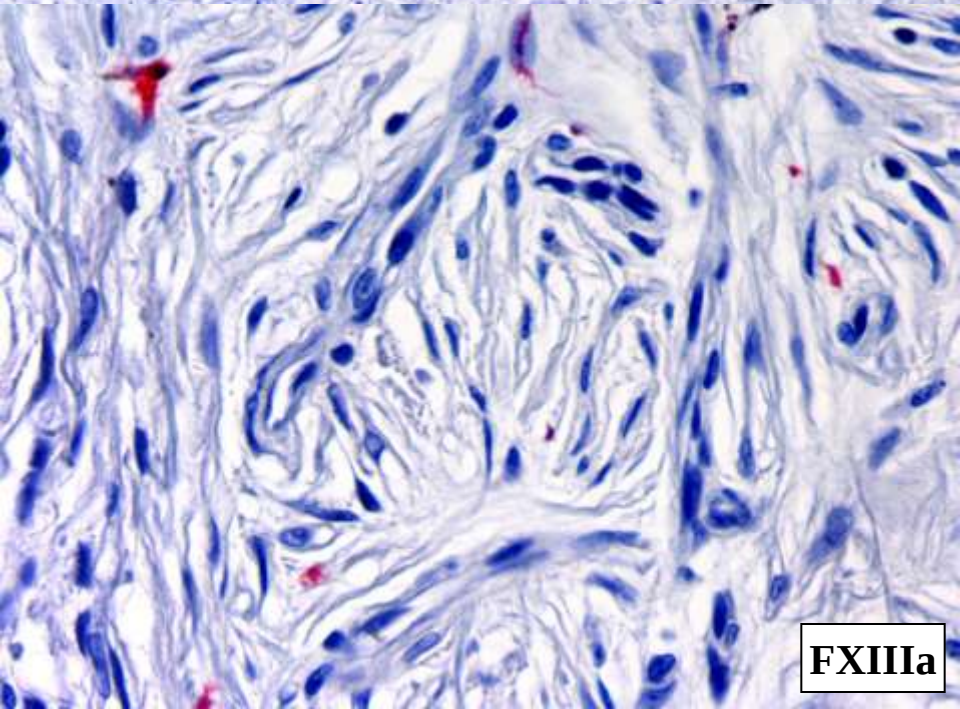
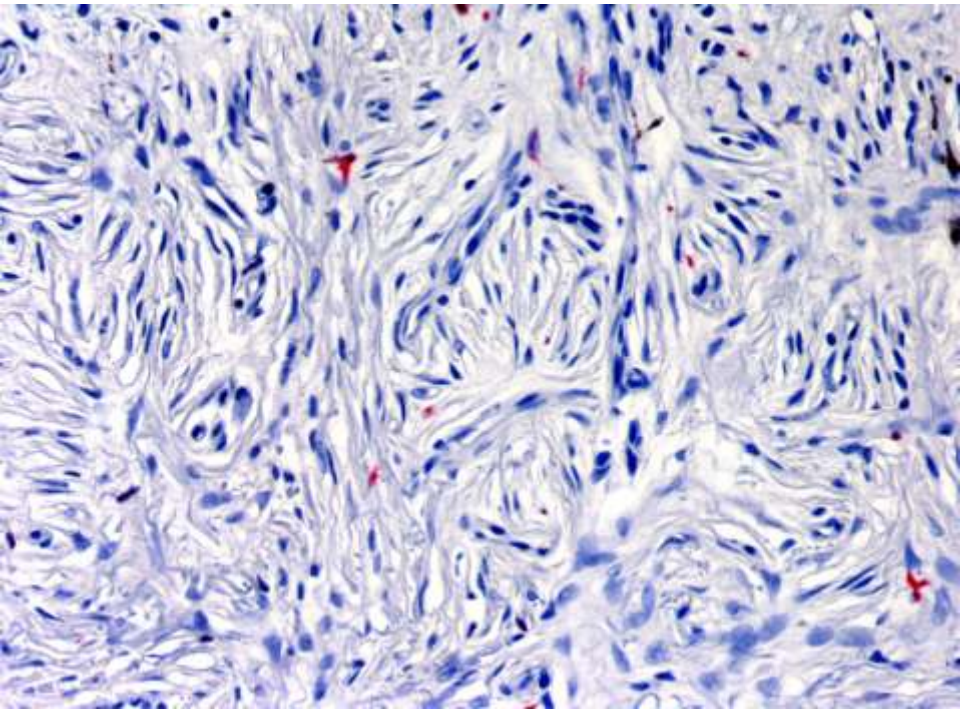
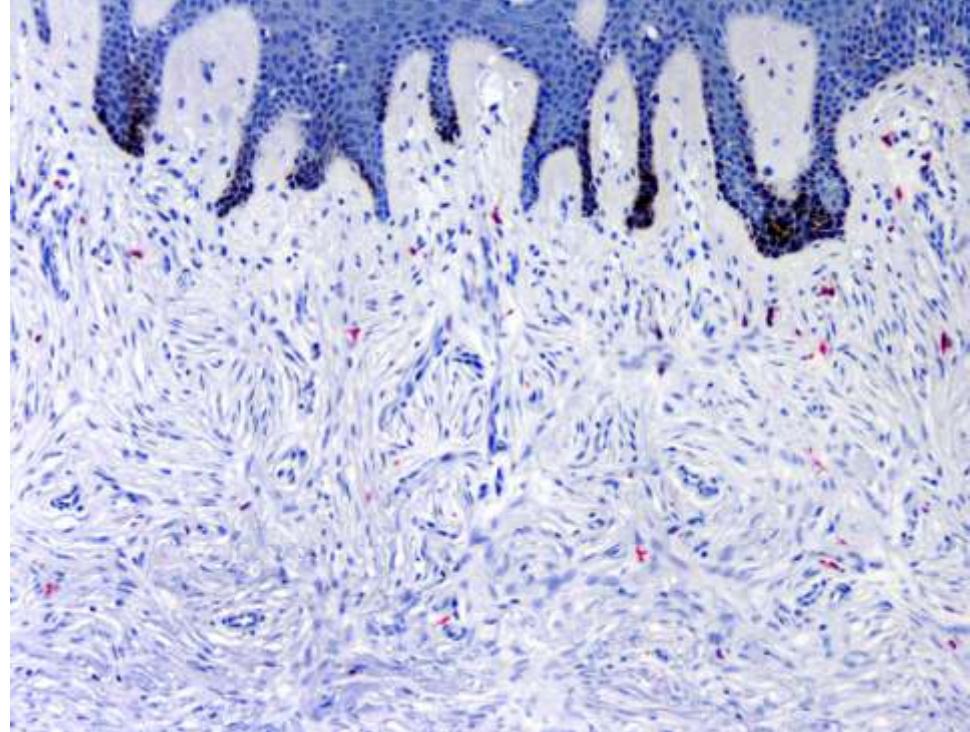
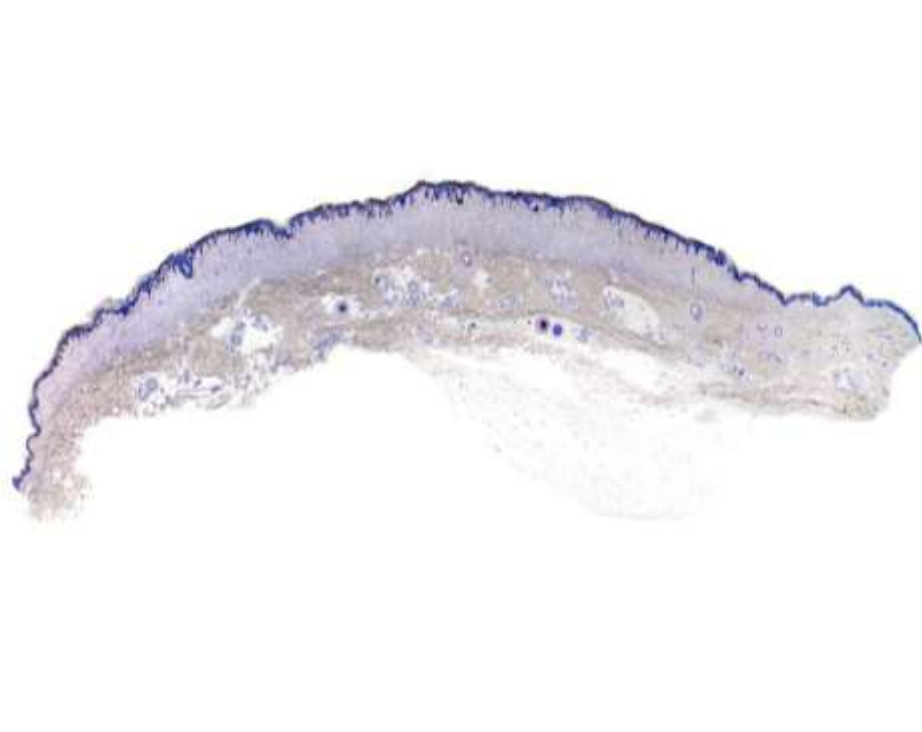


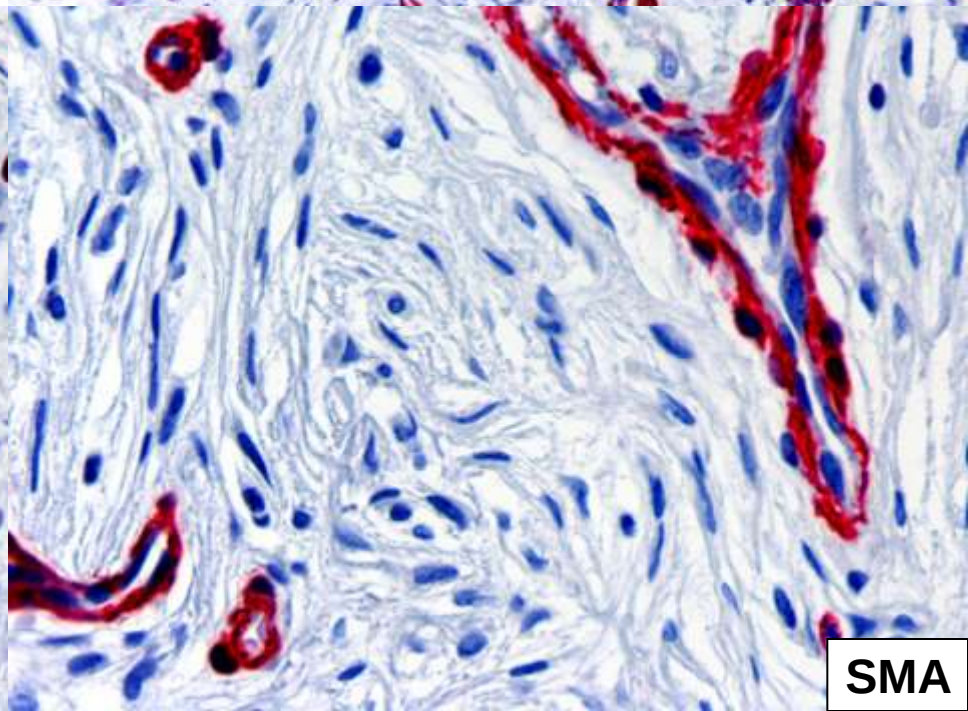
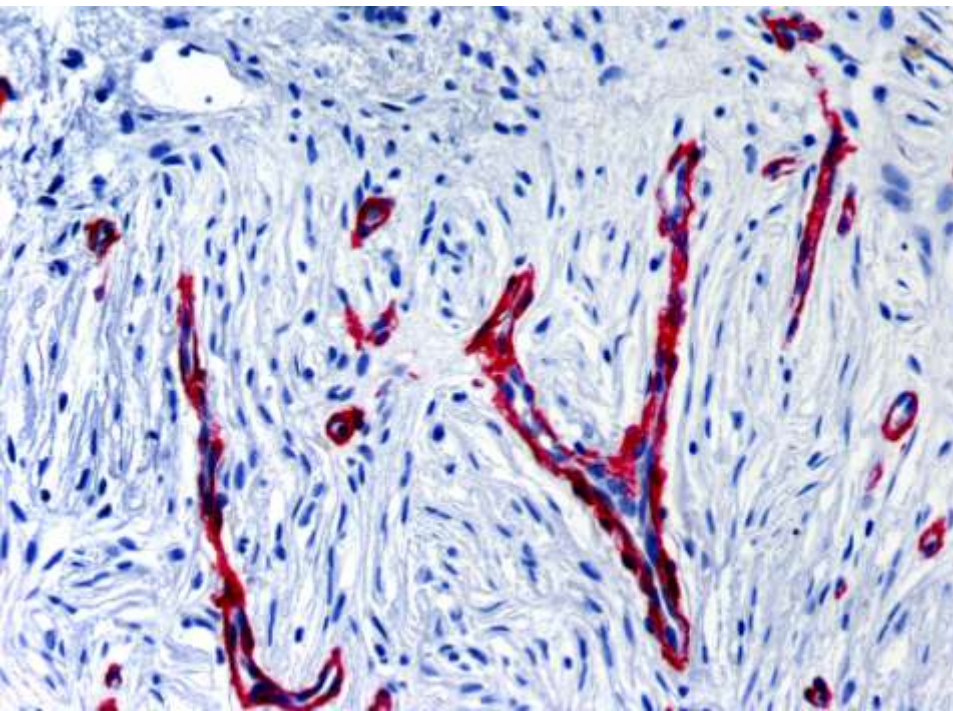
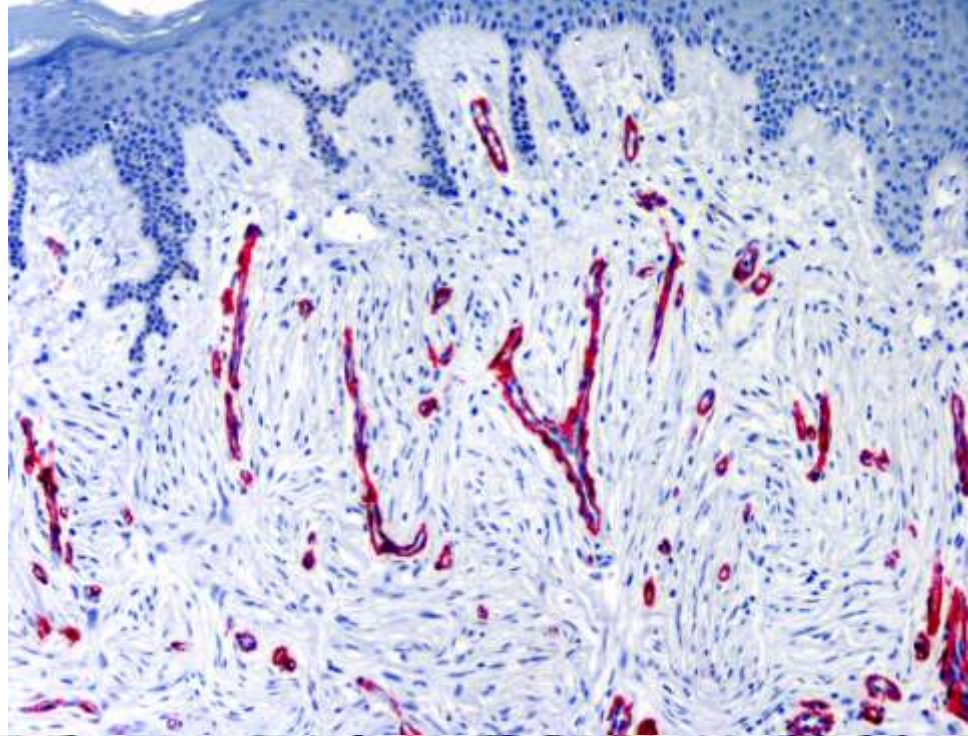
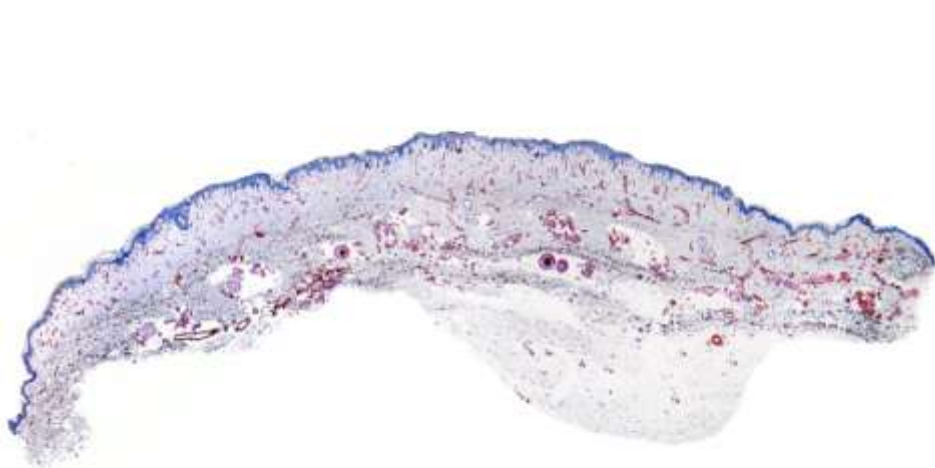


CD34

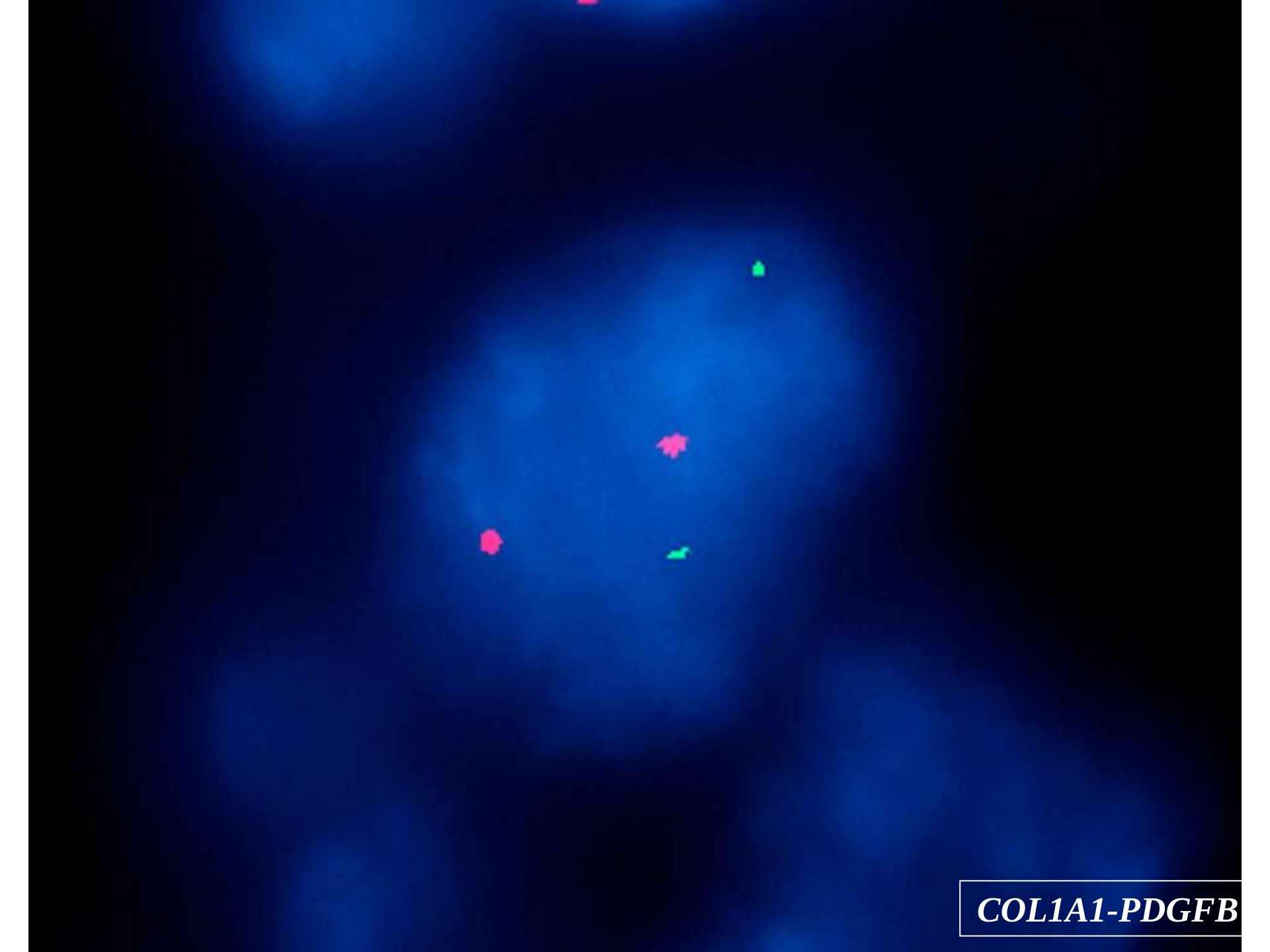


CD34





SMA



A fluorescence microscopy image showing a cell with a blue nucleus and several red and green fluorescent spots. The red spots are located in the lower-left and center-right areas, while the green spots are in the upper-right and lower-center areas. The background is dark blue.

COL1A1-PDGFB

Plaque-like CD34-positive Dermal Fibroma ("Medallion-like Dermal Dendrocyte Hamartoma")

Clinicopathologic, Immunohistochemical, and Molecular Analysis of 5 Cases Emphasizing its Distinction From Superficial, Plaque-like Dermatofibrosarcoma Protuberans

Heinz Kutzner, MD,* Thomas Mentzel, MD,* Gabriele Palmedo, PhD,* Markus Hantschke, MD,*
Arno Rütten, MD,* Bruno E. Paredes, MD,* Leo Schärer, MD,* Carlos Serra Guillen, MD,†
and Luis Requena, MD‡

TABLE 3. Clinical and Molecular-genetic Data of 5 Cases of PDF and 7 Cases of Incipient Intradermal (Plaque-like) DFSP

Patient	Age/ Sex	Location	Size (cm)	Initial Clinical Diagnosis	Histologic Diagnosis	Archival Tissue, Storage Time (y)	RT- PCR	<i>COL1A1</i> <i>PDGFB</i> FISH	% of Rearranged Cells (FISH)	Treatment/ Course/ Follow-up (y)
1	9/M	Neck	3.5	Congenital nevus	PDF	—	Negative	Negative	None	B/tumor in situ/-
2	52/M	Forearm	2.5	Nevus	PDF	5.5	NF	Negative	None	E/FOD/5.5
3	69/F	Thigh	1.5	Lichen Planus Like Keratosis	PDF	3.5	Negative	Negative	None	E/FOD/4
4	64/F	Foot	1.5	Dysplastic Nevus	PDF	—	Negative	Negative	None	E/FOD/1
5	65/F	Thigh	2.0	Dermatofibroma	PDF	—	Negative	Negative	None	E/FOD/0.5
6	53/M	Thigh	2.0	Dermatofibroma	DFSP	8.5	NF	+	26.9	WE/FOD/8.9
7	43/F	Axilla	1.0	Morphea, Collagenous Nevus	DFSP	12	NF	+	75	WE/FOD/12
8	66/F	Sternum	1.5	Basal Cell Carcinoma	DFSP	4.5	NF	+	52.1	WE/FOD/4.5
9	17/F	Forearm	1.5	Mastocytoma, Neurofibroma, Leiomyoma	DFSP	7	NF	+	46.7	WE/FOD/7
10	33/F	Thigh	0.5	Atypical Nevus	DFSP	3.5	Negative	+	70.6	WE/FOD/4
11	68/F	Lumbar	2.5	Pseudolymphoma	DFSP	—	Negative	+	76.2	WE/FOD/0.5
12	64/F	Abdomen	3.0	Granuloma annulare	DFSP	—	+	+	75	WE/FOD/1

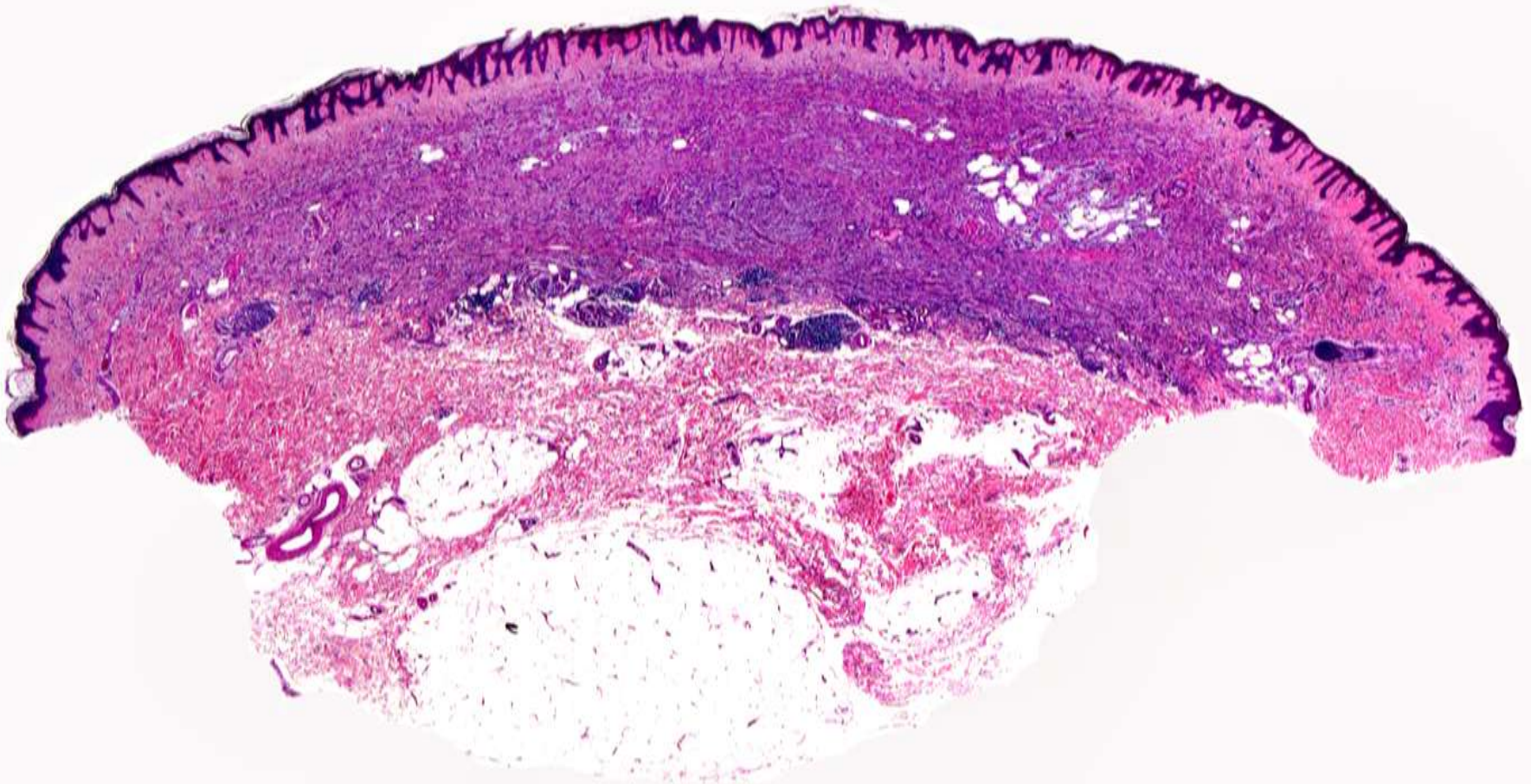
B indicates biopsy; *COL1A1*, collagen type 1 α 1; DFSP, dermatofibrosarcoma protuberans; E, excision with narrow margins; F, female; FISH, fluorescence in-situ hybridization; FOD, free of disease (no recurrences); M, male; NF, RT-PCR not feasible due to lack of amplifiable RNA (RNA degradation or insufficient RNA quantity); PDF, plaque-like dermal fibroma; *PDGFB*, platelet-derived growth factor β ; RT-PCR, reverse transcription polymerase chain reaction; WE, wide excision with margins exceeding 1 cm.

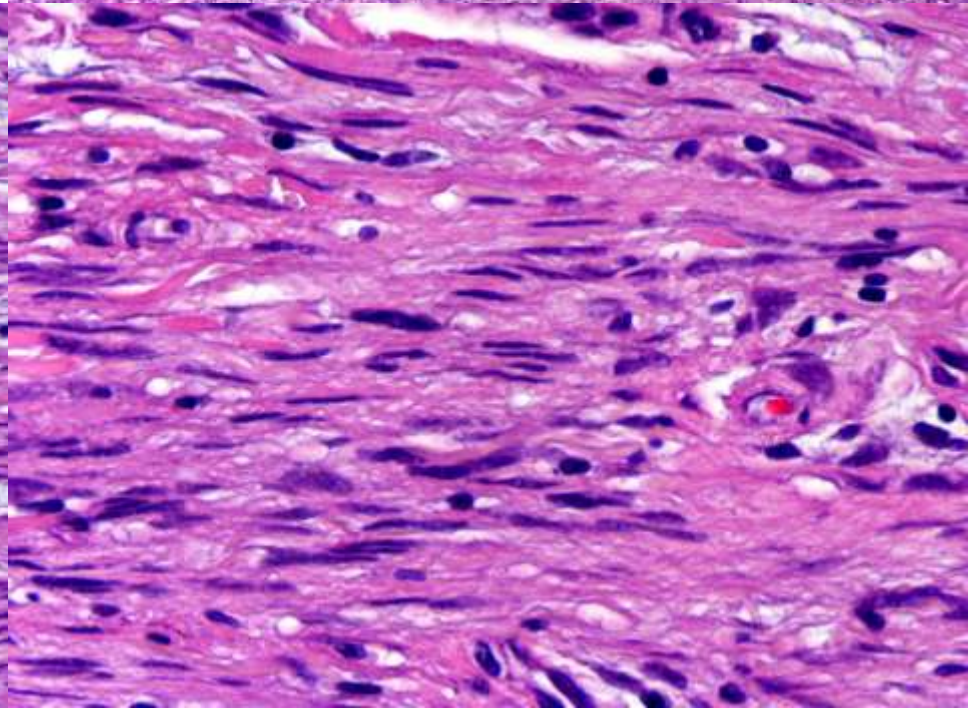
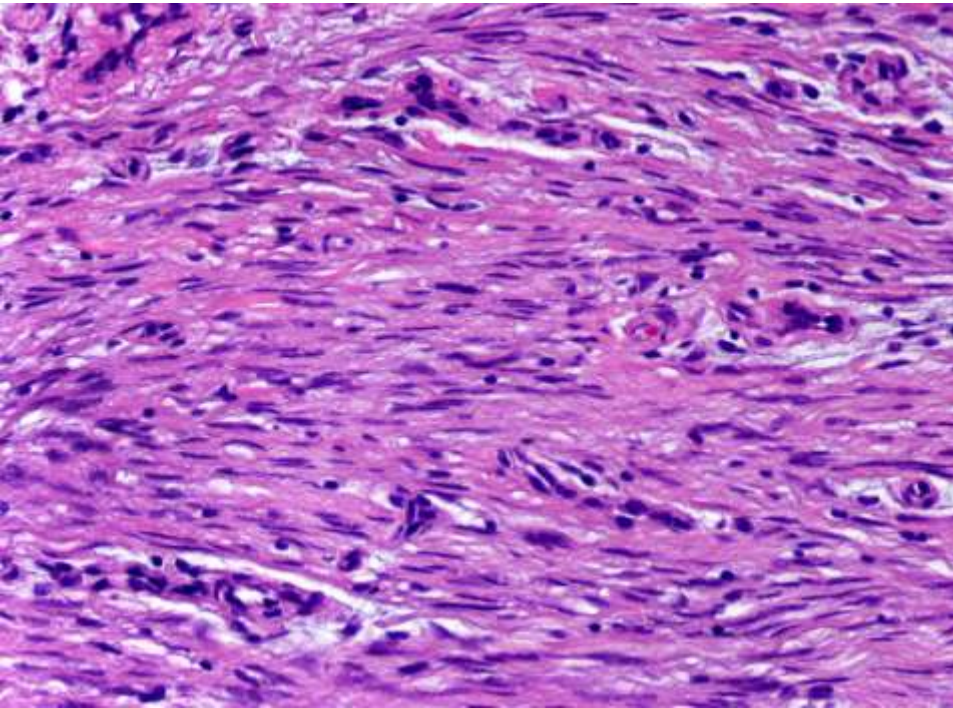
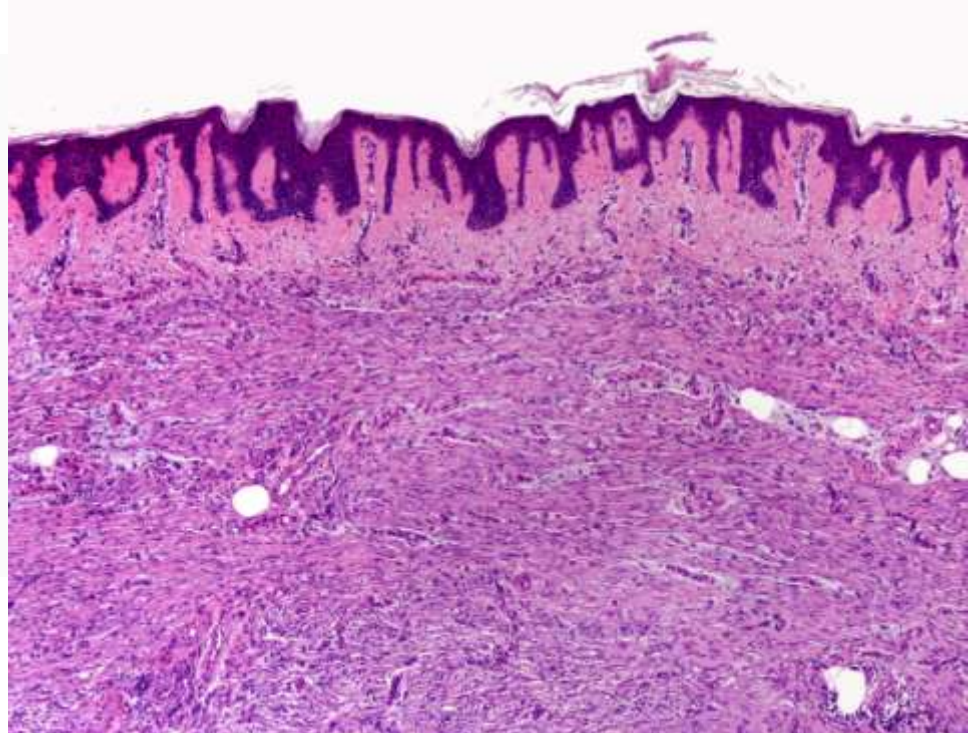
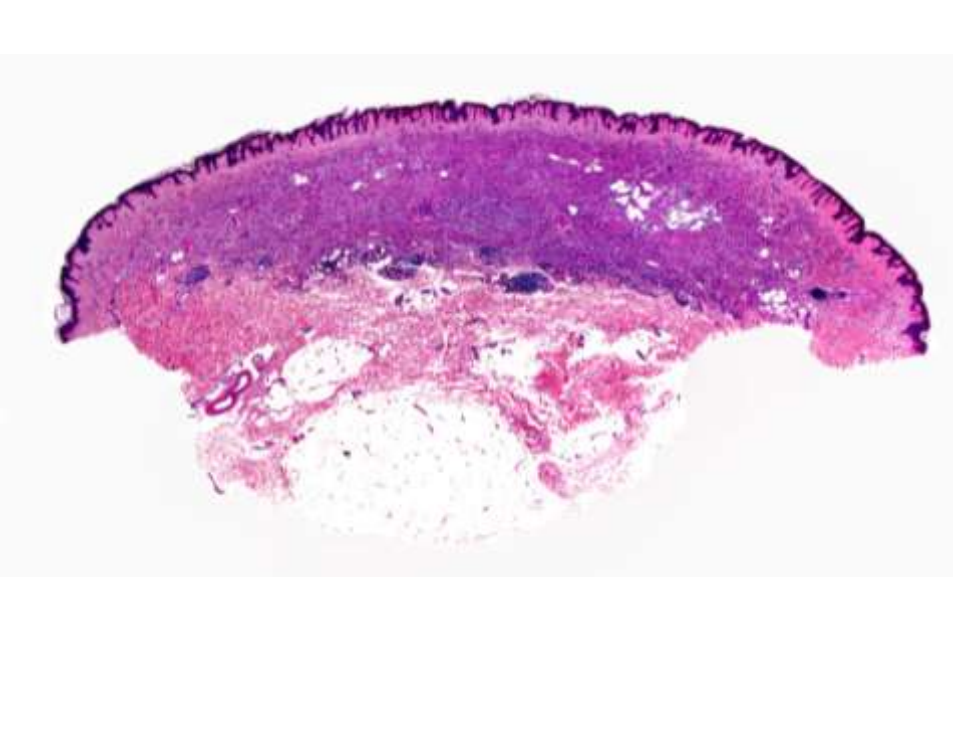
Fibroma en placa CD34+

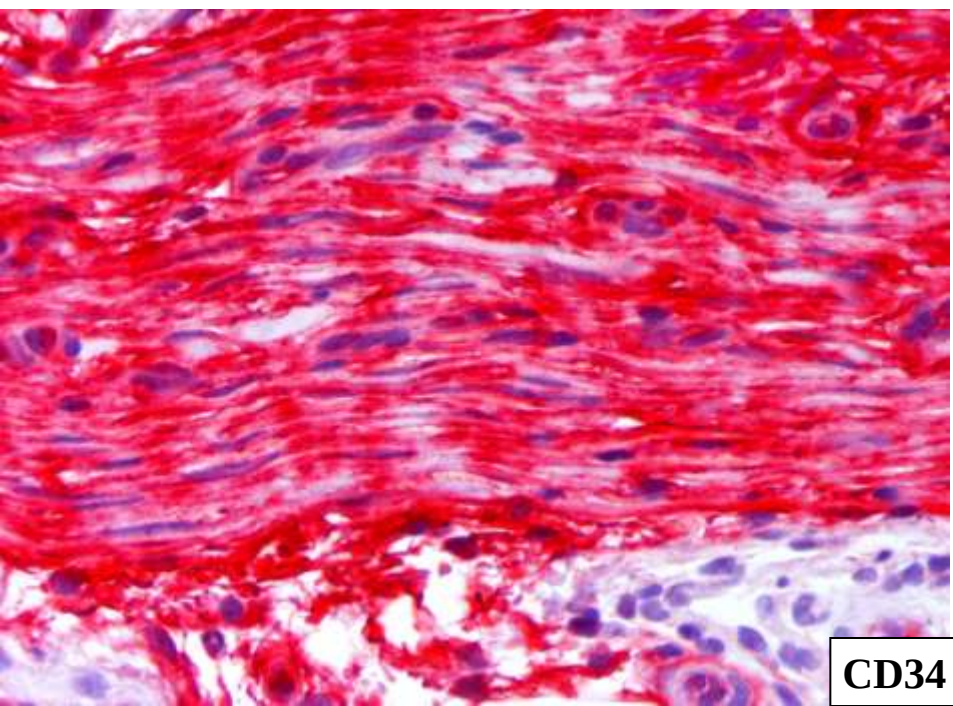
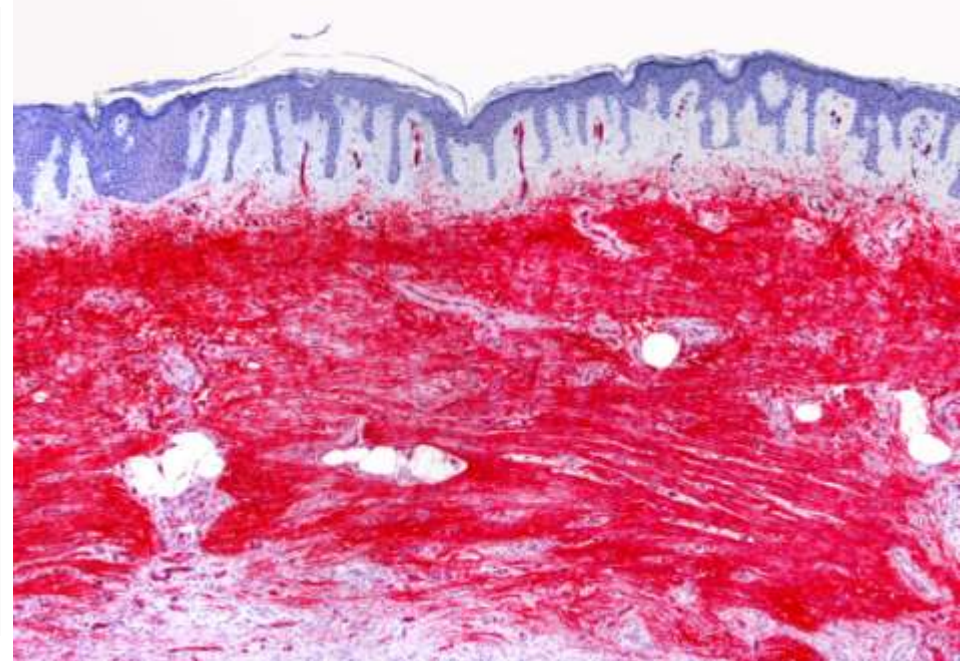
- Congénito o adquirido en la vida adulta
- Probablemente es más correcto considerar esta lesión como una neoplasia benigna que como un hamartoma. Por lo tanto, la denominación de fibroma dérmico en placa CD34+ parece más acertada que la de hamartoma dendrocítico en medallón
- Inmohistoquímicamente la lesión expresa CD34. El FXIIIa sólo ha sido positivo en 4 de los 15 casos descritos
- En caso de dificultad para el diagnóstico diferencial histopatológico con un DFSP en placa incipiente, lo mejor es el estudio del gen de fusión *COL1A1/PDGFB*, que resulta negativo en todos los casos de fibroma dérmico en placa CD34+ y positivo en el DFSP

Diagnóstico diferencial

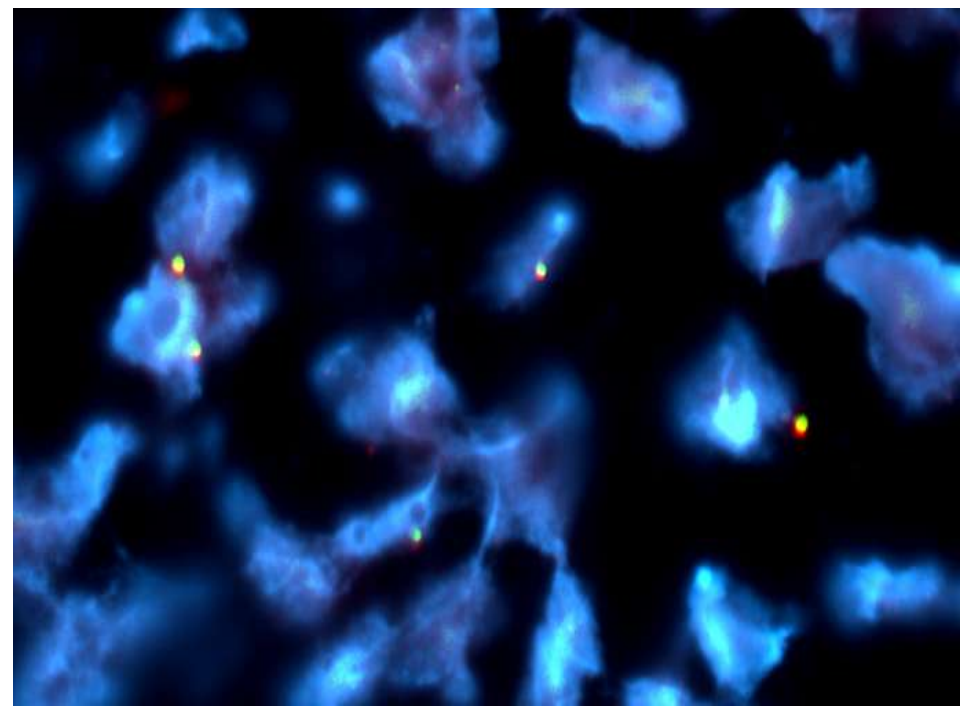
DFSP en placa

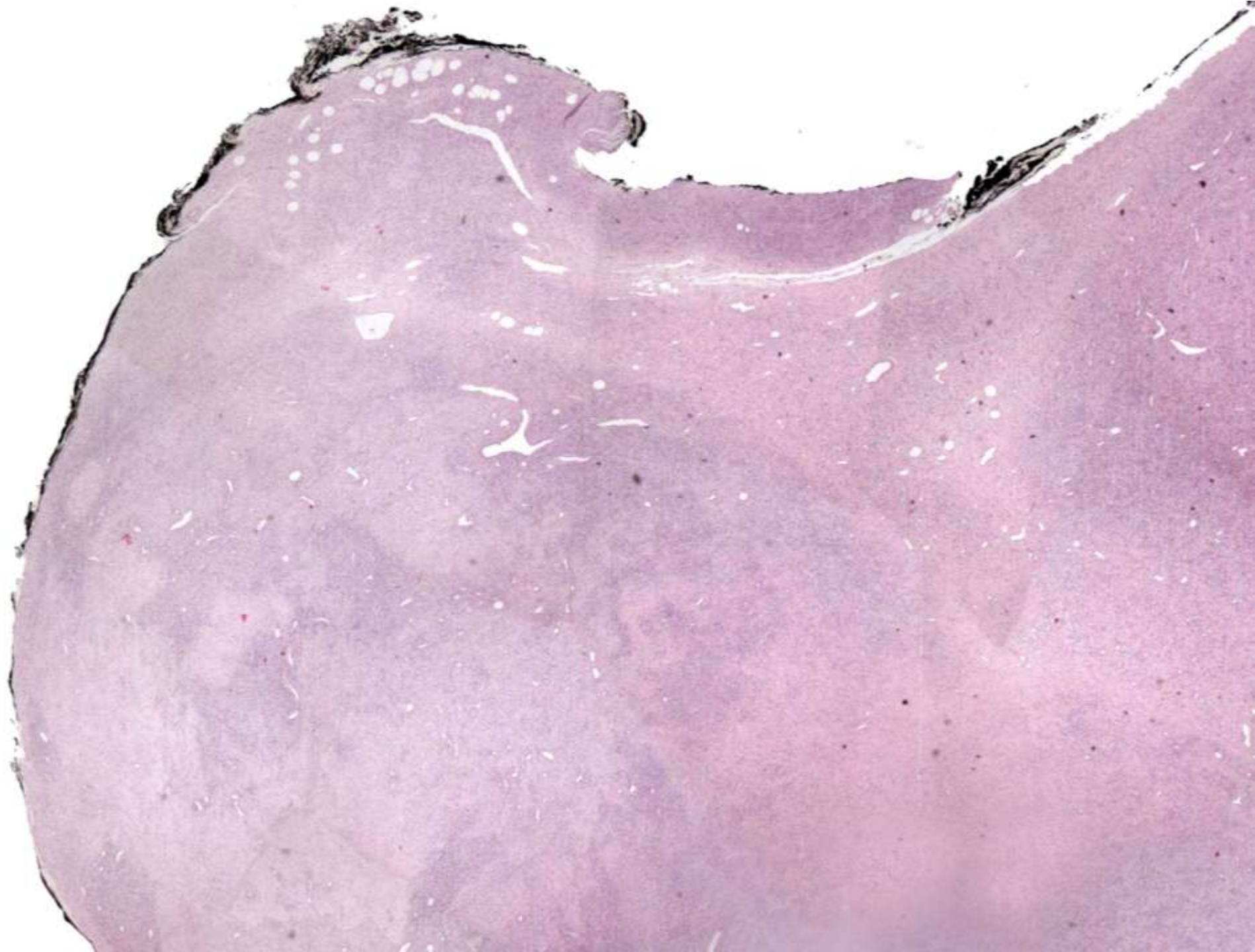


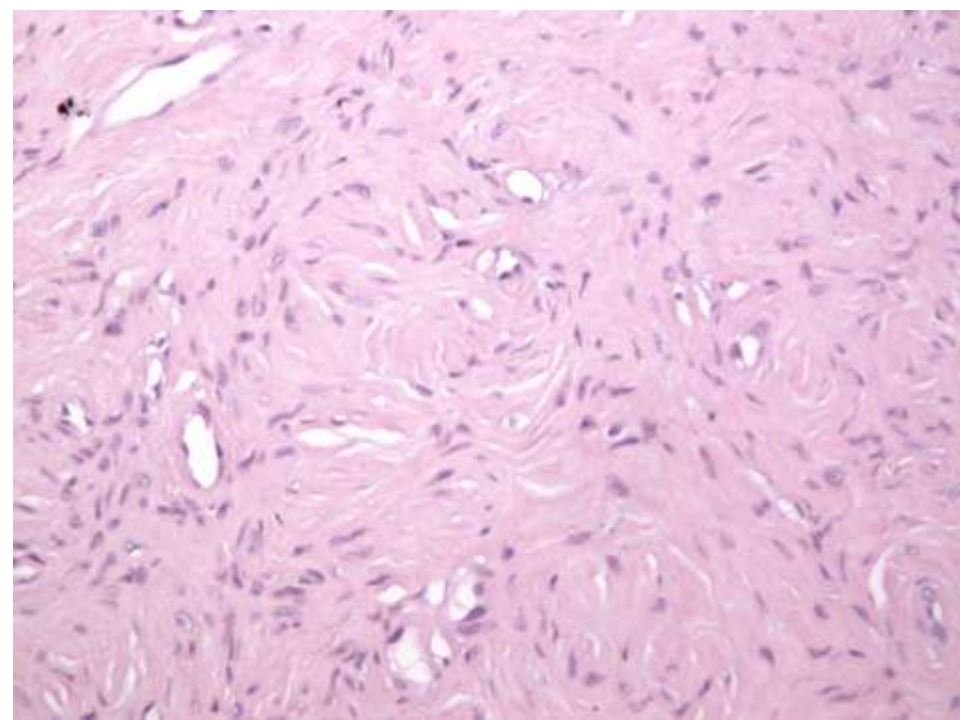
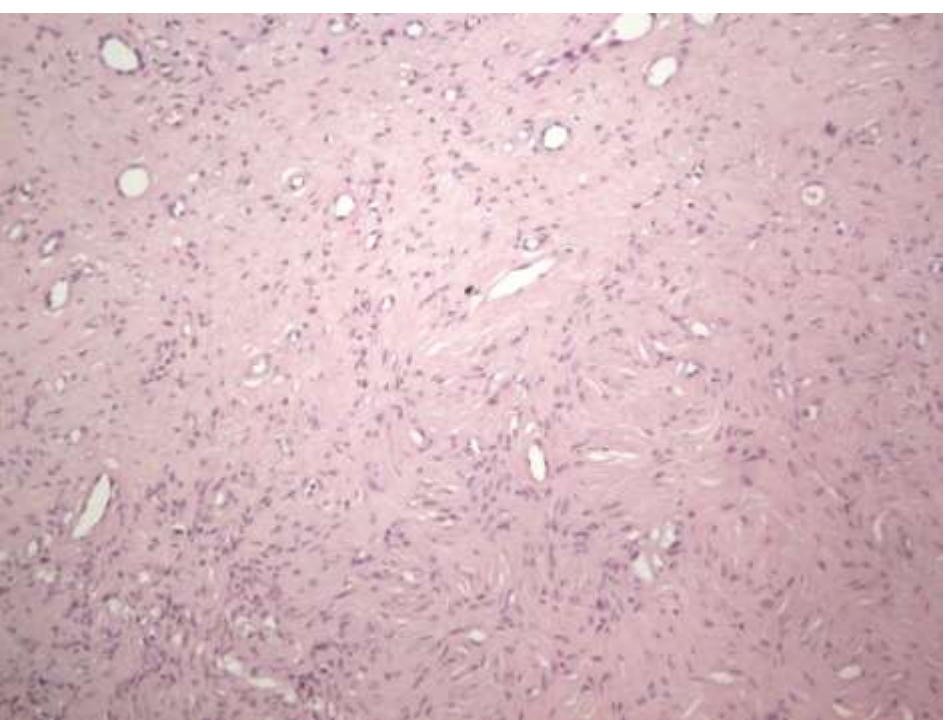
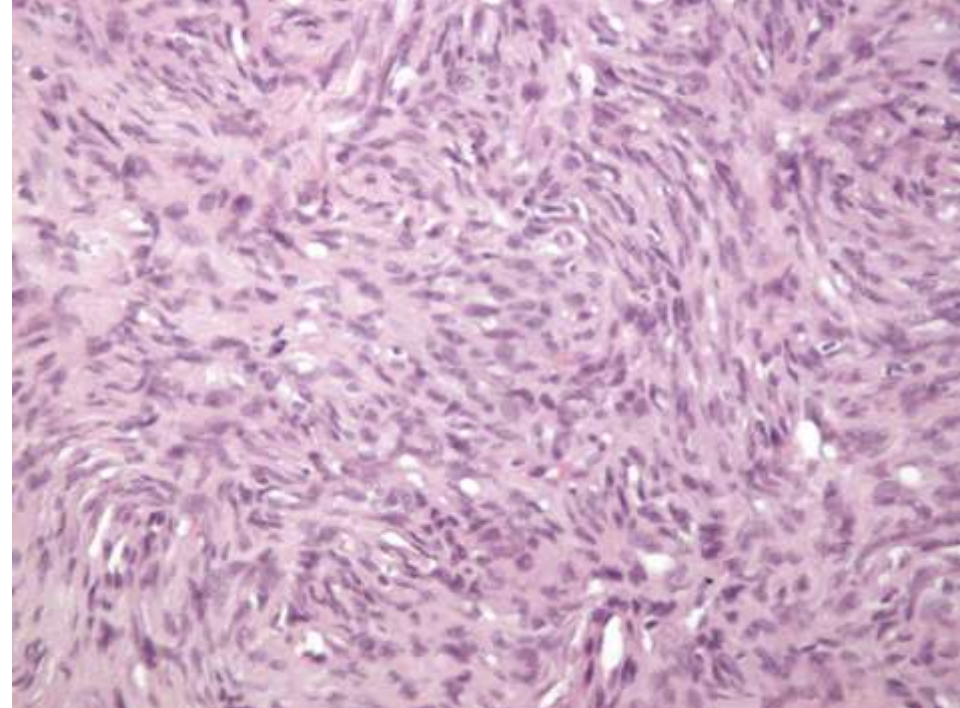


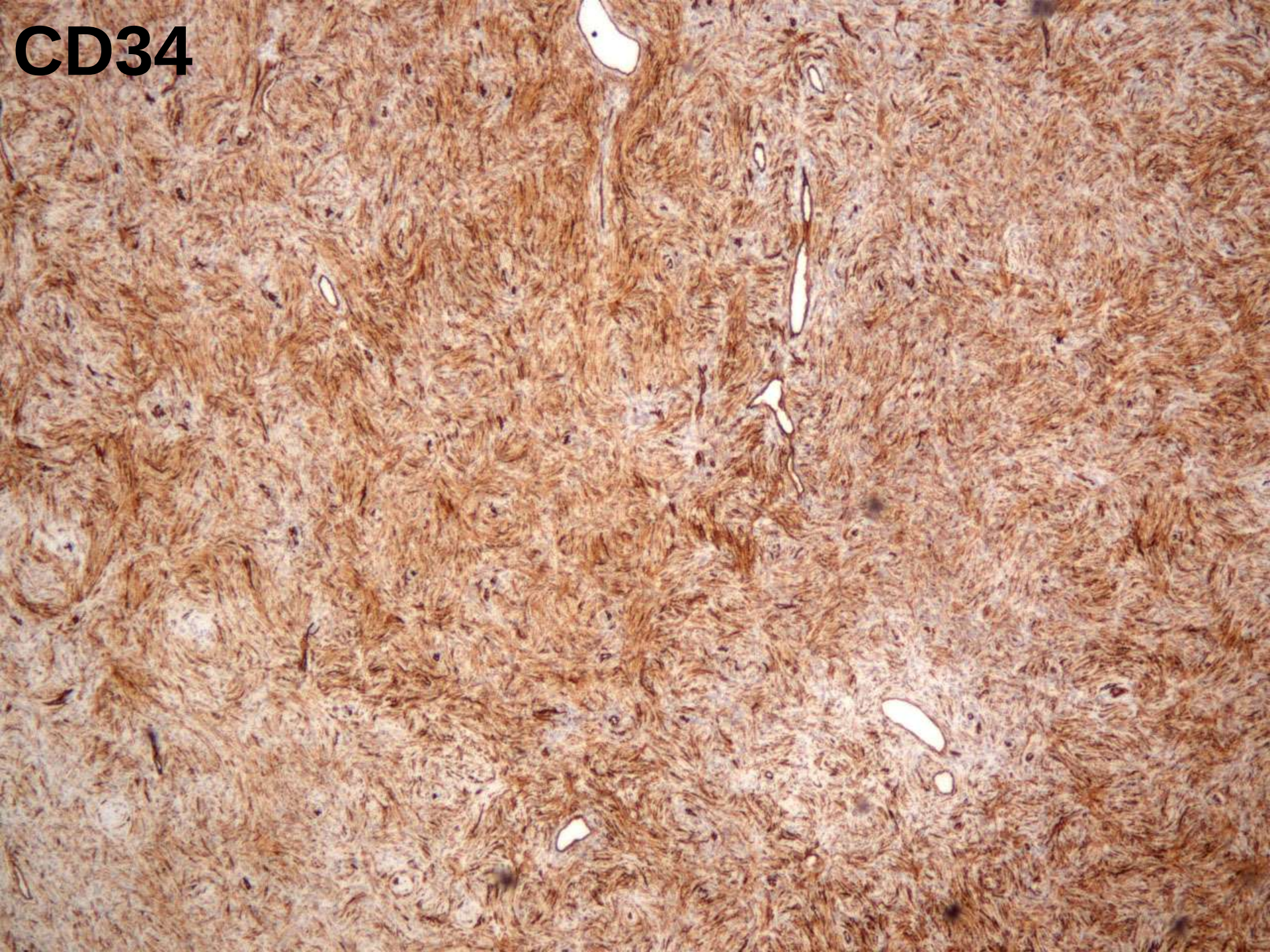


CD34









CD34

REVIEW

Solitary fibrous tumour and haemangiopericytoma: evolution of a concept

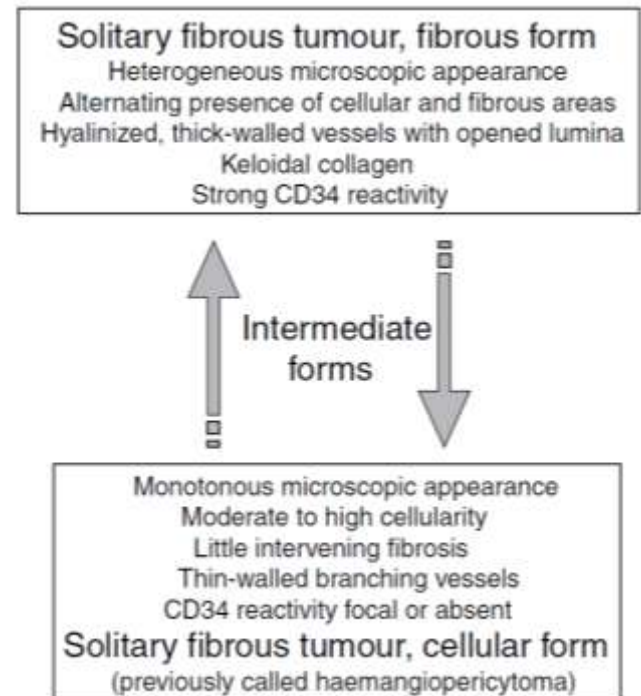
C Gengler & L Guillou

University Institute of Pathology, Lausanne, Switzerland

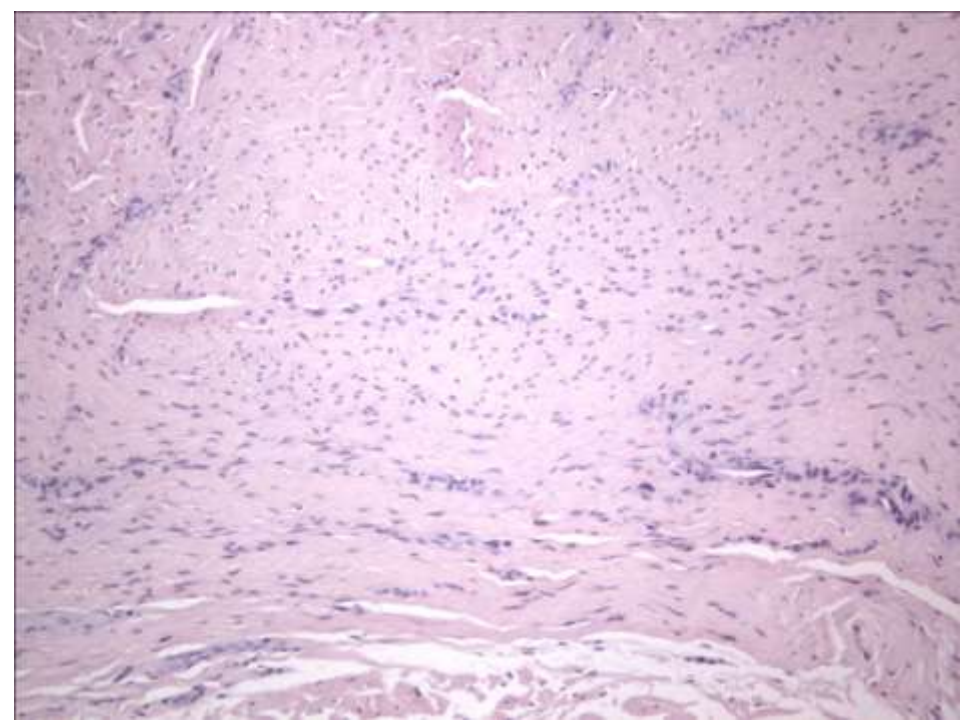
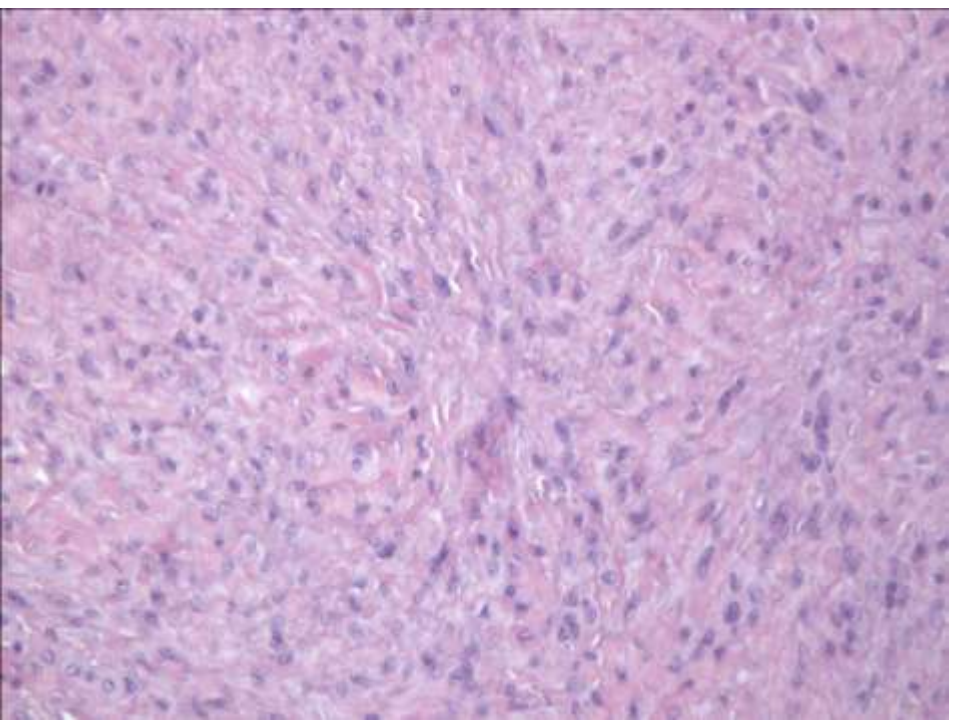
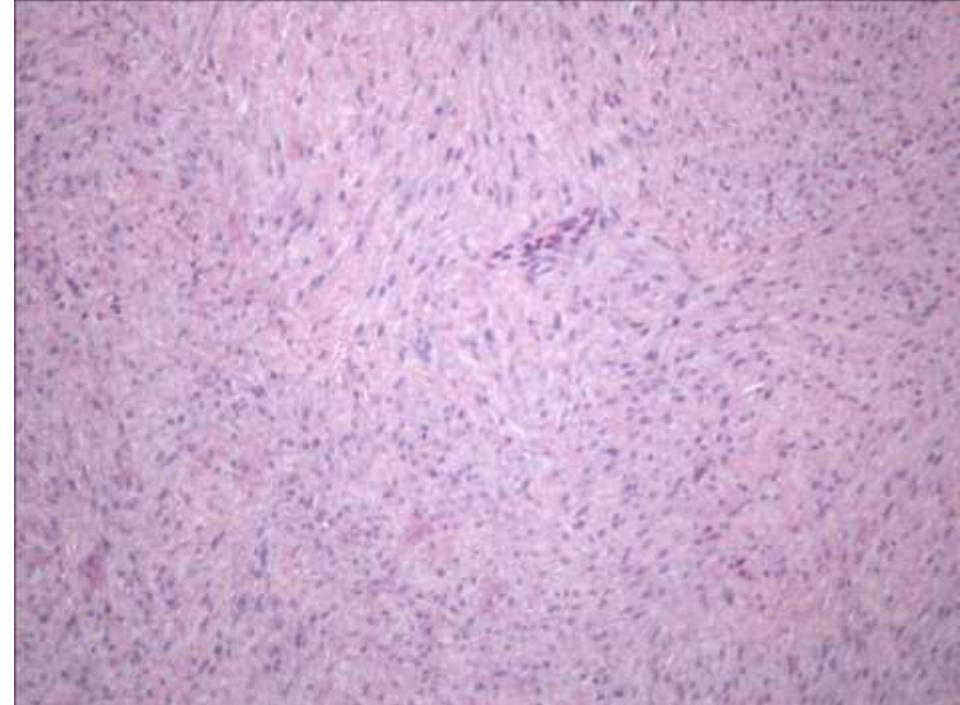
**CD34 > CD99 > bcl-2
(EMA, AML-α)**

Table 2. Solitary fibrous tumour (SFT) spectrum: a reappraisal and a proposal

Old designation	New designation
Conventional SFT	Fibrous variant of SFT
Conventional (adult-type) haemangiopericytoma	Cellular variant of SFT
Lipomatous haemangiopericytoma	Fat-forming variant of SFT
Giant cell angiofibroma	Giant cell-rich variant of SFT
Deep fibrous histiocytoma (deep FH)	FH-like variant of SFT?





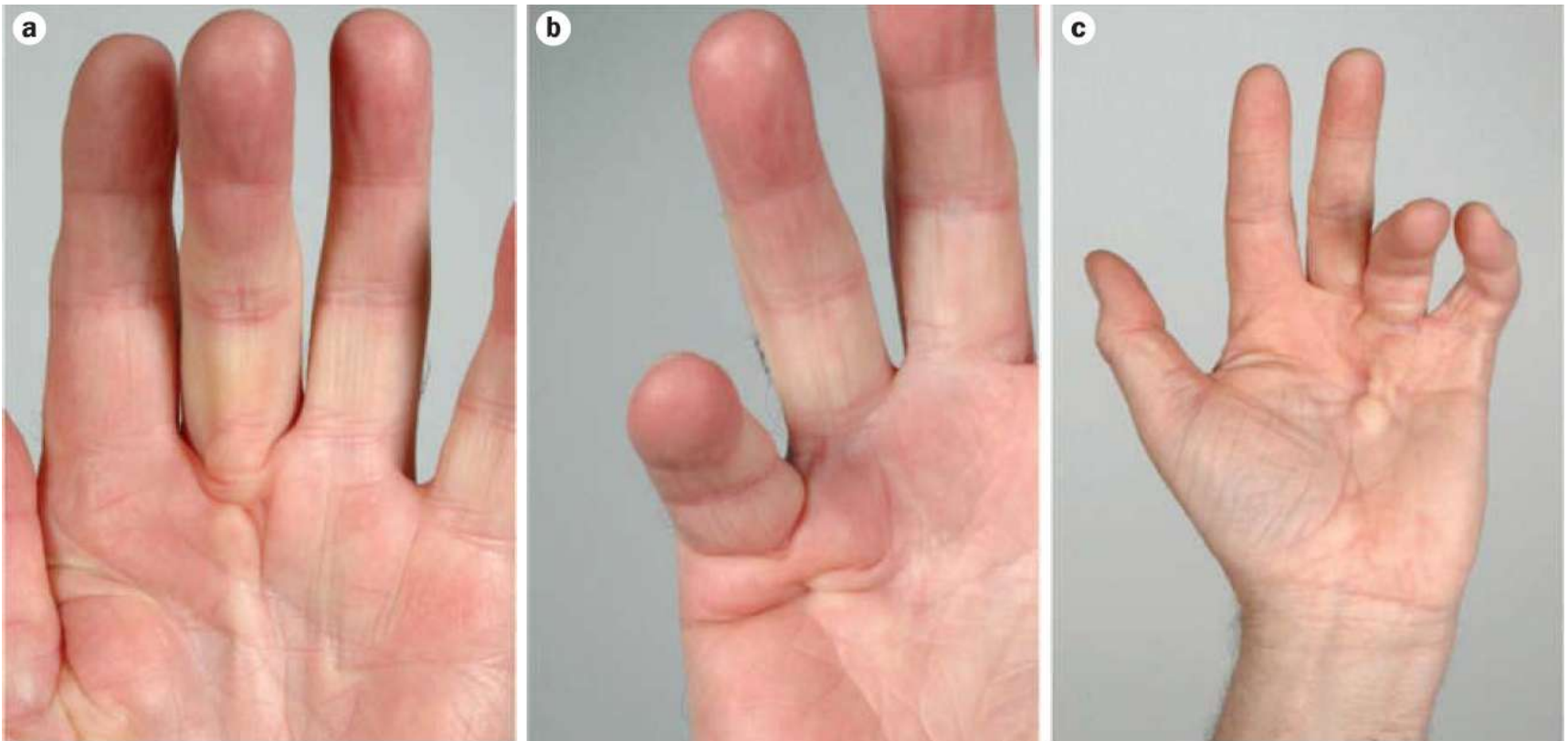


Fibromatosis superficiales

- **Palmar: Dupuytren**
- **Plantar: Ledderhose**
- **Pene: Peyronie**

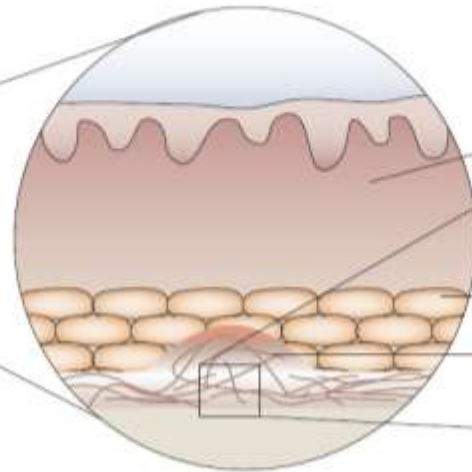
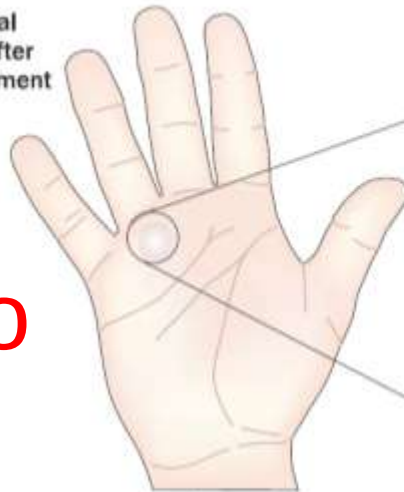
Scientific understanding and clinical management of Dupuytren disease

Barbara Shih and Ardeshir Bayat

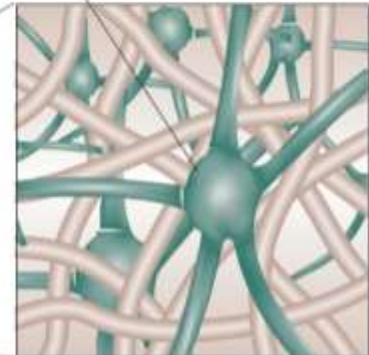


Dupuytren

Abnormal
fascia after
development
of DD



Abnormal
fibroblast/
myofibroblast



Abnormal
skin

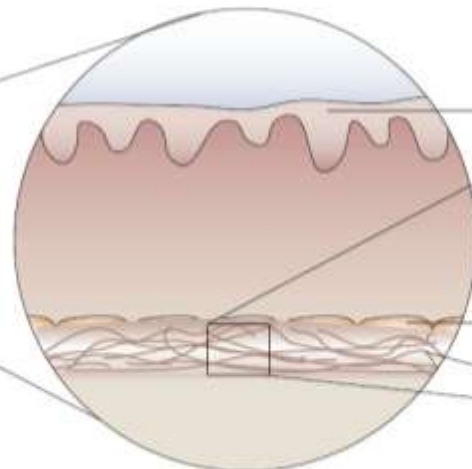
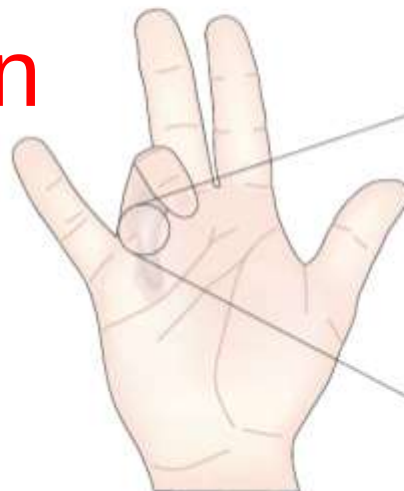
Abnormal
subcutaneous
fat
Nodule

Histological features (nodule)

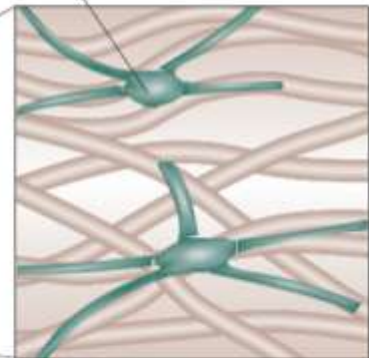
- Rich in fibroblasts
- Fibroblasts are not aligned along lines of stress

c

Cordón



Abnormal
fibroblast/
myofibroblast



Abnormal
skin

Abnormal
subcutaneous
fat
Cord

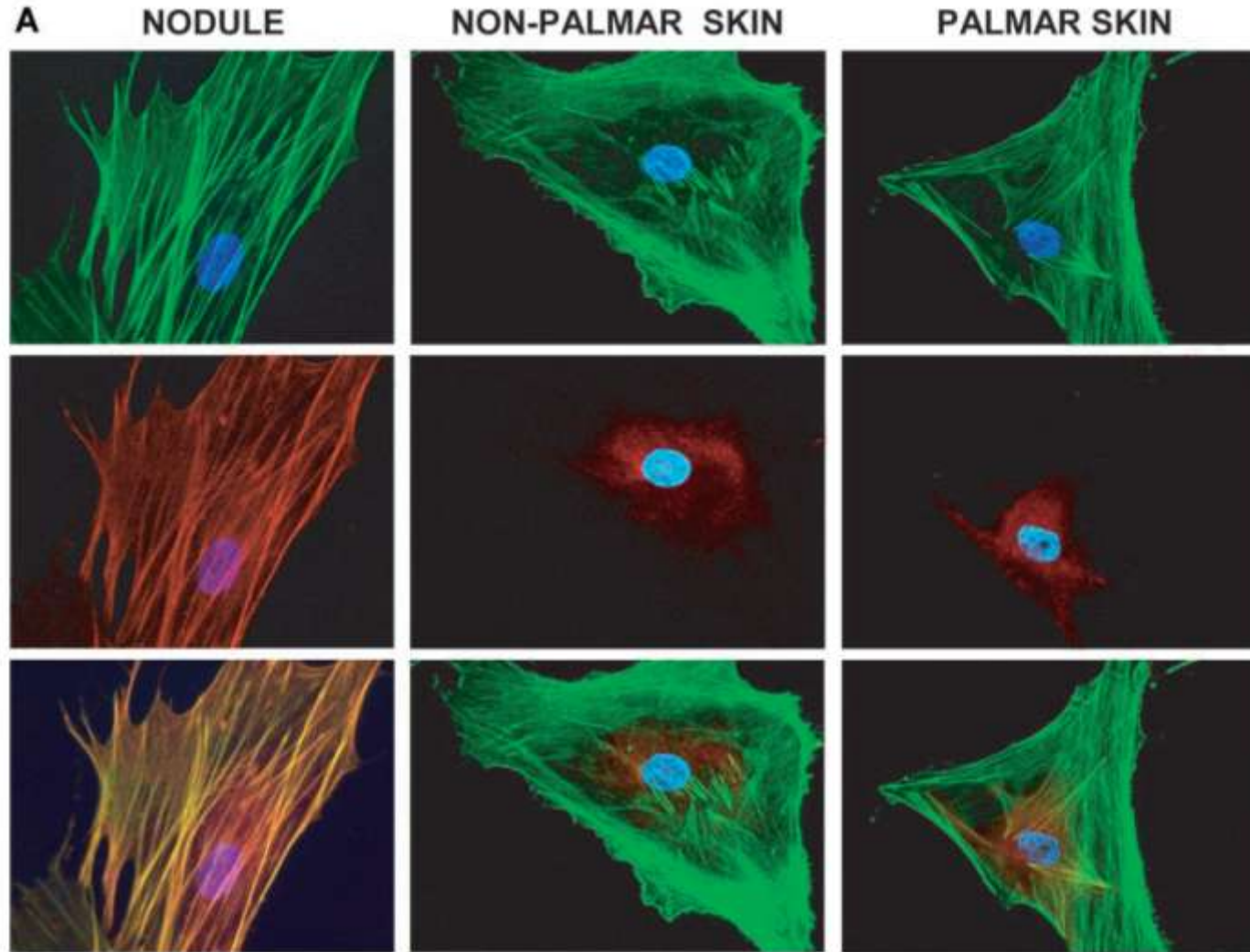
Histological features (cord)

- Alignment of fibroblasts along stress fibers
- Reduced cellularity

Dupuytren

Post-Transcriptional Regulation of α -Smooth Muscle Actin Determines the Contractile Phenotype of Dupuytren's Nodular Cells

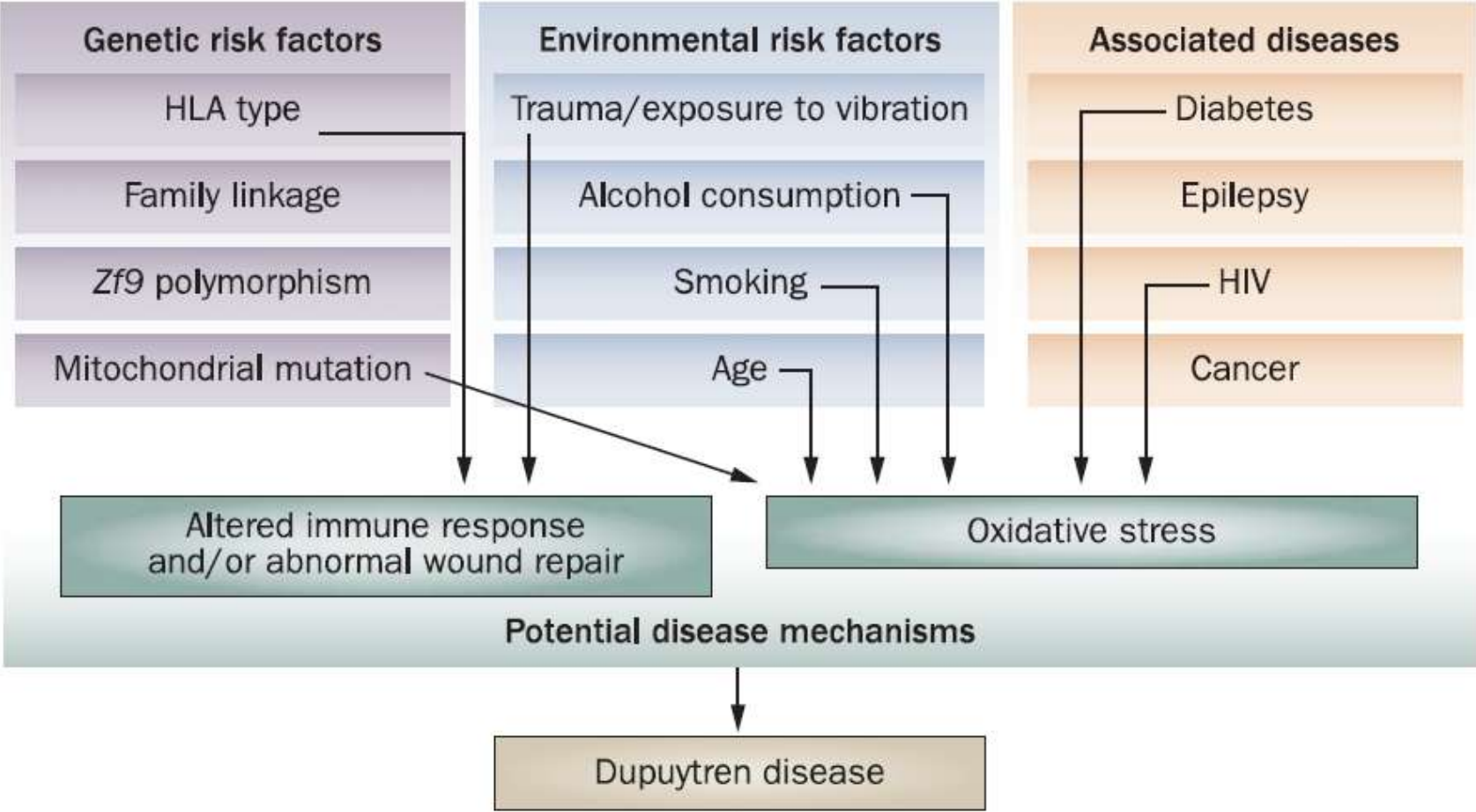
UAQUAT SULEMAN VERJEE,^{1*} KIM MIDWOOD,¹ DOMINIQUE DAVIDSON,² MARK EASTWOOD,² AND JAGDEEP NANCHAHAL¹

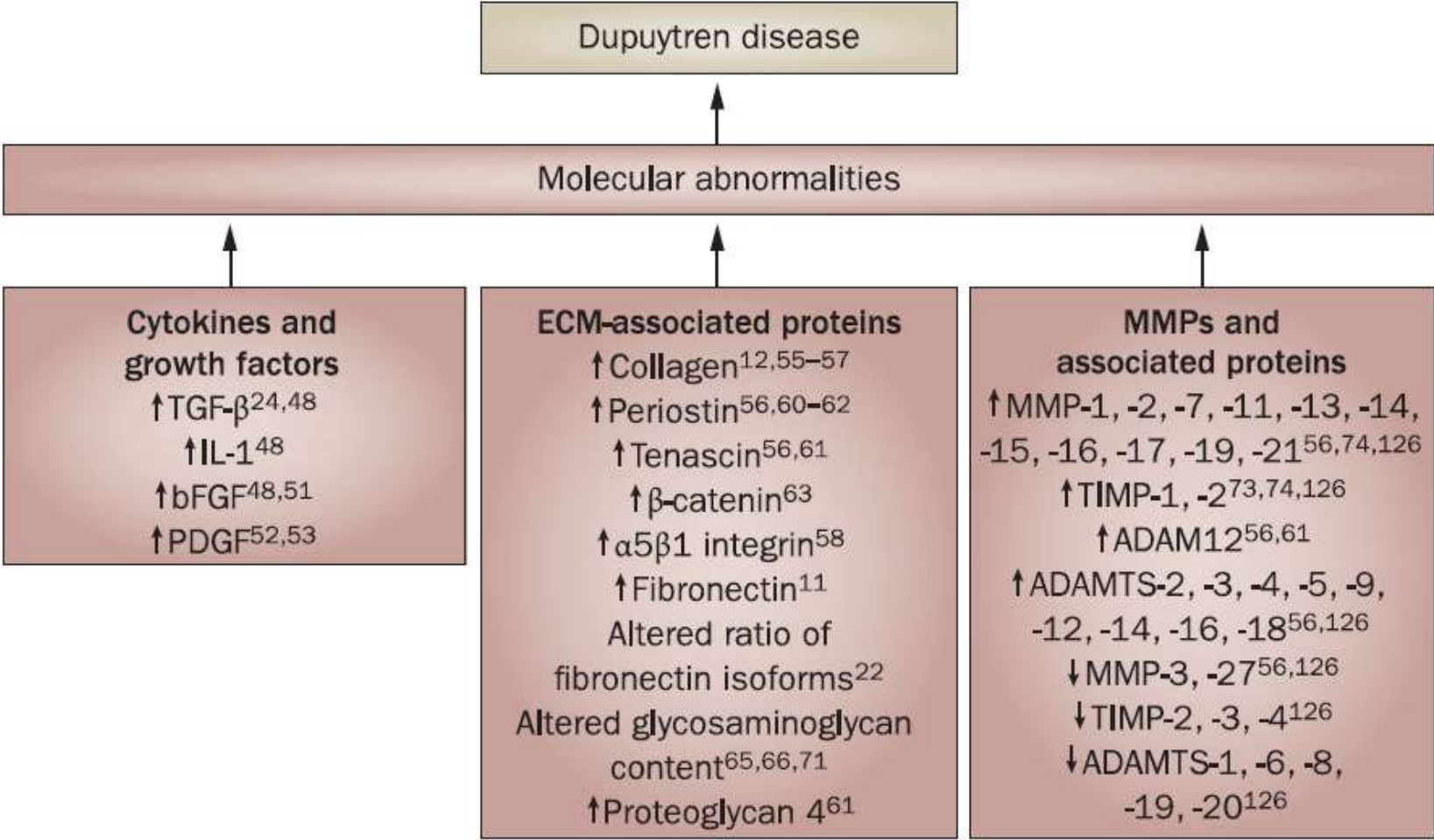


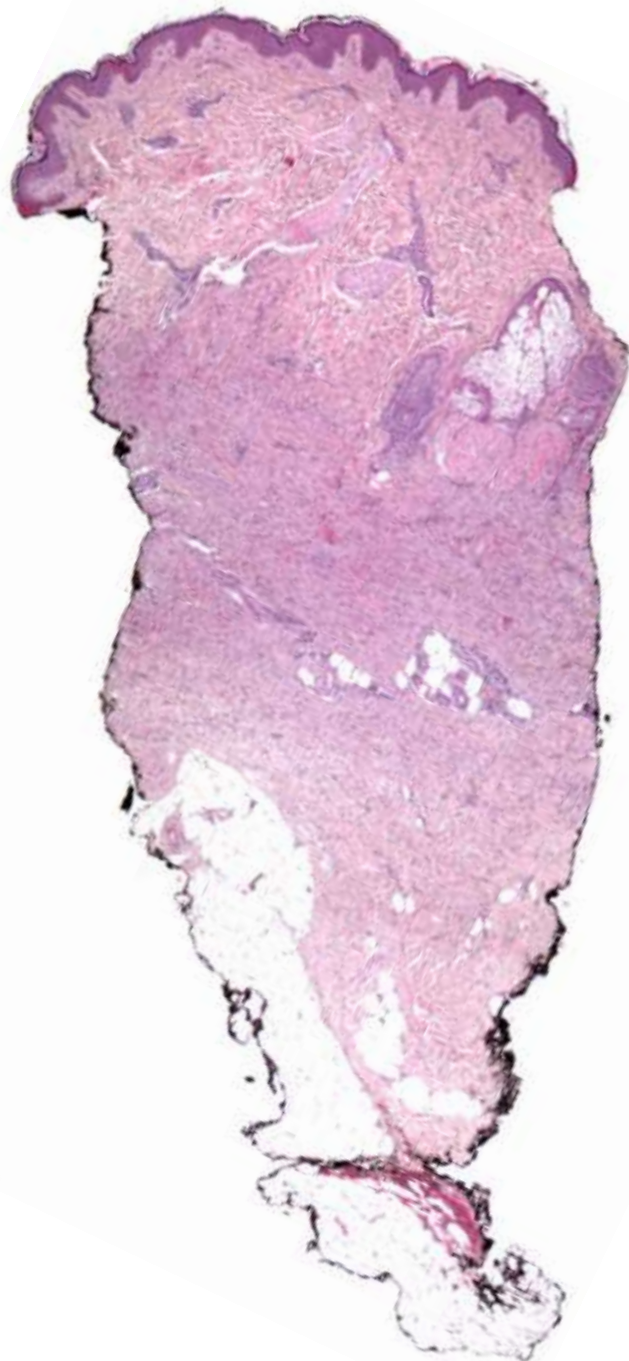
Rojo: AML- α

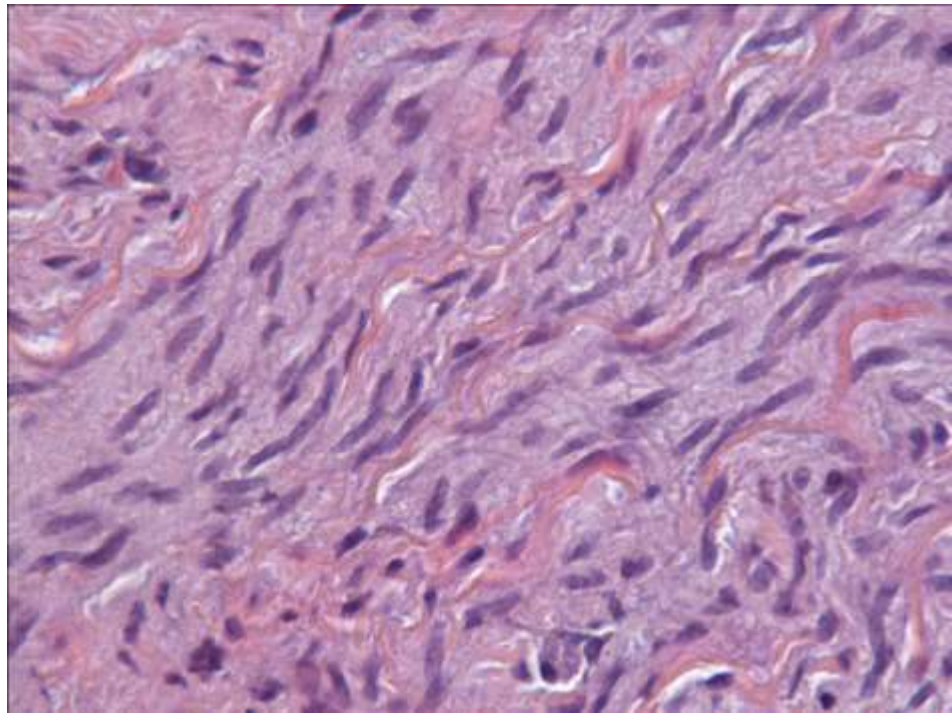
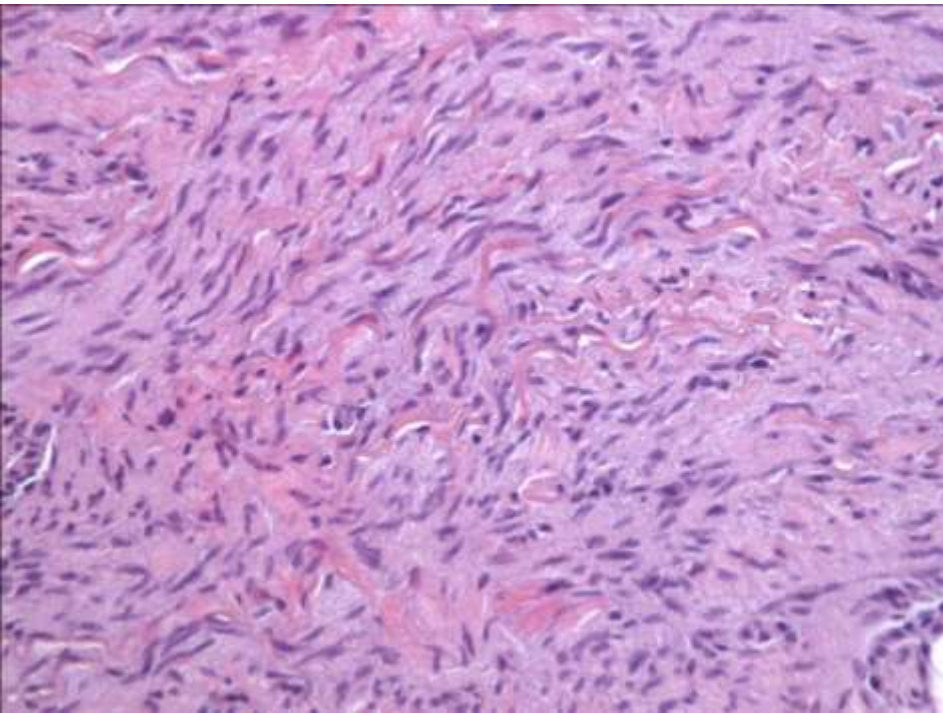
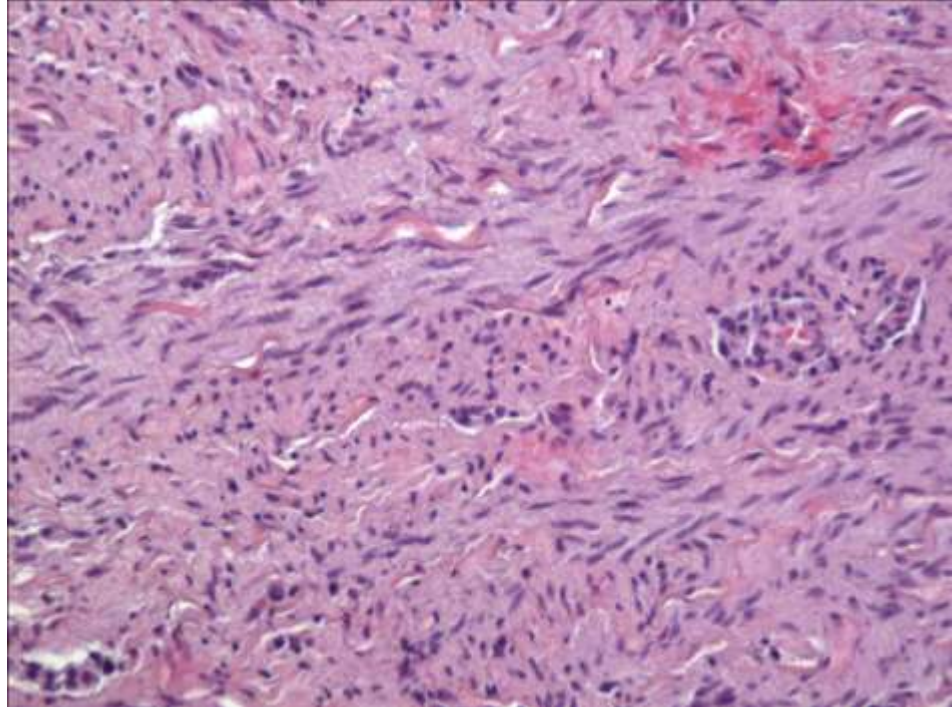
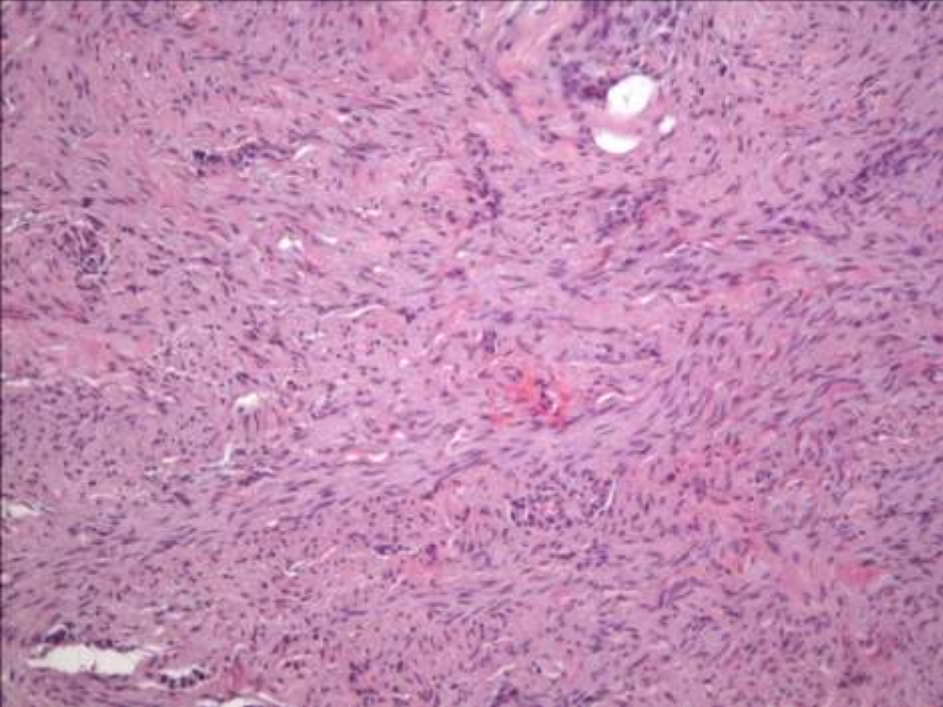
Verde: Faloidina

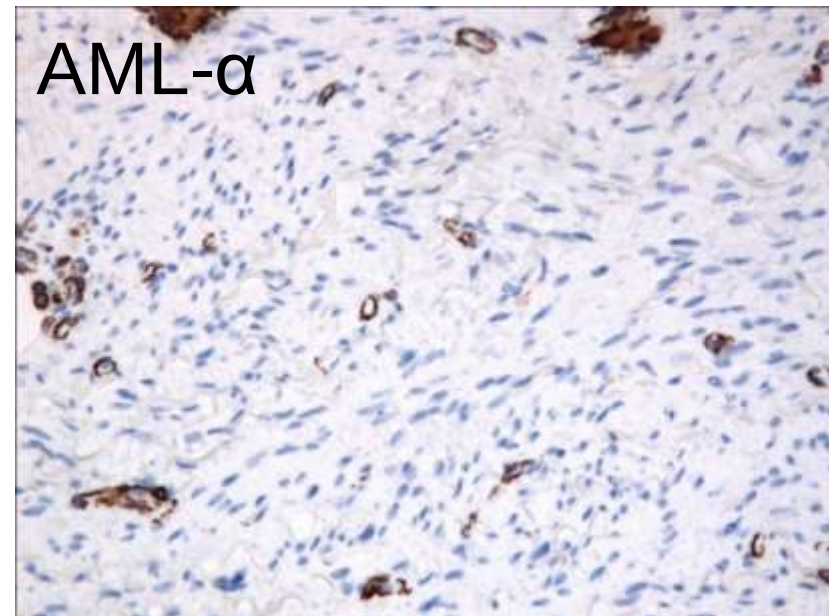
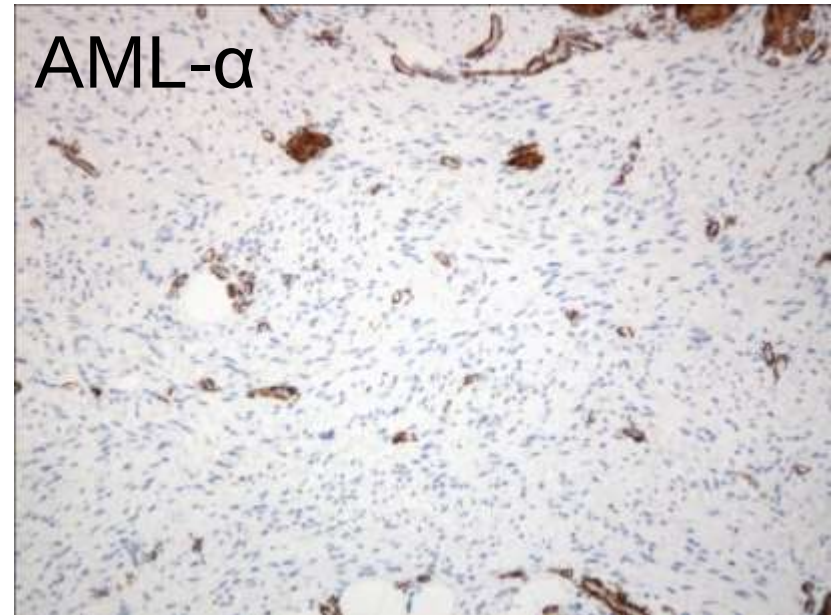
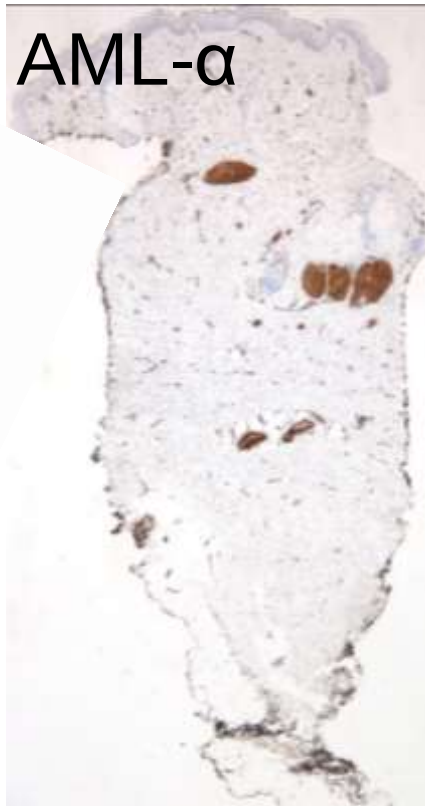
Dupuytren







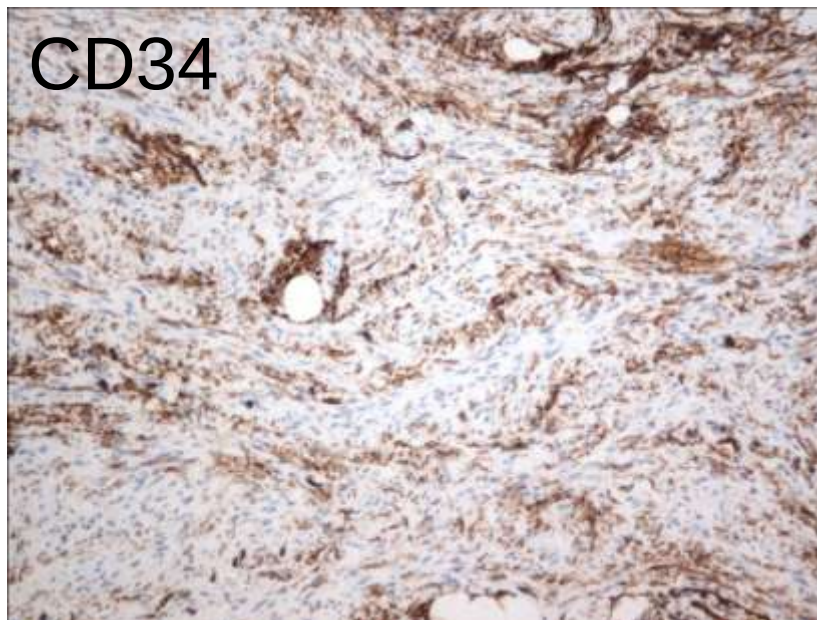




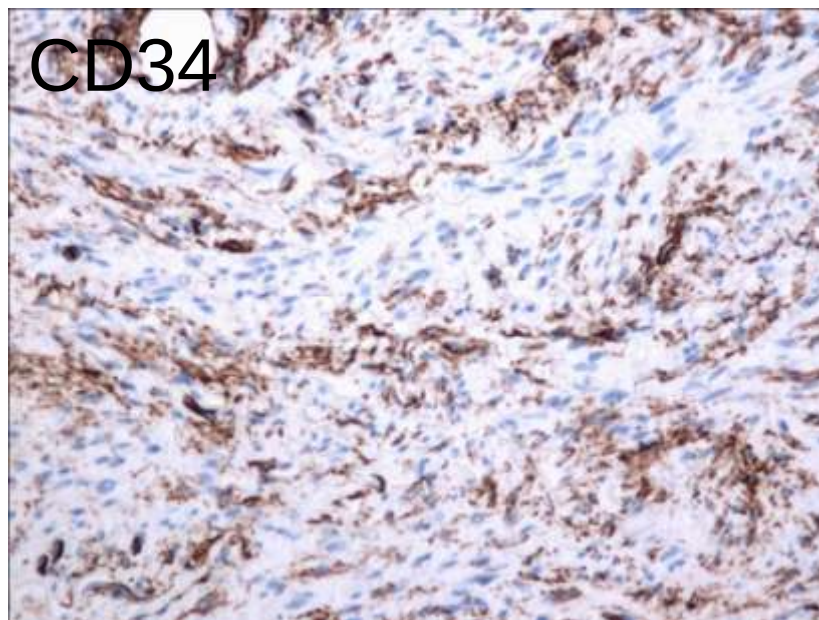
CD34



CD34



CD34

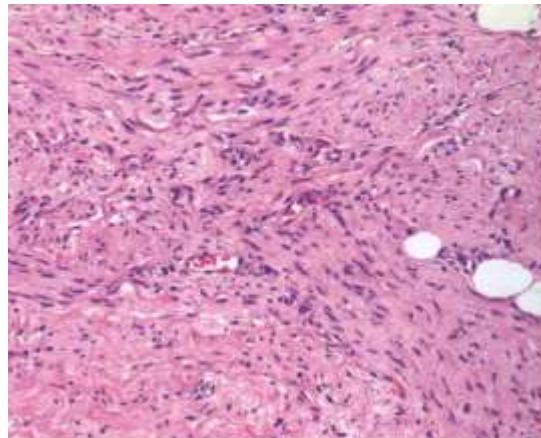
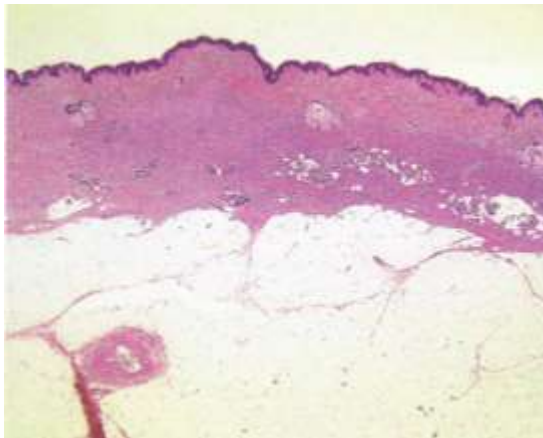


DERMATOMIOFIBROMA

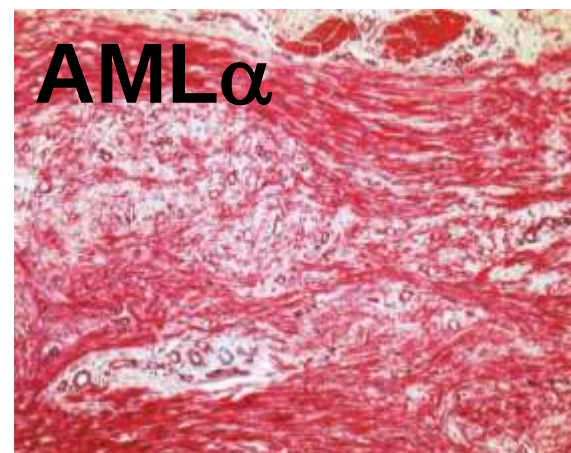
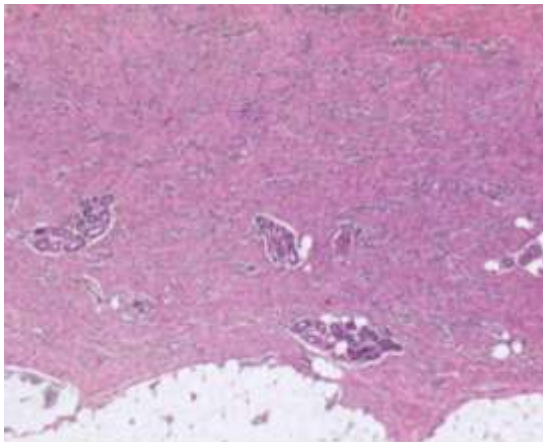
(se le llamó fibromatosis en placa)

Dermatomyofibroma: Clinicopathologic and Immunohistochemical Analysis of 56 Cases and Reappraisal of a Rare and Distinct Cutaneous Neoplasm

Thomas Mentzel, MD and Heinz Kutzner, MD



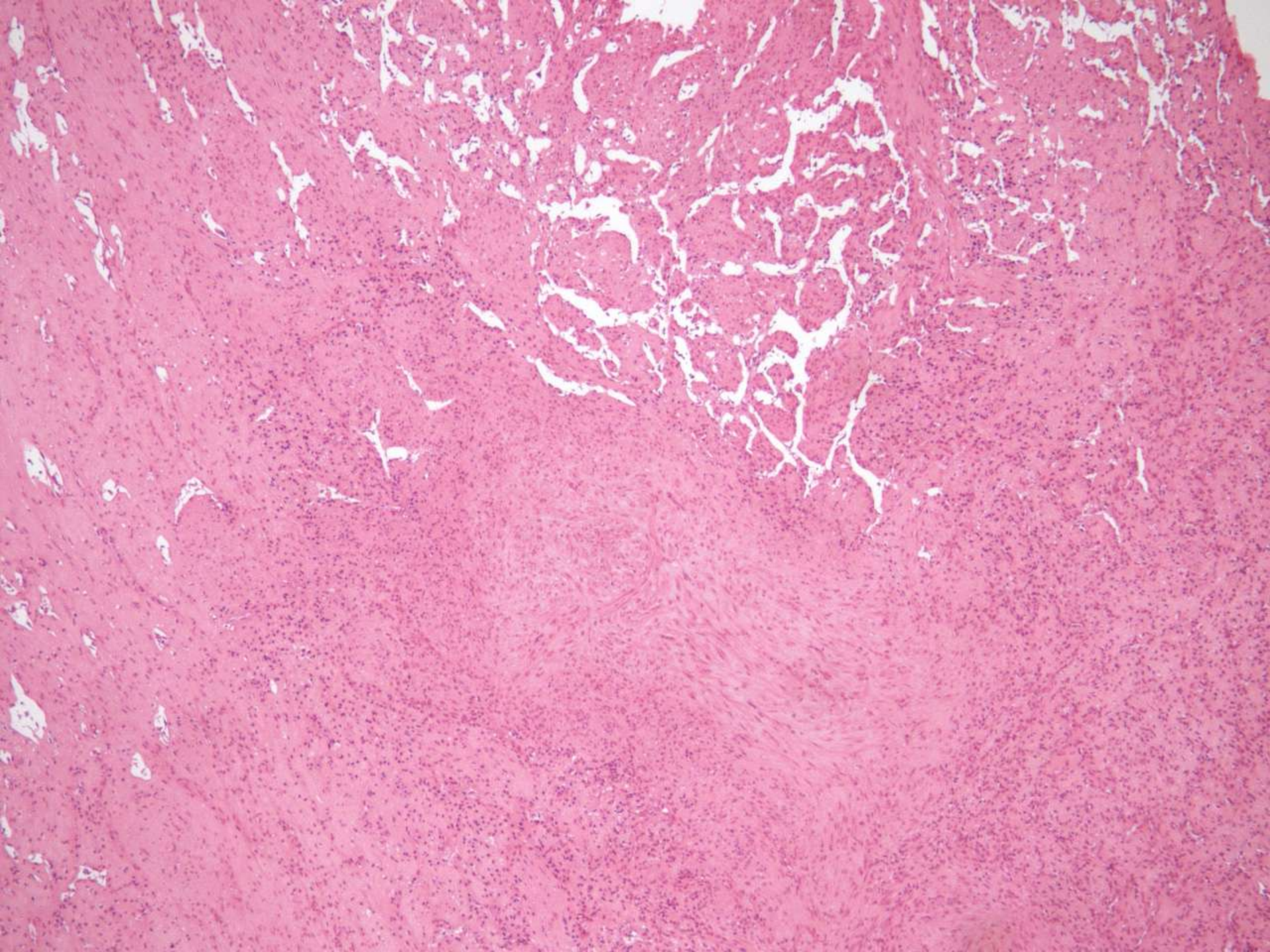
Niños y adultos
Hombros, brazo, cuello,
espalda, muslo...
No recidiva

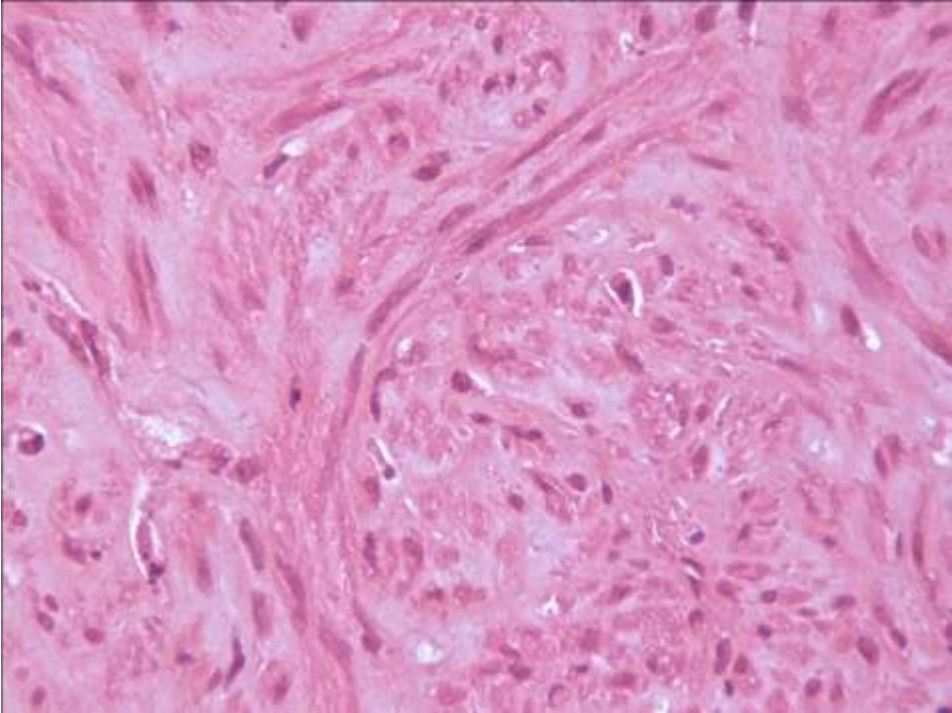
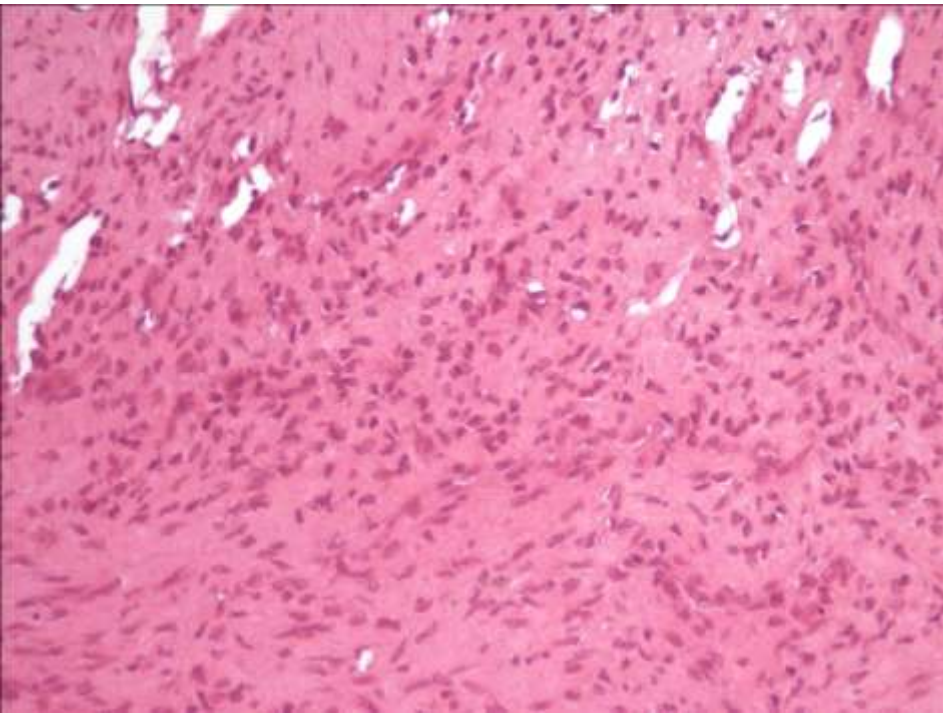
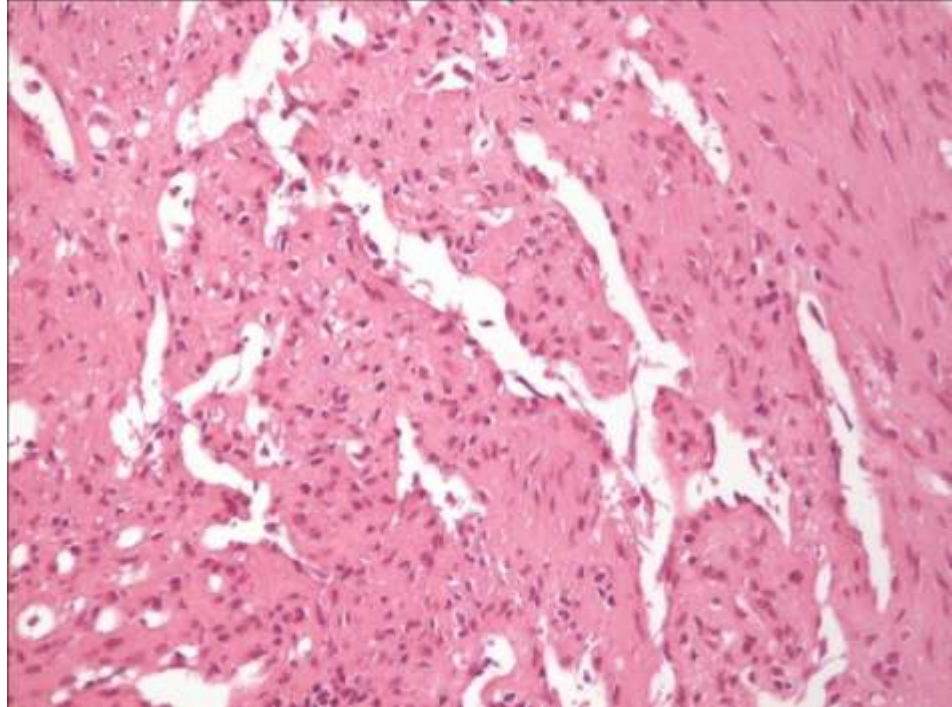
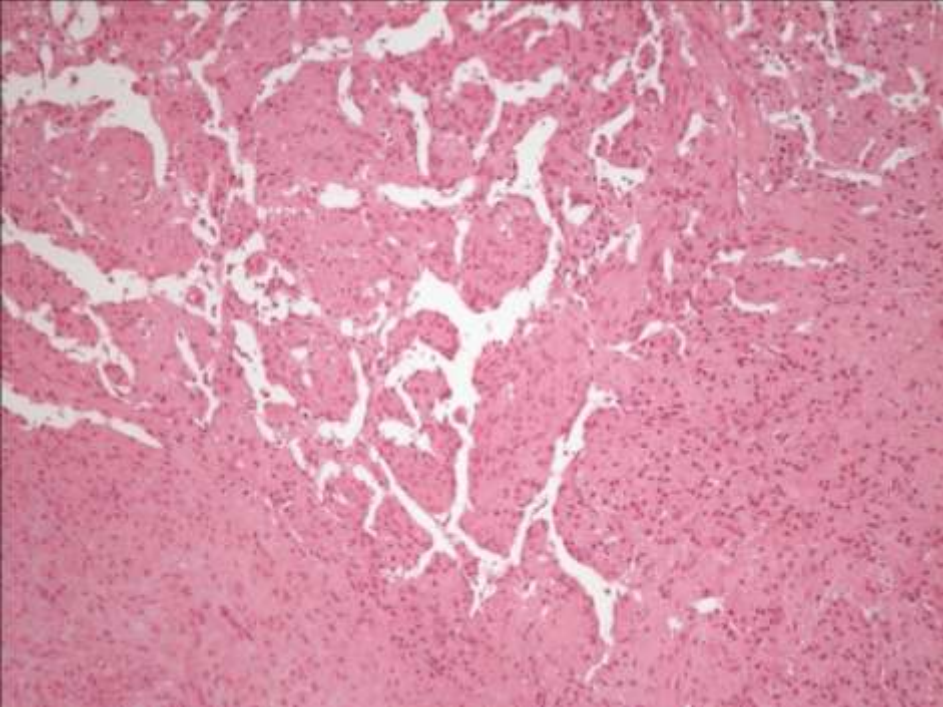


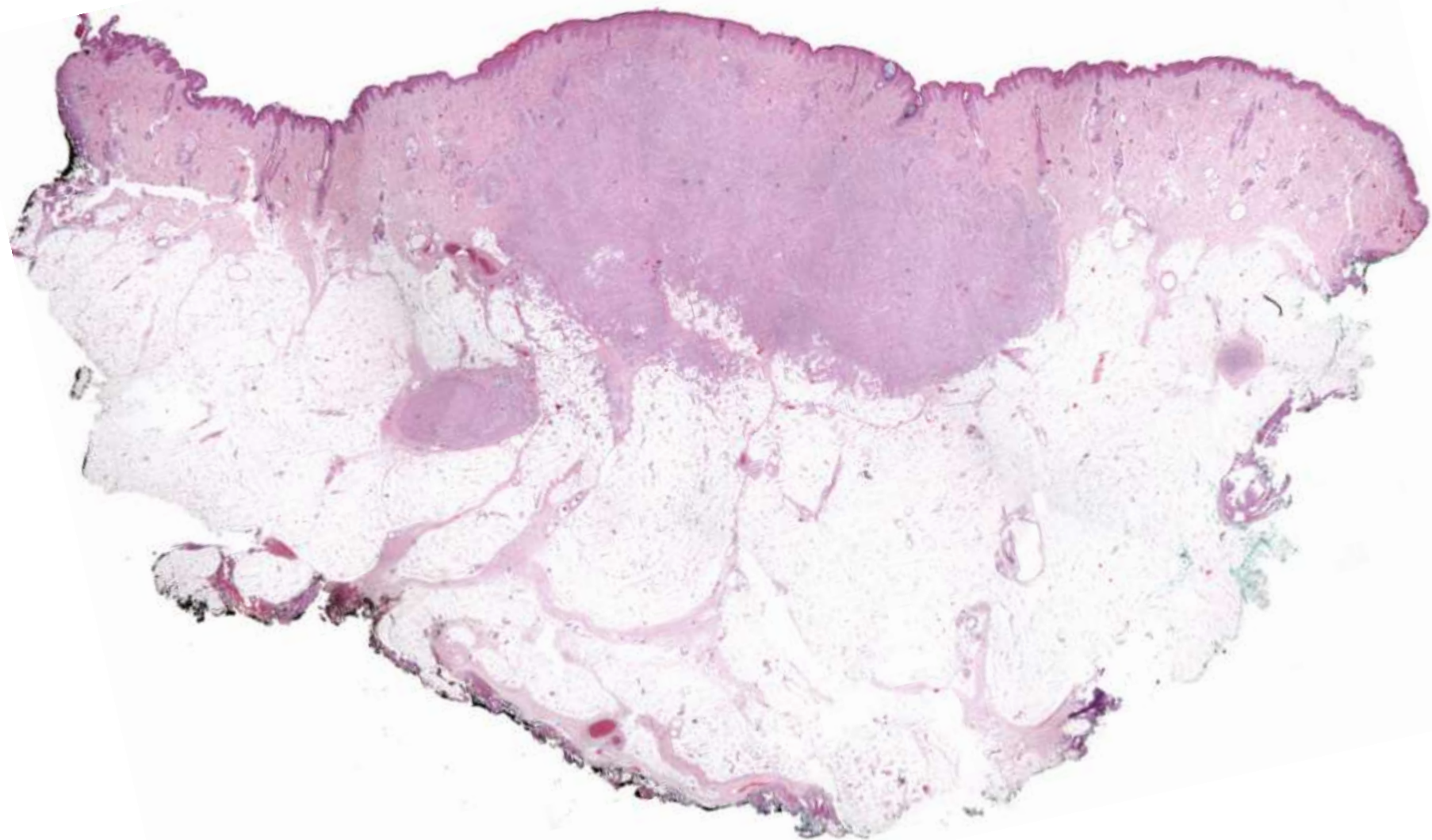
AML α

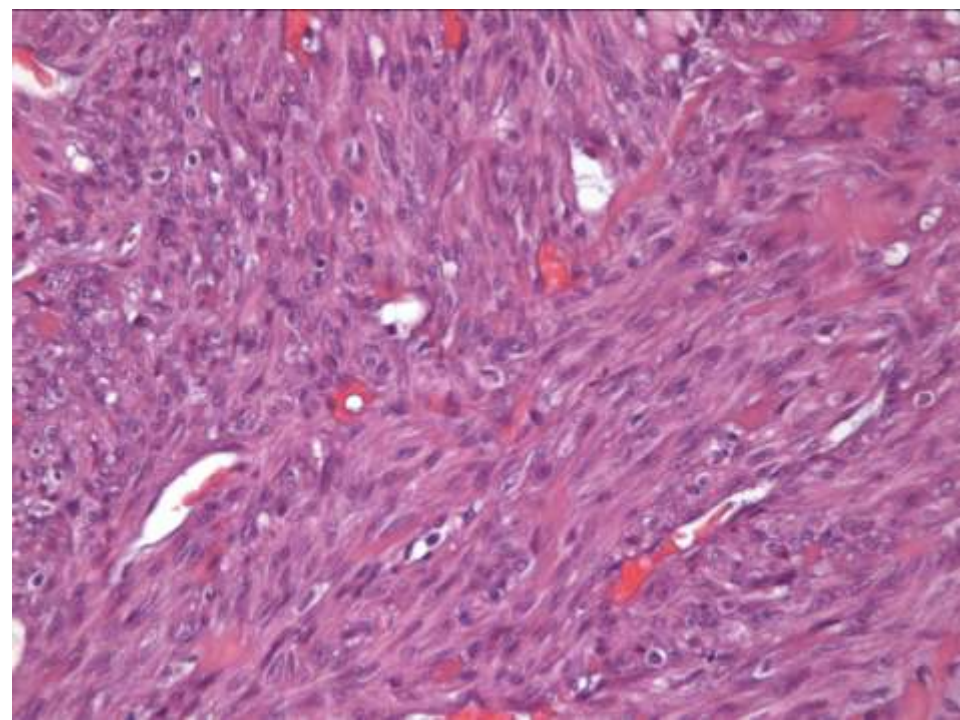
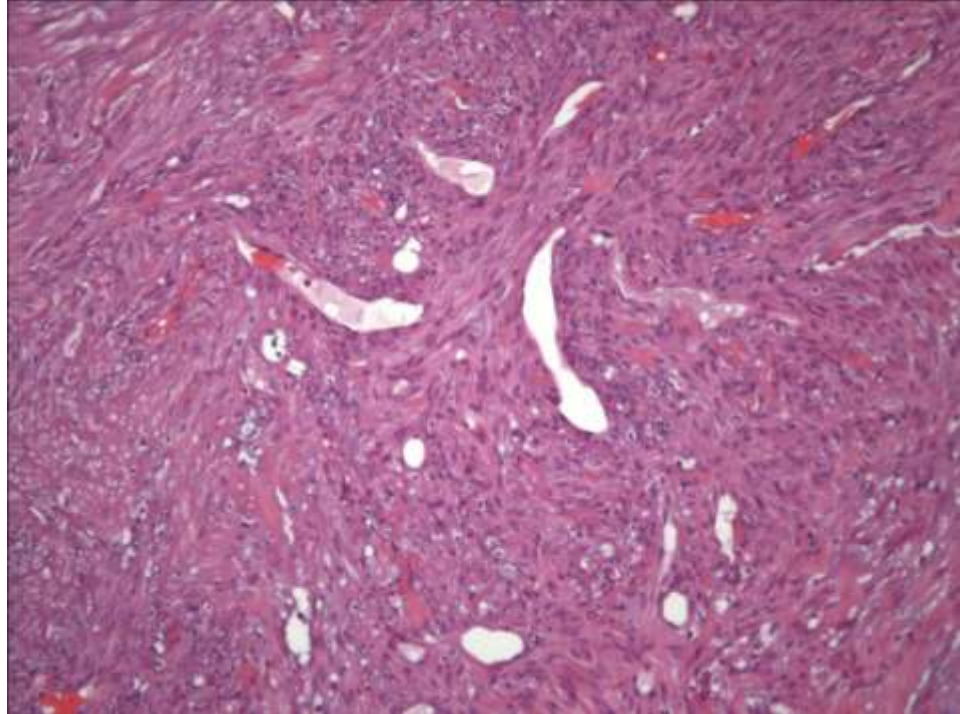
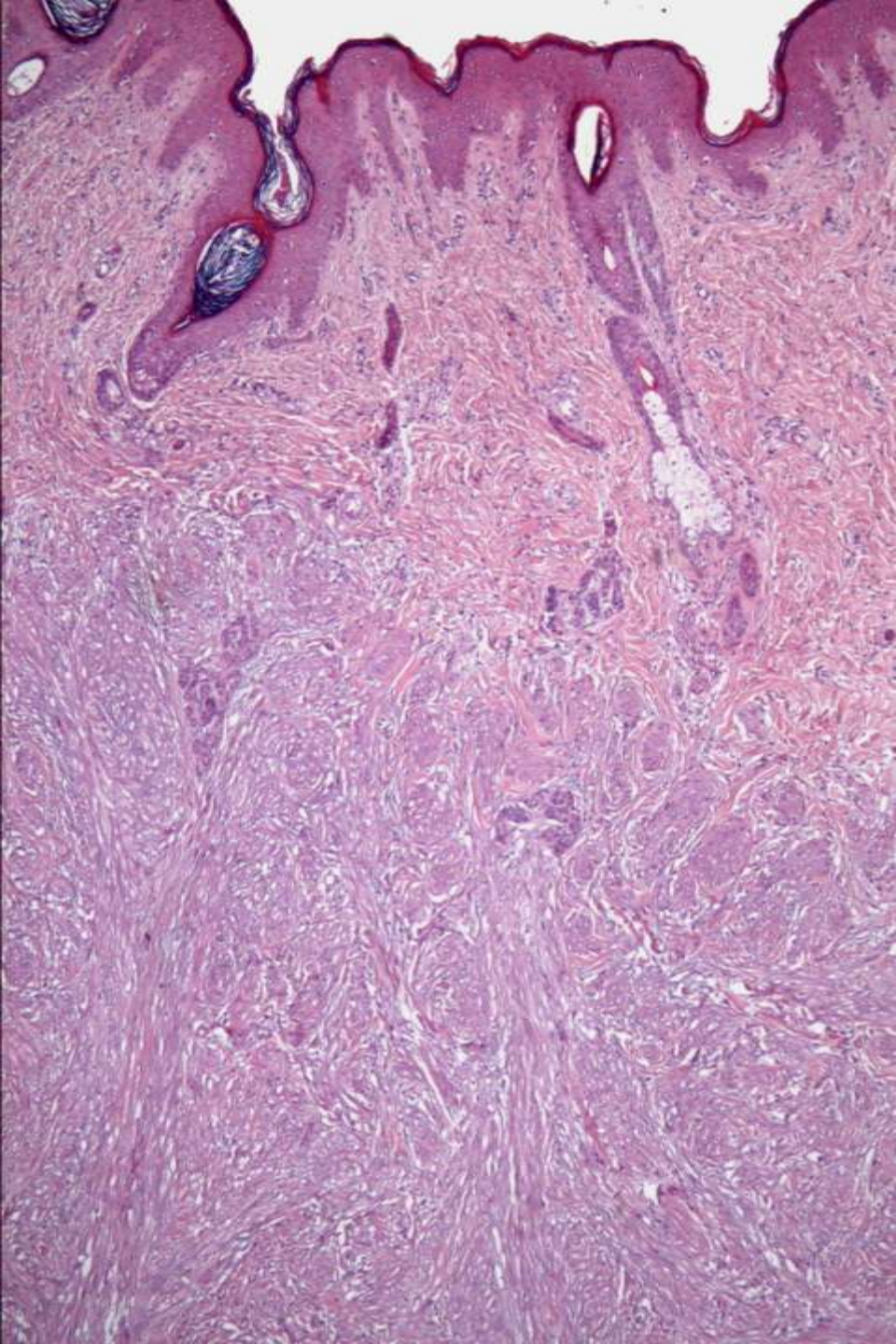
**¡¡AML- α :
 $\frac{3}{4}$ negativo
o focal!!**











Miofibromatosis infantil

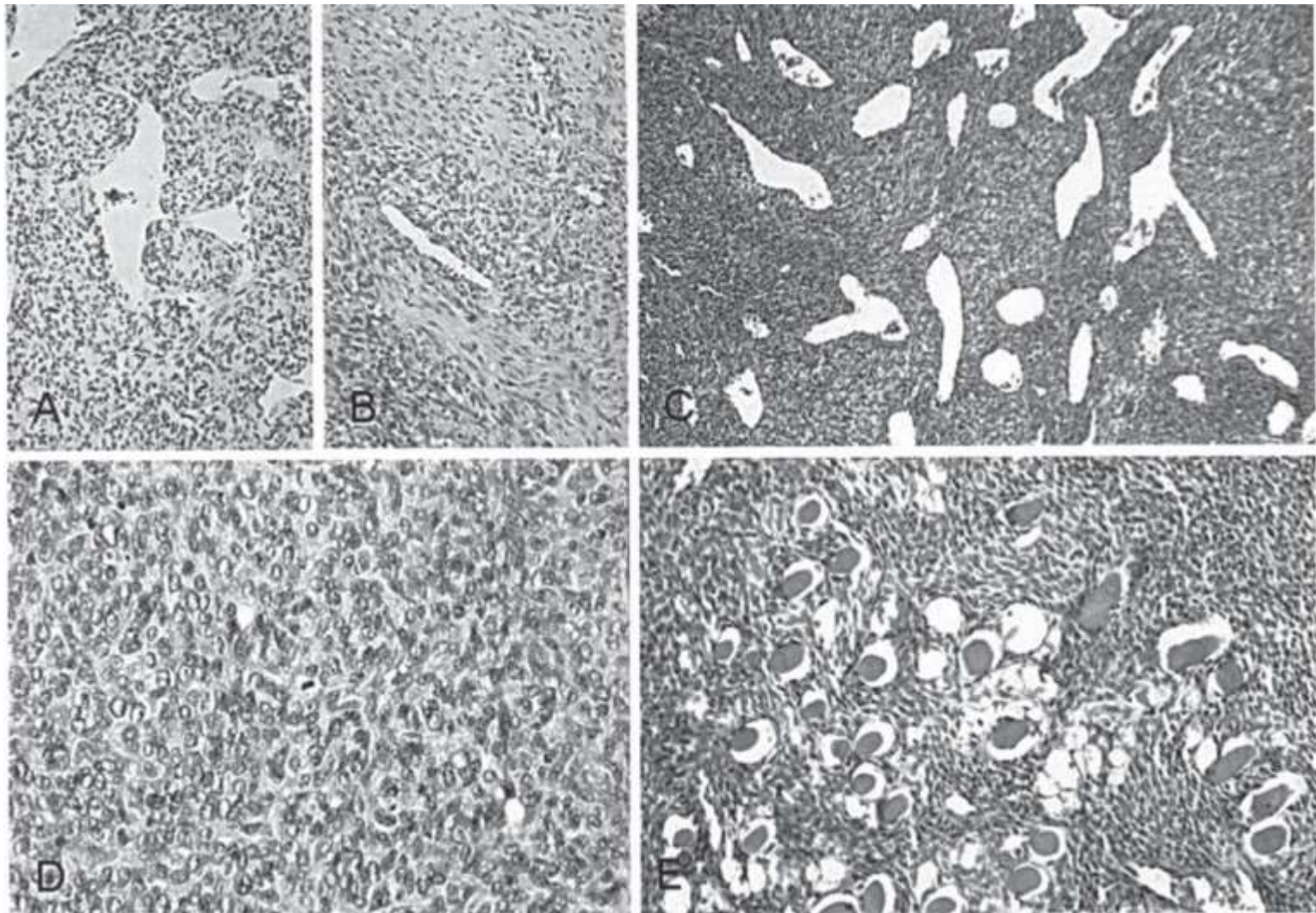
Miofibromatosis infantil

- El tumor fibroso más frecuente de la infancia
- Niños < 2 años. Congénitos 60%
- Formas:
 - Solitaria
 - Múltiple
 - Generalizada: afectación visceral (pulmón) peor pronóstico
- Clínicamente: nódulo/s sugestivos de tumor vascular
- Nódulos de unos 2 cm, con frecuente necrosis central y/o áreas hemorrágicas
- Zonación:
 - Periferia: fusocelular-mioide +/- hialinización
 - Central: células redondas, poligonales o fusiformes, con núcleos hipercrómicos + vasos hemangiopericíticos +/- necrosis + crecimiento intravascular subendotelial (polipoide). Generalmente escasas mitosis (en algunos casos pueden ser numerosas)
- Las formas solitaria y múltiple regresan espontáneamente con frecuencia
- Positividad: actina muscular, desmina, S-100
- D. Diferencial: Fibrosarcoma infantil

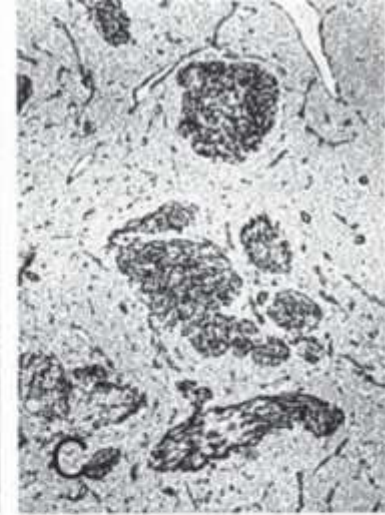
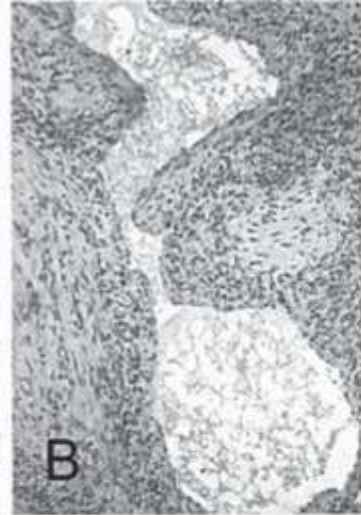
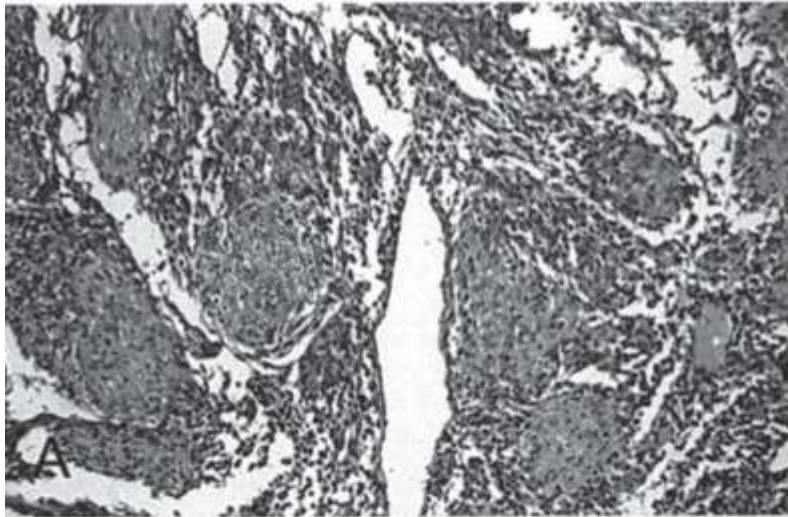
Morphologic Overlap between Infantile Myofibromatosis and Infantile Fibrosarcoma: A Pitfall in Diagnosis

RITA ALAGGIO,¹ DONATELLA BARISANI,² VITO NINFO,¹ ANGELO ROSOLEN,³ AND CHERYL M. COFFIN^{4*}

Describen solapamiento de ambas entidades, con casos indeterminados morfológicamente (“compuestos”), y que requieren estudio de la fusión génica del fibrosarcoma infantil para ser tipificados



Miofibromatosis infantil “compuesta”



Fibrosarcoma infantil

Fibrosarcoma infantil

- Raro. Niños menores de 3 años
- Profundos o superficiales, en extremidades > tronco-cabeza-cuello
- Masas lobulares de límites imprecisos, con agresividad local y recidivas pero muy excepcionales metástasis
- Fascículos de células fusiformes y rara vez redondas, con núcleos grandes pero uniformes
- La fracción de proliferación puede ser alta
- Frecuentes áreas de necrosis y hemorragia, así como vasos hemangiopericíticos
- Variable positividad para actina muscular lisa y desmina
- Translocación t(12;15)(p13;q25) con fusión génica ETV6-NTRK3 (activación oncogénica de NTRK3)

SARCOMAS

FS-DFSP

mixofibrosarcoma

**fibromixioide
bajo grado**

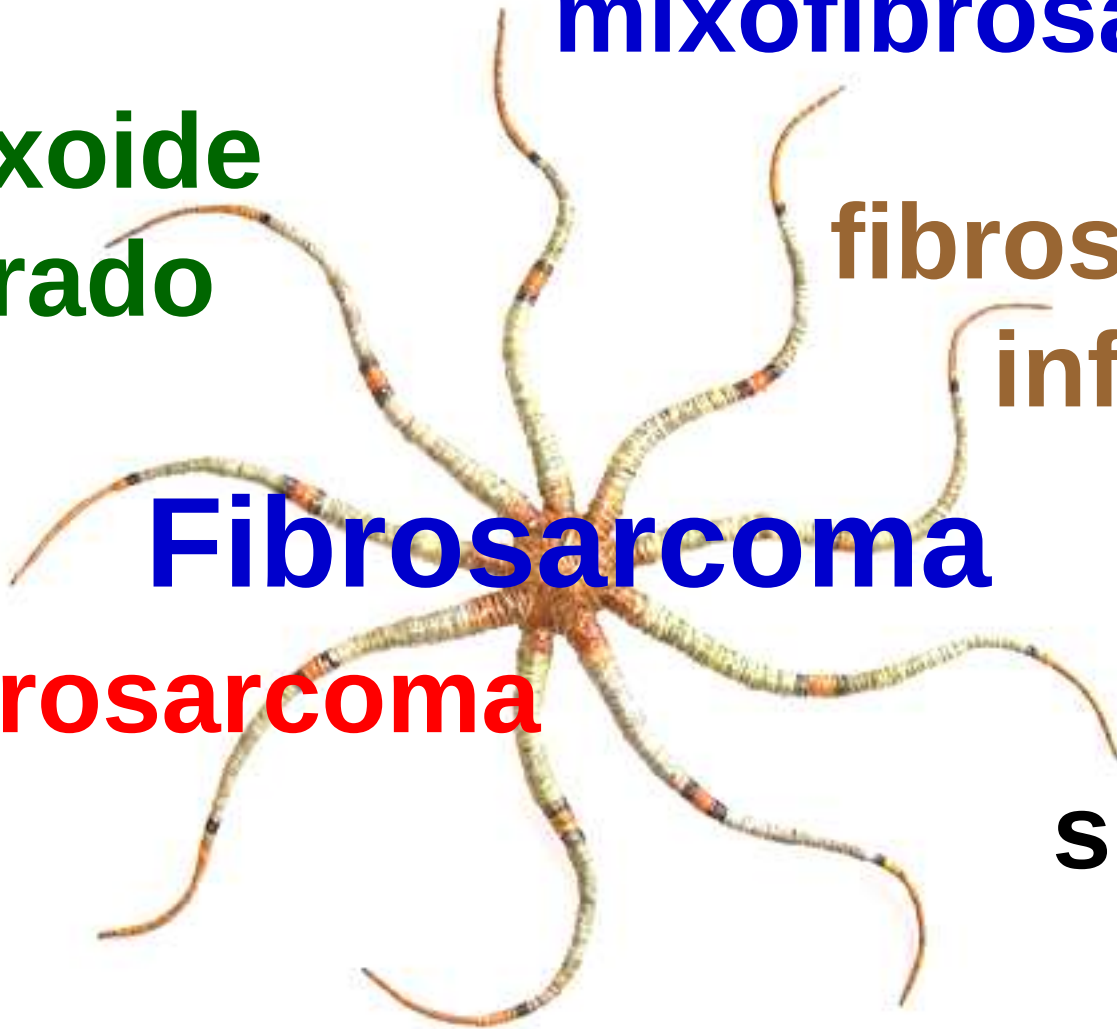
**fibrosarcoma
infantil**

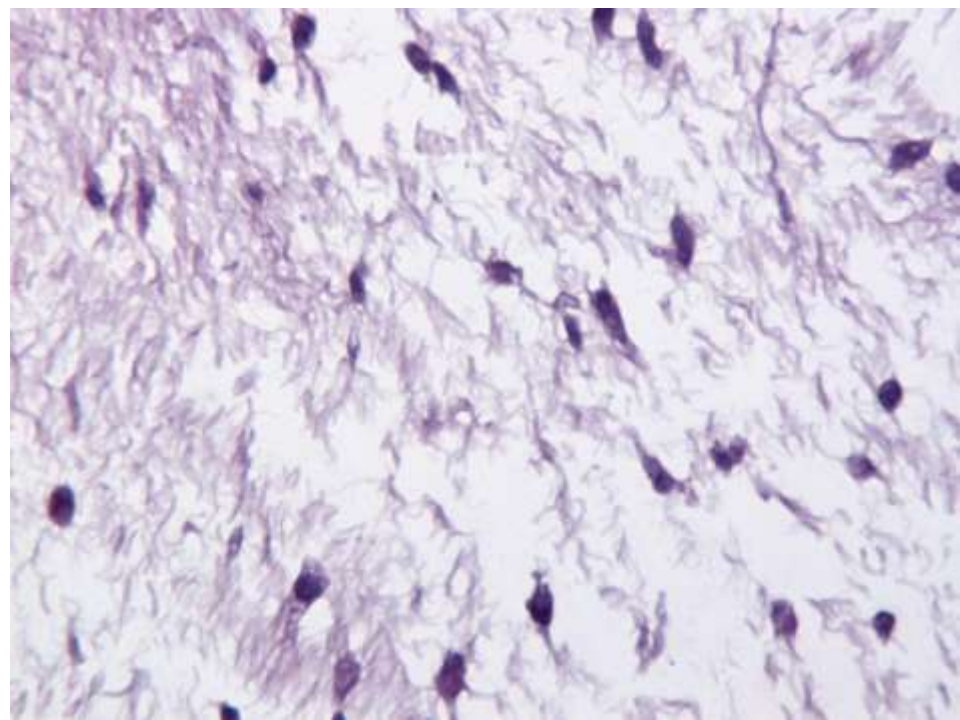
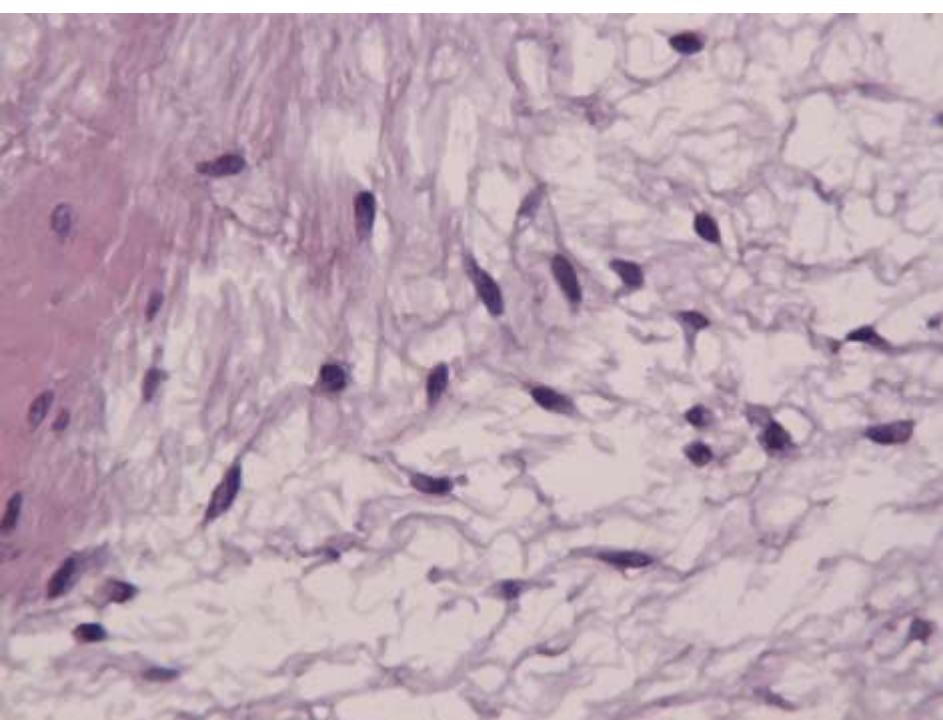
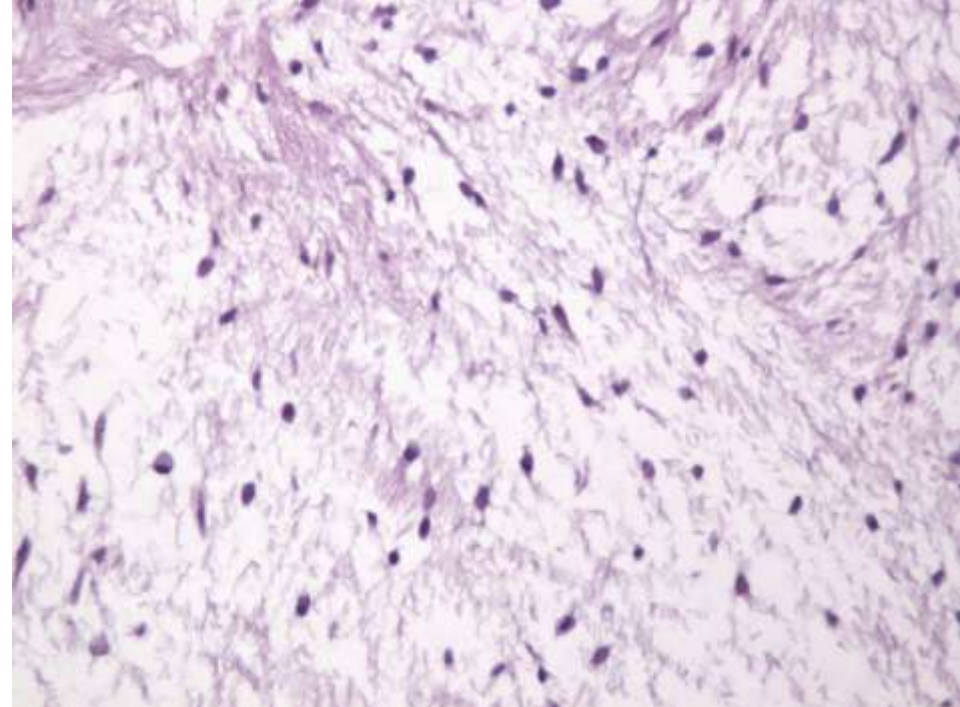
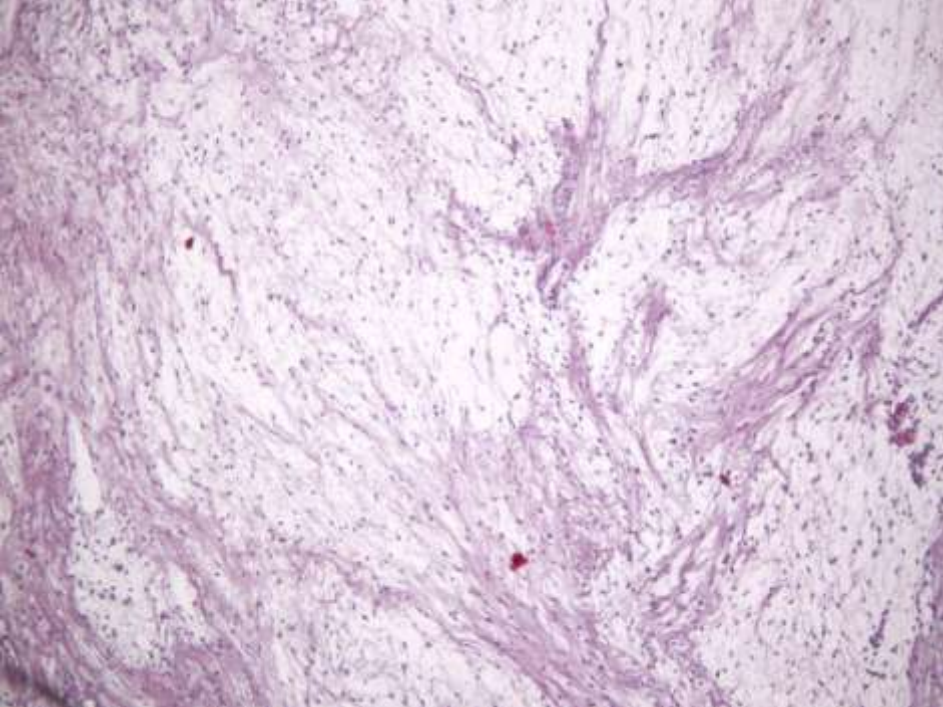
Fibrosarcoma

miofibrosarcoma

sinovial

mixoinflamatorio acral

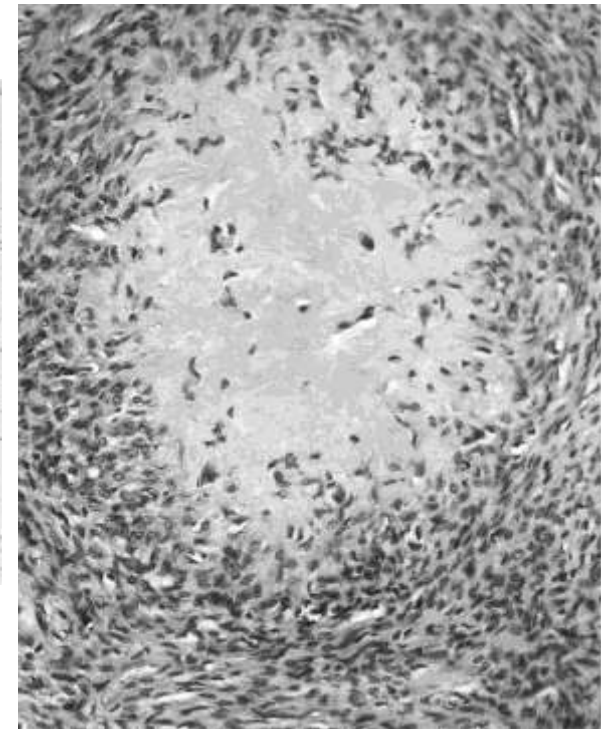
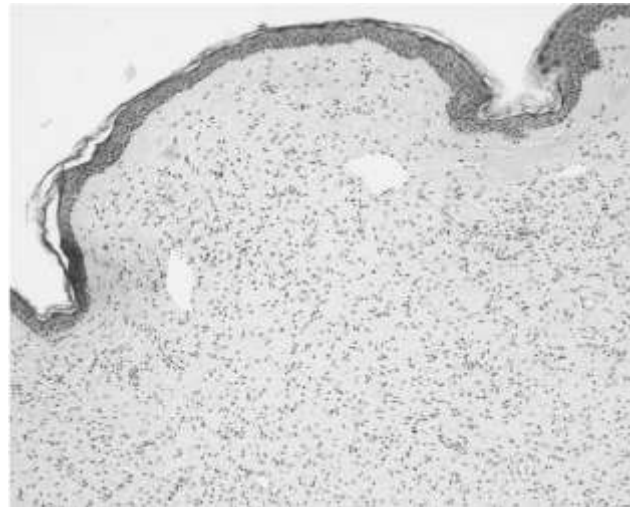




Superficial Low-grade Fibromyxoid Sarcoma (Evans Tumor)

*A Clinicopathologic Analysis of 19 Cases With a Unique Observation
in the Pediatric Population*

Steven D. Billings, MD, Georgeta Giblen, MD,† and Julie C. Fanburg-Smith, MD‡*

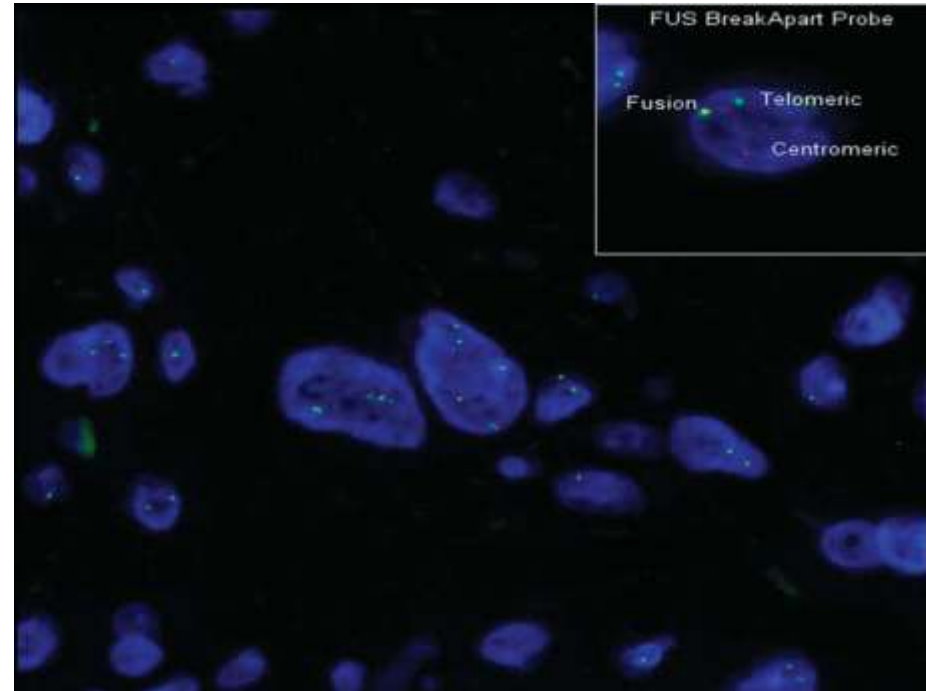
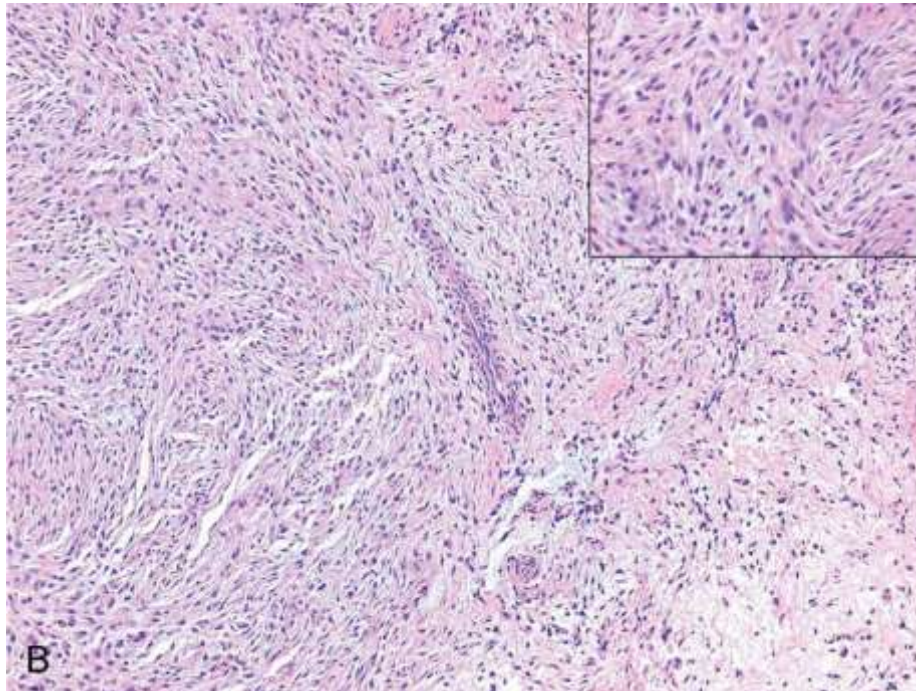


Sarcoma fibromixioide de bajo grado SUPERFICIAL

- Jóvenes y niños (37%)
- Extremidades inferiores > nalgas > tronco
- Subcutáneos (raros dérmicos). Clínicamente aspecto benigno
- Masas bien circunscritas
- Celularidad escasa a moderada
- Células fusiformes, ovals o estrelladas, poco atípicas
- Mitosis muy escasas (0-6 /50 campos). Necrosis isquémica (1/3)
- Patrones: arremolinado, estoriforme, fascicular
- Matriz mixoide y colágena (interfase abrupta o en transición)
- Rosetas colágenas en 1/3 casos. Menos frecuente la variante fusocelular hialinizante con rosetas gigantes
- Vasos curvilíneos o ramificados (más numerosos en áreas mixoides que en las más colágenas)
- **Focal positividad: actina muscular lisa α , actina muscular específica, EMA y CD68. Negativas: desmina, S-100, y CD34**
- Excepcional recidiva. Prácticamente NO metástasis
- Translocación t(7;16)(q34;p11) con fusión génica FUS/CREB3L2 (67%)

FUS (16p11) Gene Rearrangement as Detected by Fluorescence In-Situ Hybridization in Cutaneous Low-Grade Fibromyxoid Sarcoma: A Potential Diagnostic Tool

Rajiv M. Patel, MD,† Erinn Downs-Kelly, DO,‡ Monisha N. Dandekar, MD,*
Julie C. Fanburg-Smith, MD,§ Steven D. Billings, MD,‡ Raymond R. Tubbs, DO,¶
and John R. Goldblum, MD‡*



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and John R. Goldblum, MD‡*

TABLE 1. FISH Results for *FUS* Rearrangements in LGFMS

Case Number	Cells Positive for <i>FUS</i> (16p11) Rearrangement, (%)	Result
1	72*	Positive
2	6	Negative
3	78*	Positive
4	2	Negative
5	80*	Positive
6	78*	Positive

*Mean: 77% positive cells/case, Range: 72–80% positive cells/case.

***FUS* (16p11) Gene Rearrangement as Detected by Fluorescence In-Situ Hybridization in Cutaneous Low-Grade Fibromyxoid Sarcoma: A Potential Diagnostic Tool**

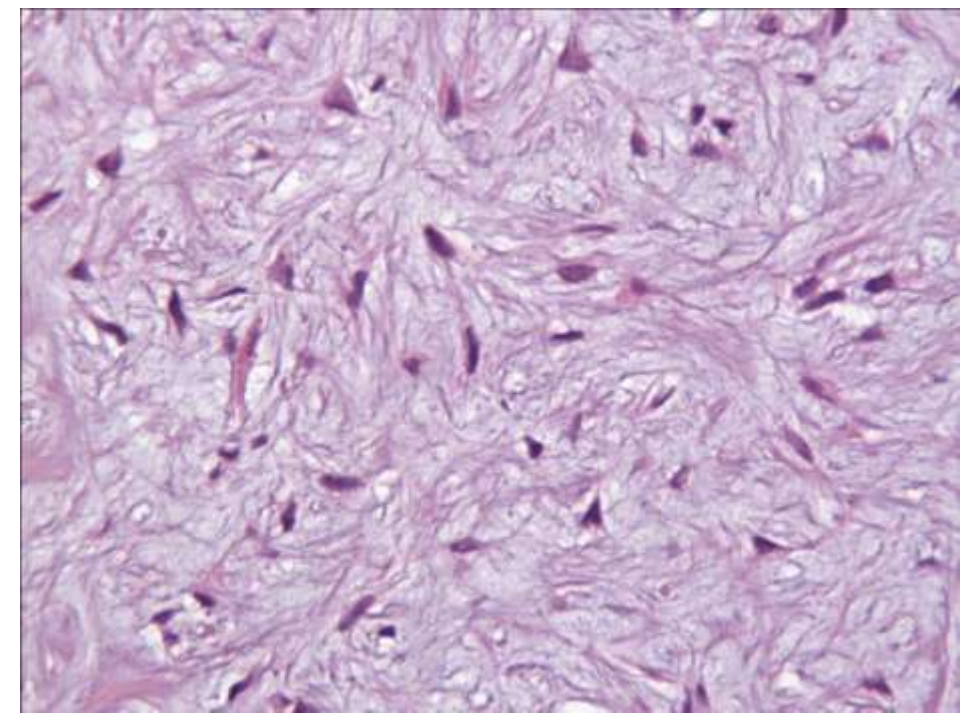
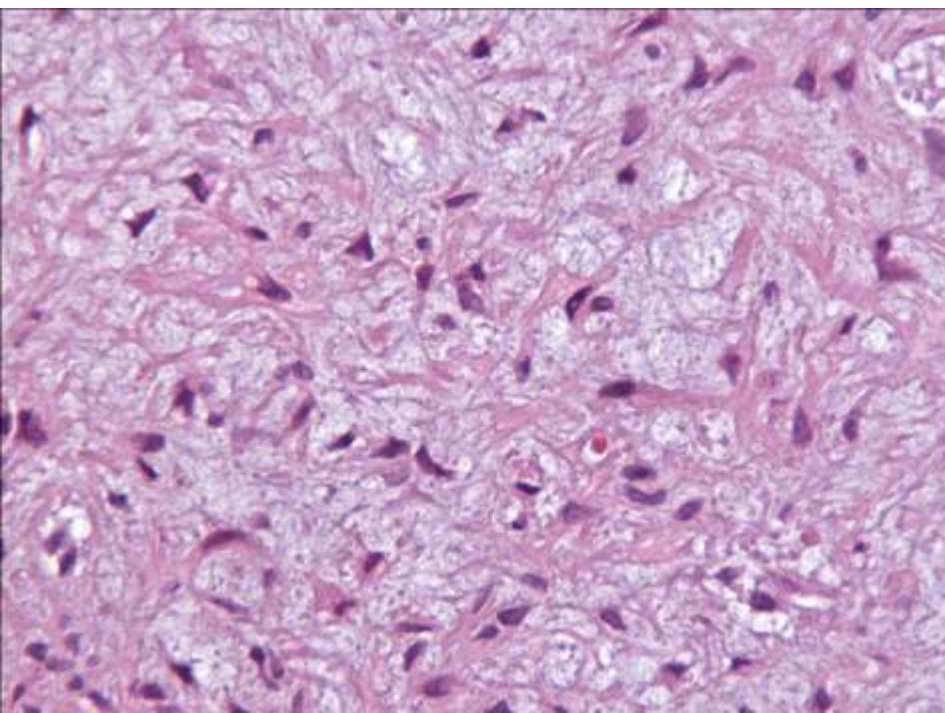
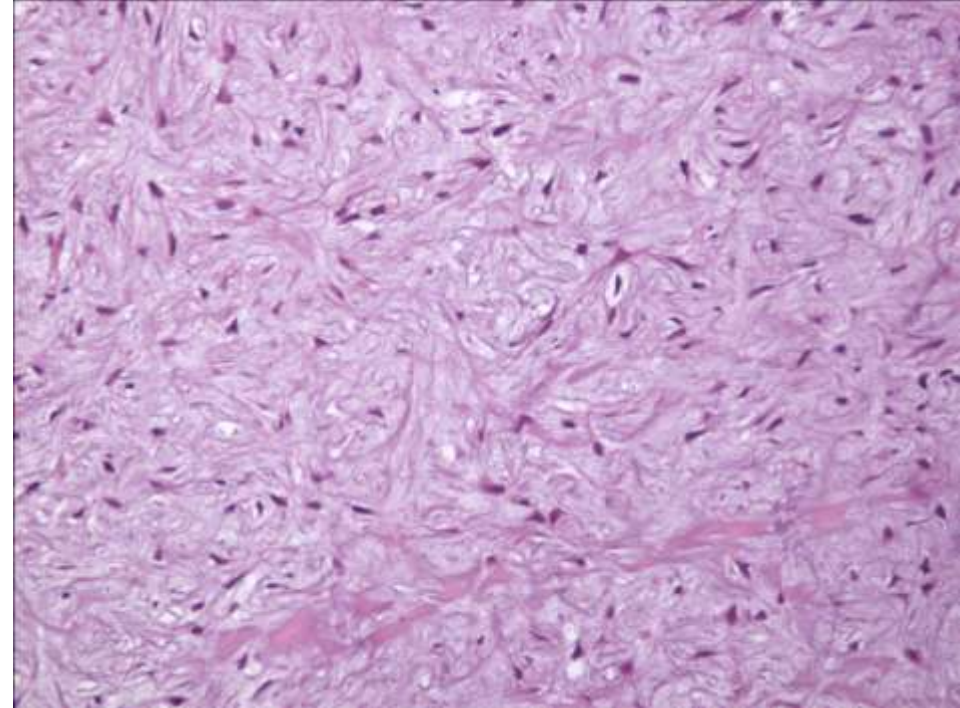
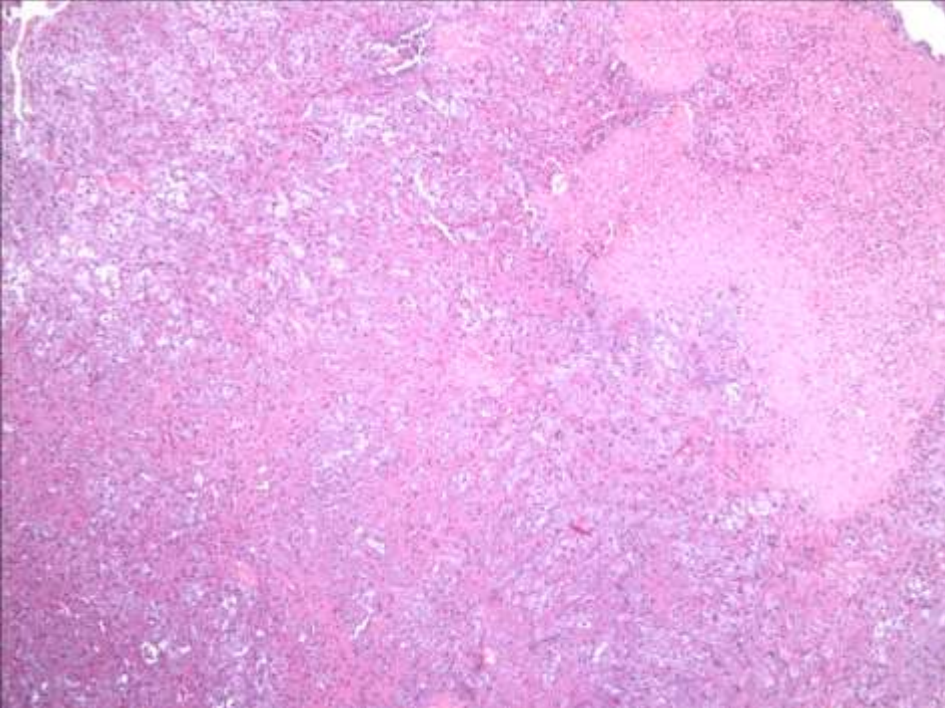
Rajiv M. Patel, MD,† Erinn Downs-Kelly, DO,‡ Monisha N. Dandekar, MD,*
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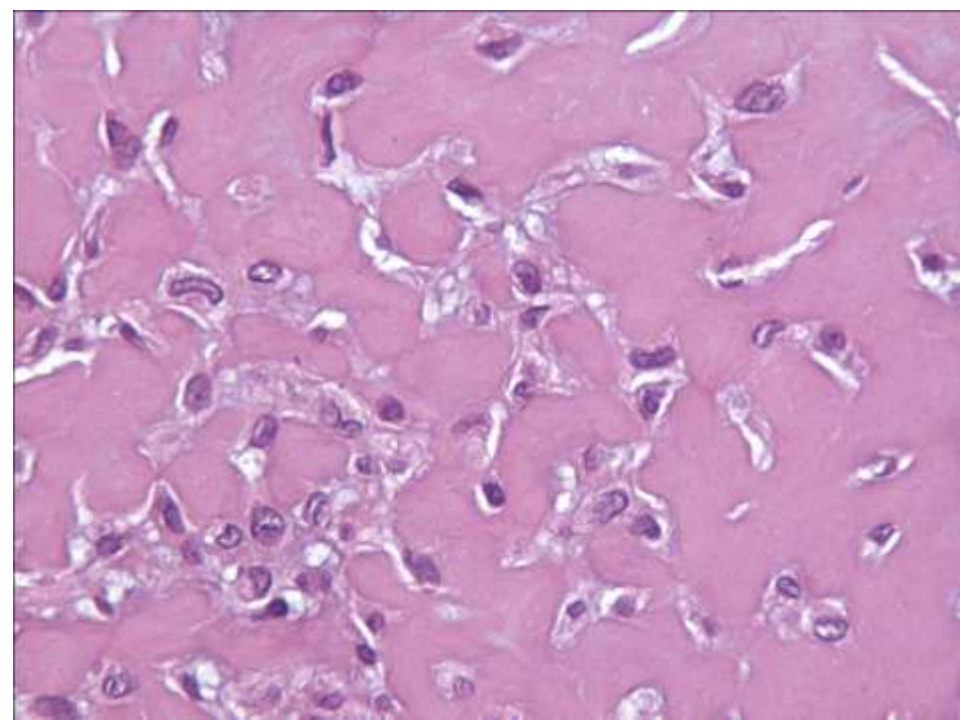
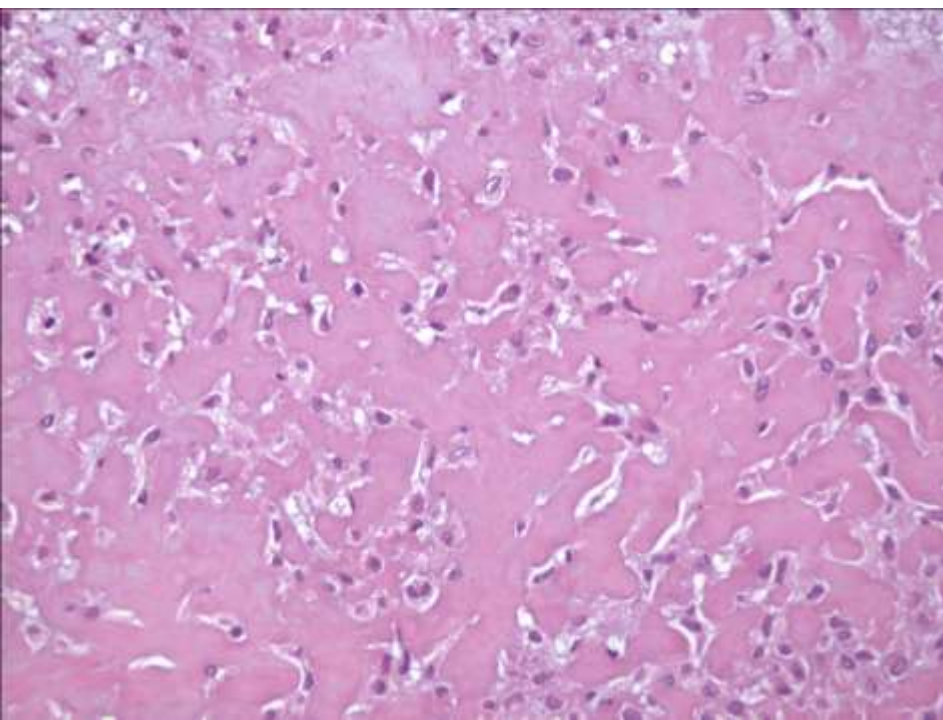
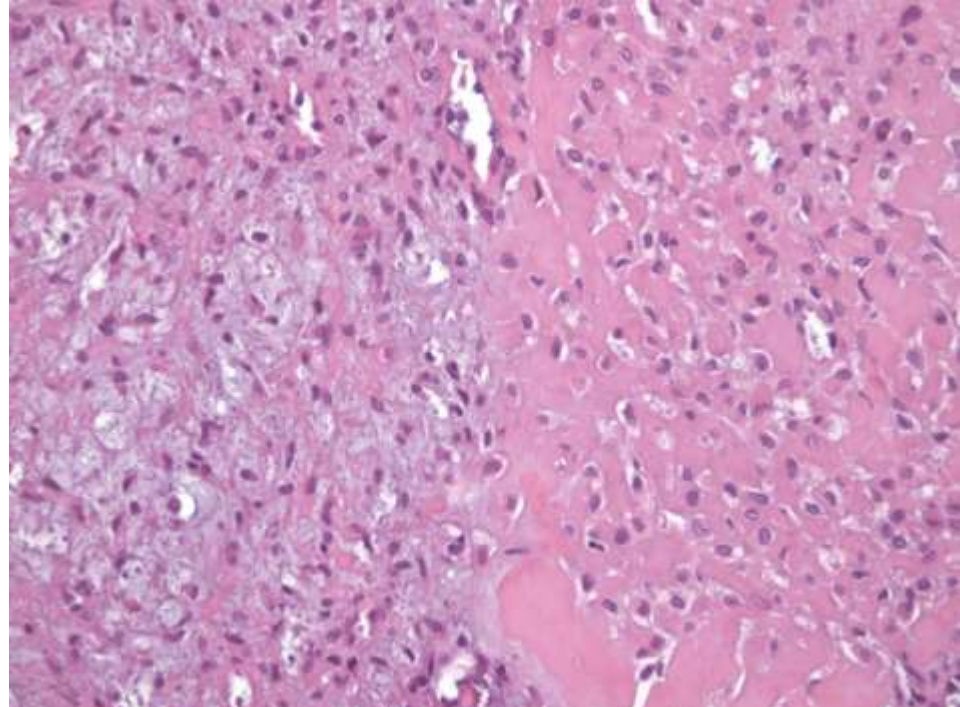
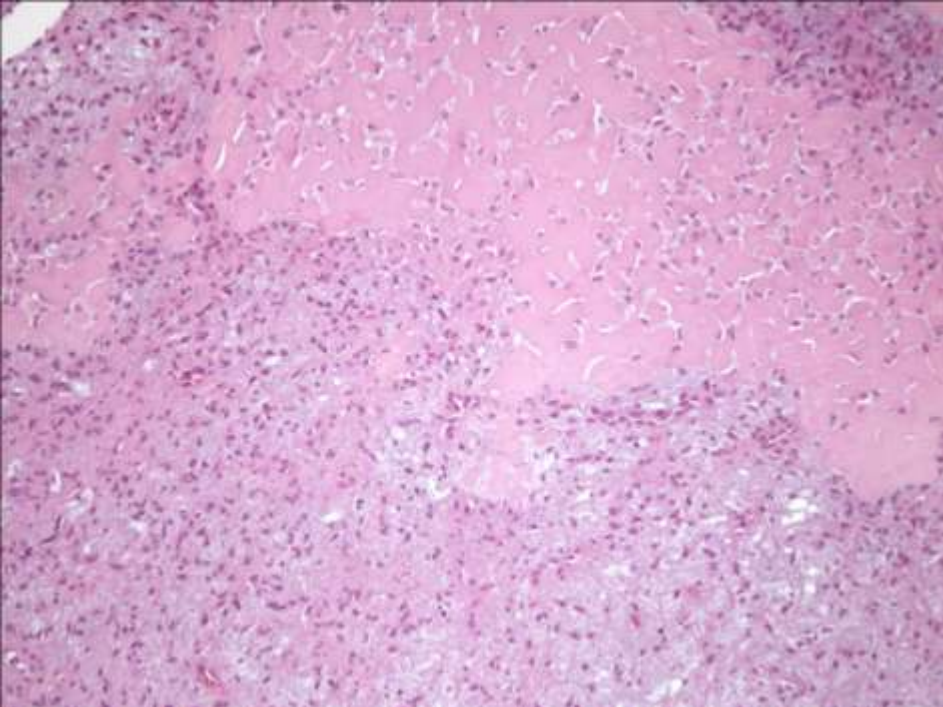
Persiste ambigüedad en la caracterización de esta entidad como lo demuestra la revisión significativa de diagnósticos tras re-evaluación histológica

FUS (16p11) Gene Rearrangement as Detected by Fluorescence In-Situ Hybridization in Cutaneous Low-Grade Fibromyxoid Sarcoma: A Potential Diagnostic Tool

Rajiv M. Patel, MD,† Erinn Downs-Kelly, DO,‡ Monisha N. Dandekar, MD,*
Julie C. Fanburg-Smith, MD,§ Steven D. Billings, MD,‡ Raymond R. Tubbs, DO,¶
and John R. Goldblum, MD‡*

*La detección de la fusión génica por FISH,
unida a una evaluación histológica precisa
puede refinar los criterios diagnósticos de la
forma superficial del sarcoma fibromixoide de
bajo grado*

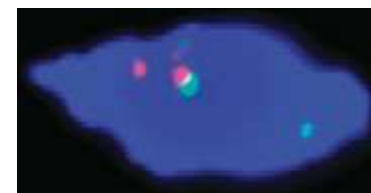
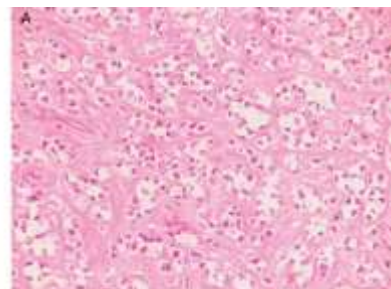
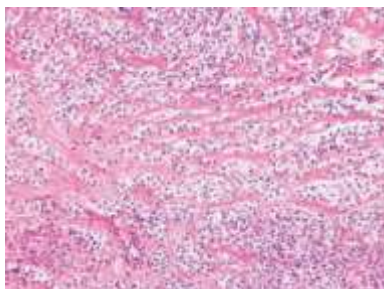
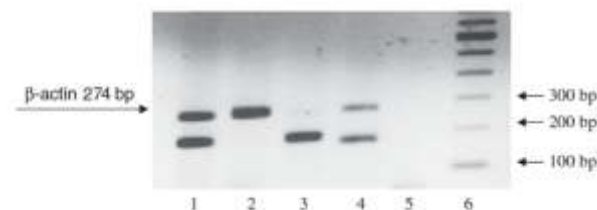
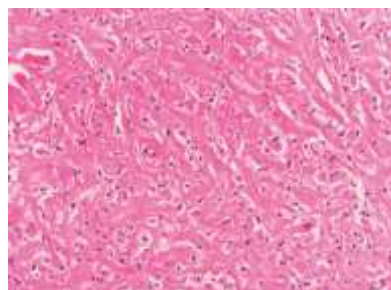
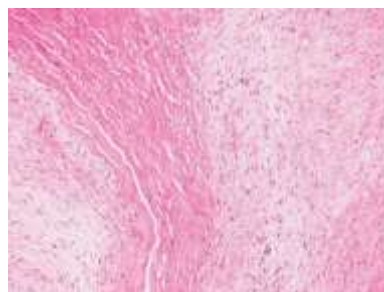




Translocation-positive Low-grade Fibromyxoid Sarcoma: Clinicopathologic and Molecular Analysis of a Series Expanding the Morphologic Spectrum and Suggesting Potential Relationship to Sclerosing Epithelioid Fibrosarcoma

A Study From the French Sarcoma Group

Louis Guillou, MD, Jean Benhattar, PhD,* Carole Gengler, MD,* Gabrielle Gallagher, Tech,*
Dominique Ranchère-Vince, MD,† Françoise Collin, MD,‡ Philippe Terrier, MD,§
Marie-José Terrier-Lacombe, MD,§ Agnès Leroux, MD,|| Bernard Marquès, MD,¶
Nicolas de Saint Aubain Somerhausen, MD,# Frédérique Keslair, BSc,**
Florence Pedeutour, PharmD, PhD,** and Jean-Michel Coindre, MD† †*



Sclerosing Epithelioid Fibrosarcoma

A Variant of Fibrosarcoma Simulating Carcinoma

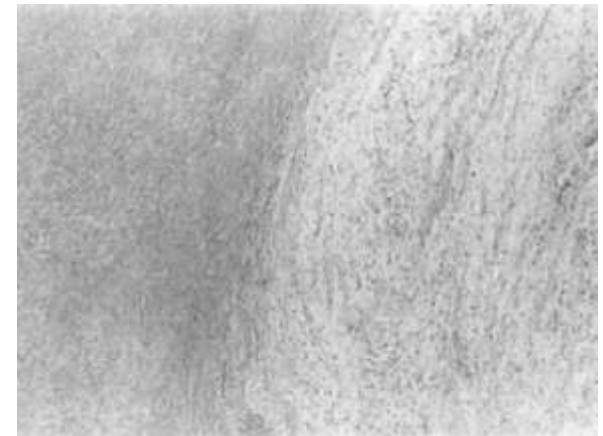
**Jeanne M. Meis-Kindblom, M.D.,
Lars-Gunnar Kindblom, M.D., Ph.D., and
Franz M. Enzinger, M.D.**

myxoid zones bore a closer resemblance to myxofibrosarcoma (myxoid fibrosarcoma) (24), so-called low-grade fibromyxoid sarcoma (12), or low-grade myxoid MFH (35).

Sclerosing Epithelioid Fibrosarcoma

A Study of 16 Cases and Confirmation of a Clinicopathologically Distinct Tumor

Cristina R. Antonescu, M.D., Marc K. Rosenblum, M.D.,
Patricia Pereira, M.D., Antonio G. Nascimento, M.D., and
James M. Woodruff, M.D.



confusion arises from the presence of both large paucicellular fibrous zones and focal myxoid areas, features also seen in low-grade fibromyxoid sarcoma.

Well and poorly delineated myxoid areas were present in fibroma-like portions of four tumors. These fibroma-like and myxoid areas resembled low-grade fibromyxoid sarcoma (Fig. 12).

MUC4 Is a Highly Sensitive and Specific Marker for Low-grade Fibromyxoid Sarcoma

Leona A. Doyle, MD, Emely Möller, PhD,† Paola Dal Cin, PhD,*
Christopher D.M. Fletcher, MD, FRCPath,* Fredrik Mertens, MD, PhD,†
and Jason L. Hornick, MD, PhD**

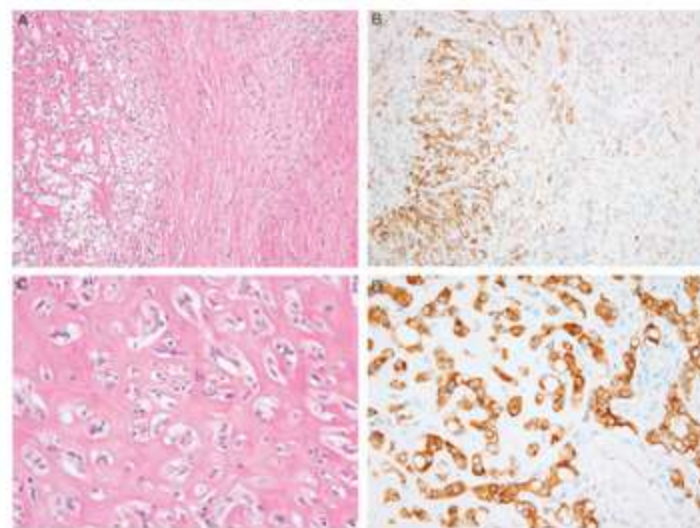
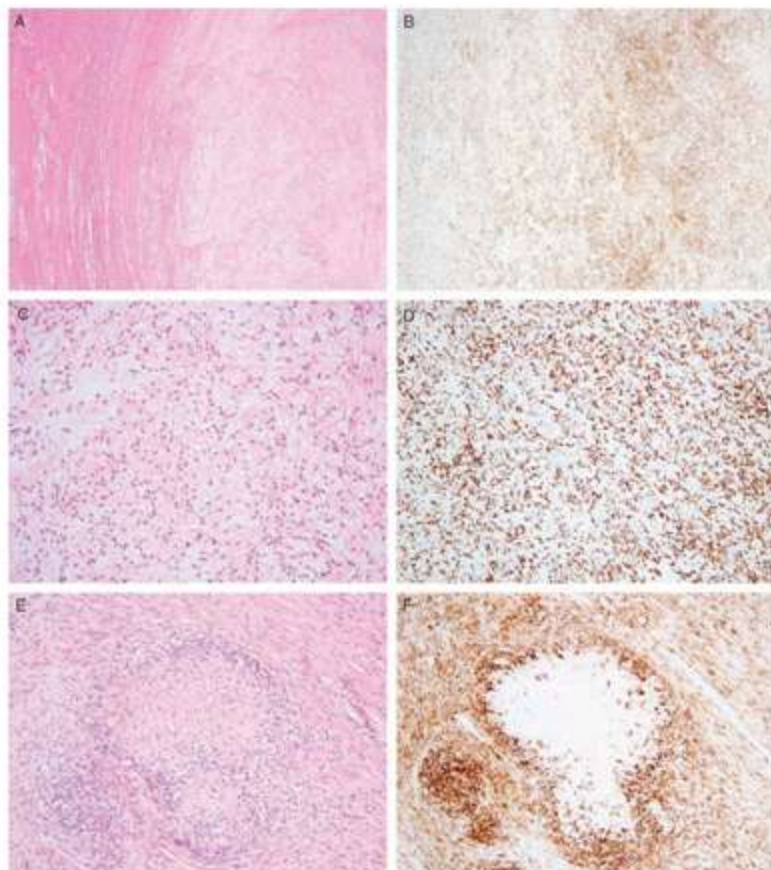


TABLE 1. Summary of Immunohistochemical Staining for MUC4

Tumor Type	Total Cases MUC4 Positive (%)	
Cellular myxoma	20	0 (0)
Dermoid fibromatosis	20	0 (0)
Dermatofibrosarcoma protuberans	20	0 (0)
Extraskeletal myxoid chondrosarcoma	10	0 (0)
Low-grade fibromyxoid sarcoma	49	49 (100)
MPNST, low-grade	20	0 (0)
Myxofibrosarcoma	40	0 (0)
Myxoid liposarcoma	10	0 (0)
Monophasic synovial sarcoma	20	6 (30)
Neurofibroma	20	0 (0)
Schwannoma	20	0 (0)
Soft tissue perineurioma	40	0 (0)
Solitary fibrous tumor	20	0 (0)

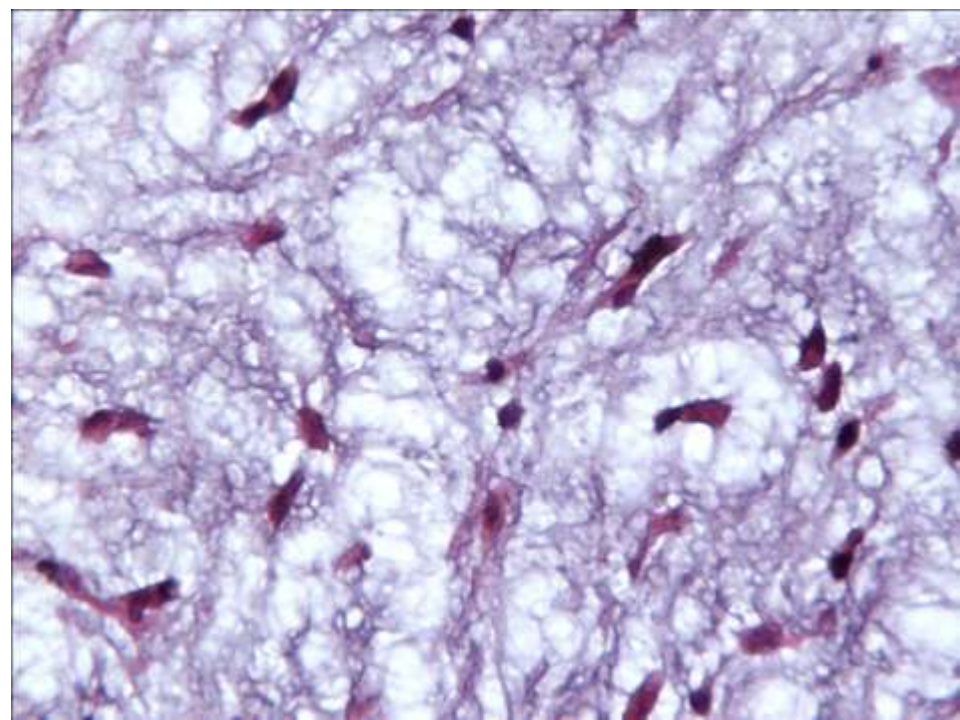
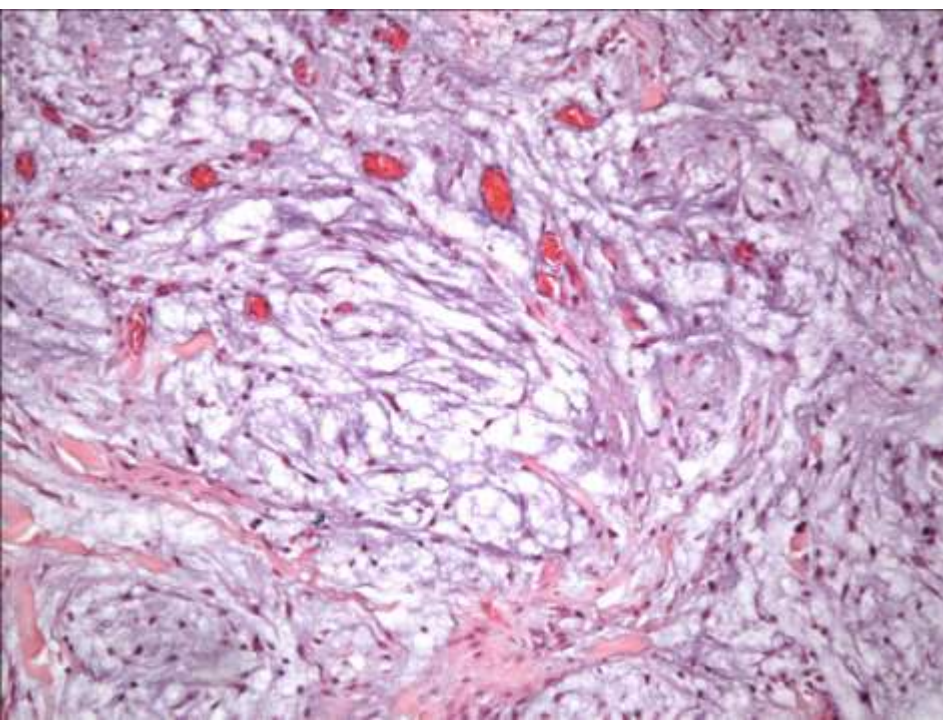
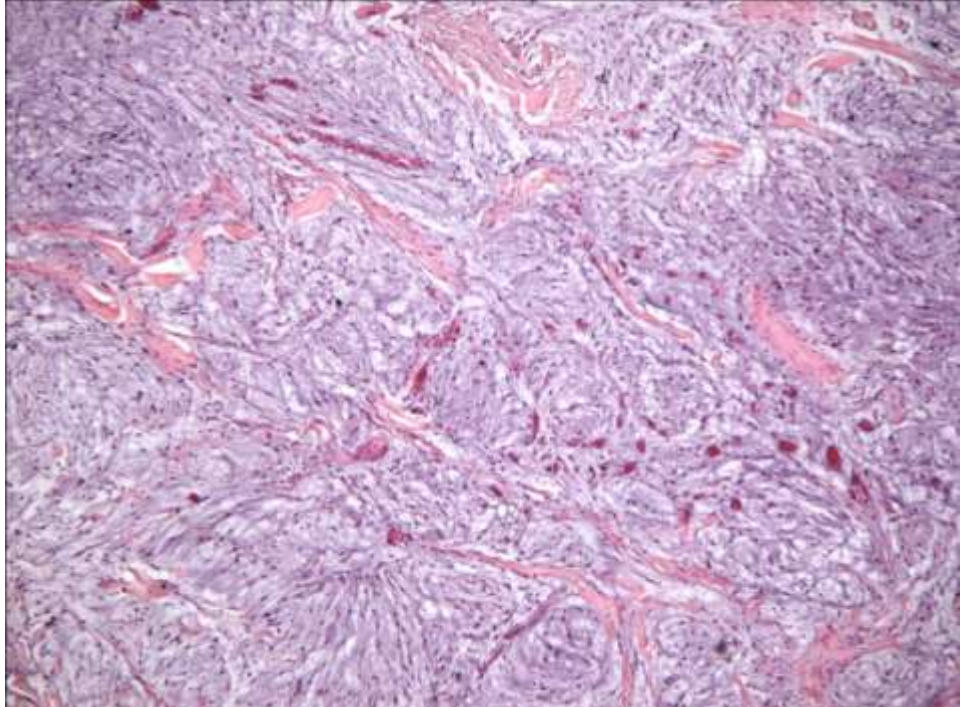
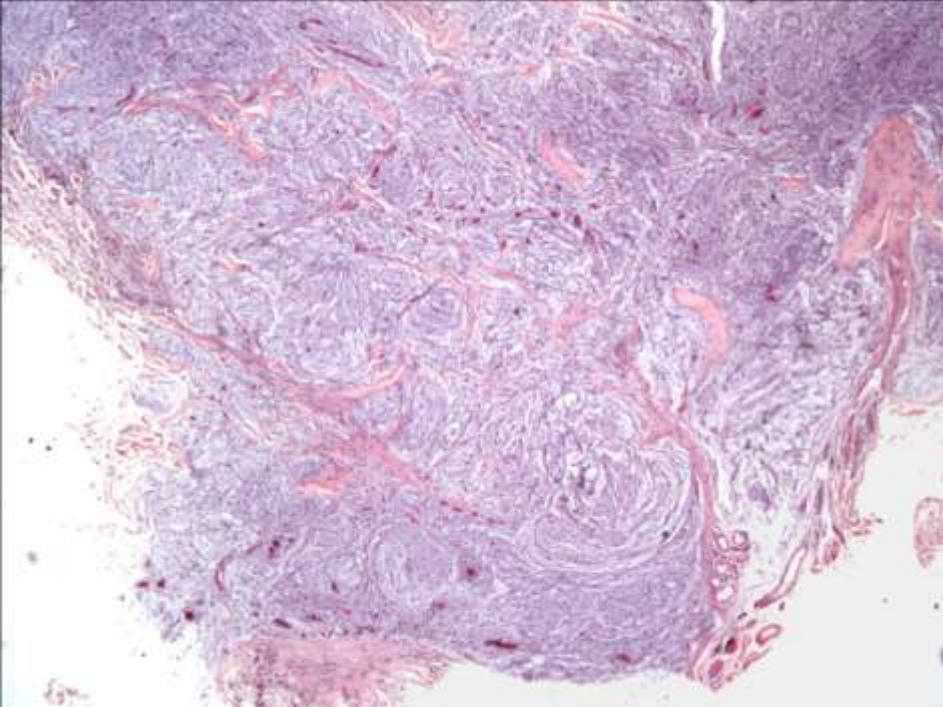
MPNST indicates malignant peripheral nerve sheath tumor.

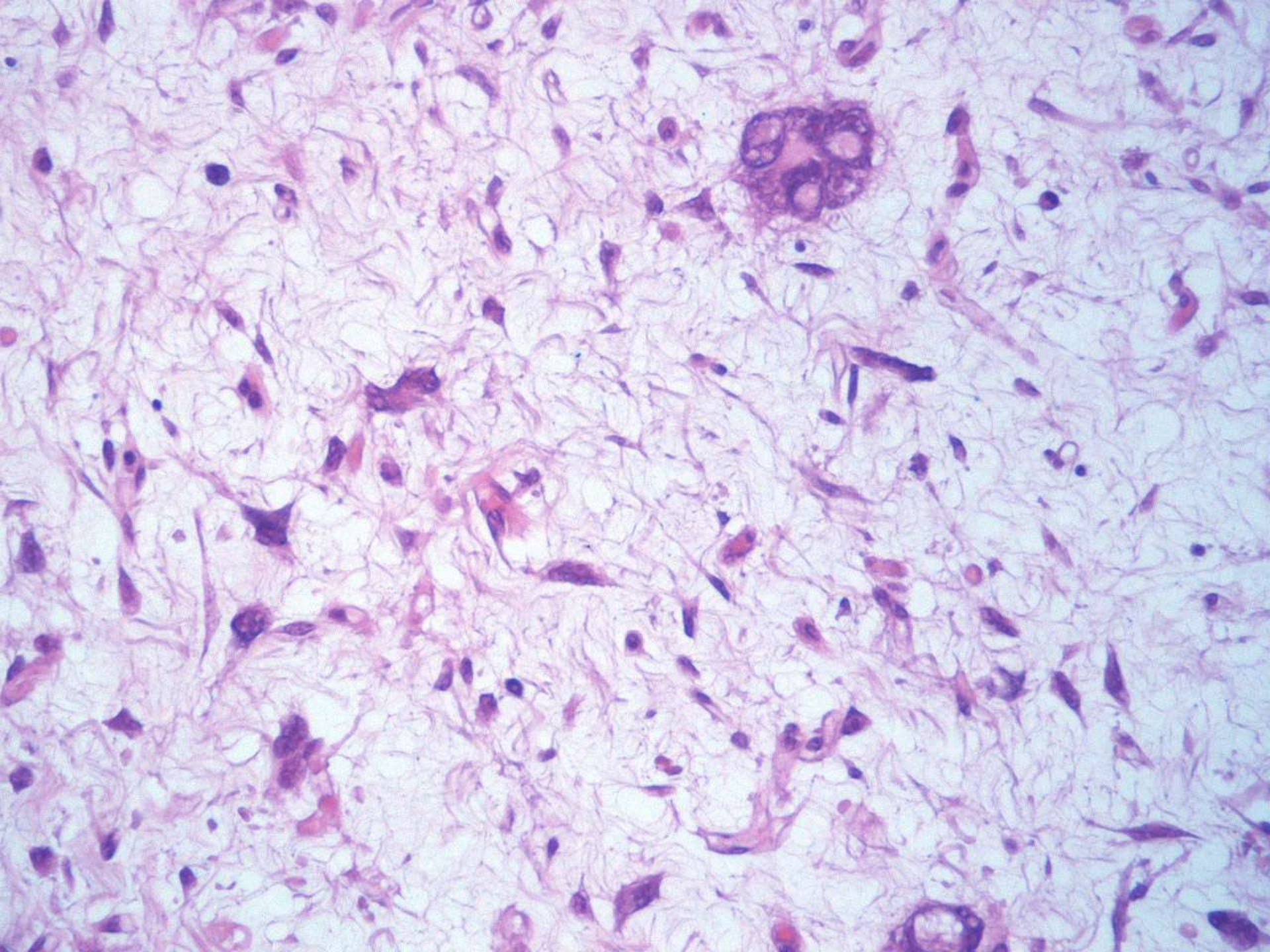
Diagnóstico diferencial

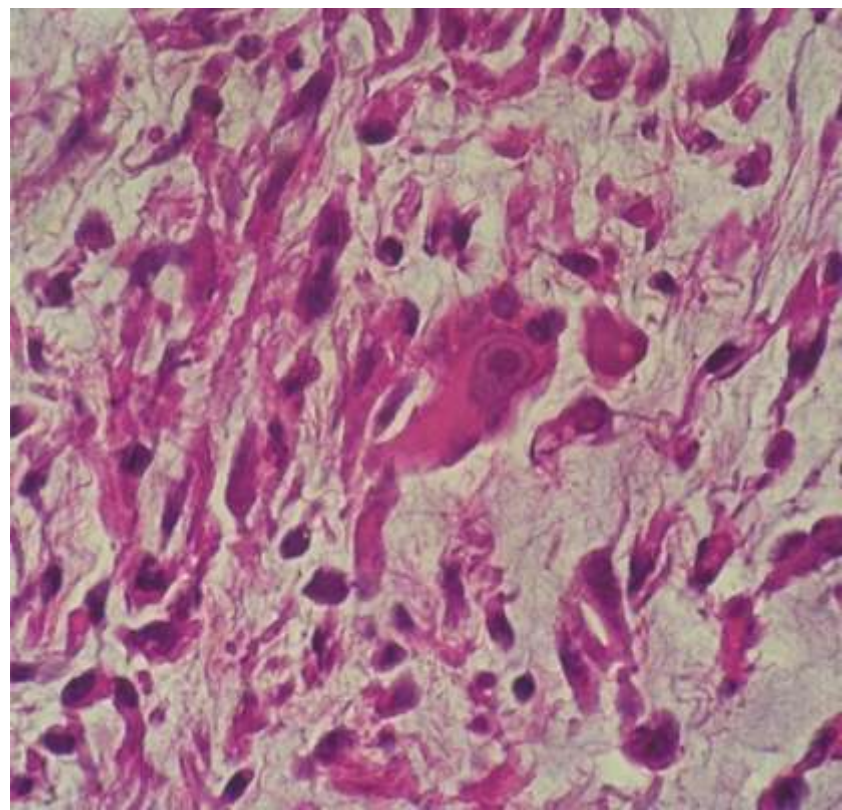
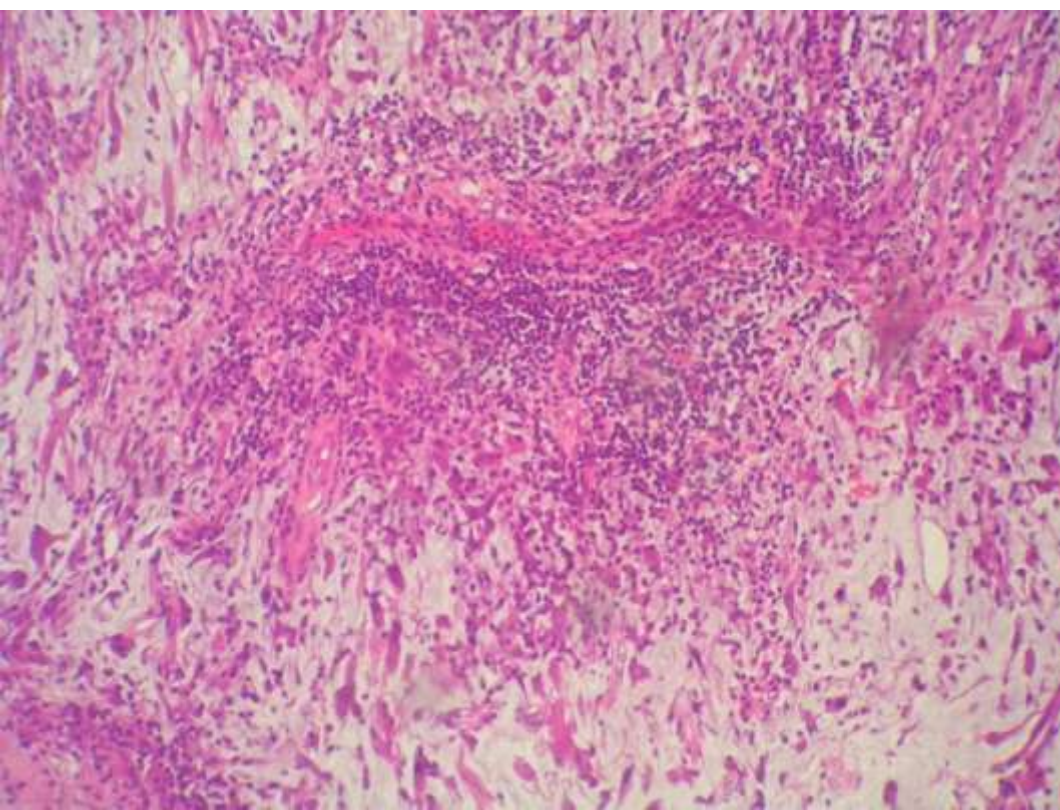
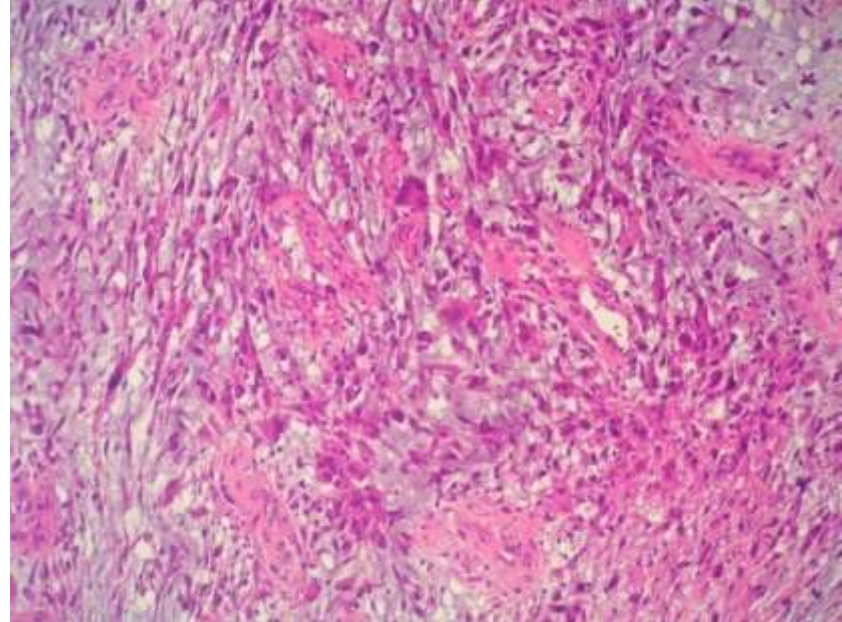
Mixofibrosarcoma

(antiguo FHM mixoide)

- Más edad
- Más atipia
- Más vasos (curvilíneos)
- Más frecuente superficial
- Más mixoide
- Menos formación de colágeno

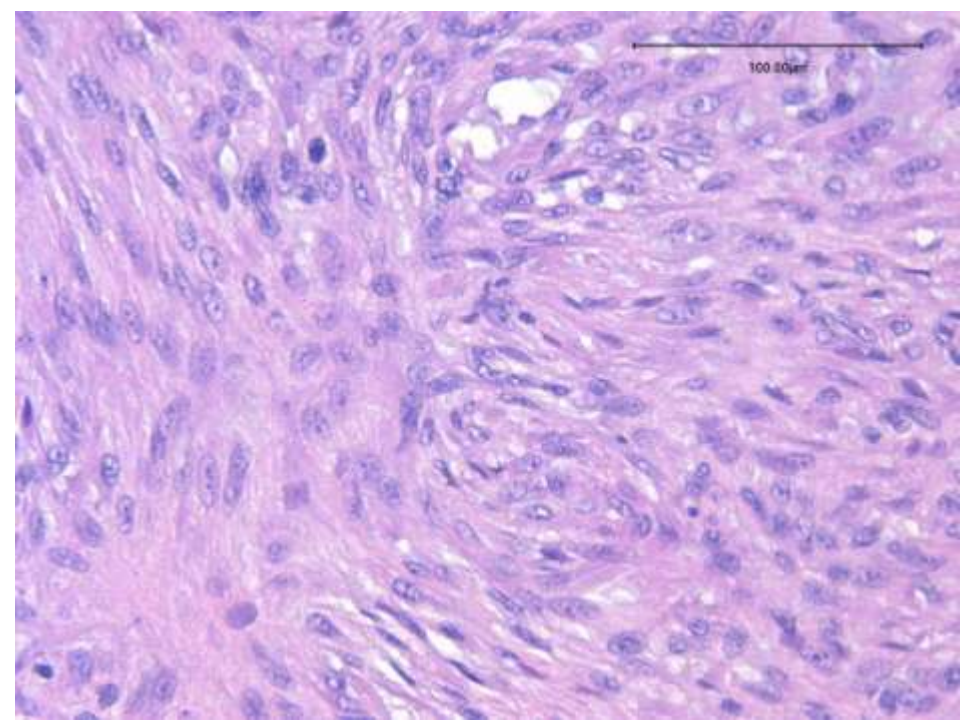
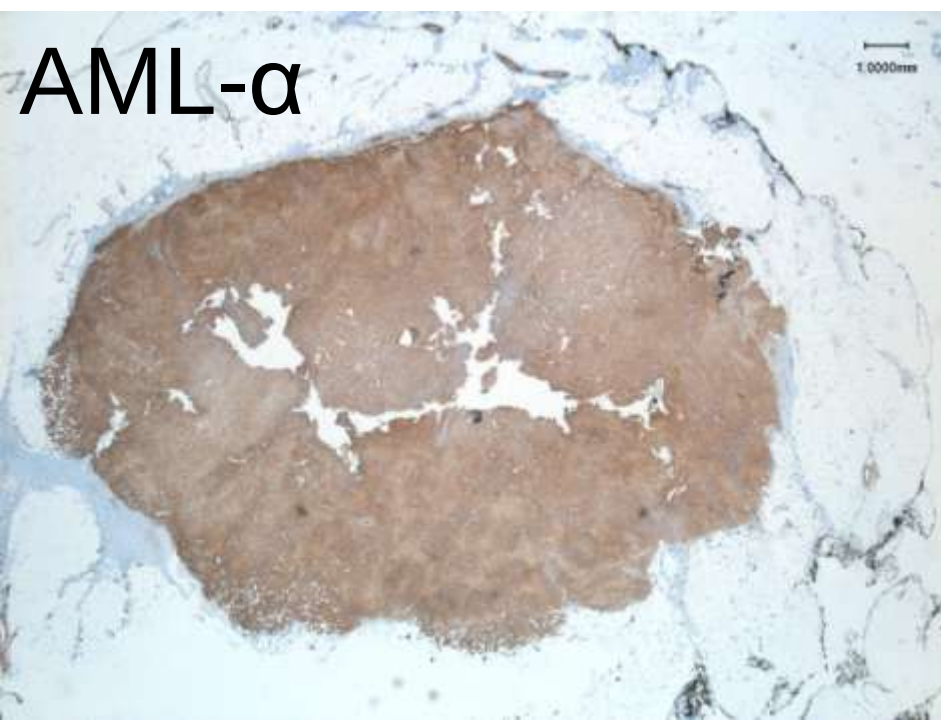
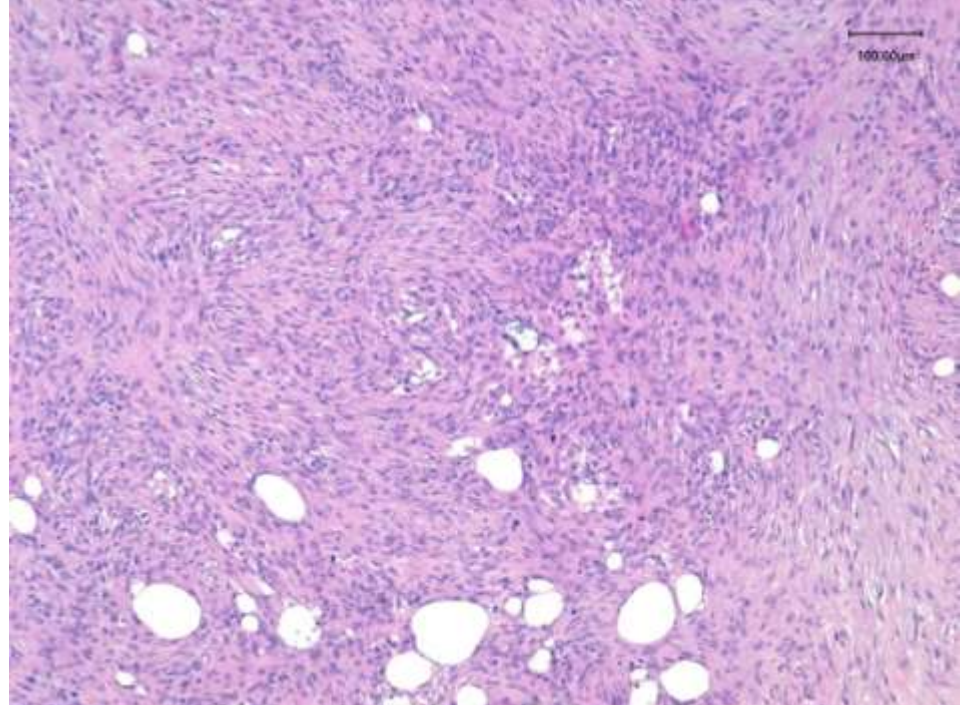
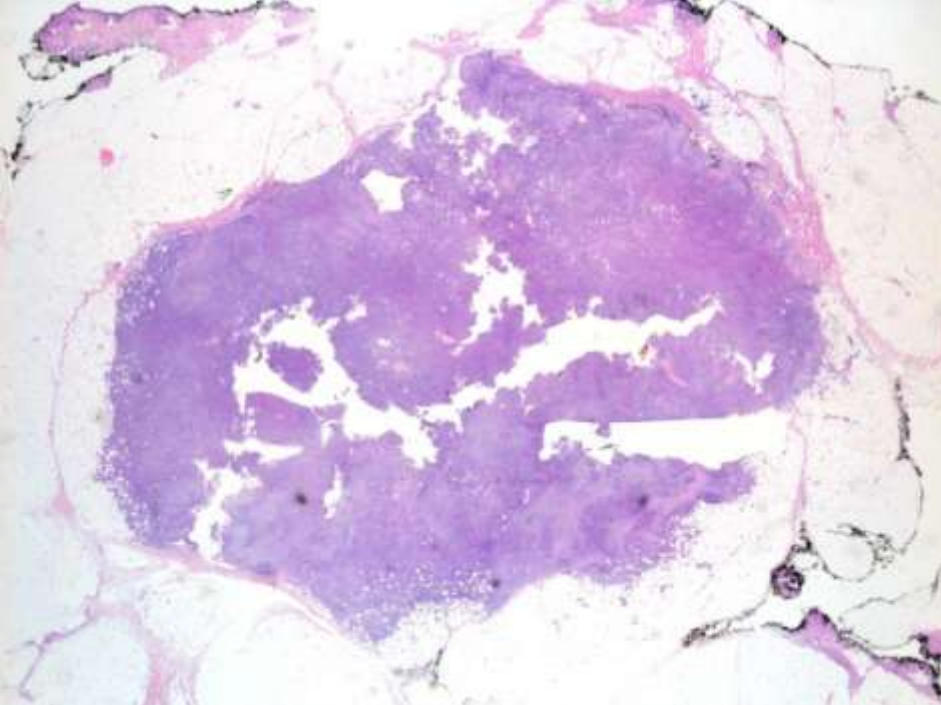






Sarcoma mixoinflamatorio acral (Tumor mixohialino inflamatorio)

- Cualquier edad y sexo
- Dedos, mano, muñeca, brazo, pie , pierna (algunas no acrales)
- Lobulado o multinodular
- Areas fibroescleróticas y mixoides con celularidad fusiforme, pleomórfica, con células Reed-Sternberg-like o virocíticas, y a veces lipoblásticas)
- Componente inflamatorio: eosinófilos, neutrófilos, linfocitos, macrófagos (espumosos y/o siderófagos)
- Puede haber mitosis típicas y atípicas. Variable necrosis
- Variable positividad para CD34, CD68, CD163, AML- α
- Frecuente recidiva. Raras metástasis





MIOFIBROSARCOMA

Myofibrosarcoma

A Clinicopathologic Study

Elizabeth Montgomery, M.D., John R. Goldblum, M.D., and
Cyril Fisher, M.D., F.R.C.Path.

TABLE 2. Clinicopathologic features of 15 patients with myofibrosarcomas

Case no.	Age (yrs)	Sex	Site	Size (cm)	Depth	Mitoses per 10 HPF	Focal necrosis	Grade	Vasc inv	SMA	MSA	DES	CK	EM	Therapy and follow up	Therapy and follow up after recurrence
1	64	M	Arm	1.5	SC	<1	No	1	No	+	+	-	-	Yes	LEX, NED 48 mos	
2	41	M	Hard palate	3.5	Bone	<1	No	1	No	+	+	+focal	-	Yes	WEX, NED 18 mos	
3	73	M	Mesentery	12	Mesentery	0	No	1	No	+		+		Yes	LEX, RT, NED 11 mos	
4	57	M	Anterior thigh	4	IM	1	No	1	No	+	+	+focal	-	Yes	WLEX, RT, NED 144 mos	
5	35	M	Palate	1.6	Submucosal	<1	No	1	No	+			-		LEX, REC 12 mos	Maxillectomy
6	63	M	Neck	4	IM	4	No	1	No	-		+focal	-			
7	48	M	Scrotum	3 × 2 × 2	Deep	<1	No	1	No	-		-	-	Yes	LEX, REC (unknown interval)	Unknown
8	44	F	Abdominal wall	2.5	SC	1	No	1	No	+focal	-	-		Yes	LEX, positive margin	LEX, NED 24 mos
9	65	M	Tibia	11	Bone	6	No	1	No	+focal	+focal	-			EXC, REC 24 mos	AKA, NED 172 mos
10	54	F	Gingiva	1.5	Submucosal	3	No	1	No	+		-	-		LEX, REC 4 mos	REX; lost to F/U
11	72	F	Breast	3.4	Breast	2	Yes	2	Yes	+	+	+focal	-	Yes	LEX, REC 5 mos	Mastectomy, Metastases (lung), 12 mos
12	69	M	Leg	U	IM	1	Yes	2	Yes	+	+	+focal	-	Yes	WLEX, Chemo-therapy, REC 8 mos	RT, further REC at 70 mos, amputation
13	33	M	Arm	U	SC/IM	11	No	2	Subend	+	+	-	-			
14	42	M	Axilla	5	SC	4	Yes	2	No	+		-	-		LEX, NED 36 mos	
15	36	F	Base Skull	3	Bone	<1	Yes	2	No	+	-	-	-	Yes	LEX, REC 18 mos	REX; NED 36 mos
						Total 13/15	Total 7/9	Total 6/14	Total 0/11							

Apo; aponeurosis; CK, cytokeratin (see *Methods* for subtypes); DES, desmin; DOD, dead of disease; EM, electron microscopy; IHC, immunohistochemistry; IM, intramuscular; INV, invasion; LEX, local excision; MSA, muscle-specific actin; NED, no evidence of disease; REC, recurrence; REX, re-excision; RT, radiation therapy; SC, subcutaneous; SMA, smooth muscle actin; Subend, subendothelial proliferation; TX, treatment; U, unknown; WLEX, wide local excision.

Sarcoma miofibroblástico bajo grado

Mentzel et al. 2006

- **Adultos**
- **Extremidades, cabeza y cuello (lengua, oral), piel, digestivo, gl. salivares, nasal/paranasal**
- **Crecimiento infiltrativo difuso por fascículos fusocelulares, generalmente muy celulares, con moderada atipia (nucleos grandes e hipercromáticos) y mitosis frecuentes**
- **Una fracción de proliferación alta y necrosis tumoral se asocian con una mayor agresividad clínica**
- **Immunofenotipo:**
 - **actina +/-desmina-**
 - **actina- /desmina+**
 - **actina+/desmina+**
 - **fibronectina +**
 - **CD34+**
 - **CD99+ (citoplásmico)**
 - **h-caldesmon, β -catenina, S-100 y CK : negativas**

Miofibrosarcoma

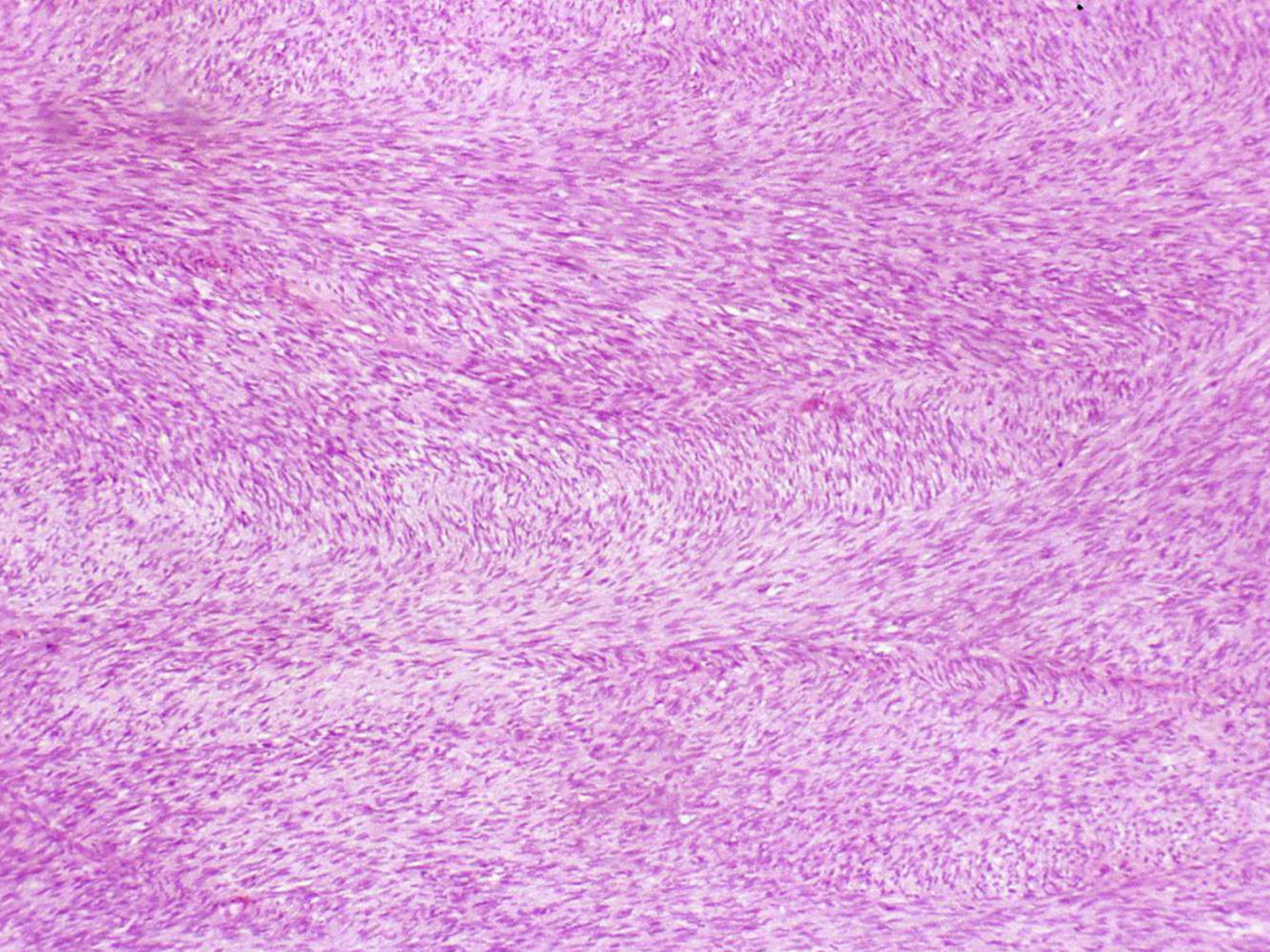
Fascículos de células fusiformes de extremos más afilados que redondeados, orientados perpendicularmente, filamentos citoplásmicos eosinófilos delicados y vacuolas paranucleares
Positivas: actina, fibronectina, calponina y, a veces, desmina

Negativas: h-caldesmon y miosina de músculo liso

Rasgos ultraestructurales de miofibroblastos

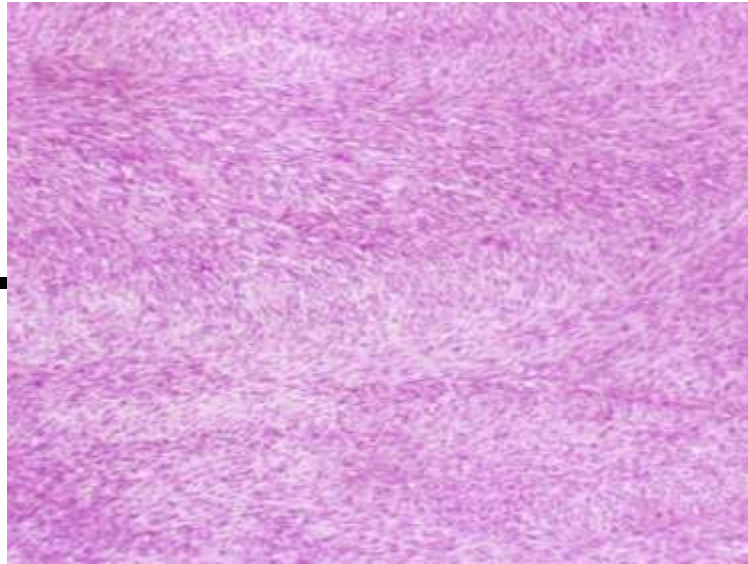
D. Diferencial: Fibrosarcomas*

However, indistinguishable cases are inevitable as fibroblasts and myofibroblasts form a morphologic continuum.



DFSP-Fibrosarcoma

Superficial



FS-infantil

Miofibrosarcoma

Profundo

S Sinovial

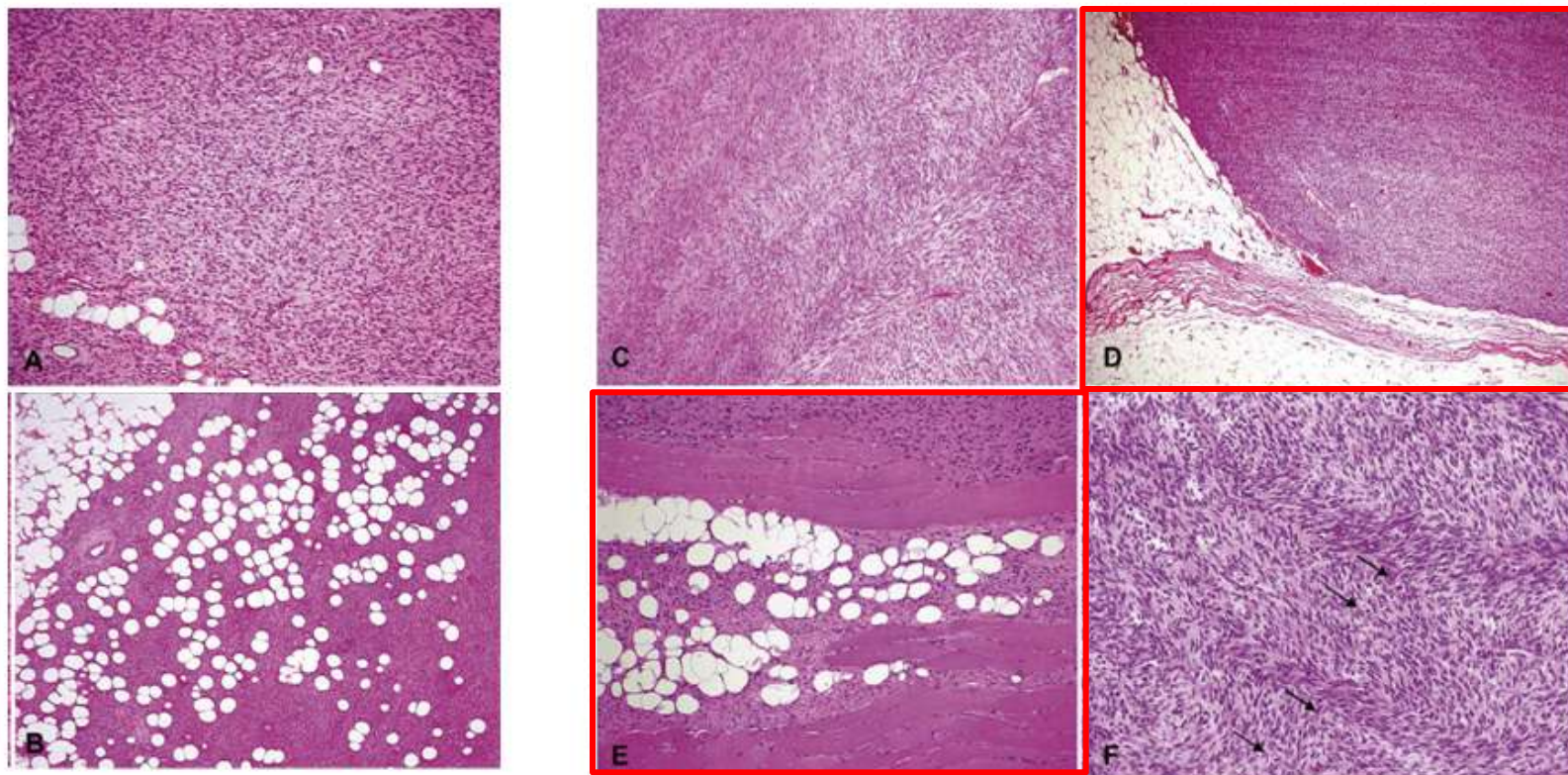
T M Vaina

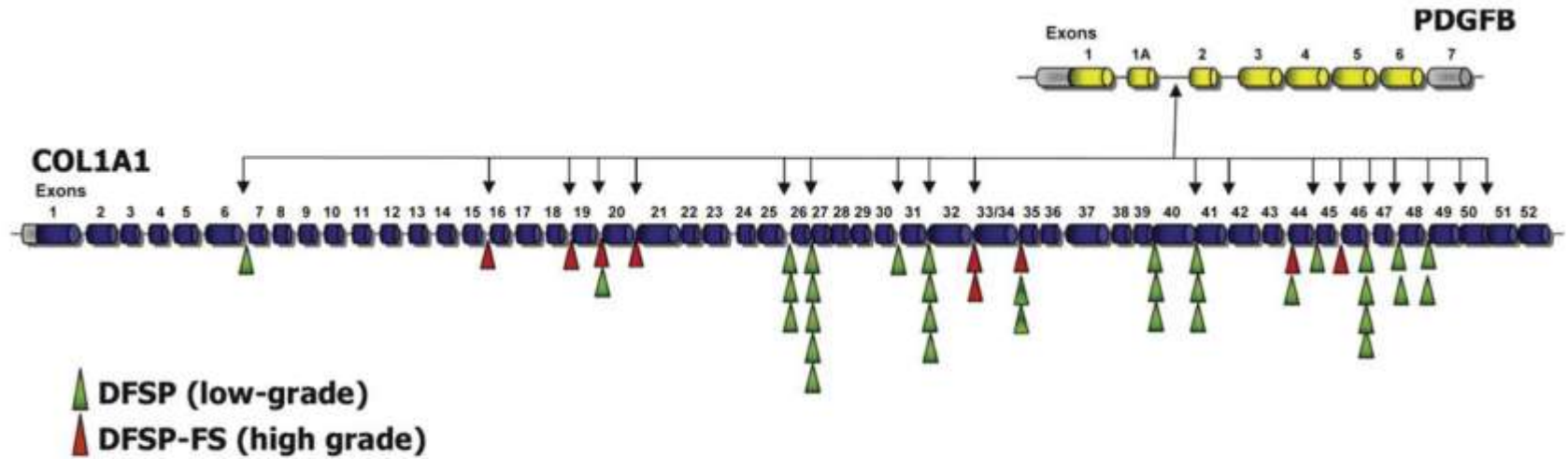
Nerviosa Perif

Transformación fibrosarcomatosa del dermatofibrosarcoma protuberans

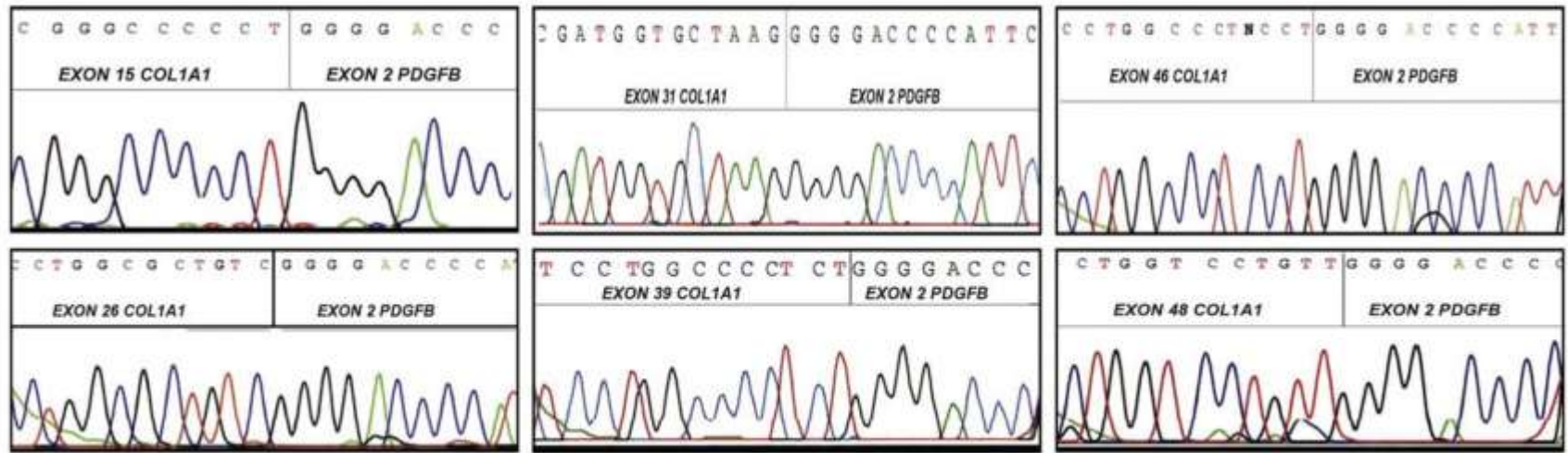
Dermatofibrosarcoma protuberans: A clinicopathological, immunohistochemical, genetic (*COL1A1-PDGFB*), and therapeutic study of low-grade versus high-grade (fibrosarcomatous) tumors

Beatriz Llombart, MD,^{a,d} Carlos Monteagudo, MD,^d Onofre Sanmartín, MD,^a José Antonio López-Guerrero,^b
Carlos Serra-Guillén, MD,^a Andrés Poveda, MD,^c Esperanza Jorda, MD,^c Antonio Fernandez-Serra,^b
Antonio Pellín, MD,^d Carlos Guillén, MD,^a and Antonio Llombart-Bosch, MD^d
Valencia, Spain

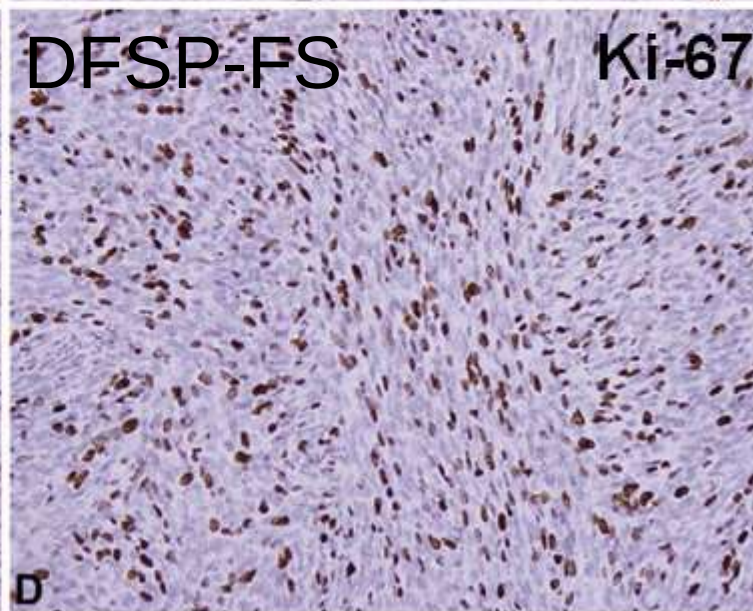
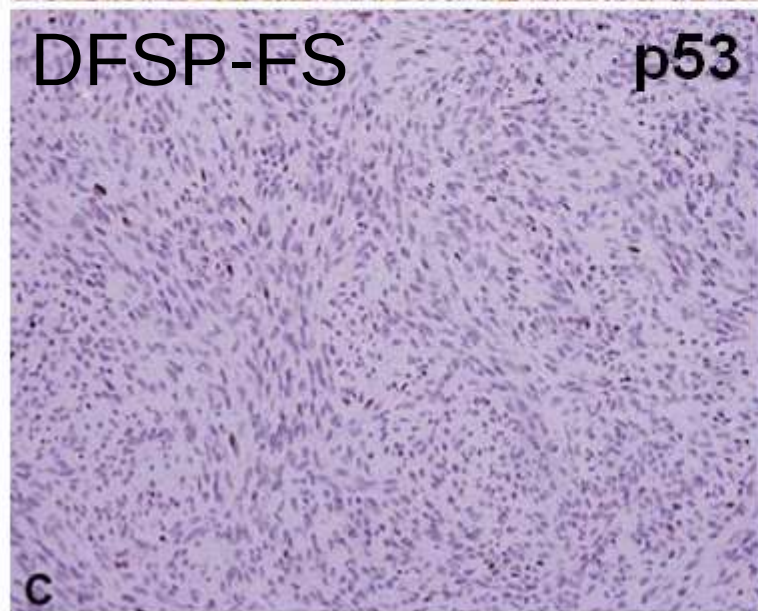
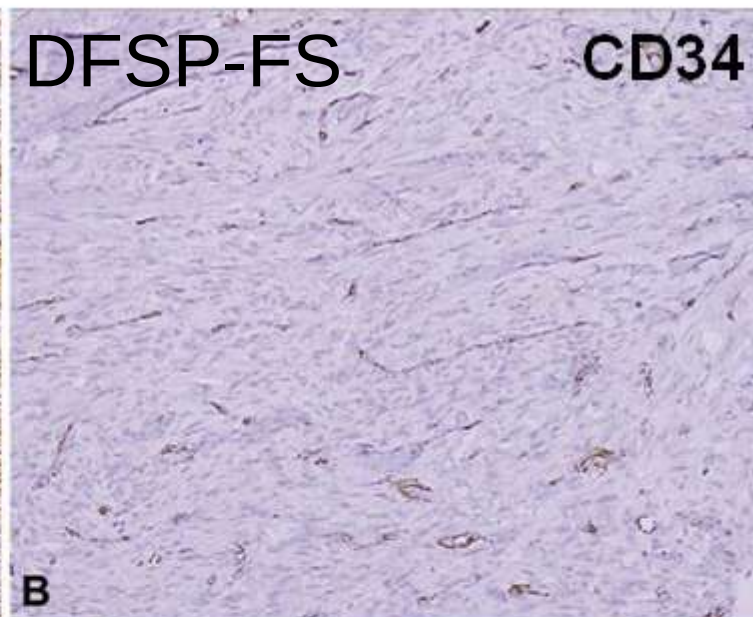
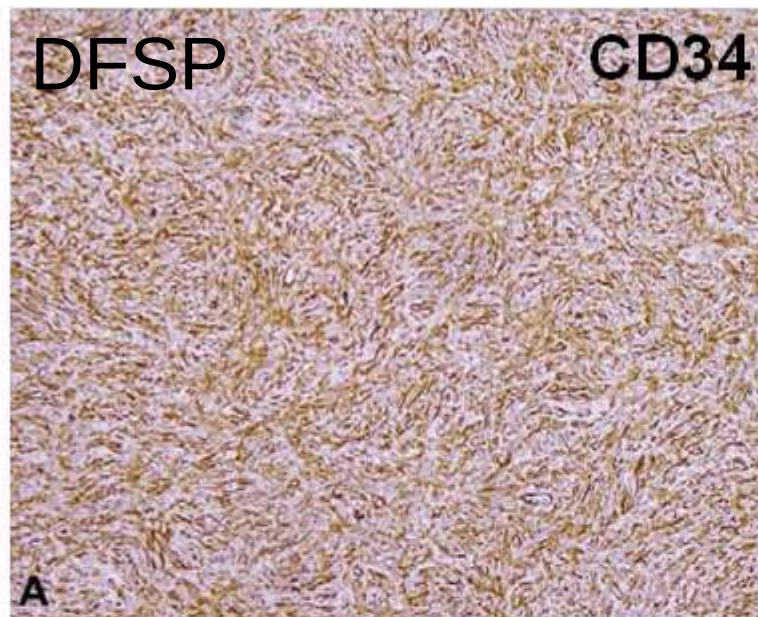


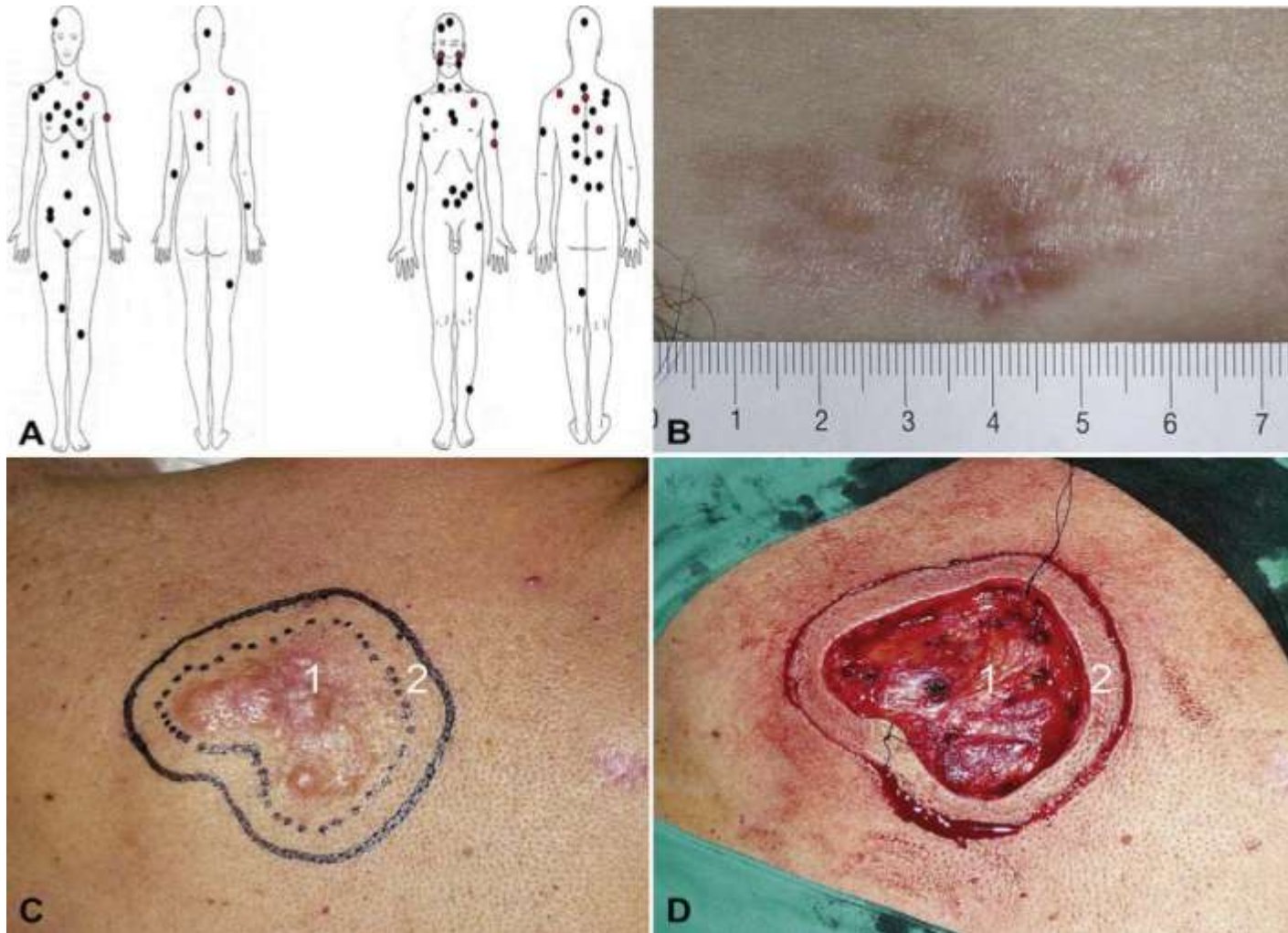


A



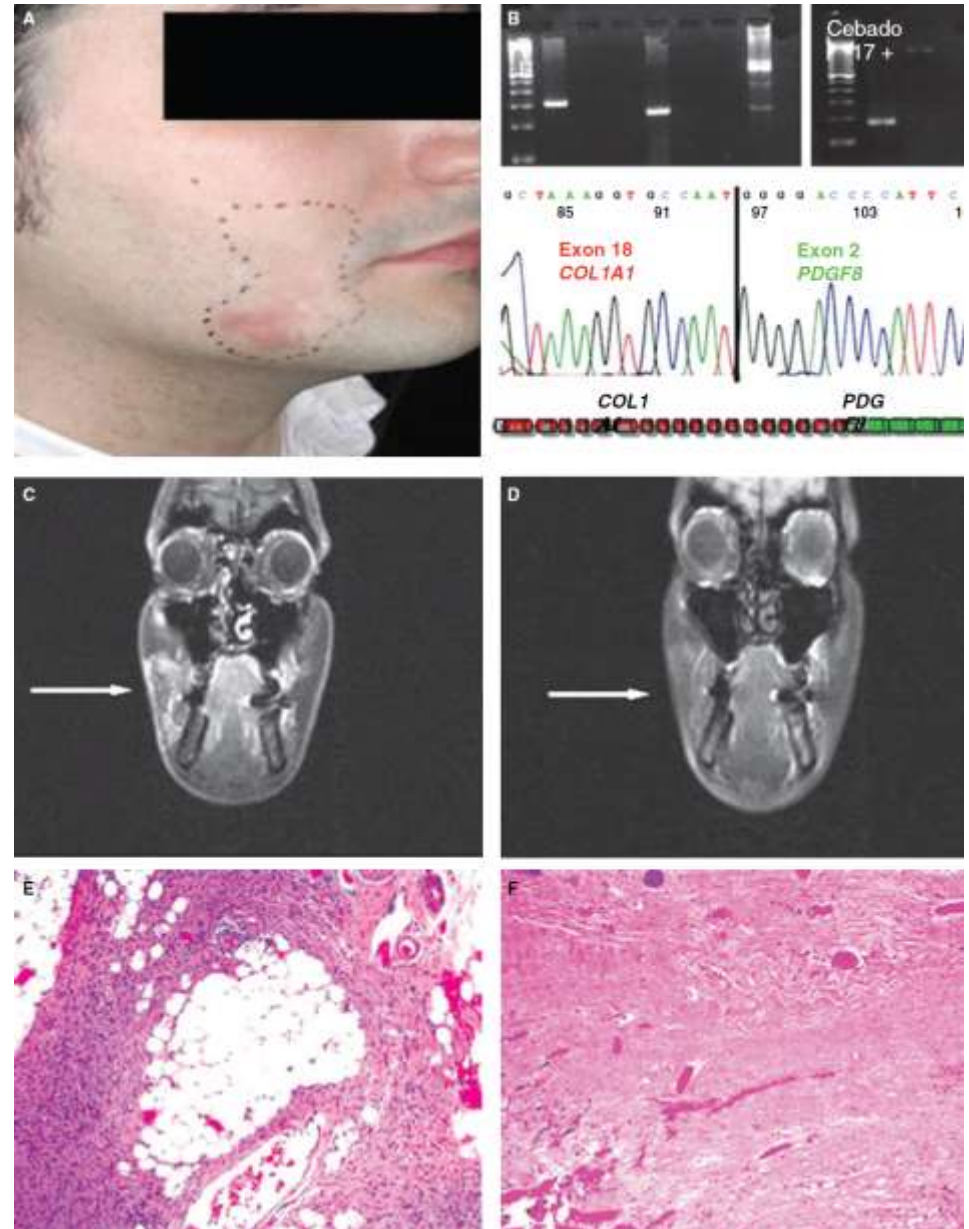
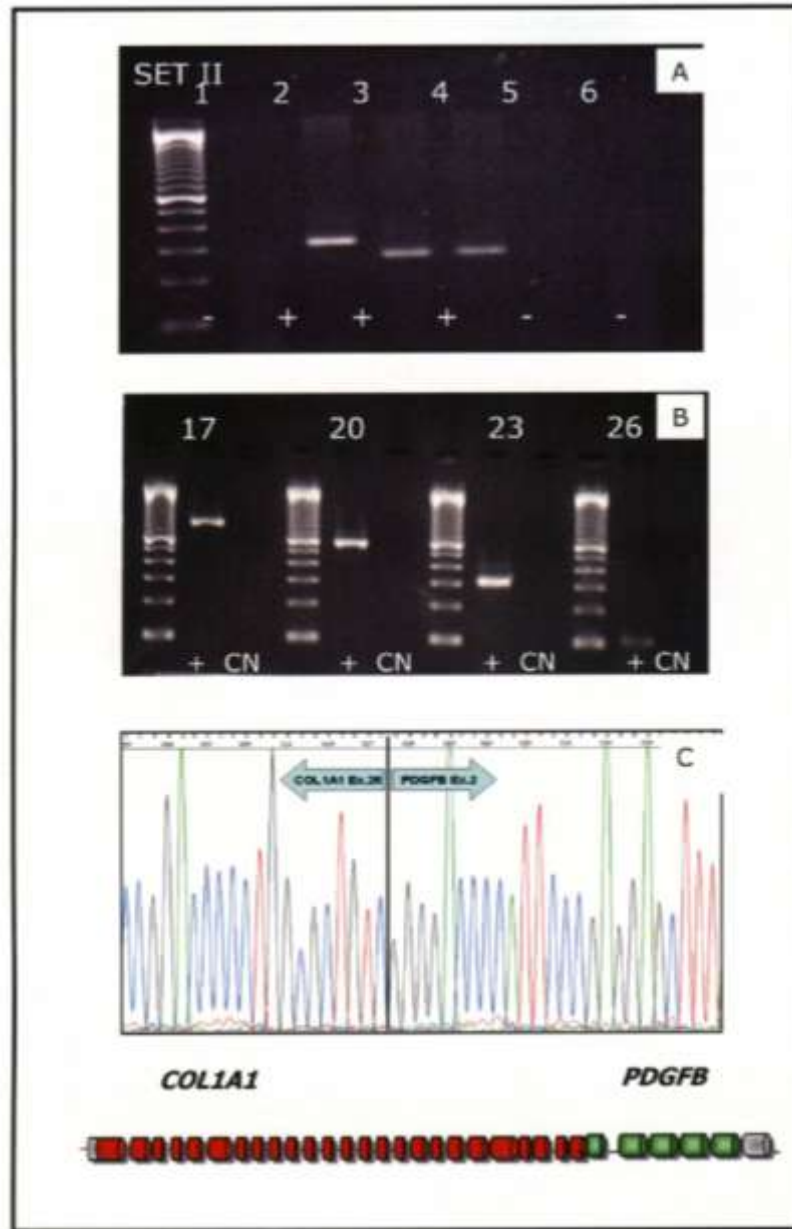
B





La cirugía de Mohs es el tratamiento de elección en todos los casos (no recidivan, salvo los excepcionales casos metastásicos)

Tratamiento con Imatinib



Molecular Diagnosis of Dermatofibrosarcoma Protuberans: A Comparison Between Reverse Transcriptase-Polymerase Chain Reaction and Fluorescence In Situ Hybridization Methodologies

Rocío Salgado,^{1,2†} Beatriz Llombart,^{3†} Ramon M. Pujol,⁴ Antonio Fernández-Serra,⁵ Onofre Sanmartín,³ Agustí Toll,⁴ Luis Rubio,⁵ Sonia Segura,⁴ Carlos Barranco,¹ Carlos Serra-Guillén,³ Mireia Yébenes,⁶ Marta Salido,¹ Víctor Traves,⁷ Carlos Monteagudo,⁸ Empar Sáez,⁹ Teresa Hernández,¹⁰ Enrique de Álava,¹⁰ Antonio Llombart-Bosch,⁸ Francesc Solé,¹ Carlos Guillén,³ Blanca Espinet,^{1‡*} and Jose A. López-Guerrero^{5‡}

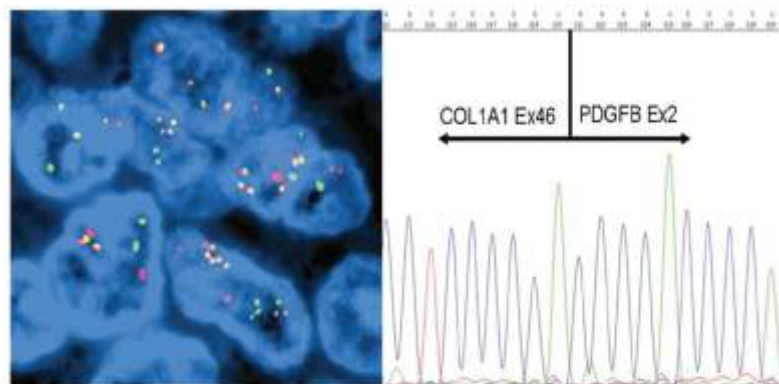


TABLE 3. Comparison of *COL1A1*/*PDGFB* Detection Between FISH and RT-PCR Techniques: Results of the Performance Test

	FISH (<i>n</i> = 106) ^a (%)	RT-PCR (<i>n</i> = 92) ^b (%)
Sensitivity	91	72
Specificity	100	100
PPV	100	100
NPV	53	30

PPV: positive predictive value; NPV: negative predictive value.

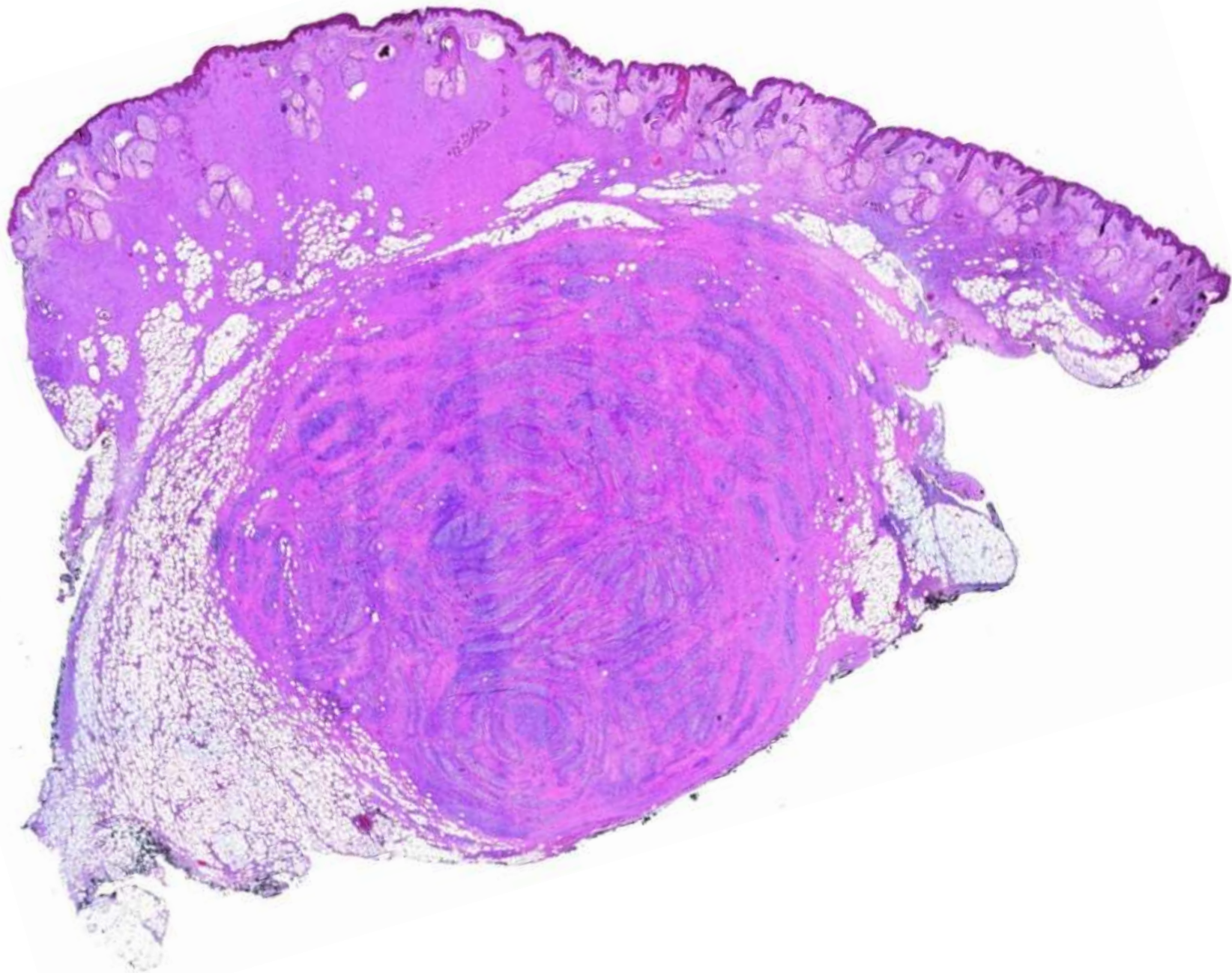
TABLE 2. Comparison of *COL1A1*/*PDGFB* Detection Between FISH and RT-PCR Techniques: Data for the Performance Test

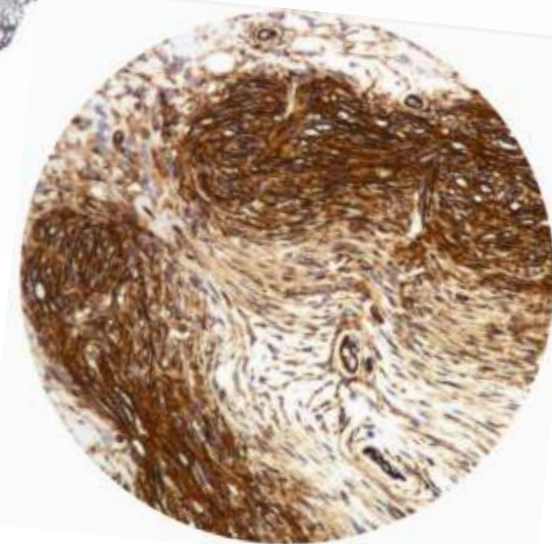
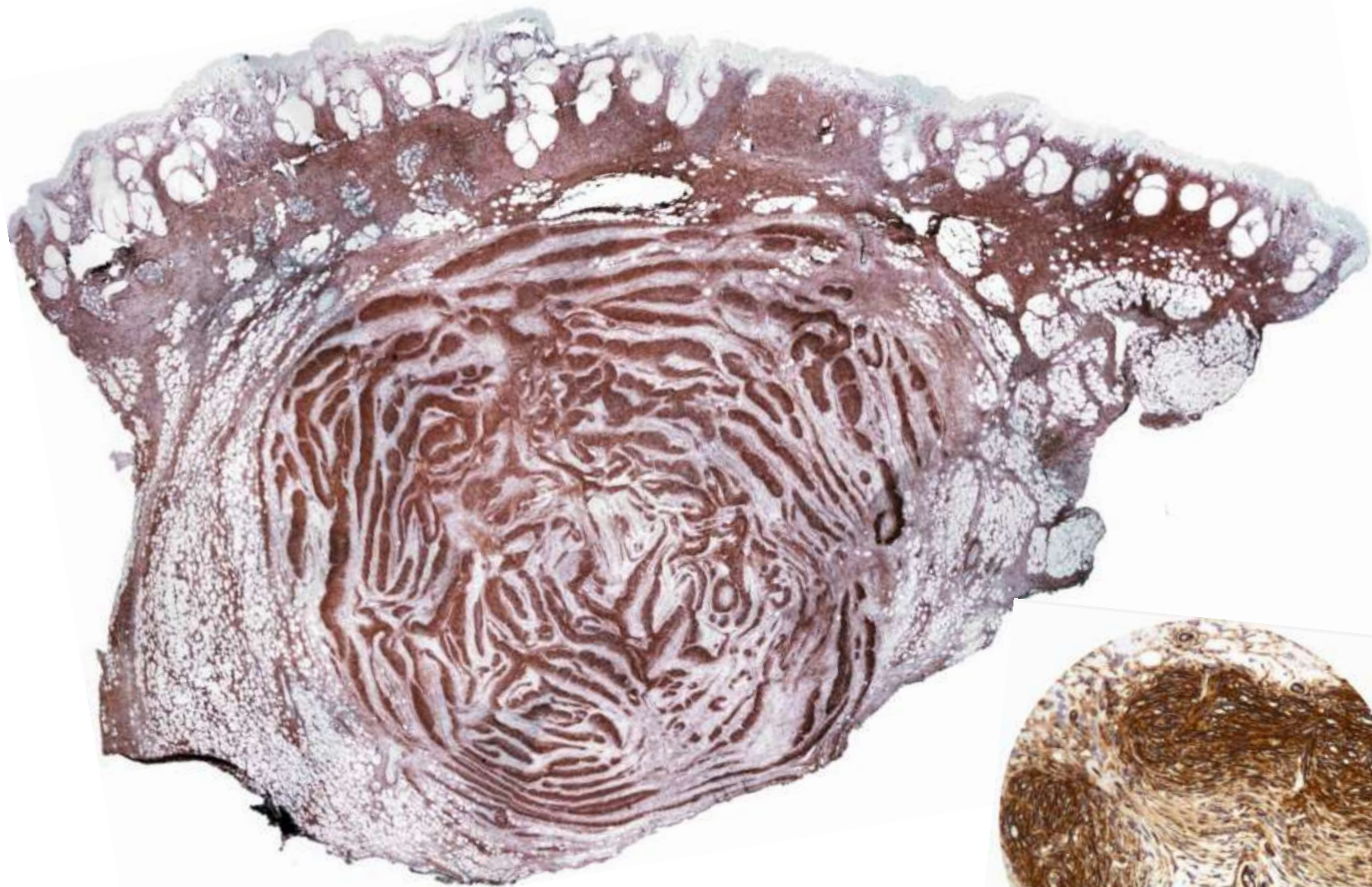
Molecular status FISH/RT-PCR	DFSP (<i>n</i> = 99) ^b	No DFSP (<i>n</i> = 10)
FISH+/RT-PCR+ (positive concordance)	54	0
FISH+/RT-PCR ni ^a	14	0
FISH ni/RT-PCR+	1	0
FISH-/RT-PCR- (negative concordance)	2	10
FISH-/RT-PCR ni	3	0
FISH ni/RT-PCR-	2	0
Discordant	23	0
FISH+/RT-PCR-	19	0
FISH-/RT-PCR+	4	0

^ani: noninformative.

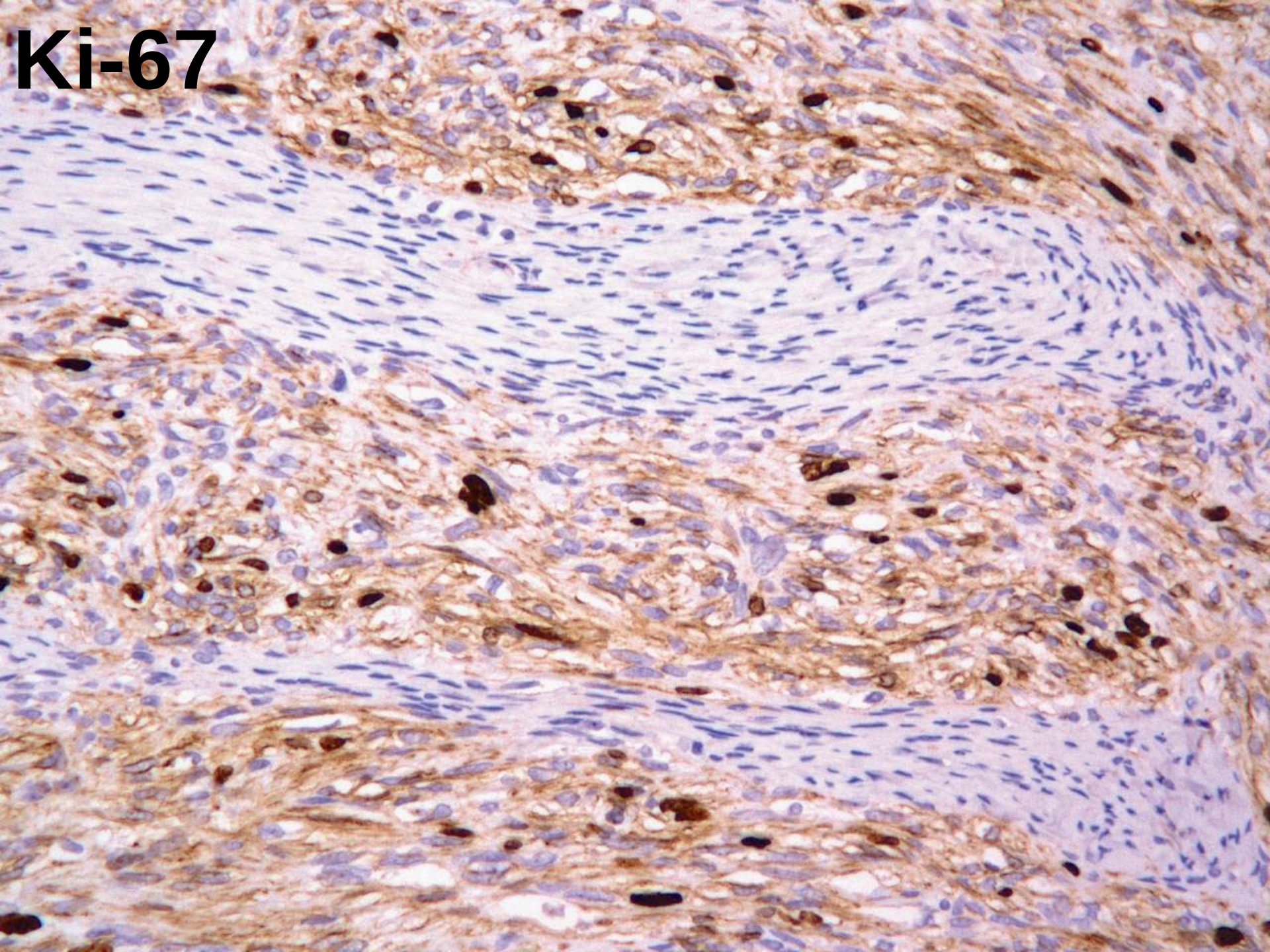
^bNoninformative cases for FISH and RT-PCR techniques (*n* = 4) are not reported in this table.

- En el DFSP-fibrosarcoma se detecta por FISH un mayor porcentaje de células con la fusión génica que en los restantes subtipos ($p < 0,001$)
- Todos los casos de DFSP-fibrosarcoma y DFSP negativos para CD34 presentaron la fusión COL1A1-PDGFB, tanto por PCR como por FISH

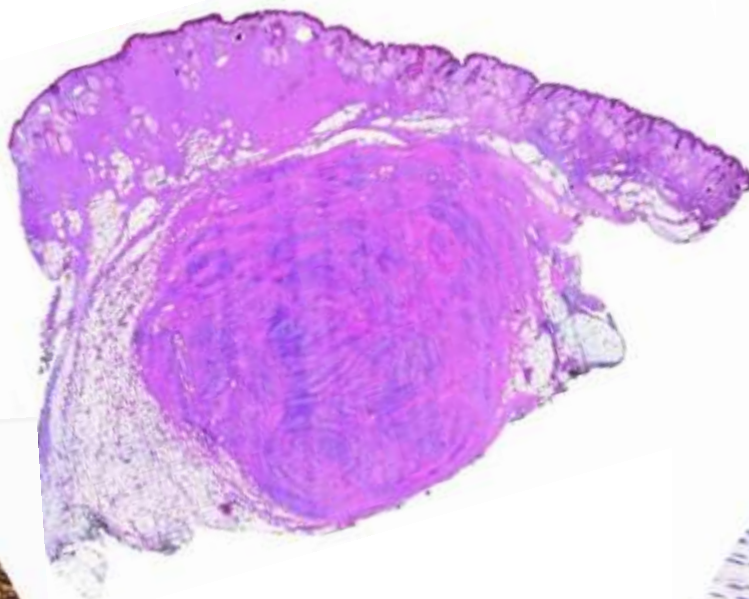
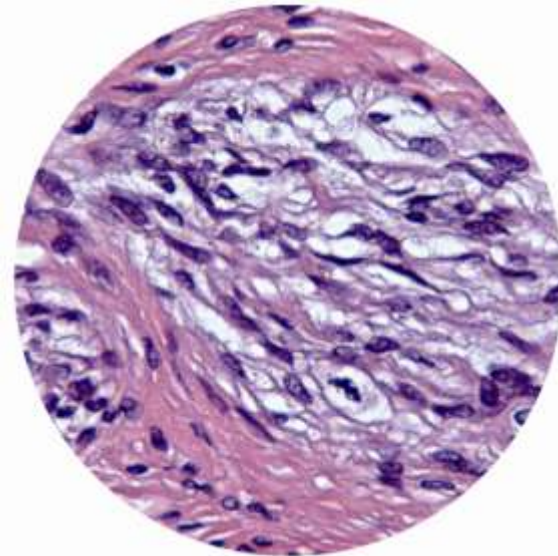
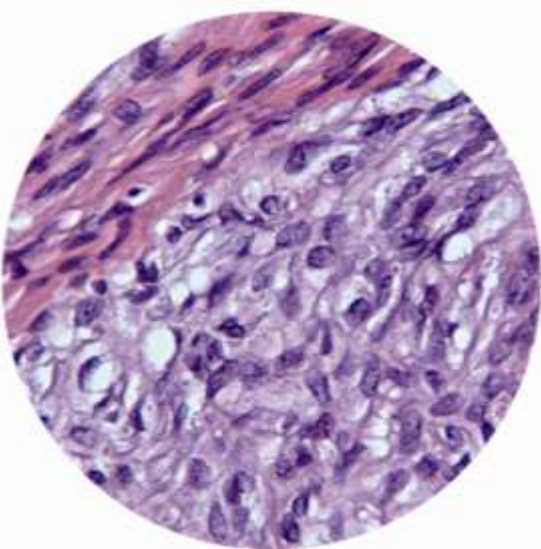




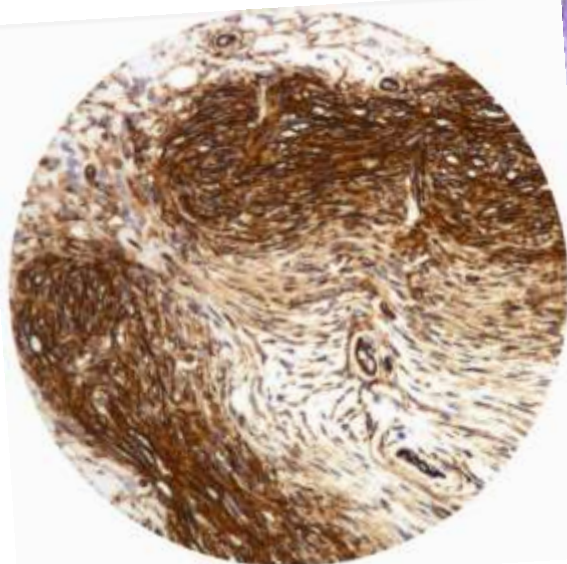
CD34



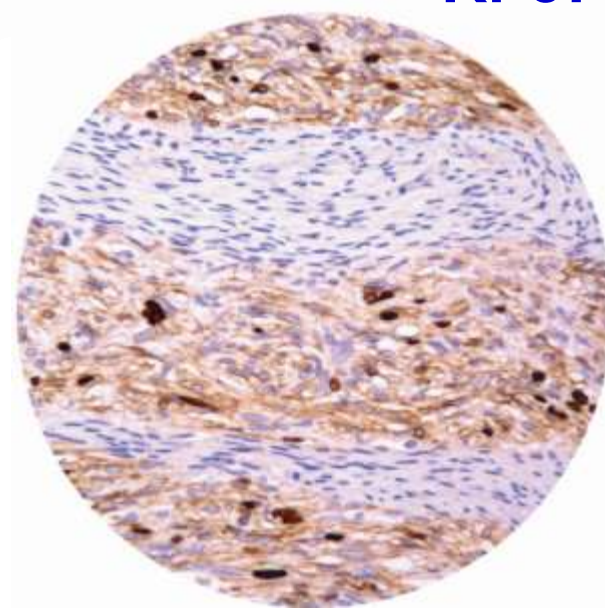
Ki-67

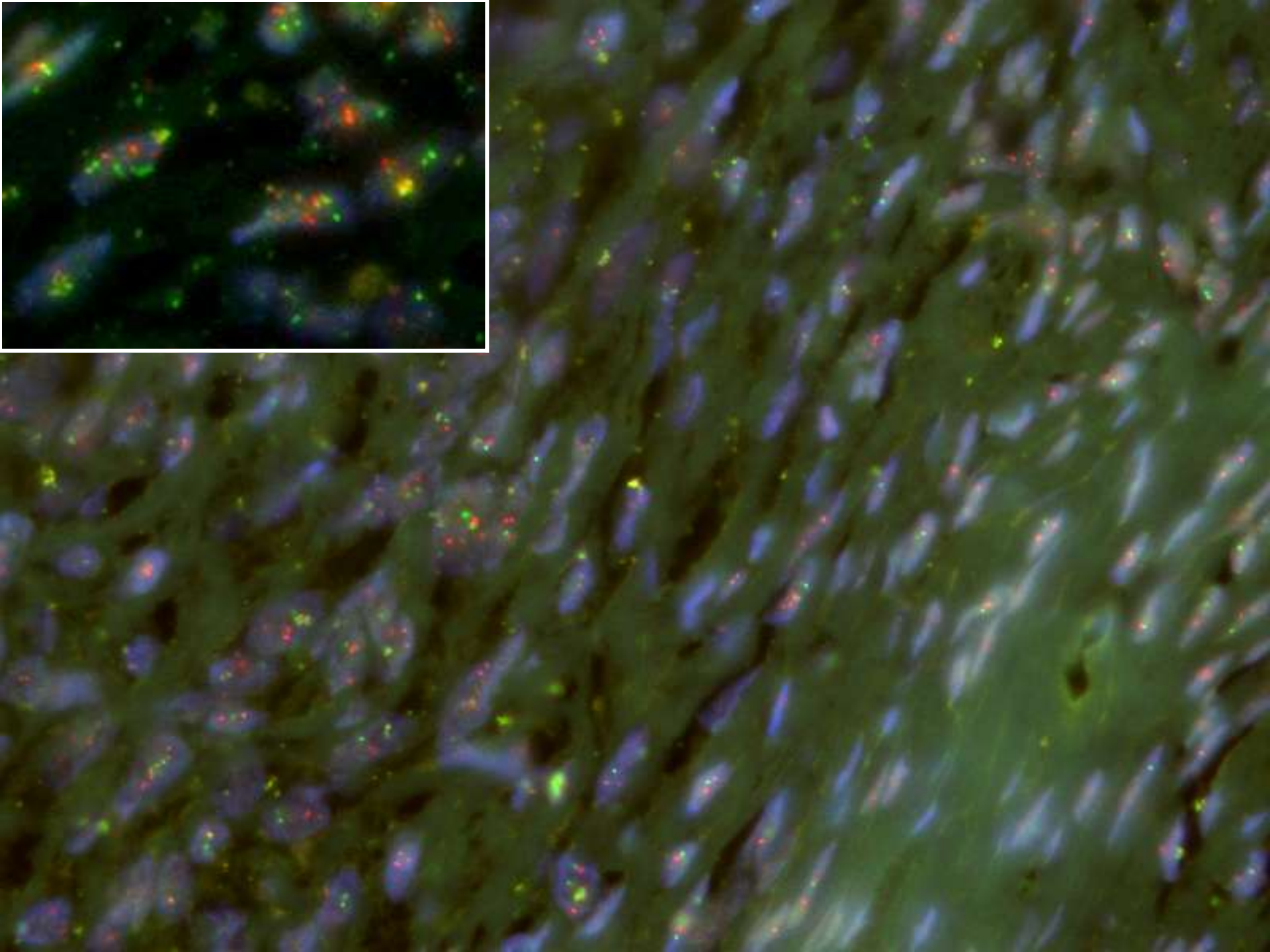
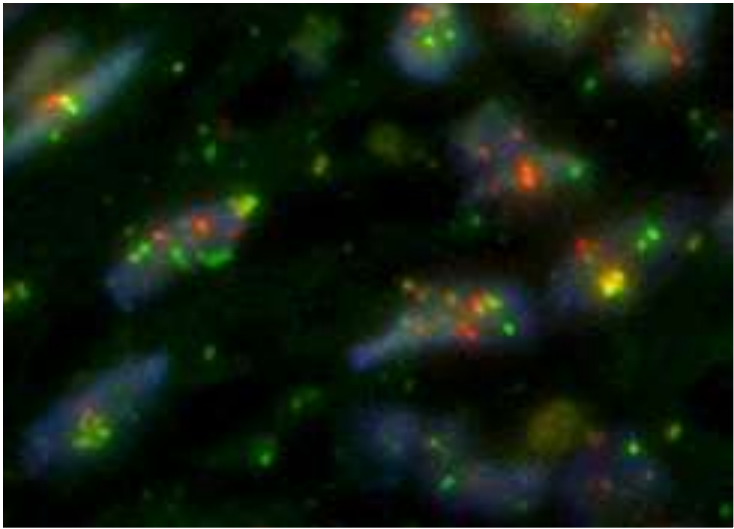


CD34



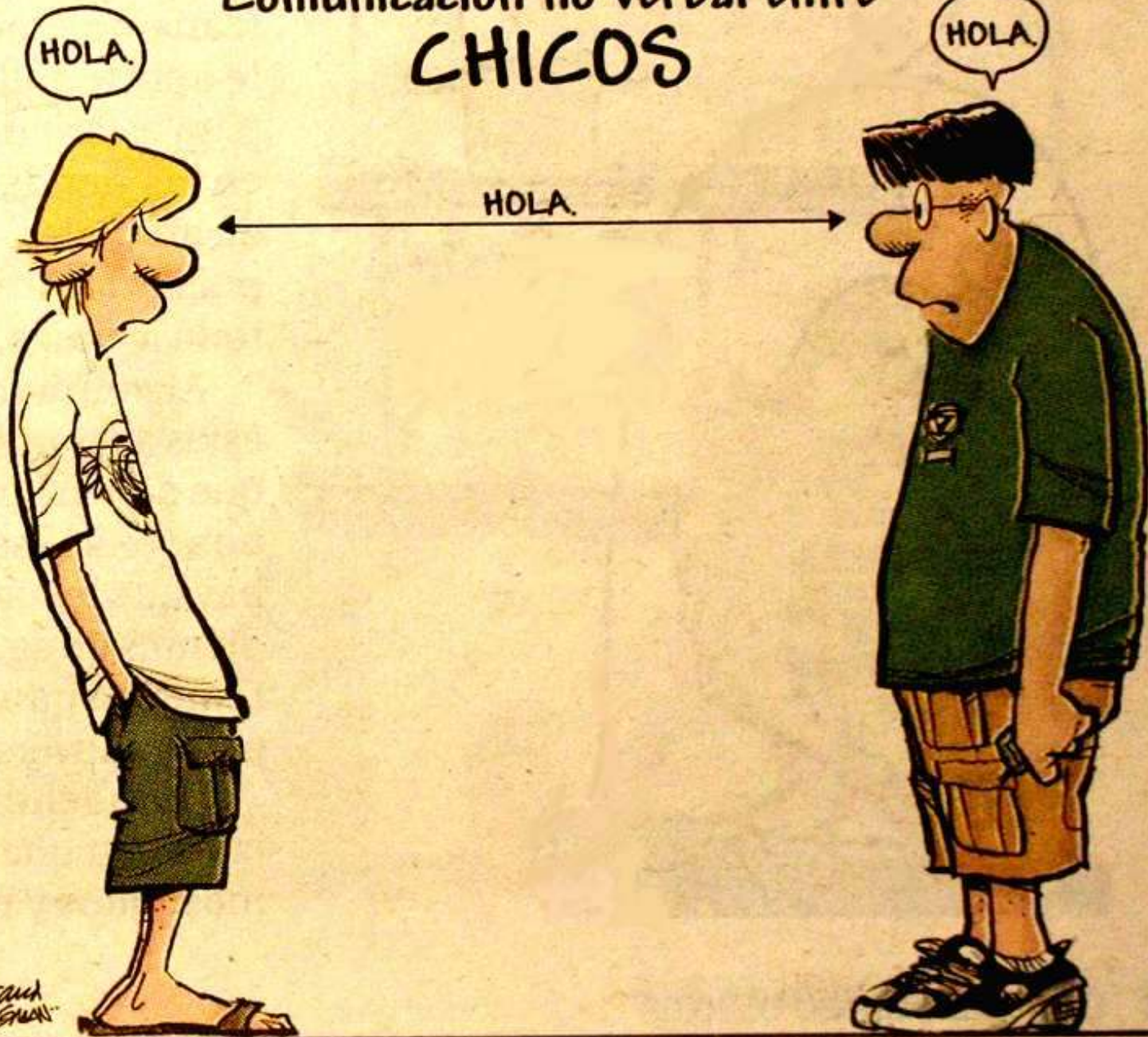
Ki-67





Reflexión final...
cuando tenemos delante un
caso difícil,
hay dos posibles actitudes...

Comunicación no verbal entre **CHICOS**



Comunicación no verbal entre CHICAS

