Memorial Sloan Kettering Cancer Center

Keeping track amidst an explosion of data: What is new in mesenchymal neoplasia

By Konstantinos Linos MD, FCAP, FASDP
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Associate Attending
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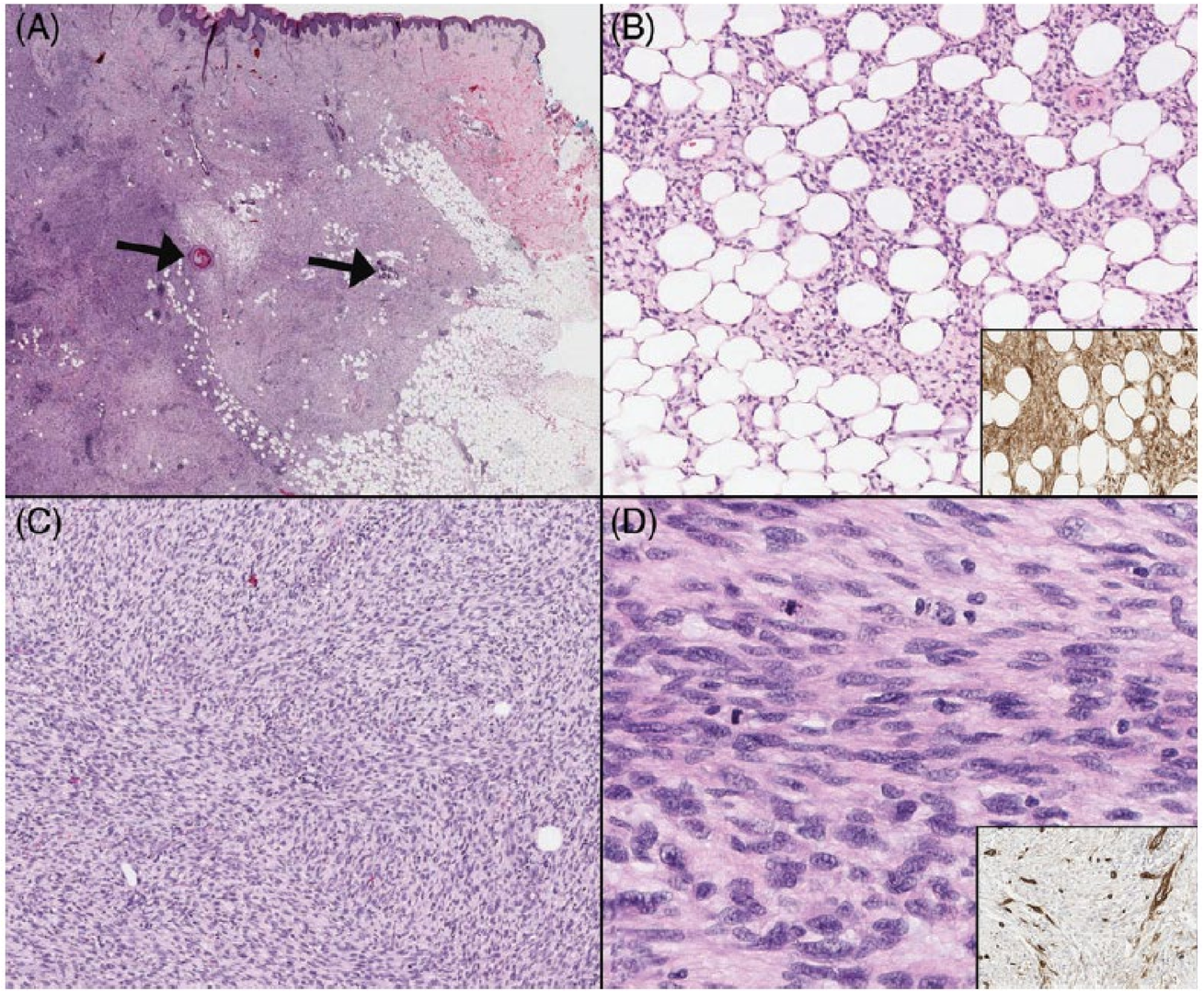
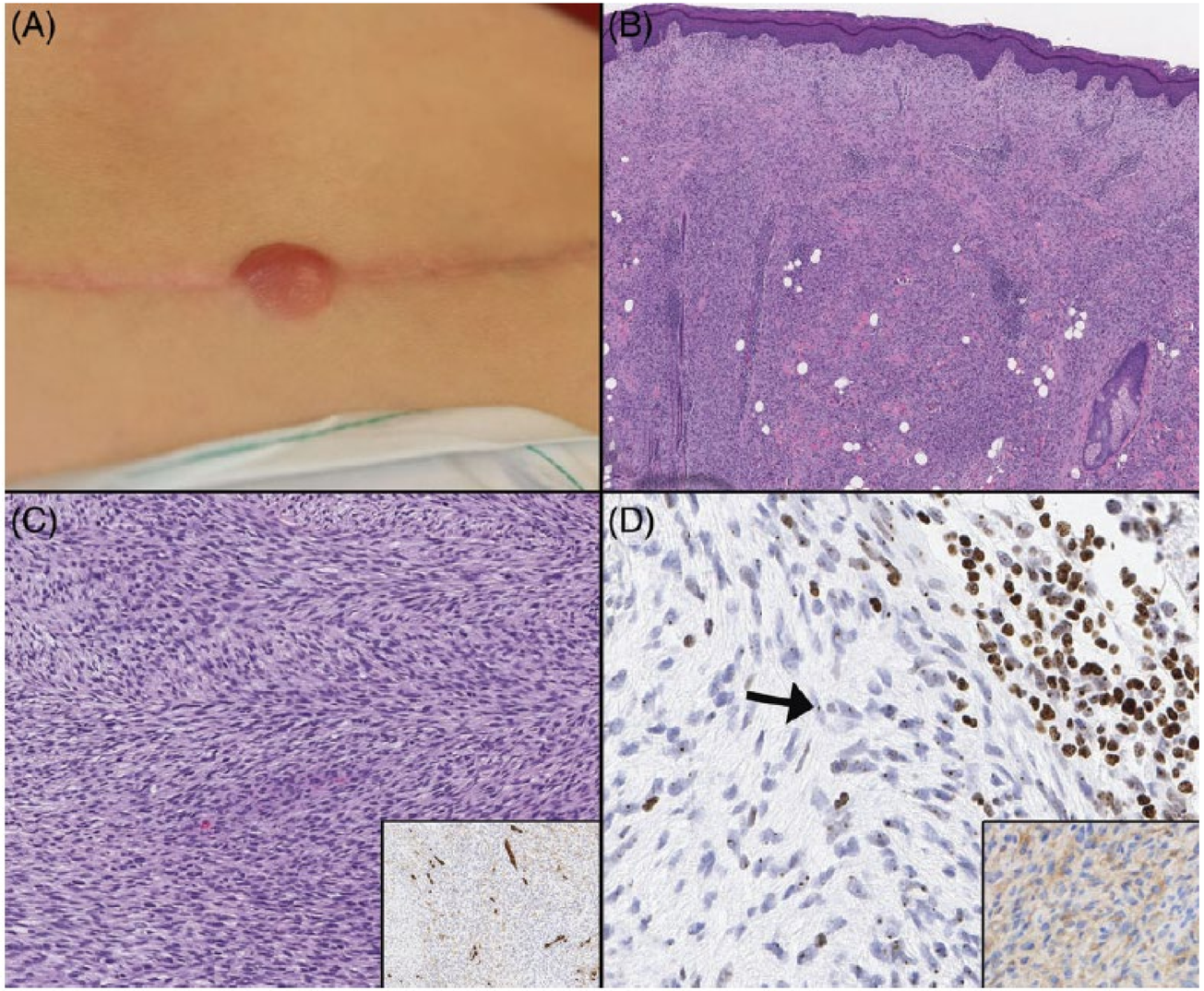
Mesenchymal Neoplasms with *NTRK* fusions



J Cutan Pathol. 2018;45:933–939.



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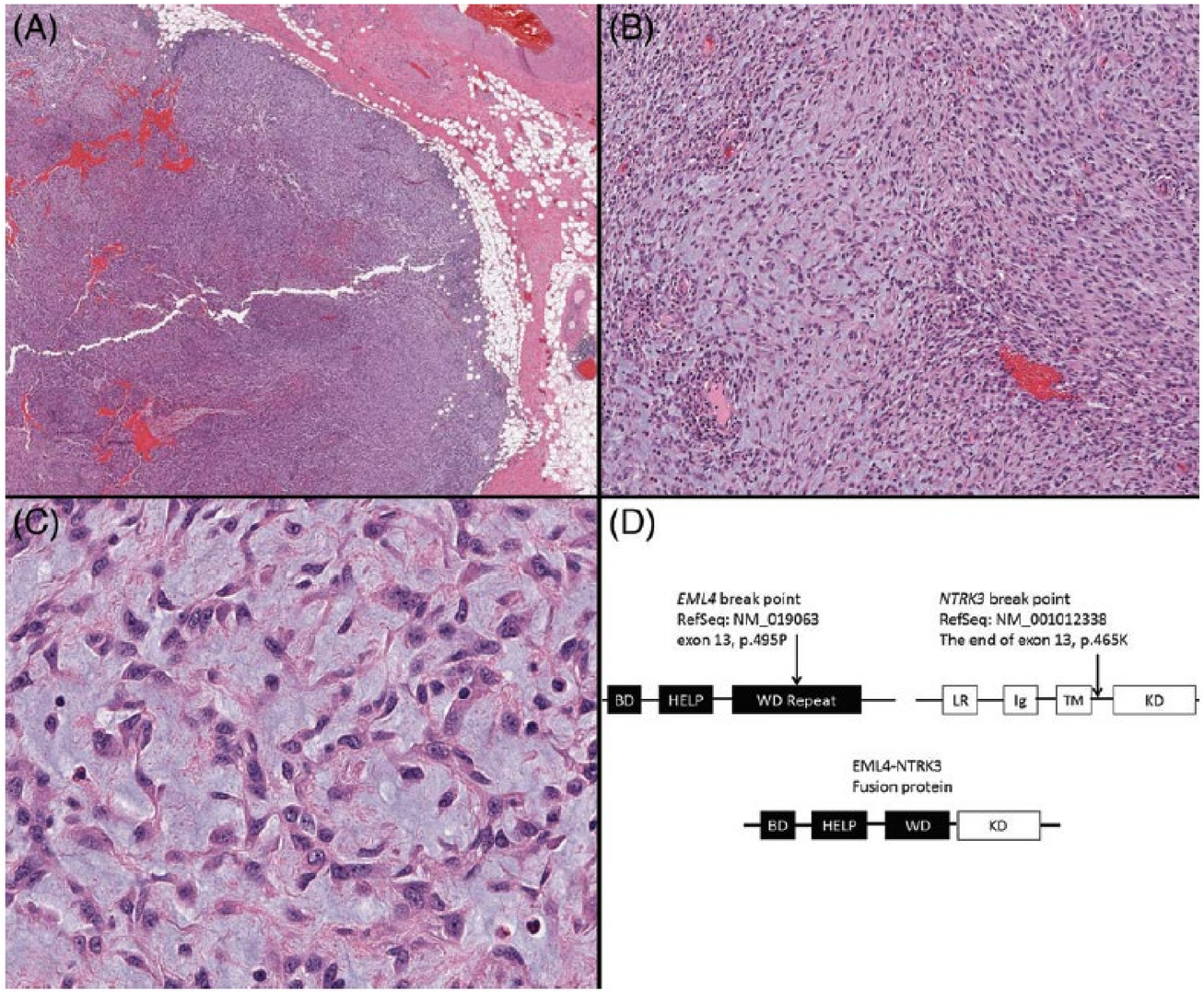

J Cutan Pathol. 2018;45:933–939.

WILEY JOURNAL OF CUTANEOUS PATHOLOGY

CASE REPORT

A novel case of an aggressive superficial spindle cell sarcoma in an adult resembling fibrosarcomatous dermatofibrosarcoma protuberans and harboring an *EML4-NTRK3* fusion

Nicholas Olson[1] | Omid Rouhi[2] | Linsheng Zhang[2] | Christina Angeles[3] | Julia Bridge[4] | Dolores Lopez-Terrada[5] | Thomas Royce[6] | Konstantinos Linos[1]

J Cutan Pathol. 2018;45:933–939.

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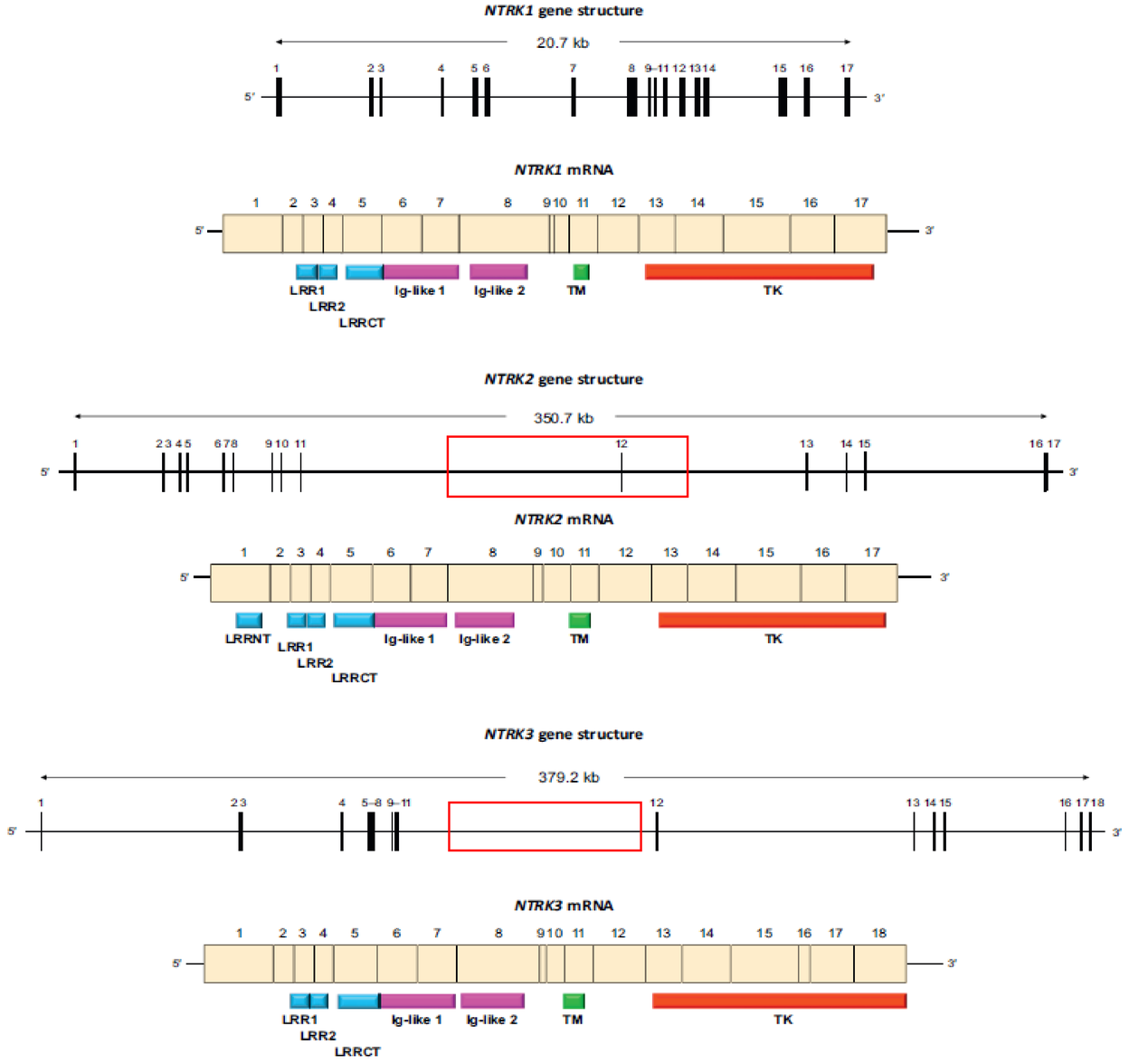
journal homepage: www.elsevier.com/locate/prp

Review

NTRK-Fusions – A new kid on the block

Bruno Märkl[a,*], Klaus Hirschbühl[b], Christine Dhillon[a]

[a] *Institute of Pathology and Molecular Diagnostics, University Clinic Augsburg, Germany*
[b] *II. Medical Clinic, University Clinic Augsburg, Germany*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20.7 kb
1 2 3 4 5 6 7 8 9–11 12 13 14 15 16 17
5′ 3′
NTRK1 mRNA
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
5′ 3′
LRR1
LRR2
LRRCT
Ig-like 1
Ig-like 2
TM
TK
NTRK2 gene structure
350.7 kb
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NTRK2 mRNA
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LRRNT
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LRR2
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Ig-like 1
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NTRK3 gene structure
379.2 kb
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NTRK3 mRNA
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5′ 3′
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LRR2
LRRCT
Ig-like 1
Ig-like 2
TM
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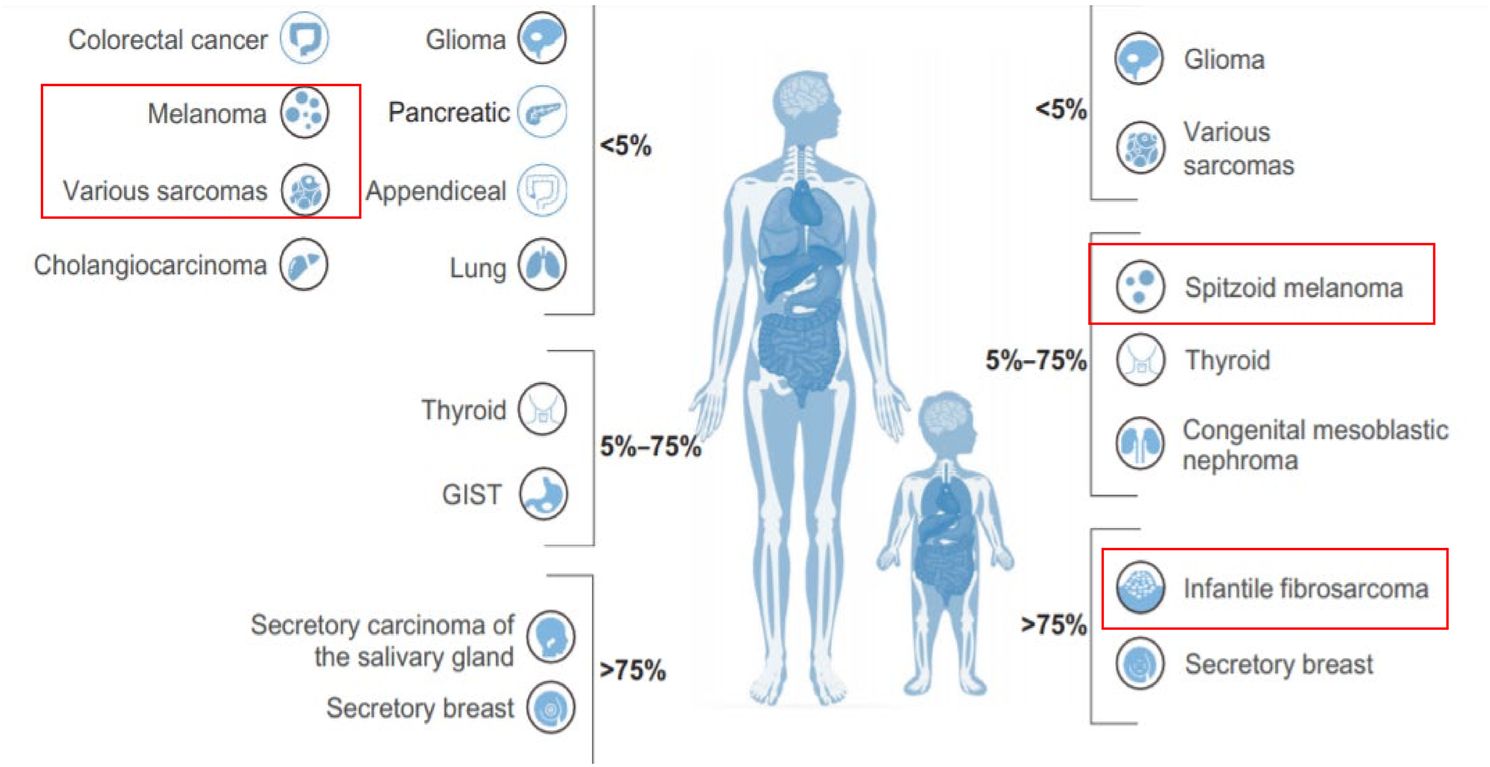


The Journal of Molecular Diagnostics, Vol. 21, No. 4, July 2019

Modern Pathology (2020) 33:38–46
https://doi.org/10.1038/s41379-019-0324-7

ARTICLE

NTRK fusion detection across multiple assays and 33,997 cases: diagnostic implications and pitfalls

James P. Solomon[1] · Irina Linkov[1] · Andrea Rosado[1] · Kerry Mullaney[1] · Ezra Y. Rosen[2] · Denise Frosina[1] · Achim A. Jungbluth[1] · Ahmet Zehir[1] · Ryma Benayed[1] · Alexander Drilon[2,3] · David M. Hyman[2,3] · Marc Ladanyi[1] · Anthony N. Sireci[4] · Jaclyn F. Hechtman[1]

	Number of cases with *NTRK* fusions	Total patients for which molecular testing was performed	Percentage
Salivary gland carcinoma	13	256	5.08%
Thyroid carcinoma	13	571	2.28%
Sarcoma	13	1915	0.68%
Lung adenocarcinoma	9	3993	0.23%
Colorectal carcinoma	9	2929	0.31%
Glioma/neuroepithelial tumor	8	1465	0.55%
Breast carcinoma	6	4458	0.13%
Pancreatic adenocarcinoma	5	1492	0.34%
Melanoma	4	1125	0.36%
Inflammatory myofibroblastic tumor	3	17	17.7%
Cholangiocarcinoma	2	787	0.25%
Appendiceal adenocarcinoma	1	208	0.48%
Neuroendocrine tumor	1	322	0.31%

REVIEW ARTICLE

WILEY

Emerging soft tissue tumors with kinase fusions: An overview of the recent literature with an emphasis on diagnostic criteria

Genes Chromosomes Cancer. 2020;59:437–444

Cristina R. Antonescu

The Journal of Molecular Diagnostics, Vol. 21, No. 4, July 2019

ELSEVIER

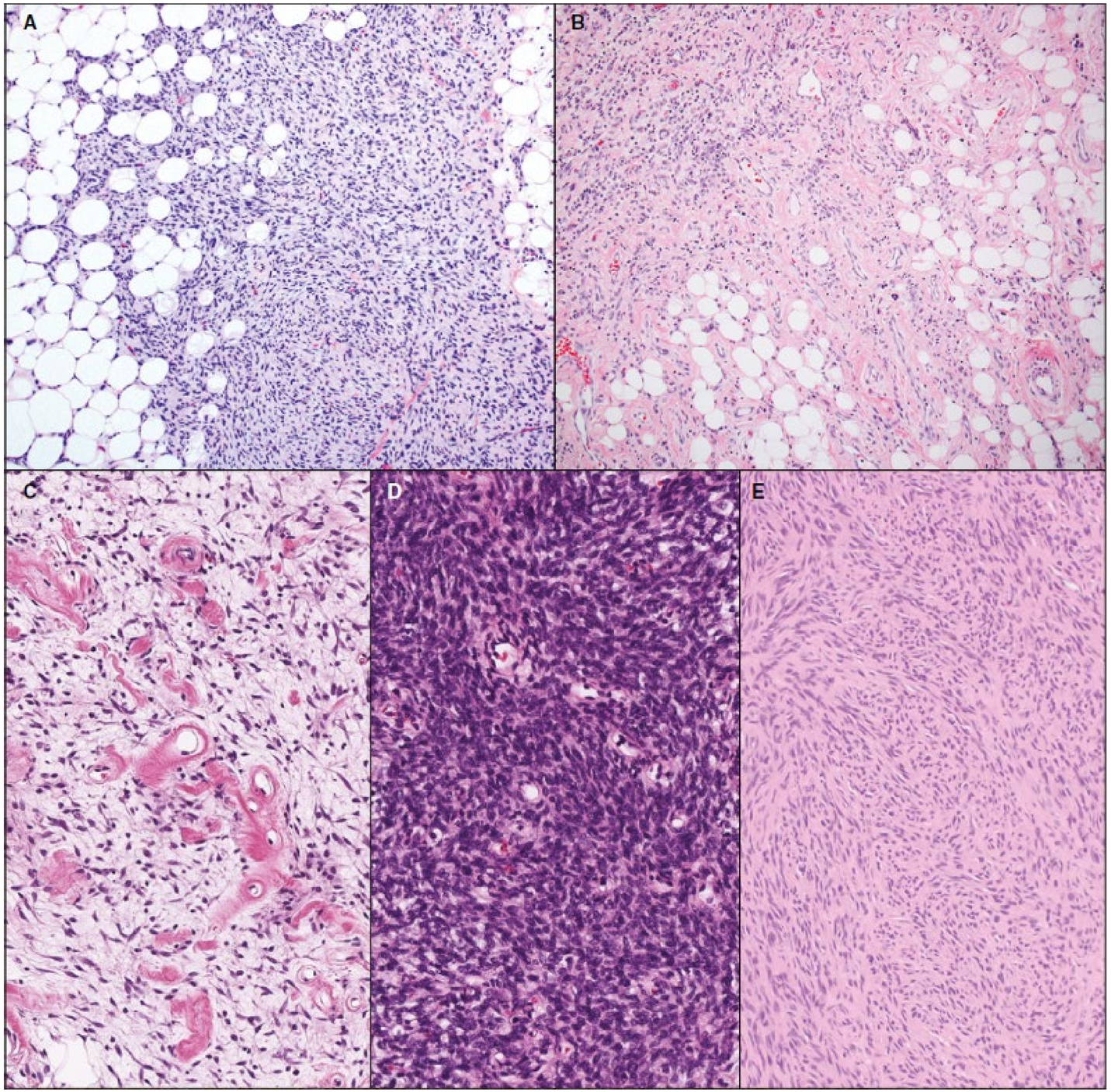
the Journal of Molecular Diagnostics

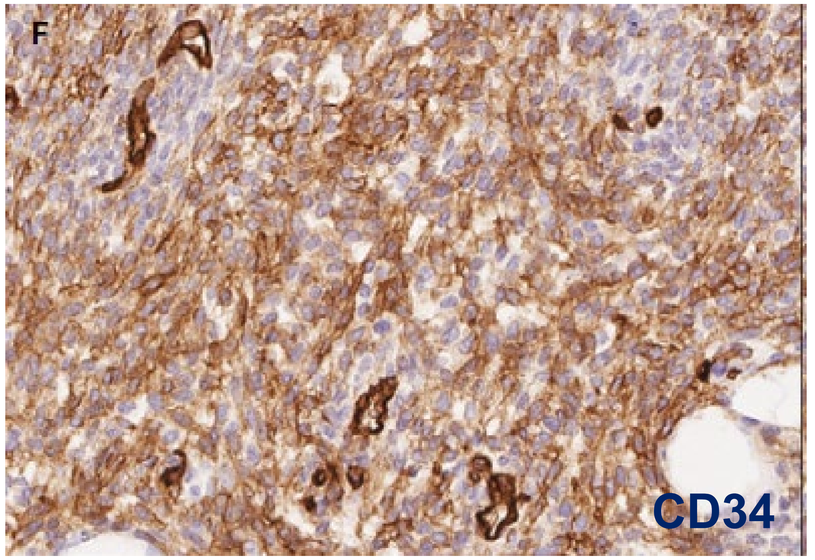
jmd.amjpathol.org

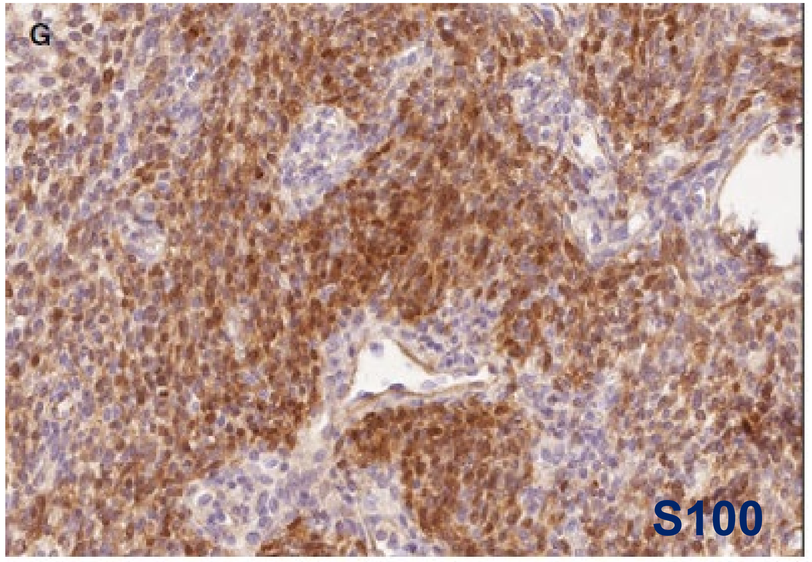
REVIEW

Detection of Tumor *NTRK* Gene Fusions to Identify Patients Who May Benefit from Tyrosine Kinase (TRK) Inhibitor Therapy

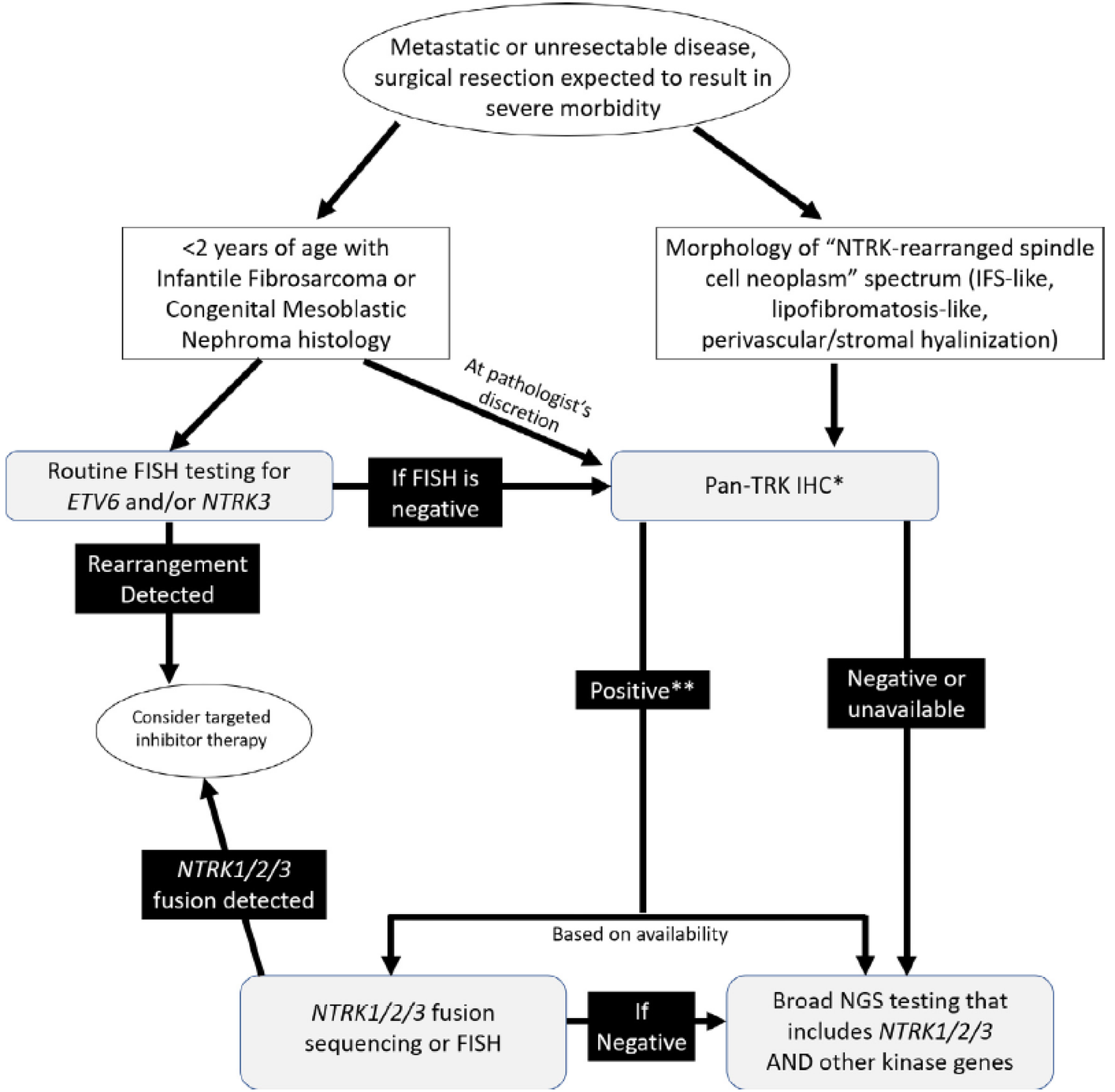
Susan J. Hsiao,* Ahmet Zehir,† Anthony N. Sireci,‡ and Dara L. Aisner§

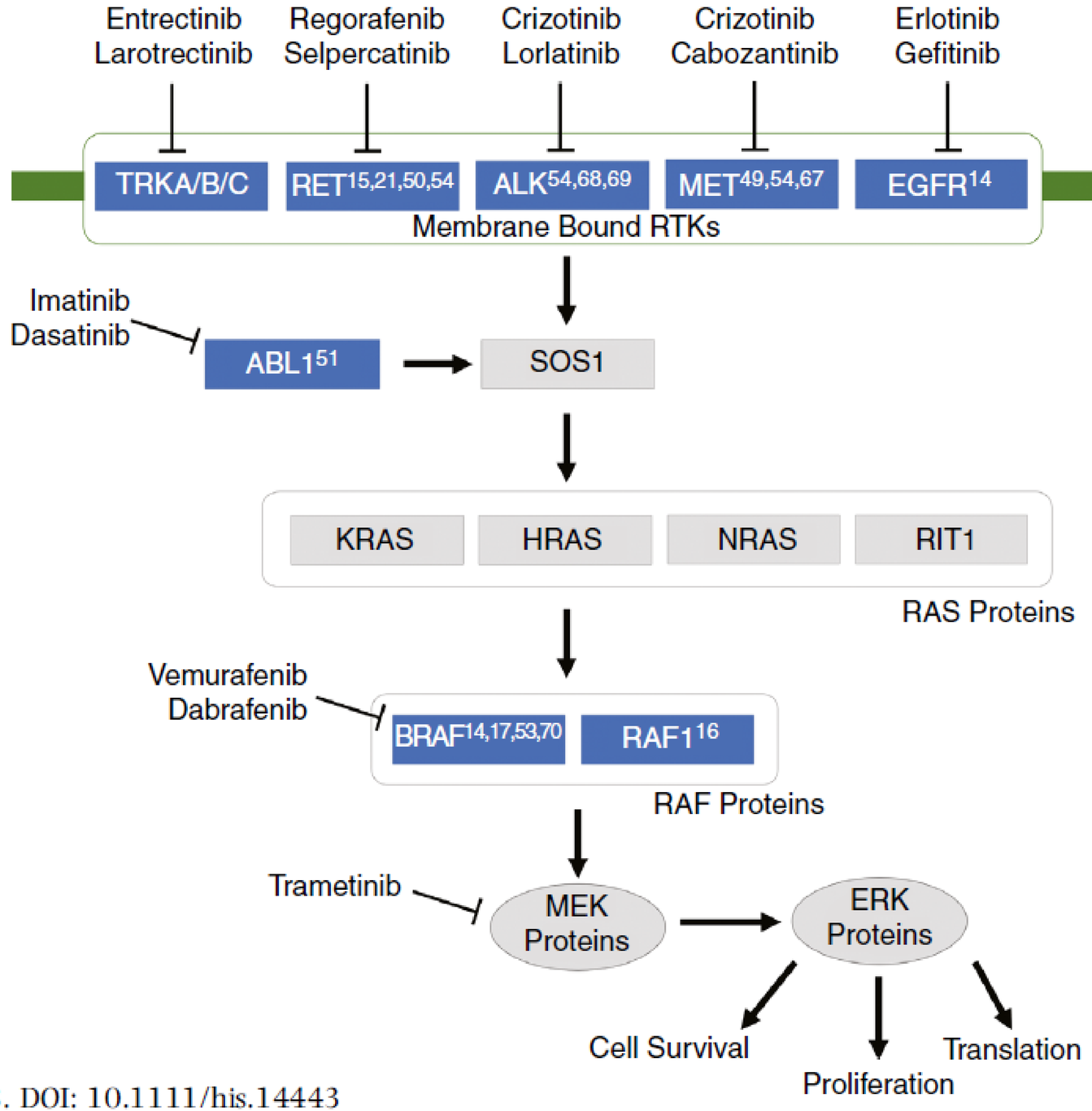






Histopathology 2022, **80**, 4–18. DOI: 10.1111/his.14443


Metastatic or unresectable disease, surgical resection expected to result in severe morbidity
<2 years of age with Infantile Fibrosarcoma or Congenital Mesoblastic Nephroma histology
Morphology of "NTRK-rearranged spindle cell neoplasm" spectrum (IFS-like, lipofibromatosis-like, perivascular/stromal hyalinization)
At pathologist's discretion
Routine FISH testing for ETV6 and/or NTRK3
If FISH is negative
Pan-TRK IHC*
Rearrangement Detected
Positive**
Negative or unavailable
Consider targeted inhibitor therapy
NTRK1/2/3 fusion detected
Based on availability
NTRK1/2/3 fusion sequencing or FISH
If Negative
Broad NGS testing that includes NTRK1/2/3 AND other kinase genes


Entrectinib
Larotrectinib
Regorafenib
Selpercatinib
Crizotinib
Lorlatinib
Crizotinib
Cabozantinib
Erlotinib
Gefitinib
TRKA/B/C
RET15,21,50,54
ALK54,68,69
MET49,54,67
EGFR14
Membrane Bound RTKs
Imatinib
Dasatinib
ABL151
SOS1
KRAS
HRAS
NRAS
RIT1
RAS Proteins
Vemurafenib
Dabrafenib
BRAF14,17,53,70
RAF116
RAF Proteins
Trametinib
MEK
Proteins
ERK
Proteins
Cell Survival
Proliferation
Translation

Larotrectinib for paediatric solid tumours harbouring NTRK gene fusions: phase 1 results from a multicentre, open-label, phase 1/2 study

Theodore W Laetsch, Steven G DuBois*, Leo Mascarenhas, Brian Turpin, Noah Federman, Catherine M Albert, Ramamoorthy Nagasubramanian, Jessica L Davis, Erin Rudzinski, Angela M Feraco, Brian B Tuch, Kevin T Ebata, Mark Reynolds, Steven Smith, Scott Cruickshank, Michael C Cox, Alberto S Pappo*, Douglas S Hawkins**

www.thelancet.com/oncology **Vol 19 May 2018**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of Larotrectinib in *TRK* Fusion–Positive Cancers in Adults and Children

A. Drilon, T.W. Laetsch, S. Kummar, S.G. DuBois, U.N. Lassen, G.D. Demetri, M. Nathenson, R.C. Doebele, A.F. Farago, A.S. Pappo, B. Turpin, A. Dowlati, M.S. Brose, L. Mascarenhas, N. Federman, J. Berlin, W.S. El-Deiry, C. Baik, J. Deeken, V. Boni, R. Nagasubramanian, M. Taylor, E.R. Rudzinski, F. Meric-Bernstam, D.P.S. Sohal, P.C. Ma, L.E. Raez, J.F. Hechtman, R. Benayed, M. Ladanyi, B.B. Tuch, K. Ebata, S. Cruickshank, N.C. Ku, M.C. Cox, D.S. Hawkins, D.S. Hong, and D.M. Hyman

N Engl J Med 2018;378:731-9.

	Targets	IC_{50} against TRKs in cell lines, nmol/L	CNS penetration	Activity against NTRK secondary mutations	Development phase in NTRK fusion-positive tumours	Approval status
Larotrectinib	TRKA, B, and C	9·8–25	Brain to plasma ratio in mice of 0·03–0·23	No	2	US FDA approved
Entrectinib	TRKA, B, and C; ROS1, ALK	0·1–1·7*	Brain to plasma ratio in mice of 0·6–1	No	2	US FDA approved
Selitrectinib (LOXO-195)	TRKA, B, and C	≤5	Brain to plasma ratio in mice of 0·017–0·025	Yes	1/2	US FDA orphan drug designation
Repotrectinib (TPX-0005)	TRKA, B, and C; ROS1, ALK	<0·2	Brain to plasma ratio in mice of 0·0281–0·0577	Yes	1/2	Not approved
DS-6051b	TRKA/B/C, ROS1	~3–20	Not reported	Yes	1	Not approved

TRK=tropomyosin receptor kinase. ROS1=c-ros oncogene 1. ALK=anaplastic lymphoma kinase. FDA=Food and Drug Administration. *Enzymatic assays.

Table: **Comparison of selected TRK inhibitors that are US FDA approval or under clinical development**

Lancet Oncol 2020

Published Online

February 24, 2020

Superficial CD34-positive Fibroblastic Tumors

Superficial CD34-positive fibroblastic tumor: report of 18 cases of a distinctive low-grade mesenchymal neoplasm of intermediate (borderline) malignancy

Jodi M Carter[1], Sharon W Weiss[2], Konstantinos Linos[2], David J DiCaudo[3] and Andrew L Folpe[1]

[1]*Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA;* [2]*Department of Pathology and Laboratory Medicine, Emory University, Atlanta, GA, U* **Modern Pathology** (2013), 1–9
Dermatology, Mayo Clinic, Scottsdale, AZ, USA

Histopathology

Histopathology 2017, 70, 394–401. DOI: 10.1111/his.13088

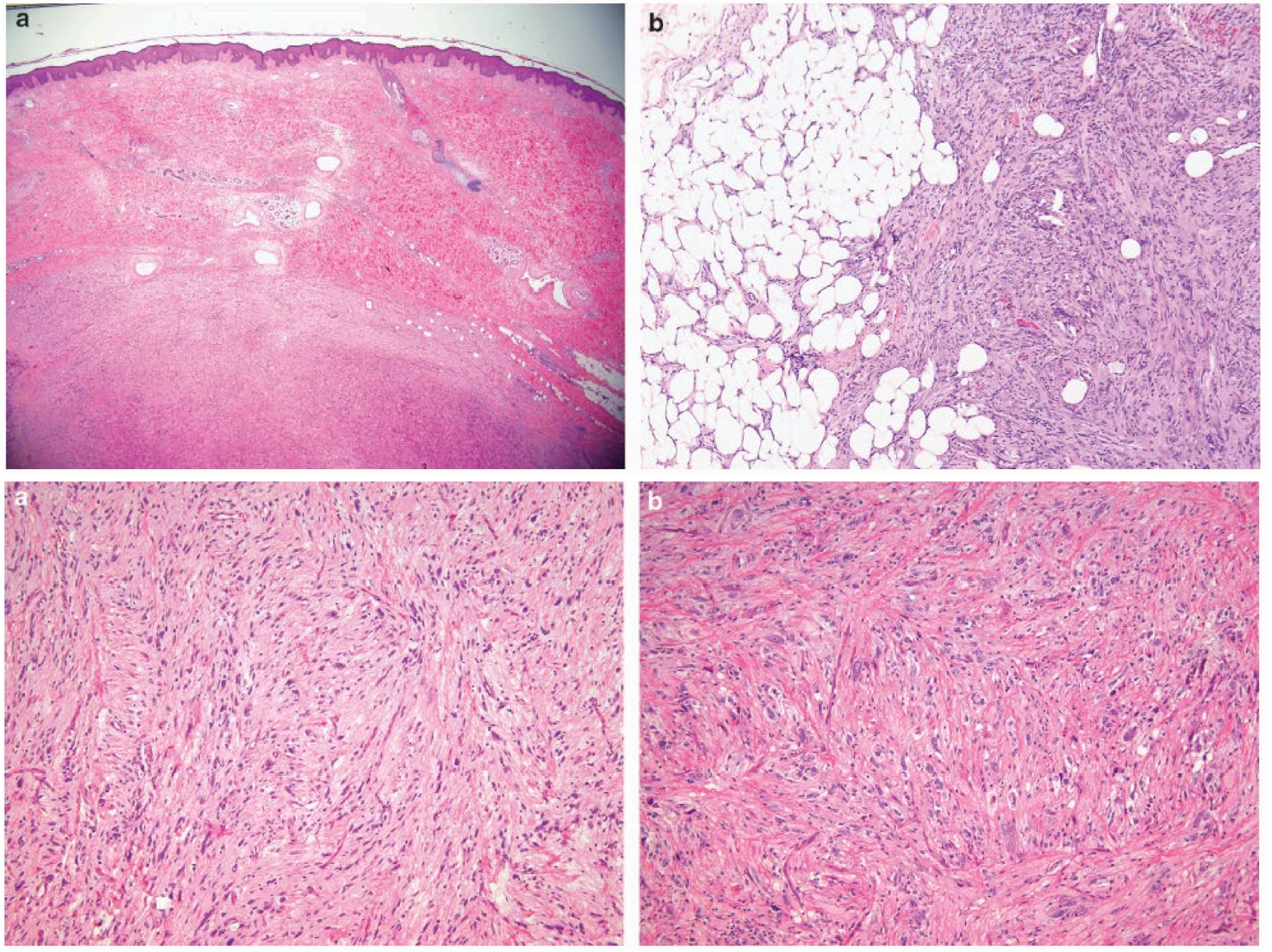
Superficial CD34-positive fibroblastic tumour: a clinicopathological and immunohistochemical study of an additional series

I Weng Lao,[1,2] Lin Yu[1,2] & Jian Wang[1,2]
[1]*Department of Pathology, Fudan University Shanghai Cancer Centre, and* [2]*Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China*

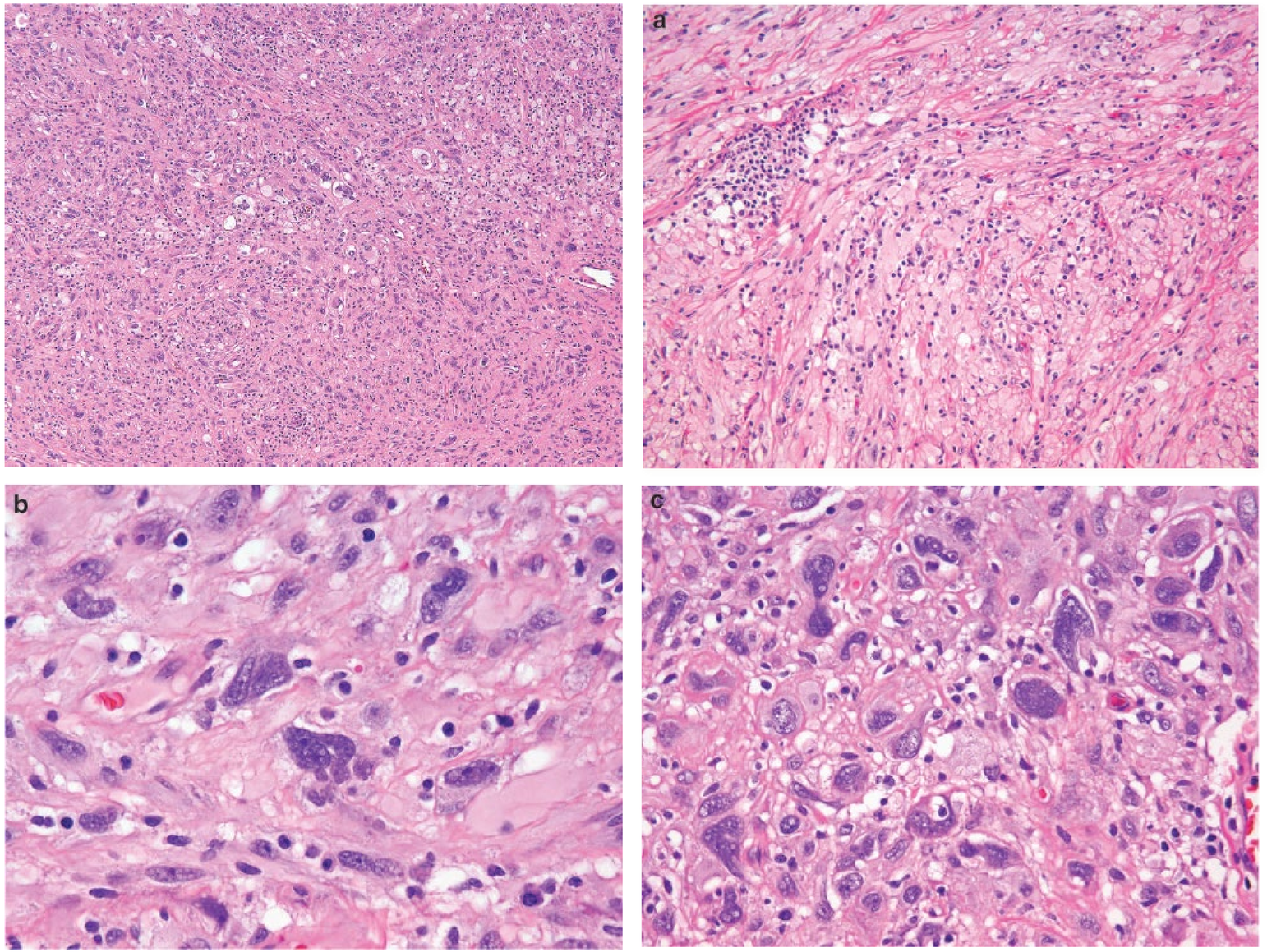
Date of submission 22 June 2016
Accepted for publication 14 September 2016
Published online *Article Accepted* 16 September 2016

Case No.	Age (year)/ sex	Site/size (cm)	Preoperative duration	Depth	Treatment/margin status	Local recurrences	Outcome/follow-up duration (months)
1	20/M	Thigh/3.1	Unknown	Suprafascial	Local excision, then interval regional lymphadenectomy/marginal	No, regional LN metastasis	ANED/104
2	21/F	Leg/2	Unknown	Suprafascial	Local excision/marginal	No	ANED/30
3	25/M	Groin/7.5	Unknown (rapid enlargement)	Suprafascial	Local excision/marginal	No	ANED/1
4	25/M	Foot/3.8	4 years	Suprafascial	Wide excision/wide	No	ANED/17
5	26/M	Thigh/6.5	Unknown	Suprafascial	Local excision, then wide excision/wide	No	ANED/7
6	26/M	Thigh/2.2	'Several years'	Suprafascial	Local excision/marginal	NA	NA
7	28/M	Thigh/1.5	Unknown	Suprafascial	Local excision/Marginal	No	ANED/24
8	32/M	Shoulder/ unknown	14 years	Suprafascial	Local excision/marginal	No	ANED/2
9	37/F	Vulva/10	Unknown	Suprafascial	Local excision/marginal	NA	NA
10	38/F	Neck/1.5	6 years	Suprafascial	Local excision/Marginal	No	ANED/38
11	44/F	Popliteal fossa/6.5	At least 1 year	Suprafascial	Local excision, then wide excisions[2] and RT/wide	No	ANED/20
12	45/M	Knee/ unknown	Unknown	Suprafascial	Local excision/marginal	NA	NA
13	46/M	Hip/2	Unknown	Suprafascial	Local excision/marginal	NA	NA
14	48/M	Arm/2.7	Unknown	Suprafascial	Local excision, preoperative RT, then wide excision/Wide	No	ANED/4
15	51/F	Arm/ unknown	Unknown	Suprafascial	Local excision/marginal	NA	NA
16	53/F	Groin/3.4	20 years	Suprafascial	Local excision, then wide excision/wide	No	ANED/53
17	57/F	Thigh/7.4	Unknown	Suprafascial	Local excision, then wide excision/wide	No	ANED/3
18	76/F	Buttock/2	'Many years'	Suprafascial	Local excision/marginal	No	ANED/3

Modern Pathology advance online publication, 26 July 2013; doi:10.1038/modpathol.2013.139



Modern Pathology advance online publication, 26 July 2013; doi:10.1038/modpathol.2013.139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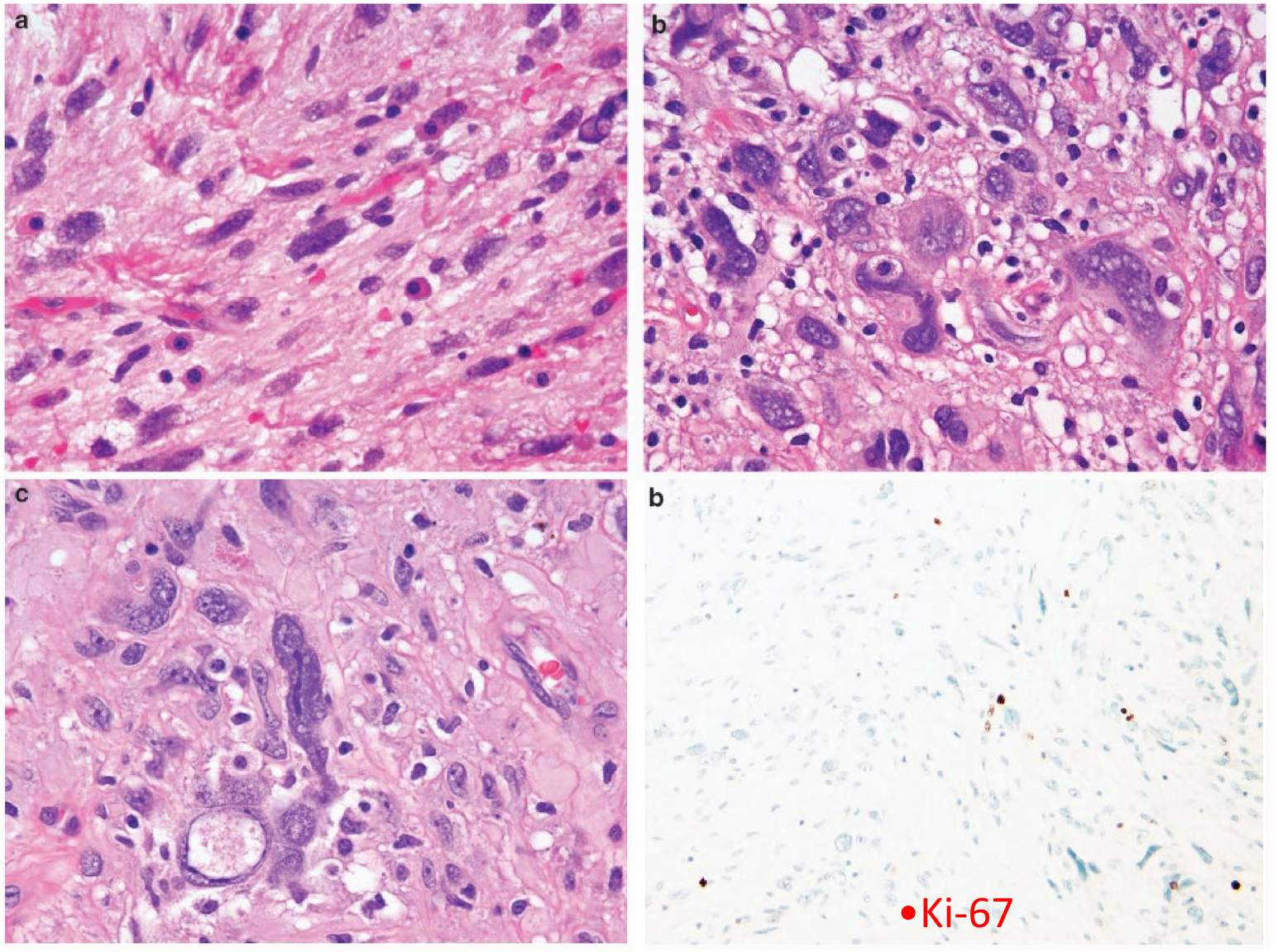

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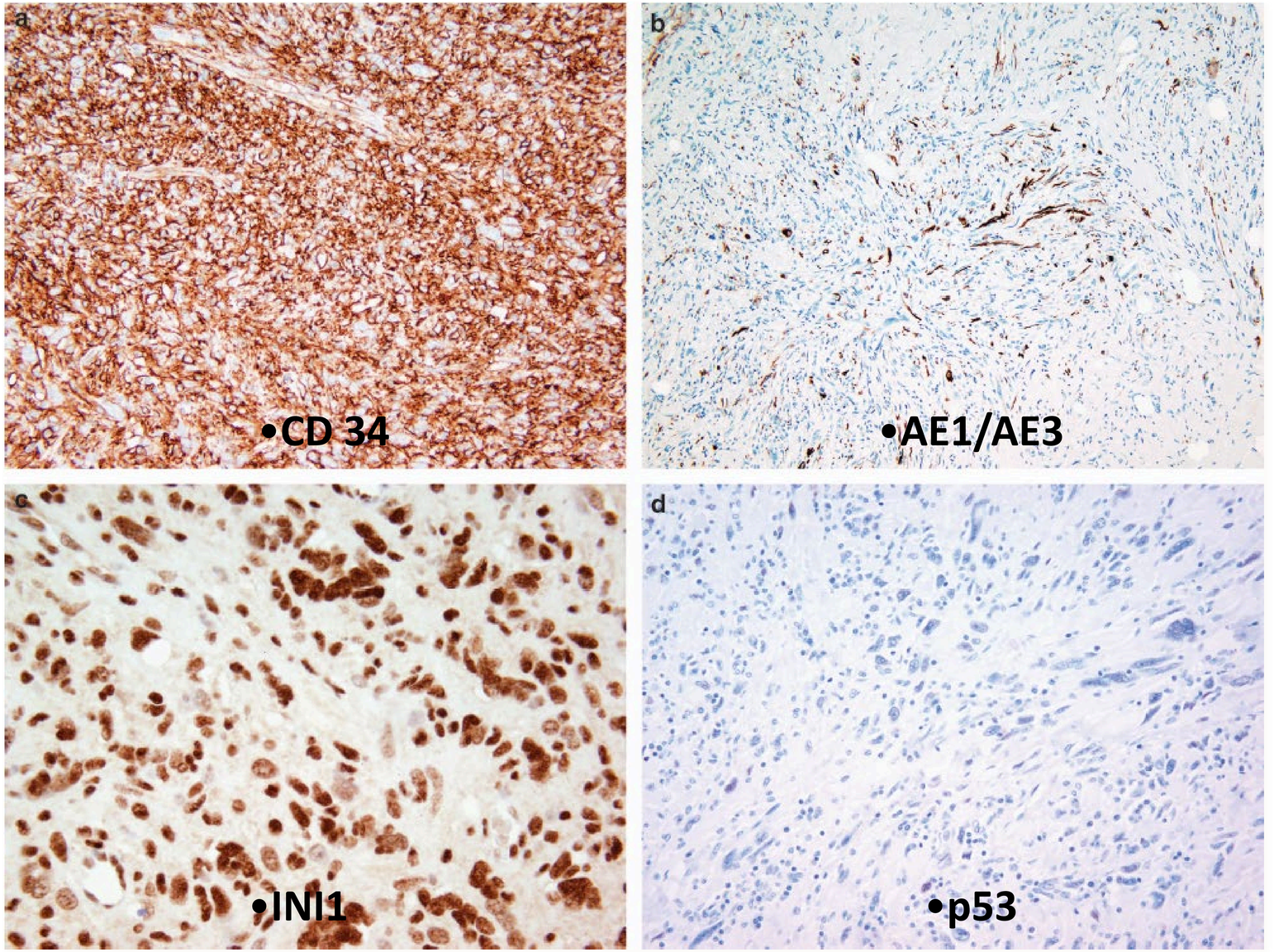


Modern Pathology advance online publication, 26 July 2013; doi:10.1038/modpathol.2013.139

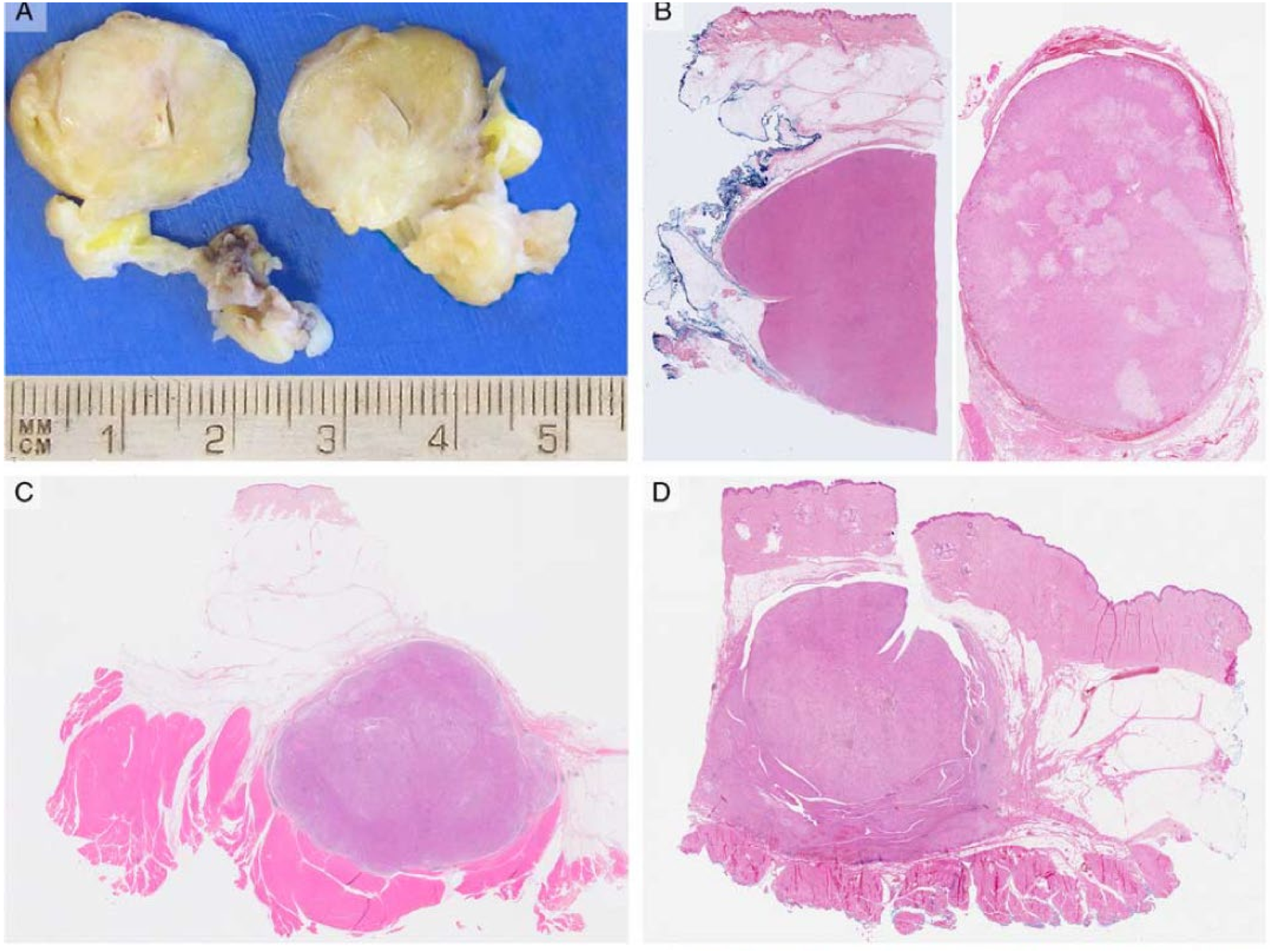
PRDM10-rearranged Soft Tissue Tumor

A Clinicopathologic Study of 9 Cases

Florian Puls, MD, FRCPath, Nischalan Pillay, MB, ChB, FRCPath, PhD,†‡*
Henrik Fagman, MD, PhD, Anne Palin-Masreliez, BSc,* Fernanda Amary, MD, PhD,†*
Magnus Hansson, MD, PhD, Lars-Gunnar Kindblom, MD, PhD,**
Tom A. McCulloch, BM, BS, FRCP, FRCPath,§ George Meligonis, MBBCh, FCPath(SA),‖
*Ronald Muc, MBBCh, FRCPath,¶ Pehr Rissler, MD, PhD,# Vaiyapuri P. Sumathi, FRCPath,***
Roberto Tirabosco, MD,† Jakob Hofvander, MSc,†† Linda Magnusson, MSc,††
Jenny Nilsson, MSc,†† Adrienne M. Flanagan, MB, BCh, PhD, FRCPath,†‡
and Fredrik Mertens, MD, PhD#††

(*Am J Surg Pathol* 2018;00:000–000)

Case	Demarcation	Myxoid Areas	Multinucleated Giant Cells	Pseudovascular Spaces	Vacuolization	Mitoses/ 50 hpf*	Original Diagnosis
1	Well demarcated	Present	Absent	Absent	Absent	7	UPS, low grade
2	Focal infiltrative	Absent	Present	Absent	Absent	7	UPS, low grade
3	Focal infiltrative	Present	Absent	Present	Single cells	1	UPS, low grade
4	Well demarcated	Present	Absent	Present	Prominent	0	PLS
5	Focal infiltrative	Present	Absent	Present	Single cells	3	PHAT
6	Well demarcated	Present	Absent	Present	Prominent	4	PLS
7	Well demarcated	Absent	Present	Absent	Single cells	7	SCD34FT
8	Focal infiltrative	Present	Present	Absent	Single cells	2	SCD34FT
9	Well demarcated	Entirely myxoid	Absent	Absent	Absent	3	SCD34FT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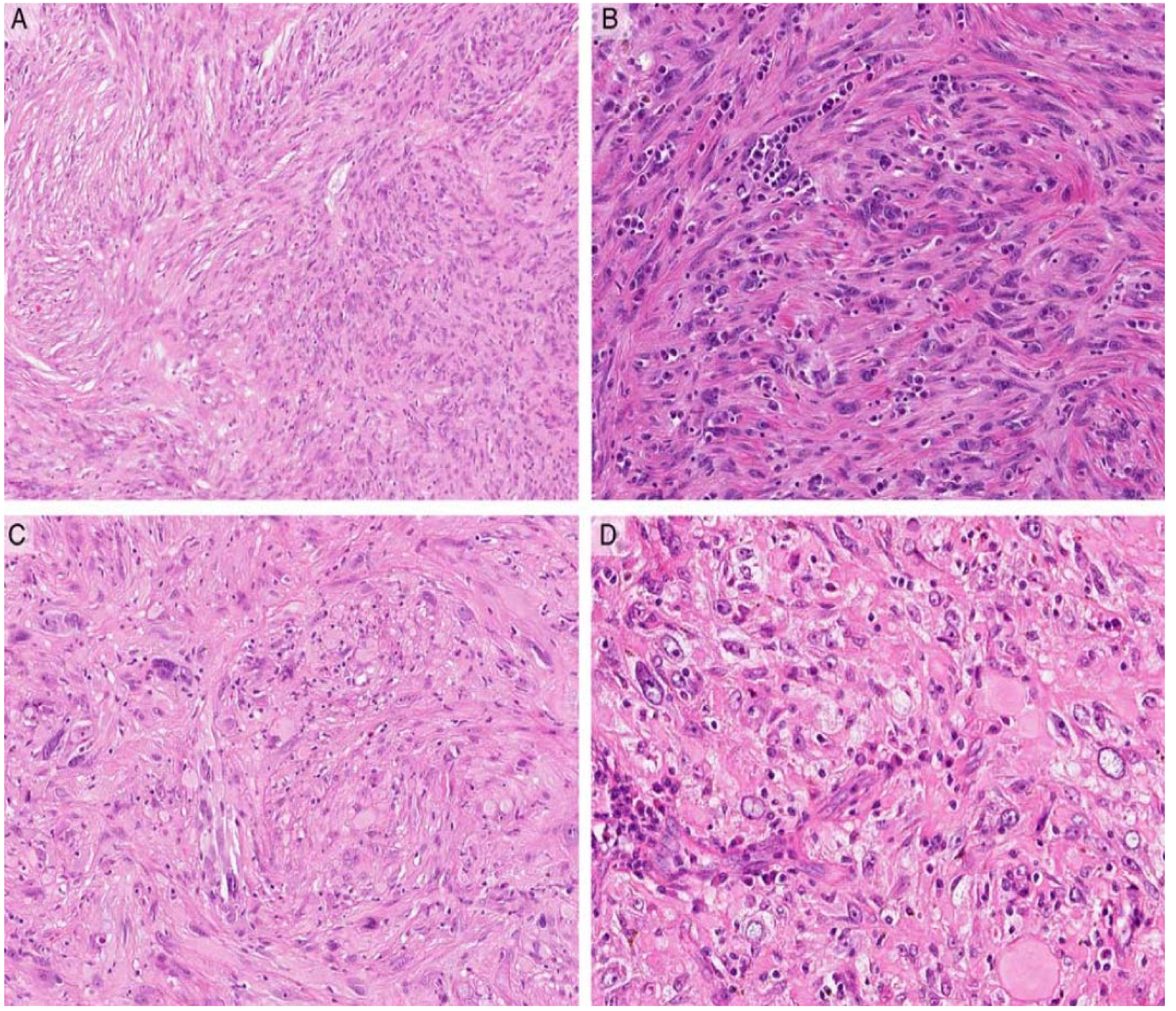
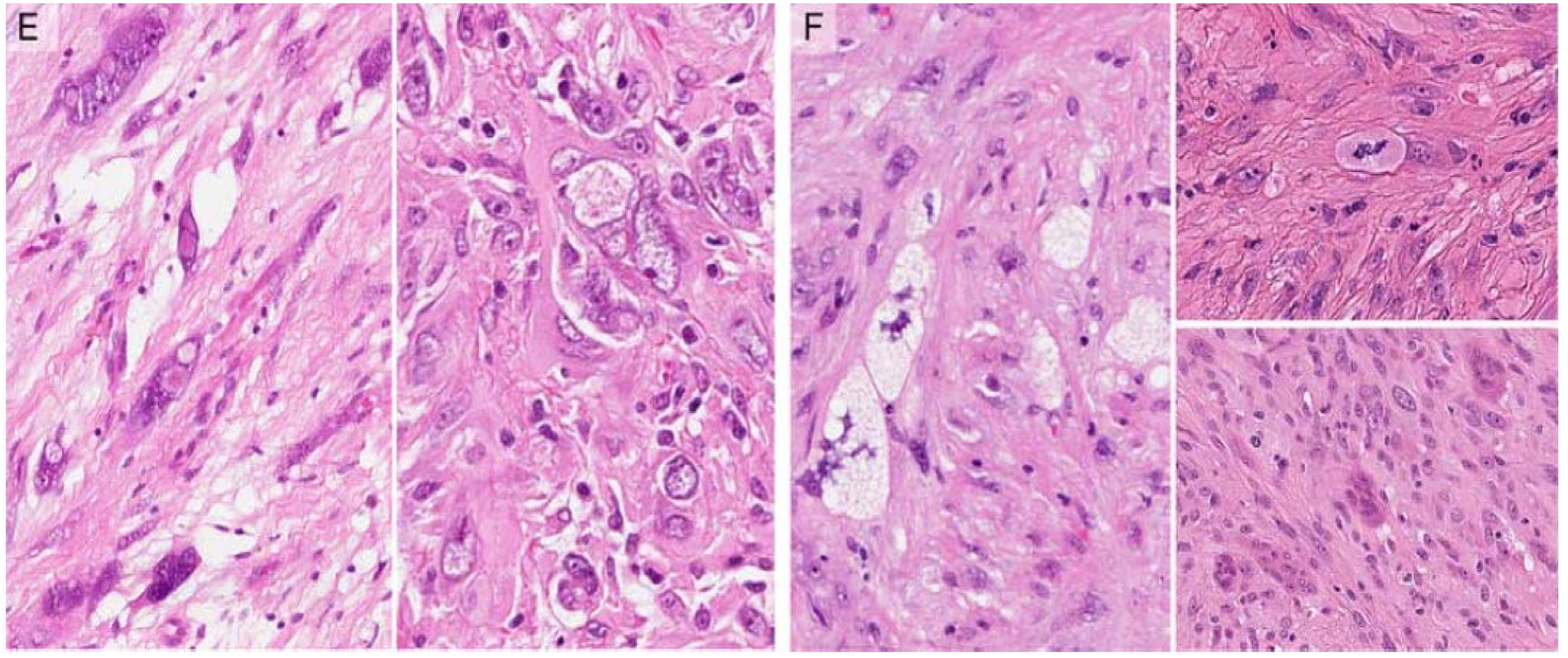


(*Am J Surg Pathol* 2018;00:000–000)



(*Am J Surg Pathol* 2018;00:000–000)

Case*	CD34	Cytokeratins AE1/AE3 or MNF116	S100 Protein	Ki-67 (%)	PRDM10 Cytoplasmic	PRDM10 Nuclear	FISH†	Fusion Transcript	Fusion Junction‡
1	Pos	Pos (focal)	Neg	5	1+ weak	4+ strong	Pos (68%)	*CITED2-PRDM10*	ex2-ex14
2	Pos	NA	NA	NA	1+ weak	3+ moderate§	Pos (93%)	*MED12-PRDM10*	ex43-ex14
3	Pos	NA	NA	NA	1+ weak	3+ moderate§	ND	*MED12-PRDM10*	ex43-ex13
4‖	Pos	NA	Neg	5	1+ weak	4+ strong	ND	*CITED2-PRDM10*	ex2-ex14
5	Pos	Pos (focal)	Neg	< 5	1+ weak	3+ moderate	Pos (36%)	Neg	NA
6	Pos	Pos (focal)	Neg	5	1+ weak	4+ strong	Pos (17%)	ND¶	NA
7	Pos	Pos (focal)	Neg	5	1+ weak	4+ moderate	Neg (8%)	*MED12-PRDM10*	ex42-ex14
8	Pos	Pos (focal)	Neg	NA	1+ weak	3+ moderate	Pos (26%)	*MED12-PRDM10*	ex43-ex13
9	Pos	Neg	Neg	NA	1+ weak	4+ strong	Neg (13%)	*CITED2-PRDM10*	ex2-ex14

Histopathology

Histopathology 2021, **79**, 810–825. DOI: 10.1111/his.14429

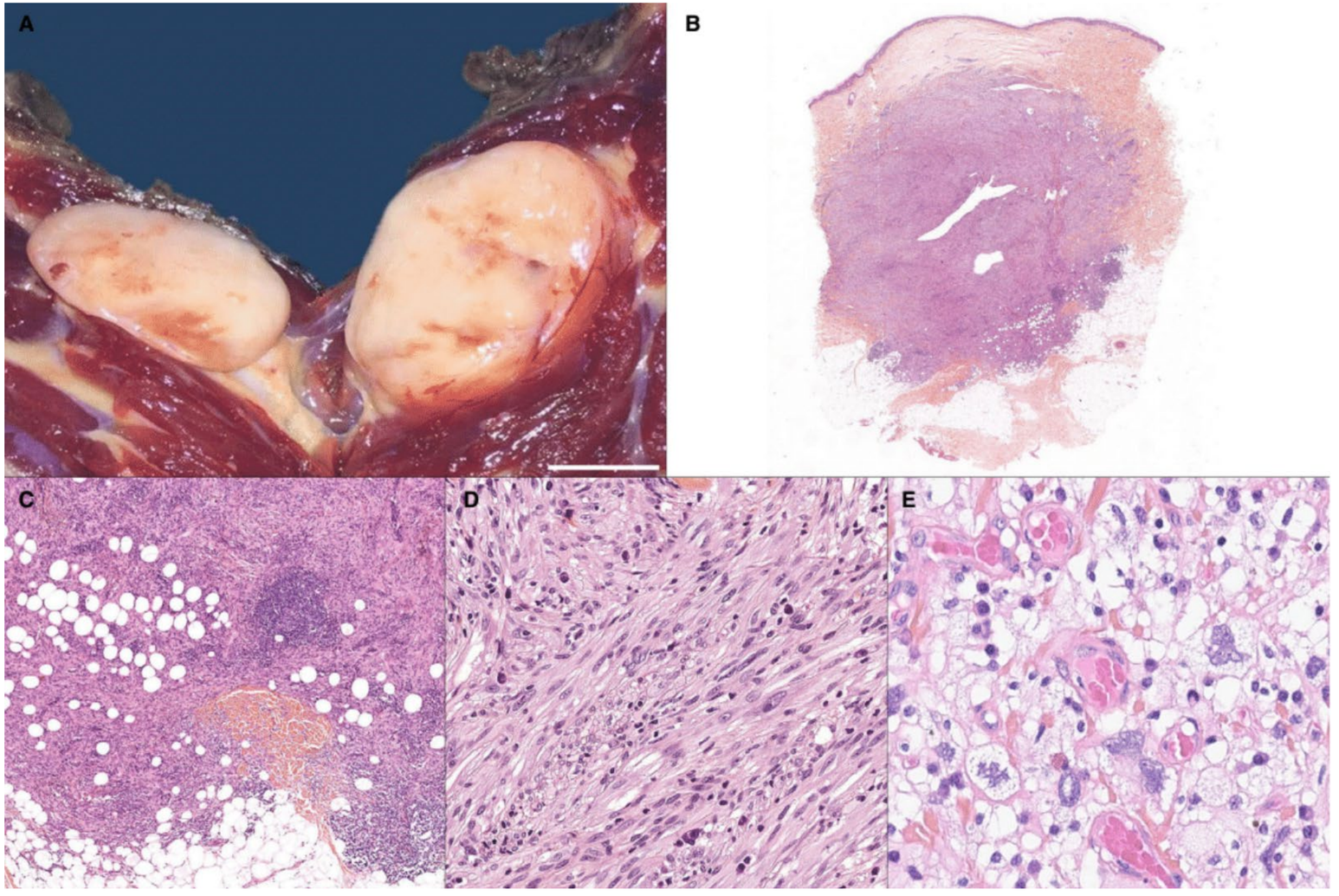
Superficial CD34-positive fibroblastic tumor and *PRDM10*-rearranged soft tissue tumor are overlapping entities: a comprehensive study of 20 cases

Raul Perret,[1] Michael Michal,[2,3] Richard A Carr,[4] Valérie Velasco,[1] Marian Švajdler,[2,3] Marie Karanian,[5,6] Alexandra Meurgey,[5] Sandrine Paindavoine,[5] Isabelle Soubeyran,[1] Jean-Michel Coindre,[1,7] Romain Boidot,[8] Céline Charon-Barra,[9] Damien Geneste,[10] Noelle Weingertner,[11] Daniel Pissaloux,[5,6] Franck Tirode,[6] Jessica Baud[7,12] &

Overlapping morphological, immunohistochemical and genetic features of superficial CD34-positive fibroblastic tumor and *PRDM10*-rearranged soft tissue tumor

Florian Puls[1,2✉], Jodi M. Carter[3], Nischalan Pillay[4,5], Thomas A. McCulloch[6], Vaiyapuri P. Sumathi[7], Pehr Rissler[8], Henrik Fagman[1,2], Magnus Hansson[1], Fernanda Amary[4], Roberto Tirabosco[4], Linda Magnusson[9], Jenny Nilsson[9], Adrienne M. Flanagan[4,5], Andrew L. Folpe[3] and Fredrik Mertens[8,9]

Modern Pathology (2022) 35:767–776;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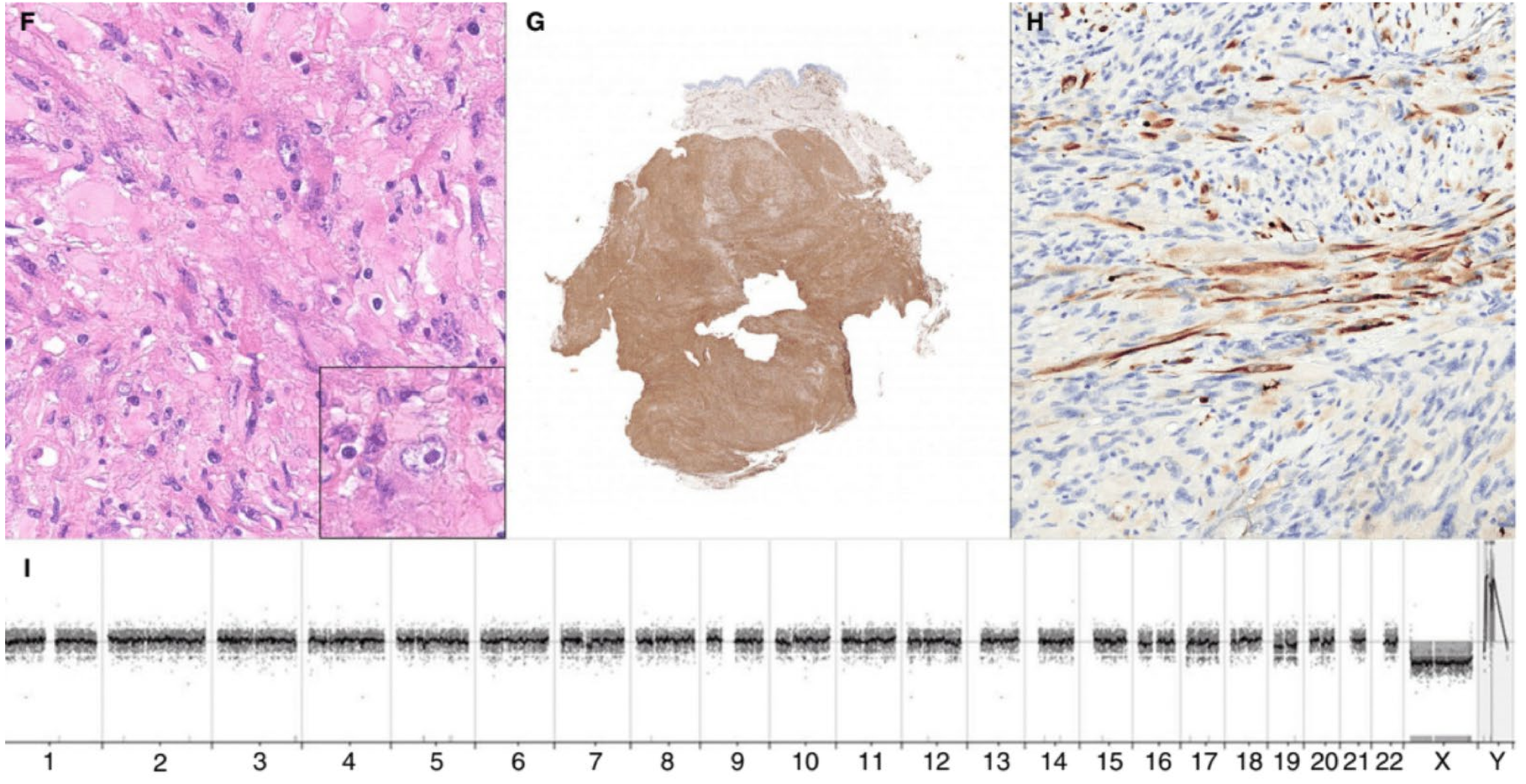
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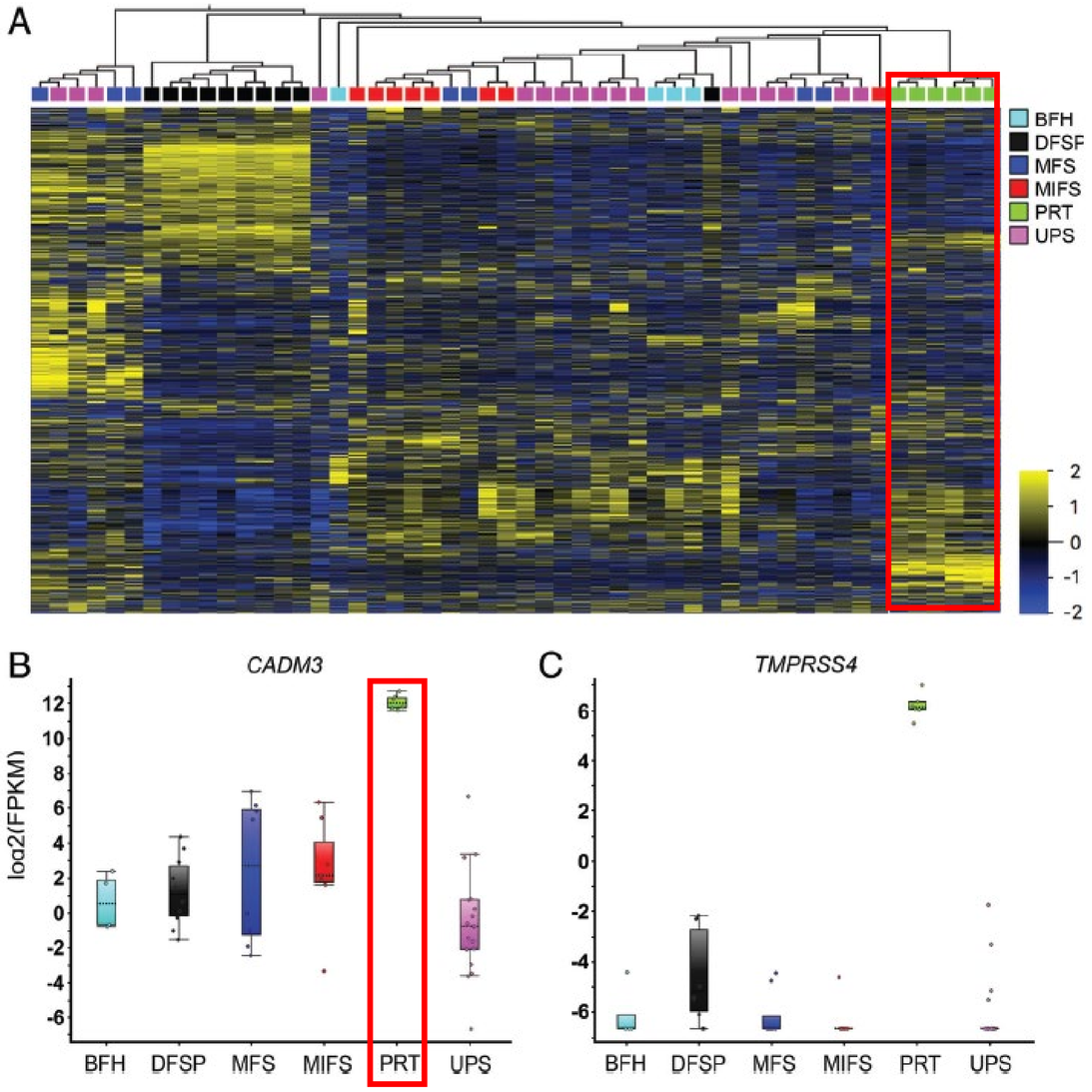
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-4
-6
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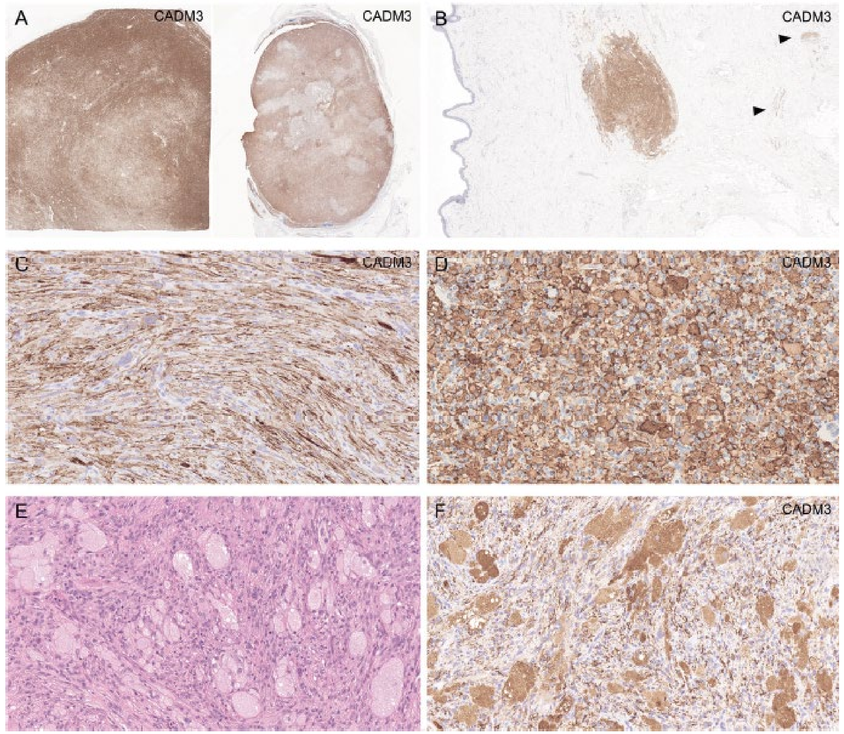
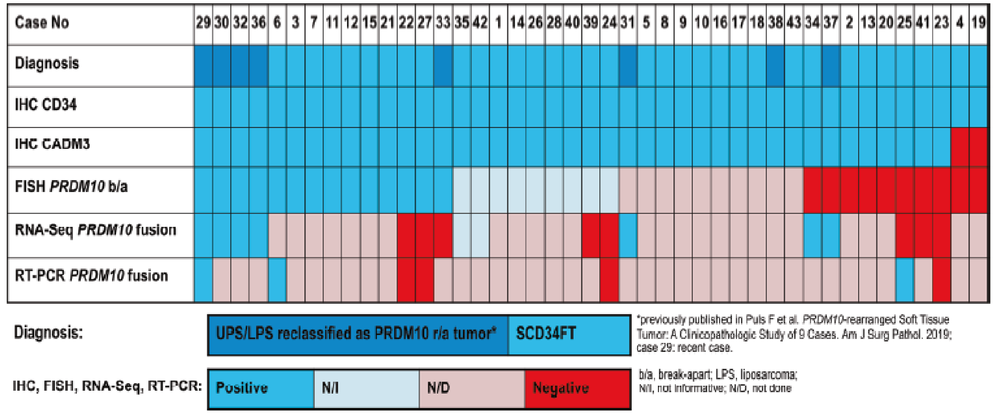
PRT
UPS

Immunohistochemistry for CAMD3





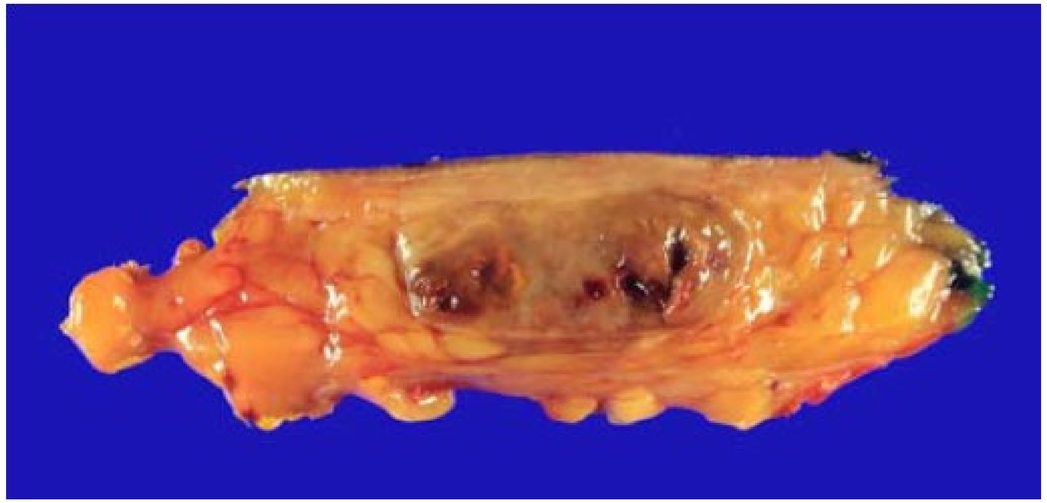
Modern Pathology (2022) 35:767–776;

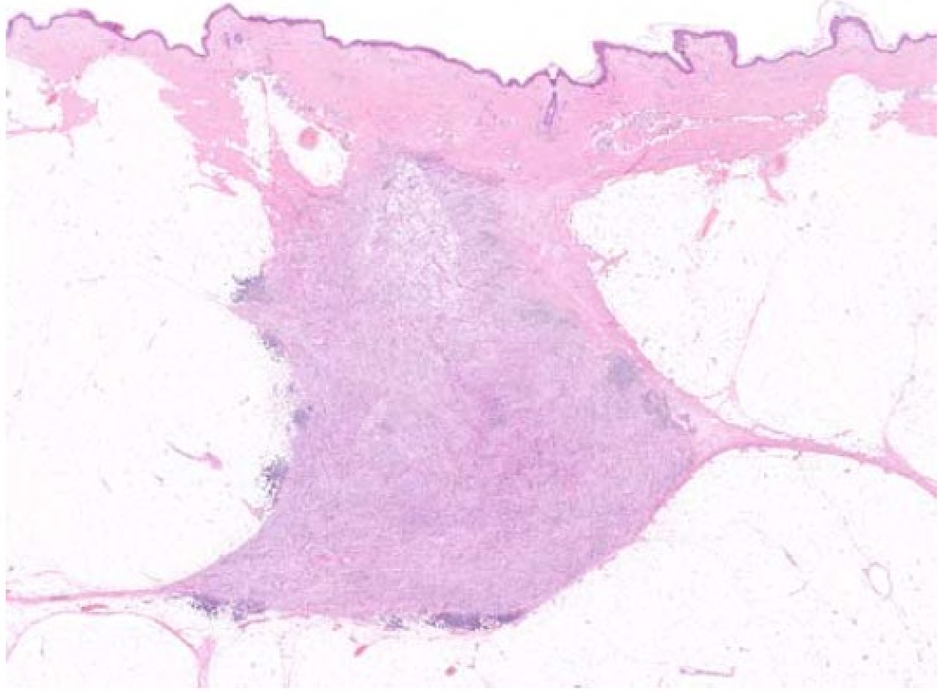
Superficial CD34-Positive Fibroblastic Tumor

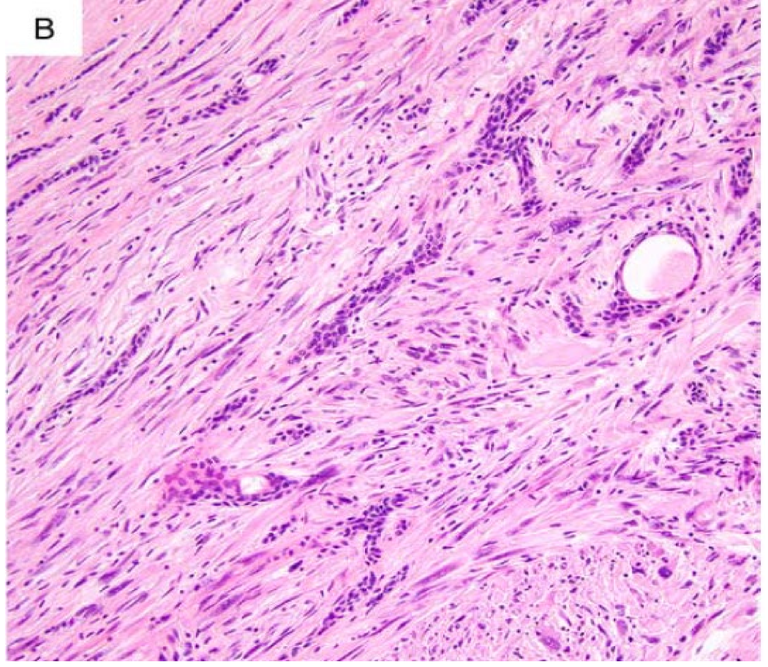
A Clinicopathologic, Immunohistochemical, and Molecular Study of 59 Cases

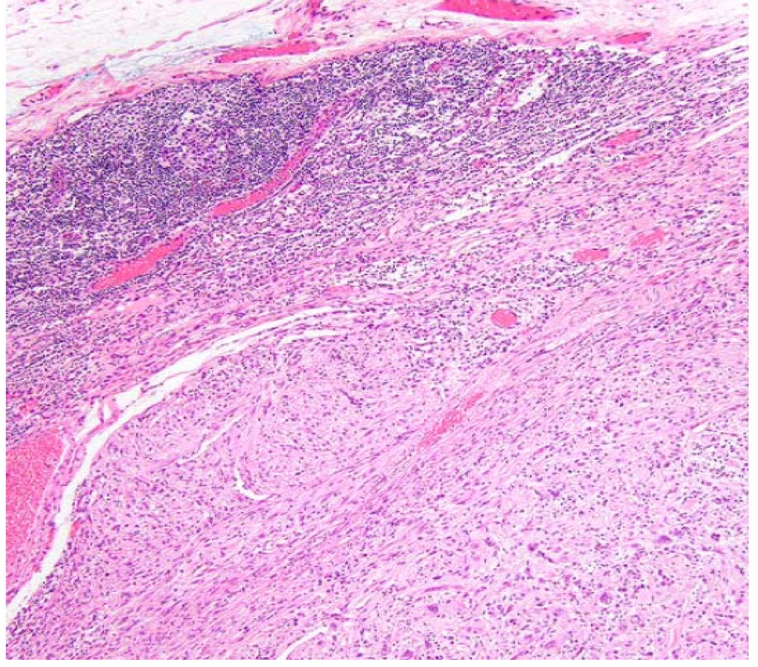
William J. Anderson, MBChB, Fredrik Mertens, MD, PhD,†‡ Adrián Mariño-Enríquez, MD, PhD,* Jason L. Hornick, MD, PhD,* and Christopher D.M. Fletcher, MD, FRCPath**

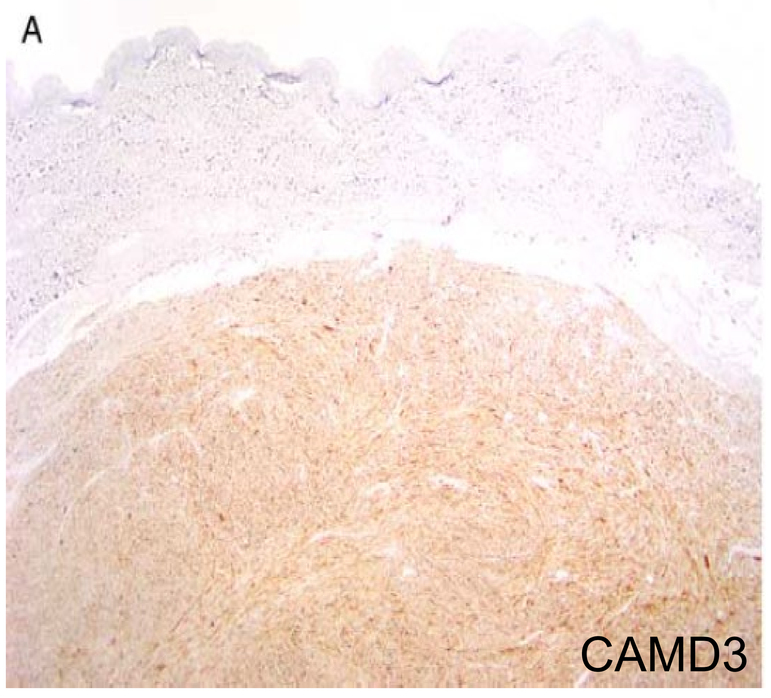
Am J Surg Pathol 2022;46:1329–1339

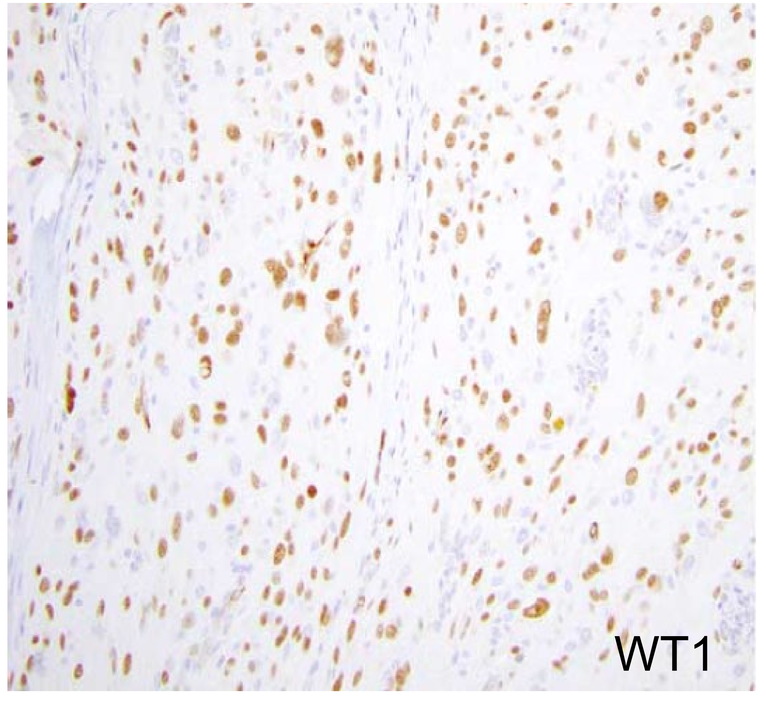






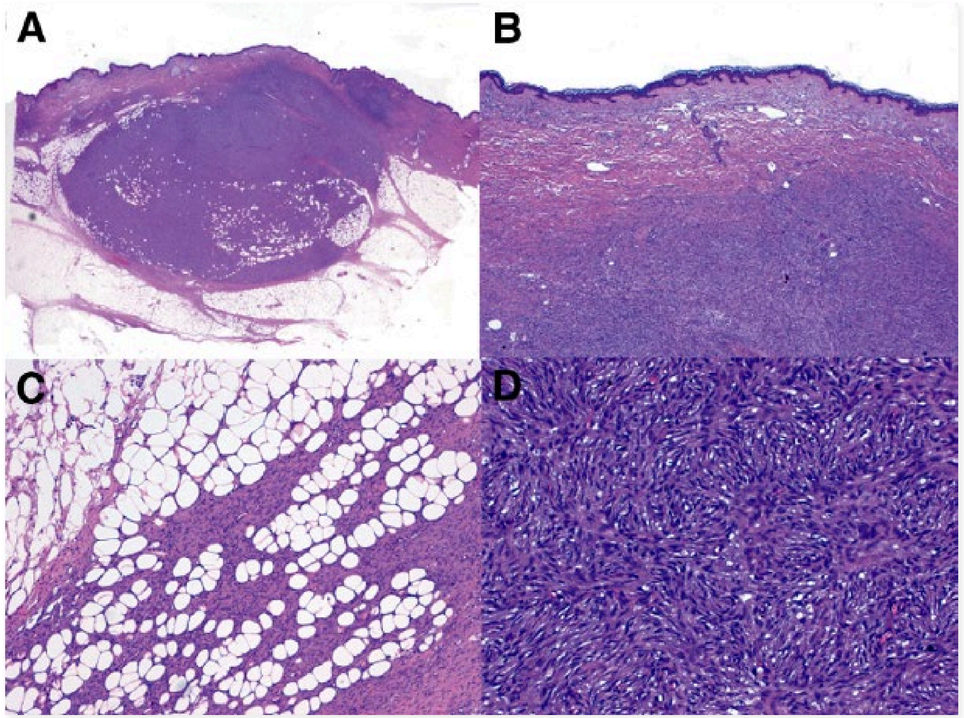


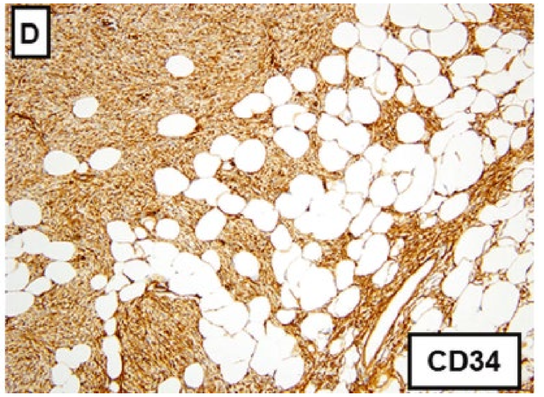




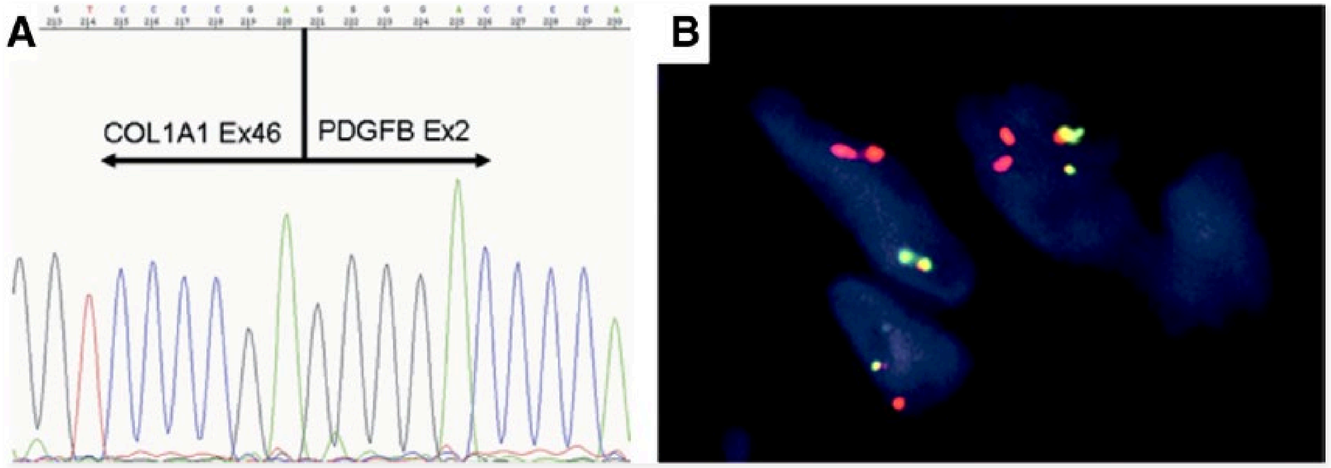
Am J Surg Pathol 2022;46:1329–1339

Dermatofibrosarcoma Protuberans (DFSP)



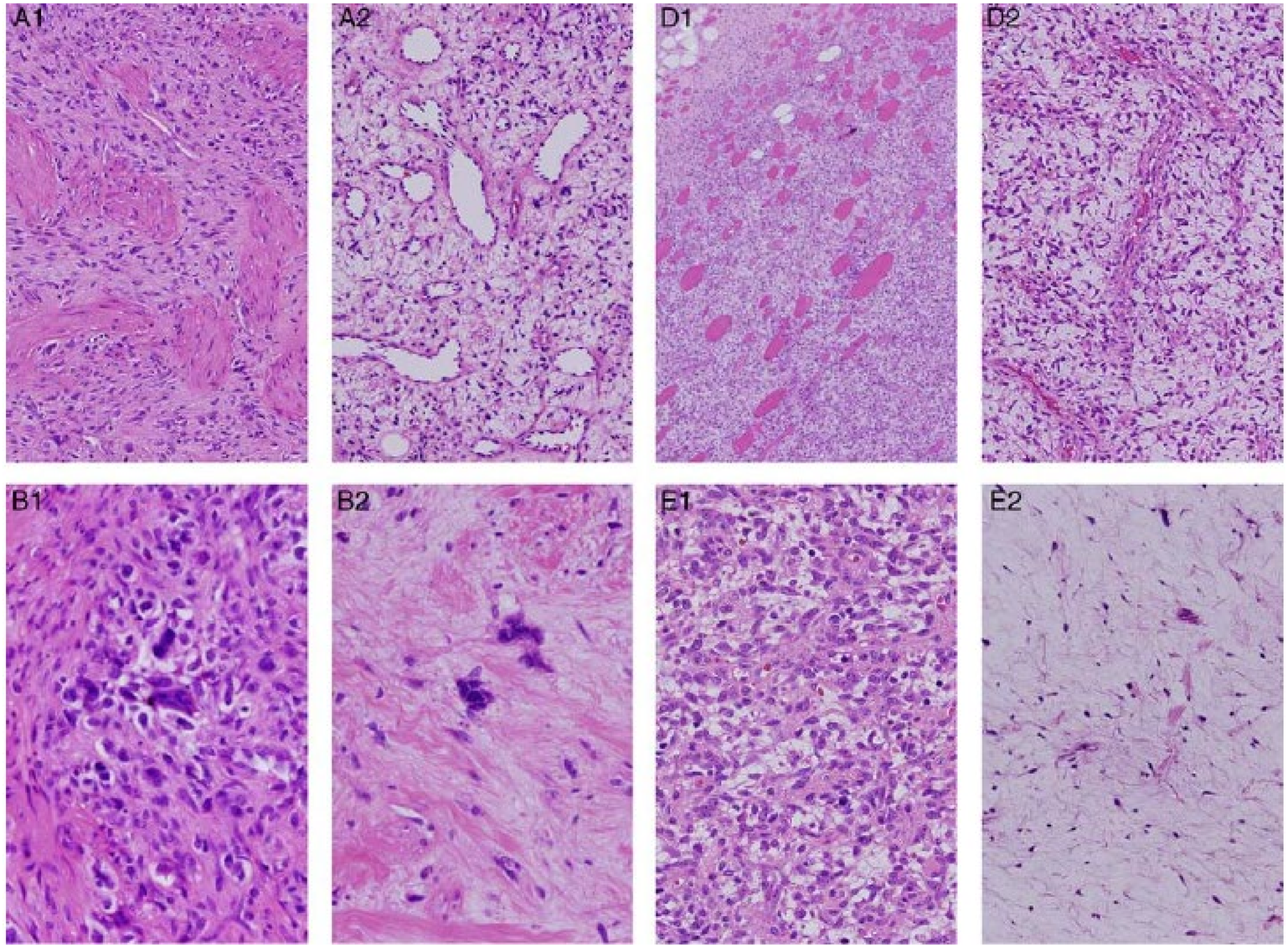


Seminars in Diagnostic Pathology (2013) 30, 13-28



- t(17;22)(q22;q13)=*COL1A1-PDGFB*

Seminars in Diagnostic Pathology (2013) 30, 13-28

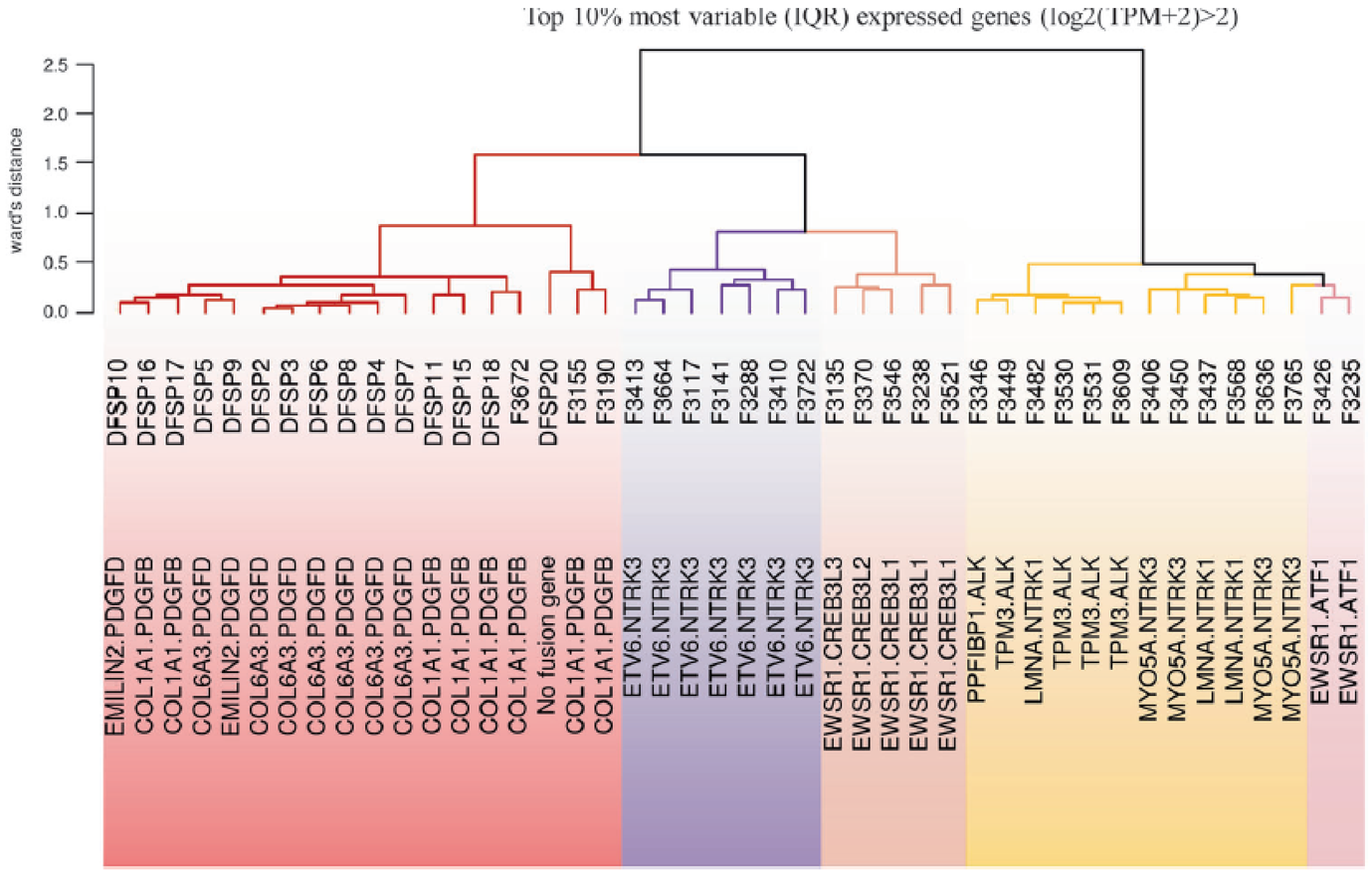

A1
A2
D1
D2
B1
B2
E1
E2

Modern Pathology
https://doi.org/10.1038/s41379-018-0089-4

ARTICLE

Alternative *PDGFD* rearrangements in dermatofibrosarcomas protuberans without *PDGFB* fusions

Bérengère Dadone-Montaudié[1] · Laurent Alberti[2,3] · Adeline Duc[3] · Lucile Delespaul[4,5,11] · Tom Lesluyes[4,5,11] · Gaëlle Pérot[6] · Agnès Lançon[3] · Sandrine Paindavoine[3] · Ilaria Di Mauro[1] · Jean-Yves Blay[2,7] · Arnaud de la Fouchardière[3] · Frédéric Chibon[4,6,11] · Marie Karanian[3] · Gaëtan MacGrogan[6] · Valérie Kubiniek[1] · Frédérique Keslair[1] · Nathalie Cardot-Leccia[8] · Audrey Michot[9] · Virginie Perrin[10] · Yanis Zekri[10] · Jean-Michel Coindre[5,6] · Franck Tirode[2,10] · Florence Pedeutour[1] · Dominique Ranchère-Vince[3] · François Le Loarer[5,6] · Daniel Pissaloux[2,3]


Top 10% most variable (IQR) expressed genes (log2(TPM+2)>2)
ward's distance
2.5
2.0
1.5
1.0
0.5
0.0
DFSP10
DFSP16
DFSP17
DFSP5
DFSP9
DFSP2
DFSP3
DFSP6
DFSP8
DFSP4
DFSP7
DFSP11
DFSP15
DFSP18
F3672
DFSP20
F3155
F3190
F3413
F3664
F3117
F3141
F3288
F3410
F3722
F3135
F3370
F3546
F3238
F3521
F3346
F3449
F3482
F3530
F3531
F3609
F3406
F3450
F3437
F3568
F3636
F3765
F3426
F3235
EMILIN2.PDGFD
COL1A1.PDGFB
COL1A1.PDGFB
COL6A3.PDGFD
EMILIN2.PDGFD
COL6A3.PDGFD
COL6A3.PDGFD
COL6A3.PDGFD
COL6A3.PDGFD
COL6A3.PDGFD
COL6A3.PDGFD
COL1A1.PDGFB
COL1A1.PDGFB
COL1A1.PDGFB
COL1A1.PDGFB
No fusion gene
COL1A1.PDGFB
COL1A1.PDGFB
ETV6.NTRK3
ETV6.NTRK3
ETV6.NTRK3
ETV6.NTRK3
ETV6.NTRK3
ETV6.NTRK3
ETV6.NTRK3
EWSR1.CREB3L3
EWSR1.CREB3L2
EWSR1.CREB3L1
EWSR1.CREB3L1
EWSR1.CREB3L1
PPFIBP1.ALK
TPM3.ALK
LMNA.NTRK1
TPM3.ALK
TPM3.ALK
TPM3.ALK
MYO5A.NTRK3
MYO5A.NTRK3
LMNA.NTRK1
LMNA.NTRK1
MYO5A.NTRK3
MYO5A.NTRK3
EWSR1.ATF1
EWSR1.ATF1

WILEY

RESEARCH ARTICLE

Dermatofibrosarcoma protuberans with a novel *COL6A3-PDGFD* fusion gene and apparent predilection for breast

Brendan C. Dickson[1] | Jason L. Hornick[2] | Christopher D. M. Fletcher[2] | Elizabeth G. Demicco[1] | David J. Howarth[1] | David Swanson[1] | Lei Zhang[3] | Yun-Shao Sung[3] | Cristina R. Antonescu[3]

Received: 16 May 2018 | Revised: 14 June 2018 | Accepted: 15 June 2018

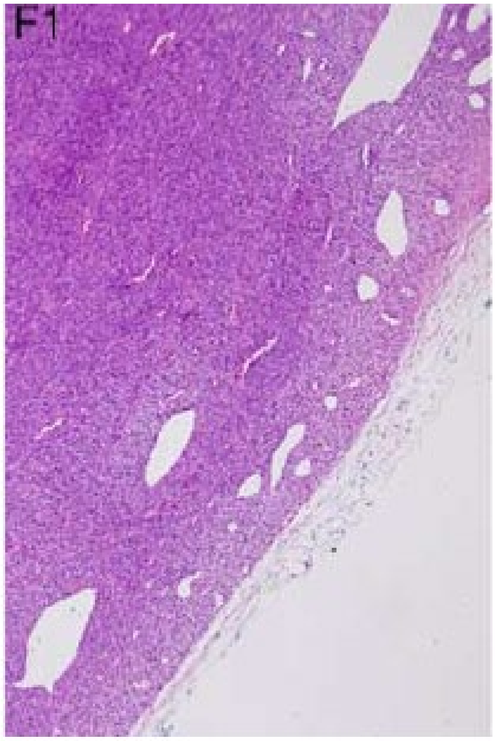
Molecular Characterization of Dermatofibrosarcoma Protuberans

The Clinicopathologic Significance of Uncommon Fusion Gene Rearrangements and Their Diagnostic Importance in the Exclusively Subcutaneous and Circumscribed Lesions

Pei-Hang Lee, MD, Shih-Chiang Huang, MD,†‡ Pao-Shu Wu, MD, PhD,§‖ Hui-Chun Tai, MD,¶ Chih-Hung Lee, MD, PhD,# Jen-Chieh Lee, MD, PhD,** Yu-Chien Kao, MD,††‡‡ Jen-Wei Tsai, MD,§§ Tsung-Han Hsieh, PhD,‖‖ Chien-Feng Li, MD, PhD,¶¶ Wan-Shan Li, MD,## Ting-Ting Liu, MD,**** Yu-Li Su, MD,††† Shih-Chen Yu, MS,* and Hsuan-Ying Huang, MD**

TABLE 2. Clinicopathologic and Molecular Findings of Cryptic *PDGFB*-rearranged and *PDGFD*-rearranged DFSPs

Case No.	Age (y)	Sex	Size (cm)	Location	Subtype	Tumor Contour	Depth
1	31	F	3.5	Groin	FS	Circumscribed	Subcutis
2	64	F	6.5	Abdominal wall	Typical	Circumscribed	Dermis
3	24	F	2.2	Back	Typical	Circumscribed	Dermis
4	30	M	NA	Back	Typical	Infiltrative	Dermis
5	18	F	2	Eyebrow	Typical	Infiltrative	Dermis
6	60	F	3	Sacral area	Typical	Infiltrative	Dermis
7	43	M	NA	Inguinal	Typical	Infiltrative	Dermis
8	34	M	3.5	Eyebrow	FS	Infiltrative	Dermis
9	24	M	3.8	Thigh	FS	Circumscribed	Subcutis
10	31	F	0.6	Flank	FS	Infiltrative	Dermis
11	14	F	3	Neck	Typical	Infiltrative	Dermis
12	20	F	2	Back	Typical	Infiltrative	Subcutis
13	32	M	3.7	Back	Typical	Circumscribed	Subcutis
14	43	M	4.5	Shoulder	FS	Circumscribed	Subcutis
15	15	F	5.0	Thigh	FS	Circumscribed	Subcutis
16	45	M	2	Leg	FS	Infiltrative	Dermis

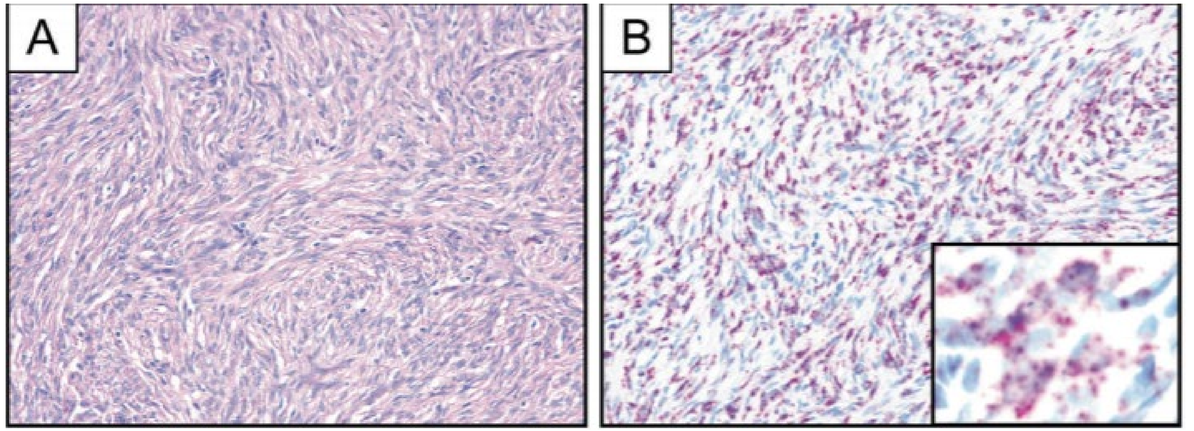


Modern Pathology
https://doi.org/10.1038/s41379-021-00800-2

ARTICLE

PDGFB RNA in situ hybridization for the diagnosis of dermatofibrosarcoma protuberans

Jeffrey M. Cloutier[1] · Grace Allard[1] · Gregory R. Bean[1] · Jason L. Hornick[2] · Gregory W. Charville[1]



Vascular Neoplasms

Memorial Sloan Kettering Cancer Center™

Vascular Tumors of Intermediate Malignancy

Retiform Hemangioendothelioma

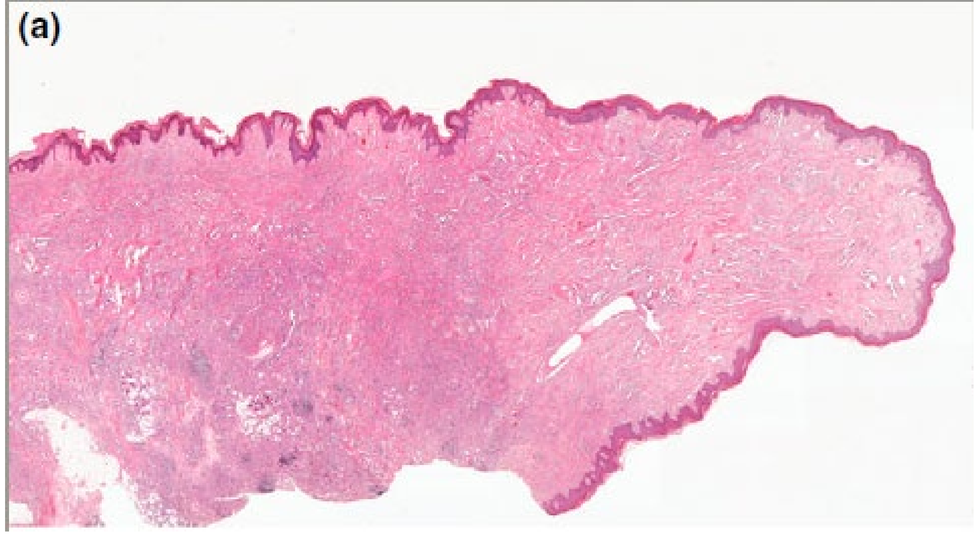
- Locally aggressive, rarely metastasizing
- Superficially located, mainly occurs in adults
- Preferentially in the **skin** and **subcutaneous tissue** of distal extremities

- **Elongated-shaped vessels resembling rete testis**

- Similarly to PILA lined by h**obnail endothelial cells** and a/w lymphocytes

- Intravascular papillary projections absent or very few

- Closely related to PILA
  - "Hobnail Hemangioendotheliomas"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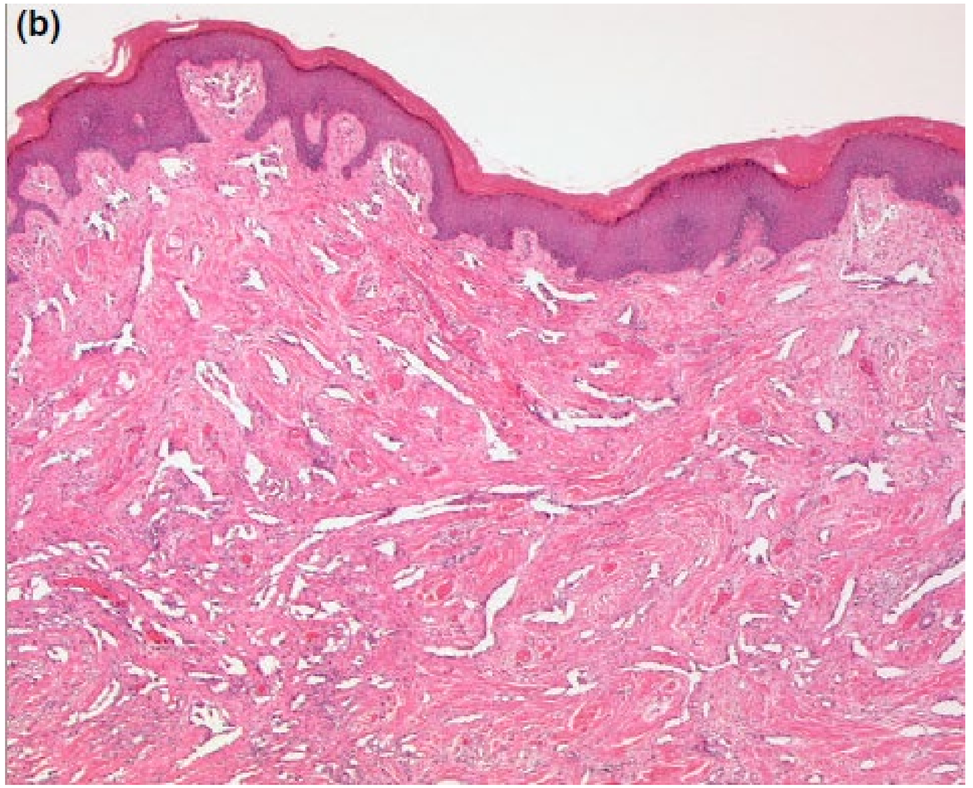
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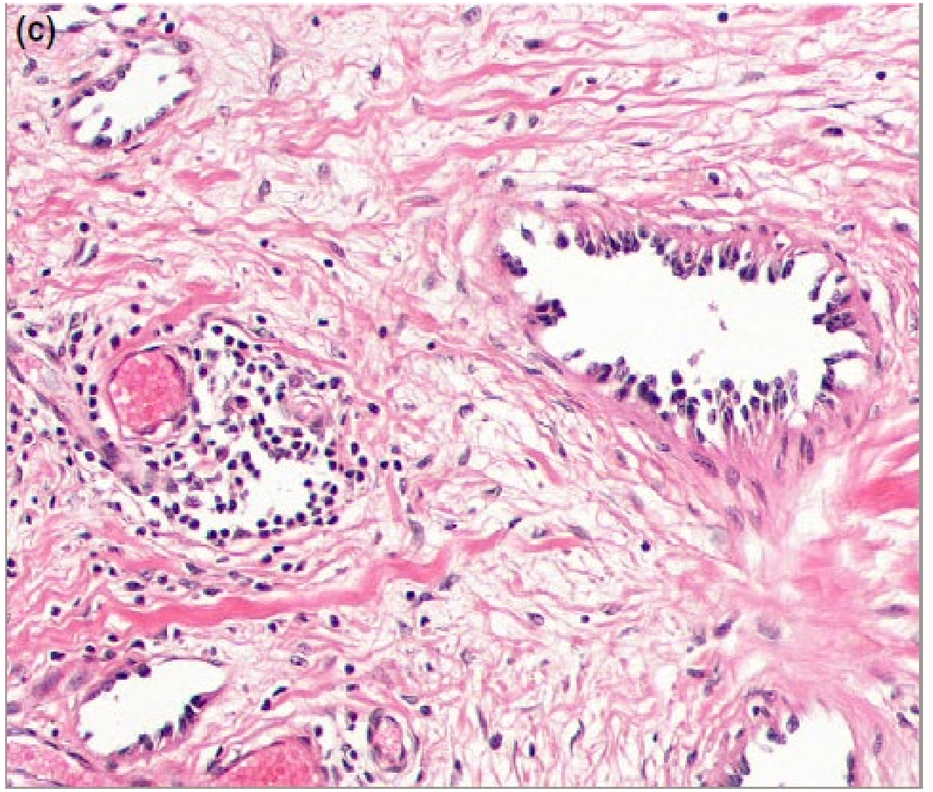
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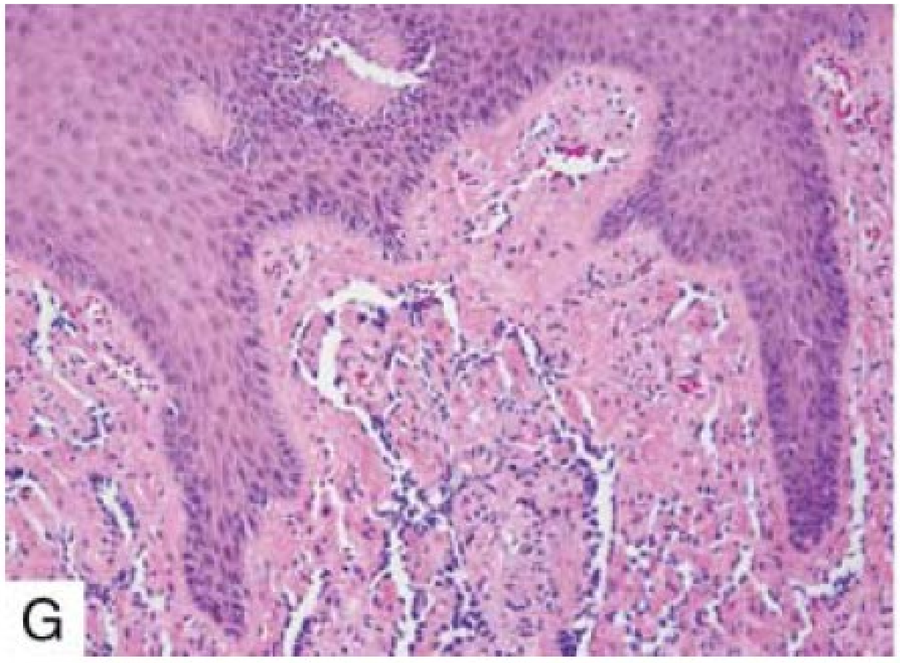
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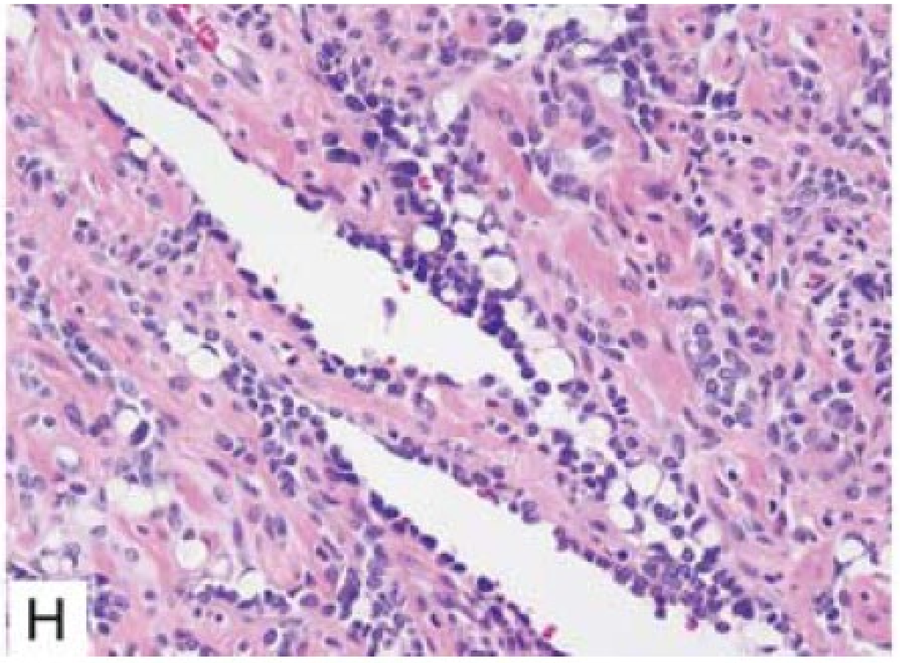
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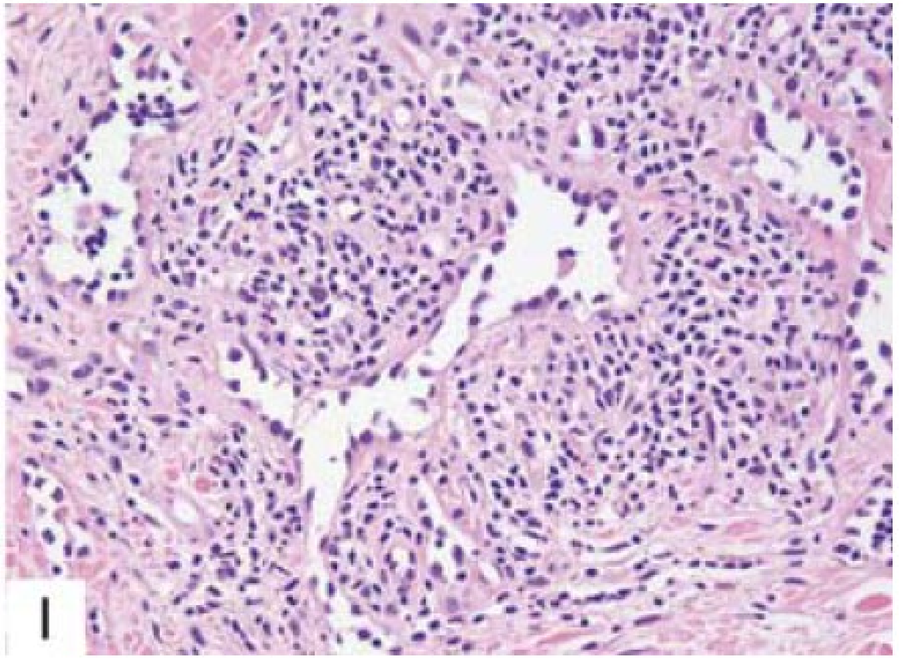

I

Recurrent *YAP1* and *MAML2* Gene Rearrangements in Retiform and Composite Hemangioendothelioma

Cristina R. Antonescu, MD, Brendan C. Dickson, MD,† Yun-Shao Sung, MSc,* Lei Zhang, MD,* Albert J.H. Suurmeijer, MD,‡ Albrecht Stenzinger, MD,§ Gunhild Mechtersheimer, MD,§ and Christopher D.M. Fletcher, MD‖*

Am J Surg Pathol 2020;44:1677–1684

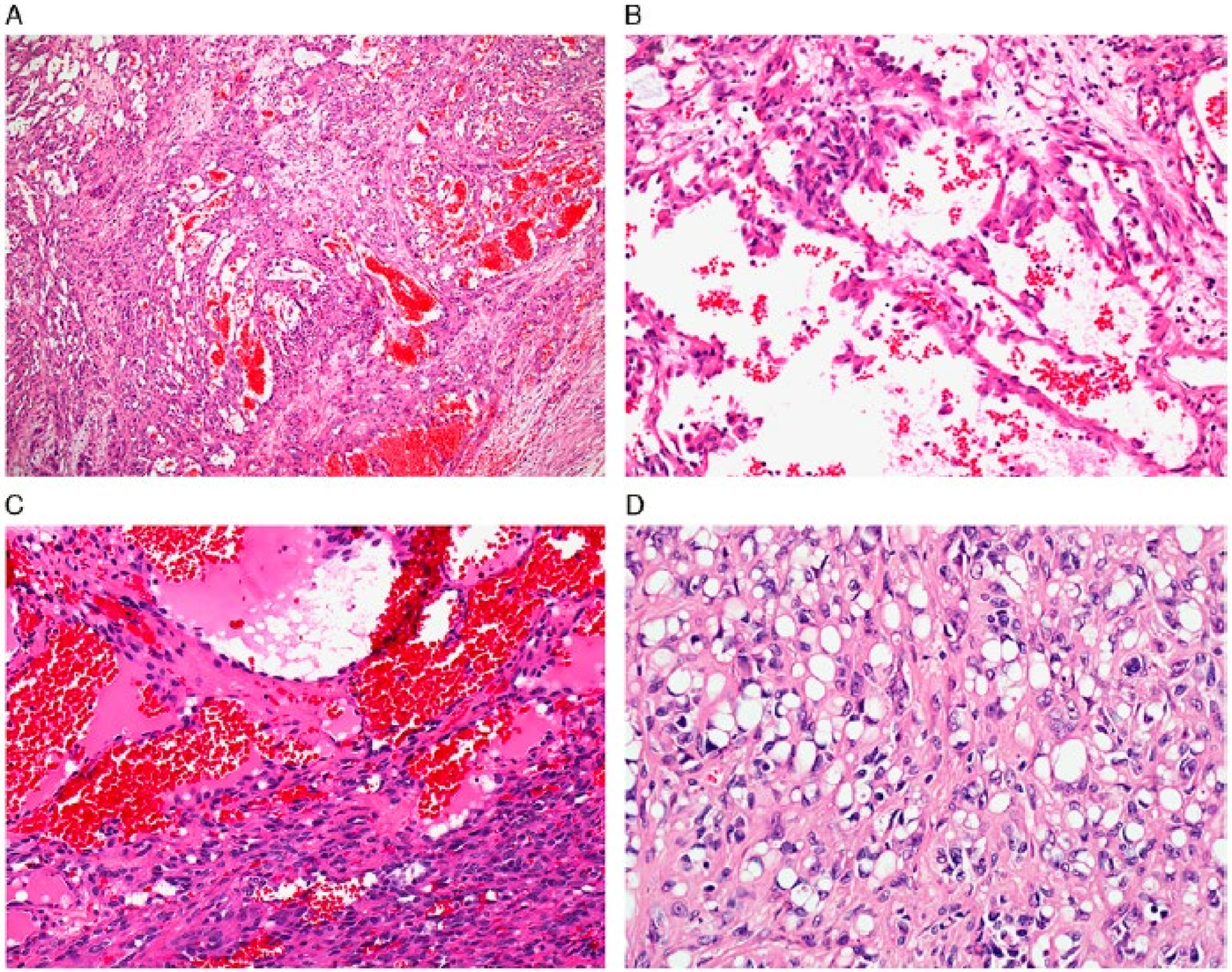
HE #	HE Type	Age/Sex	Site	Genetic Abnormality
1	RHE	10/male	Knee	*YAP1-MAML2**†
2	RHE	31/male	Shoulder	*YAP1*†
3	RHE	23/male	Fourth toe	*YAP1-MAML2*†
4	RHE	10/male	Buttock	*YAP1*†
5	RHE	50/female	Knee	*YAP1*†
6	CHE	9/female	Foot	*YAP1-MAML2*†
7	CHE	9/female	Heel	*YAP1-MAML2*†
8	CHE	7/female	Middle finger	*YAP1-MAML2*†
9	NE-CHE	37/male	Pancreas, liver, and lung lesions	*PTBP1-MAML2**

Composite Hemangioendothelioma

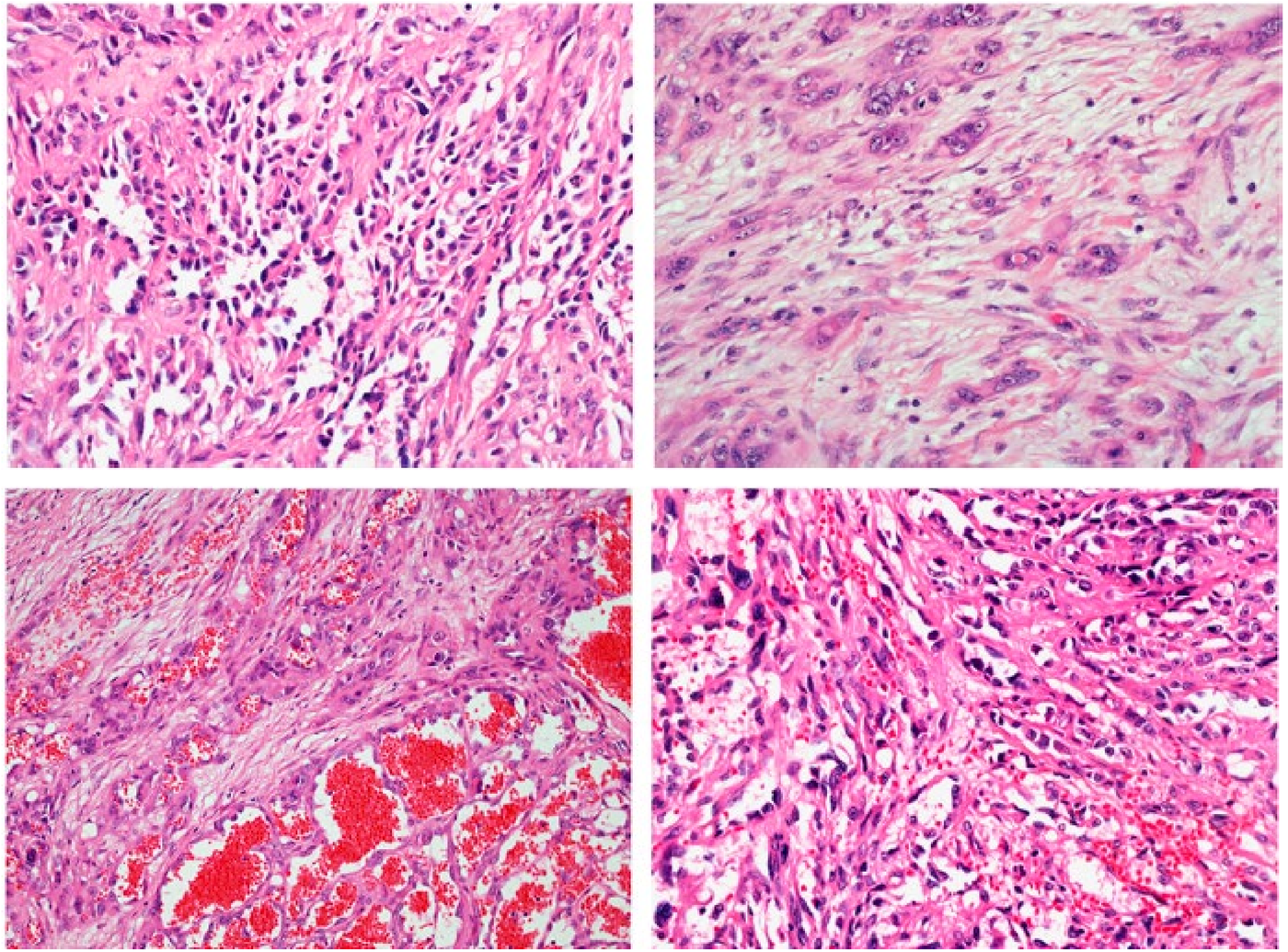
- Locally aggressive, rarely metastasizing vascular neoplasm, containing an admixture of histologically distinct components
- Chiefly in adults
  - Very rare pediatric or congenital cases
- Predominantly skin and superficial soft tissues
- High rate of local recurrence (50%)
- Low risk of lymph node (6%) or distant metastases(1%)

Morphological patterns

- Retiform Hemangioendothelioma-like
- Epithelioid Hemangioendothelioma-like
- Spindle cell Hemangioma-like
- Low-Grade Angiosarcoma-like



(*Adv Anat Pathol* 2015;22:254–259)



(*Adv Anat Pathol* 2015;22:254–259)

Recurrent *YAP1* and *MAML2* Gene Rearrangements in Retiform and Composite Hemangioendothelioma

Cristina R. Antonescu, MD, Brendan C. Dickson, MD,† Yun-Shao Sung, MSc,* Lei Zhang, MD,* Albert J.H. Suurmeijer, MD,‡ Albrecht Stenzinger, MD,§ Gunhild Mechtersheimer, MD,§ and Christopher D.M. Fletcher, MD‖*

Am J Surg Pathol 2020;44:1677–1684

HE #	HE Type	Age/Sex	Site	Genetic Abnormality
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7	CHE	9/female	Heel	*YAP1-MAML2*†
8	CHE	7/female	Middle finger	*YAP1-MAML2*†
9	NE-CHE	37/male	Pancreas, liver, and lung lesions	*PTBP1-MAML2**

ARTICLE

Check for updates

Loss of expression of YAP1 C-terminus as an ancillary marker for epithelioid hemangioendothelioma variant with *YAP1-TFE3* fusion and other YAP1-related vascular neoplasms

William J. Anderson[1], Christopher D. M. Fletcher[1] and Jason L. Hornick[1]✉

Modern Pathology; https://doi.org/10.1038/s41379-021-00854-2

Tumor type	Total cases	YAP1-CT lost	YAP1-CT retained
Epithelioid hemangioendothelioma with *YAP1-TFE3*	13	10	3
Epithelioid hemangioendothelioma with *WWTR1-CAMTA1*	20	1	19
Retiform hemangioendothelioma	4	4	0
Composite hemangioendothelioma	2	2	0
Pseudomyogenic hemangioendothelioma	10	0	10
Epithelioid hemangioma	19	0	19
Epithelioid angiosarcoma	10	0	10

MODERN PATHOLOGY (2017) 30, 1589–1602

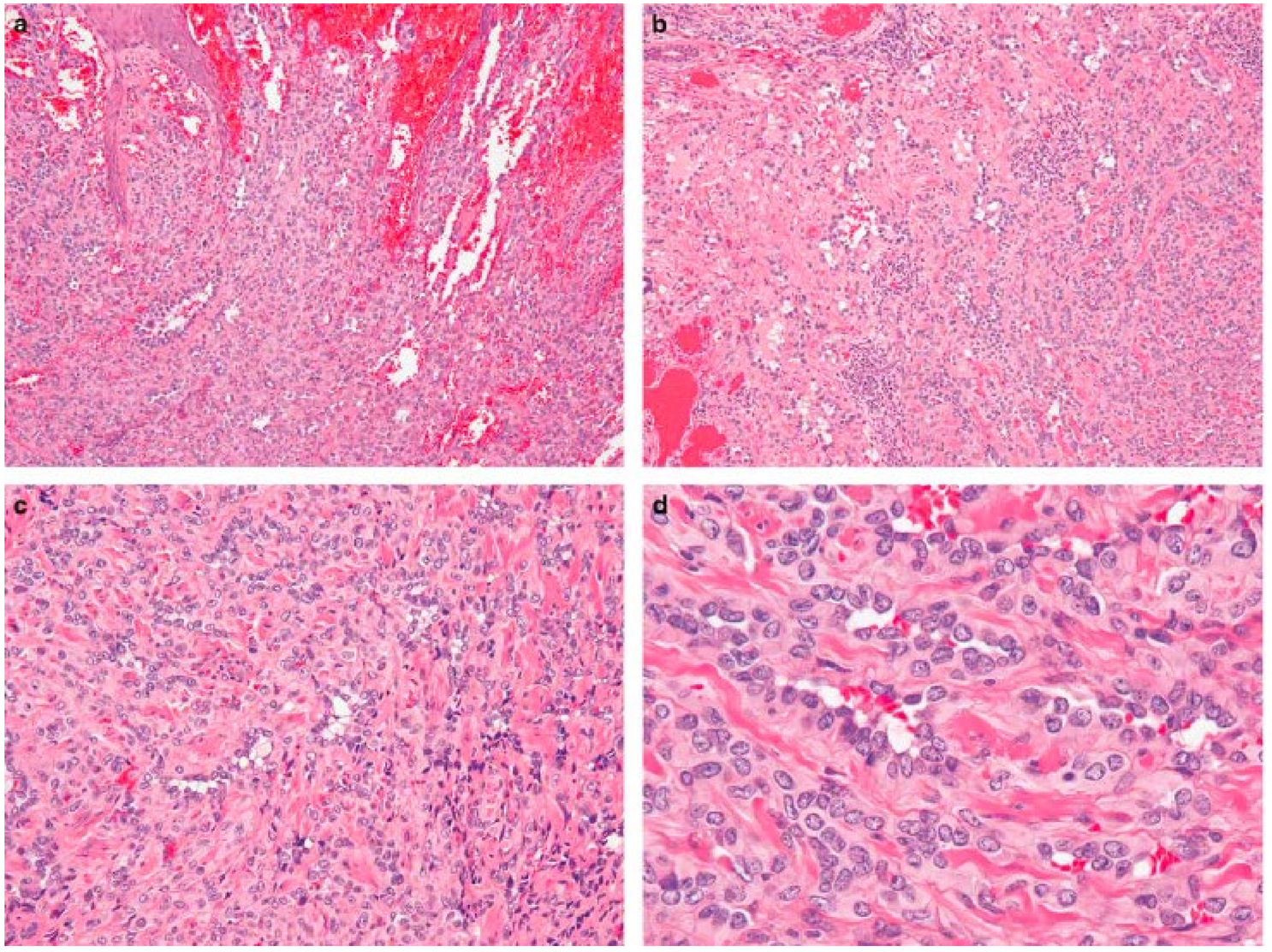
Composite hemangioendothelioma with neuroendocrine marker expression: an aggressive variant

Kyle D Perry[1], Alyaa Al-Ibraheemi[2], Brian P Rubin[3], Jin Jen[1,4], Hongzheng Ren[1], Jin Sung Jang[4], Asha Nair[1], Jaime Davila[4], Stefan Pambuccian[5], Andrew Horvai[6], William Sukov[1], Henry D Tazelaar[7] and Andrew L Folpe[1]

[1]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA; [2]Department of Pathology, Boston Children's Hospital, Boston, MA, USA; [3]Robert J Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, OH, USA; [4]Genome Analysis Core, Medical Genome Facility, Center for Individualized Medicine, Mayo Clinic, Rochester, MN, USA; [5]Department of Pathology, Loyola University Medical Center, Maywood, IL, USA; [6]Department of Pathology, University of California San Francisco, San Francisco, CA, USA and [7]Department of Laboratory Medicine and Pathology, Mayo Clinic, Scottsdale, AZ, USA

Table 1 Clinicopathological, immunohistochemical, and genetic results

Case	*Sex*	*Age (years)*	*Site*	*Size (cm)*	*LR*	*Met*	*Status*	*CD31*	*ERG*	*FLI-1*	*CD34*	*D2-40*	*SYN*	*CGA*	*CD56*	*CK*	*CAMTA1*	*Genetics*
1	M	47	Wrist	7.7	Yes	Liver/lung/humerus	DOD	+	+	+	−	−	+	−	+	−	−	ND
2	F	48	Right ankle	N/A	Yes	—	AWOD	+	+	+	+	−	+	−	−	−	ND	ND
3	F	36	Periaortic	2.1	—	Sacrum	AWD	+	+	+	−	+	+	−	+	−	−	*PTBP1-MAML2*
4	F	48	Vertebral	N/A	—	Lung	AWD	+	+	+	−	+	+	−	−	−	−	ND
5	M	27	Pulmonary vein	N/A	—	Brain	AWD	+	+	+	−	−	+	+	+	−	−	*EPC1-PHC2*
6	F	14	Ear	3.0	—	—	N/A	+	+	+	+	+	+	−	+	−	−	ND
7	F	55	Superficial hip	0.4	—	—	AWOD	+	+	+	−	+	+	−	−	−	ND	ND
8	M	55	Liver	6.9	—	—	AWOD	ND	ND	ND	ND	ND	+	−	−	−	ND	ND
9	M	15	Foot	1.2	—	—	AWOD	+	ND	+	+	+	+	−	−	−	−	ND
10	F	59	Cheek	9.5	—	—	N/A	+	+	+	+	+	+	−	+	−	ND	ND
11	M	9	Index finger	N/A	—	—	N/A	+	+	+	+	+	+	−	−	−	ND	ND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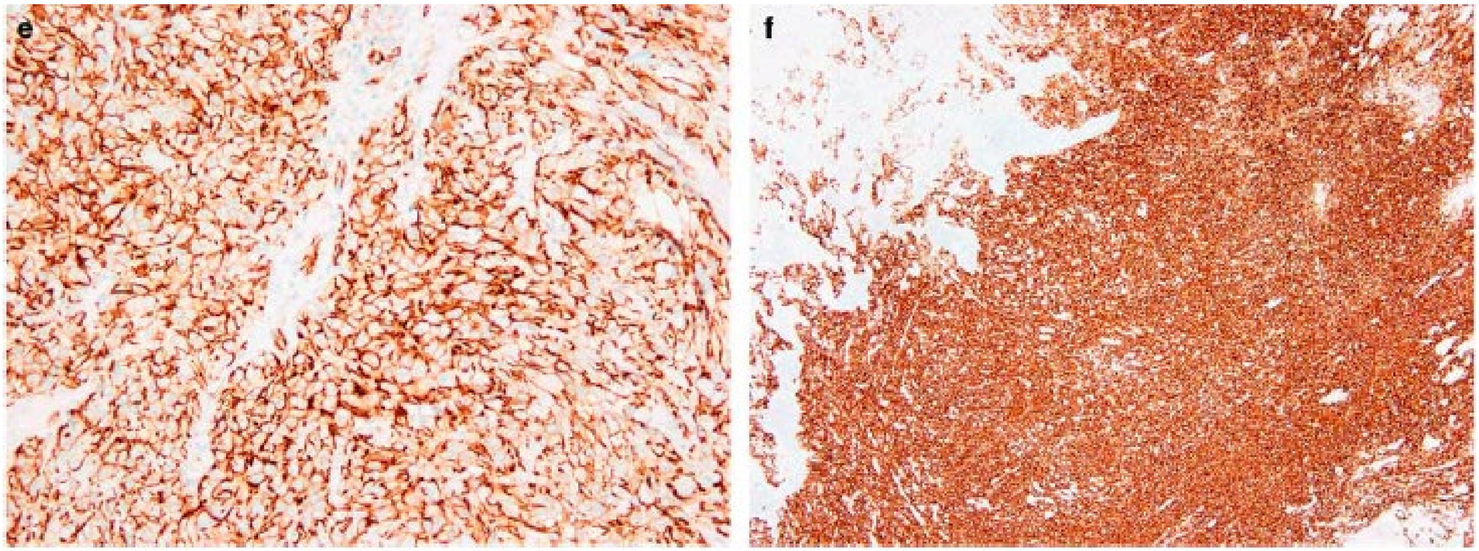
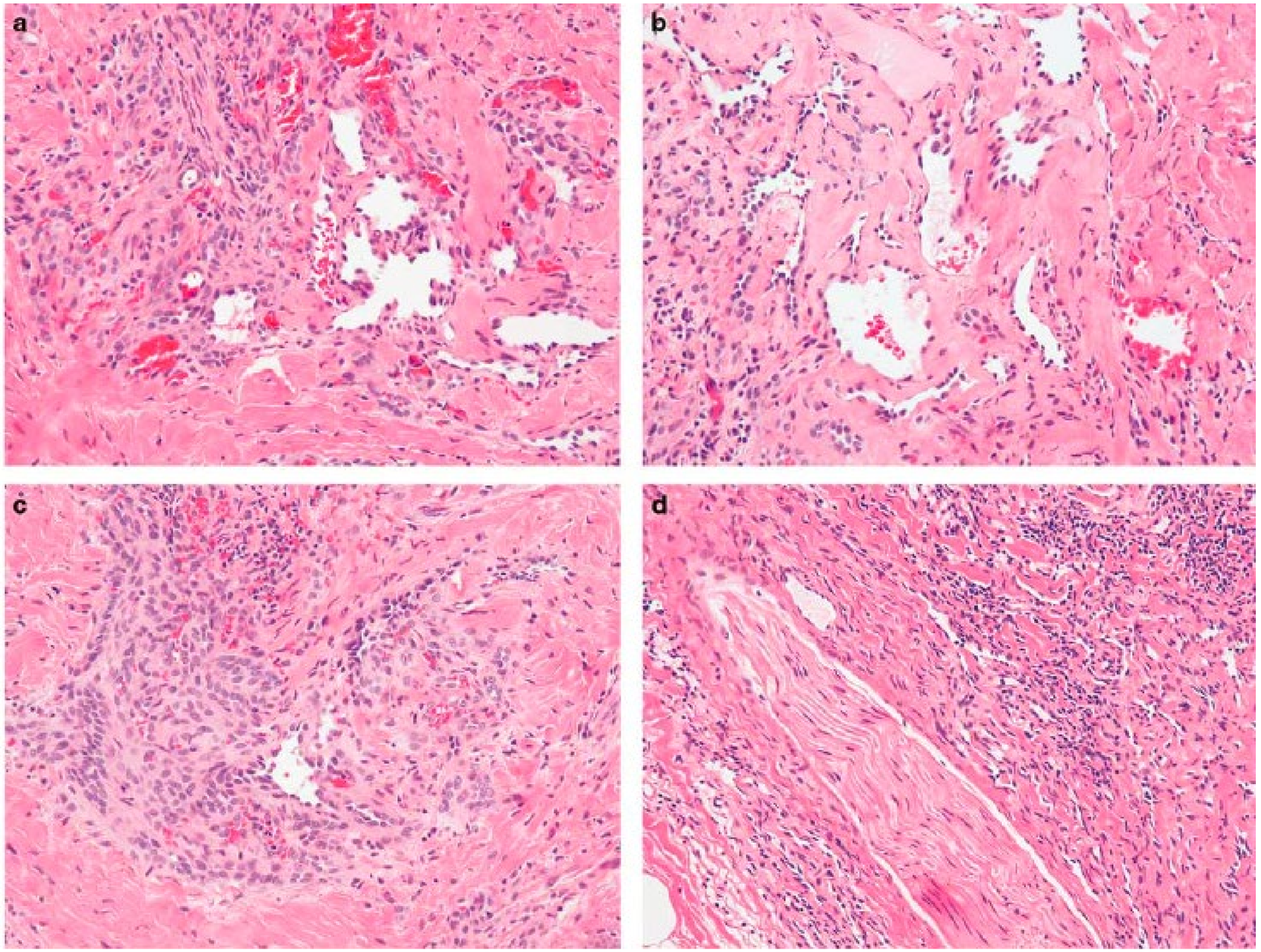
CD31

Synaptophysin



MODERN PATHOLOGY (2017) 30, 1589–1602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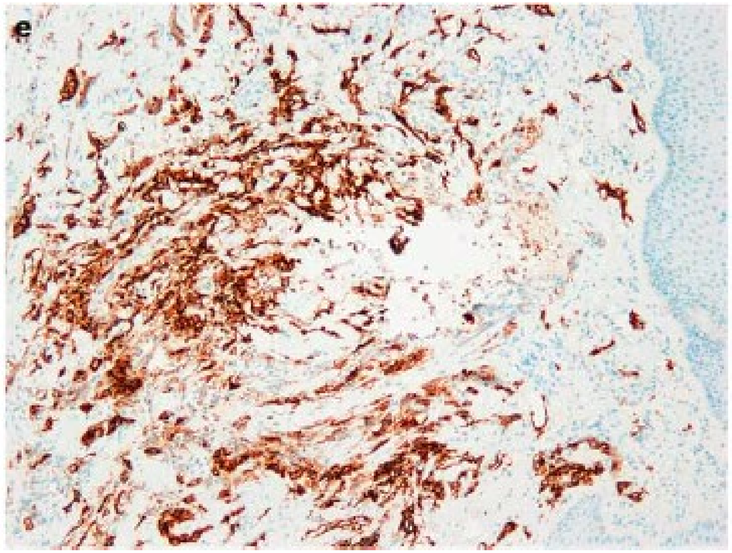
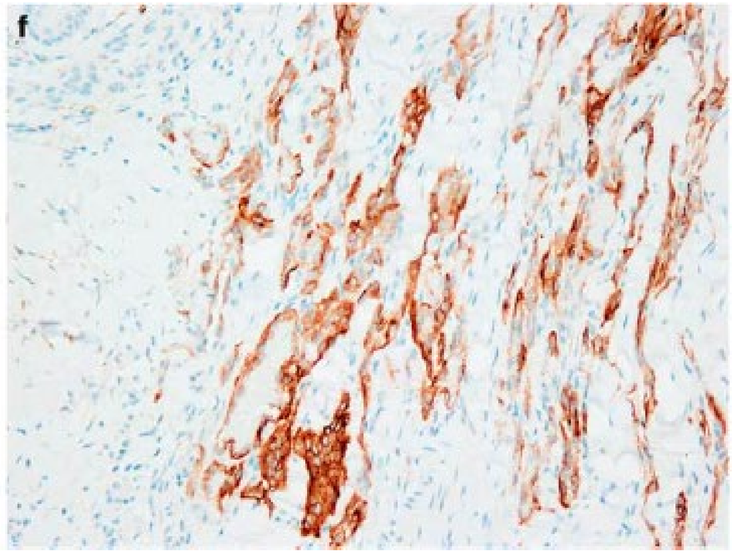
D2-40



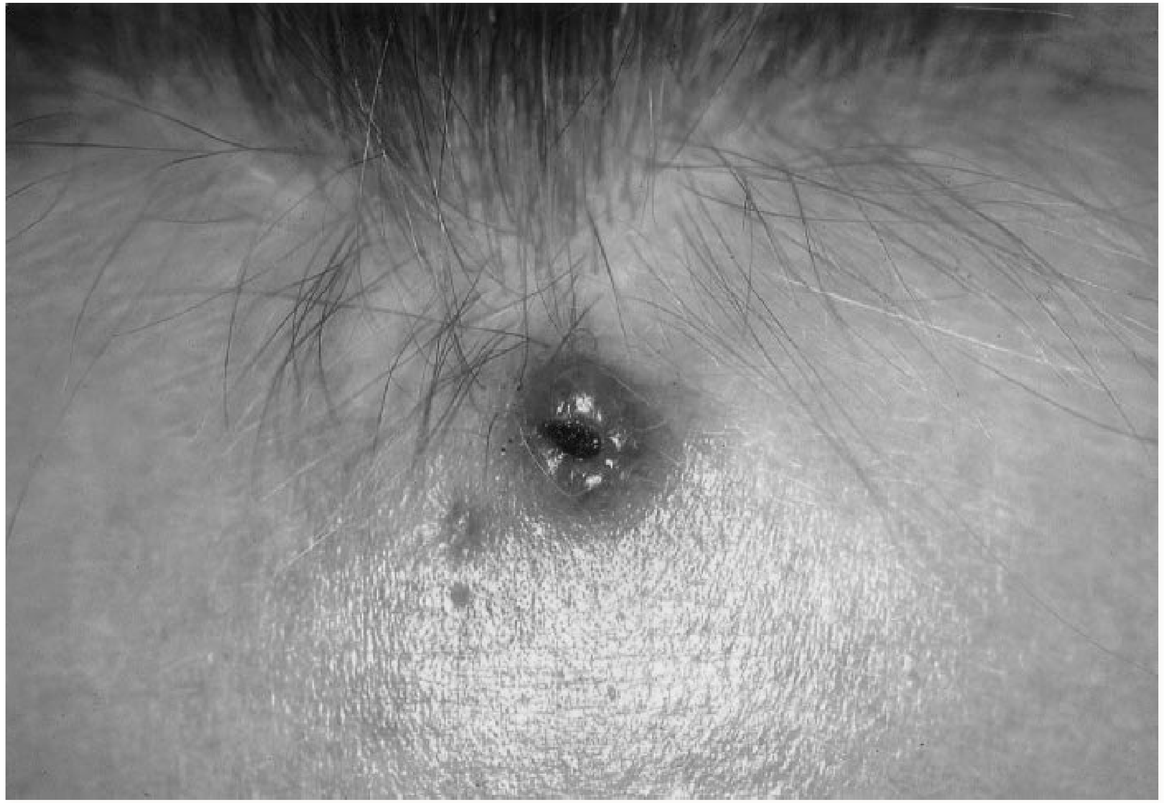
Synaptophysin

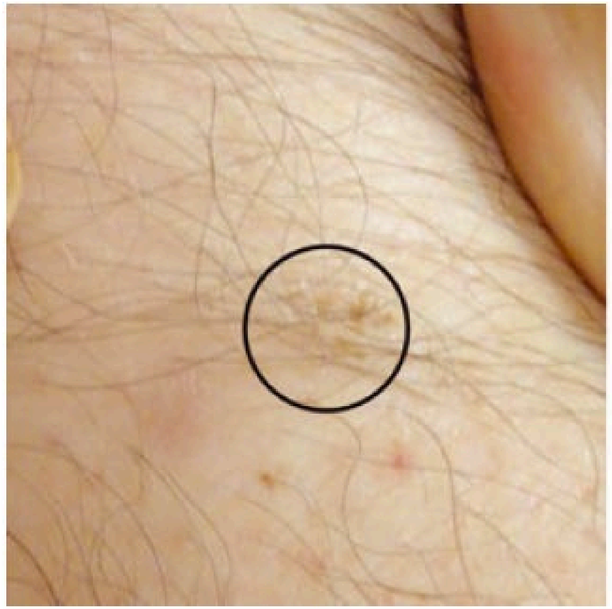


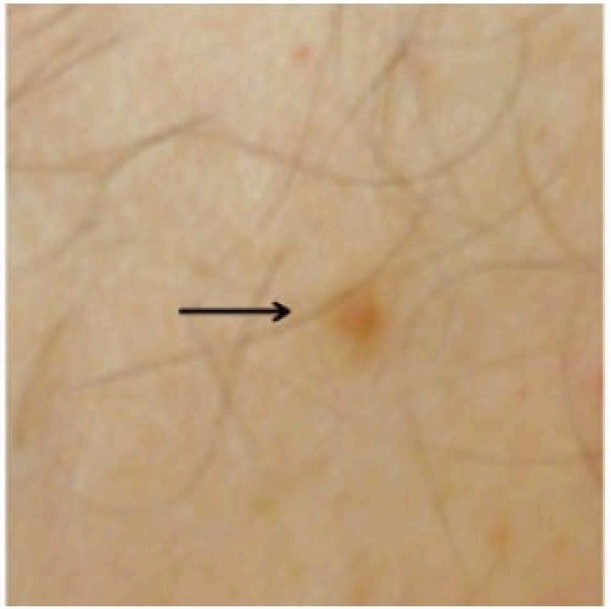
MODERN PATHOLOGY (2017) 30, 1589–1602

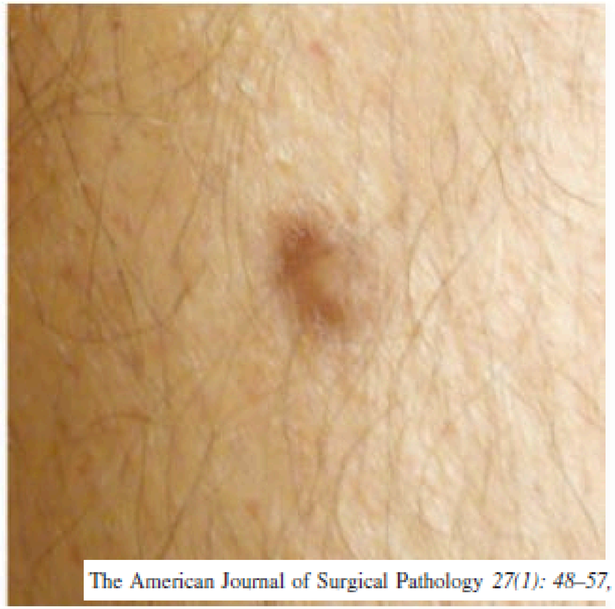
Pseudomyogenic Hemangioendothelioma

- Typically young adults with marked male (4:1) predilection
- Rare soft tissue of **intermediate biological potential**
  - Propensity for local recurrence or frequent (and characteristic) development of additional nodules in the same region
  - Metastasis is rare
- Conservative management is the mainstay of therapy



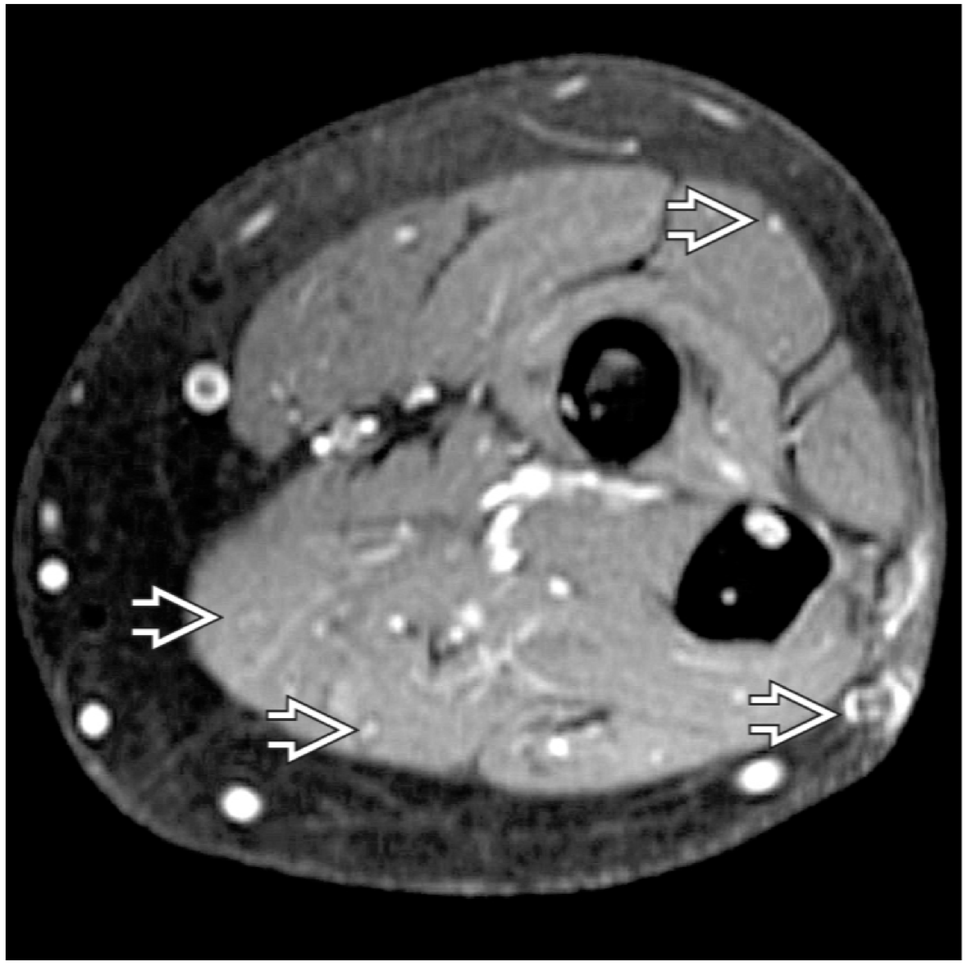






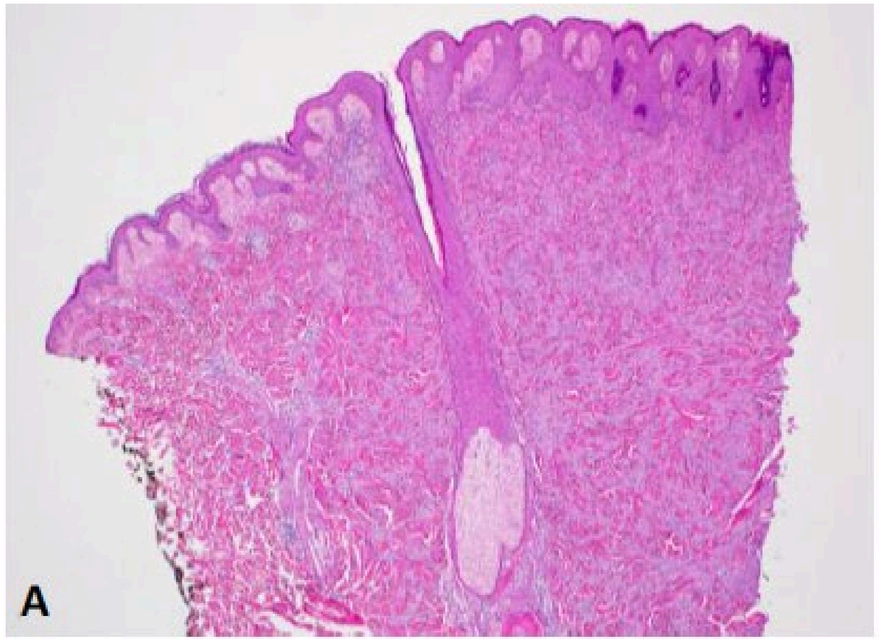
The American Journal of Surgical Pathology *27(1): 48–57, 2003*

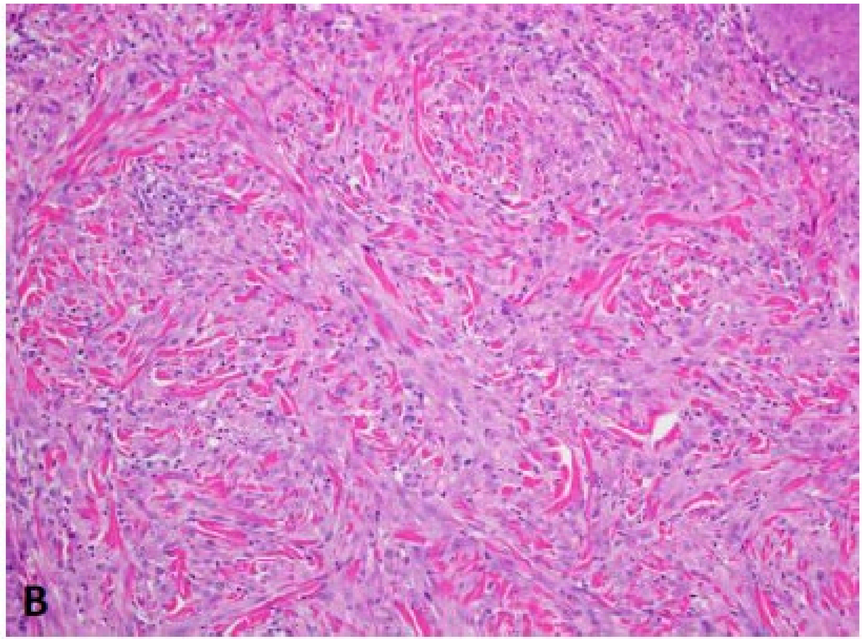
Radiologic findings

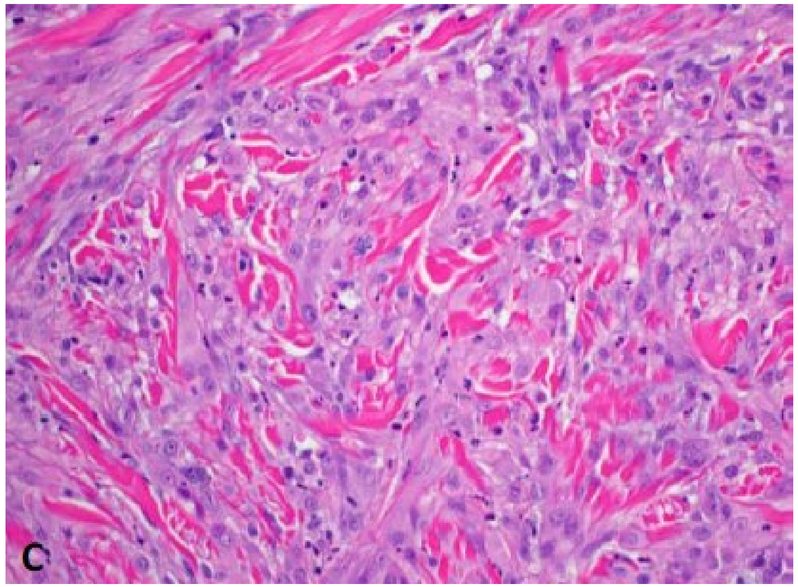


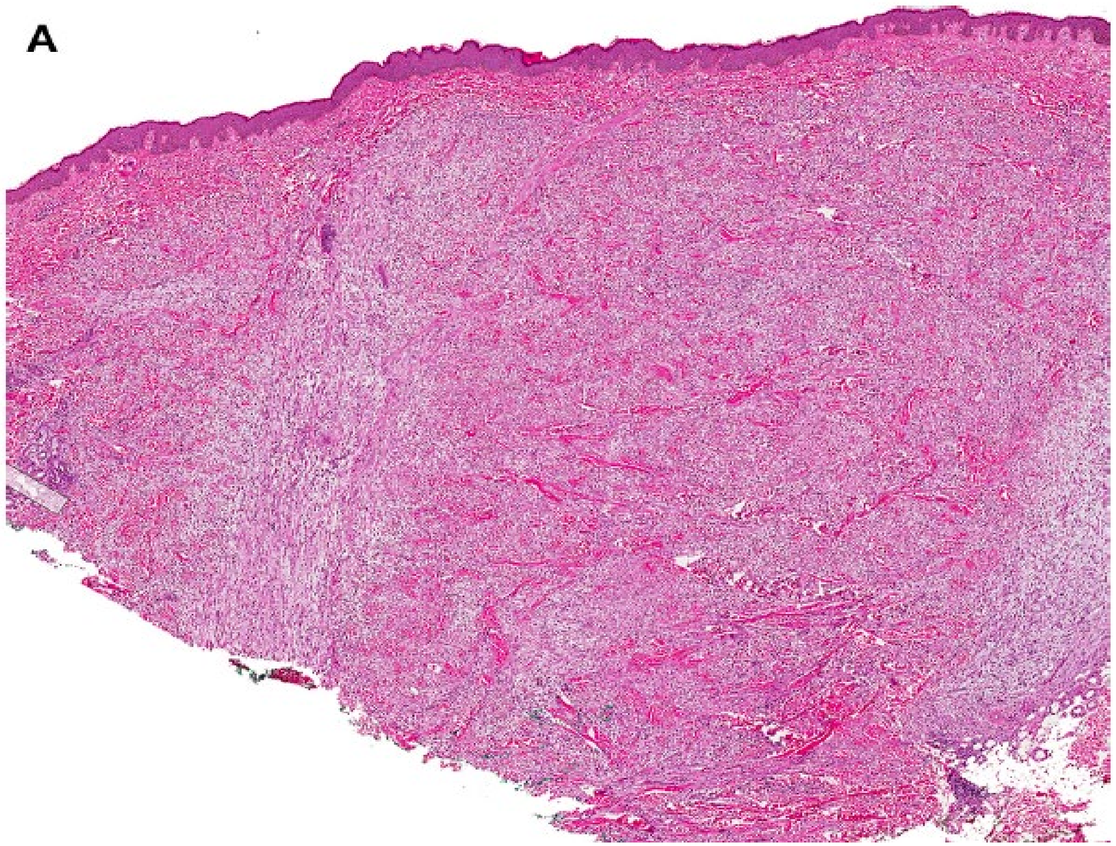
•Diagnostic Pathology: Soft Tissue Tumors 2nd Ed 2015, Elsevier

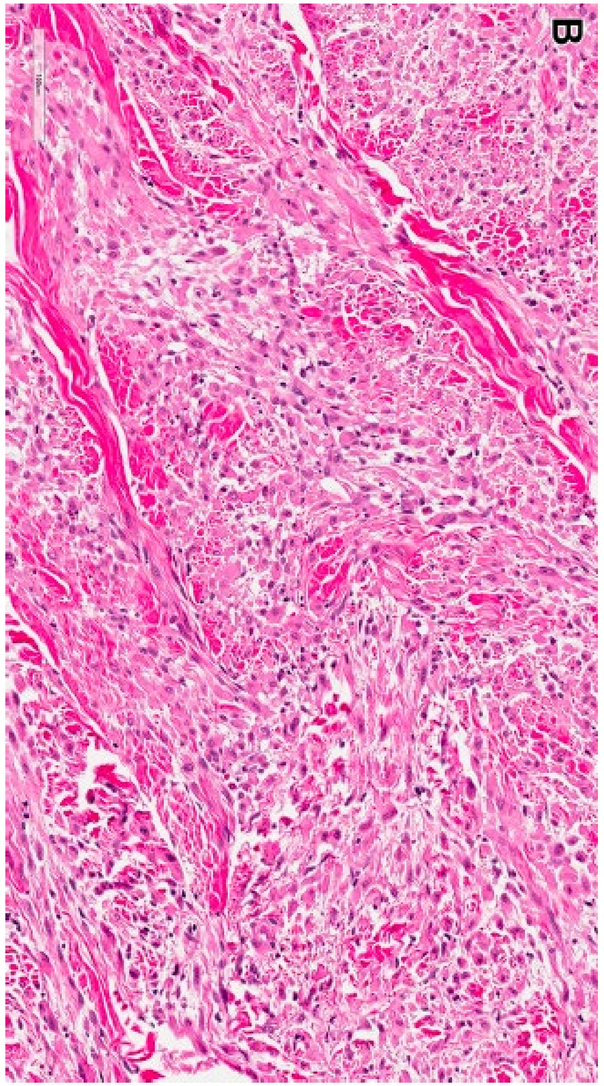
Microscopic findings



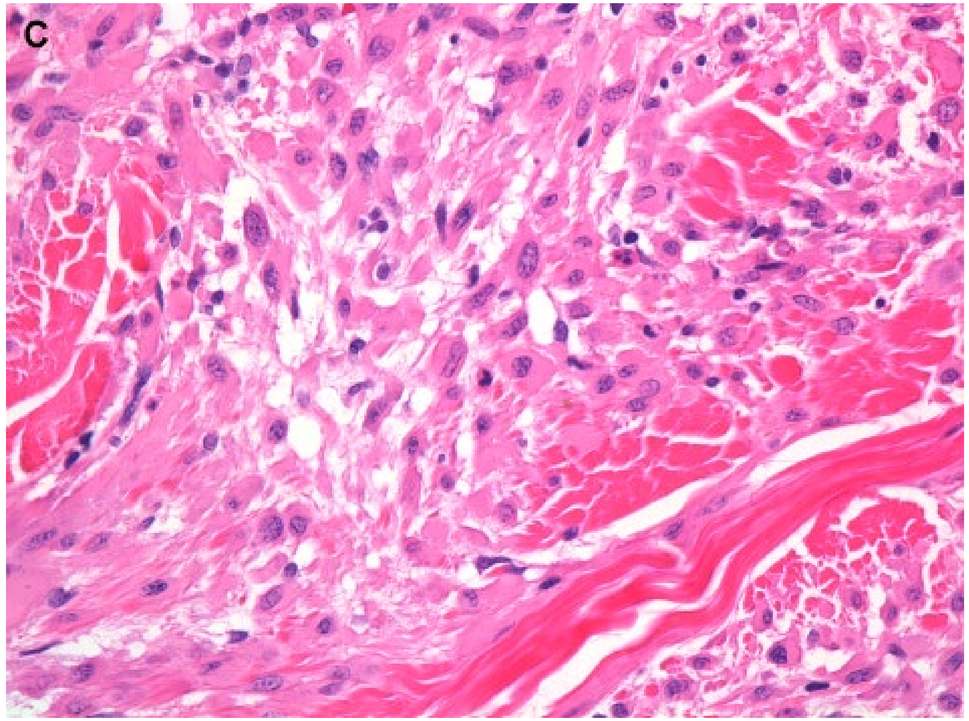


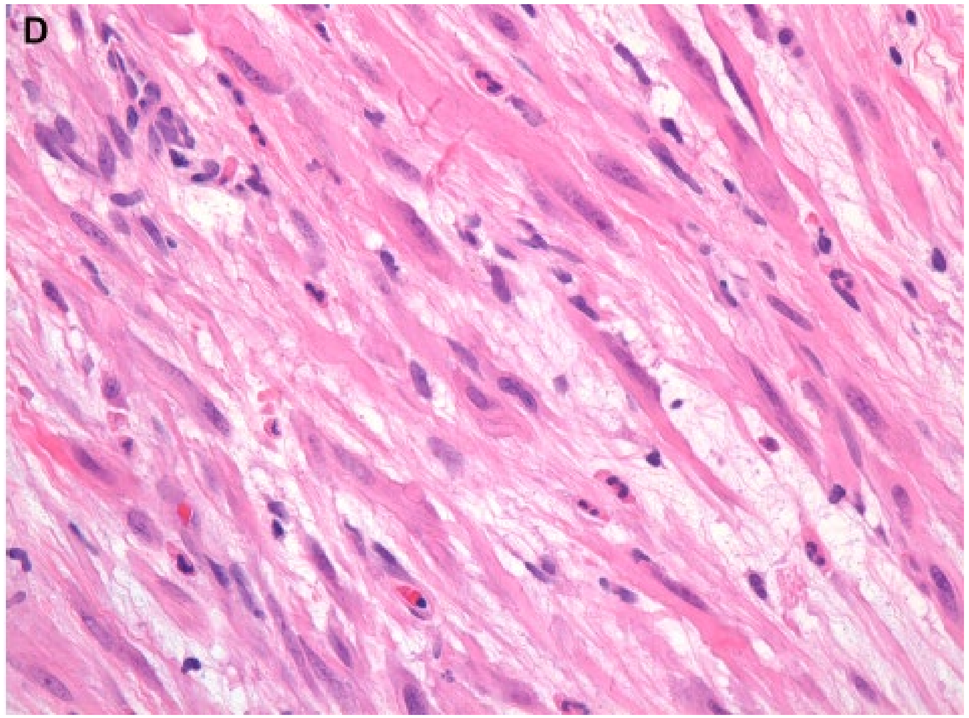






Memorial Sloan Kettering Cancer Center





POSITIVE

CKAE1/3

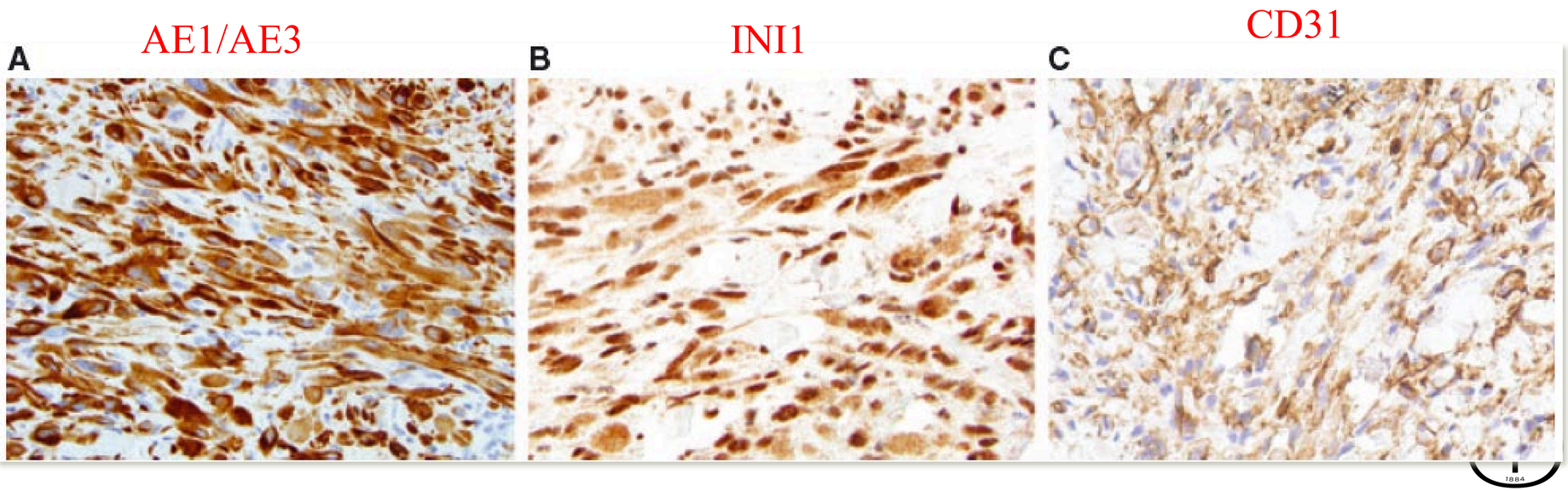
ERG

CD31 (variable)

NEGATIVE

CD34

INI-1 (SMRCB1) is retained



Other Differential Diagnosis

- Spindle cell squamous cell carcinoma
- Cellular benign fibrous histiocytoma
- Smooth muscle neoplasms
- Epithelioid Hemangioendothelioma

Journal of Pathology
J Pathol 2014; **232:** 534–540
Published online 29 January 2014 in Wiley Online Library
(wileyonlinelibrary.com) DOI: 10.1002/path.4322

ORIGINAL PAPER

A novel *SERPINE1–FOSB* fusion gene results in transcriptional up-regulation of *FOSB* in pseudomyogenic haemangioendothelioma

Charles Walther,[1,2*] Johnbosco Tayebwa,[1] Henrik Lilljebjörn,[1] Linda Magnusson,[1] Jenny Nilsson,[1] Fredrik Vult von Steyern,[3] Ingrid Øra,[4] Henryk A Domanski,[2] Thoas Fioretos,[1] Karolin H Nord,[1] Christopher DM Fletcher[5] and Fredrik Mertens[1]

Expanding the Spectrum of Genetic Alterations in Pseudomyogenic Hemangioendothelioma With Recurrent Novel *ACTB-FOSB* Gene Fusions

Narasimhan P. Agaram, MBBS, Lei Zhang, MD, Paolo Cotzia, MD, and Cristina R. Antonescu, MD

(*Am J Surg Pathol* 2018;42:1653–1661)

Fusion of the Genes *WWTR1* and *FOSB* in Pseudomyogenic Hemangioendothelioma

IOANNIS PANAGOPOULOS[1], INGVILD LOBMAIER[2], LUDMILA GORUNOVA[1] and SVERRE HEIM[1,3]

CANCER GENOMICS & PROTEOMICS *16*: 293-298 (2019)

A novel *CLTC-FOSB* gene fusion in pseudomyogenic hemangioendothelioma of bone

Julia A. Bridge[1,2] | Janos Sumegi[1] | Thomas Royce[1] | Michael Baker[3] | Konstantinos Linos[3]

Genes Chromosomes Cancer. 2021;60:38–42

Novel *EGFL7–FOSB* fusion in pseudomyogenic haemangioendothelioma with widely metastatic disease

Histopathology 2021

Primary pseudomyogenic haemangioendothelioma of the testis with a novel *POTEI::FOSB* gene fusion

Sugita et al. Diagnostic Pathology (2016) 11:75
DOI 10.1186/s13000-016-0530-2

Diagnostic Pathology

RESEARCH Open Access

Diagnostic utility of FOSB immunohistochemistry in pseudomyogenic hemangioendothelioma and its histological mimics

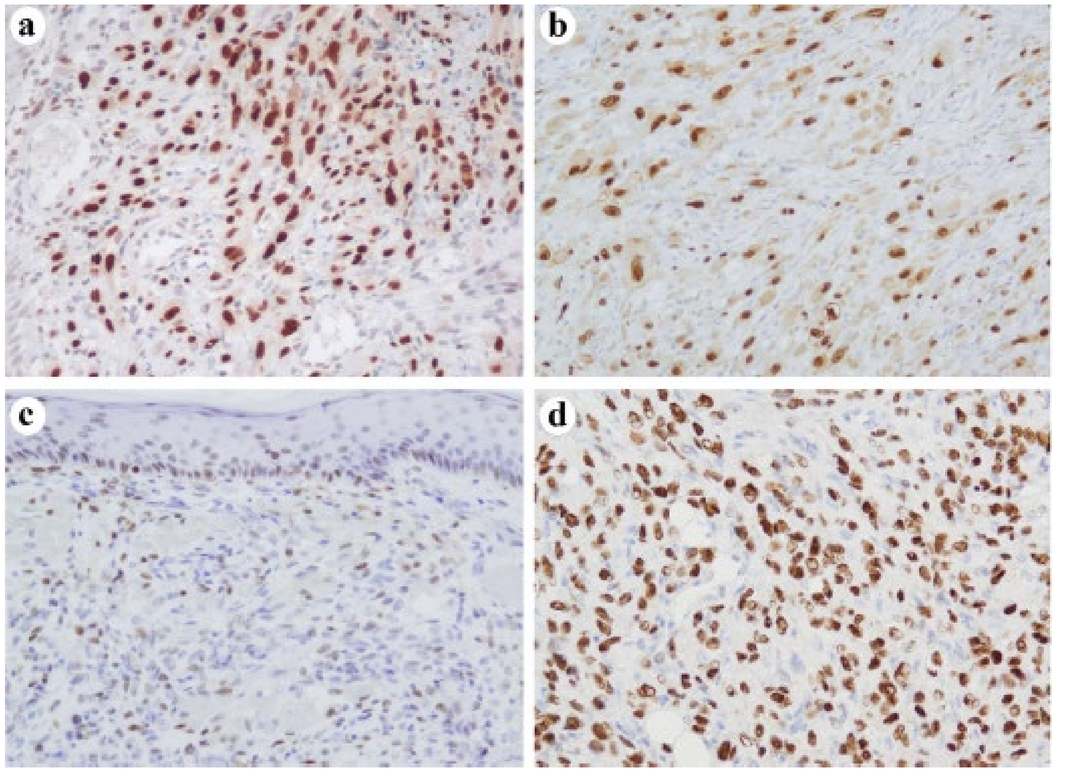
Shintaro Sugita[1], Hiroshi Hirano[1], Noriaki Kikuchi[1], Terufumi Kubo[1], Hiroko Asanuma[1], Tomoyuki Aoyama[1], Makoto Emori[2] and Tadashi Hasegawa[1*]

FOSB is a Useful Diagnostic Marker for Pseudomyogenic Hemangioendothelioma

Yin P. Hung, MD, PhD, Christopher D.M. Fletcher, MD, FRCPath, and Jason L. Hornick, MD, PhD

(*Am J Surg Pathol* 2016;00:000–000)

Case	Age (y)/sex	Histology	Location	FOSB		CAMTA1	
				%	Intensity	%	Intensi
1	20/F	PHE	Bone (mul)[a]	100	Strong	-	-
2	36/M	PHE	Bone (mul)[a]	100	Strong	NA	NA
3	15/F	PHE	Thigh	100	Strong	-	-
4	54/M	PHE	Calcaneus	100	Strong	-	-
5	62/F	EHE	Forehead	-	-	100	Moder
6	71/F	EHE	Femur	10	Weak	100	Moder
7	73/F	EHE	Liver (mul)	-	-	100	Strong
8	86/F	EHE	Upper arm	10	Weak	100	Strong
9	68/F	EHE	Forearm	10	Weak	100	Strong
10	32/M	EHE	Liver (mul)	-	-	100	Strong
11	72/M	AS	Vertebra	10	Weak	-	-
12	48/M	AS	Humerus	10	Weak	10	Weak
13	89/M	AS	Head	-	-	10	Weak
14	62/F	AS	Head	10	Weak	-	-
15	70/M	AS	Head	10	Weak	10	Weak
16	82/F	AS	Head	-	-	-	-
17	74/F	AS	Upper arm	10	Weak	10	Weak
18	77/M	AS	Head	10	Weak	10	Weak
19	89/F	KS	Trunk, limbs (mul)	10	Weak	-	-
20	68/M	KS	Trunk, limbs (mul)	10	Weak	10	Weak
21	76/M	KS	Larynx, limbs (mul)	10	Weak	-	-
22	82/M	KS	Limbs (mul)	10	Weak	-	-
23	75/F	ES	Thigh	10	Weak	-	-
24	73/F	ES	Thigh	10	Weak	-	-
25	55/M	ES	Forearm	-	-	-	-
26	30/M	ES	Thigh	10	Weak	-	-
27	80/F	ES	Genital region	-	-	-	-

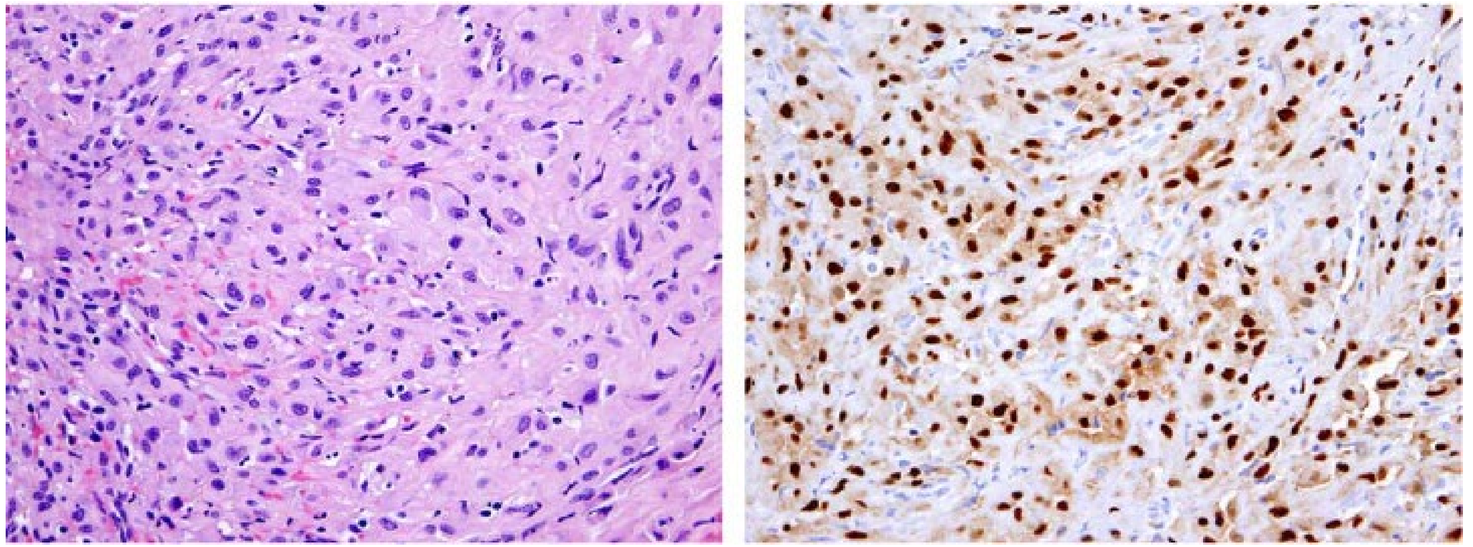


Sugita *et al. Diagnostic Pathology* (2016) 11:75
DOI 10.1186/s13000-016-0530-2

TABLE 1. Summary of Immunohistochemical Staining for FOSB

Tumor Type	Total Cases	FOSB Positive (%)*	0	1+	2+	3+	4+
Pseudomyogenic hemangioendothelioma	50	48 (96)	2	0	0	1	47
Epithelioid hemangioma	24	13 (54)	6	4	1	6	7
Conventional	8	6 (75)	0	1	1	4	2
Cellular	10	1 (10)	6	3	0	0	1
Angiolymphoid hyperplasia with eosinophilia	6	6 (100)	0	0	0	2	4
Other endothelial neoplasms and histologic mimics	200	7 (4)	142	42	9	4	3
Epithelioid angiosarcoma	20	1 (5)	11	7	1	0	1
Spindle-cell angiosarcoma	10	1 (10)	9	0	0	1	0
Epithelioid hemangioendothelioma	20	1 (5)	15	4	0	1	0
Epithelioid angiomatous nodule	10	0	9	1	0	0	0
Epithelioid sarcoma	20	0	10	10	0	0	0
Spindle-cell squamous cell carcinoma	20	0	16	4	0	0	0
Spindle-cell rhabdomyosarcoma	20	0	19	1	0	0	0
Leiomyosarcoma	20	0	18	2	0	0	0
Cellular benign fibrous histiocytoma	20	0	12	4	4	0	0
Nodular fasciitis	20	2 (10)	7	7	4	2	0
Proliferative fasciitis	20	2 (10)	16	2	0	0	2

0, <5%; 1+, 5% to 25%; 2+, 25% to 50%; 3+, 50% to 75%; 4+, 75% to 100%.
*FOSB positivity was defined as moderate-to-strong nuclear staining in at least 50% of cells.



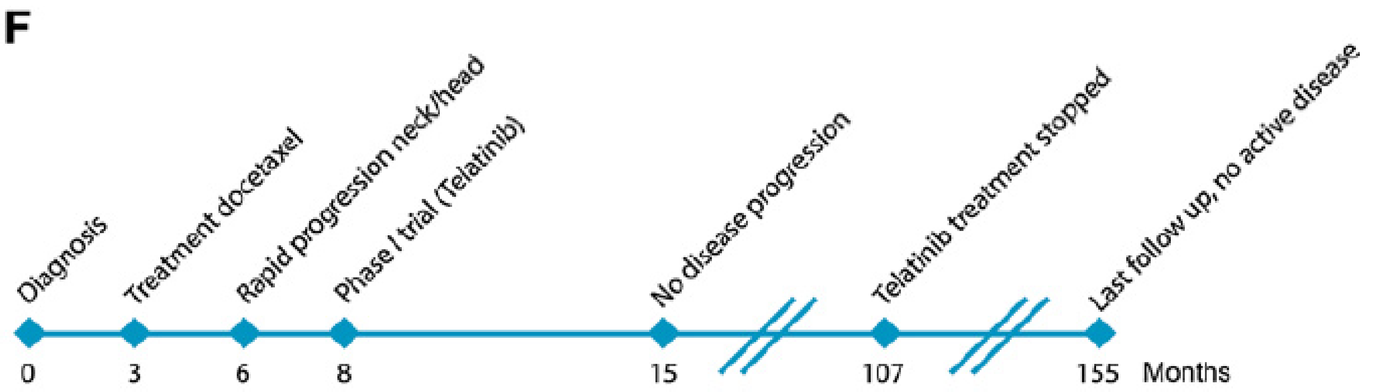
Biology of Human Tumors

Clinical Cancer Research

Telatinib Is an Effective Targeted Therapy for Pseudomyogenic Hemangioendothelioma

David G.P. van IJzendoorn[1], Stefan Sleijfer[2], Hans Gelderblom[3], Ferry A.L.M. Eskens[2], Geert J.L.H. van Leenders[4], Karoly Szuhai[5], and Judith V.M.G. Bovée[1]

Clin Cancer Res; 24(11) June 1, 2018



Memorial Sloan Kettering Cancer Center

Malignant Vascular Tumors

Epithelioid Hemangioendothelioma (EHE) and **CAMTA1**

- Rare low-grade, malignant vascular neoplasm that shows endothelial differentiation

- Less aggressive than angiosarcoma
  - Risk of metastasis in ~ 20-30% of cases
  - Death in approximately 15% of cases

J Cutan Pathol 2008: 35: 236–240
doi: 10.1111/j.1600-0560.2007.00790.x
Blackwell Munksgaard. Printed in Singapore

Journal of
Cutaneous Pathology

Cutaneous epithelioid hemangioendothelioma

Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor of endothelial cell origin. We describe an EHE arising on the plantar surface of the foot that was treated as verruca vulgaris for several years before a biopsy showed EHE. We discuss the clinical and histopathologic differential diagnoses for these tumors and review additional cases in which EHE has been mistaken for benign entities clinically.

Loren E. Clarke[1], Robert Lee[2], Giuseppe Militello[2], Rosalie Elenitsas[2] and Jacqueline Junkins-Hopkins[2]

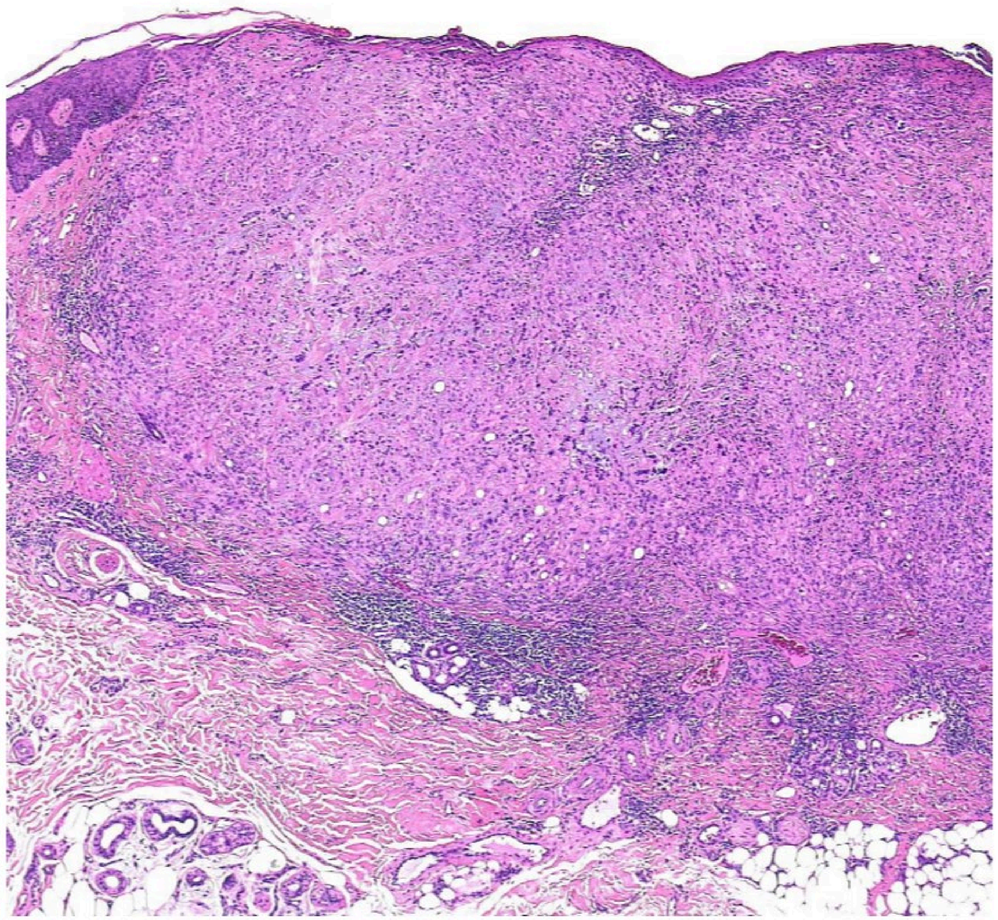
[1]Department of Pathology, Penn State Milton S. Hershey Medical Center, Hershey, PA, USA, and
[2]Department of Dermatology, The Hospital of the University of Pennsylvania, Philadelphia, PA, USA

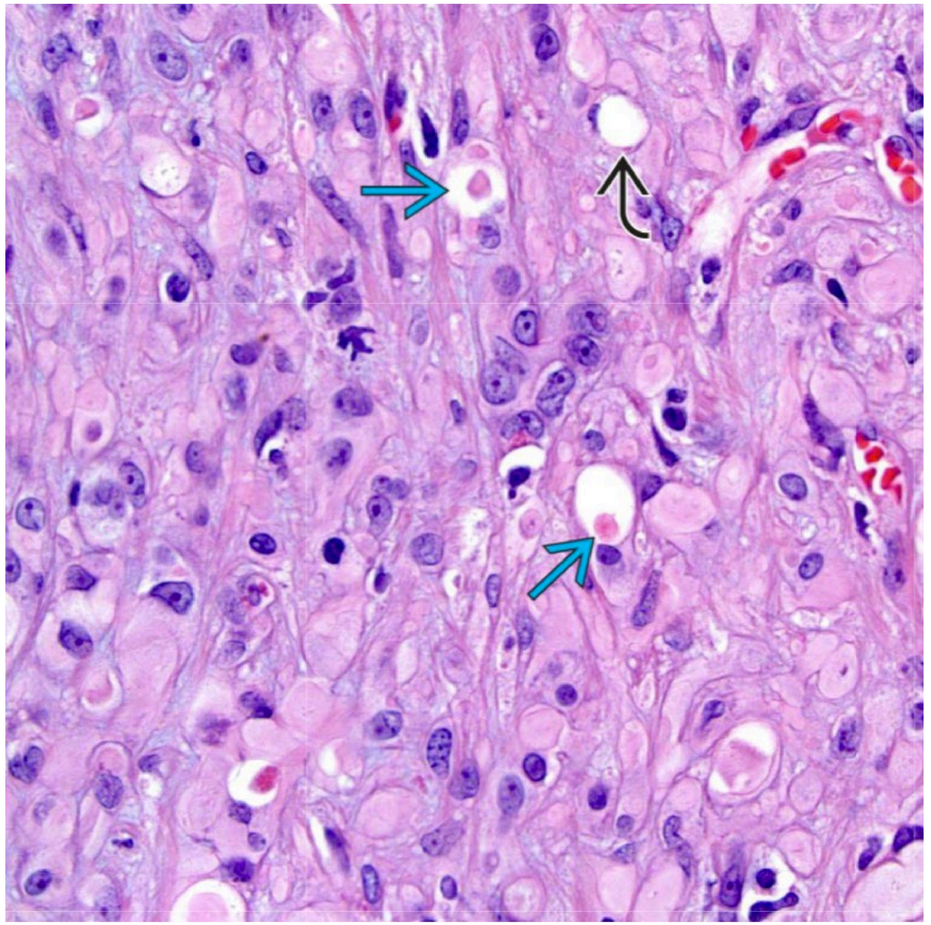
Clinical Features

- Affects patients of all ages but rare during childhood
- Typically solitary lesion on the extremities
- Can involve larger preexisting vessels

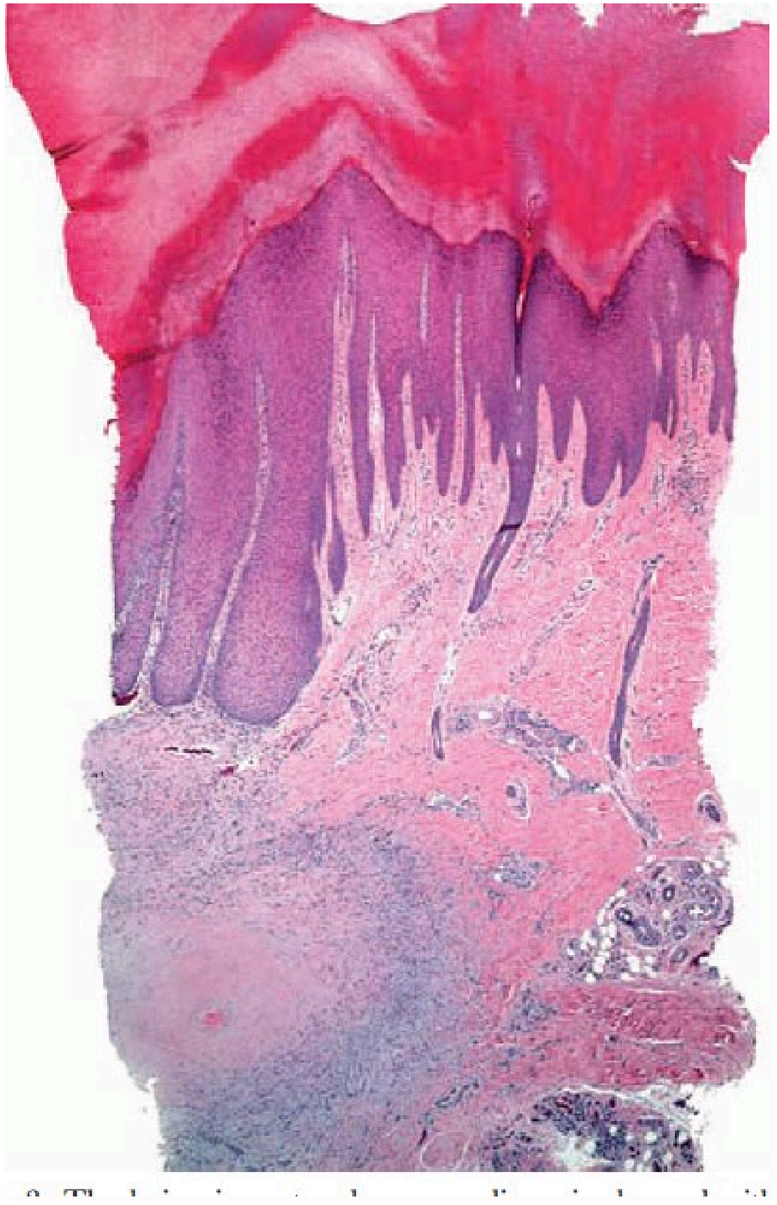
<u>Multiple cutaneous nodules</u>

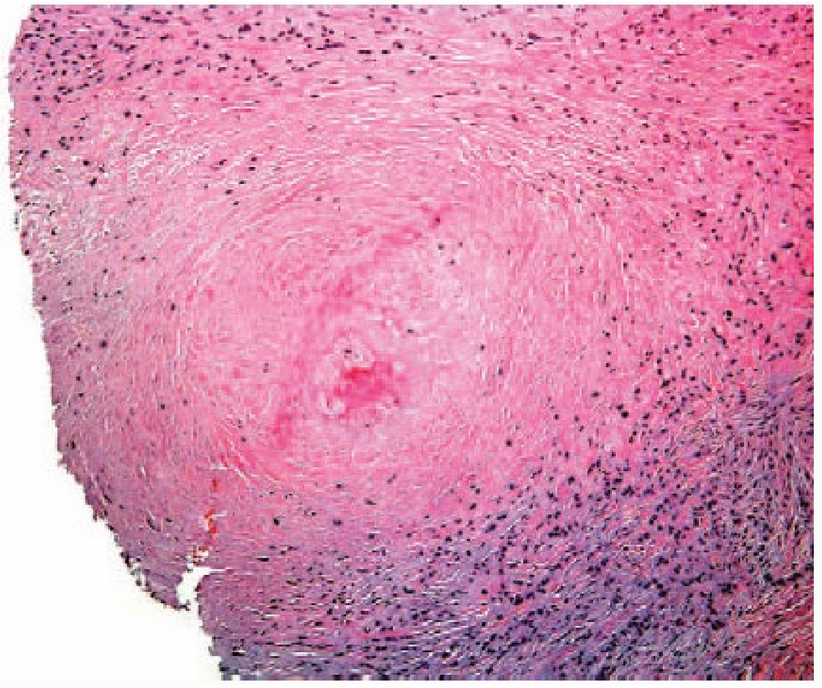
- !!!!**Metastasizing deep soft tissue or osseous EHE should be ruled out**!!!!

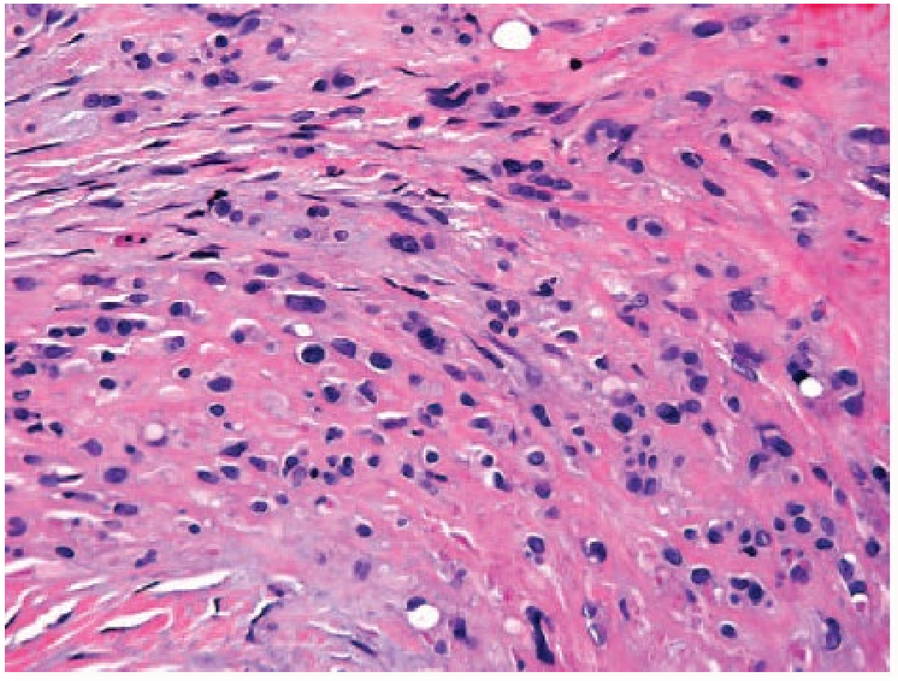


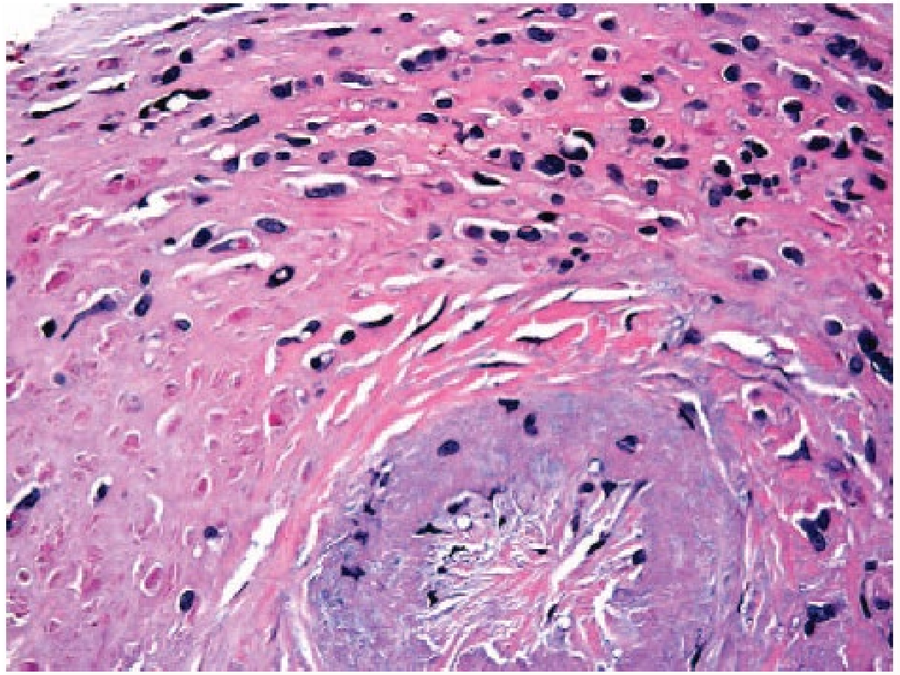


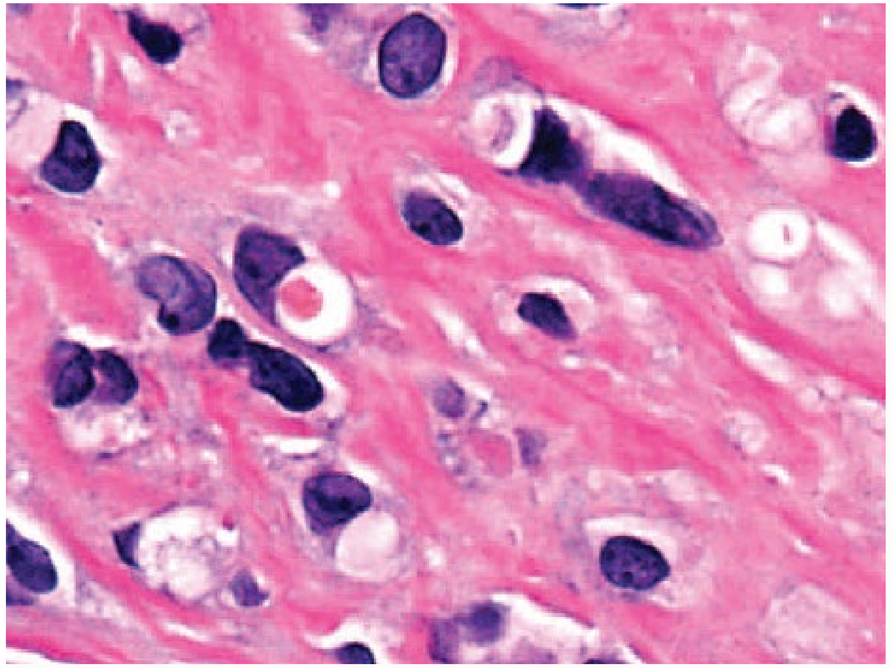
•Diagnostic Pathology: Vascular 2016 Elsevier

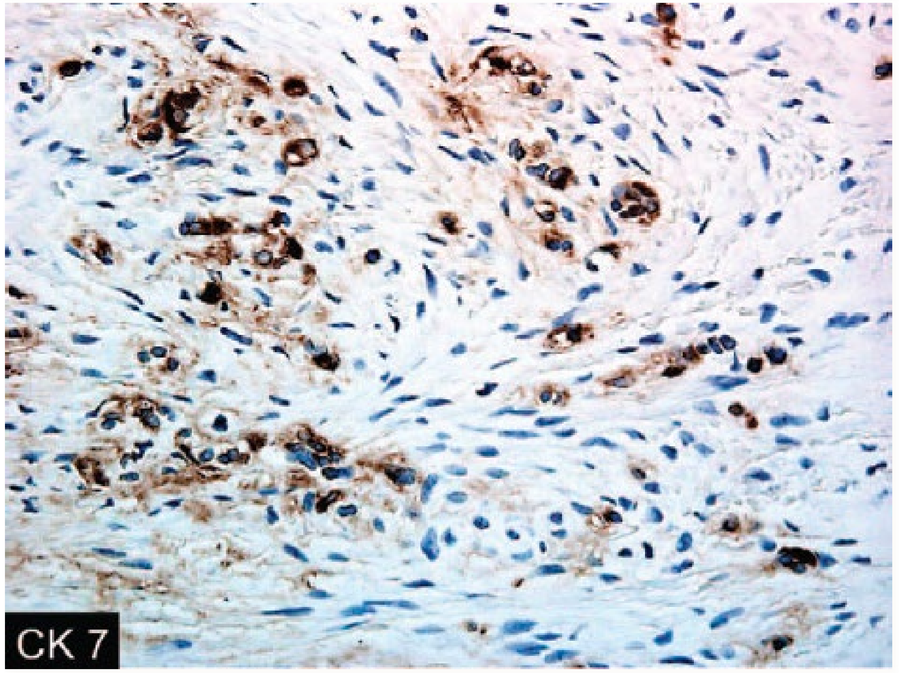


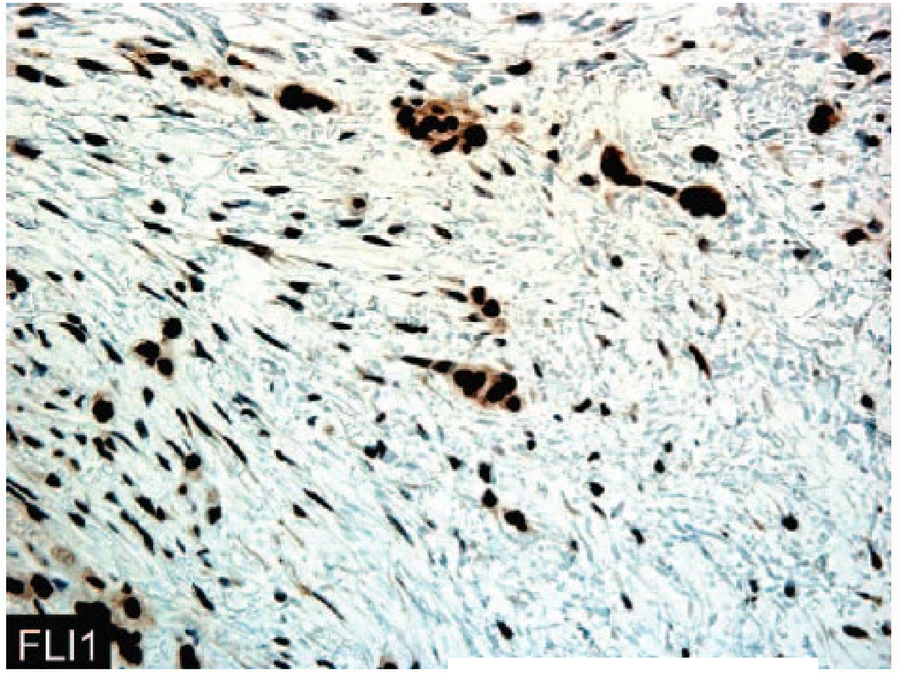









CK 7


FLI1

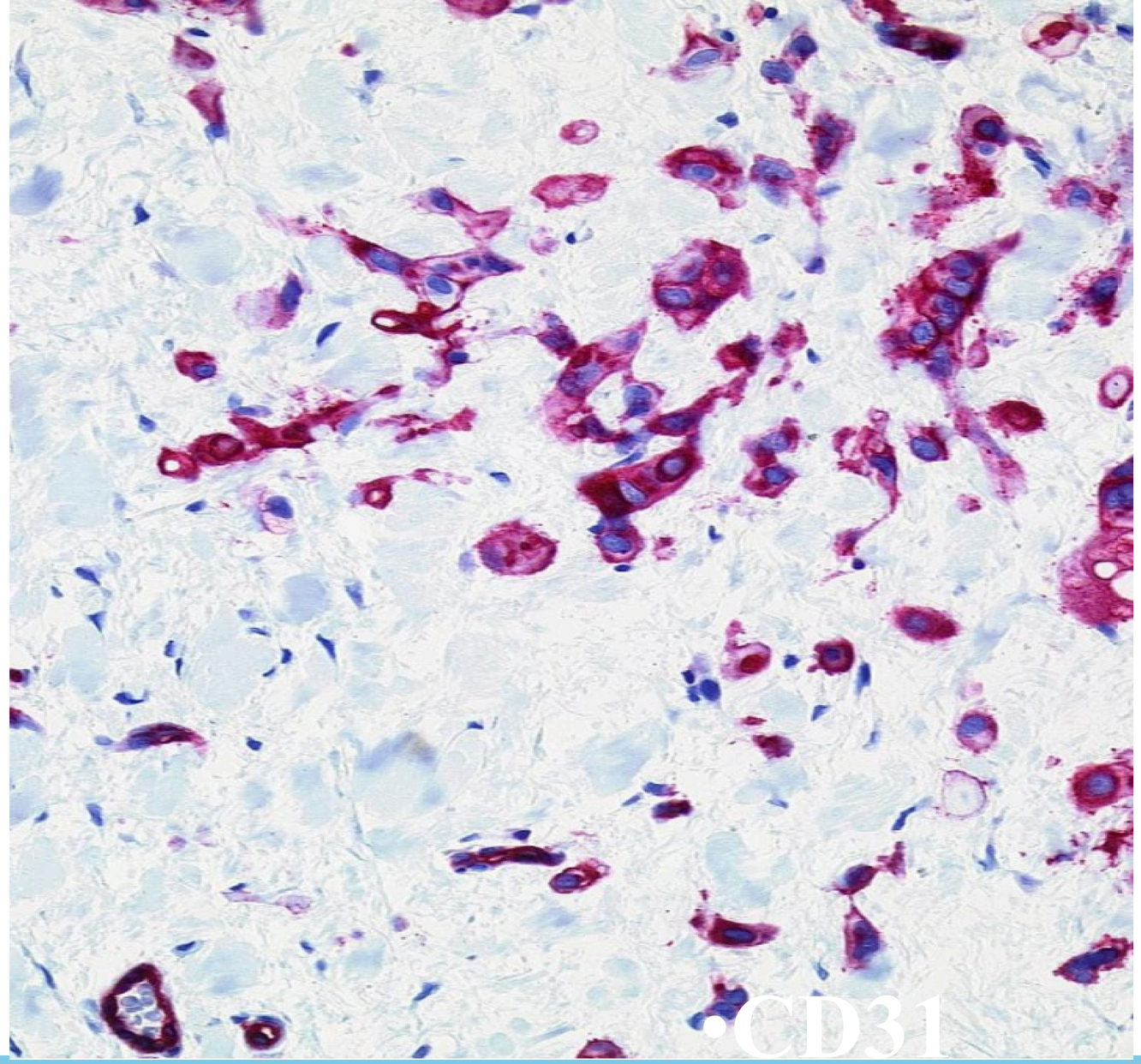
Immunohistochemistry

POSITIVE

- CD31
- CD34
- ERG
- AE1/AE3 in 25% of cases

NEGATIVE

- S100 protein
- Desmin
- EMA



Molecular

- Recurrent translocation t(1;3)(p36;q25) involving **WWTR1** (3q25) and **CAMTA1** (1p36)
  - Approximately 90% of EHE with classic morphology and not identified in histologic mimics

- A subset shown to harbor **YAP1-TFE3**

CAMTA1 is a useful immunohistochemical marker for diagnosing epithelioid haemangioendothelioma

Ryo Shibuya, Atsuji Matsuyama, Eisuke Shiba, Hiroshi Harada, Kei Yabuki & Masanori Hisaoka

Department of Pathology and Oncology, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

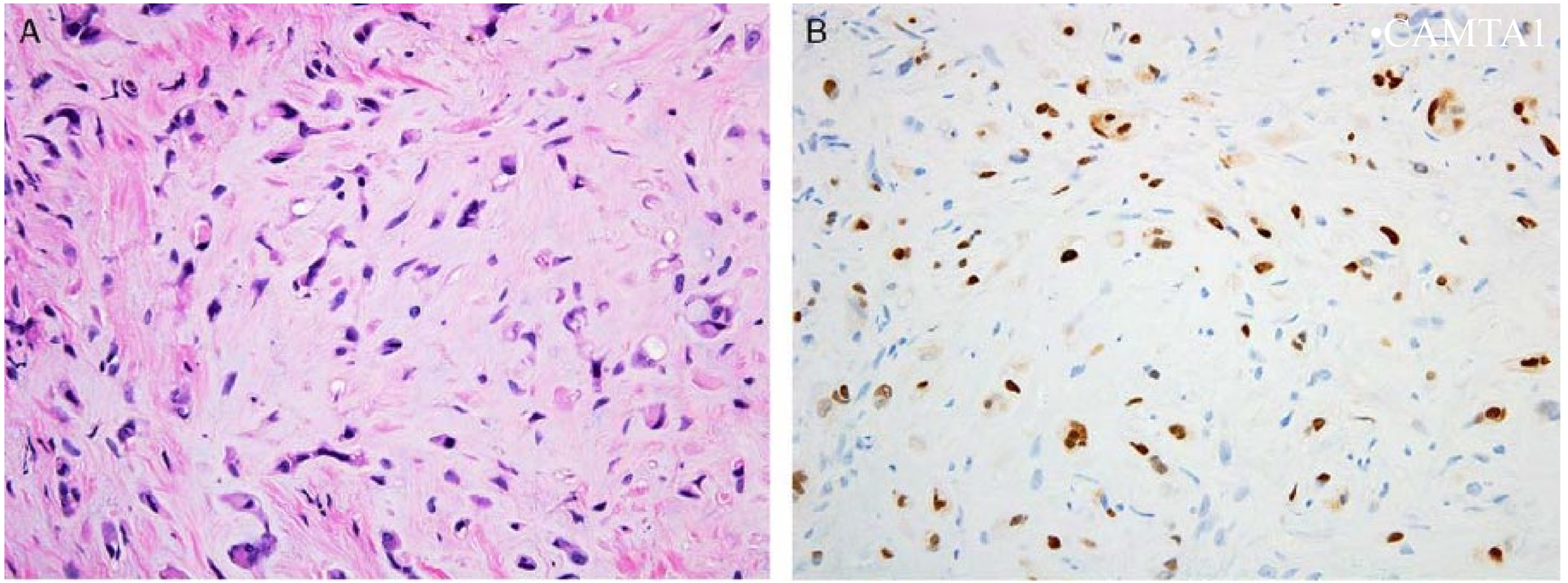
Histopathology 2015, 67, 827–835.

Nuclear Expression of CAMTA1 Distinguishes Epithelioid Hemangioendothelioma From Histologic Mimics

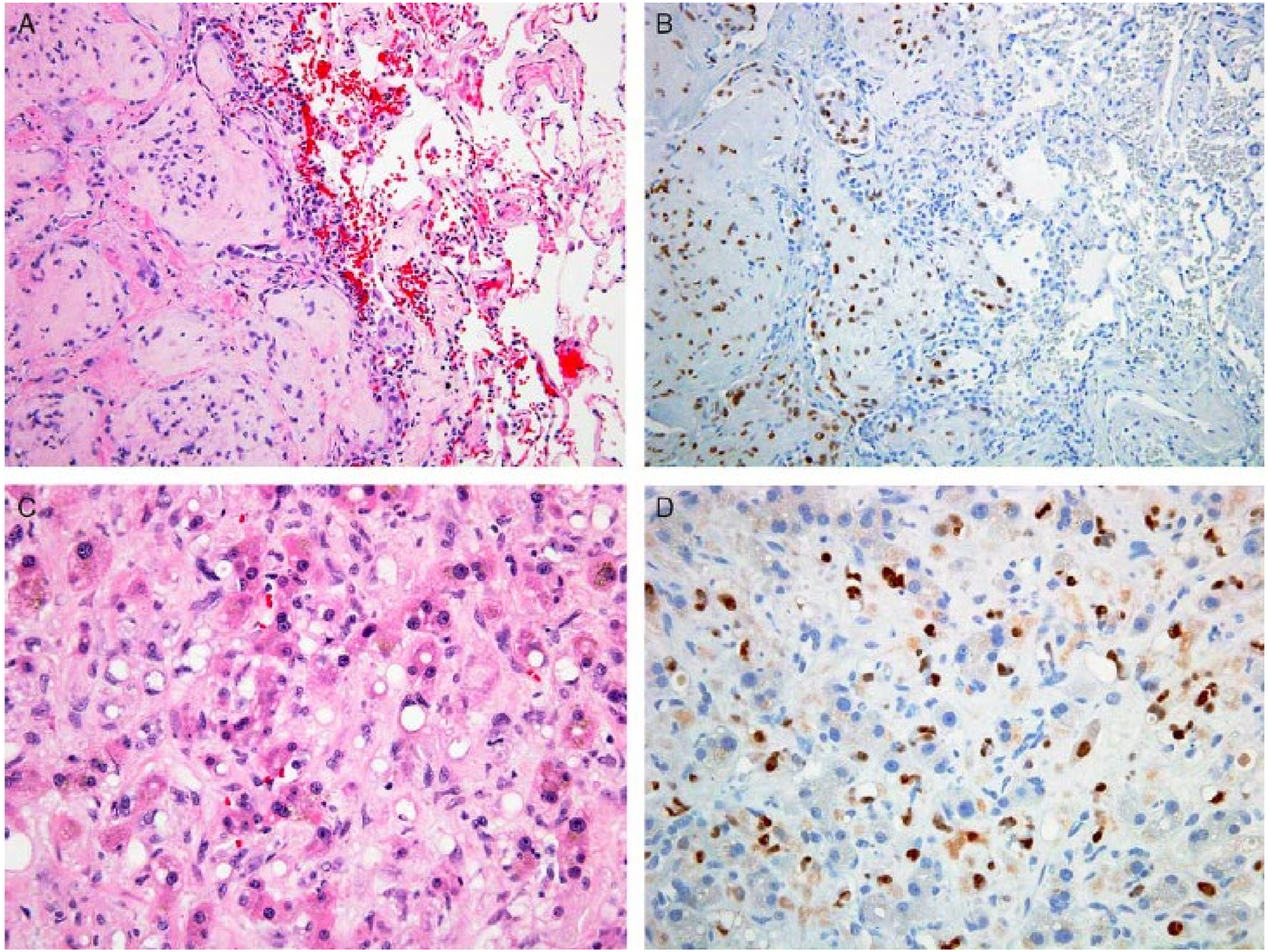
Leona A. Doyle, MD, Christopher D.M. Fletcher, MD, FRCPath, and Jason L. Hornick, MD, PhD

(*Am J Surg Pathol* 2016;40:94–102)

Tumor Type	Total Cases	CAMTA1 Positive (%)
EHE	59	51 (86)*
Epithelioid hemangioma	20	0 (0)
Epithelioid angiomatous nodule	10	0 (0)
Epithelioid angiosarcoma	25	1 (4)
Composite hemangioendothelioma	5	0 (0)
Pseudomyogenic hemangioendothelioma	10	0 (0)
Epithelioid sarcoma	25	0 (0)
Sclerosing epithelioid fibrosarcoma	10	0 (0)
Myoepithelial neoplasms of soft tissue	10	0 (0)
PEComa	10	0 (0)
Alveolar soft part sarcoma	10	0 (0)
Ossifying fibromyxoid tumor	10	0 (0)



(*Am J Surg Pathol* 2016;40:94–102)



(*Am J Surg Pathol* 2016;40:94–102)

Tumour type	CAMTA1 positivity
Carcinomas	1/169
Adenocarcinoma, bile duct	0/5
Adenocarcinoma, colon	0/24
Adenocarcinoma, ductal, breast	1/37
Adenocarcinoma, endometrium	0/5
Adenocarcinoma, lobular, breast	0/9
Adenocarcinoma, lung	0/6
Adenocarcinoma, ovary	0/6
Adenocarcinoma, prostate	0/6
Adenocarcinoma, stomach (7 signet ring cell)	0/12
Basal cell carcinoma, skin	0/7
Carcinoma of thyroid (4 papillary, 1 follicular, 1 medurally)	0/6
Hepatocellular carcinoma	0/6
Renal cell carcinoma	0/7
Squamous cell carcinoma, oesophagus	0/7
Squamous cell carcinoma, lung	0/6
Squamous cell carcinoma, skin	0/7
Squamous cell carcinoma, uterine cervix	0/6
Urothelial carcinoma	0/7

Tumour type	CAMTA1 positivity
Epithelioid haemangioendothelioma (EHE)	14/16
Non-EHE tumours	1/276
Non-epithelial tumours other than EHE	0/107
Alveolar soft part sarcoma (*ASPL–TFE3* fusion +)	0/4
Anaplastic large cell lymphoma	0/4
Angiomatoid fibrous histiocytoma	0/3
Angiosarcoma (2 epithelioid)	0/12
Clear cell sarcoma	0/5
Composite haemangioendothelioma	0/1
Desmoplastic small round cell tumour	0/2
Epithelioid angiomyolipoma	0/5
Epithelioid haemangioma	0/6
Epithelioid neurofibroma	0/2
Epithelioid sarcoma	0/8
Epithelioid schwannoma	0/1
Extraskeletal myxoid chondrosarcoma	0/6
Gastrointestinal stromal tumour (epithelioid)	0/2
Leiomyosarcoma (epithelioid)	0/2
Malignant melanoma	0/13
Malignant mesothelioma (epithelioid)	0/6
Malignant peripheral nerve sheath tumour (epithelioid)	0/3
Malignant perivascular epithelioid cell tumour (PEComa)	0/2
Myoepithelioma of soft tissue	0/4
Ossifying fibromyxoid tumour	0/2
Pseudomyogenic haemangioendothelioma	0/4
Sclerosing epithelioid fibrosarcoma	0/2
Solitary fibrous tumour (epithelioid)	0/2
Synovial sarcoma (biphasic type)	0/6

Variant *WWTR1* gene fusions in epithelioid hemangioendothelioma—A genetic subset associated with cardiac involvement

Albert J. H. Suurmeijer[1] | Brendan C. Dickson[2] | David Swanson[2] | Yun S. Sung[3] | Lei Zhang[3] | Cristina R. Antonescu[3]

Genes Chromosomes Cancer. 2020;59:389–395.

Case 1[a]	WWTR1-MAML2	EHE	76/F	Heart, left atrium	N/A
Case 2	*WWTR1-MAML2*	EHE	21/M	Bone, vertebra T11	NED, 70 months (s/p resection)
Case 3[a]	*WWTR1-ACTL6A*	Malignant EHE	73/F	Heart, right ventricle	DOD, 9 months
Case 4[a]	*WWTR1* rearrangement	EHE	72/F	Heart, left atrium	DOD, 15 months (s/p chemo Adriamycin +DTIC), soft tissue metastases
Case 5[a]	*WWTR1* rearrangement	EHE	67/M	Heart, left atrium	Lung metastases at diagnosis
Case 6	*WWTR1* rearrangement	Malignant EHE	65/M	Pelvic mass	Recent case

Virchows Arch. 2021 Jul 6. doi: 10.1007/s00428-021-03143-0. Online ahead of print.

Novel detection of the CAMTA1-WWTR1 fusion gene in extra-adrenal myelolipoma-like lesion: a case report

Hirofumi Watanabe [1], Kazuhiro Murakami [2], Toru Motoi [3], Keigo Murakami [2], Yayoi Aoyama [4], Hideki Mitomo [5], Naoya Ishibashi [5], Takashi Sugawara [5], Toshiharu Tabata [5], Tomonori Matsuura [6], Hironobu Sasano [4], Yasuhiro Nakamura [2]

Int J Surg Pathol. 2019 Sep;27(6):664-668. doi: 10.1177/1066896919837611. Epub 2019 Apr 3.

Epithelioid Hemangioendothelioma Arising Within Mediastinal Myelolipoma: A WWTR1-Driven Composite Neoplasm

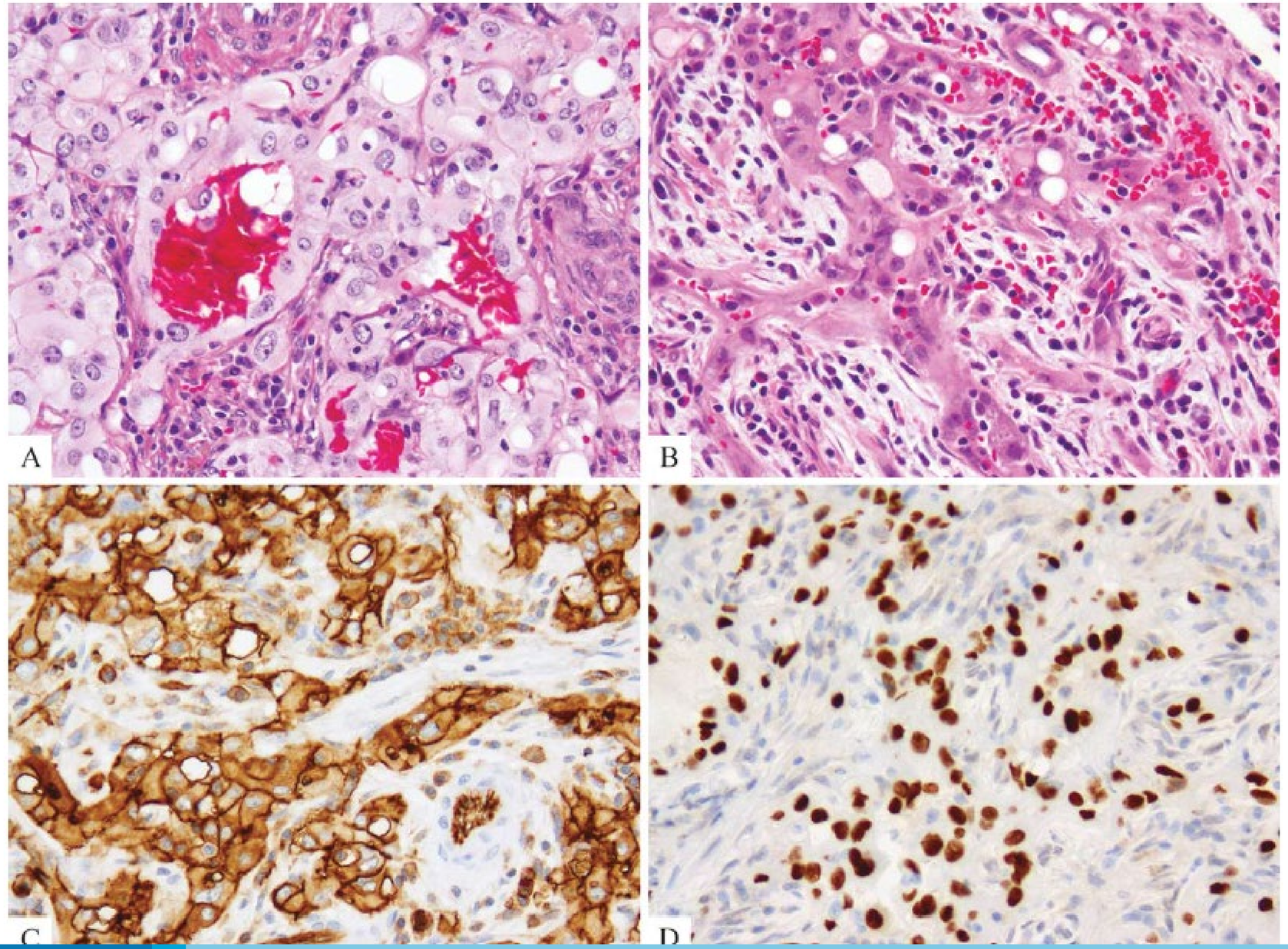
Julio A Diaz-Perez [1], Jaylou Velez-Torres [1], Oleksii Iakymenko [1], Nestor Villamizar [2], Andrew E Rosenberg [1]

Novel *YAP1-TFE3* Fusion Defines a Distinct Subset of Epithelioid Hemangioendothelioma

Cristina R. Antonescu,[1]* Francois Le Loarer,[1] Juan-Miguel Mosquera,[2] Andrea Sboner,[2,3] Lei Zhang,[1] Chun-Liang Chen,[1] Hsiao-Wei Chen,[1] Nursat Pathan,[4] Thomas Krausz,[5] Brendan C. Dickson,[6] Ilan Weinreb,[7] Mark A. Rubin,[2] Meera Hameed,[1] and Christopher D. M. Fletcher[8]*

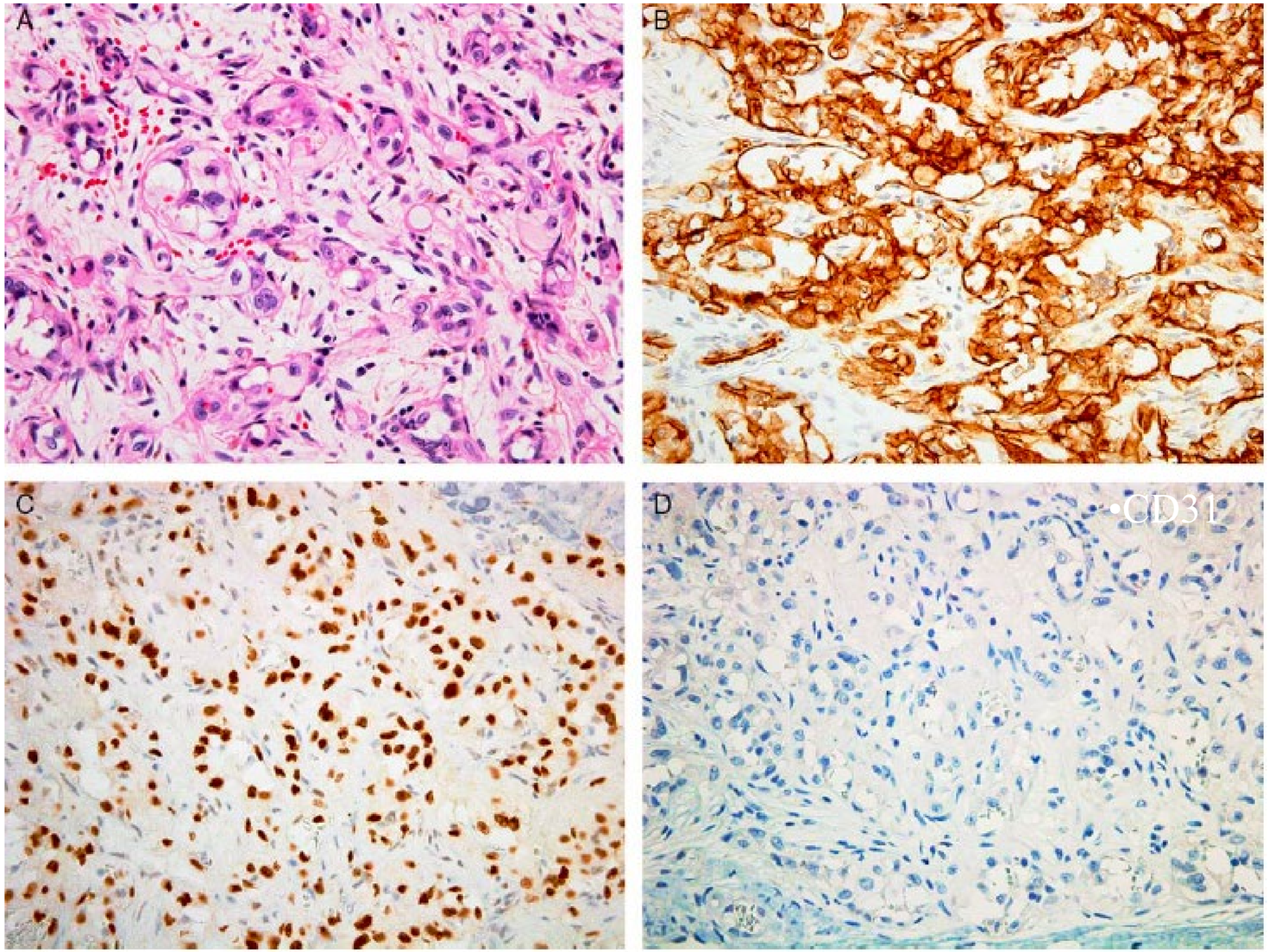
[1]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY
[2]Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, NY
[3]Institute for Computational Biomedicine, Weill Medical College of Cornell University, New York, NY
[4]Department of Pathology, Raritan Bay Medical Center, Raritan Bay, NJ
[5]Department of Pathology, University of Chicago, Chicago, IL
[6]Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada
[7]Department of Pathology, University Health Network and Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada
[8]Department of Pathology, Brigham & Women's Hospital and Harvard Medical School, Boston, MA

GENES, CHROMOSOMES & CANCER 52:775–784 (2013)



Memorial Sloan Kettering Cancer Center

Antonescu et al, Genes, Chromosomes and Cancer 52, 772-784, 2013



(*Am J Surg Pathol* 2016;40:94–102)

ARTICLE

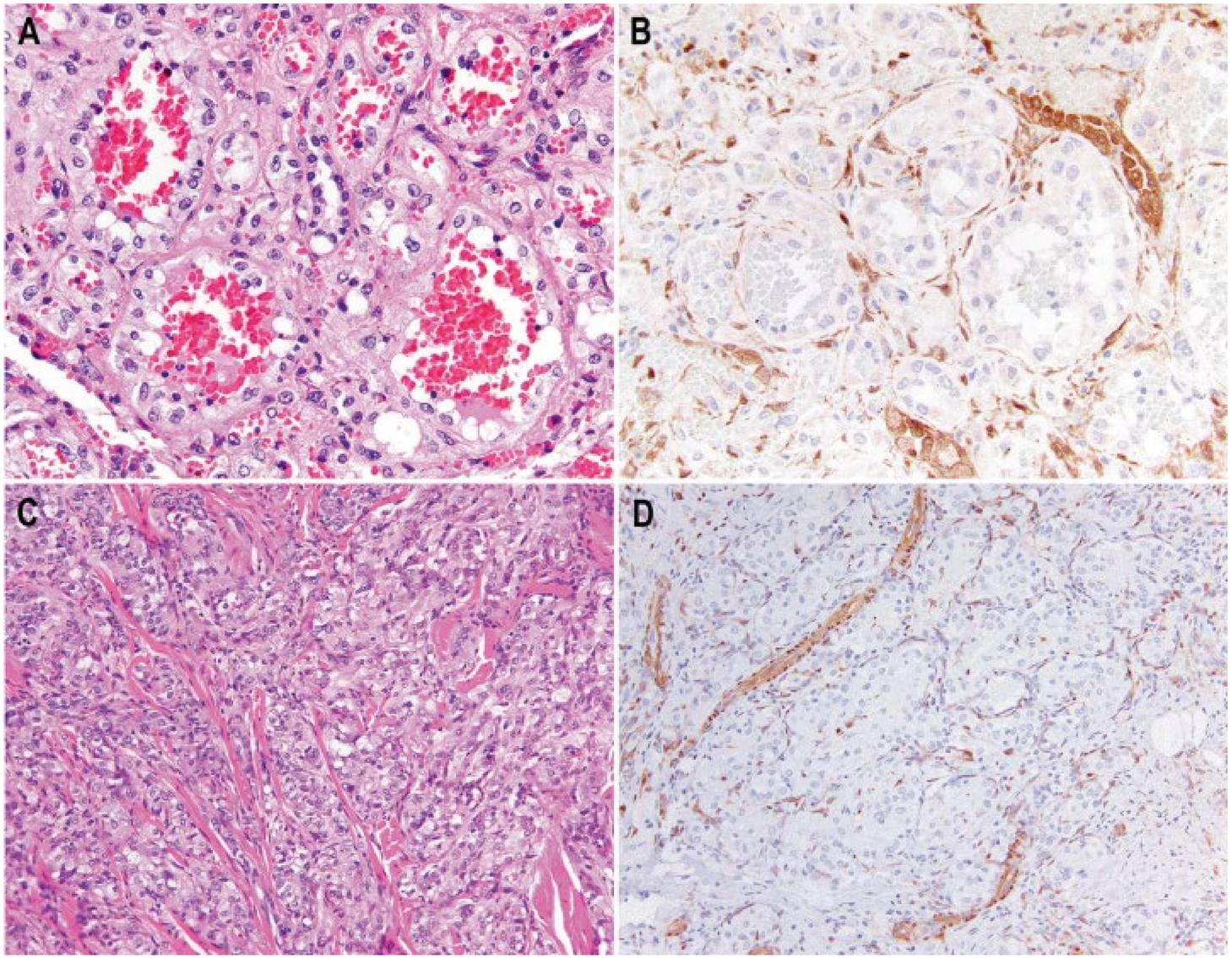
Check for updates

Loss of expression of YAP1 C-terminus as an ancillary marker for epithelioid hemangioendothelioma variant with *YAP1-TFE3* fusion and other YAP1-related vascular neoplasms

William J. Anderson[1], Christopher D. M. Fletcher[1] and Jason L. Hornick[1]✉

Modern Pathology; https://doi.org/10.1038/s41379-021-00854-2

Tumor type	Total cases	YAP1-CT lost	YAP1-CT retained
Epithelioid hemangioendothelioma with *YAP1-TFE3*	13	10	3
Epithelioid hemangioendothelioma with *WWTR1-CAMTA1*	20	1	19
Retiform hemangioendothelioma	4	4	0
Composite hemangioendothelioma	2	2	0
Pseudomyogenic hemangioendothelioma	10	0	10
Epithelioid hemangioma	19	0	19
Epithelioid angiosarcoma	10	0	10

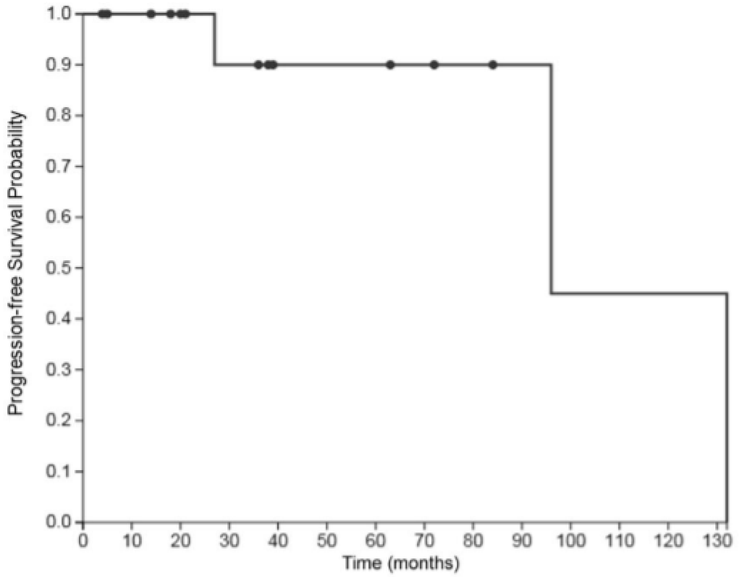


Modern Pathology; https://doi.org/10.1038/s41379-021-00854-2

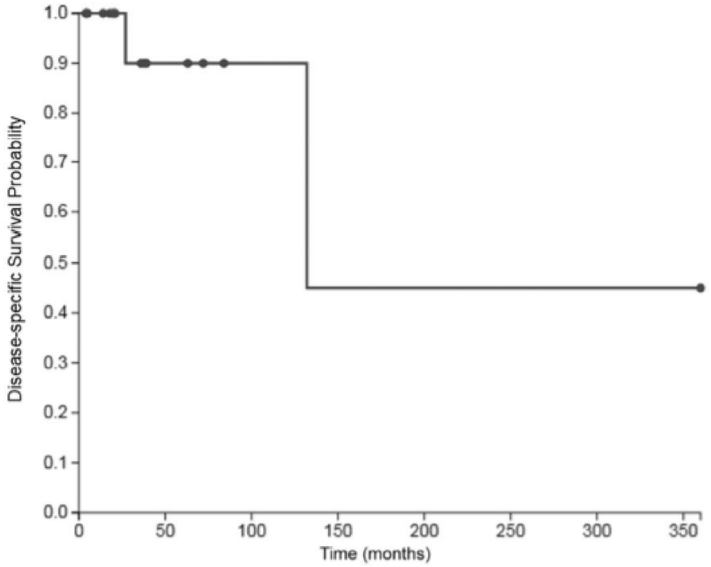
YAP1-TFE3-fused hemangioendothelioma: a multi-institutional clinicopathologic study of 24 genetically-confirmed cases

Josephine K. Dermawan[1], Elizabeth M. Azzato[1], Steven D. Billings[1], Karen J. Fritchie[1], Sebastien Aubert[2], Armita Bahrami[3], Marta Barisella[4], Daniel Baumhoer[5], Veronika Blum[6], Beata Bode[7], Scott W. Aesif[1], Judith V. M. G. Bovée[8], Brendan C. Dickson[9], Mari van den Hout[10], David R. Lucas[11], Holger Moch[12], Gabriel Oaxaca[1], Alberto Righi[13], Raf Sciot[14], Vaiyapuri Sumathi[15], Akihiko Yoshida[16] and Brian P. Rubin[1]✉

A



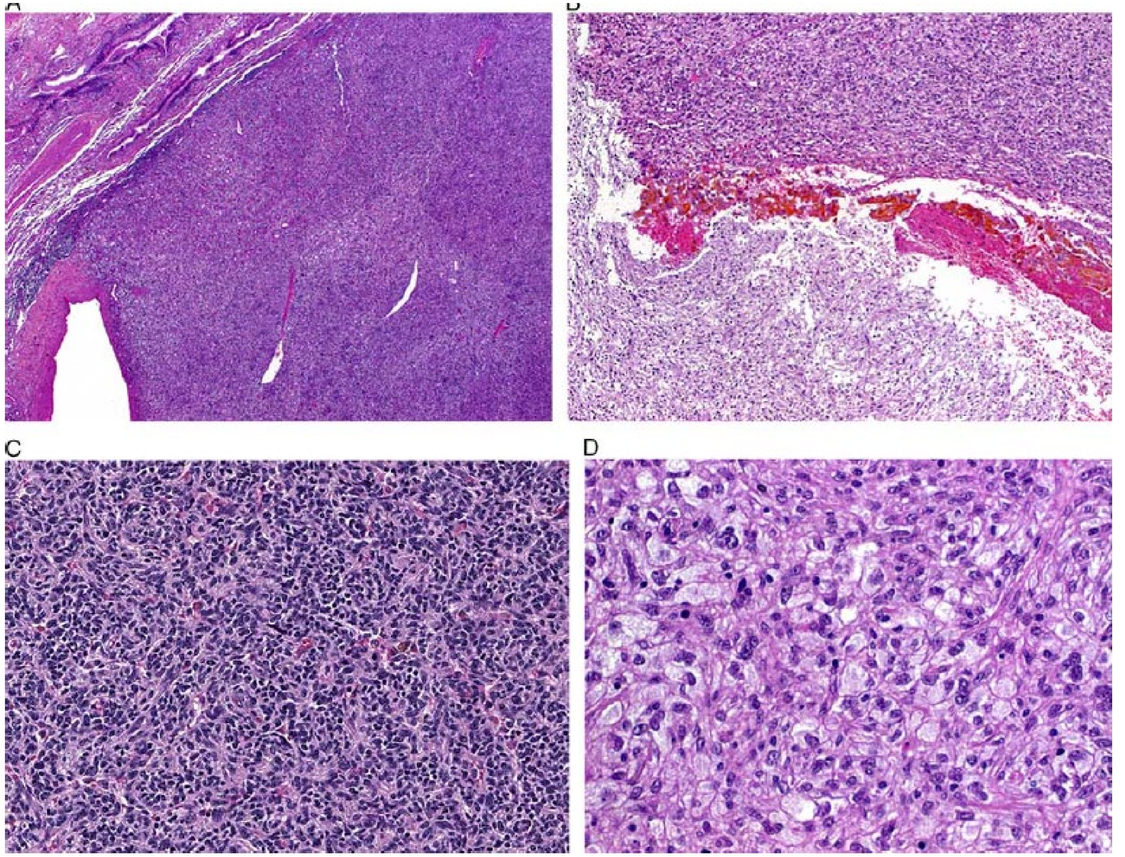
B



Recurrent *YAP1-TFE3* Gene Fusions in Clear Cell Stromal Tumor of the Lung

Abbas Agaimy, MD, Robert Stoehr, PhD,* Michael Michal, MD,†‡ Petros Christopoulos, MD,§‖ Hauke Winter, MD,‖¶ Lei Zhang, MD,# Albrecht Stenzinger, MD,** Michal Michal, MD,†‡ Gunhild Mechtersheimer, MD,** and Cristina R. Antonescu, MD#*

Am J Surg Pathol 2021;00:000–000



Epithelioid hemangioendotheliomas with *TFE3* gene translocations are compossible with *CAMTA1* gene rearrangements

Seok Joo Lee[1], Woo Ick Yang[1], Woo-Suk Chung[2] and Sang Kyum Kim[1]

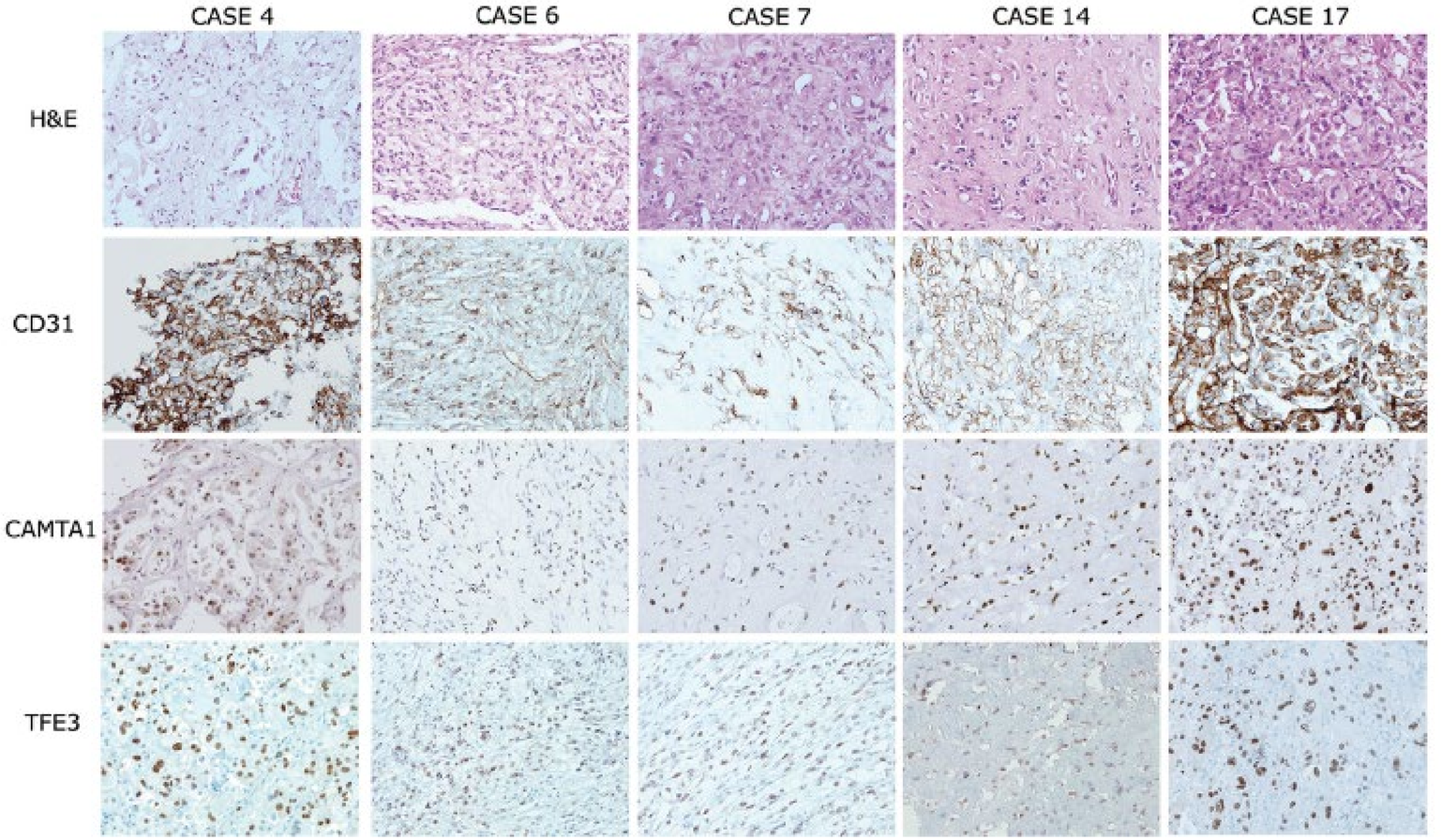
[1] Department of Pathology, Yonsei University Medical Center, Seoul, South Korea

[2] Department of Diagnostic Radiology, Konyang University Hospital, Daejeon, South Korea

Correspondence to: Sang Kyum Kim, email: nicekyumi@yuhs.ac

***Keywords**: epithelioid hemangioendothelioma, TFE3, YAP1, CAMTA1, WWTR1, Pathology Section*

***Received**: September 02, 2015* ***Accepted**: January 21, 2016* ***Published**: January 28, 2016*

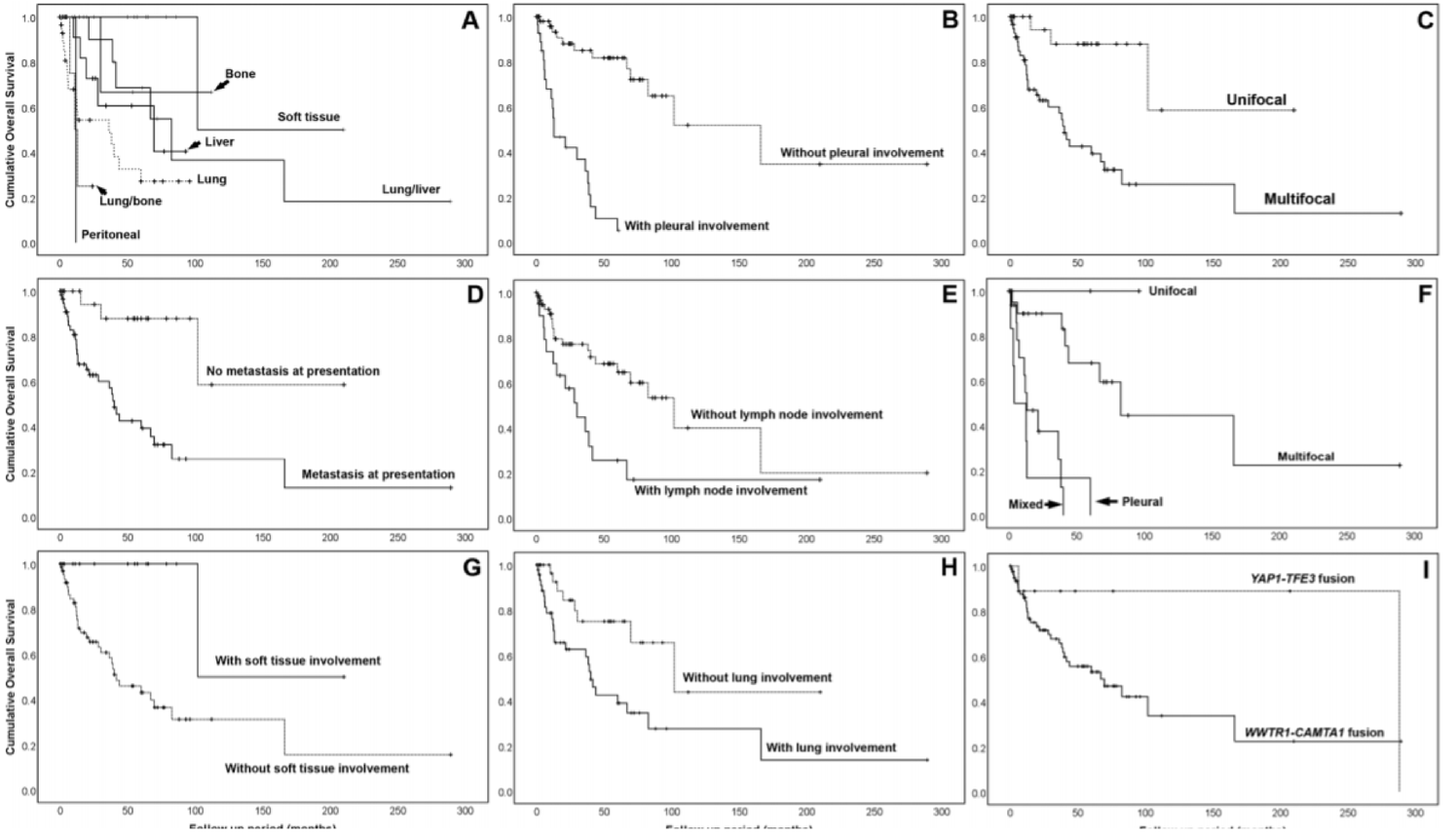


Modern Pathology (2020) 33:591–602
https://doi.org/10.1038/s41379-019-0368-8

ARTICLE

Prognostic stratification of clinical and molecular epithelioid hemangioendothelioma subsets

Evan Rosenbaum[1] · Bhumika Jadeja[2] · Bin Xu[3] · Lei Zhang[3] · Narasimhan P. Agaram[3] · William Travis[3] · Samuel Singer[2] · William D. Tap[1,4] · Cristina R. Antonescu[3]

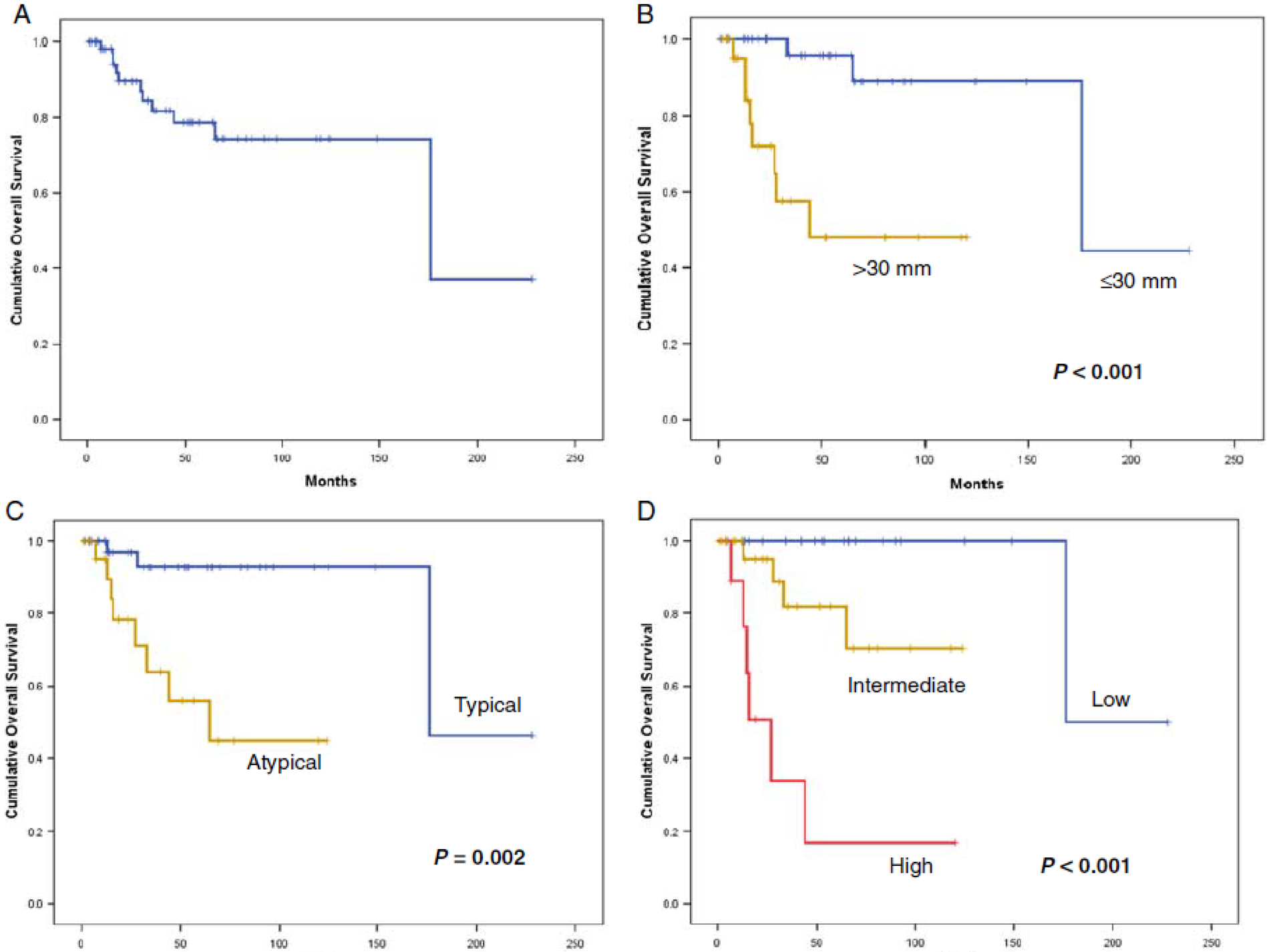


Am J Surg Pathol 2021;45:616–626

Clinicopathologic Characterization of Epithelioid Hemangioendothelioma in a Series of 62 Cases

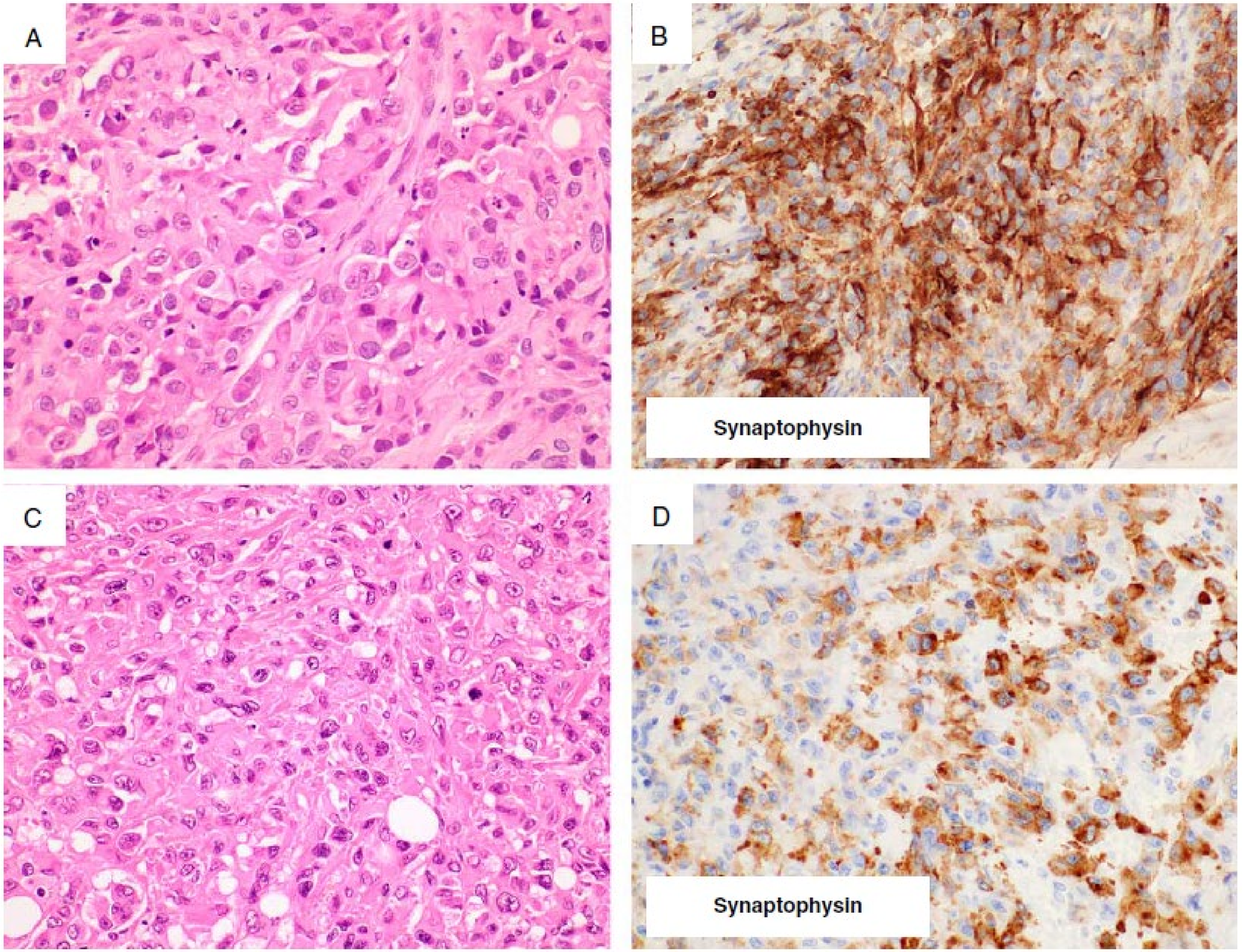
A Proposal of Risk Stratification and Identification of a Synaptophysin-positive Aggressive Subset

Takahiro Shibayama, MD, Naohiro Makise, MD, PhD,† Toru Motoi, MD, PhD,‡ Taisuke Mori, DMD, PhD,* Nobuyoshi Hiraoka, MD, PhD,* Kan Yonemori, MD, PhD,§‖ Shun-ichi Watanabe, MD, PhD,¶ Minoru Esaki, MD, PhD,# Chigusa Morizane, MD, PhD,‖** Tomotake Okuma, MD, PhD,†† Akira Kawai, MD, PhD,‖‡‡ Tetsuo Ushiku, MD, PhD,† Yasushi Yatabe, MD, PhD,* and Akihiko Yoshida, MD, PhD*‖*


A
B
C
D
Cumulative Overall Survival
Months
>30 mm
≤30 mm
P < 0.001
Typical
Atypical
P = 0.002
Intermediate
Low
High
P < 0.001

Risk Factors	Score
Tumor size (mm)	
≤30	0
>30	1
Histology	
Typical	0
Atypical*	1
Risk category	Total score
Low	0
Intermediate	1
High	2

*Atypical histology is defined as having at least 2 of the following 3 findings: mitosis > 1/2 mm^2, high nuclear grade, and coagulative tumor necrosis. Any tumor histology that does not meet these criteria is considered typical.


A
B
Synaptophysin
C
D
Synaptophysin

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REVIEW

Epithelioid hemangioendothelioma, an ultra-rare cancer: a consensus paper from the community of experts

S. Stacchiotti[1*], A. B. Miah[2], A. M. Frezza[1], C. Messiou[3], C. Morosi[4], A. Caraceni[5], C. R. Antonescu[6], J. Bajpai[7], E. Baldini[8], S. Bauer[9], R. Biagini[10], S. Bielack[11], J. Y. Blay[12], S. Bonvalot[13], I. Boukovinas[14], J. V. M. G. Bovee[15], K. Boye[16], T. Brodowicz[17], D. Callegaro[18], E. De Alava[19,20], M. Deoras-Sutliff[21], A. Dufresne[12], M. Eriksson[22], C. Errani[23], A. Fedenko[24], V. Ferraresi[25], A. Ferrari[26], C. D. M. Fletcher[27], X. Garcia del Muro[28], H. Gelderblom[29], R. A. Gladdy[30], F. Gouin[31], G. Grignani[32], J. Gutkovich[21,33], R. Haas[34,35], N. Hindi[36], P. Hohenberger[37], P. Huang[38], H. Joensuu[39], R. L. Jones[40], C. Jungels[41], B. Kasper[42], A. Kawai[43], A. Le Cesne[44], F. Le Grange[45], A. Leithner[46], H. Leonard[47], A. Lopez Pousa[48], J. Martin Broto[49], O. Merimsky[50], P. Merriam[51], R. Miceli[52], O. Mir[53], M. Molinari[54], M. Montemurro[55], G. Oldani[56], E. Palmerini[57], M. A. Pantaleo[58], S. Patel[59], S. Piperno-Neumann[60], C. P. Raut[61,62,63], V. Ravi[59], A. R. A. Razak[64], P. Reichardt[65], B. P. Rubin[66], P. Rutkowski[67], A. A. Safwat[68], C. Sangalli[69], G. Sapisochin[70], M. Sbaraglia[71], S. Scheipl[72], P. Schöffski[73], D. Strauss[74], S. J. Strauss[75], K. Sundby Hall[16], W. D. Tap[76], A. Trama[77], A. Tweddle[78], W. T. A. van der Graaf[79], M. A. J. Van De Sande[80], W. Van Houdt[81], G. van Oortmerssen[82], A. J. Wagner[51], M. Wartenberg[83], J. Wood[84], N. Zaffaroni[85], C. Zimmermann[86], P. G. Casali[1], A. P. Dei Tos[71] & A. Gronchi[18]

Memorial Sloan Kettering Cancer Center
1884

Angiosarcoma

- **Angiosarcoma** arises in four typical clinical settings:
  - **Chronically sun-damaged skin**, particularly the scalp or face
  - **Sporadic visceral angiosarcoma**
  - In the setting of **chronic lymphedema** (eg, after mastectomy in Stewart-Treves syndrome)
  - In areas of prior **therapeutic radiation**, such as for the management of breast carcinoma.

- **Atypical vascular proliferations**, which have been described under various nomenclature designations, occur **in areas of prior radiation**

- In some cases may be difficult to distinguish from vasoformative angiosarcoma.

MYC

- MYC proto-oncogene is a transcription factor located on the long arm of **chromosome 8** (8q24.21)
- **Nuclear expression of MYC** occurs **in the vast majority of secondary angiosarcomas**
- Only very rarely seen in primary angiosarcoma
- Not detected in atypical or benign vascular lesions occurring in irradiated skin.

The American Journal of Pathology, Vol. 176, No. 1, January 2010

DOI: 10.2353/ajpath.2010.090637

Short Communication

MYC High Level Gene Amplification Is a Distinctive Feature of Angiosarcomas after Irradiation or Chronic Lymphedema

Consistent *MYC* and *FLT4* Gene Amplification in Radiation-Induced Angiosarcoma But Not in Other Radiation-Associated Atypical Vascular Lesions

Tianhua Guo,[1] Lei Zhang,[1] Ning-En Chang,[1] Samuel Singer,[2] Robert G. Maki,[3] and Cristina R Antonescu[1]*

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[2]Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY
[3]Department of Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY

GENES, CHROMOSOMES & CANCER 50:25–33 (2011)

Postradiation cutaneous angiosarcoma after treatment of breast carcinoma is characterized by *MYC* amplification in contrast to atypical vascular lesions after radiotherapy and control cases: clinicopathological, immunohistochemical and molecular analysis of 66 cases

T Mentzel[1], HU Schildhaus[2], G Palmedo[1], R Büttner[2] and H Kutzner[1]

[1]*Dermatopathologie Bodensee, Friedrichshafen, Germany and* [2]*Institute of Pathology, University Hospital Cologne, Cologne, Germany*

Modern Pathology (2012) 25, 75–85

J Cutan Pathol 2012: 39: 234–242
doi: 10.1111/j.1600-0560.2011.01843.x
John Wiley & Sons. Printed in Singapore

Journal of
Cutaneous Pathology

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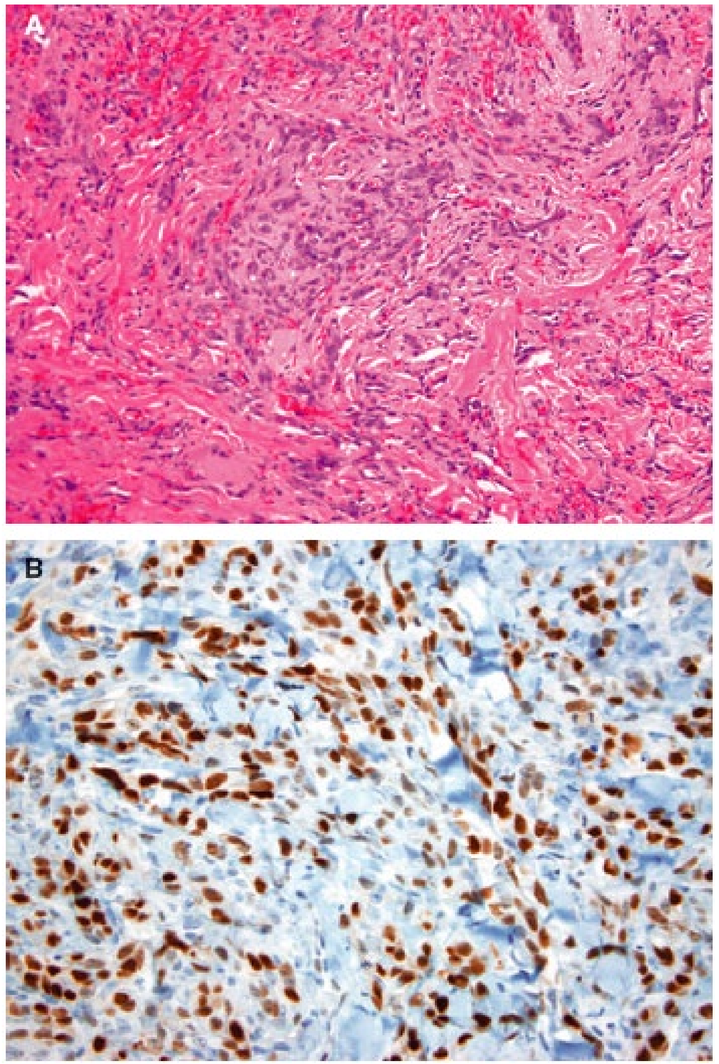
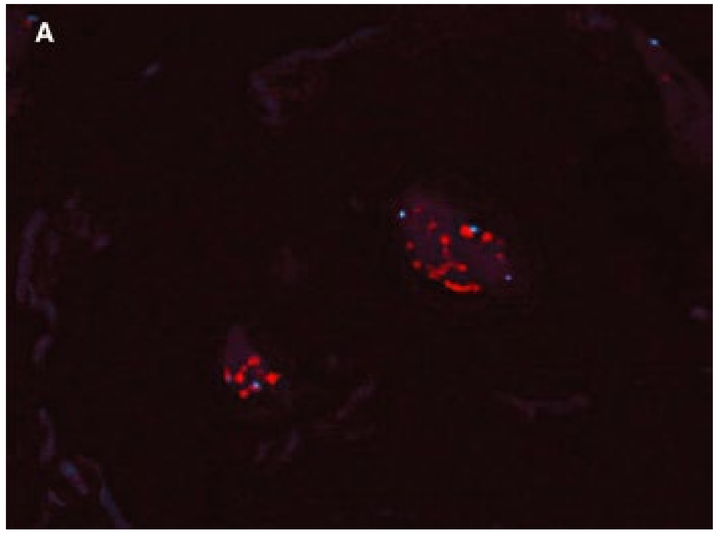
FISH for MYC amplification and anti-MYC immunohistochemistry: useful diagnostic tools in the assessment of secondary angiosarcoma and atypical vascular proliferations

Angiosarcoma





J Cutan Pathol 2012: 39: 234–242

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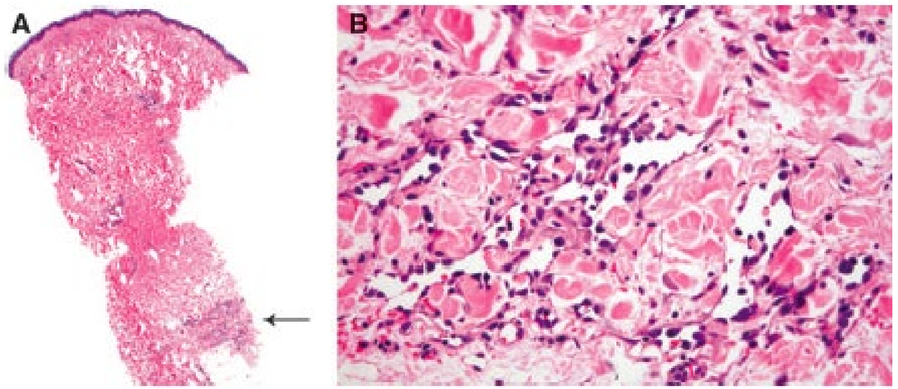
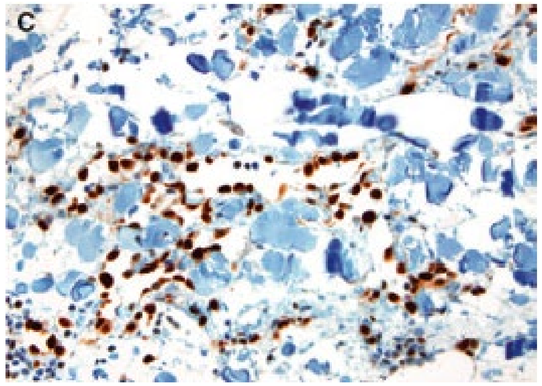
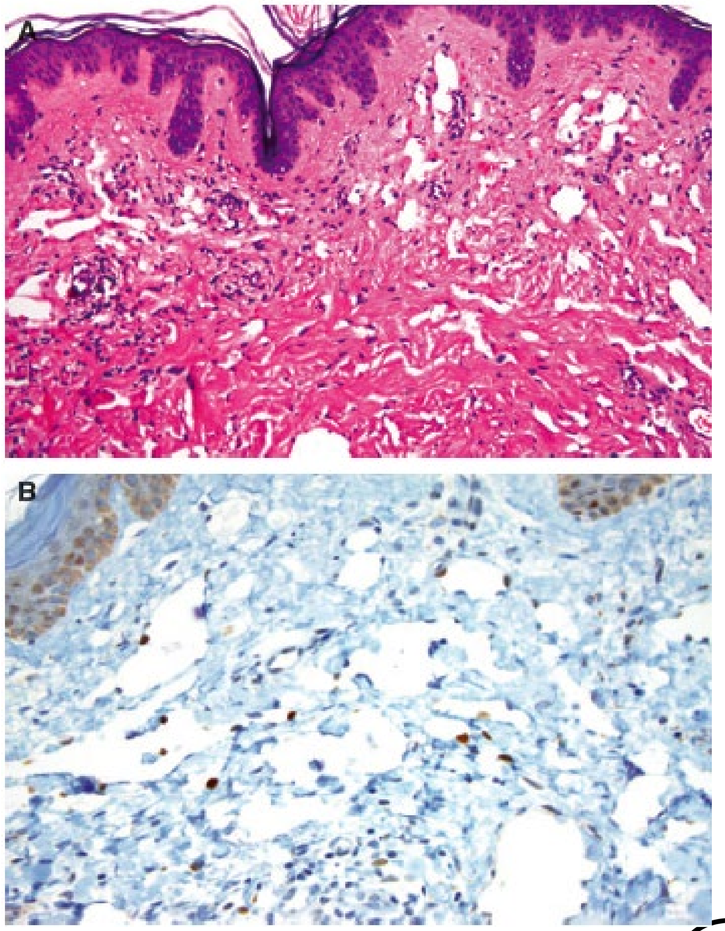
Angiosarcomas







J Cutan Pathol 2012: 39: 234–242

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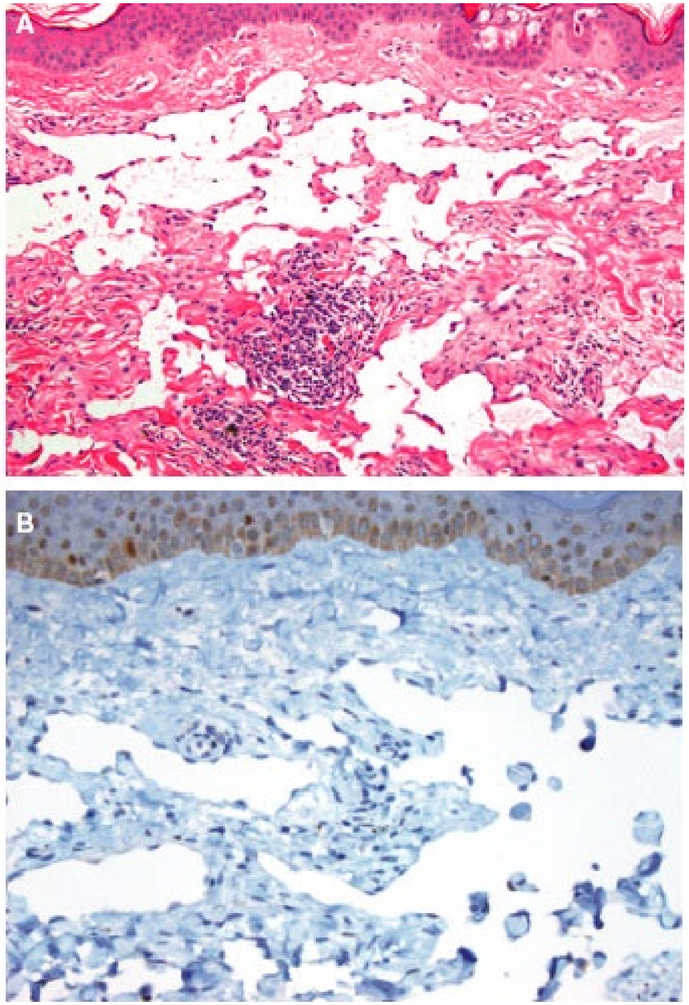
Atypical Vascular lesion (AVL)



J Cutan Pathol 2012: 39: 234–242

Memorial Sloan Kettering Cancer Center

MYC amplification and overexpression in primary cutaneous angiosarcoma: a fluorescence *in-situ* hybridization and immunohistochemical study

Wonwoo Shon[1], William R Sukov[1], Sarah M Jenkins[2] and Andrew L Folpe[1]

[1]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA and [2]Department of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA

MODERN PATHOLOGY (2014) 27, 509–515

Conclusion

- MYC immunohistochemistry is therefore useful **in differentiating atypical or benign vascular lesions occurring in irradiated skin from secondary postradiation angiosarcomas**.

MYC gene amplification by fluorescence in situ hybridization and MYC protein expression by immunohistochemistry in the diagnosis of cutaneous angiosarcoma: Systematic review and appropriate use criteria

Kiran Motaparthi[1] | Scott R. Lauer[2] | Rajiv M. Patel[3,4] | Claudia I. Vidal[5] | Konstantinos Linos[6]

J Cutan Pathol. 2021;48:578–586

J Cutan Pathol. 2021 Sep 18. doi: 10.1111/cup.14135. Online ahead of print.

Appropriate Use Criteria (AUC) for Ancillary Diagnostic Testing in Dermatopathology: New Recommendations for 11 tests and 220 clinical scenarios from the American Society of Dermatopathology AUC Committee

Maxwell A Fung [1], Claudia I Vidal [2], Eric A Armbrecht [3], Aleodor A Andea [4], David S Cassarino [5], Nneka I Comfere [6], Patrick O Emanuel [7], Tammie Ferringer [8], Alexandra C Hristov [4], Jinah Kim [9], Scott R Lauer [10], Konstantinos Linos [11], Tricia A Missall [12], Kiran Motaparthi [12], Roberto A Novoa [13], Rajiv Patel [4], Sara C Shalin [14], Uma Sundram [15], Antoanella Calame [16], Daniel D Bennett [17], Lyn M Duncan [18], Dirk M Elston [19], Gregory A Hosler [20], Yadira M Hurley [21], Alexander J Lazar [22], Lori Lowe [4], Jane Messina [23], Jonathan Myles [24], Jose A Plaza [25], Victor G Prieto [26], Vijaya Reddy [27], András Schaffer [28], Antonio Subtil [29]

Neoplasm	Genetic alteration (prevalence)	Immunohistochemical markers (sensitivity)
Epithelioid hemangioma	*WWTR1-FOSB*, *ZFP36-FOSB* (20% cellular subtype); *FOS-VIM*, *FOS-MBLNI*, *FOS-lincRNA*, *FOS*-(unknown) (50% cellular subtype)	FOSB (75% conventional subtype; 100% ALHE subtype; 10% cellular subtype)
Tufted angioma/kaposiform hemangioendothelioma	*GNA14* mutation (unknown)	No specific markers
Anastomosing hemangioma Hepatic small vessel neoplasm Lobular capillary hemangioma	*GNA11* mutation, *GNA14* mutation, *GNAQ* mutation (? nearly 100%)	No specific markers
Composite hemangioendothelioma	*PTBP1-MAML2* (rare) *EPC1-PHC2* (rare)	Synaptophysin (subset of aggressive cases; unknown sensitivity overall)
Pseudomyogenic hemangioendothelioma	*SERPINE1-FOSB* (? 55%) *ACTB-FOSB* (? 45%)	FOSB (nearly 100%)
Epithelioid hemangioendothelioma	*WWTR1-CAMTA1* (85%) *YAP1-TFE3* (5%)	CAMTA1 (85%) TFE3 (5%)
Post-radiation angiosarcoma	*MYC* amplification (100%) *FLT4* amplification (25%) *PTPBR* mutation (45%) *PLCG1* mutation (15%)	MYC (nearly 100%)
Primary angiosarcoma	Complex karyotype (? 25%) *KDR* mutation (25%) *CIC* rearrangement or point mutation (10%)	No specific markers

Virchows Archiv
https://doi.org/10.1007/s00428-019-02651-4

Received: 10 June 2021 | Revised: 29 June 2021 | Accepted: 1 July 2021

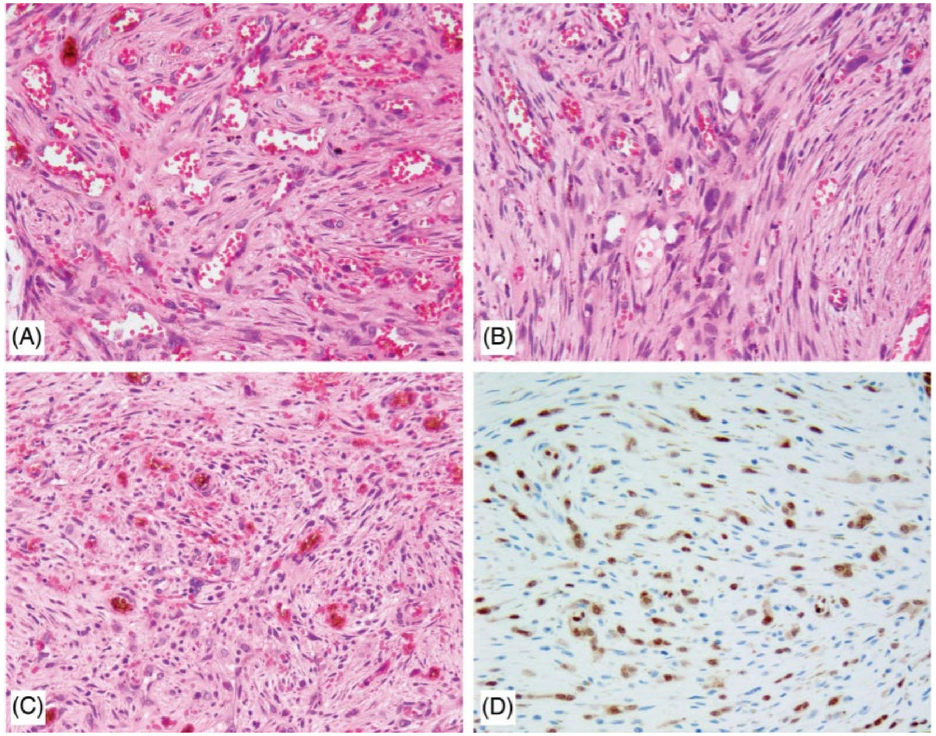
DOI: 10.1002/gcc.22984

RESEARCH ARTICLE

WILEY

A unique epithelioid vascular neoplasm of bone characterized by *EWSR1/FUS-NFATC1/2* fusions

Nooshin K. Dashti[1] | Brendan C. Dickson[2] | Lei Zhang[3] | Ziyu Xie[3] | Gunnlaugur Pétur Nielsen[4] | Cristina R. Antonescu[3]



Virchows Archiv
https://doi.org/10.1007/s00428-019-02651-4

REVIEW ARTICLE

What is new in endothelial neoplasia?

David J. Papke Jr[1] · Jason L. Hornick[1]

Received: 11 June 2019 / Revised: 30 July 2019 / Accepted: 13 August 2019

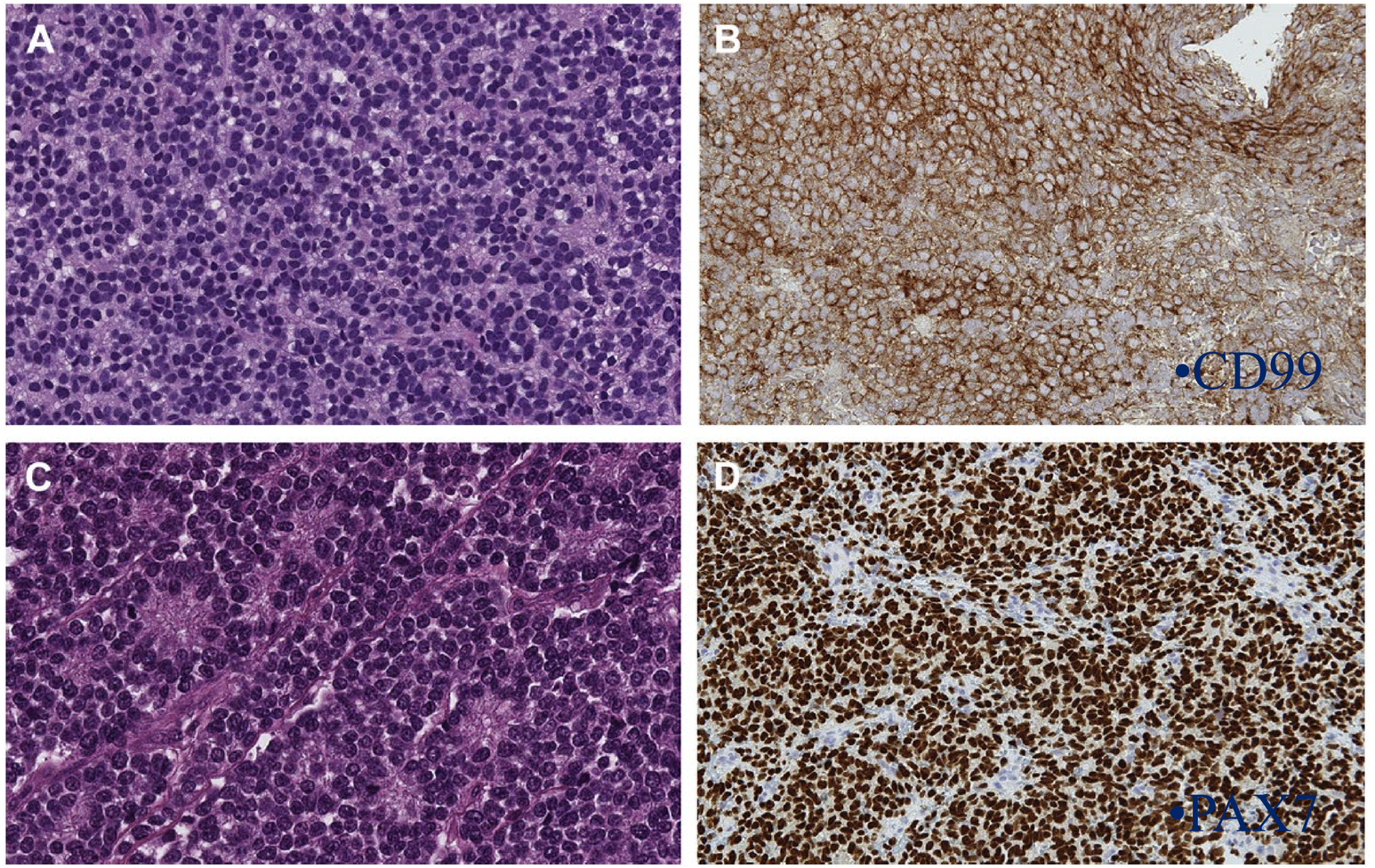
Abstract

The classification of vascular neoplasms continues to evolve as we accumulate more genetic and clinical data, particularly for rare tumor types. Because of tumor rarity, changes to classification schema, overlapping histologic features, and in some cases, lack of morphologic evidence of vasoformation, vascular neoplasms present a diagnostic challenge. Here, we discuss recent developments in our understanding of vascular tumors, with a detailed discussion of epithelioid hemangioma, tufted angioma, kaposiform hemangioendothelioma, composite hemangioendothelioma, pseudomyogenic hemangioendothelioma, epithelioid hemangioendothelioma, and angiosarcoma.

Keywords Hemangioendothelioma · Hemangioma · Angiosarcoma · Gene fusion · Immunohistochemistry

Undifferentiated Round Cell Sarcomas

Ewing Sarcoma



Surgical Pathology 12 (2019) 191–215

Ewing sarcoma	t(11;22)(q24;q12)	EWSR1-FLI1 (85%)
	t(21;22)(q22;q12)	EWSR1-ERG (10%)
		EWSR1-ETS gene family
		FUS-ETS gene family
EWSR1 RCS-non-ETS partners	t(20;22)(q13.2;q12)	EWSR1-NFATC2
	t(20;16)(q13.2;p11.2)	FUS-NFATC2
	inv(22)(q12; q12)	EWSR1-PATZ1

Virchows Archiv
https://doi.org/10.1007/s00428-019-02720-8

Undifferentiated small round cell sarcomas other than Ewing

- Round cell morphology similar to Ewing Sarcoma
- Lack of *EWSR1-ETS* rearrangements
- No other signs of a specific line of differentiation

World Health Organization 2020

CIC-rearranged sarcoma (*CIC-DUX4*)

- Largest subset (at least 70%)

Sarcoma with ***BCOR* genetic alterations**

Round cell sarcoma **with *EWSR1*-non-ETS fusions**

Sarcomas With CIC-rearrangements Are a Distinct Pathologic Entity With Aggressive Outcome

A Clinicopathologic and Molecular Study of 115 Cases

Cristina R. Antonescu, MD, Adepitan A. Owosho, DDS,† Lei Zhang, MD,* Sonja Chen, MD,* Kemal Deniz, MD,‡ Joseph M. Huryn, MD,† Yu-Chien Kao, MD,*§ Shih-Chiang Huang, MD,*‖ Samuel Singer, MD,† William Tap, MD,¶ Inga-Marie Schaefer, MD,# and Christopher D. Fletcher, MD#*

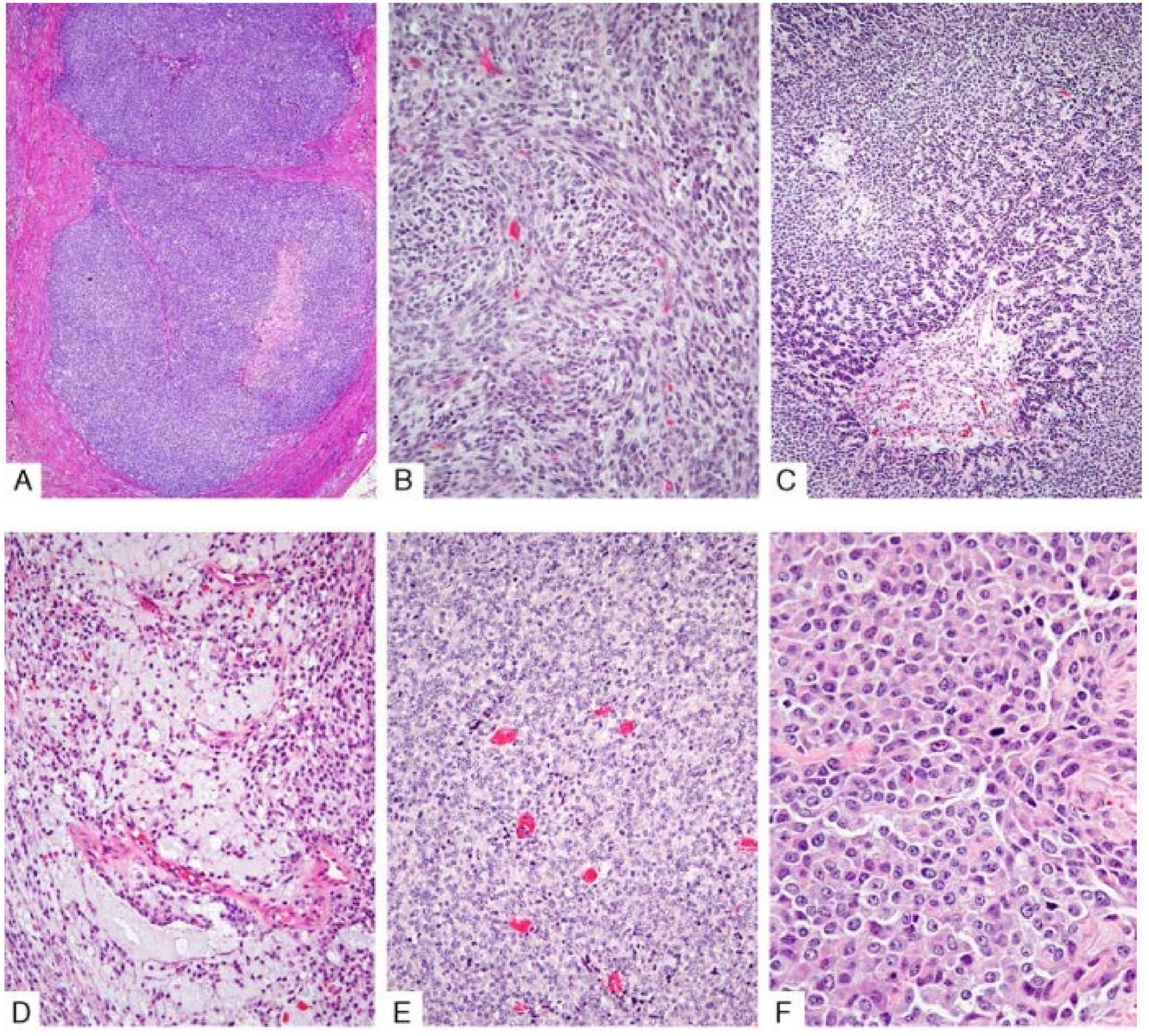
(*Am J Surg Pathol* 2017;41:941–949)

- t(4;19) translocation involving ***CIC-DUX4***
- t(10;19) translocation ***CIC-DUX4L***
- Distinct transcriptional signature with poor clinical outcomes

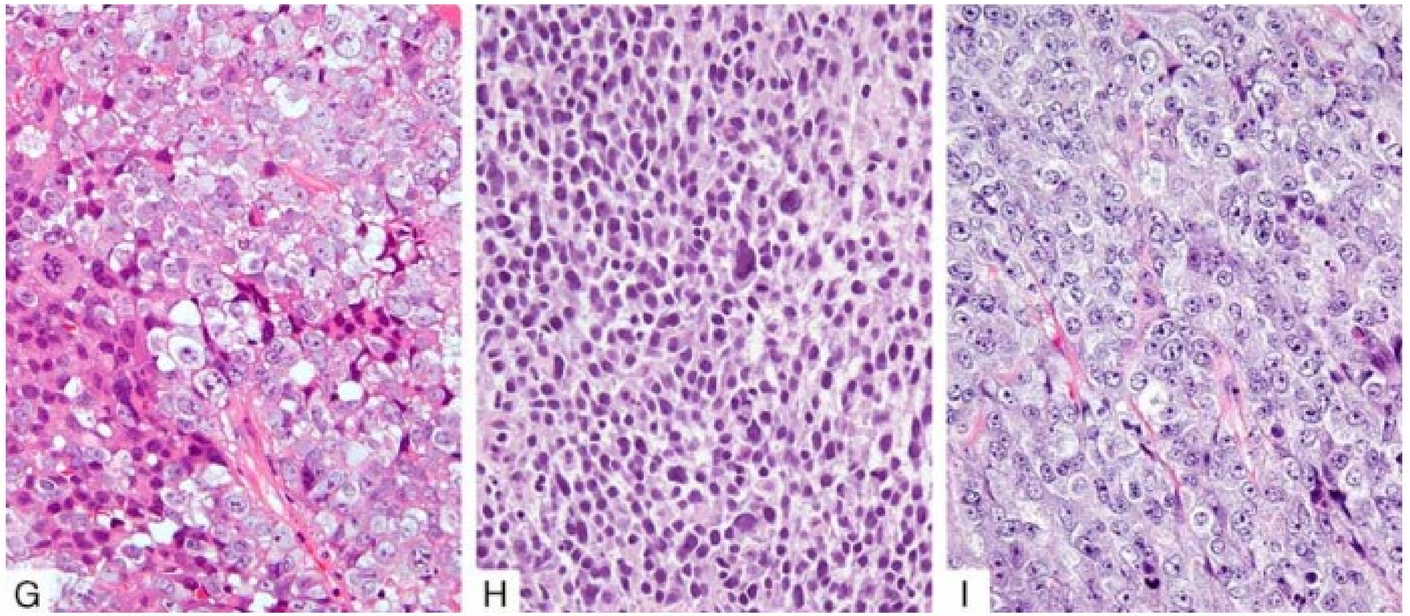
- Wide age range (6-81 years)
  - Most commonly present in **young adults** (mean 30 years)

- Nearly 90% arise in **soft tissues**
  - Split evenly between **extremities** and **trunk/pelvis**
  - Minority of cases (10%) in visceral organs

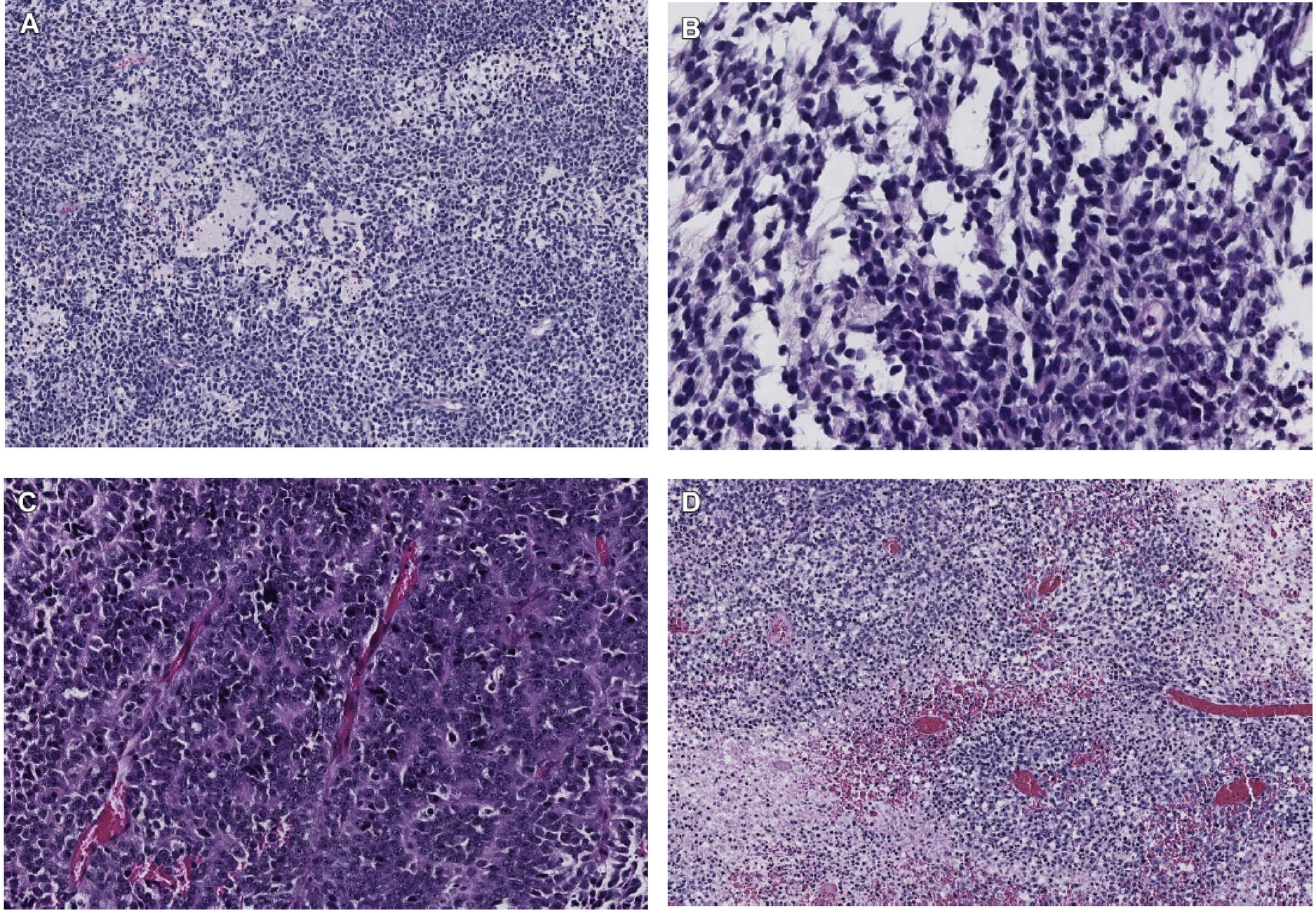
- <5% arise in bone
  - In stark contrast to Ewing Sarcoma
  - Frequent dissemination site in advanced stages



(*Am J Surg Pathol* 2017;41:941–949)



(*Am J Surg Pathol* 2017;41:941–949)


A
B
C
D

Evaluation of ETV4 and WT1 expression in *CIC*-rearranged sarcomas and histologic mimics

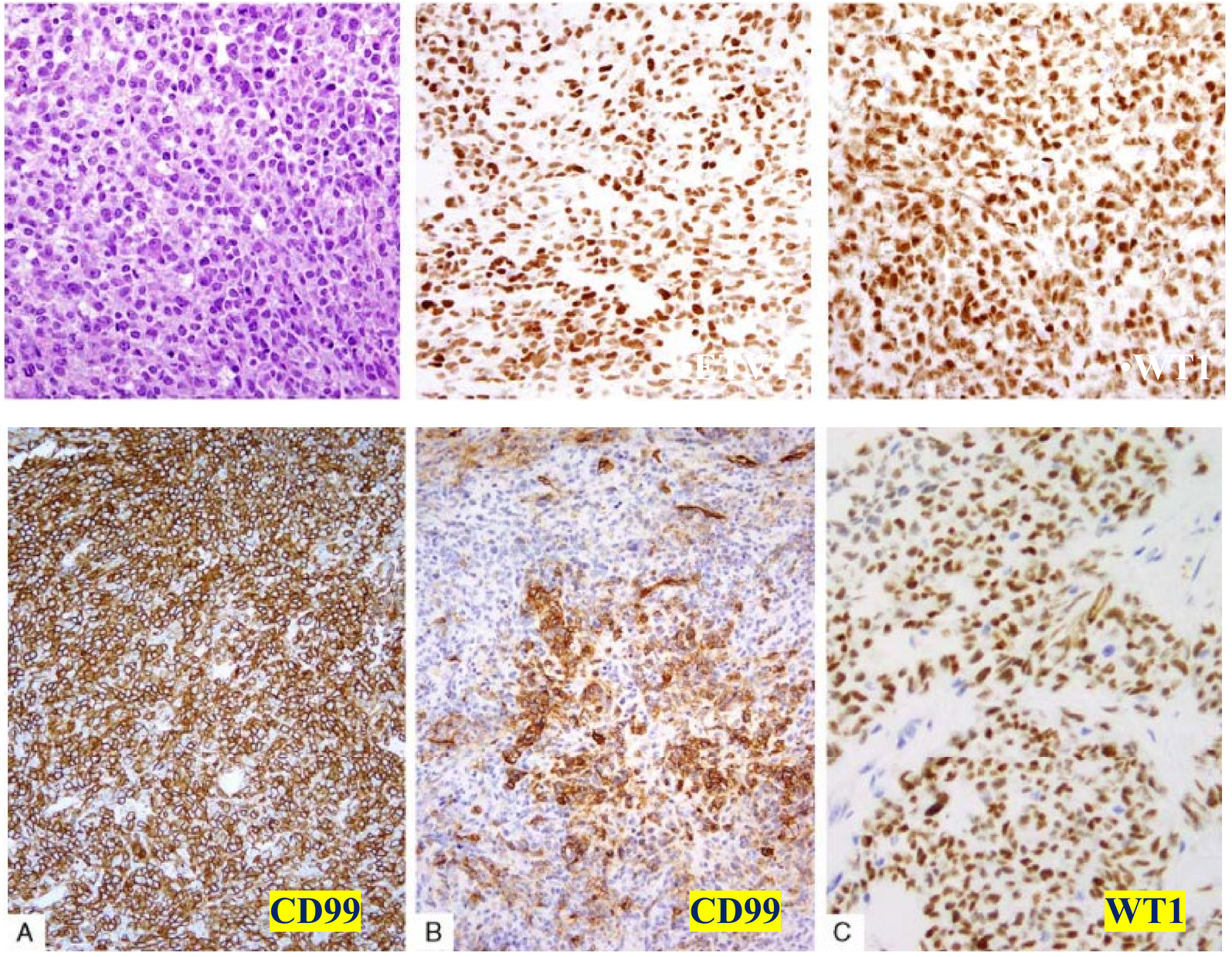
Yin P Hung, Christopher DM Fletcher and Jason L Hornick

Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

Modern Pathology (2016) 29, 1324–1334

- Upregulation of **WT1** and ETV1/4/5 in CIC-rearranged sarcomas **ETV4** (ETS Variant 4)

- Member of the PEA3 subgroup in the ETS transcription factor family


CD99
CD99
WT1
A
B
C

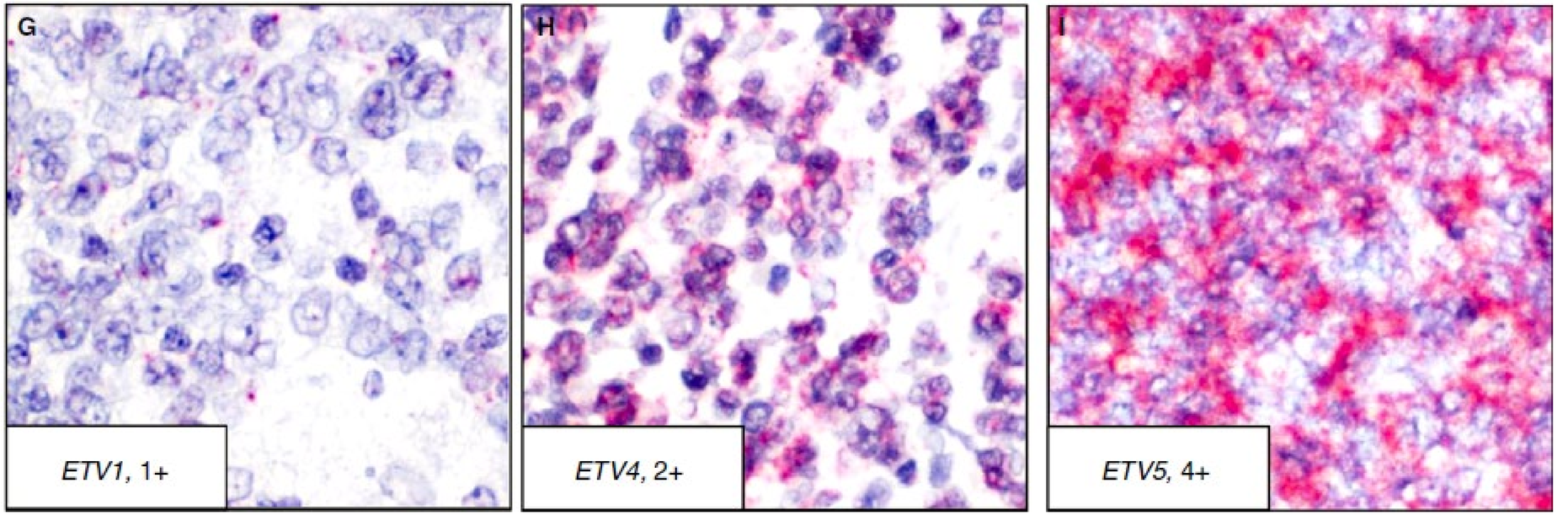
Tumor type	*Total cases*	*ETV4 positive (%)*[a]	*0*	*1+*	*2+*	*3+*	*4+*	*Both ETV4 and WT1 positive (%)*[b]
CIC-rearranged sarcoma	40	36 (90)	2	1	1	4	32	34 (85)
Non-*CIC*-rearranged tumors	200	10 (5)	145	33	11	4	7	8 (4)[c]
Ewing sarcoma	40	0 (0)	28	12	0	0	0	0 (0)
BCOR-CCNB3 sarcoma	4	0 (0)	4	0	0	0	0	0 (0)
Unclassified round cell sarcoma	6	5 (83)	1	0	0	0	5	5 (83)
Synovial sarcoma, poorly differentiated	10	0 (0)	6	3	1	0	0	0 (0)
Myxoid liposarcoma, high grade (round cell)	10	0 (0)	8	2	0	0	0	0 (0)
Lymphoblastic lymphoma	10	0 (0)	9	1	0	0	0	0 (0)
Alveolar rhabdomyosarcoma	10	0 (0)	8	2	0	0	0	0 (0)
Embryonal rhabdomyosarcoma	10	0 (0)	8	1	1	0	0	0 (0)
Mesenchymal chondrosarcoma	10	0 (0)	10	0	0	0	0	0 (0)
Merkel cell carcinoma	10	0 (0)	10	0	0	0	0	0 (0)
Neuroblastoma	10	0 (0)	9	0	1	0	0	0 (0)
Olfactory neuroblastoma	10	0 (0)	9	1	0	0	0	0 (0)
NUT midline carcinoma	5	0 (0)	5	0	0	0	0	0 (0)
Desmoplastic small round cell tumor	5	1 (20)	3	1	0	1	0	0 (0)
Wilms tumor	10	2 (20)	3	2	3	1	1	2 (22)
Small cell carcinoma	20	1 (5)	16	3	0	1	0	0 (0)
Melanoma	20	1 (5)	8	5	5	1[d]	1	1 (5)

The utility of *ETV1*, *ETV4* and *ETV5* RNA *in-situ* hybridization in the diagnosis of *CIC–DUX* sarcomas

Steven C Smith,[1,2,*] Nallasivam Palanisamy,[3,4,*] Elizabeth Martin,[1] Jorge Almenara,[1] Jonathan B McHugh,[4] Eun-Young K Choi,[4] David R Lucas,[4] Bryan L Betz,[4] Dafydd Thomas[4] & Rajiv M Patel[4,5]

[1]*Department of Pathology, VCU School of Medicine, Richmond, VA, USA,* [2]*Department of Surgery, VCU School of Medicine, Richmond, VA, USA,* [3]*Department of Urology, Henry Ford Health System, Detroit, MI, USA,* [4]*Department of Pathology, University of Michigan, Ann Arbor, MI, USA, and* [5]*Department of Dermatology, University of Michigan, Ann Arbor, MI, USA*

Histopathology 2017, 70, 657–663. DOI: 10.1111/his.13112

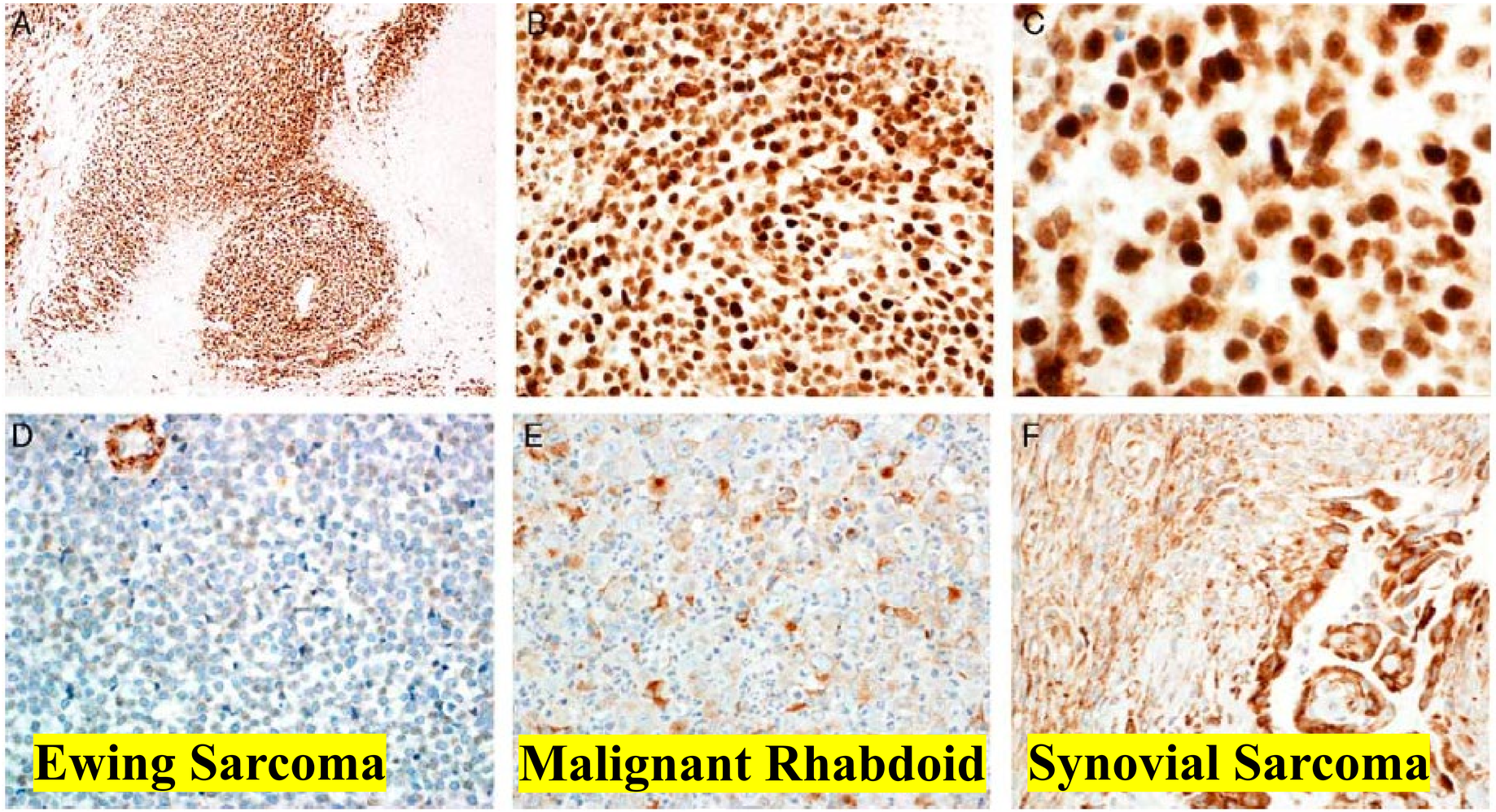


DUX4 Immunohistochemistry Is a Highly Sensitive and Specific Marker for CIC-DUX4 Fusion-positive Round Cell Tumor

Bradford Siegele, MD, JD,†‡ Jon Roberts, BA,† Jennifer O. Black, MD,*† Erin Rudzinski, MD,§ Sara O. Vargas, MD,‡ and Csaba Galambos, MD, PhD*†*

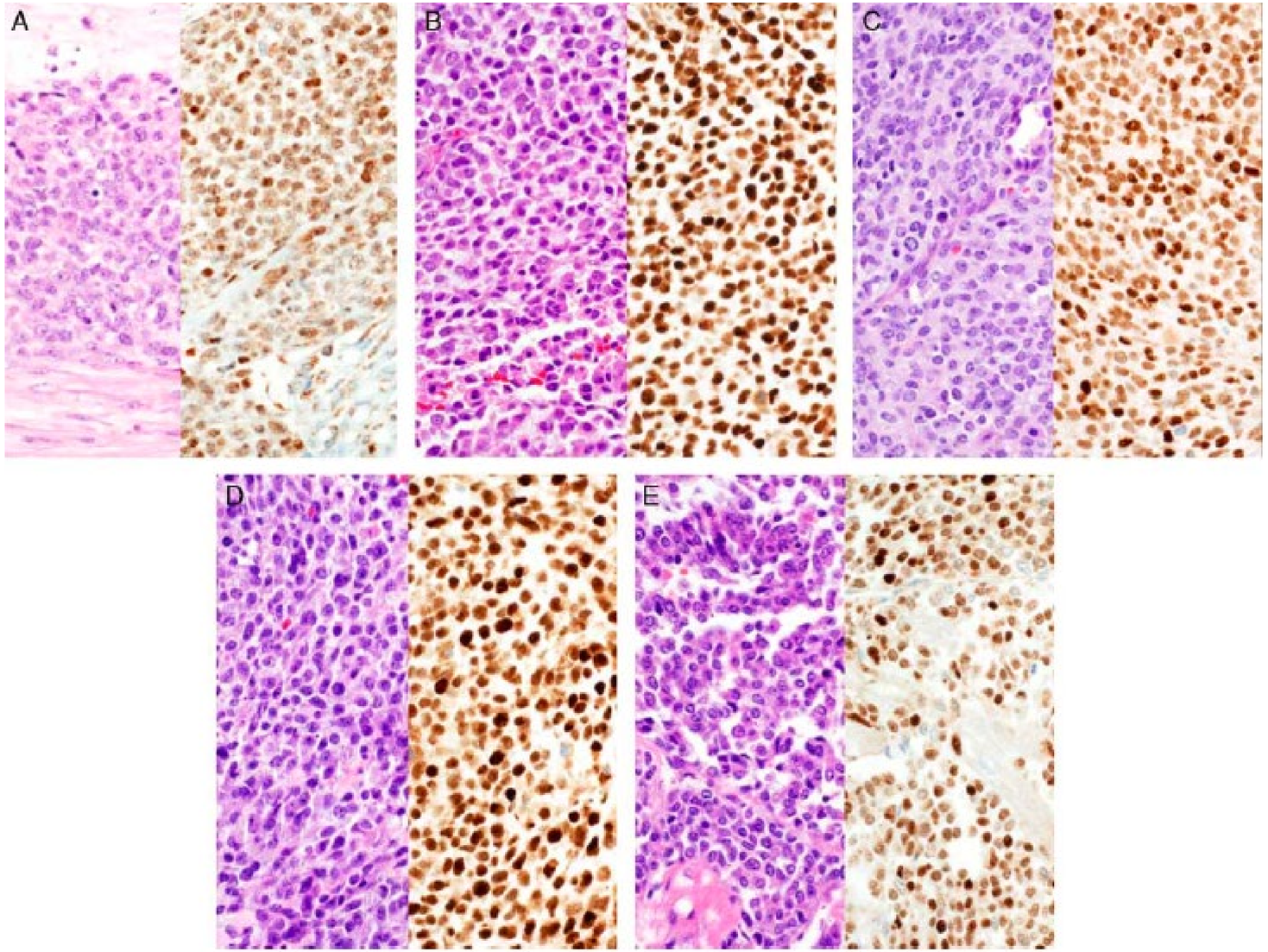
(*Am J Surg Pathol* 2017;41:423–429)

Case	Age/ Sex	Location	Translocation/Genetic Confirmation	CD99	WT1	CK	Desmin	Myogenin	Clinical Course and Outcome
S1	10/F	Neck	*CIC* translocation FISH	+ (mem/ cyt)	+	–	–	–	Surgical resection Chemotherapy and radiation Alive at 12 mo, lung nodules
S2	19/F	Pelvis	t(4;19) Conventional karyotype	+ (mem)	–	+ (foc)	–	–	Neoadjuvant chemotherapy Surgical resection Alive, NED at 24 mo
S3	13/F	Neck	t(4;19) RT-PCR	+	+	+ (foc)	–	–	Neoadjuvant chemotherapy and local proton-beam radiation Surgical resection with negative margins DFS 16 mo (lung metastases) Alive at 22 mo, lung nodules
S4	15/M	Pelvis	t(4;19) FISH	+ (foc mem)	+	ND	–	–	Neoadjuvant chemotherapy and radiation Hemipelvectomy Alive, at 7.5 mo
S5	14/M	Paraspinal	t(10;19) Conventional karyotype	+ (mem)	+	+ (foc)	–	–	Neoadjuvant chemotherapy and radiation Surgical resection DFS 6 mo (myocardial metastasis) Died, OS 7 mo



(*Am J Surg Pathol* 2017;41:423–429)

Memorial Sloan Kettering Cancer Center



(*Am J Surg Pathol* 2017;41:423–429)

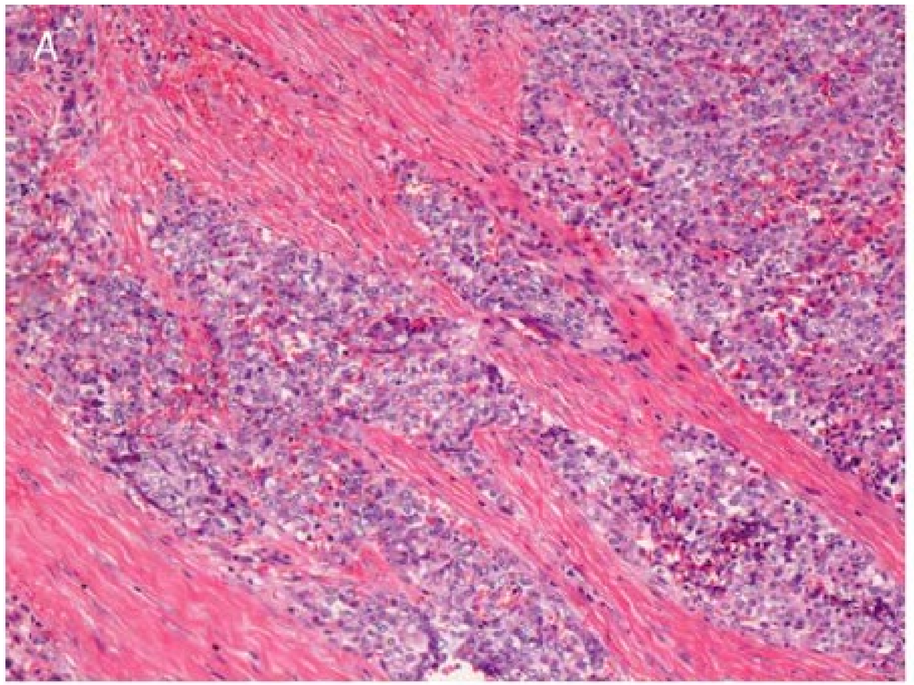
Memorial Sloan Kettering Cancer Center

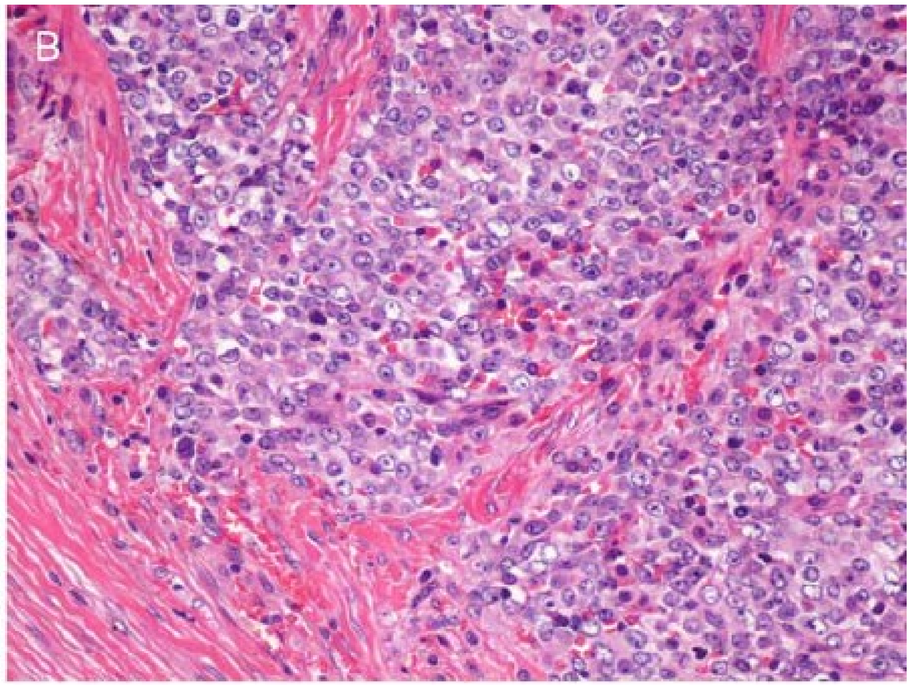
A Novel *CIC-FOXO4* Gene Fusion in Undifferentiated Small Round Cell Sarcoma

A Genetically Distinct Variant of Ewing-like Sarcoma

Shintaro Sugita, MD, PhD, Yasuhito Arai, PhD,† Akiko Tonooka, MD, PhD,‡ Natsuko Hama, MS,† Yasushi Totoki, BS,† Tomoki Fujii, MD,§ Tomoyuki Aoyama, MT,* Hiroko Asanuma, MT, PhD,* Tomohide Tsukahara, MD, PhD,‖ Mitsunori Kaya, MD, PhD,¶ Tatsuhiro Shibata, MD, PhD,† and Tadashi Hasegawa, MD, PhD**

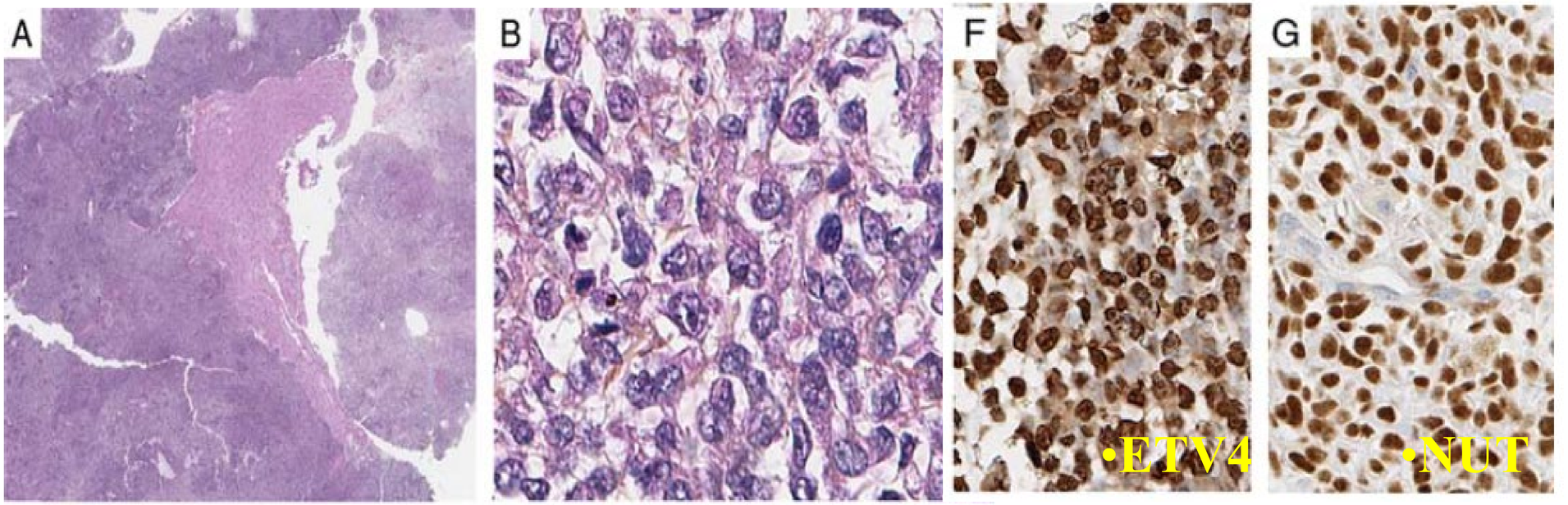
(*Am J Surg Pathol* 2014;38:1571–1576)





Clinicopathologic Features of *CIC-NUTM1* Sarcomas, a New Molecular Variant of the Family of *CIC*-Fused Sarcomas

François Le Loarer, MD, PhD,†‡ Daniel Pissaloux, PhD,§‖ Sarah Watson, MD, PhD,¶ Catherine Godfraind, MD, PhD,# Louise Galmiche-Rolland, MD,** Karen Silva, MSc,†† Laetitia Mayeur, MSc,* Antoine Italiano, MD, PhD,†‡‡‡ Audrey Michot, MD,§§ Gaëlle Pierron, PhD,‖‖ Alexandre Vasiljevic, MD, PhD,†† Dominique Ranchère-Vince, MD,§ Jean Michel Coindre, MD,*†‡ and Franck Tirode, PhD‖¶¶*



Human Pathology (2017) 65, 225–230

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Human PATHOLOGY

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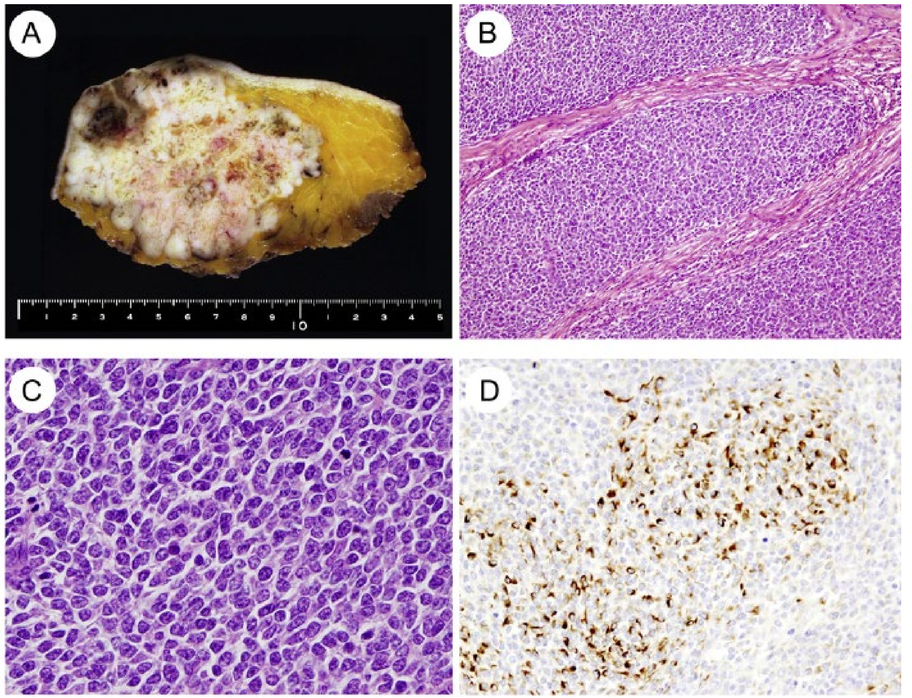
Case study

NUTM2A-CIC fusion small round cell sarcoma: a genetically distinct variant of *CIC*-rearranged sarcoma☆,☆☆

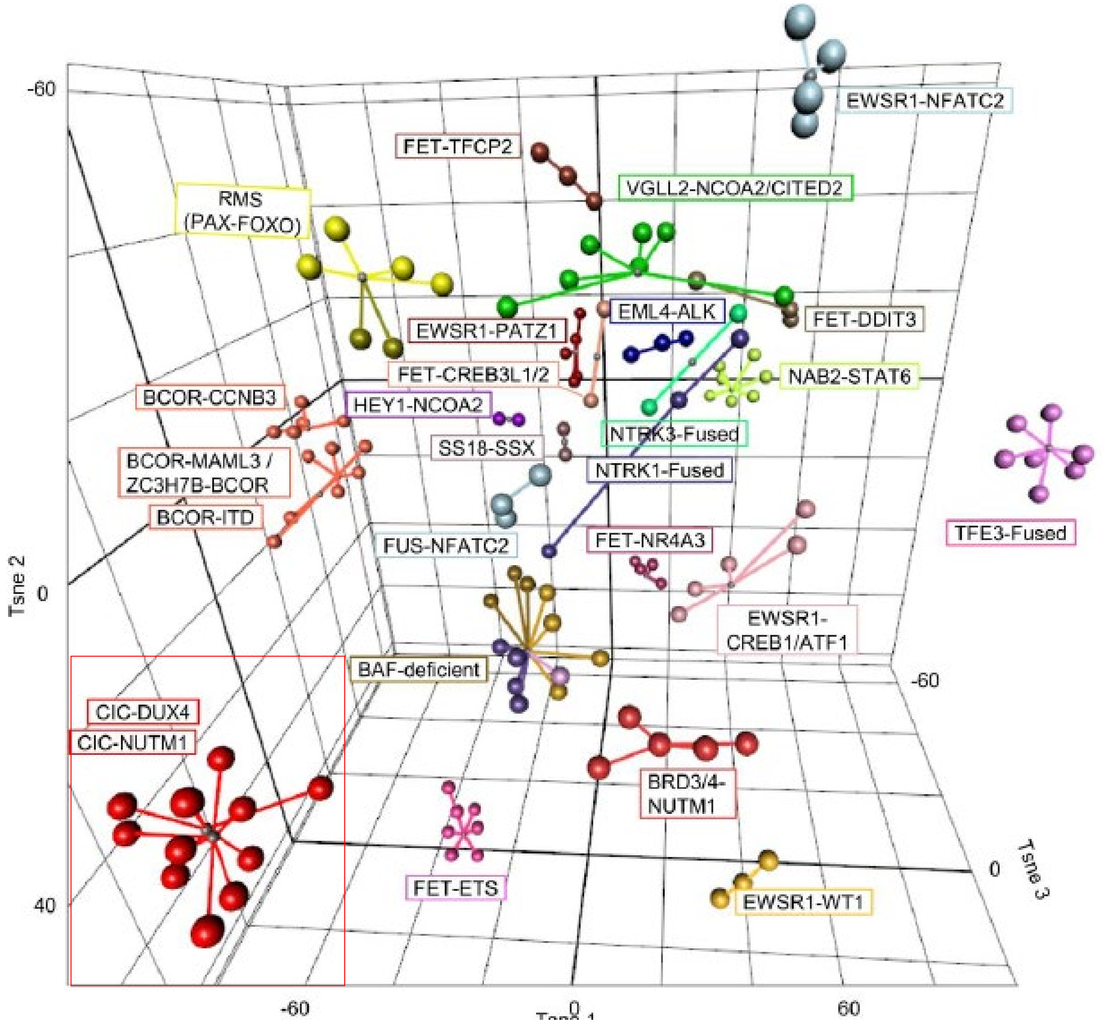
Shintaro Sugita MD, PhD[a], Yasuhito Arai PhD[b], Tomoyuki Aoyama MT[a], Hiroko Asanuma PhD[a], Wakako Mukai BS[b], Natsuko Hama MS[b], Makoto Emori MD, PhD[c], Tatsuhiro Shibata MD, PhD[b], Tadashi Hasegawa MD, PhD[a,*]

[a]*Department of Surgical Pathology, Sapporo Medical University, School of Medicine, Sapporo, Hokkaido 060-8543, Japan*
[b]*Division of Cancer Genomics, National Cancer Center Research Institute, Tokyo 104-0045, Japan*
[c]*Department of Orthopedic Surgery, Sapporo Medical University, School of Medicine, Sapporo, Hokkaido 060-8543, Japan*



Transcriptomic definition of molecular subgroups of small round cell sarcomas

Sarah Watson[1,2], Virginie Perrin[1,2], Delphine Guillemot[3], Stephanie Reynaud[3], Jean-Michel Coindre[4,5], Marie Karanian[6], Jean-Marc Guinebretière[7], Paul Freneaux[8], François Le Loarer[4,5], Megane Bouvet[3], Louise Galmiche-Rolland[9,10], Frédérique Larousserie[11], Elisabeth Longchampt[12], Dominique Ranchere-Vince[6], Gaelle Pierron[3]*, Olivier Delattre[1,2,3,13]†*, Franck Tirode[1,2,14 †*]



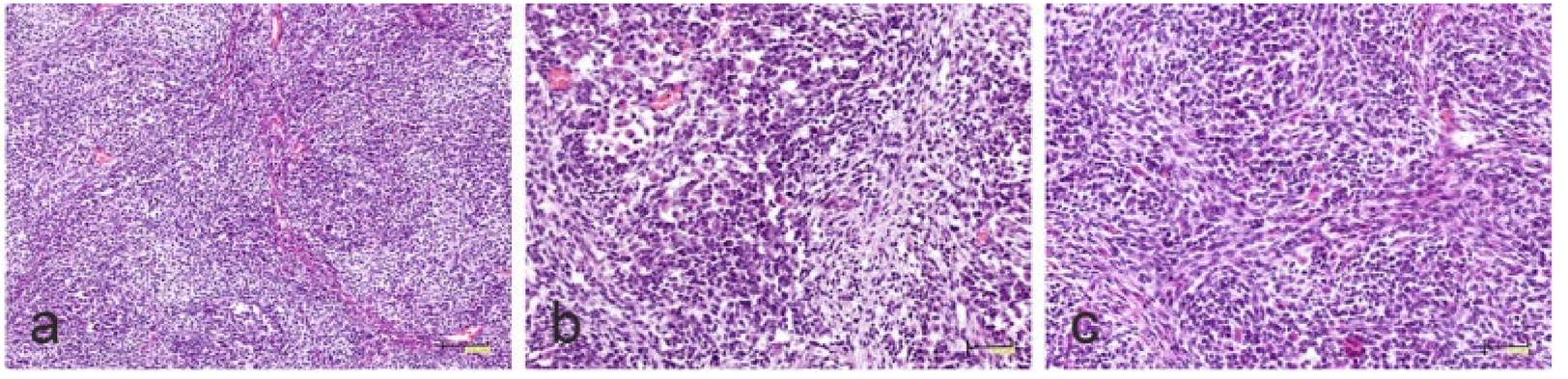
Łastowska et al. Acta Neuropathologica Communications (2020) 8:105
https://doi.org/10.1186/s40478-020-00984-9

Acta Neuropathologica Communications

RESEARCH Open Access

Molecular identification of CNS NB-FOXR2, CNS EFT-CIC, CNS HGNET-MN1 and CNS HGNET-BCOR pediatric brain tumors using tumor-specific signature genes

Maria Łastowska[1,2*], Joanna Trubicka[1], Anna Sobocińska[2], Bartosz Wojtas[3], Magdalena Niemira[4], Anna Szałkowska[4], Adam Krętowski[4], Agnieszka Karkucińska-Więckowska[1], Magdalena Kaleta[1], Maria Ejmont[1], Marta Perek-Polnik[5], Bożenna Dembowska-Bagińska[5], Wiesława Grajkowska[1] and Ewa Matyja[2]



ARTICLE

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DOI: 10.1038/ncomms11790 OPEN

Identification of *ETV6-RUNX1*-like and *DUX4*-rearranged subtypes in paediatric B-cell precursor acute lymphoblastic leukaemia

Henrik Lilljebjörn[1], Rasmus Henningsson[2], Axel Hyrenius-Wittsten[1], Linda Olsson[1], Christina Orsmark-Pietras[1], Sofia von Palffy[1], Maria Askmyr[1], Marianne Rissler[1], Martin Schrappe[3], Gunnar Cario[3], Anders Castor[4], Cornelis J.H. Pronk[4], Mikael Behrendtz[5], Felix Mitelman[1], Bertil Johansson[1,6], Kajsa Paulsson[1], Anna K. Andersson[1], Magnus Fontes[2] & Thoas Fioretos[1,6]

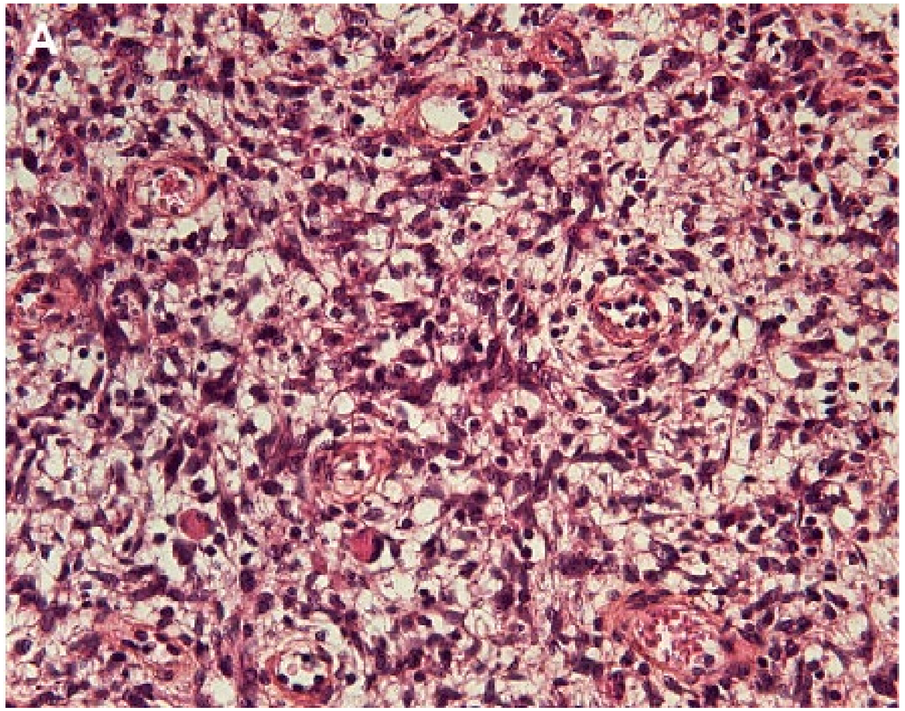
Recurrent *DUX4* fusions in B cell acute lymphoblastic leukemia of adolescents and young adults

Takahiko Yasuda[1,2], Shinobu Tsuzuki[3], Masahito Kawazu[4], Fumihiko Hayakawa[2], Shinya Kojima[1], Toshihide Ueno[1], Naoto Imoto[2], Shinji Kohsaka[4], Akiko Kunita[5], Koichiro Doi[6], Toru Sakura[7], Toshiaki Yujiri[8], Eisei Kondo[9], Katsumichi Fujimaki[10], Yasunori Ueda[11], Yasutaka Aoyama[12], Shigeki Ohtake[13], Junko Takita[14], Eirin Sai[4], Masafumi Taniwaki[15], Mineo Kurokawa[16], Shinichi Morishita[6], Masashi Fukayama[5], Hitoshi Kiyoi[2], Yasushi Miyazaki[17], Tomoki Naoe[18] & Hiroyuki Mano[1]

Fusion of *EWSR1* with the *DUX4* facioscapulohumeral muscular dystrophy region resulting from t(4;22)(q35;q12) in a case of embryonal rhabdomyosarcoma

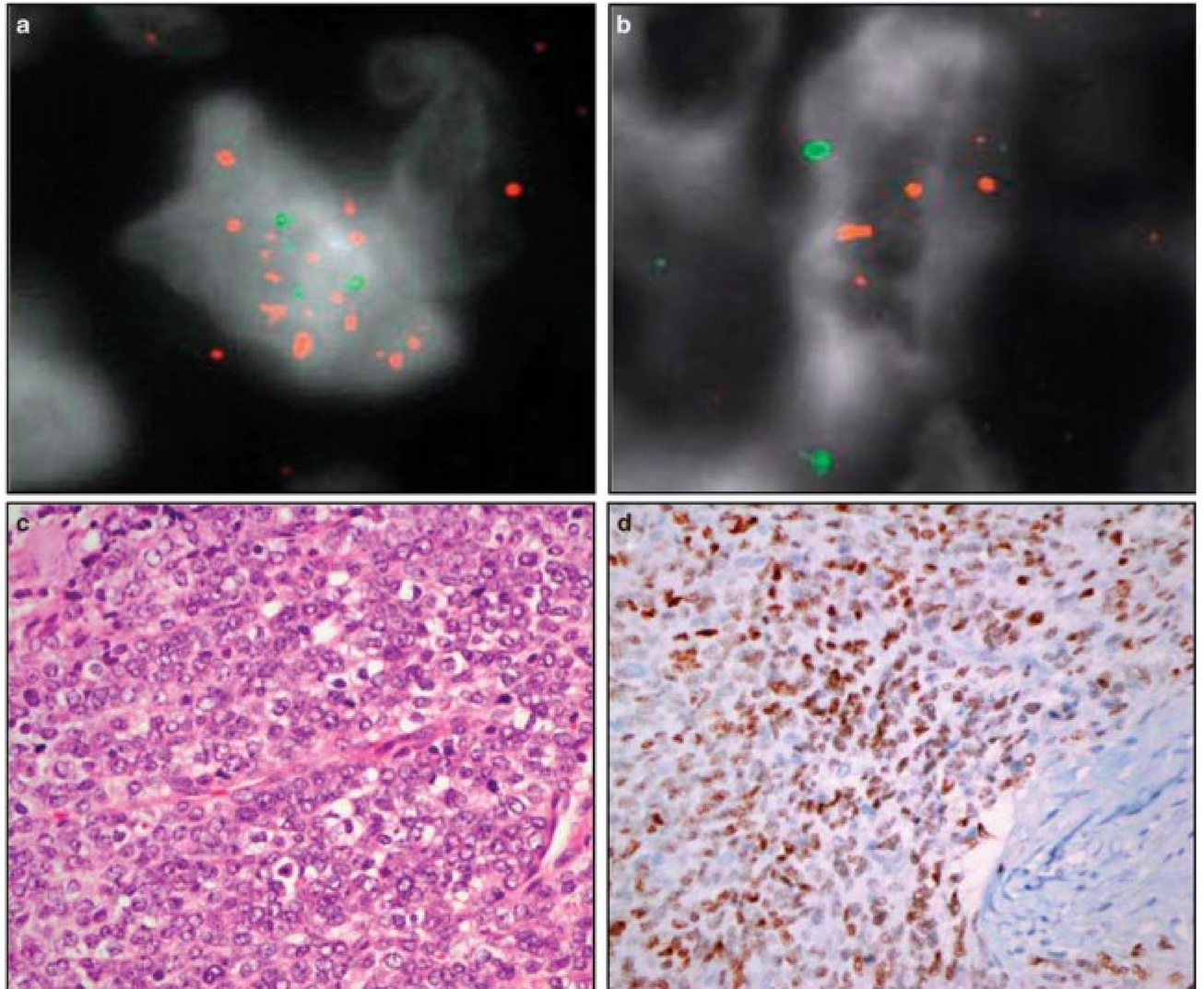
Nicolas Sirvent[a,b,c,*], Martine Trassard[d], Nathalie Ebran[a,b], Rita Attias[a,b], Florence Pedeutour[a,b]

Cancer Genetics and Cytogenetics 195 (2009) 12–18

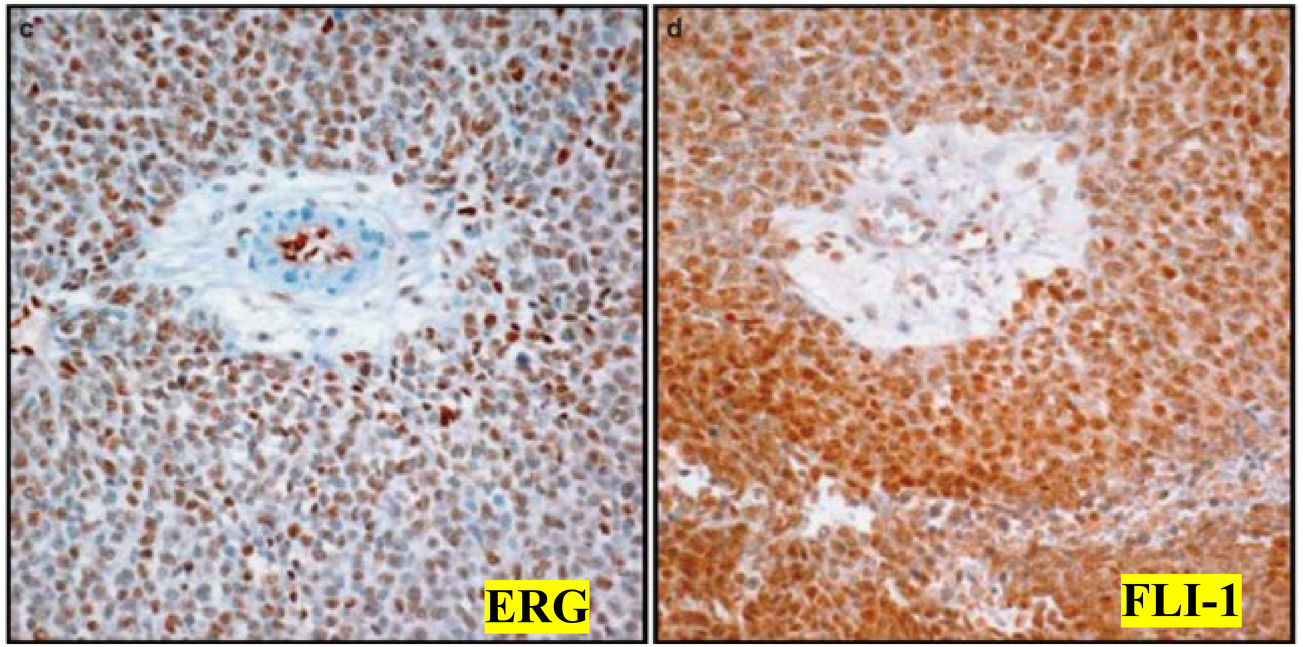


CIC-DUX sarcomas demonstrate frequent MYC amplification and ETS-family transcription factor expression

Steven Christopher Smith[1,2,6,7], Darya Buehler[3,6], Eun-Young Karen Choi[1], Jonathan B McHugh[1], Brian P Rubin[4], Steven D Billings[4], Bonnie Balzer[2], Dafydd G Thomas[1], David R Lucas[1], John R Goldblum[4] and Rajiv M Patel[1,5]



Induction of ETS-family transcription



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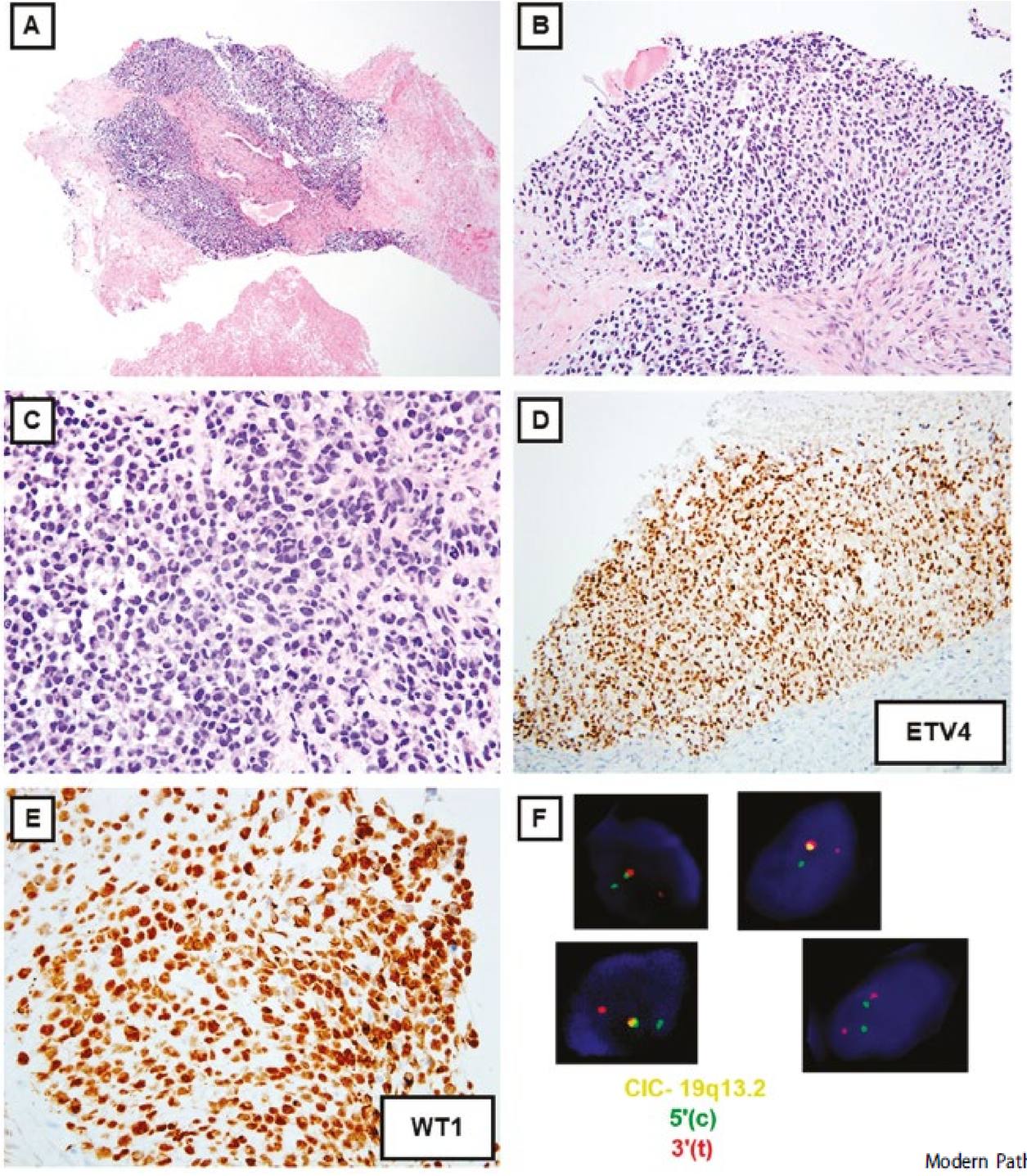
Other IHC

- Focal expression of desmin, S100 protein, MUC4, EMA, cytokeratins, and calretinins have been reported

- NKX2.2 is negative

IHC

- **ETV4** diffusely expressed with nuclear pattern ~93% of cases
  - Rare cases patchy or negative staining (~3.5%)
  - Not entirely specific
    - Focal staining 10% Ewing Sarcoma
    - Occasionally desmoplastic small round cell tumor, rhabdomyosarcoma and melanoma
- Nuclear **WT1** positive in 75% of cases
  - N and C terminus quite sensitive for tumors with *CIC-DUX4* fusions

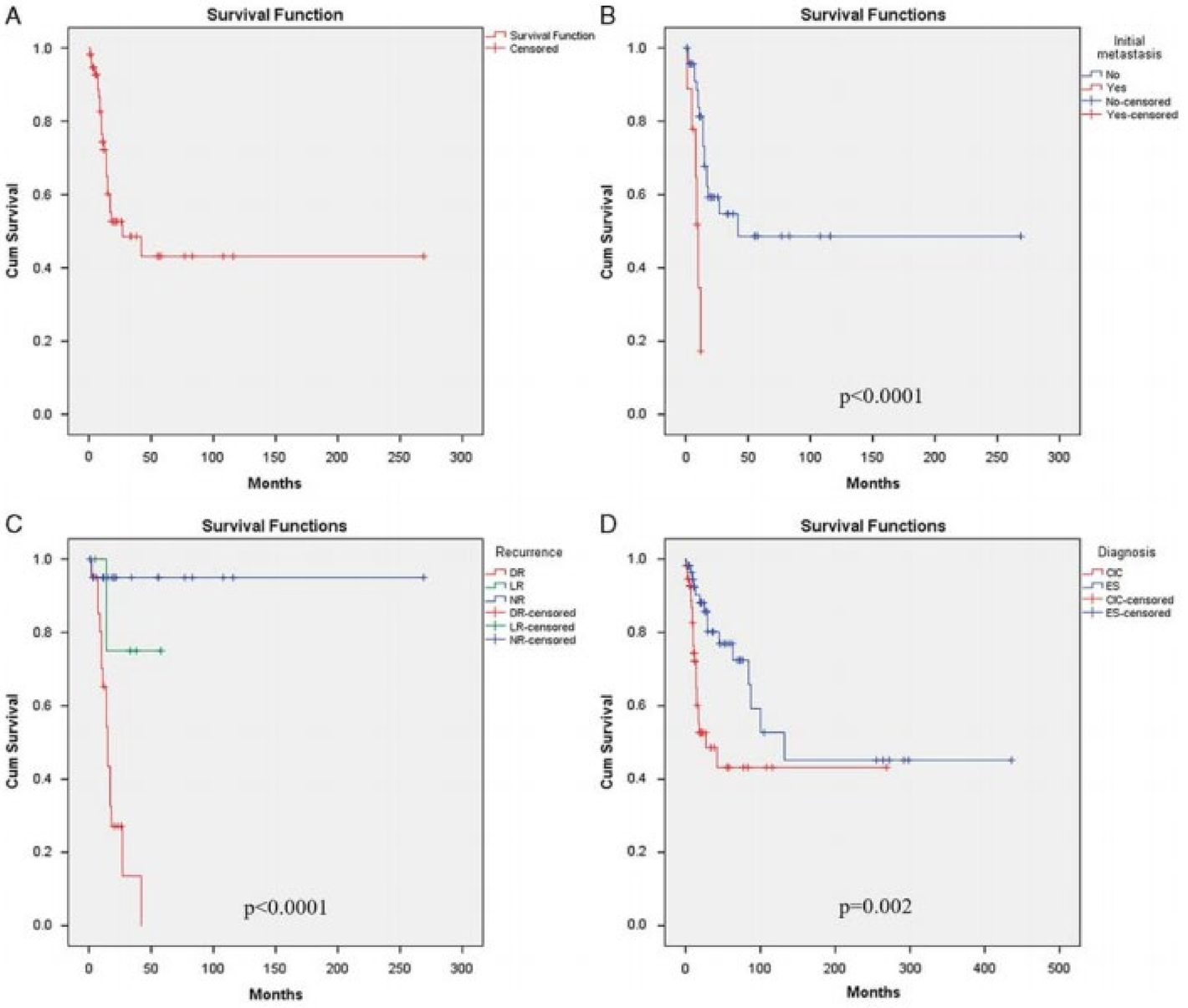

A
B
C
D
ETV4
E
WT1
F
CIC- 19q13.2
5'(c)
3'(t)

ETV transcriptional upregulation is more reliable than RNA sequencing algorithms and FISH in diagnosing round cell sarcomas with *CIC* gene rearrangements

Yu-Chien Kao[1,2] | Yun-Shao Sung[1] | Chun-Liang Chen[1] | Lei Zhang[1] | Brendan C Dickson[3] | David Swanson[3] | Sumathi Vaiyapuri[4] | Farida Latif[5] | Abdullah Alholle[6] | Shih-Chiang Huang[7] | Jason L. Hornick[8] | Cristina R Antonescu[1]

Genes Chromosomes Cancer. 2017;56:501–510

- ~15% of cases are CIC FISH negative
- Cryptic rearrangements
- Upregulation of ETV4 appears more sensitive than FISH


A
Survival Function
Survival Function
Censored
Cum Survival
Months
B
Survival Functions
Initial metastasis
No
Yes
No-censored
Yes-censored
p<0.0001
C
Survival Functions
Recurrence
DR
LR
NR
DR-censored
LR-censored
NR-censored
p<0.0001
D
Survival Functions
Diagnosis
CIC
ES
CIC-censored
ES-censored
p=0.002

Expanding the differential of superficial tumors with round-cell morphology: Report of three cases of *CIC*-rearranged sarcoma, a potentially under-recognized entity

Nolan Maloney MD[1] | Stephen M. Smith MD[2] | Sara B. Peters MD, PhD[2] | Anna Batistatou MD[3] | Zoi Evangelou MD[3] | Paul W. Harms MD[4] | May P. Chan MD[4] | Cristina R. Antonescu MD[5] | Konstantinos Linos MD[1]

J Cutan Pathol. 2020;47:535–540.

Superficial sarcomas with *CIC* rearrangement are aggressive neoplasms: A series of eight cases

Jennifer S. Ko MD, PhD[1] | Zlatko Marusic MD, PhD[2] | Elizabeth M. Azzato MD, PhD[1] | Daniel H. Farkas PhD[1] | John Van Arnam MD[3] | Sven Seiwerth MD, PhD[2,4] | Karen Fritchie[3] | Rajiv M. Patel MD[5] | Brian P. Rubin MD, PhD[1] | Steven D. Billings MD[1]

J Cutan Pathol. 2020;47:509–516.

A few home take points

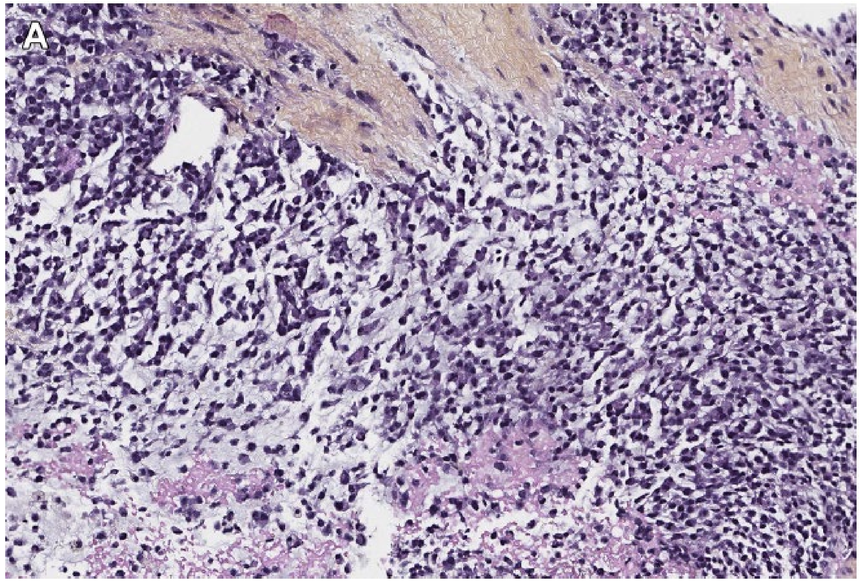
- **Atypical morphologic findings** common in CIC-rearranged sarcomas
- CIC-sarcomas in **bones** correspond to **secondary site**
  - Bone primary location exceptional
- **Nuclear** expression of **WT1** C-terminal
  - Ddx DSRCT in the setting of intraabdominal mass
- A subset of EWSR1-ETS and EWSR1-Non ETS round cell sarcoma can display atypia and high-grade features

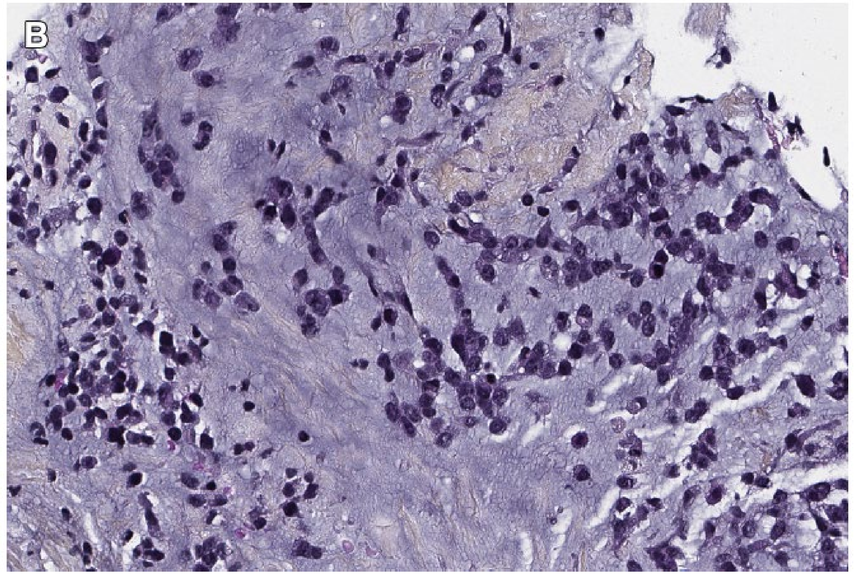
A few take home points

- **Calretinin** and **cytokeratin** expression may occasionally be seen
  - Ddx carcinoma or mesothelioma

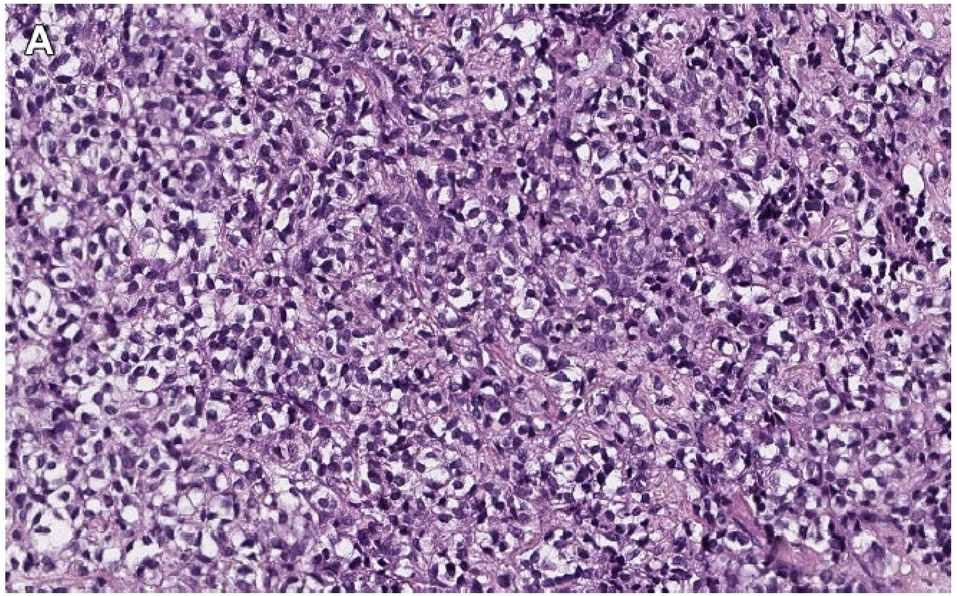
- **ERG** and **FLI1** do **not** discriminate CIC-sarcoma from Ewing Sarcoma

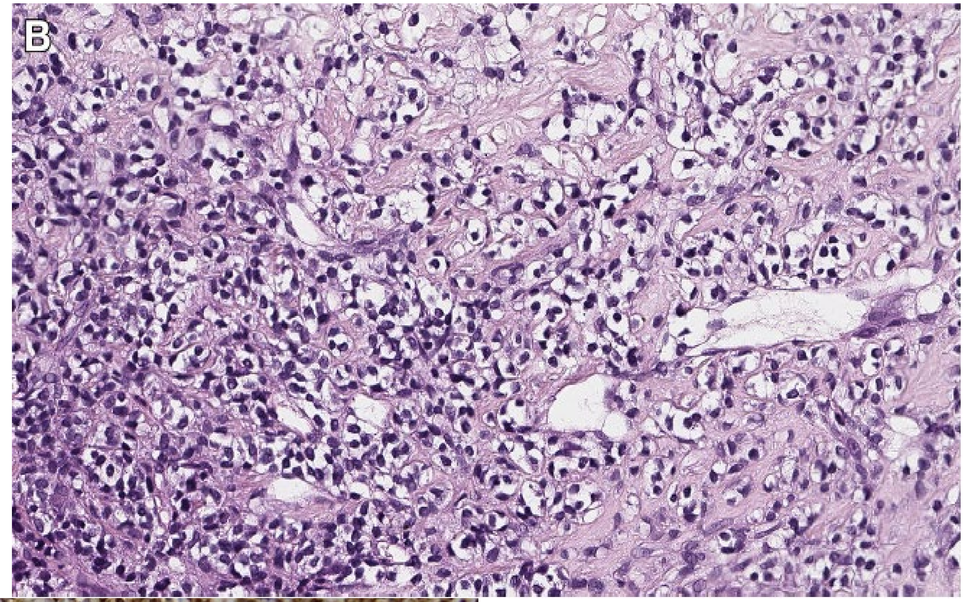
CIC with myxoid changes
DDx Extraskeletal Myxoid Chondrosarcoma and Myoepithelial tumor

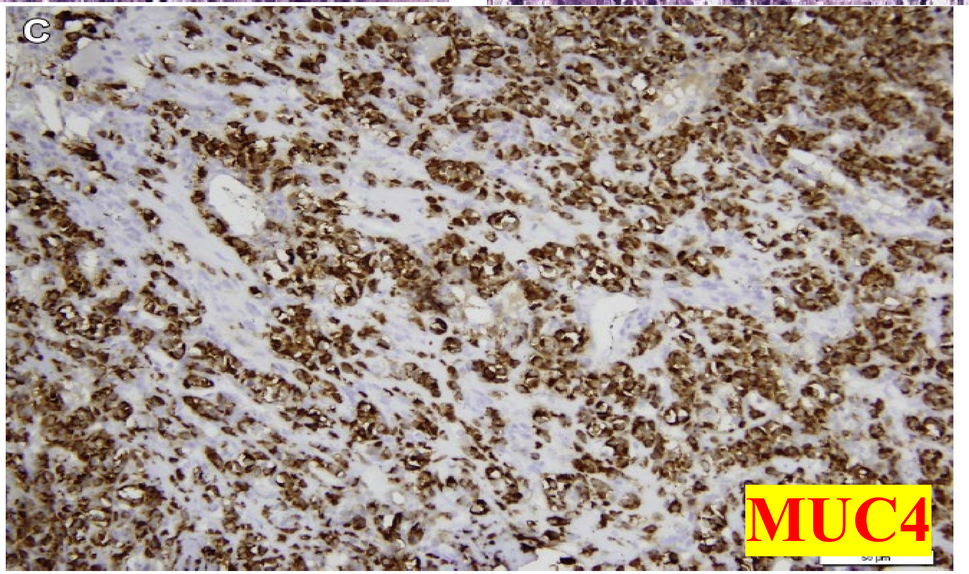




Sclerosing epithelioid fibrosarcoma







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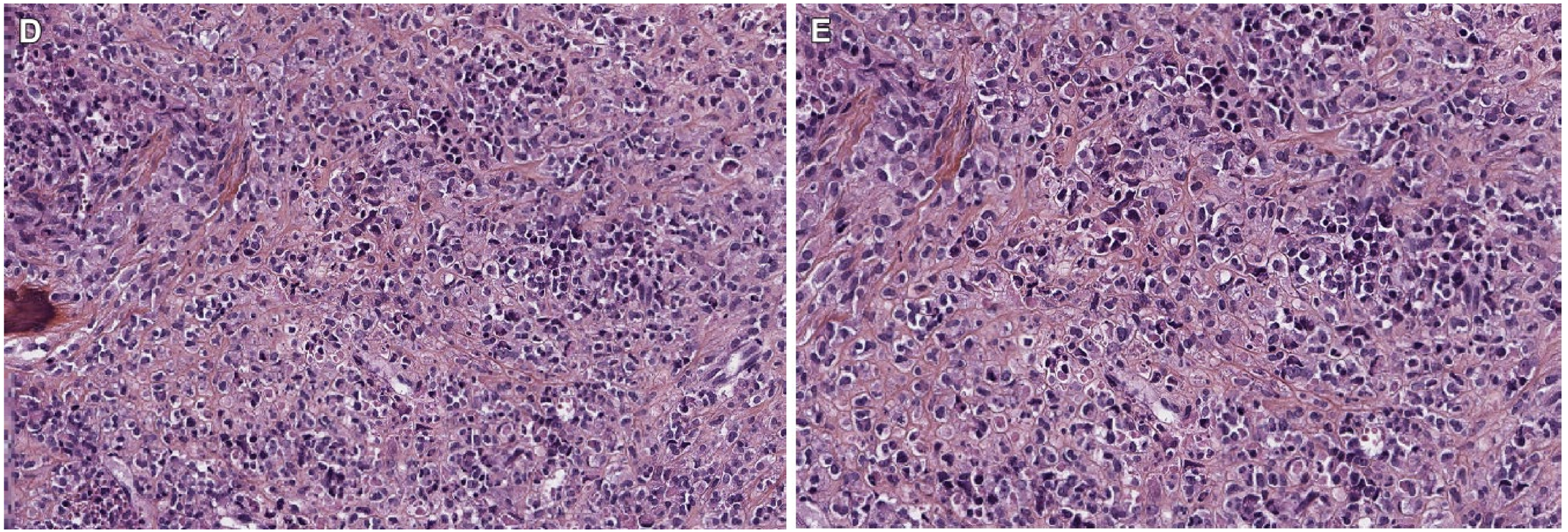
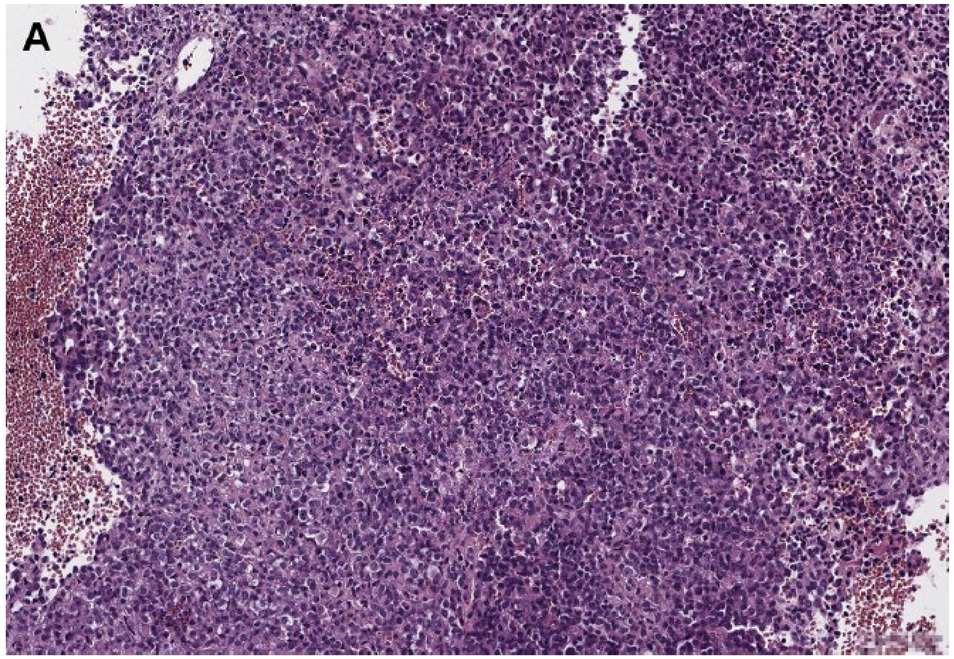
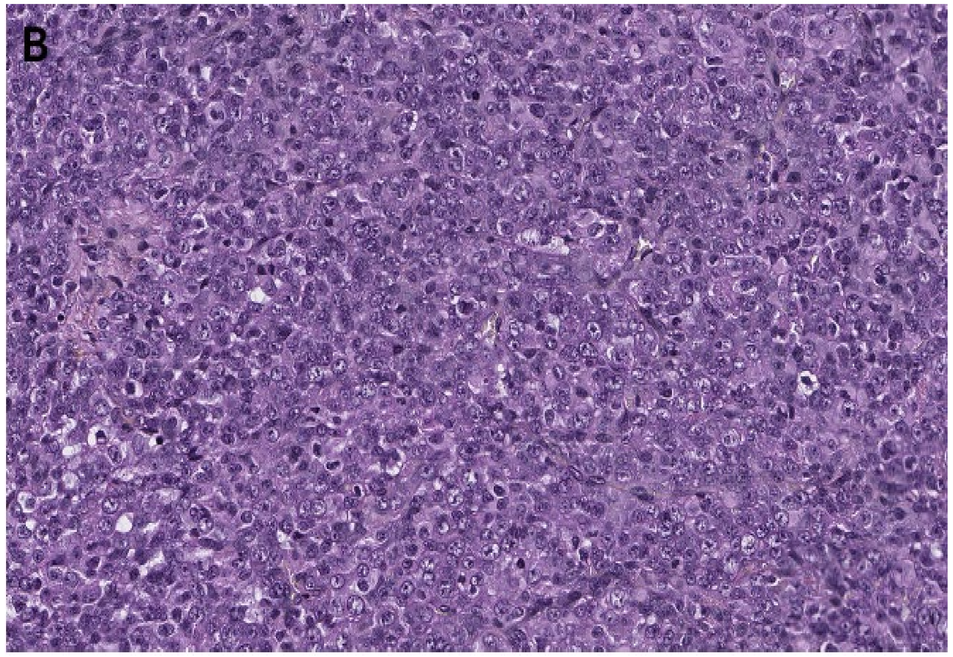
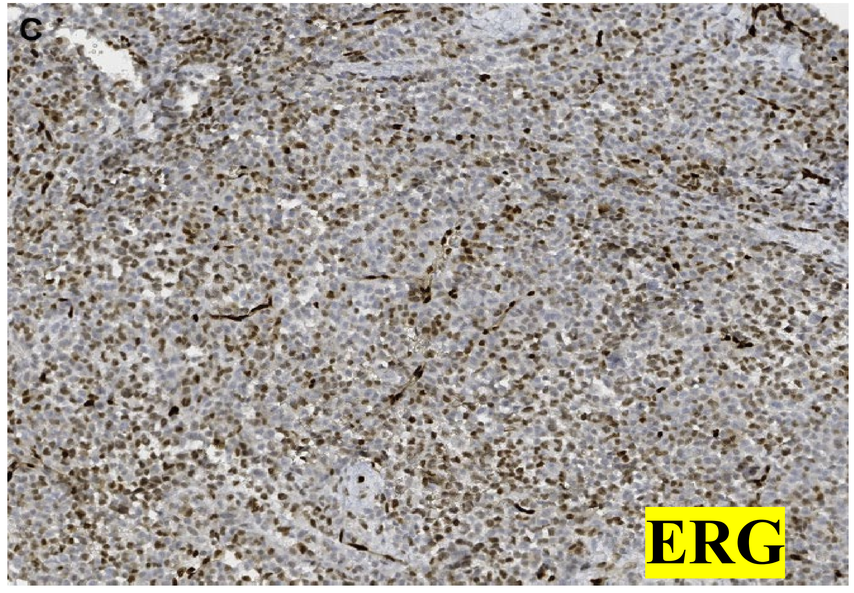
CIC-rearranged sarcoma mimicking sclerosing epithelioid sarcoma



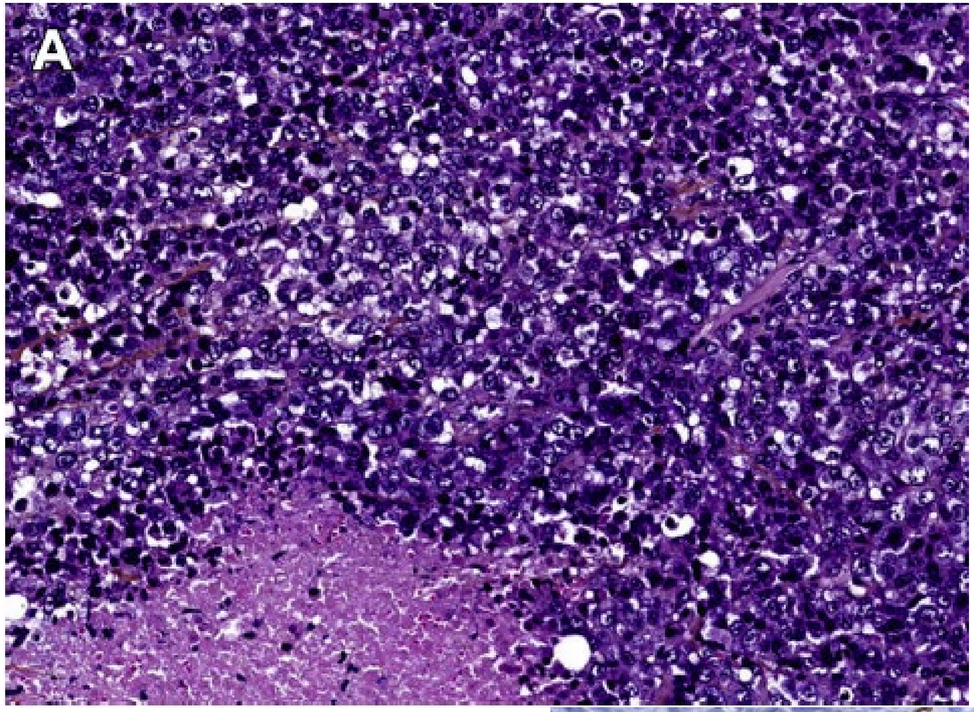
CIC with epithelioid features

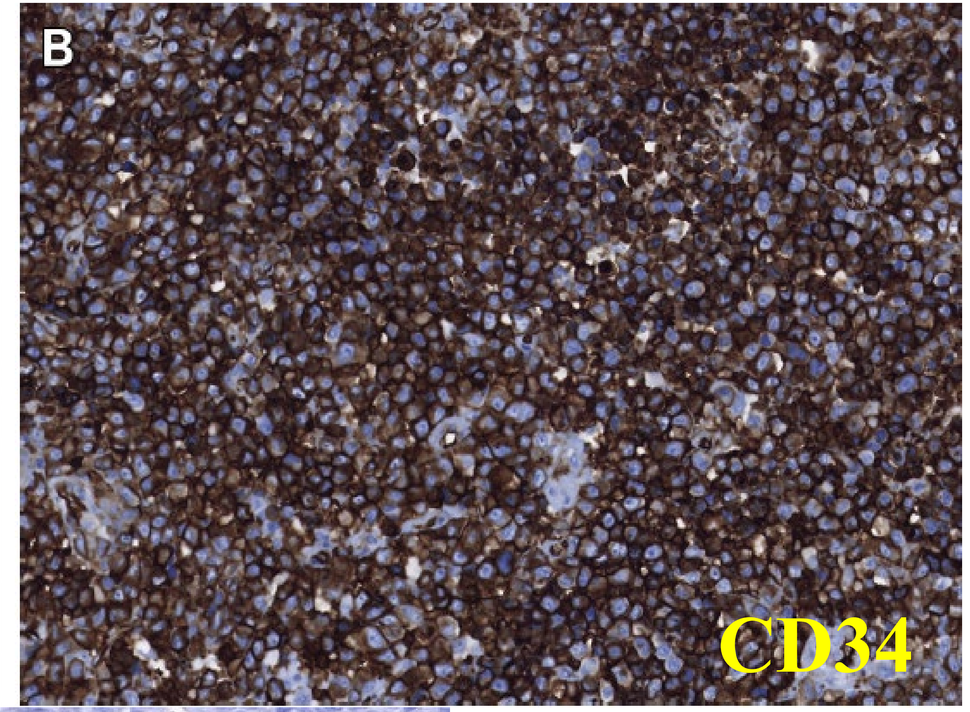


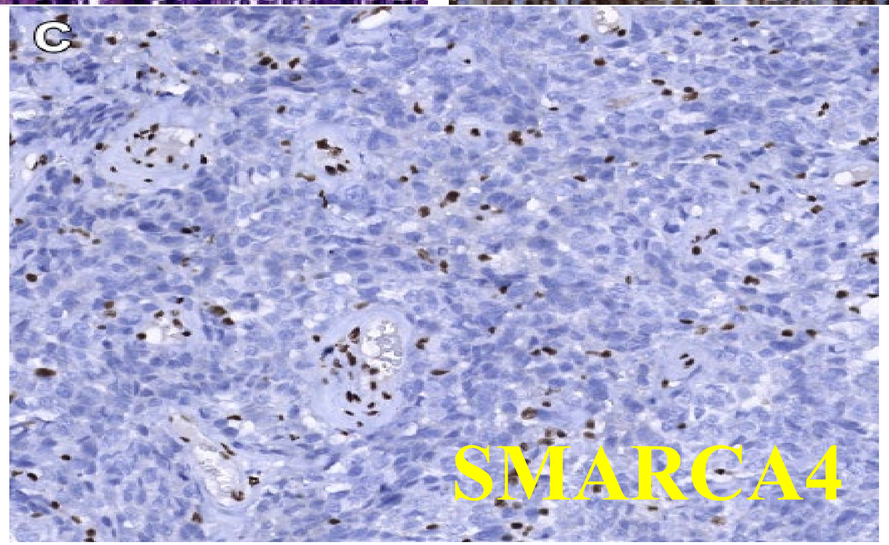




SMARCA4-deficient thoracic sarcoma







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Nevus, Melanoma or Something Else? Mesenchymal Tumors with Melanocytic Differentiation

By Konstantinos Linos MD, FCAP, FASDP
Bone, Soft Tissue and Dermatopathology
Associate Attending
Memorial Sloan Kettering Cancer Center
Department of Pathology and Laboratory Medicine
NY, USA

Malignant melanotic nerve sheath tumor

Acceptable: melanotic schwannoma; psammomatous melanotic schwannoma; malignant melanotic schwanian tumor

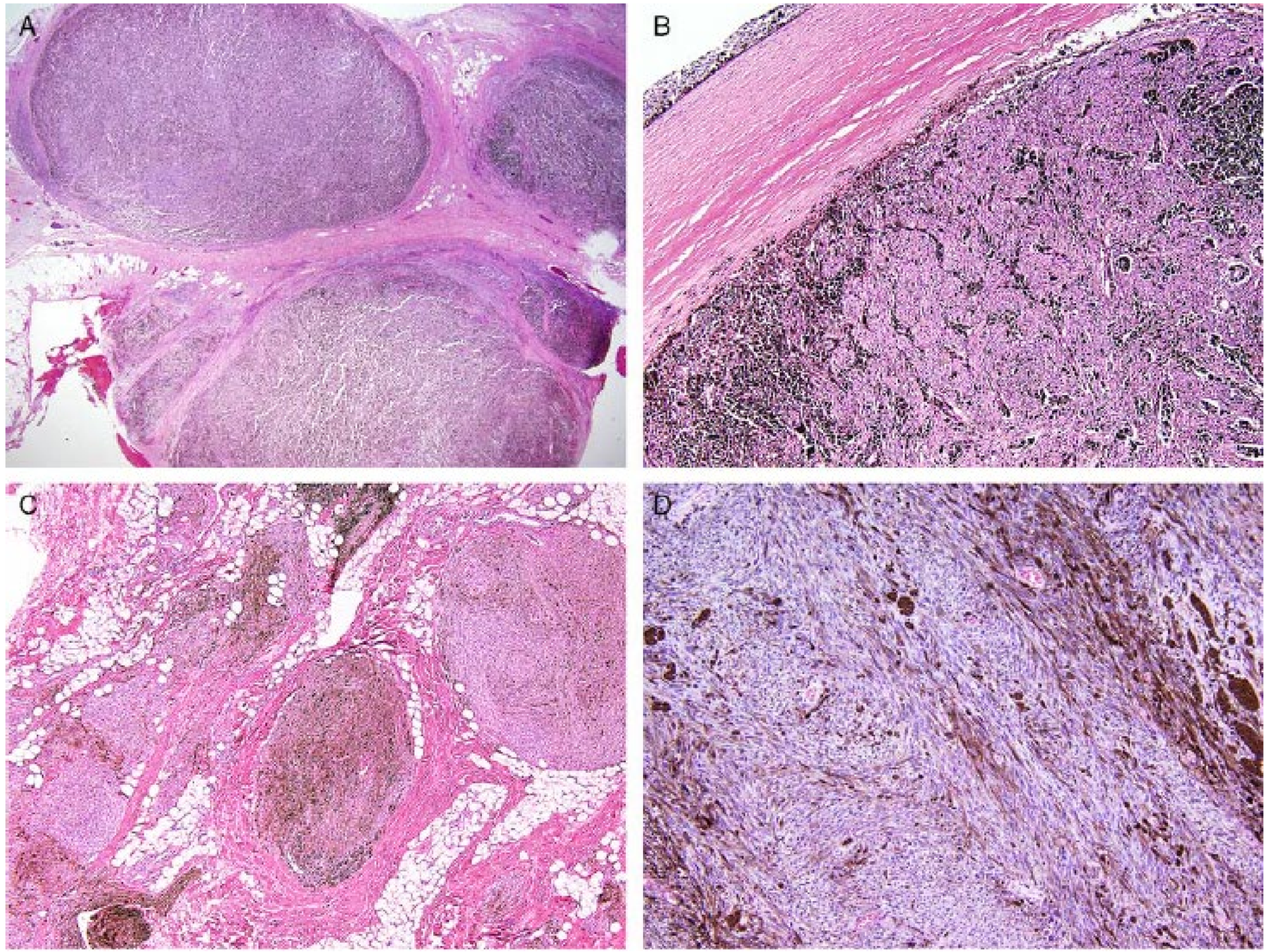
- Rare tumor of putative **neural crest origin**
- Most often in **paraspinal nerve roots and gastrointestinal tract**
- Association with other stigmata of **Carney complex**
  - Skin pigmentary abnormalities, myxomas, endocrine tumors/endocrine hyperactivity
  - Mutations in *PRKAR1A* gene

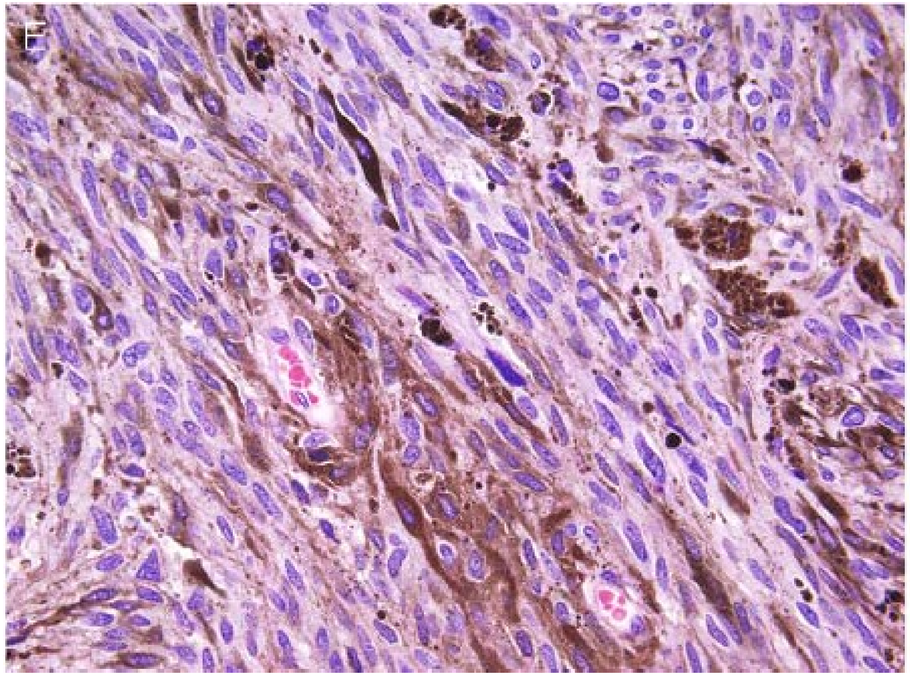
Unknown ‘cell of origin”

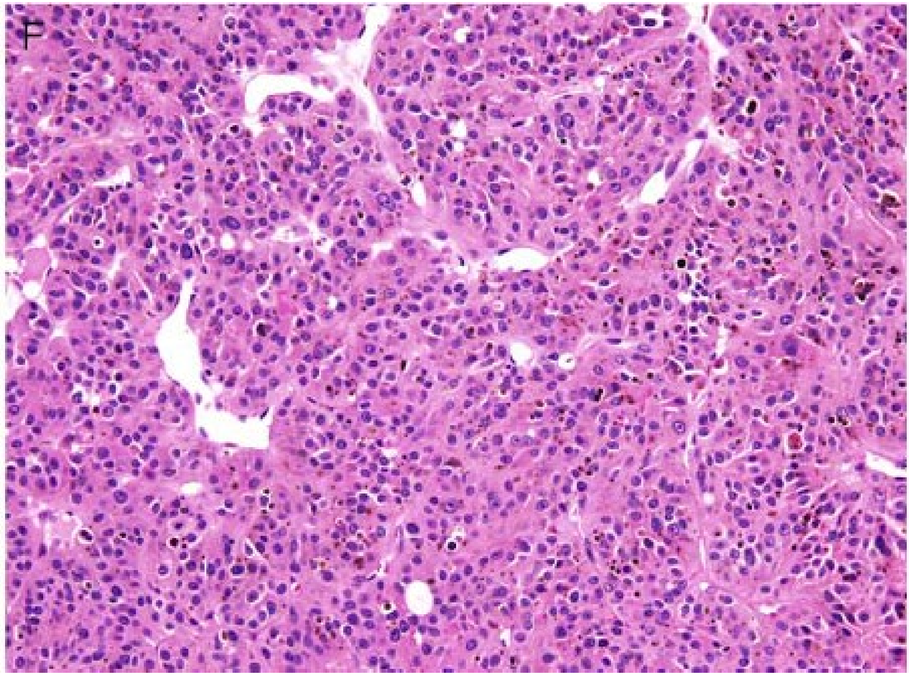
- **Hybrid light microscopic and ultrastructural features of Schwann cells and melanocytes**

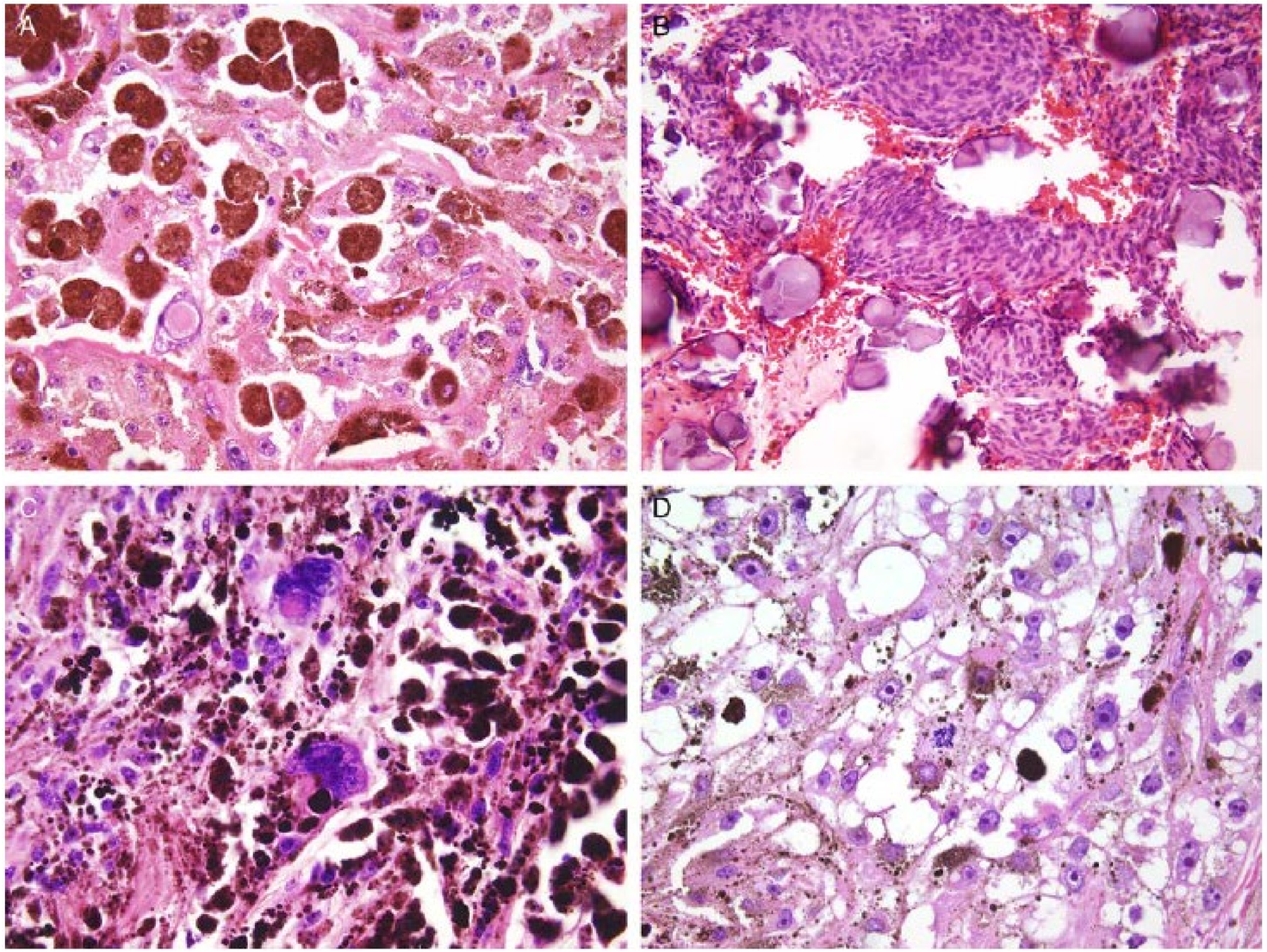
Unpredictable behavior

- **13-26% metastases** including histologically benign-appearing tumors


A
B
C
D






A
B
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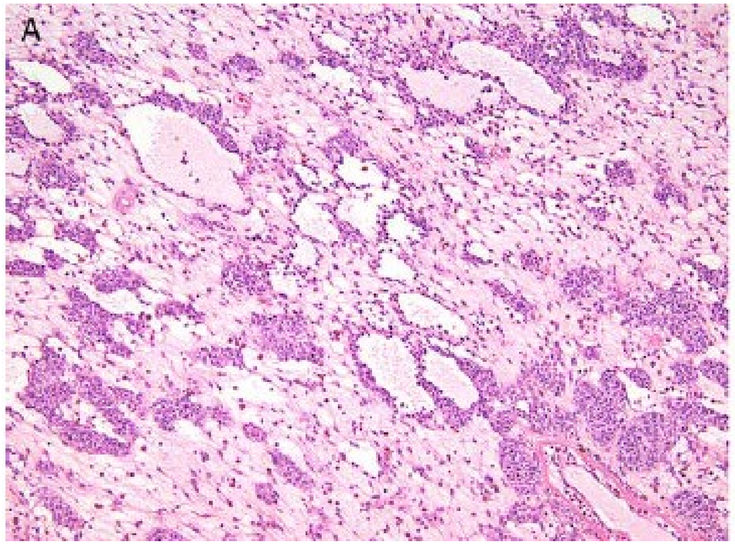
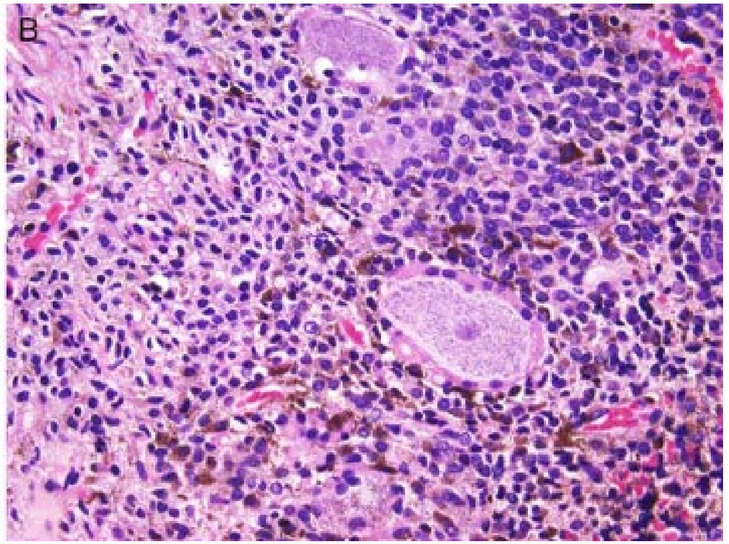
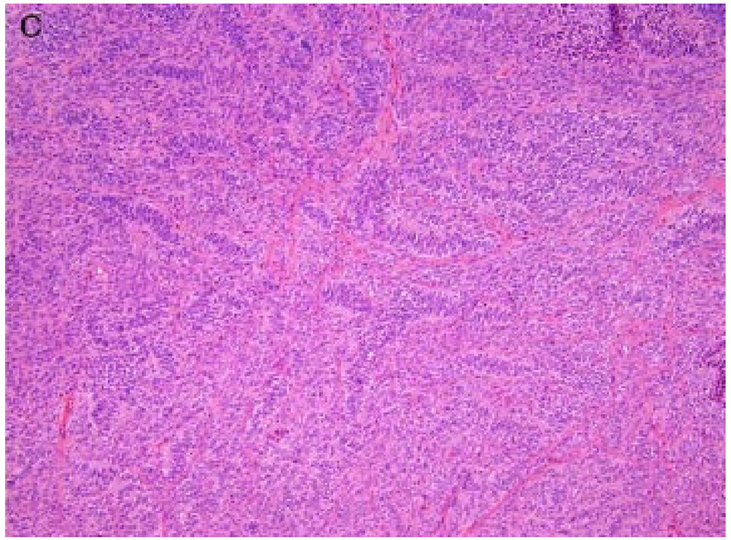
Myxoid Change



“Small cell pattern”

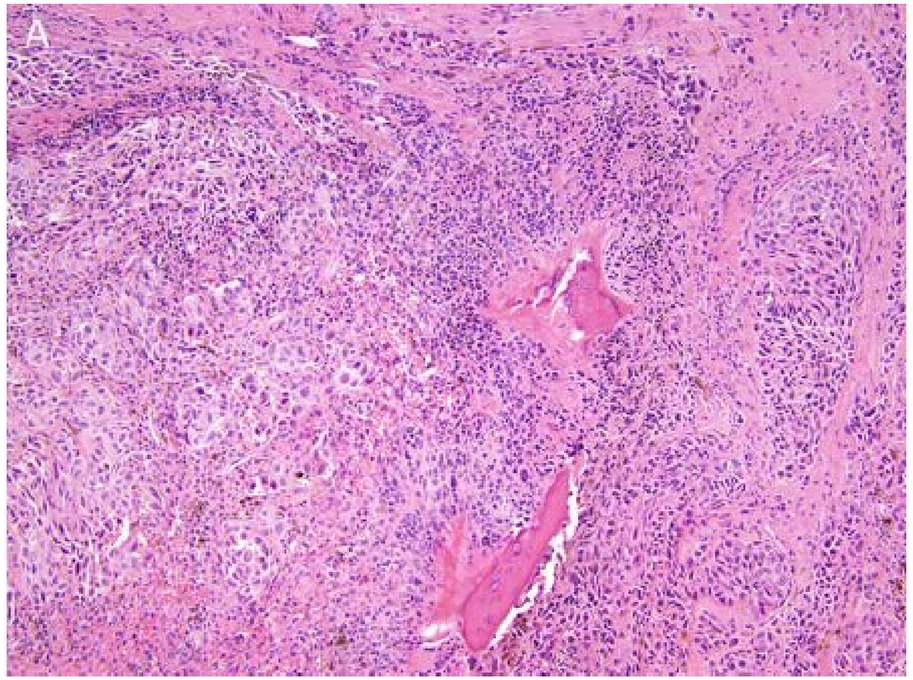


“Rippled pattern”

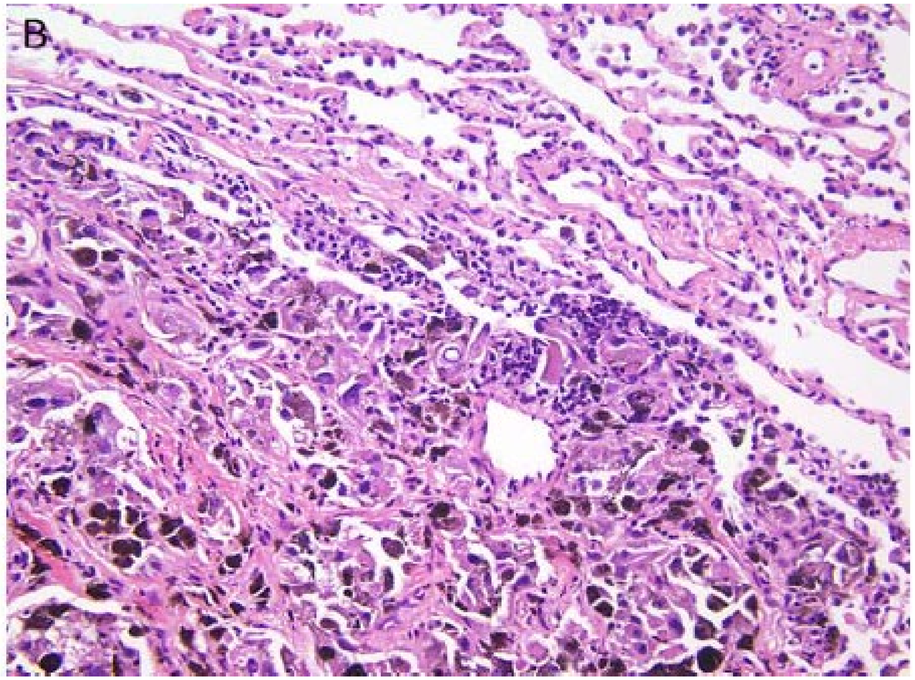


Am J Surg Pathol • Volume 38, Number 1, January 2014

Bone Invasion



Pulmonary Metastasis



Am J Surg Pathol • Volume 38, Number 1, January 2014

Malignant Melanotic Schwannian Tumor

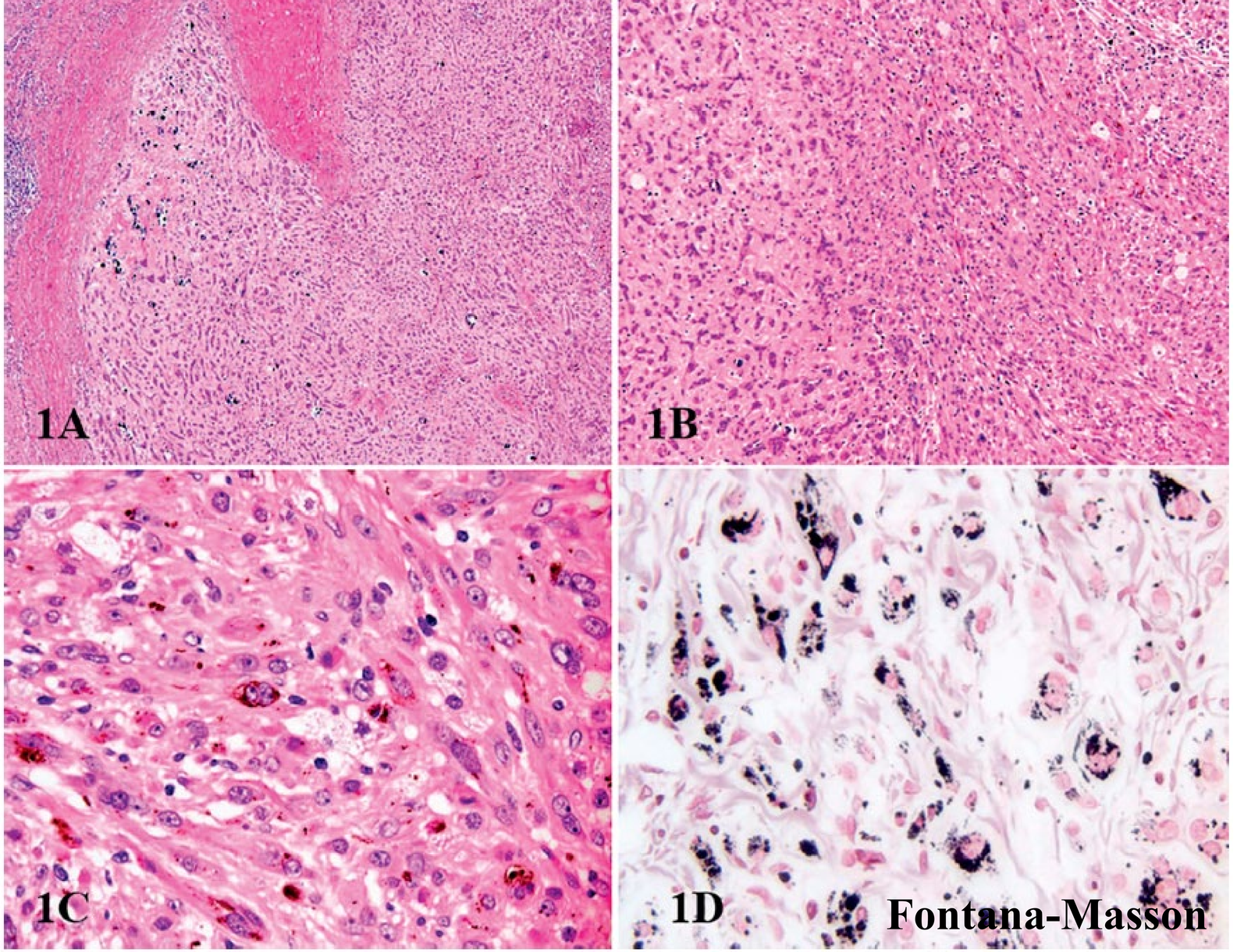
A Clinicopathologic, Immunohistochemical, and Gene Expression Profiling Study of 40 Cases, With a Proposal for the Reclassification of "Melanotic Schwannoma"

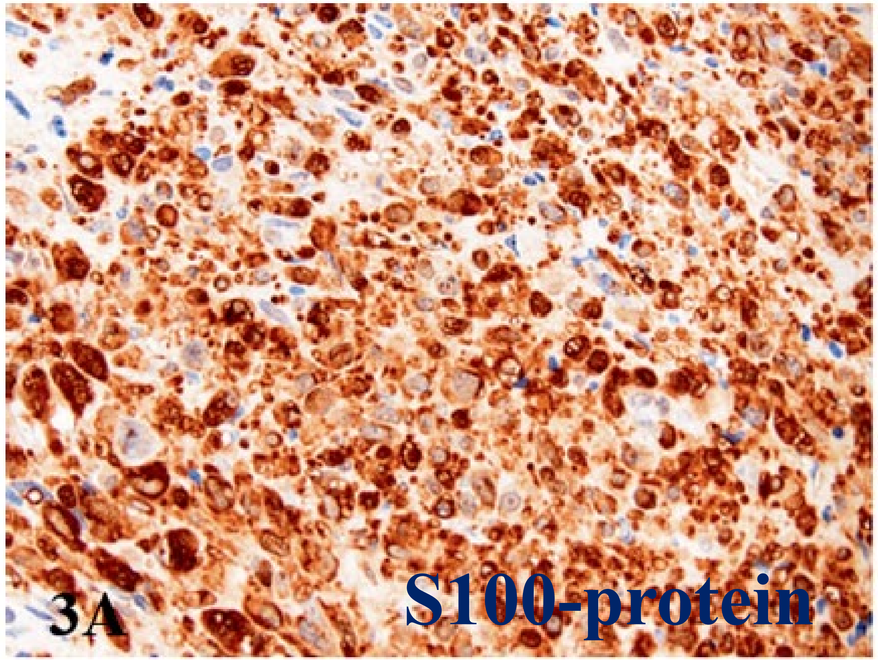
Jorge Torres-Mora, MD, Sarah Dry, MD,† Xinmin Li, PhD,† Scott Binder, MD,† Mitual Amin, MD,‡ and Andrew L. Folpe, MD**

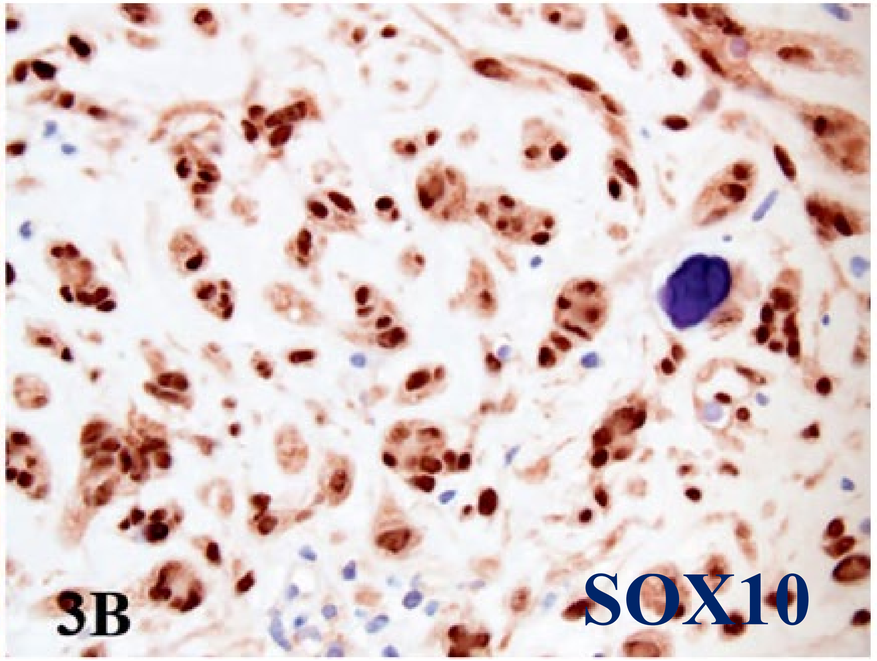
(*Am J Surg Pathol* 2014;38:94–105)

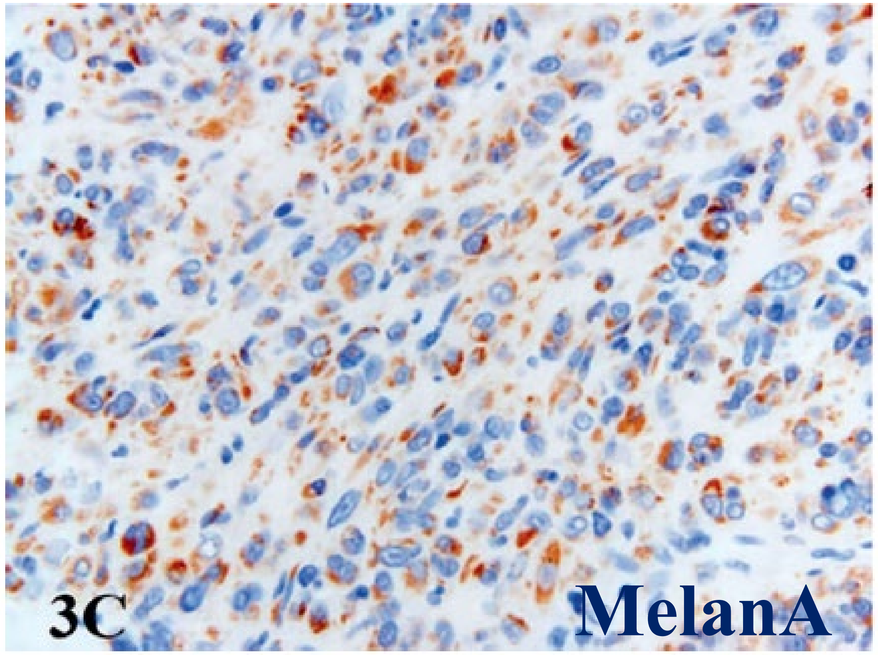
TABLE 3. IHC Results

Antibody	S100 (%)	Melan-A (%)	HMB45 (%)	Tyrosinase (%)	EMA (%)	SMARCB1 (%)	GFAP (%)	Ki-67 < 5 (%)	Ki-67 > 5 (%)	PRKAR1A Loss (%)	ASMTL (%)
MS	21/25 (84)	23/25 (92)	25/25 (100)	25/25 (100)	0/9 (0)	25/25 (100)	0/24 (0)	23/25 (92)	2/25 (8)	7/21 (35)	5/19 (26)

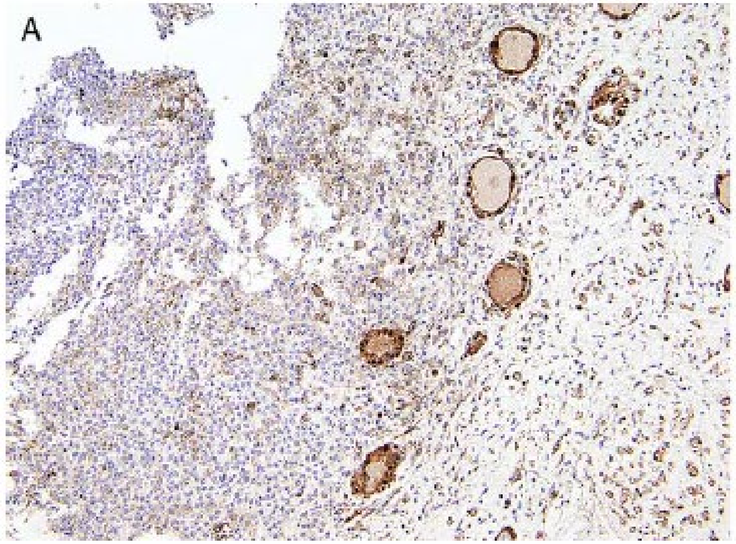

1A
1B
1C
1D
Fontana-Masson


3A
S100-protein

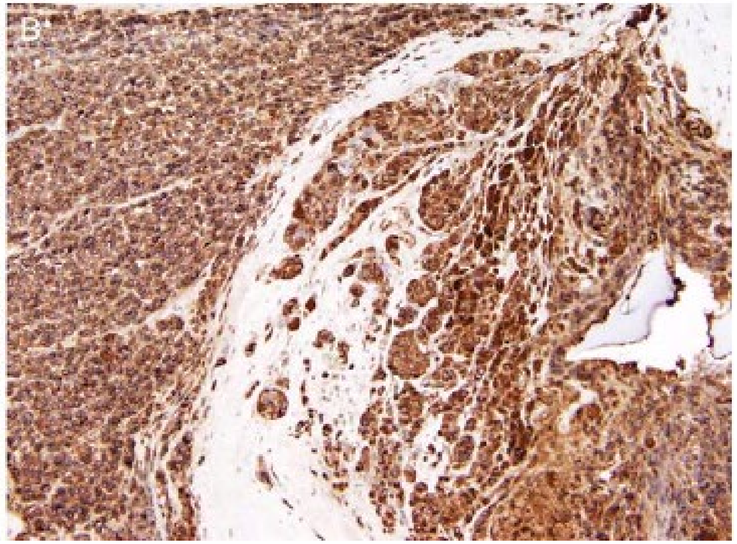

3B
SOX10


3C
MelanA

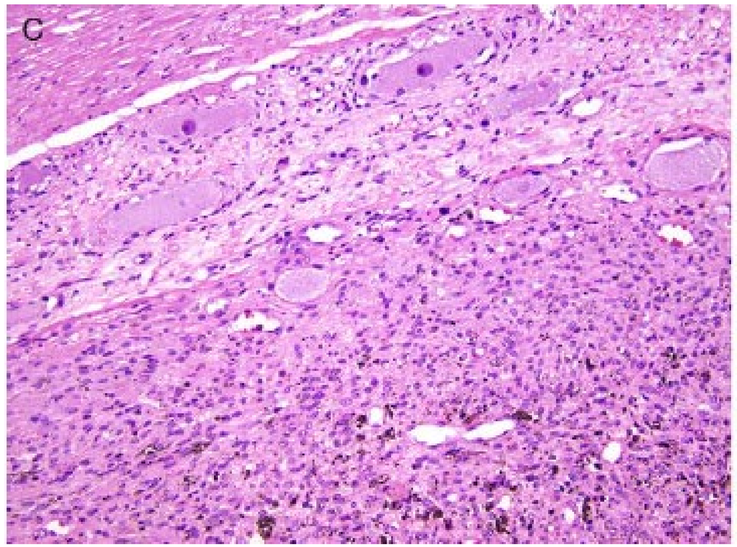
S100-protein



HMB45



Loss of PRKAR1A



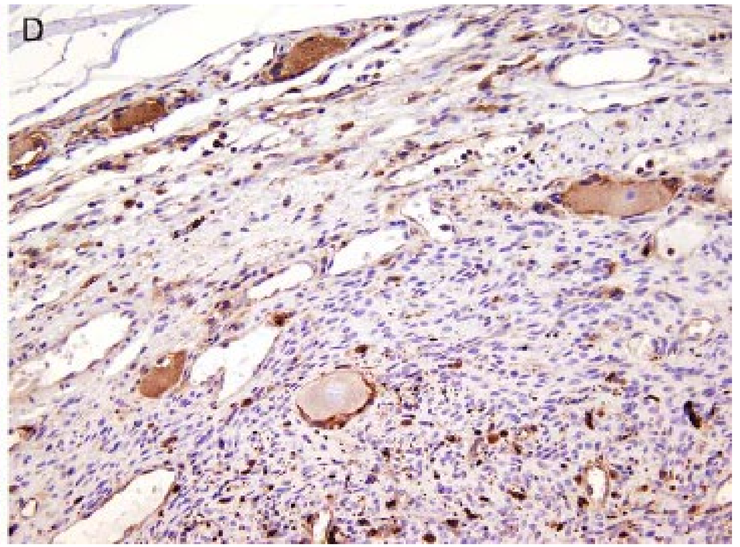
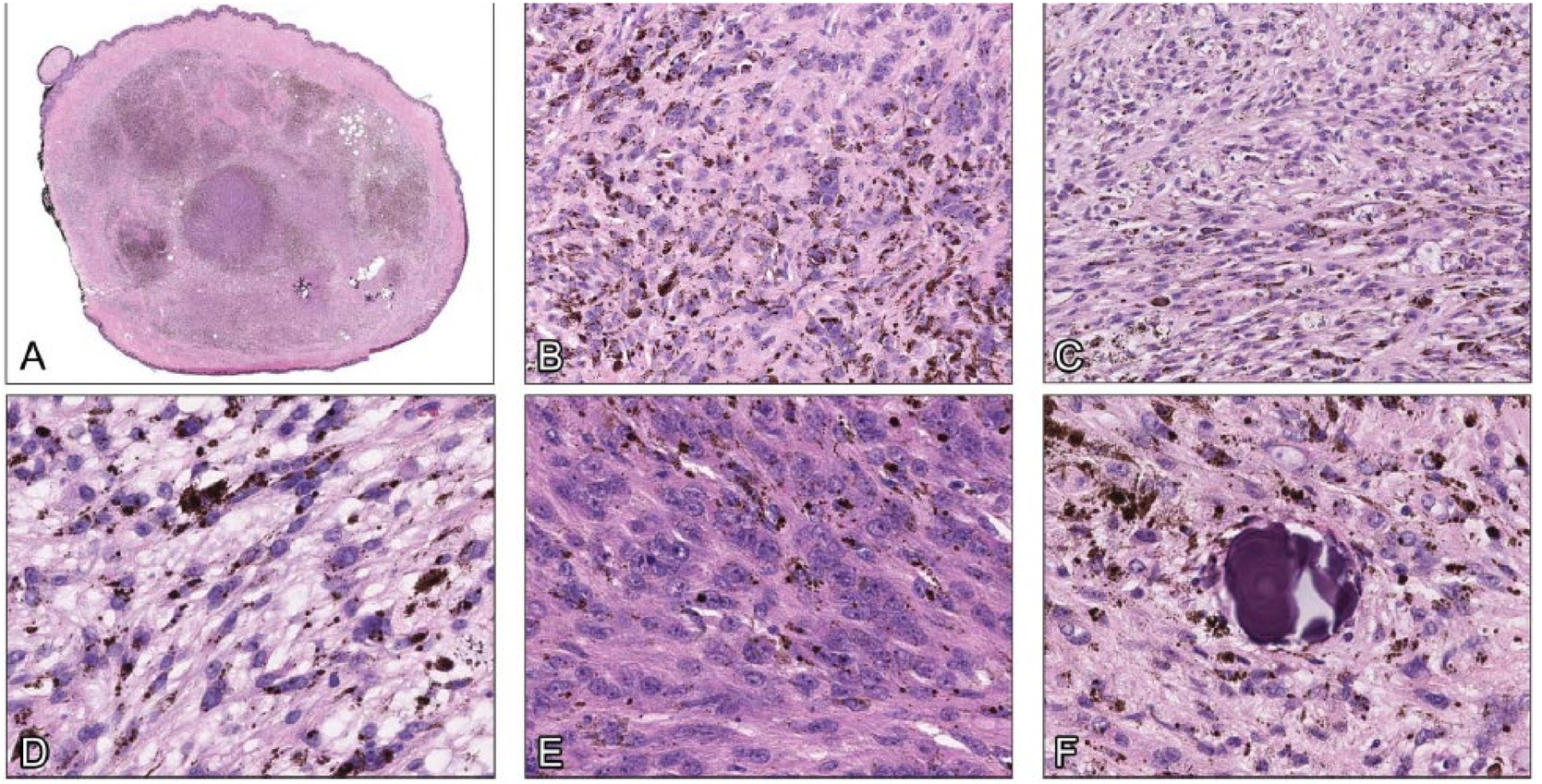


TABLE 2. Correlation of Pathologic Features With Metastases

Pathologic Feature	Metastases	*P* (Fisher Exact Test)
Mitotic activity > 1/10 HPF		
Present	5/5	0.008
Absent	6/20	
Necrosis		
Present	3/7	1 (NS)
Absent	8/18	
Macronucleoli		
Present	5/11	1 (NS)
Absent	6/14	
Small cell change		
Present	2/3	0.56 (NS)
Absent	9/22	
Nuclear pleomorphism		
Present	4/8	1 (NS)
Absent	7/17	
Psammoma bodies		
Present	4/10	1 (NS)
Absent	7/15	

Melanotic Schwannoma of the Vulva: A Case Report and Review of the Literature

Jarish N. Cohen, MD, PhD,† Iwei Yeh, MD, PhD,*†‡§ and Philip E. LeBoit, MD*†§*



(*Am J Dermatopathol* 2019;00:1–6)

TABLE 1. Clinicopathologic Characteristics of Primary Cutaneous Melanotic Schwannomas Reported in the Literature

Age/Sex	Site	Size	Clinical Follow-up	Carney's Complex	Psammoma Bodies	IHC	EM	Genetics	Reference
53/F	L foot	20 mm	NR	NR	N	NR	Prominent basal lamina, cytoplasmic processes, melanosomes, and premelanosomes	NR	5
45/F	L shoulder	25 mm	NED, 7 yrs	NR	N	NR	Thin continuous basal lamina, blunt cytoplasmic processes, melanosomes, and premelanosomes	NR	6
11/M	R axilla	15 mm	NR	Y	Y	S100+	External lamina, elongated cytoplasmic processes, and premelanosomes	NR	7
31/F	NR	NR	NR	Y	Y	S100 + HMB-45+ vimentin+	Reduplicated basal lamina, long cytoplasmic processes, melanosomes, and premelanosomes	NR	8
45/M	L shoulder	30 mm	NED, 4 yrs	NR	Y	S100 + HMB-45+	NR	NR	9
37/M	Chest	NR	NED, 2 yrs	Y	Y	S100 + HMB-45+	NR	NR	9
34/F	L preauricular	40 mm	NED, local recurrence 3 yrs after initial resection	N	N	S100 + MelanA+	NR	NR	10
11/F	Lumbosacral	15 mm	NED, 3 yrs	N	NR	NR	NR	NR	2
44/M	Chest	NR	NR	Y	N	S100 + HMB45 + collagen IV+	NR	NR	11
34/F	R vulva	15 mm	Unavailable	N	Y	S100 + Melan-A + collagen IV + BRAF V600E- *PRKAR1A*-	NP	*PRKAR1A* p.S299fs, CNLOH distal Ch 17q	Current case

Cutaneous malignant melanotic nerve sheath tumor

- Tend to arise in the trunk (67%)
- Largely equal gender distribution
- Can be associated with Carney Complex (56%)

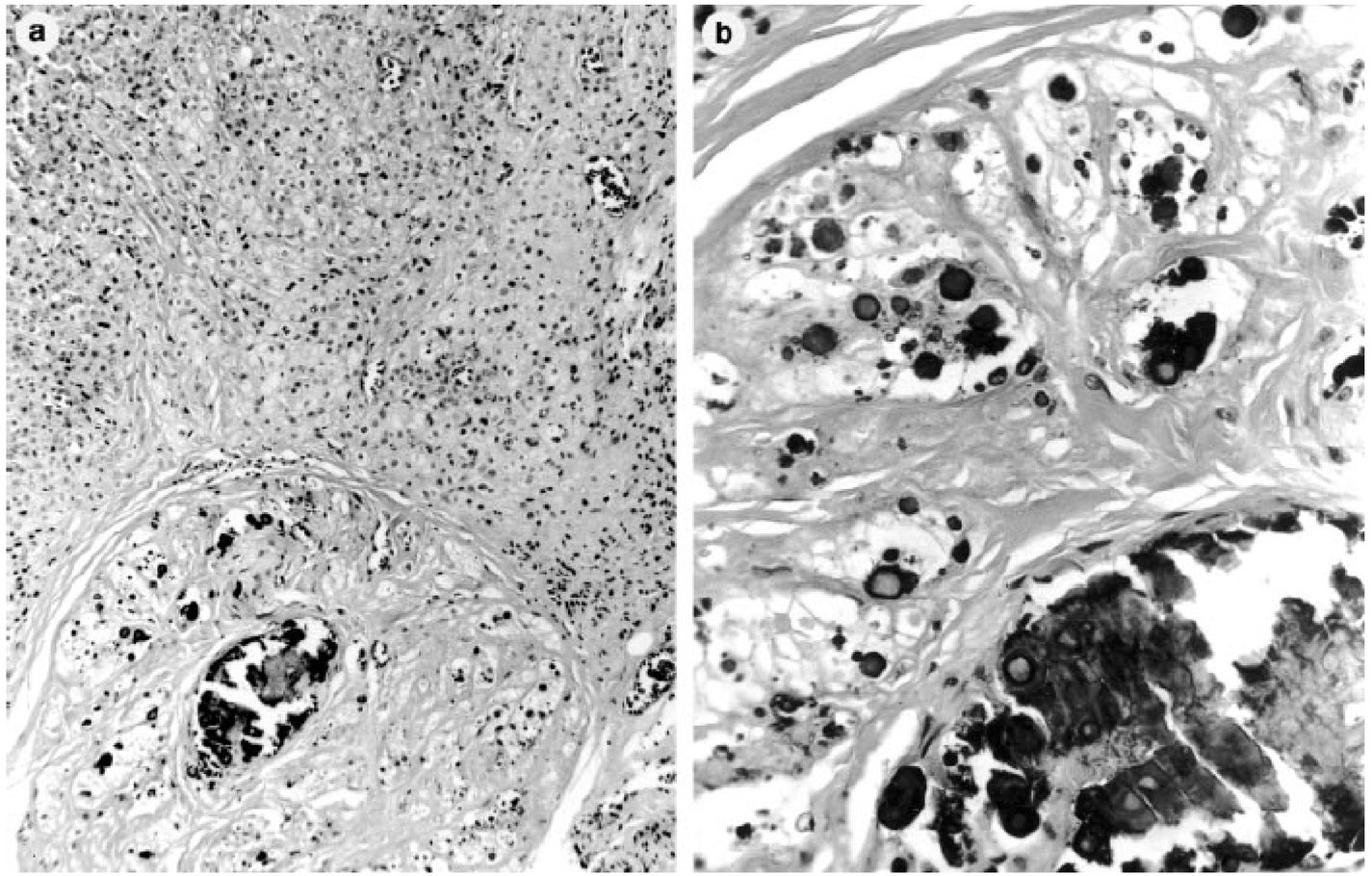
Differential Diagnosis

- Melanotic neurofibroma
- Pigmented Epithelioid Melanocytoma (PEM)
- Variants of blue nevi
- Pigmented Epithelioid Melanoma

Histopathology 2001, **39**, 493–497

Psammomatous malignant melanoma arising in an intradermal naevus

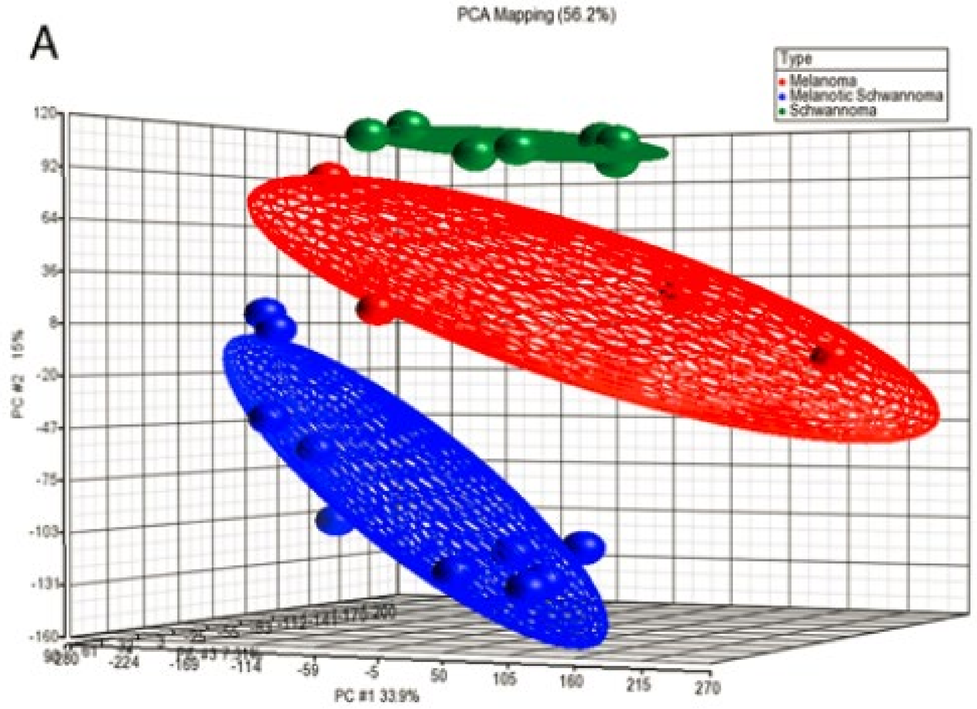
C Monteagudo, A Ferrández, M González-Devesa & A Llombart-Bosch
Department of Pathology, Hospital Clínico Universitario, University of Valencia, Valencia, Spain

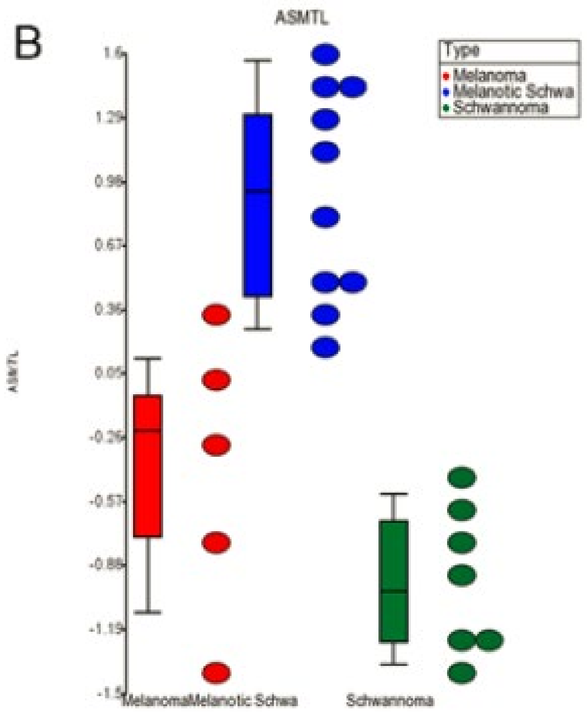


Malignant melanotic nerve sheath tumor vs Melanoma

- **No individual clinicopathologic features that are completely specific**
- Melanotic Schwannoma
  - Paravertebral, predominantly spindled, heavy melanin pigmentation, psammoma bodies, striking nuclear pleomorphism with low mitotic activity
- Detailed clinical history
- Careful dermatologic examination

Gene Expression Profiling





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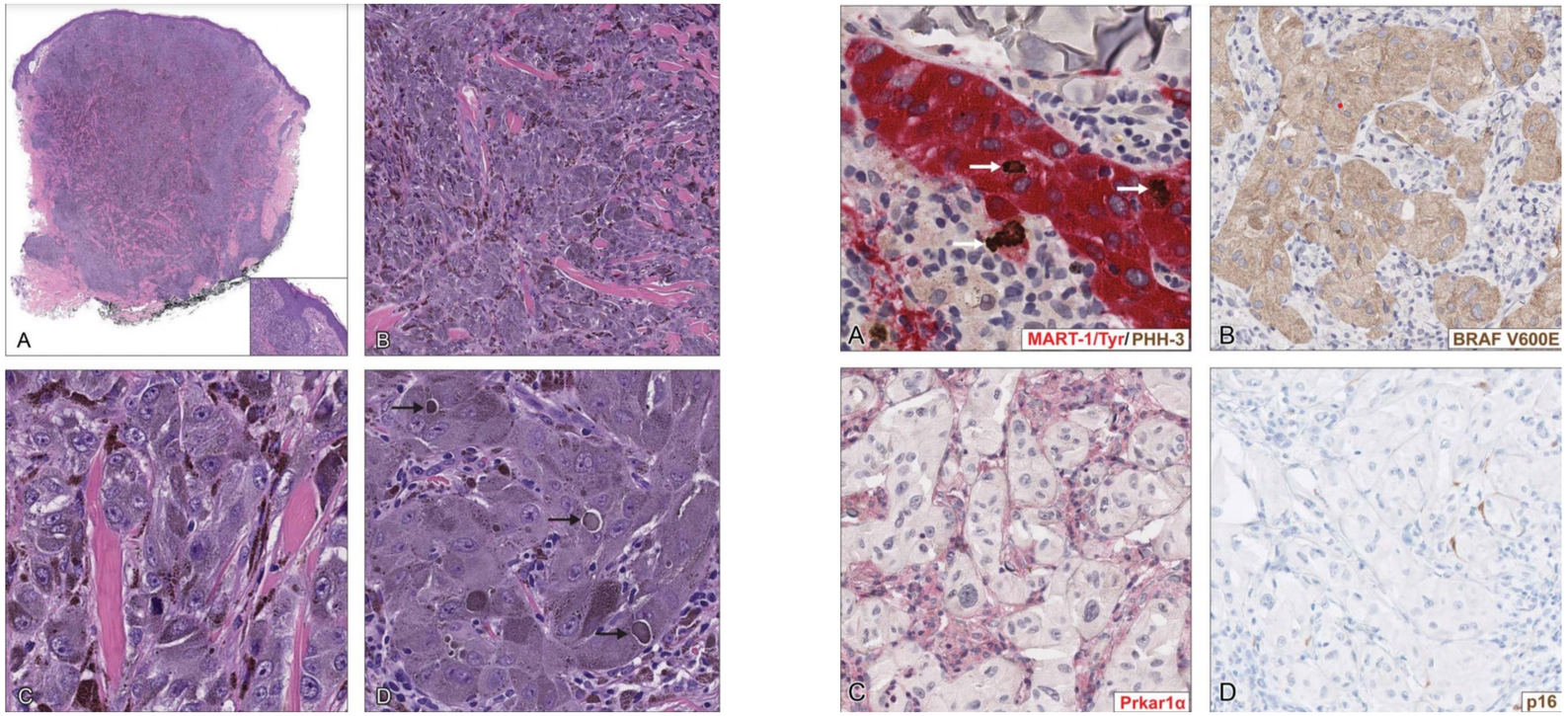
Am J Surg Pathol • Volume 38, Number 1, January 2014

Heavily Pigmented Epithelioid Melanoma With Loss of Protein Kinase A Regulatory Subunit-α Expression

Jarish N. Cohen, MD, PhD,† Jessica A. Spies, MD,‡ Fawn Ross, NP-C,§ Angela Bohlke, MD,§ and Timothy H. McCalmont, MD*†*



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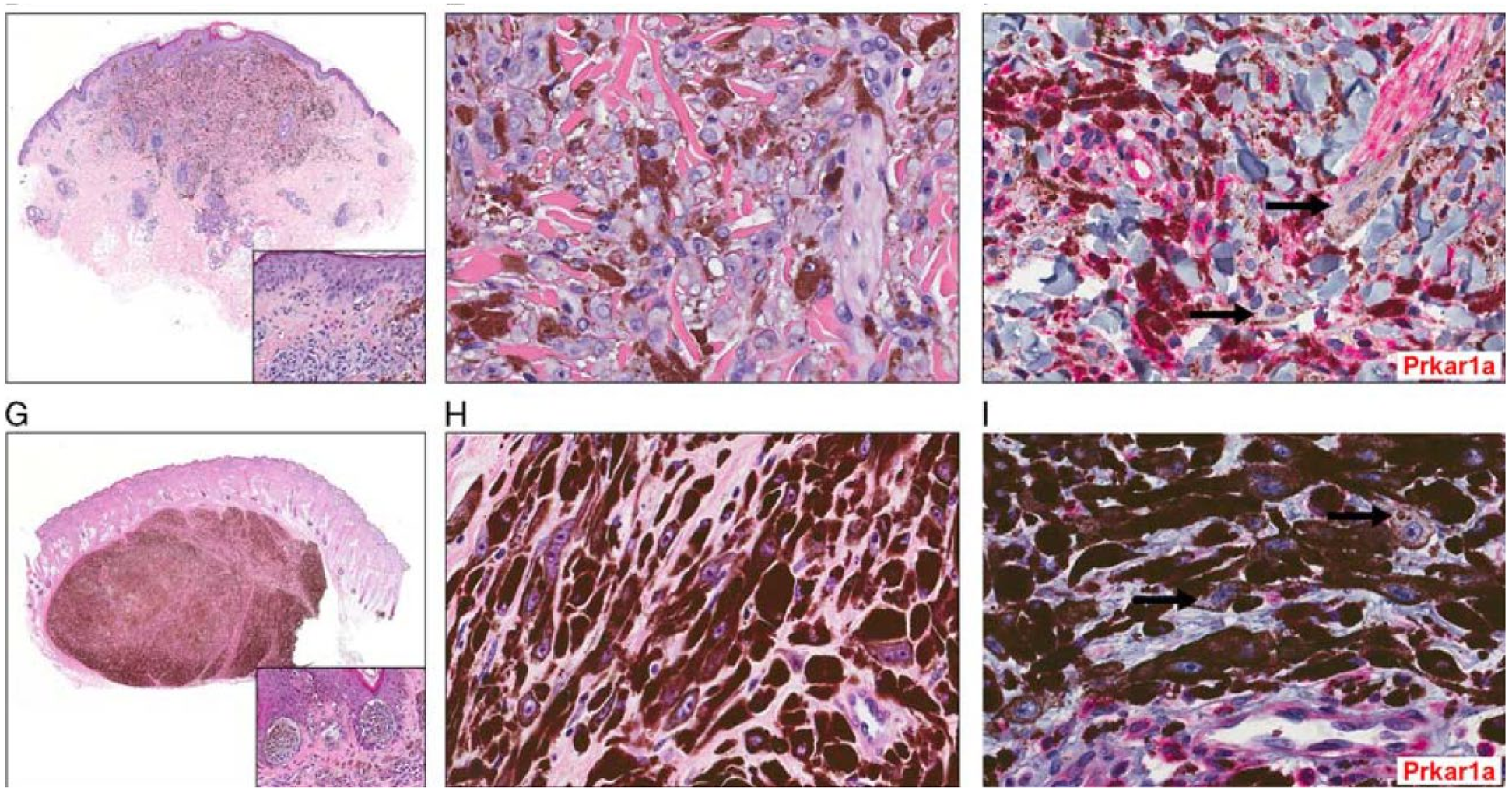
(*Am J Dermatopathol* 2018;40:912–916)



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(*Am J Surg Pathol* 2017;41:1333–1346)

Attempting to Solve the Pigmented Epithelioid Melanocytoma (PEM) Conundrum

PRKAR1A Inactivation Can Occur in Different Genetic Backgrounds (Common, Blue, and Spitz Subgroups) With Variation in Their Clinicopathologic Characteristics

Arnaud de la Fouchardiere, MD, PhD,† Franck Tirode, PhD,*† Christine Castillo, MD,‡ Adrien Buisson, PharmD,† Felix Boivin, MSc,* Nicolas Macagno, MD, PhD,†§ and Daniel Pissaloux, PhD*†*

	All Cases	Common Group	Blue Group	Spitz Group	*PRKCA*-fused Group
N	21	9	5	6	1
Genetic data					
BRAF mutation	9/21	9/9	—	—	—
CYSLTR2 mutation	4/21	—	4/5	—	—
GNAQ mutation	1/21	—	1/5	—	—
MAP3K8 fusion	2/21	—	—	2/6	—
MAP3K3 fusion	1/21	—	—	1/6	—
RET fusion	1/21	—	—	1/6	—
HRAS G13R mutation	1/21	—	—	1/6	—
MAP2K1 mutation	1/21	—	—	1/6	—
PRKCA fusion	1/21	—	—	—	1/1

Perivascular Epithelioid Cell Tumor (PEComa)

- Mesenchymal tumor composed of perivascular epithelioid cells (PEC)
  - Distinctive neoplastic cell **with no known normal counterpart**
- Unique as it **shows immunoreactivity for both melanocytic and smooth muscle markers**

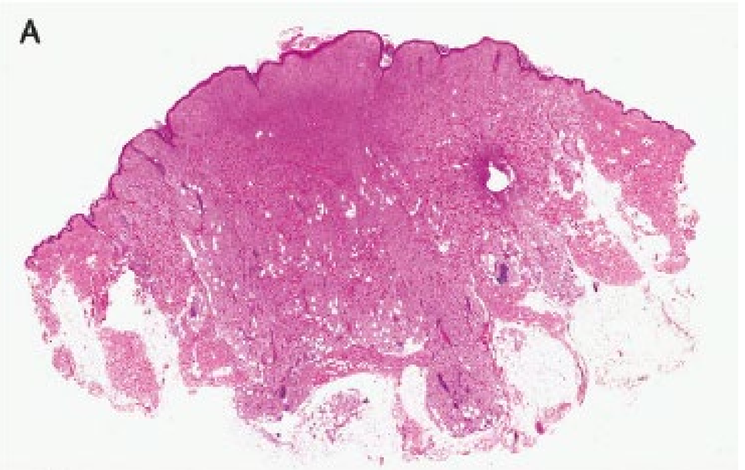
Group of mesenchymal neoplasms

- Angiomyolipoma
- Clear cell “sugar” tumor of the lung and extrapulmonary sites
- Lymphangioleiomyomatosis
- Clear cell myomelanocytic tumor of the falciform ligament/ligamentum teres

Primary Cutaneous PEComa: Distinctive Clear Cell Lesions of Skin

Bernadette Liegl, MD,† Jason L. Hornick, MD, PhD,* and Christopher D. M. Fletcher, MD, FRCPath**

(*Am J Surg Pathol* 2008;32:608–614)



Case	Age (y)/Sex	Site (Depth)	Size (cm)	Duration Before Excision	Margin Status	Status (Last Follow-up)
1	78/M	Forearm (d)	0.7	NA	Positive	NA
2	34/F	Shin (d, sc)	2	NA	Positive	NA
3	50/F	Back (d, sc)	2	1-2 mo	Marginal	ANED, 61 mo (no known recurrence)
4	53/F	Buttock (d, sc)	1	12 mo	Wide (after reexcision and sentinal lymph node biopsy)	ANED, 37 mo
5	15/F	Buttock (d, sc)	1.2	24 mo	Wide (after reexcision)	ANED, 36 mo
6	60/F	Thigh (d, sc)	1.5	6 mo	Wide (after reexcision)	ANED, 36 mo
7	81/F	Calf (d, sc)	1.5	NA	Wide (after reexcision)	Lost in follow-up
8	44/M	Leg (d, sc)	1.3	Several months	Positive	ANED, 108 mo
9	52/F	Lower spine (d, sc)	1.5	Not known	Marginal	ANED, 3 mo
10	49/F	Leg (d, sc)	2	2 mo	Wide (after reexcision)	Recent case

Primary cutaneous perivascular epithelioid cell tumor (PEComa): Five new cases and review of the literature

Lauren N. Stuart[1] | Russell G. Tipton[2] | Michael R. DeWall[3] | Douglas C. Parker[4,5] | Christina D. Stelton[6] | Annie O. Morrison[7] | Landon W. Coleman[8] | Scott W. Fosko[9] | Claudia I. Vidal[2,10] | Maria Yadira Hurley[2,10] | Amy H. Deeken[11] | Jerad M. Gardner[3]

J Cutan Pathol. 2017;44:713–721.

Case	Gender/age	Location	Size (cm)	Clinical impression	Follow-up (mo)	Actin	Desmin	Melan-A/ MART-1	HMB-45	S100 protein	SOX-10	CD10	TFE3
1	F/67	Thigh	1.2	Lipoma	NED; 31	N/A	N/A	Focally +	+	–	N/A	+	–
2	F/43	Thigh	0.6	DF, DFSP	NED; 16	–	–	–	+	–	–	N/A	–
3	F/59	Thigh	0.3	Cyst	Lost	–	–	Focally +	Focally +	–	N/A	N/A	N/A
4	M/72	Distal Leg	1.2	Amelanotic melanoma, NMSC, Sarcoma, Cyst	NED; 15	–	–	–	+	N/A	–	+	N/A
5	F/35	Thigh	4	Cyst	NED; 6	Patchy +	Patchy +	–	Patchy	–	–	+	N/A

Histologic Features

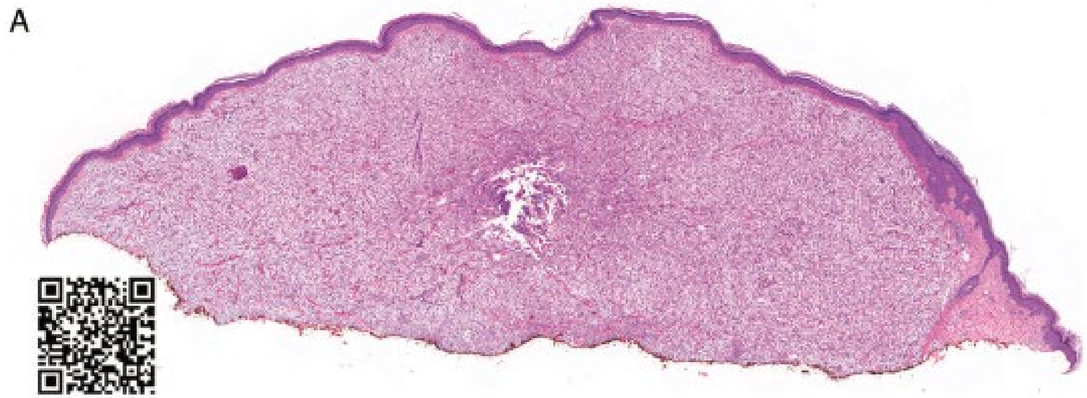
- Ill-defined dermal proliferation of epithelioid cells
- Arrangement in **nests and trabeculae** within an arborizing network of delicate capillaries
- Uniform round to ovoid vesicular nuclei
- **Pink clear or granular cytoplasm**
- Nuclei usually bland
- Low-mitotic activity
- Occasional multinucleated giant cells

Immunohistochemistry

- **Distinct immunophenotype**
  - **Melanocytic**
    - HMB45, MiTF, Melan-A, tyrosinase
  - **Smooth muscle**
    - Desmin, SMA, calponin

- HMB45 the most sensitive

- Primary cutaneous less likely to demonstrate immunoreactivity for smooth muscle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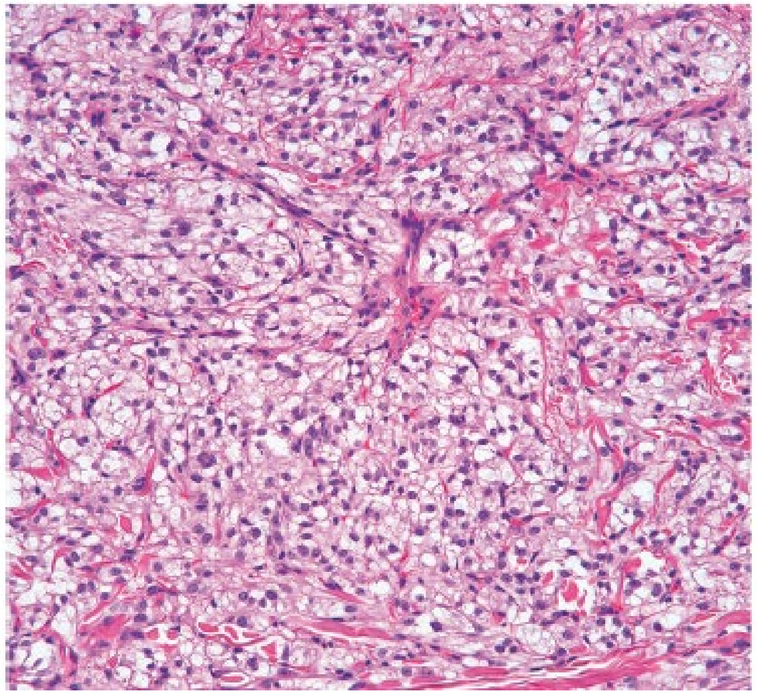
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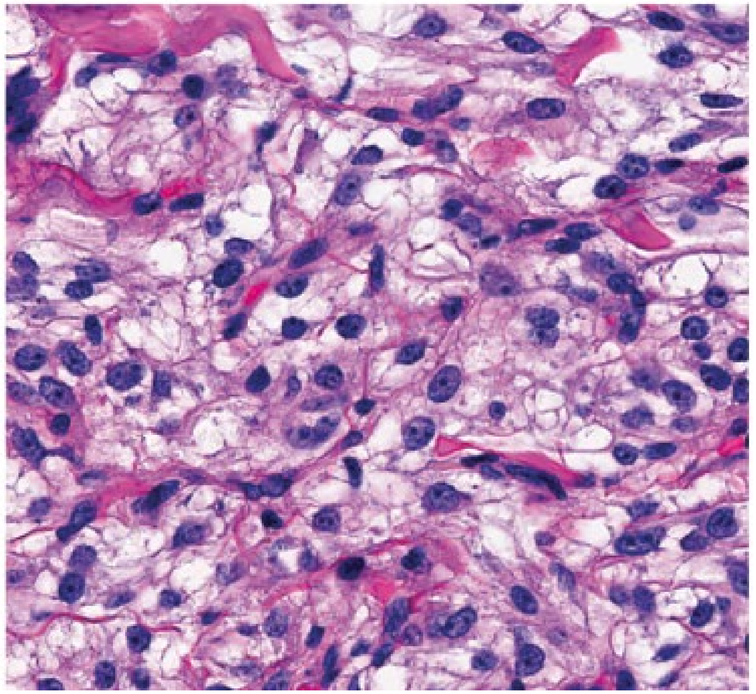
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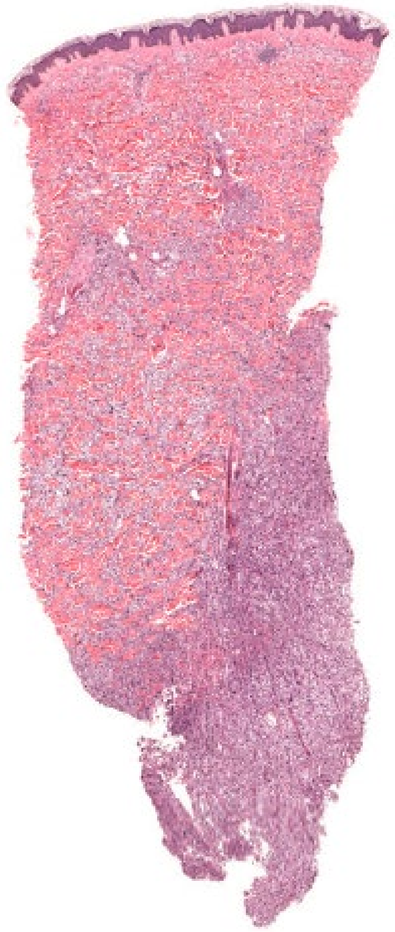
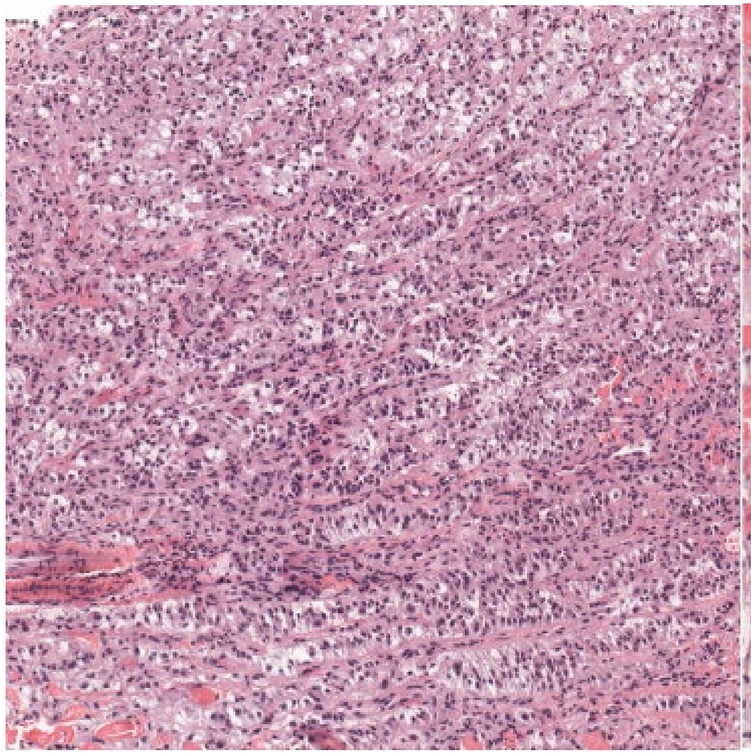
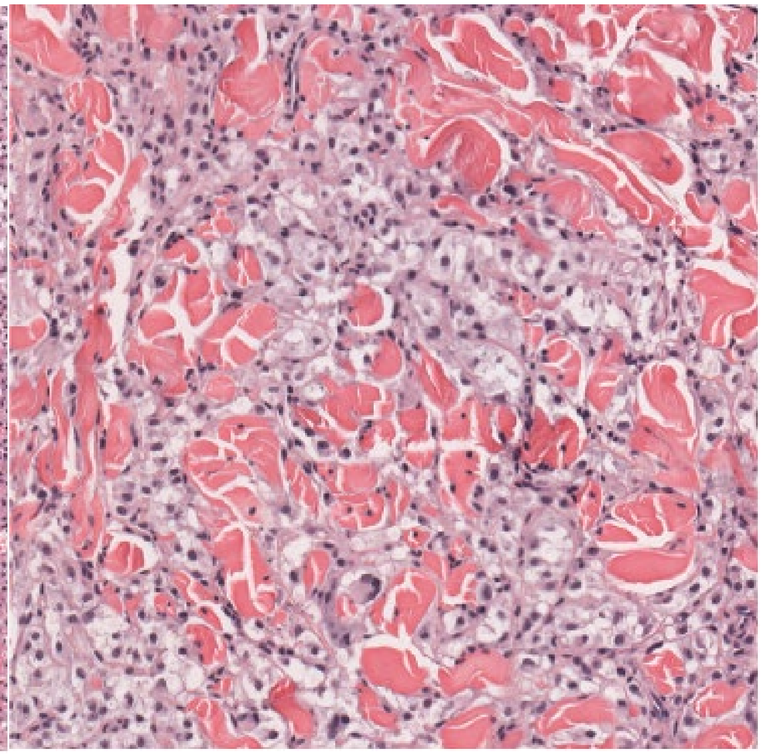


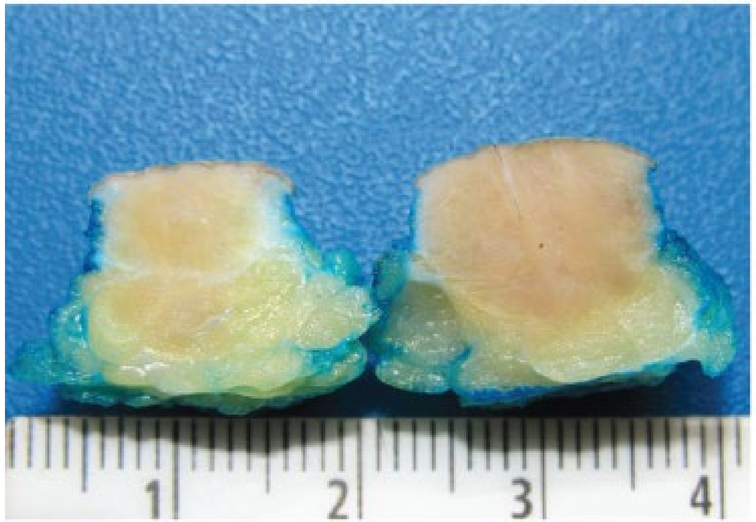


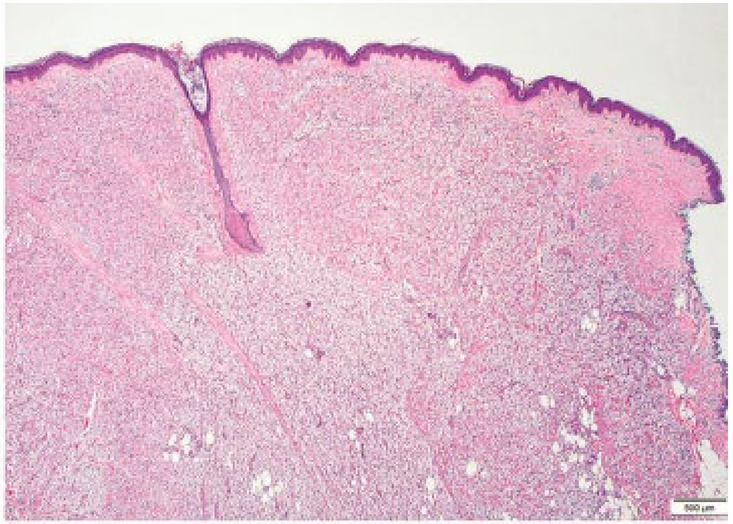


Memorial Sloan Kettering Cancer Center

1884

J Cutan Pathol. 2017;44:713–721.





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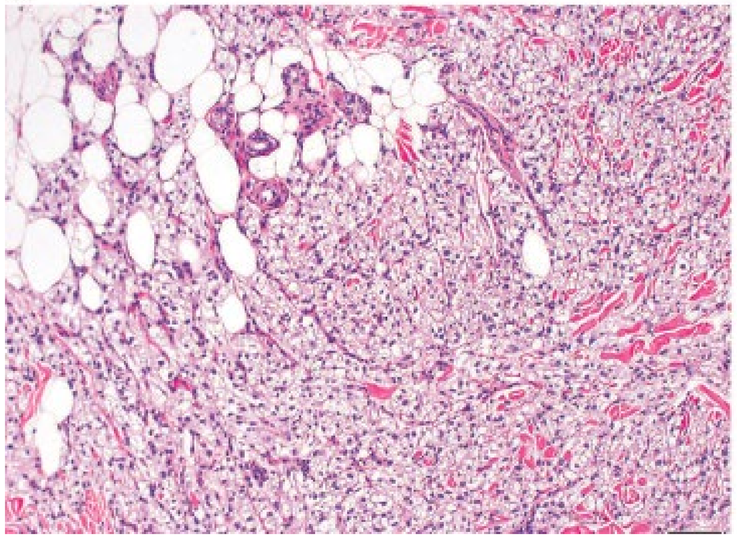

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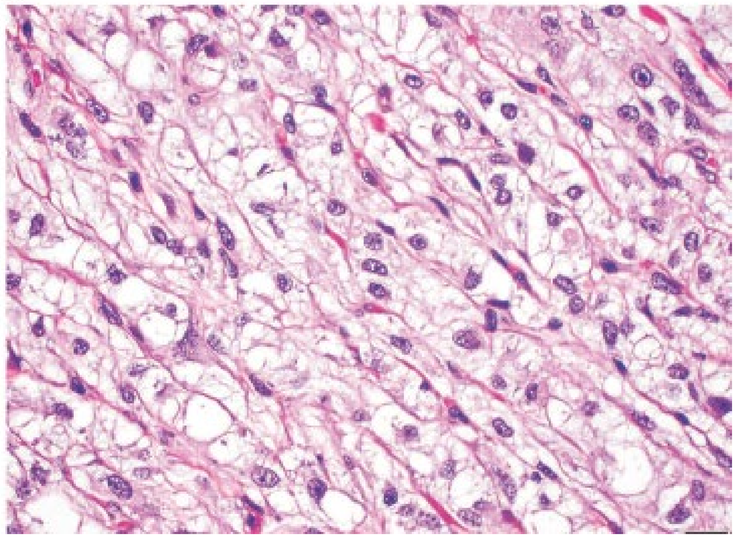
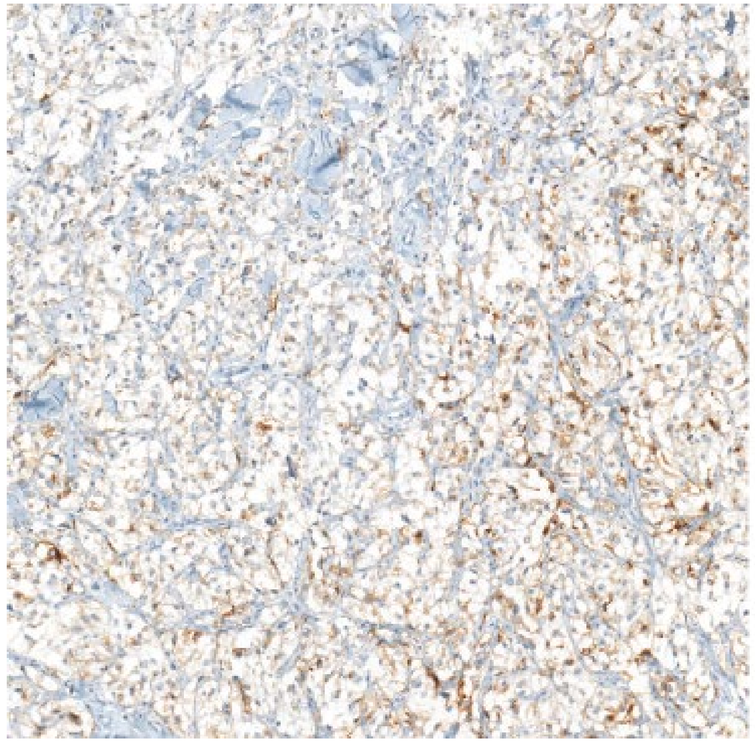
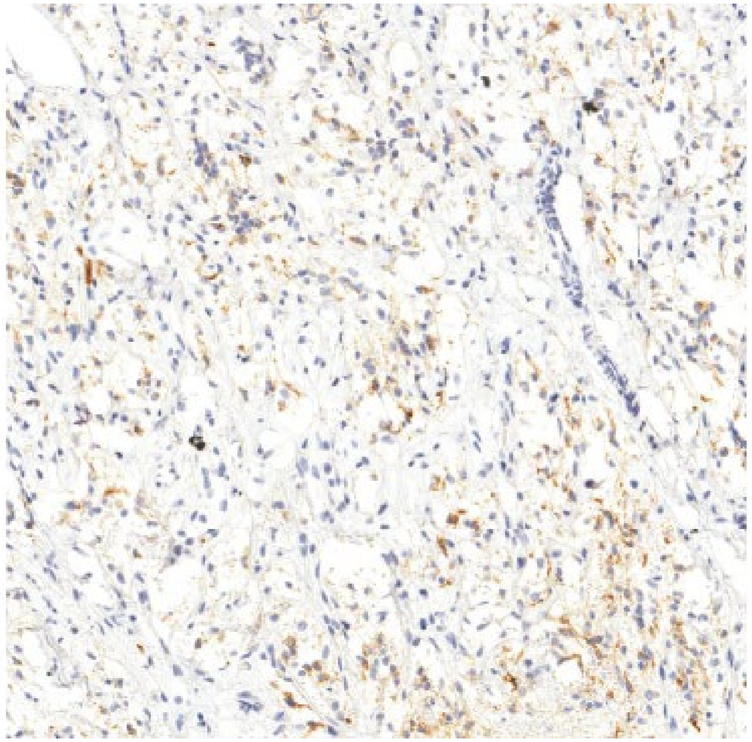


J Cutan Pathol. 2017;44:713–721.

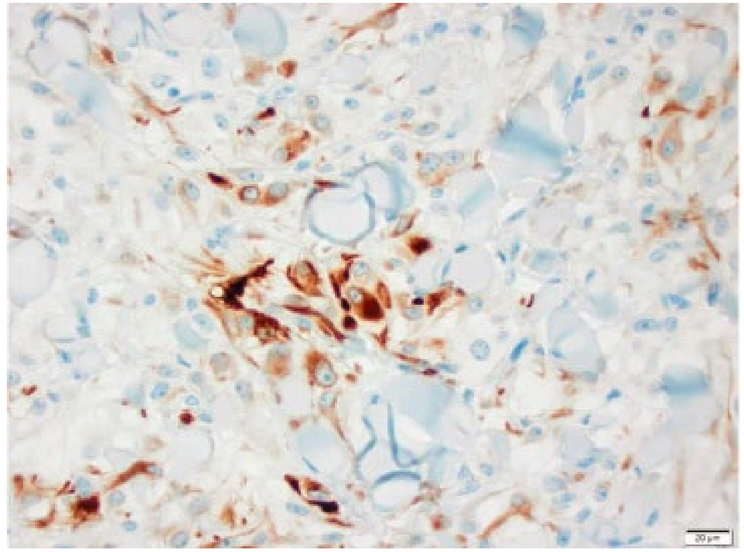
HMB45



MelanA



Desmin



J Cutan Pathol. 2017;44:713–721.

Primary cutaneous perivascular epithelioid cell tumor: A clinicopathological and molecular reappraisal

Yann Charli-Joseph, MD,[a,b] Andrea Saggini, MD,[a,b] Swapna Vemula, MS,[a]
Jingly Weier, PhD,[a] Sonia Mirza, MBBS,[a] and Philip E. LeBoit, MD[a,b,c]
San Francisco, California

J Am Acad Dermatol
December 2014

Table III. Detailed immunohistochemical findings in the current study

Case	1	2	3	4	5	6	7	8
S100	Faint	+	+	Faint	-	Faint	+	+
S100-D	-	Faint	Faint	ND	ND	ND	-	Faint
MiTF	+	+	+	+	+	+	+	+
Melan-A	-	-	-	-	-	-	-	-
HMB-45	Focal +	Focal +	-	Focal +	Focal +	Focal +	Focal +	Focal +
SOX10	-	-	-	-	-	-	ND	-
SMA	Focal +	Focal +	Focal +	Focal +	Focal +	Focal +	-	Focal +
MSA	-	-	-	ND	ND	ND	Focal +	Focal +
Desmin	-	+	-	-	-	-	-	-
Calponin	-	-	-	ND	ND	ND	Faint	-
Keratin cocktail	-	-	-	-	ND	ND	-	-
NKIC3	+	+	+	+	+	+	+	+
CD68	+	Faint	+	Faint	ND	+	+	Faint
CD56	-	-	-	ND	ND	ND	-	-
BCL-1	+	+	Focal +	+	+	+	+	+
p16	-	Few cells +	Few cells +	ND	ND	ND	-	Few cells +
4EBP1	+	+	+	+	+	-	+	+
CatK	+	+	+	+	+	+	+	+
E-cadherin	Focal +	+	+	+	+	+	+	+
c-Myc	-	-	-	Few cells +	Few cells +	-	-	Few cells +
Ki67	~30%	<5%	<5%	<5%	<5%	<5%	<5%	<5%

Table IV. Immunohistochemical staining pattern in primary cutaneous perivascular epithelioid cell tumors

		S100	HMB-45	Melan-A	MiTF	SOX10	NKIC3	SMA	MSA	Desmin	Calponin	Caldesmon	CK	CD68
Crowson et al[12]	2003	0/1	1/1	ND/NR	ND/NR	ND/NR	ND/NR	1/1	ND/NR	0/1	ND/NR	ND/NR	0/1	ND/NR
de Saint Aubain Somerhausen et al[13]	2005	0/1	1/1	ND/NR	ND/NR	ND/NR	ND/NR	1/1	ND/NR	1/1	ND/NR	0/1	0/1	ND/NR
Mentzel et al[2]	2005	0/7	7/7	1/7	7/7	ND/NR	6/6	1/7	0/6	1/6	2/4	ND/NR	0/7	5/7
Tan et al[14]	2007	0/2	2/2	2/2	ND/NR	ND/NR	ND/NR	1/2	ND/NR	0/2	ND/NR	ND/NR	0/2	2/2
Liegl et al[15]	2008	1/10	10/10	5/7	5/5	ND/NR	ND/NR	1/10	ND/NR	5/10	0/10	0/10	0/10	2/10
Calder et al[16]	2008	0/1	1/1	1/1	ND/NR	ND/NR	ND/NR	1/1	ND/NR	ND/NR	ND/NR	ND/NR	0/1	ND/NR
Ghazali et al[17]	2010	ND/NR	0/1	1/1	1/1	ND/NR	ND/NR	1/1	ND/NR	1/1	ND/NR	1/1	0/1	ND/NR
Chaplin et al[18]	2010	0/1	1/1	ND/NR	1/1	ND/NR	ND/NR	0/1	0/1	1/1	ND/NR	ND/NR	0/1	ND/NR
Llamas-Velasco et al[19]	2013	ND/NR	ND/NR	ND/NR	ND/NR	0/5	ND/NR	ND/NR	ND/NR	ND/NR	ND/NR	ND/NR	ND/NR	ND/NR
Ieremia and Robson[20]	2013	0/1	1/1	0/1	1/1	ND/NR	ND/NR	0/1	ND/NR	0/1	0/1	0/1	0/1	0/1
Current study	2014	3/8	7/8	0/7	8/8	0/7	8/8	7/8	2/5	1/8	1/5	ND	0/6	7/8
Total cases assessed		33	33	26	23	12	14	33	12	33	20	13	31	28
Positive cases, %		12	94	35	100	0	100	42	17	30	15	8	0	57

J Am Acad Dermatol
December 2014

HMB45- 94%

MelanA- 35%

NKI/C3- 100%

MiTF- 100%

MSA-17%

SMA-42%

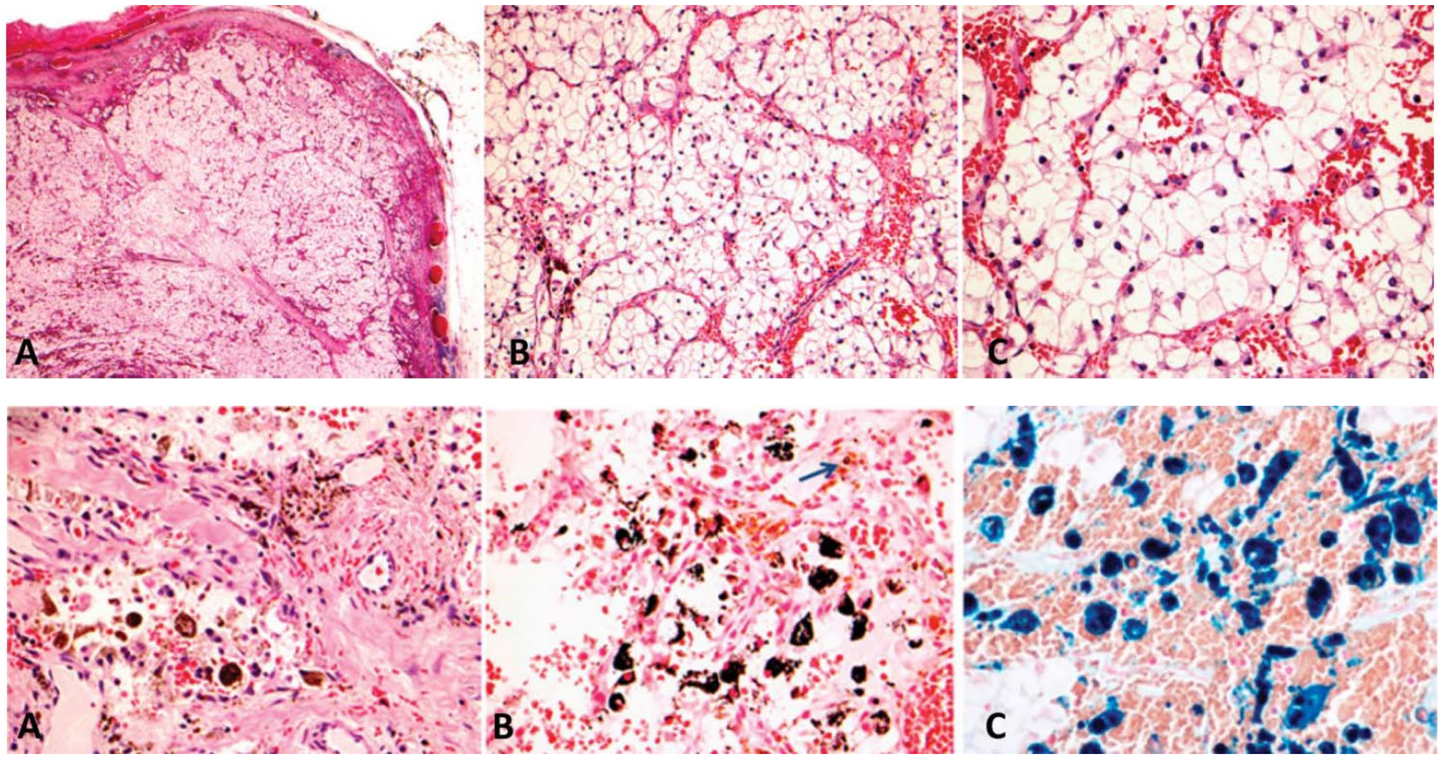
Desmin-30%

Calponin-15%

Caldesmon-8%

Pigmented Perivascular Epithelioid Cell Tumor of the Skin: First Case Report

Pooja Navale, MD, Masoud Asgari, MD,† and Sheng Chen, MD, PhD*‡*



Fontana-Masson **Perl's Stain**

(*Am J Dermatopathol* 2015;37:866–869)

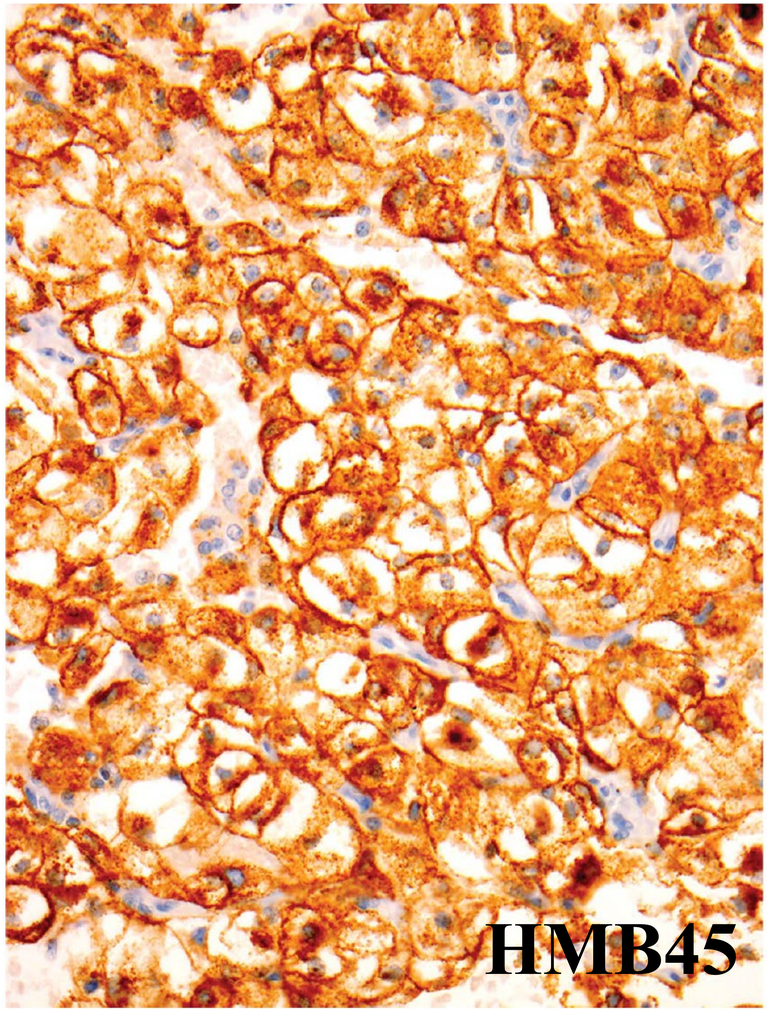


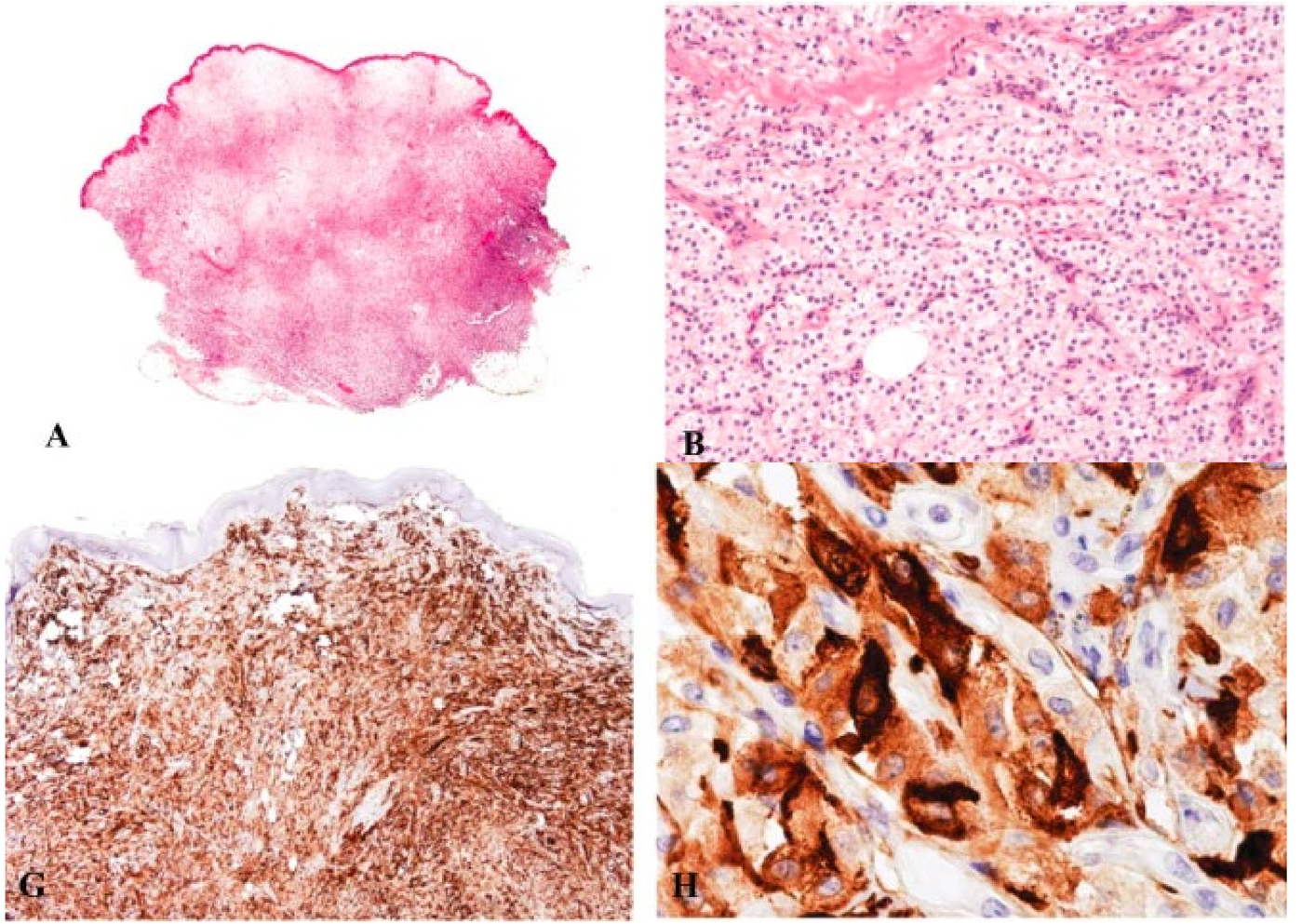
TABLE 1. Immunoprofile of pigmented PEComa

Positive	Negative
HMB-45 (diffuse)	S100, Melan-A, CD31, CD34, PAX8, CD10, Vimentin, HMWCK, Cam 5.2, EMA, Hepar, Calcitonin, Synaptophysin, Thyroglubulin, TTF-1, Inhibin, SMA

Cutaneous PEComas Express CD10: Implications for the Classification of PEComas and the Differential Diagnosis With Metastatic Renal Cell Carcinoma

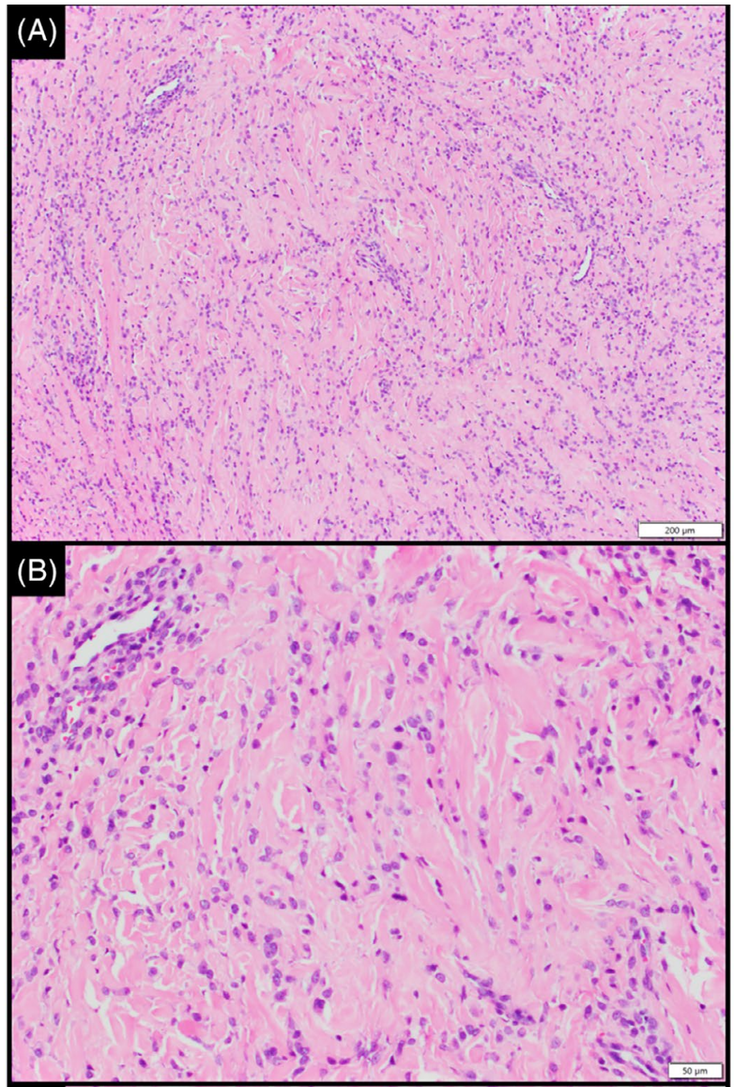
Angel Fernandez-Flores, MD, PhD, Catherine M. Nguyen, BS,† and David S. Cassarino, MD‡*

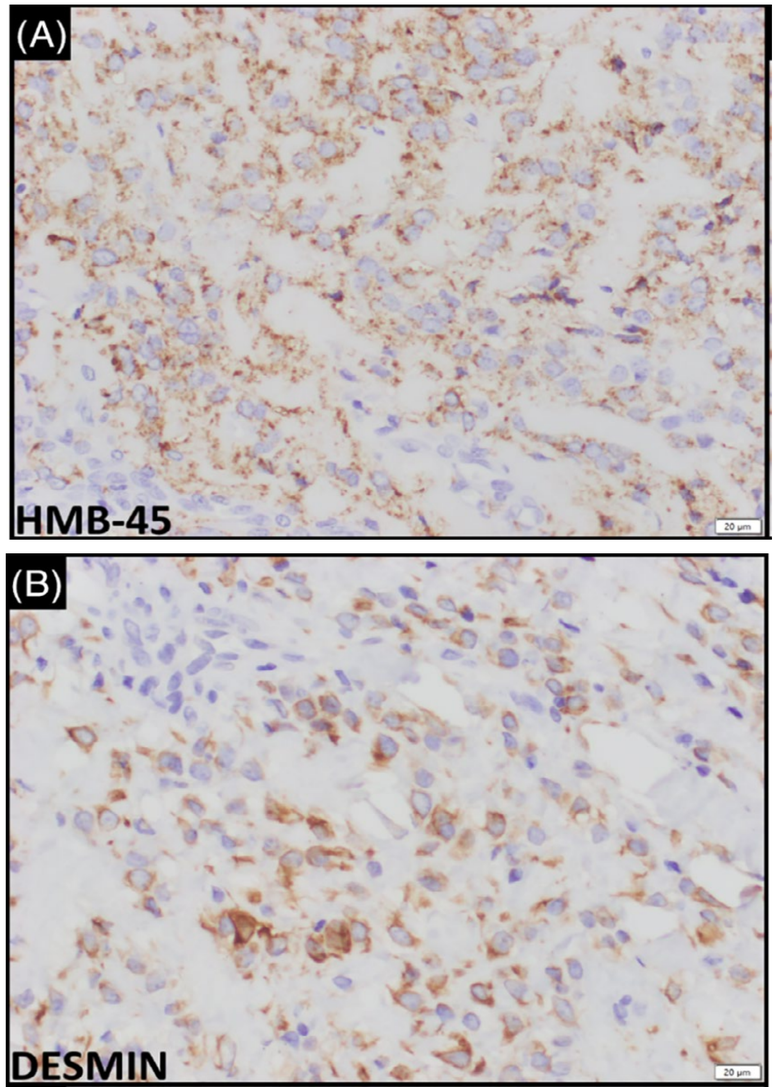
(*Am J Dermatopathol* 2016;38:645–652)



Cutaneous “fibroma-like” perivascular epithelioid cell tumor: A case report and review of literature

Eugene I. G. Odoño[1] | Kong-Bing Tan[2] | Sok Yan Tay[3] | Victor Kwan Min Lee[2]





J Cutan Pathol. 2020;47:548–553.

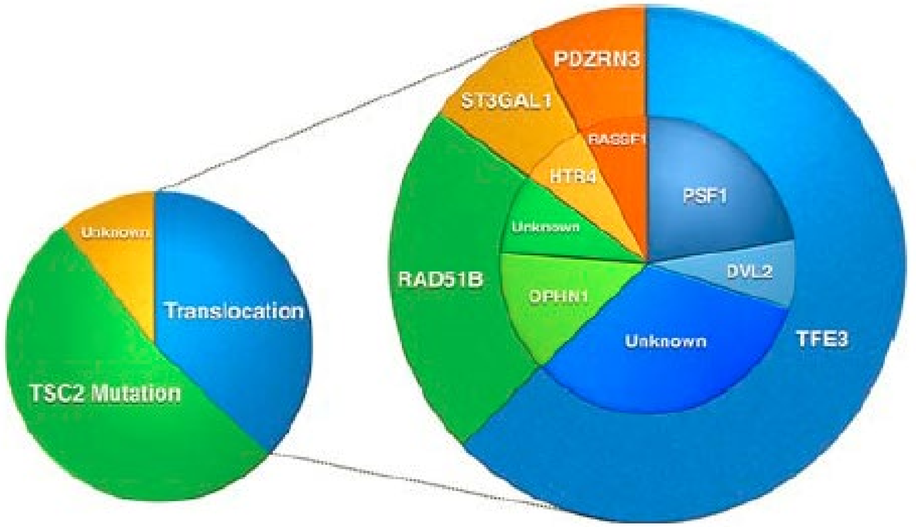
TABLE 1 Clinical features of the reported "fibroma-like" PEComas

Case	Age/sex	TS† status	Location	Size (cm)	Duration before diagnosis	Presentation	Recurrence	Metastasis	Follow-up
Case 1 in Larque et al[13]	4/F	Known TS	Wrist	5.9	24 months	Painless bump, progressively enlarging	None	None	ANED‡, 6 months
Case 2 in Larque et al[13]	25/F	Known TS	Chest Wall	2.8	None	Incidental	None	None	ANED, 29 months
Case 3 in Larque et al[13]	51/F	Known TS	Foot	5	<12 months	Painless bump, progressively enlarging	None	None	ANED, 131 months
Case 4 in Harvey et al[14]	44/M	Known TS	Knee	6.5	10 years	Incidental, progressively enlarging, became painful	Not specified	Not specified	Not specified
Case 5 (current case)	20 months/F	Known TS	Lip	1.3	7 months	Painless bump, progressively enlarging	None	None	ANED, 1 month

Dichotomy of Genetic Abnormalities in PEComas With Therapeutic Implications

Narasimhan P. Agaram, MBBS, Yun-Shao Sung, MS,* Lei Zhang, MD, MS,* Chun-Liang Chen, MS,* Hsiao-Wei Chen, MS,* Samuel Singer, MD,† Mark A. Dickson, MD,‡ Michael F. Berger, PhD,*§ and Cristina R. Antonescu, MD**

(*Am J Surg Pathol* 2015;00:000–000)



Differential Diagnosis

- Balloon Cell Nevus
- “Clear cell” melanoma
- Clear cell sarcoma
  - Lack of strong diffuse positivity for S100-protein and SOX10
- Dermal Clear Mesenchymal Neoplasm (DCCMN)
- Metastatic clear cell carcinoma
  - Positive for PAX8, RCC, negative for melanocytic markers (except melanotic Xp11 translocation renal cell cancer)

Differential diagnosis	HMB-45	Melan-A/MART-1	Actin	Desmin	S100 protein	SOX-10	Other
pcPEComa	+	+	+/−	+/−	−	−	CD10+
DCCMN	−	−	N/A	N/A	−	N/A	
metRCC	−	−	−	−	−	−	CD10+, CK+, PAX-8+, RCC+
Melanocytic	+	+	−	−	+	+	
CCS	+	+	−	−	+	+	

J Cutan Pathol. 2017;44:713–721.

- S100-protein and/or SOX10
- MelanA
- HMB45
- SMA
- Desmin

Prognosis

Perivascular Epithelioid Cell Neoplasms of Soft Tissue and Gynecologic Origin

A Clinicopathologic Study of 26 Cases and Review of the Literature

Andrew L. Folpe, MD, Thomas Mentzel, MD,† Hans-Anton Lehr, MD, PhD,‡ Cyril Fisher, MD,§ Bonnie L. Balzer, MD, PhD,* and Sharon W. Weiss, MD**

(*Am J Surg Pathol* 2005;29:1558–1575)

TABLE 5. Proposed Classification of PEComas

	Criteria	Percentage Fulfilling Criteria With Aggressive Behavior	Comment
Benign	No worrisome features (<5 cm, non-infiltrative, non-high nuclear grade and cellularity, mitotic rate ≤1/50HPF, no necrosis, no vascular invasion)	0 of 22 (0%)	
Uncertain malignant potential	1) Nuclear pleomorphism/multinucleated giant cells only *or*	1) 0 of 6 (0%)	1) "Symplastic" PEComa-probably benign, but few reported cases
	2) Size >5 cm only	2) 2 of 17 (12%)	2) Large tumors should be extensively sampled to exclude areas with other worrisome features
Malignant	Two or more worrisome features (>5 cm, infiltrative, high nuclear grade and cellularity, mitotic rate ≥1/50HPF, necrosis, vascular invasion)	12 of 17 (71%)	

Malignant perivascular epithelioid cell tumor ('PEComa'): a case report and literature review of cutaneous/ subcutaneous presentations

Kenneth B. Calder[1], Scott Schlauder[1] and Michael B. Morgan[1,2]

[1]Department of Pathology University of South Florida College of Medicine, Tampa, FL, USA, and
[2]James A. Haley Veterans Hospital, Department of Pathology, Tampa, FL, USA

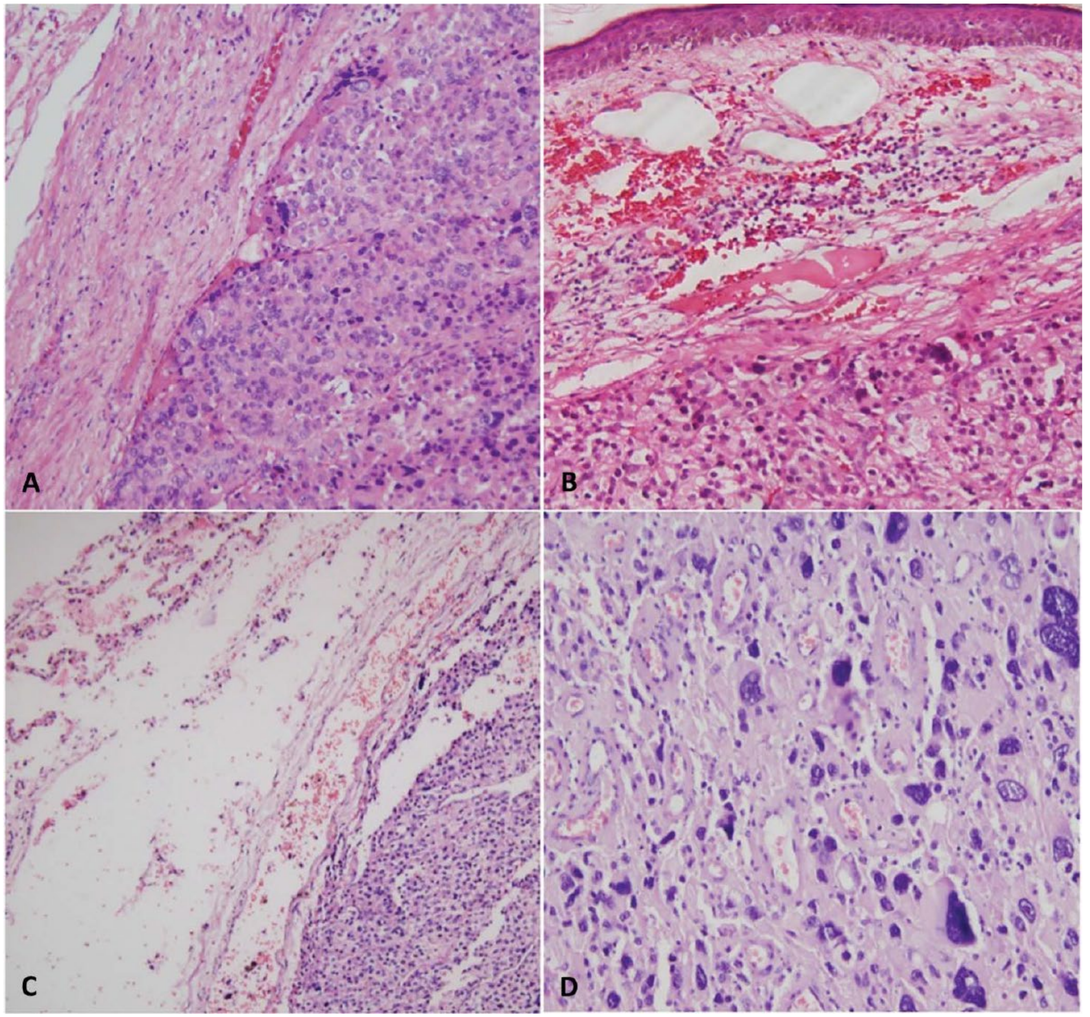
J Cutan Pathol 2008: 35: 499–503

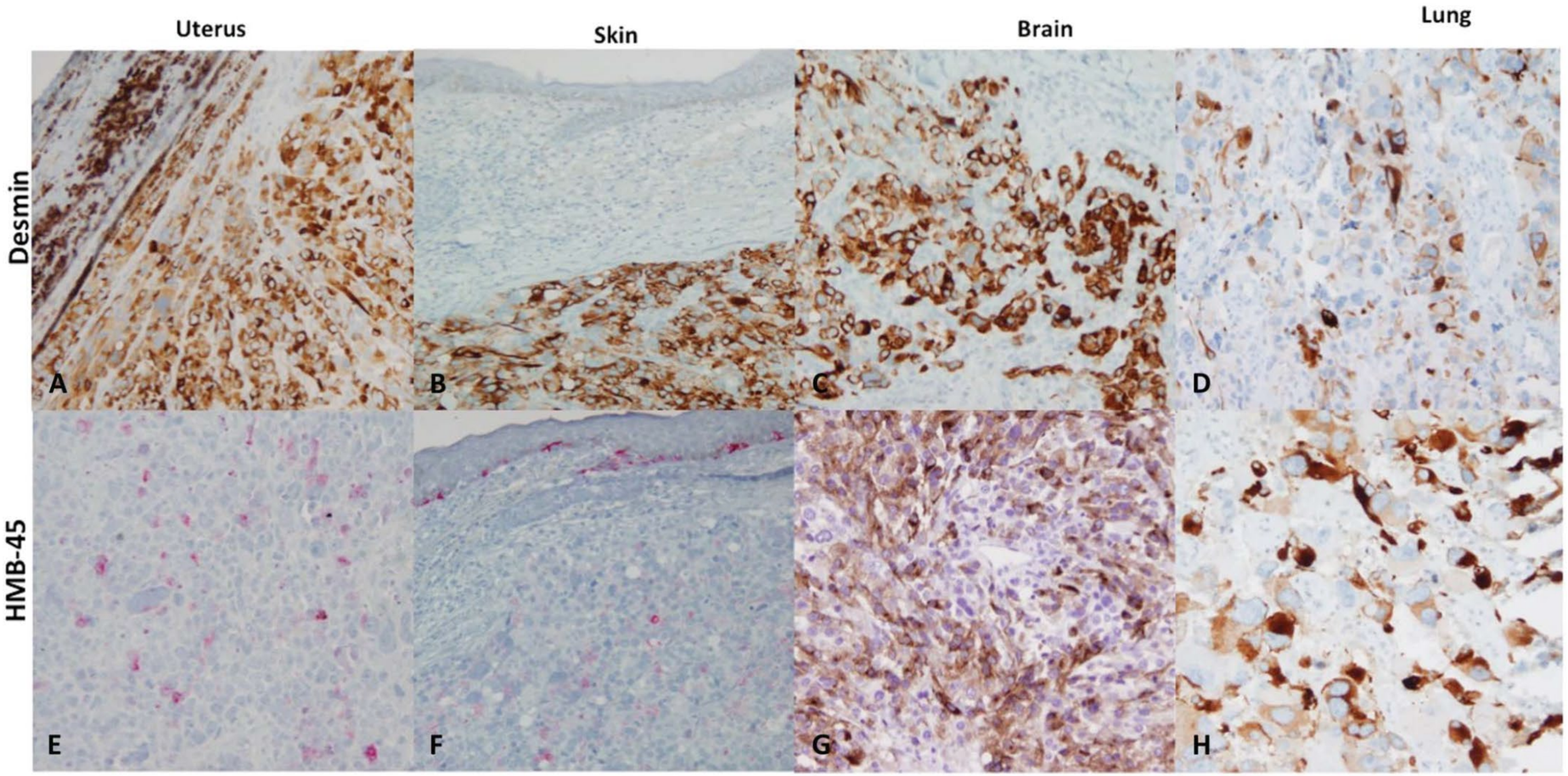
Malignant perivascular epithelioid cell tumor: A case report of a cutaneous tumor on the cheek of a male patient

Karin Greveling, MD,[a] Veronique J. L. Winnepenninckx, MD, PhD,[b] Ivo F. Nagtzaam, MD,[a] Martin Lacko, MD, PhD,[c,f] Stephania M. H. Tuinder, MD,[d] Jos M. A. de Jong, MD, PhD,[e] and Nicole W. J. Kelleners-Smeets, MD, PhD[a,f]

Cutaneous Perivascular Epithelioid Cell Tumor of Gynecologic Origin Metastatic to Skin, Lung, Stomach, and Brain

Rafael Parra-Medina, MD*†
Samuel D. Morales, MD*†
*Department of Pathology, National Institute of Cancer, Bogotá, Colombia
†Department of Pathology, Fundación Universitaria de Ciencias de la Salud, Bogotá, Colombia




Uterus
Skin
Brain
Lung
Desmin
HMB-45
A
B
C
D
E
F
G
H

Clear Cell Tumor With Melanocytic Differentiation and *ACTIN-MITF* Translocation

Report of 7 Cases of a Novel Entity

Arnaud de la Fouchardiere, MD, PhD, Daniel Pissaloux, PhD,* Franck Tirode, PhD,* Marie Karanian, MD,* Christopher D.M. Fletcher, MD,† and John Hanna, MD, PhD†*

Am J Surg Pathol 2021;45:962–968

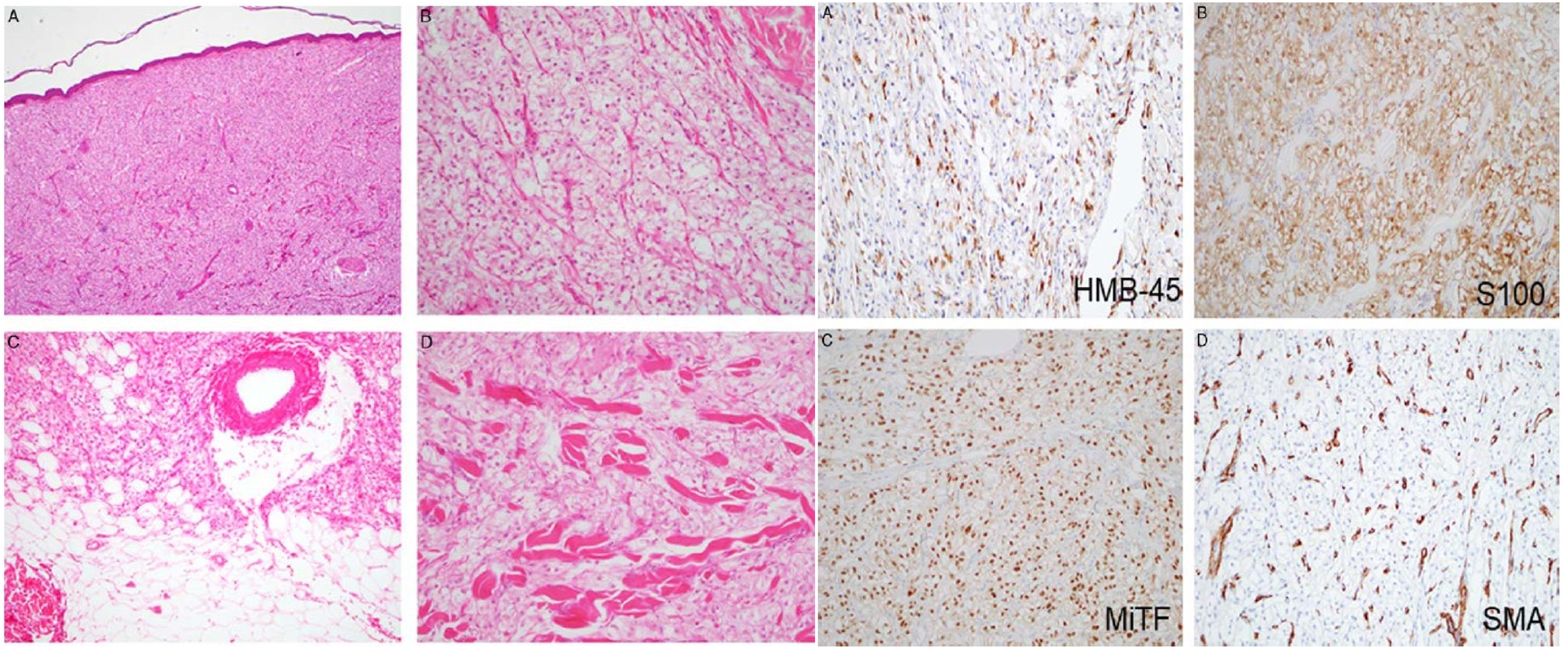
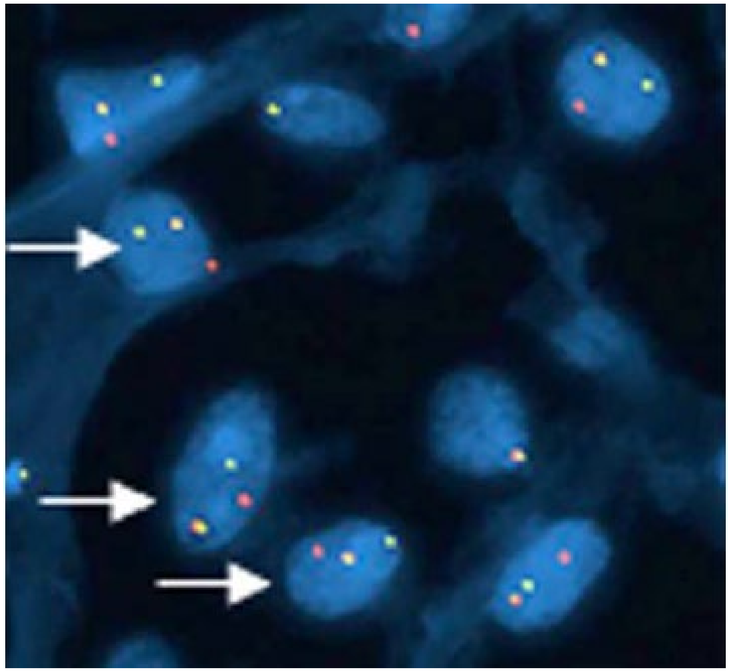


TABLE 2. IHC Features

Case No.	S100	HMB-45	Melan-A/Mart-1	MITF	SMA	Desmin	Keratin	EMA
1	+++	+++	+++	ND	ND	ND	–	–
2	+++	++	ND	ND	ND	ND	–	–
3	+	+++	++	+++	–	–	ND	–
4	+	+	–	+++	–	+	–	–
5	+++	++	–	+++	–	+	ND	ND
6	–	+++	+	ND	–	ND	–	ND
7	–	–	+++	ND	–	–	–	ND

TABLE 3. Summary of Molecular Results

Case No.	Result	Method
1	NA	NA
2	*ACTG1-MITF* fusion	RNAseq
3	*ACTB-MITF* fusion	RNAseq
4	*MITF* gene rearrangement	FISH
5	*ACTB-MITF* fusion	RNAseq
6	*ACTG1-MITF* fusion	RNAseq
7	*ACTG1-MITF* fusion	RNAseq



Clear Cell Sarcoma

CLEAR-CELL SARCOMA OF TENDONS AND APONEUROSES

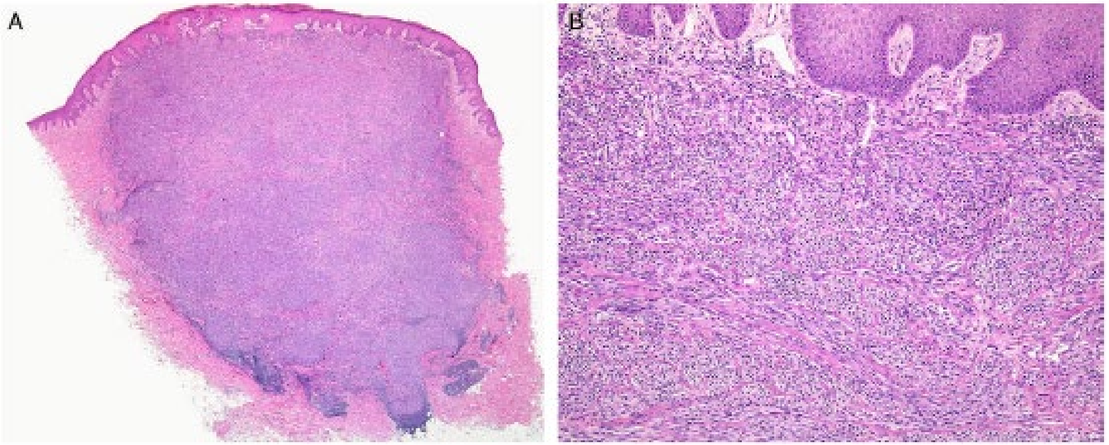
An Analysis of 21 Cases

FRANZ M. ENZINGER, M.D.

Cutaneous Clear Cell Sarcoma: A Clinicopathologic, Immunohistochemical, and Molecular Analysis of 12 Cases Emphasizing its Distinction from Dermal Melanoma

Markus Hantschke, MD, Thomas Mentzel, MD,* Arno Rütten, MD,* Gabriele Palmedo, PhD,* Eduardo Calonje, MD,† Alexander J. Lazar, MD,‡ and Heinz Kutzner, MD**

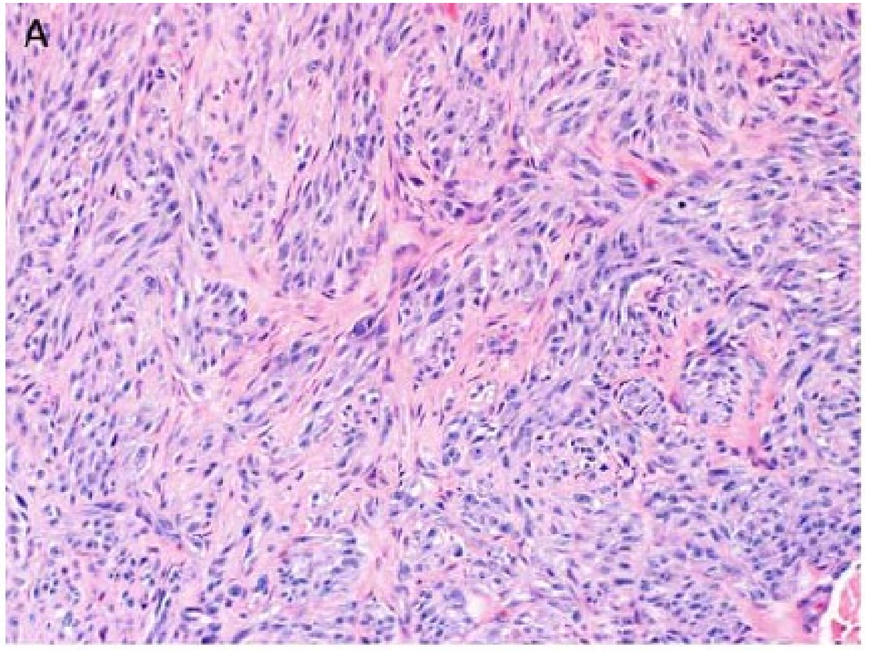
(*Am J Surg Pathol* 2010;34:216–222)

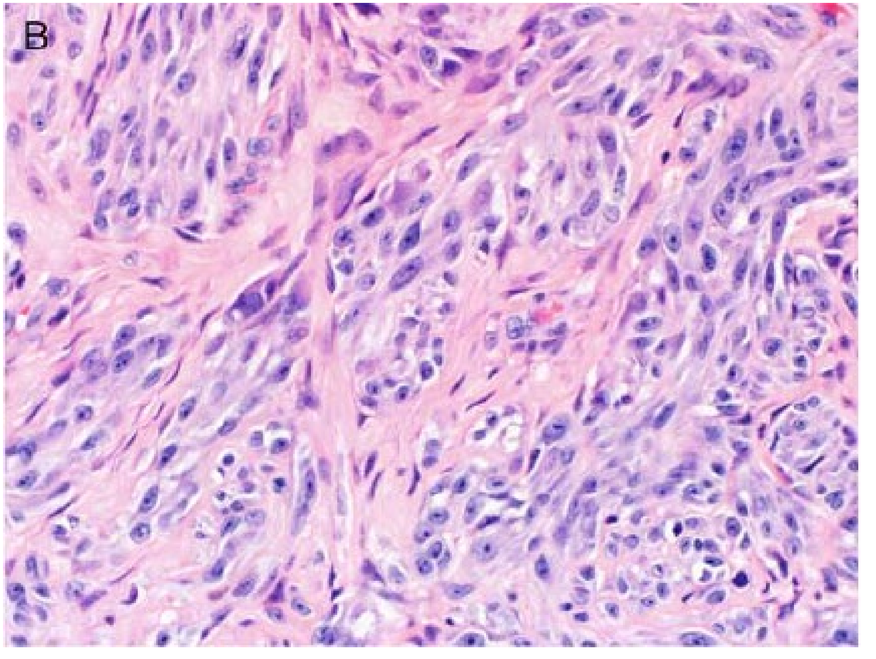


- Usually lesions relatively small (<5cm)
  - Primary cutaneous <1cm
    - Otherwise similar clinical and pathologic features

- Natural history clinically protracted
  - Multiple local recurrences
  - Late metastases in lymph nodes, lung, bone

- Wide local excision with adjuvant radiation


A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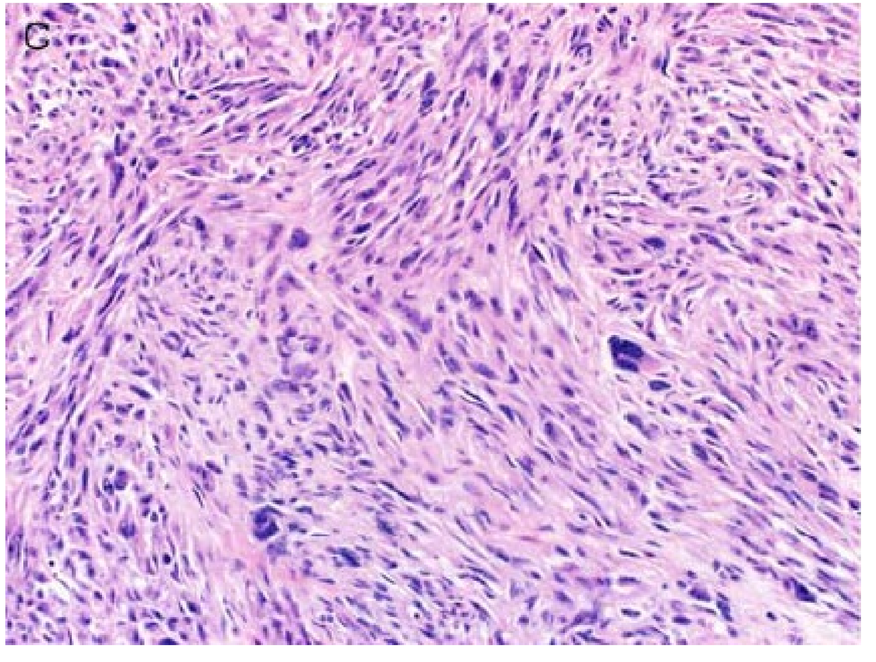
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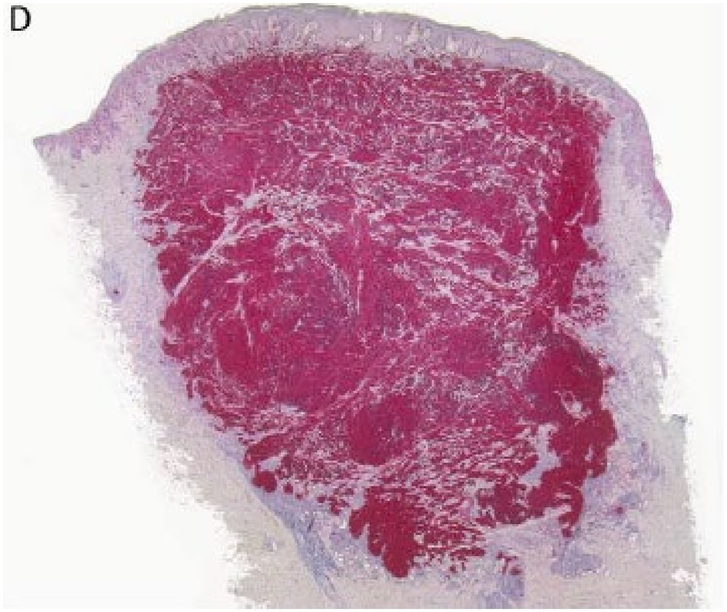
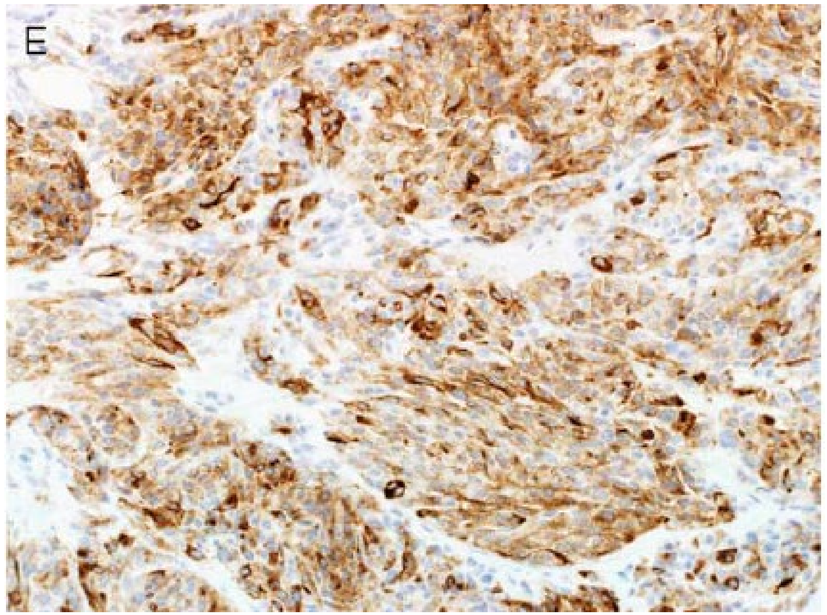
S100-Protein



Melan-A



J Cutan Pathol 2013: 40: 950–954
doi: 10.1111/cup.12197
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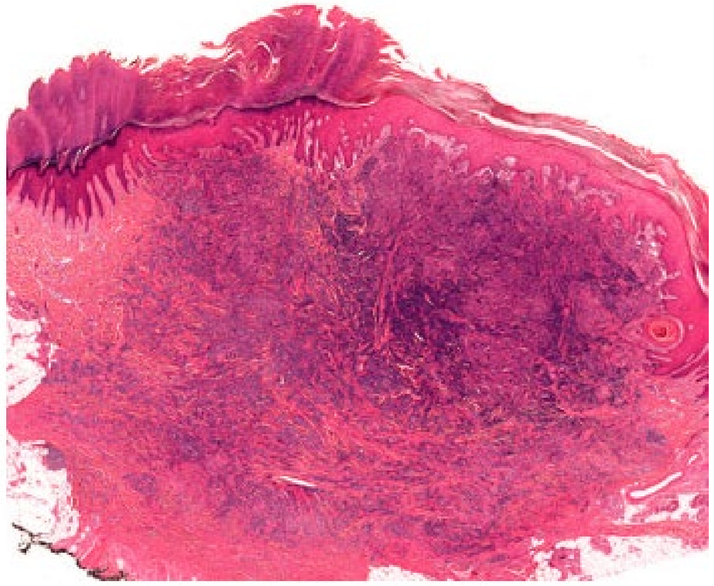
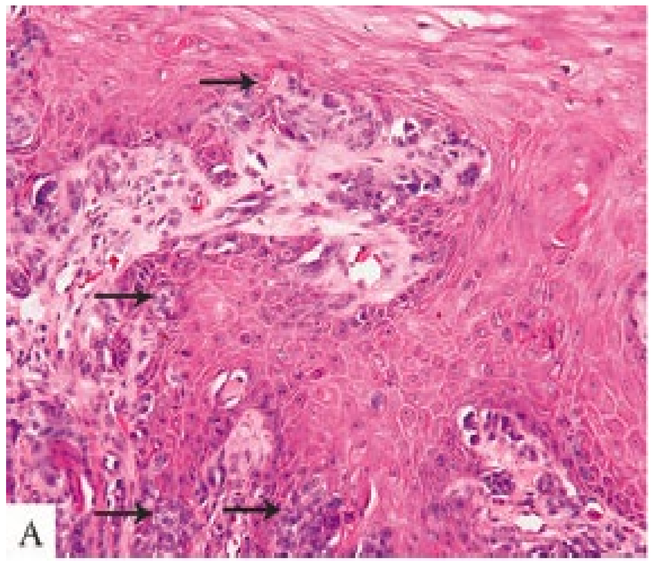
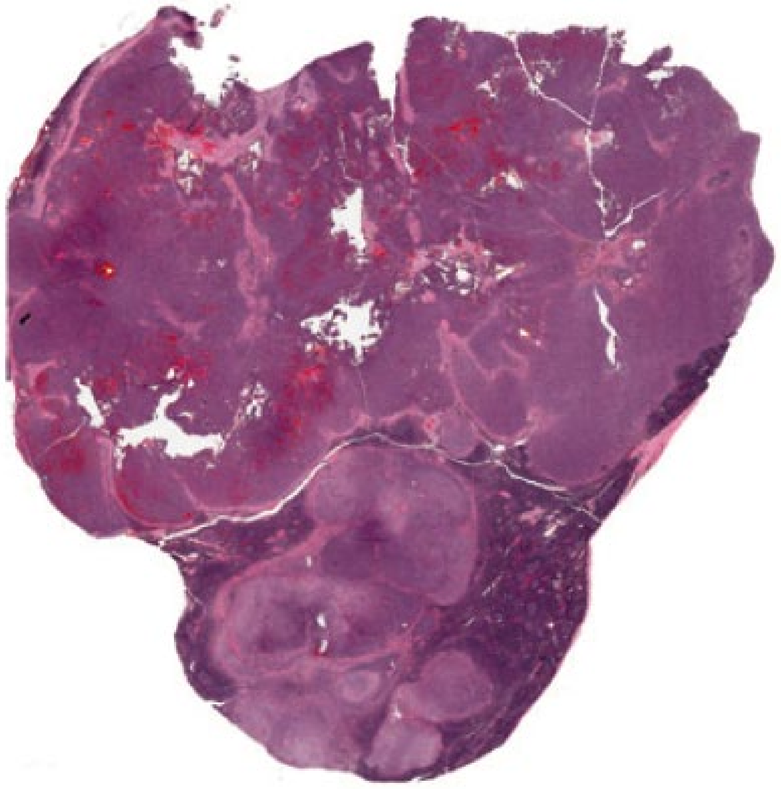
Journal of
Cutaneous Pathology

Compound clear cell sarcoma misdiagnosed as a Spitz nevus

Maija Kiuru[1,2], Meera Hameed[3] and Klaus J. Busam[3]







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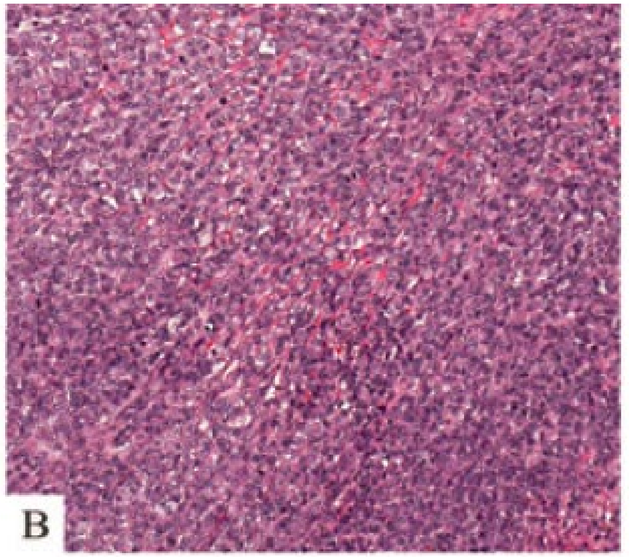
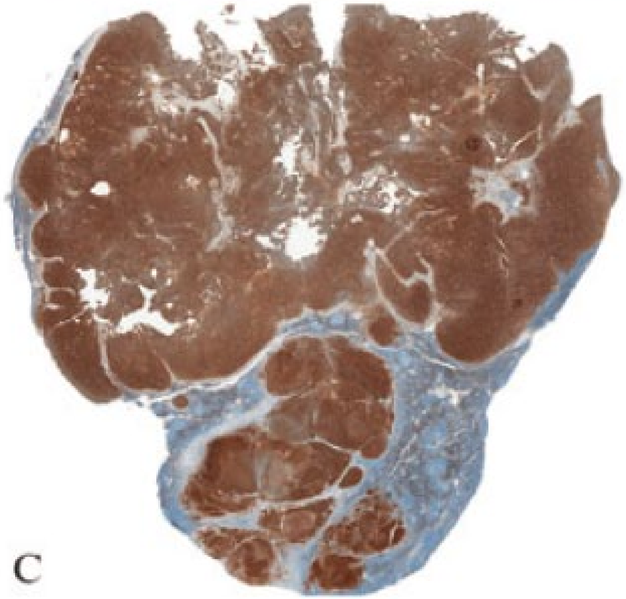


B



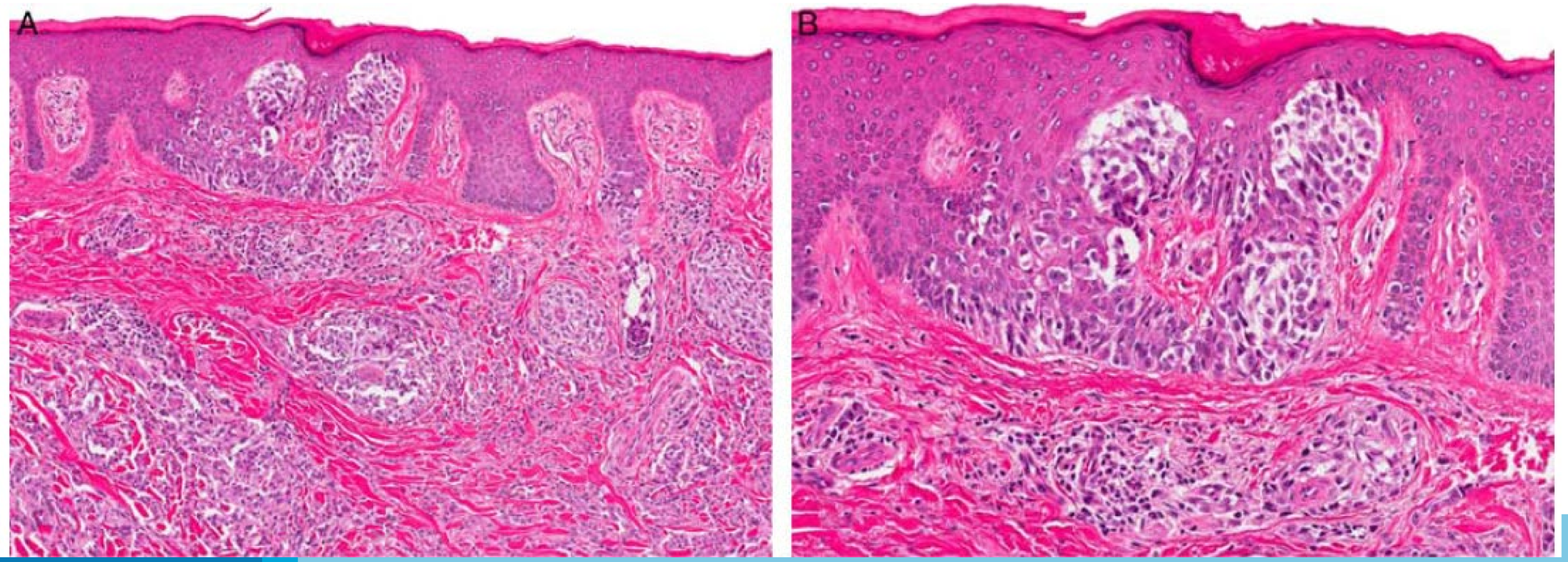
C

Compound Clear Cell Sarcoma of the Skin—A Potential Diagnostic Pitfall

Report of a Series of 4 New Cases and a Review of the Literature

Boštjan Luzar, MD, PhD, Steven D. Billings, MD,† Arnaud de la Fouchardiere, MD, PhD,‡§ Daniel Pissaloux, PhD,‡§ Laurent Alberti, PhD,‡§ and Eduardo Calonje, MD, Dip RCPath‖*

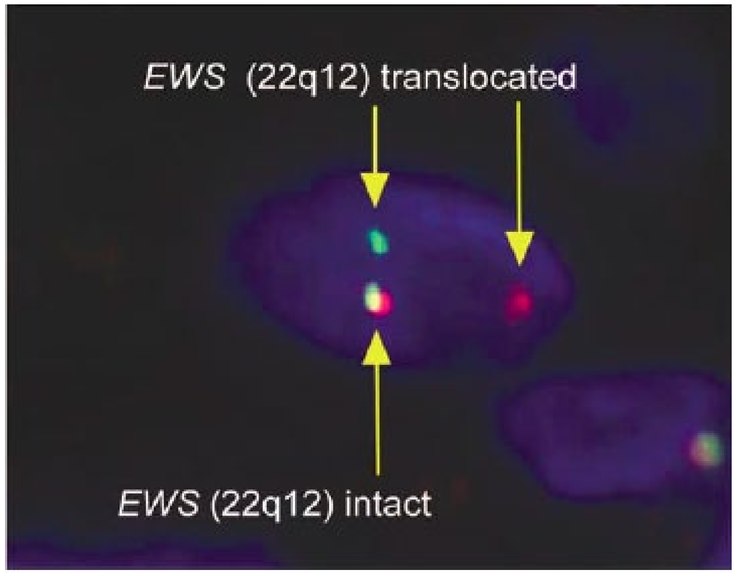
Am J Surg Pathol 2020;44:21–29



Dual-color, break-apart fluorescence *in situ* hybridization for *EWS* gene rearrangement distinguishes clear cell sarcoma of soft tissue from malignant melanoma

Rajiv M Patel[1], Erinn Downs-Kelly[2], Sharon W Weiss[1], Andrew L Folpe[1], Raymond R Tubbs[2], Ralph J Tuthill[2], John R Goldblum[2] and Marek Skacel[2]

Modern Pathology (2005) 18, 1585–1590



- *EWSR1-ATF1*
- *EWSR1-CREB1*

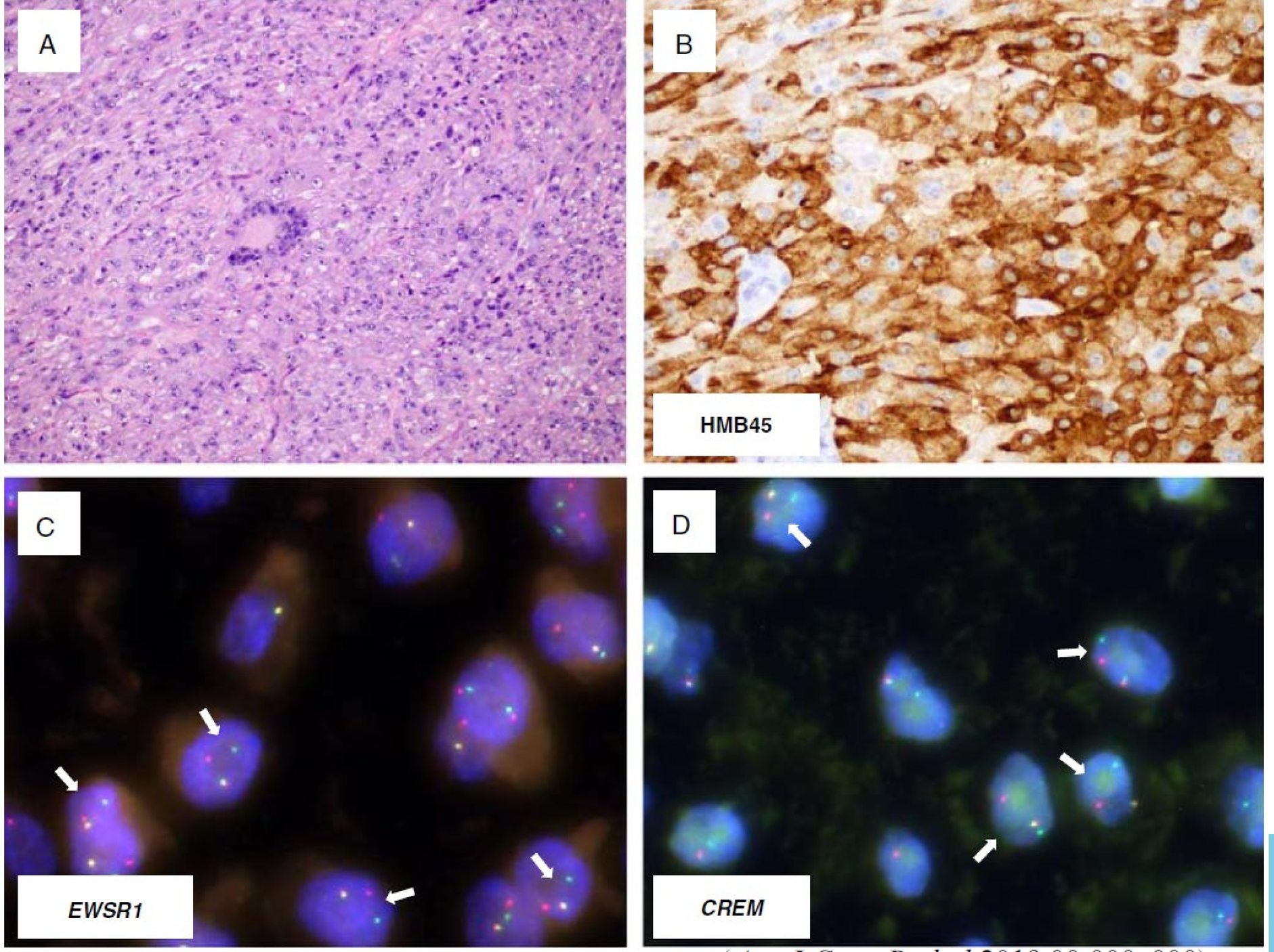
Expanding the Phenotypic Spectrum of Mesenchymal Tumors Harboring the *EWSR1-CREM* Fusion

Akihiko Yoshida, MD, PhD,† Susumu Wakai, CT,* Eijitsu Ryo, PhD,‡ Kazuyuki Miyata, MD, PhD,§ Masahisa Miyazawa, MD, PhD,‖ Ken-ichi Yoshida, MD,* Toru Motoi, MD, PhD,¶ Chitose Ogawa, MD,# Shintaro Iwata, MD, PhD,†** Eisuke Kobayashi, MD, PhD,†** Shun-ichi Watanabe, MD,†† Akira Kawai, MD, PhD,†** and Taisuke Mori, DMD, PhD*‡*

(*Am J Surg Pathol* 2019;00:000–000)

TABLE 2. Clinicopathologic Summary of Mesenchymal Tumors Harboring the *EWSR1-CREM* Fusion

Case	Age (y)/Sex	Primary Site	Histology	Treatment	Outcome (mo)
1	49/F	Hand	Clear cell sarcoma	Resection	AWD (39)
2	47/M	Lung	Myxoid AFH	Lobectomy	NED (58)
3	50/M	Finger	Myxoid AFH	Ray amputation	NED (45)
4	54/M	Hand	Myxoid AFH	Ray amputation	NED (51)
5	15/M	Abdominal cavity	Unclassifiable spindle cell tumor (CK^+, $CD34^+$, ALK^+)	Chemotherapy	DOD (18)
6	63/F	Chest wall	Unclassifiable round cell tumor ($MUC4^+$, $synapto^+$)	Wide resection	NED (17)



(*Am J Surg Pathol* 2019;00:000–000)

WILEY JOURNAL OF CUTANEOUS PATHOLOGY

REVIEW

Review of the medical literature and assessment of current utilization patterns regarding the use of two common fluorescence in situ hybridization assays in the diagnosis of dermatofibrosarcoma protuberans and clear cell sarcoma

Konstantinos Linos[1] | Jessica A. Kozel[2] | Maria Yadira Hurley[3] | Aleodor A. Andea[4]

Appropriate use criteria in dermatopathology: Initial recommendations from the American Society of Dermatopathology

Task Force / Committee Members:

Claudia I. Vidal[1] | Eric A. Armbrect[2] | Aleodor A. Andea[3] | Angela K. Bohlke[4] | Nneka I. Comfere[5] | Sarah R. Hughes[6] | Jinah Kim[7] | Jessica A. Kozel[8] | Jason B. Lee[9] | Konstantinos Linos[10] | Brandon R. Litzner[11,12] | Tricia A. Missall[1] | Roberto A. Novoa[7] | Uma Sundram[13] | Brian L. Swick[14] | Maria Yadira Hurley (Chair)[1] |

Rating Panel:

Murad Alam[15] | Zsolt Argenyi[16] | Lyn M. Duncan[17] | Dirk M. Elston[18] | Patrick O. Emanuel[19] | Tammie Ferringer[20] | Maxwell A. Fung[21] | Gregory A. Hosler[22] | Alexander J. Lazar[23] | Lori Lowe[3] | Jose A. Plaza[24] | Victor G. Prieto[23] | June K. Robinson[25] | Andras Schaffer[26] | Antonio Subtil[27] | Wei-Lien Wang[28]

J Cutan Pathol. 2018;45:563–580.

J Cutan Pathol. 2018;45:905–913.

Receptor Tyrosine Kinase Pathway Analysis Sheds Light on Similarities Between Clear-Cell Sarcoma and Metastatic Melanoma

Tiziana Negri,[1†] Silvia Brich,[1†] Elena Conca,[1] Fabio Bozzi,[1] Marta Orsenigo,[1] Silvia Stacchiotti,[2] Marco Alberghini,[3] Valentina Mauro,[1] Alessandro Gronchi,[4] Giuseppina F. Dusio,[5] Giuseppe Pelosi,[1] Piero Picci,[6] Paolo G. Casali,[2] Marco A. Pierotti,[7*] and Silvana Pilotti[1]

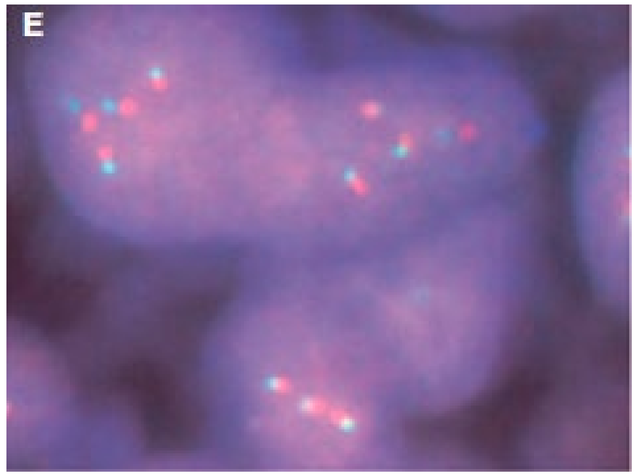
GENES, CHROMOSOMES & CANCER 51:111–126 (2012)

		Frozen and FFPE material (18 cases)			FFPE material (24 cases)				TOTAL (42 cases) Frozen + FFPE material			
		Sequencing		FISH		Sequencing		FISH		Sequencing		FISH
	Number of cases	Mutated BRAF	Mutated NRAS	Gain of chr 22 and 8	Number of cases	Mutated BRAF	Mutated NRAS	Gain of chr 22 and 8	Number of cases	Mutated BRAF	Mutated NRAS	Gain of chr 22 and 8
EWSR1+ CCS	6	1 V600E	–	N.D.	6	1 V600E	–	N.D.	12	2 V600E	–	N.D.
EWSR1- CCS	5	1 V600E	2 Q61R	5	4	2 V600E	–	4	9	3 V600E	–	9
Metastatic melanoma	7	3 V600E	2 Q61R Q61L	1	14	6 V600E	4 Q61R Q61L	2	21	9 V600E	6 Q61R Q61L	3

Atypical Ewing sarcoma breakpoint region 1 fluorescence *in-situ* hybridization signal patterns in bone and soft tissue tumours: diagnostic experience with 135 cases

A Cristina Vargas,[1,*] Christina I Selinger,[1,*] Laveniya Satgunaseelan,[1,2] Wendy A Cooper,[1,3,4] Ruta Gupta,[1,3] Paul Stalley,[5,6,8,9,10] Wendy Brown,[7] Judy Soper,[7] Julie Schatz,[7] Richard Boyle,[5,6,8,9,10] David M Thomas,[11] Martin H N Tattersall,[3,5] Vivek A Bhadri,[3,5] Fiona Maclean,[2] S Fiona Bonar,[2,8,12] Richard A Scolyer,[1,3] Rooshdiya Z Karim,[1,3] Stanley W McCarthy,[1,3] Annabelle Mahar[1] & Sandra A O'Toole[1,3,11]

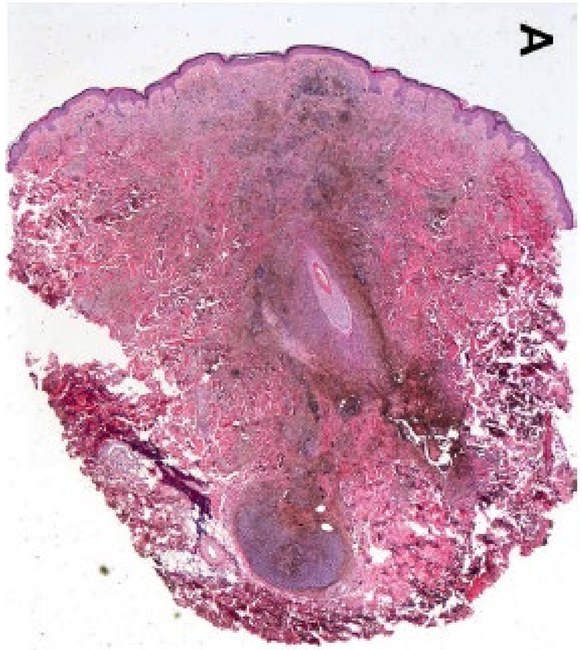
Histopathology 2016, **69**, 1000–1011. DOI: 10.1111/his.13031

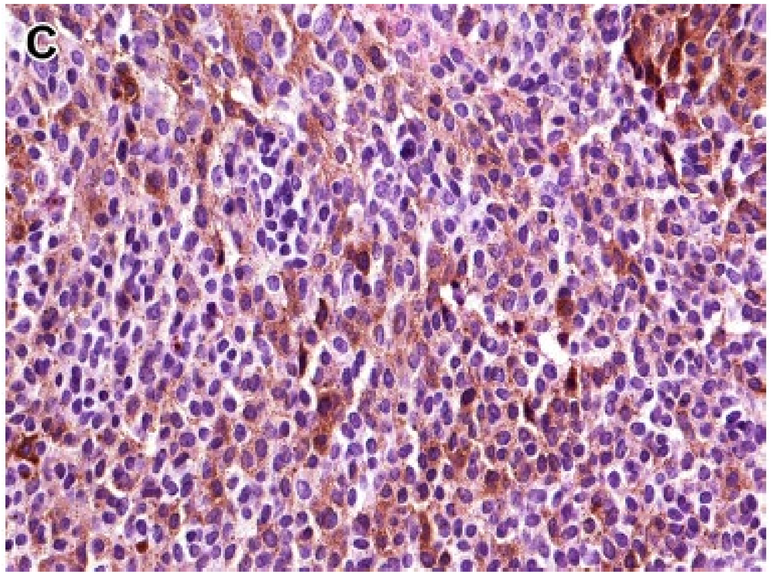


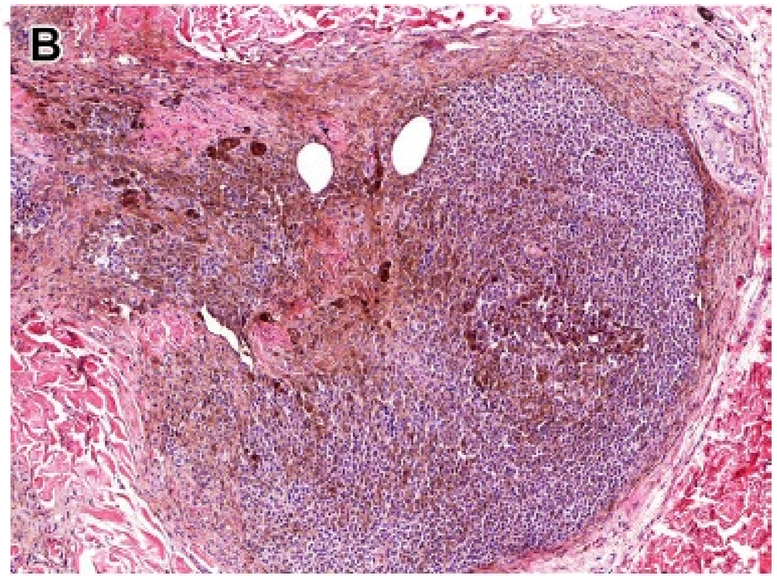
Differential Diagnosis

- Melanoma
- Perivascular Epithelioid Cell Neoplasm (PEComa)
- Cellular Blue Nevus
- Cutaneous Melanocytic Tumor with *CRTC1-TRIM11* Fusion

Cellular Blue Nevus

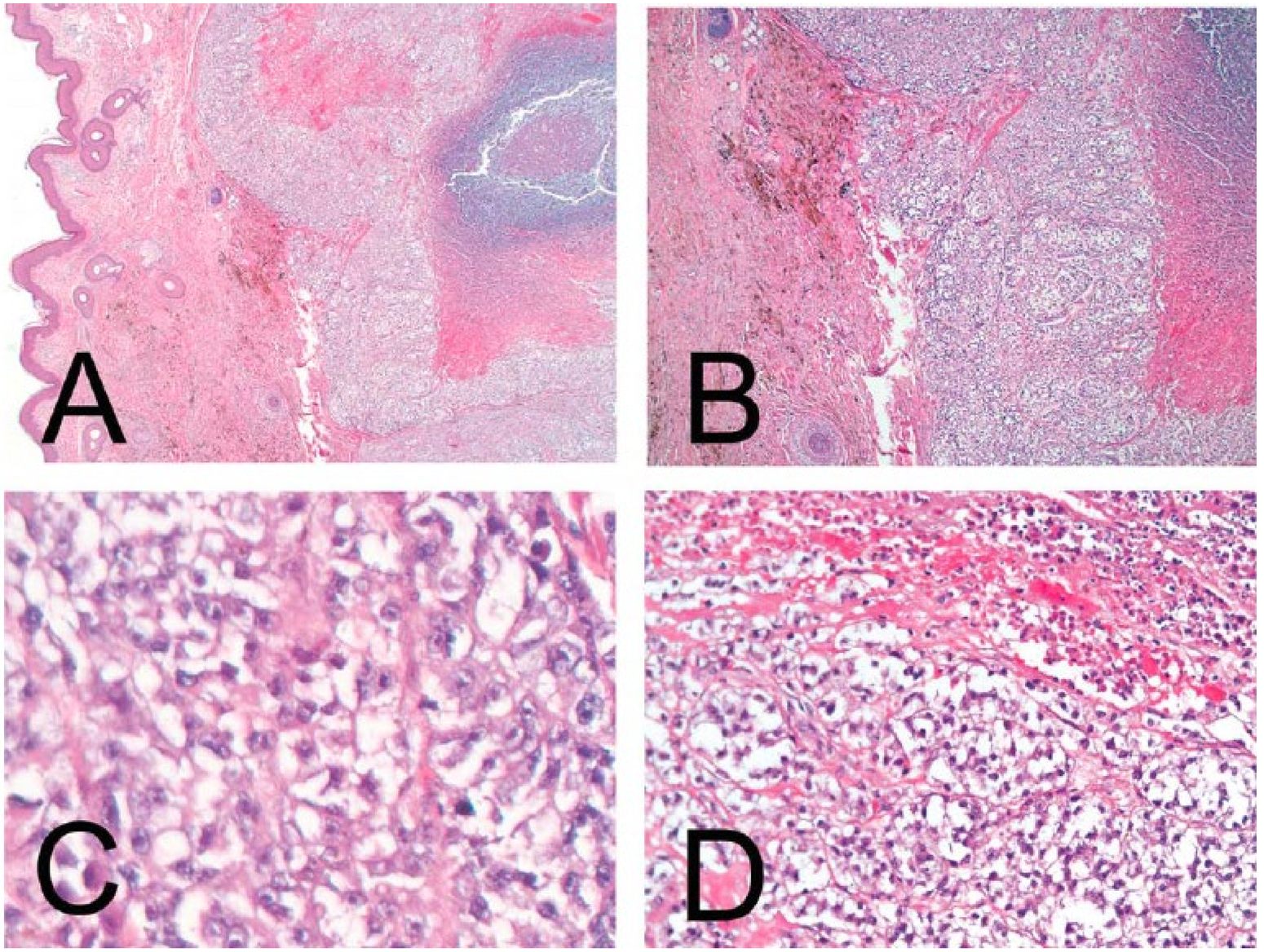






Clin Lab Med 37 (2017) 401–415

Melanoma ex blue nevus



Arch Pathol Lab Med—Vol 135, March 2011

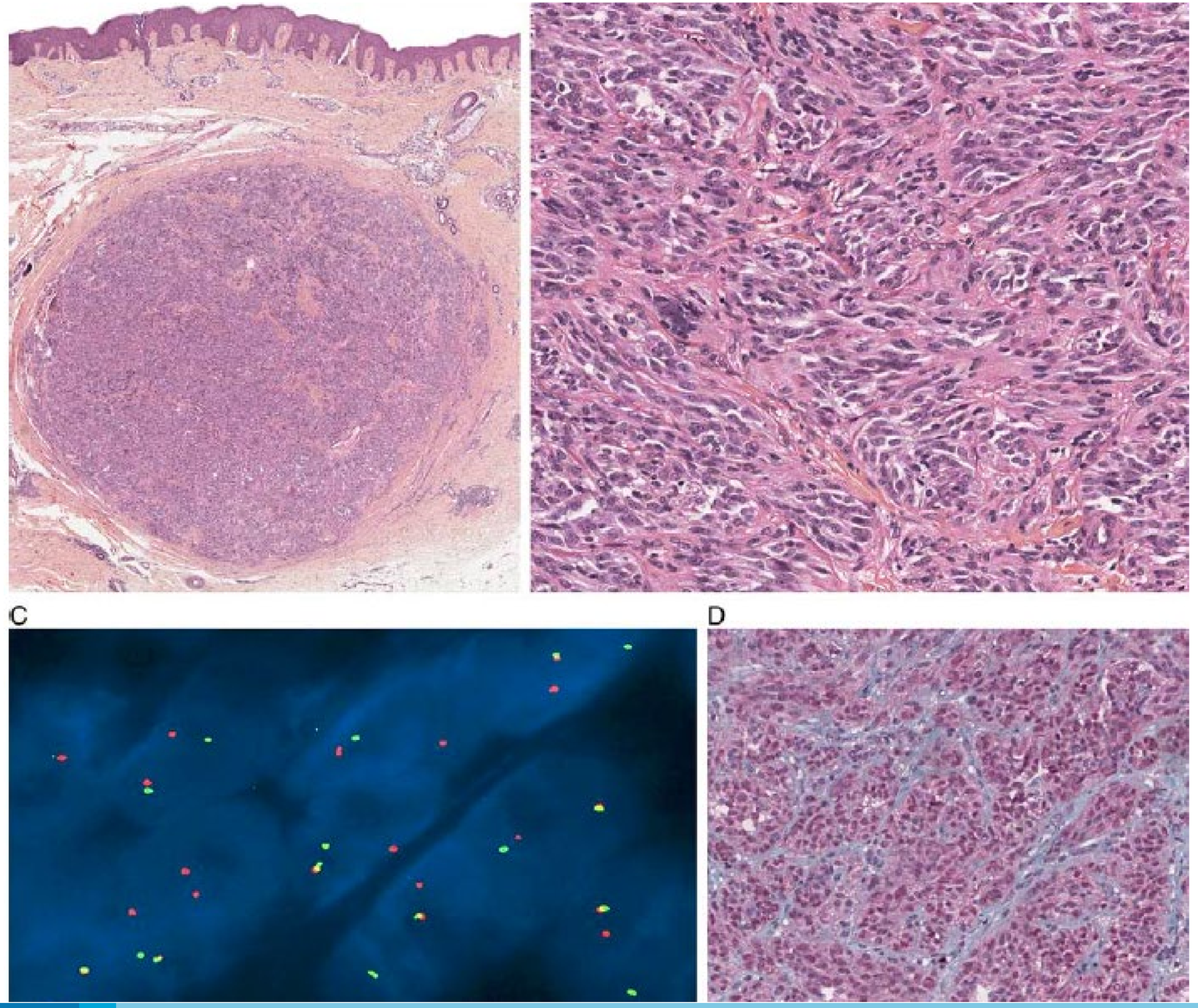
Cutaneous Melanocytoma With *CRTC1-TRIM11* Fusion

Report of 5 Cases Resembling Clear Cell Sarcoma

Lucie Cellier, MD, Emilie Perron, MD, MSc,*†‡ Daniel Pissaloux, PhD,* Marie Karanian, MD,* Veronique Haddad, PharmD,* Laurent Alberti, PhD,* and Arnaud de la Fouchardière, MD, PhD**

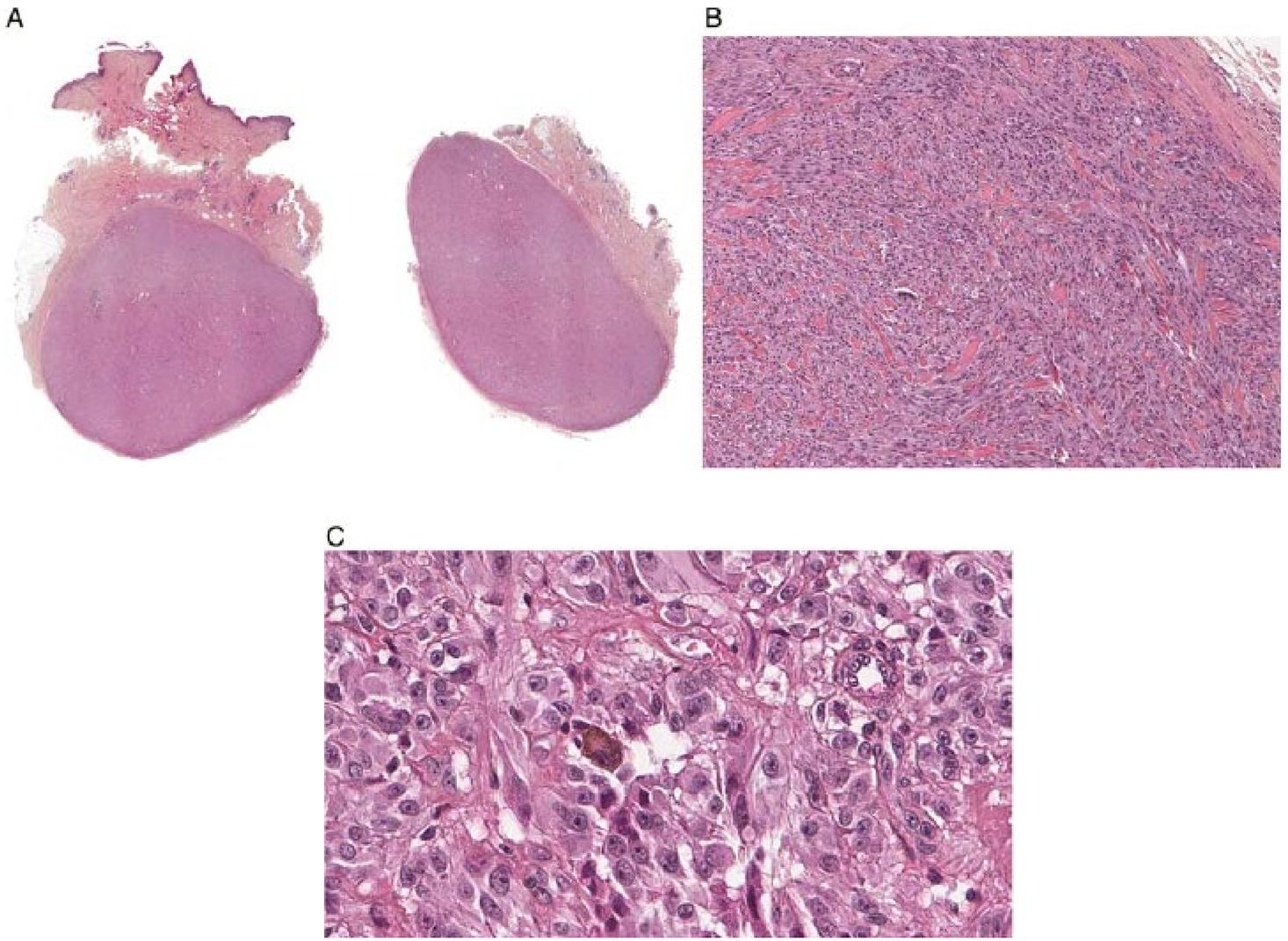
(*Am J Surg Pathol* 2017;00:000–000)

	Immunhistochemistry								FISH			RNA Sequencing	
Case No.	S100	MelanA	HMB45	Sox10	MITF	Ki67%	NTRK1	TRIM11	*EWSR1*	*NTRK1*	*TRIM11*	*CRTC1(e1)-TRIM11(e2)*	CGH
1	+	Focal +	Few + cells	+	+	5-10	+ (weak)	+	−	−	+	+	+7
2	+	Focal +	Focal +	+	+	5-10	+ (strong)	+	ND	−	+	+	NA
3	Focal +	Few + cells	−	+	+	20	+ (strong)	ND	−	−	+	+	ND
4	+	Few + cells	Few + cells	+	+	15	+ (weak)	+	−	ND	+	+	+7
5	+	−	Few + cells	+	+	5-10	+ (strong)	+	−	ND	+	+	ND

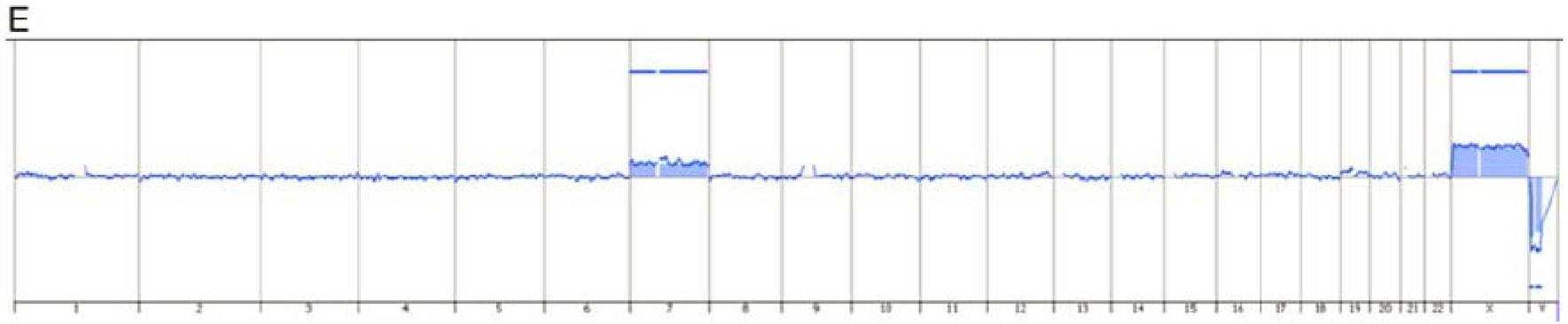


Memorial Sloan Kettering Cancer Center

(*Am J Surg Pathol* 2017;00:000–000)



(*Am J Surg Pathol* 2017;00:000–000)

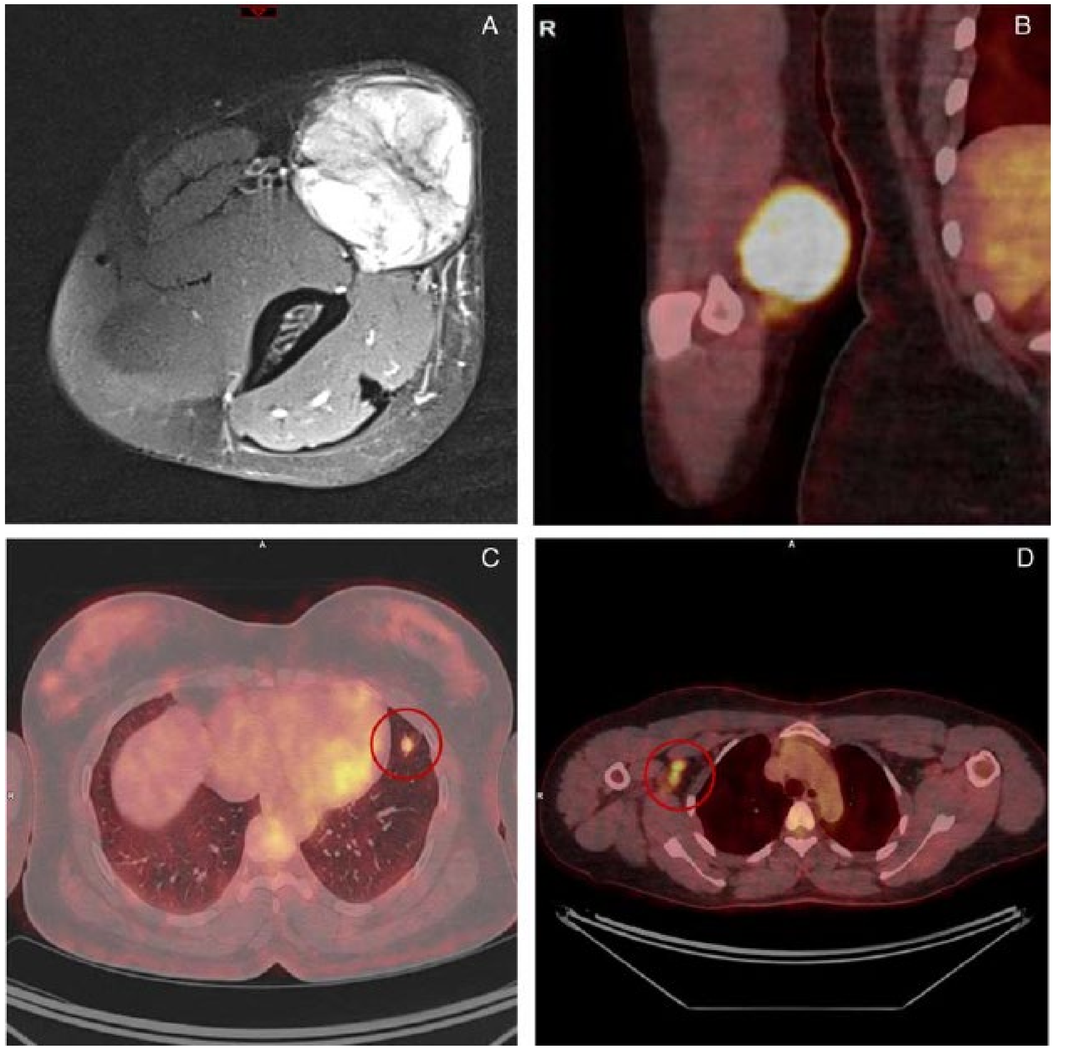


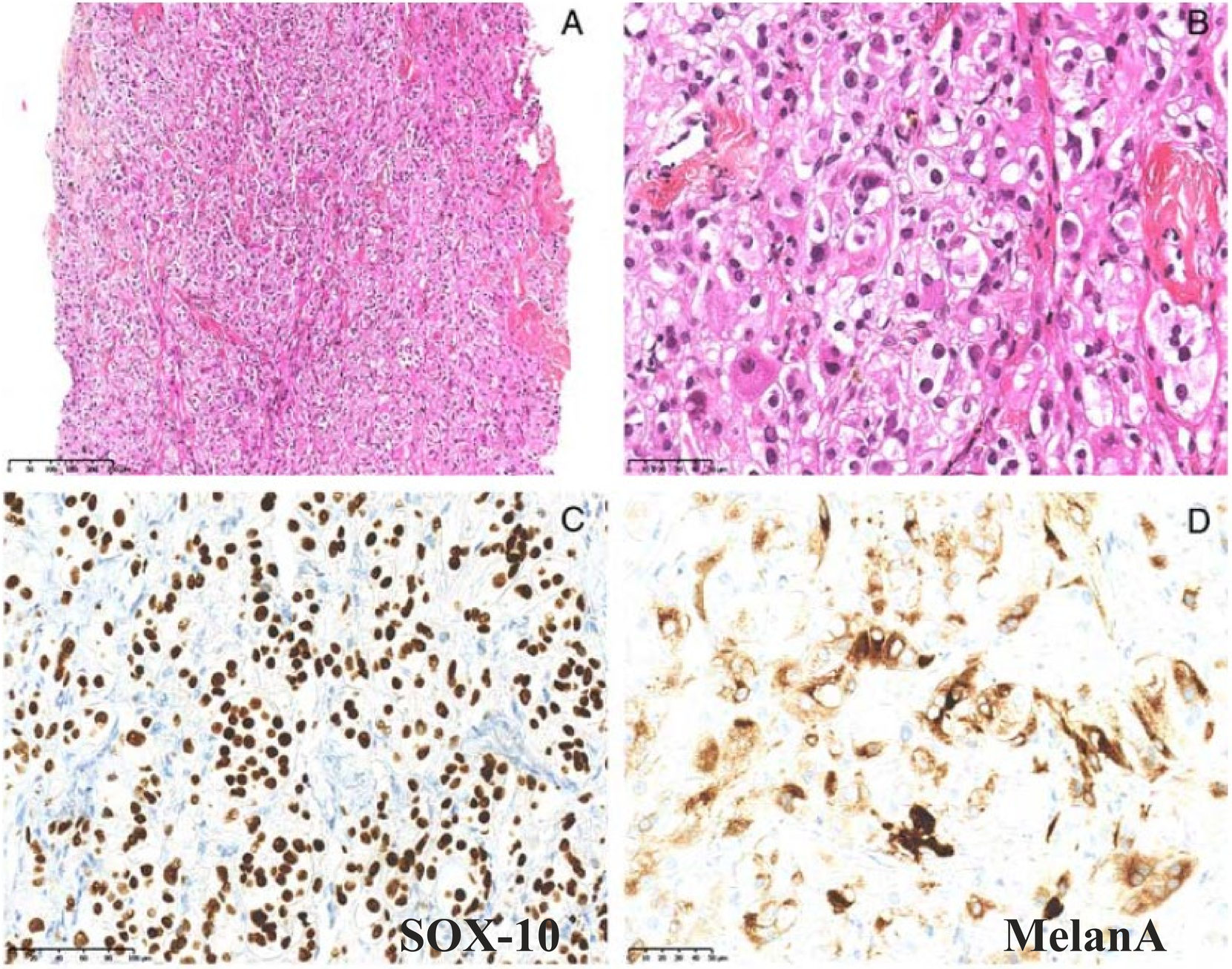
- No activating mutations of the MAP-kinase pathway such as BRAF and NRAS
- No hTERT mutations
- In some cases only a whole gain of chromosome 7
- No local recurrences or metastatic evolution (short follow-up)

CRTC1-TRIM11 Fusion in a Case of Metastatic Clear Cell Sarcoma

Are CRTC1-TRIM11 *Fusion-bearing Tumors Melanocytomas or Clear Cell Sarcomas?*

Christophe Bontoux, MD*
Barouyr Baroudjian, MD†
Christine Le Maignan, MD‡
Laetitia Vercellino, MD, PhD§
Cécile Farges, MD‖
Delphine Guillemot, MD¶
Gaëlle Pierron, MD, PhD¶
Céleste Lebbé, MD, PhD†#
Maxime Battistella, MD, PhD***
Departments of *Pathology
†Dermatology
‡Oncology
§Nuclear Medicine
‖Radiology, Hôpital Saint-Louis, APHP
¶Department of Genetics, Institut Curie, PSL Research University
#INSERM UMR_S976

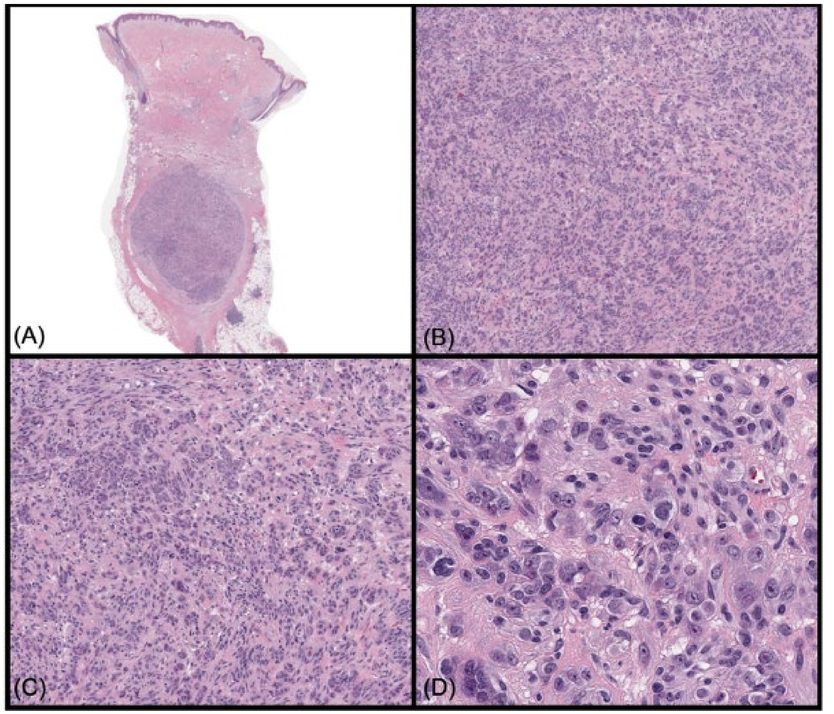



A
B
C
SOX-10
D
MelanA

Dermal melanocytic tumor with *CRTC1-TRIM11* fusion: Report of two additional cases with review of the literature of an emerging entity

Ourania Parra[1] | Julia A. Bridge[2,3] | Klaus J. Busam[4] | Sara C. Shalin[5] | Konstantinos Linos[1,6]

J Cutan Pathol. 2021;48:915–924.

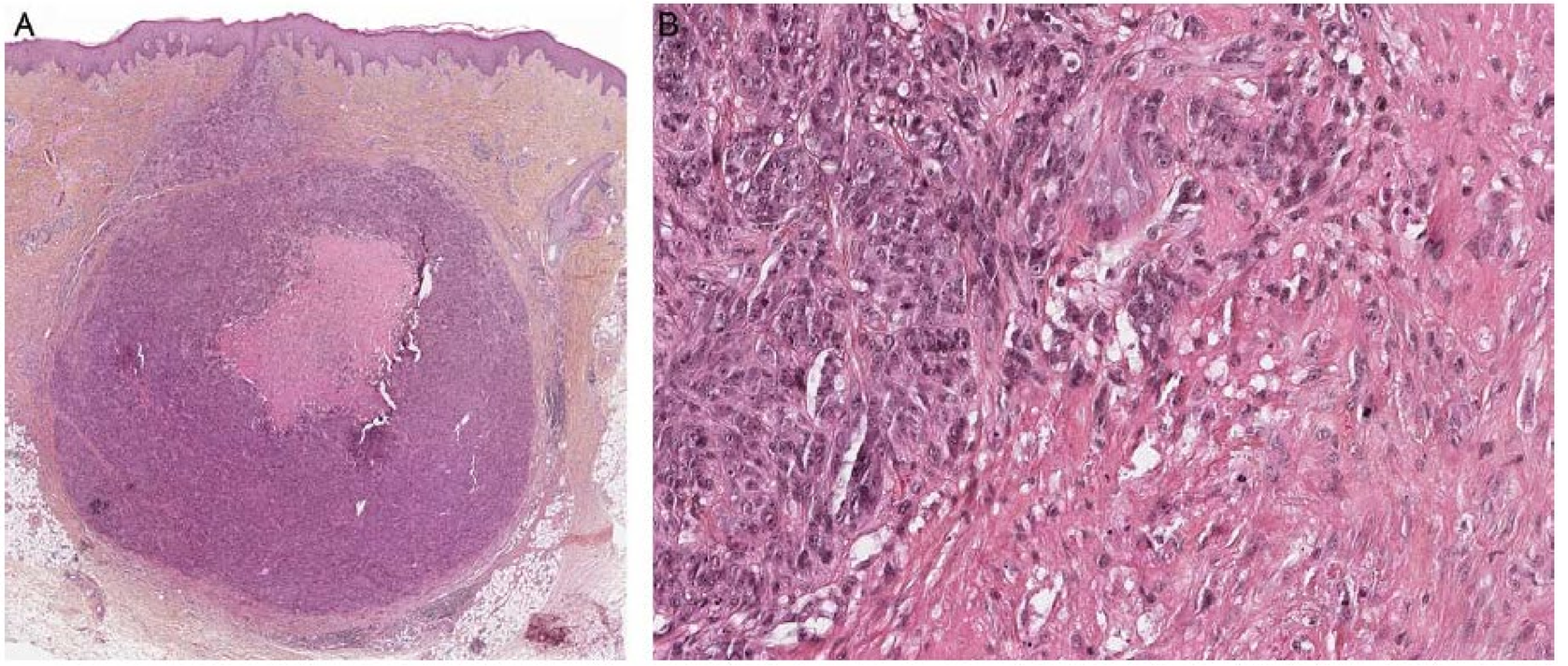


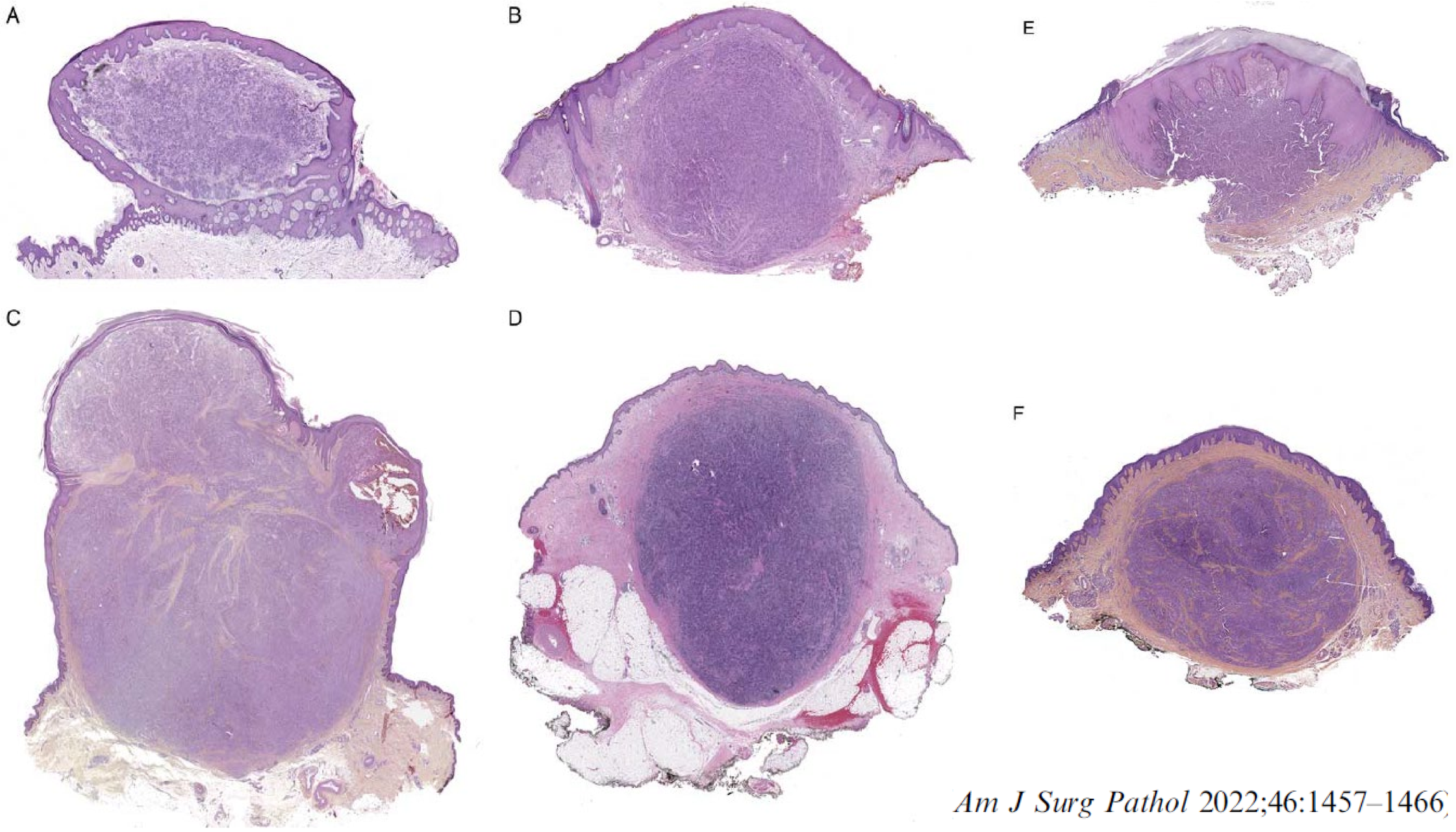
Cutaneous Melanocytic Tumor With *CRTC1::TRIM11* Translocation

An Emerging Entity Analyzed in a Series of 41 Cases

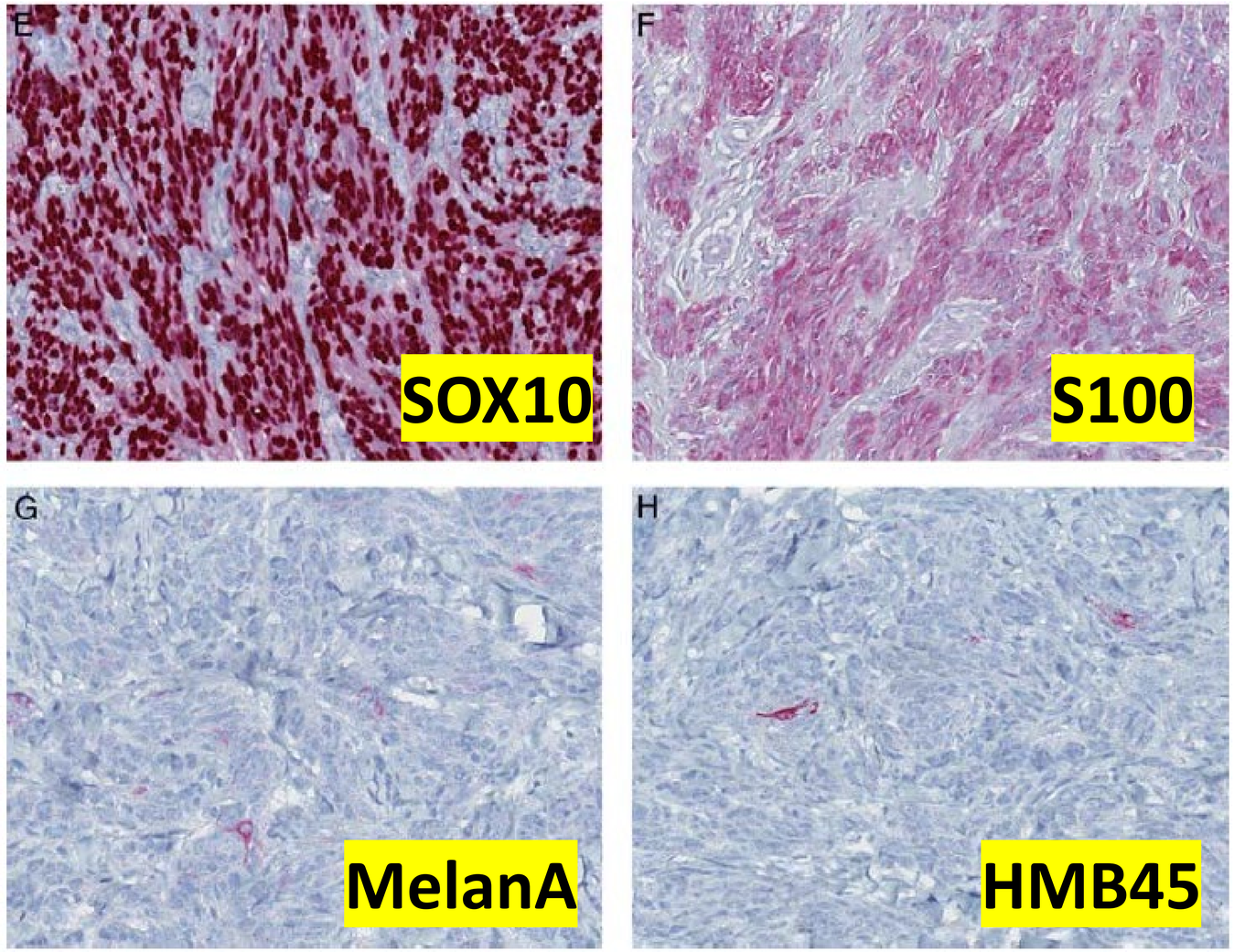
John Hanna, MD, PhD, Jennifer S. Ko, MD, PhD,† Steven D. Billings, MD,† Felix Boivin, MSc,‡ Olivia Beaudoux, MD,§ Daniel Pissaloux, PhD,‡‖ Franck Tirode, PhD,‡ Alvaro Laga, MD,* Christopher D.M. Fletcher, MD,* and Arnaud de la Fouchardiere, MD, PhD‡‖*

Am J Surg Pathol 2022;46:1457–1466



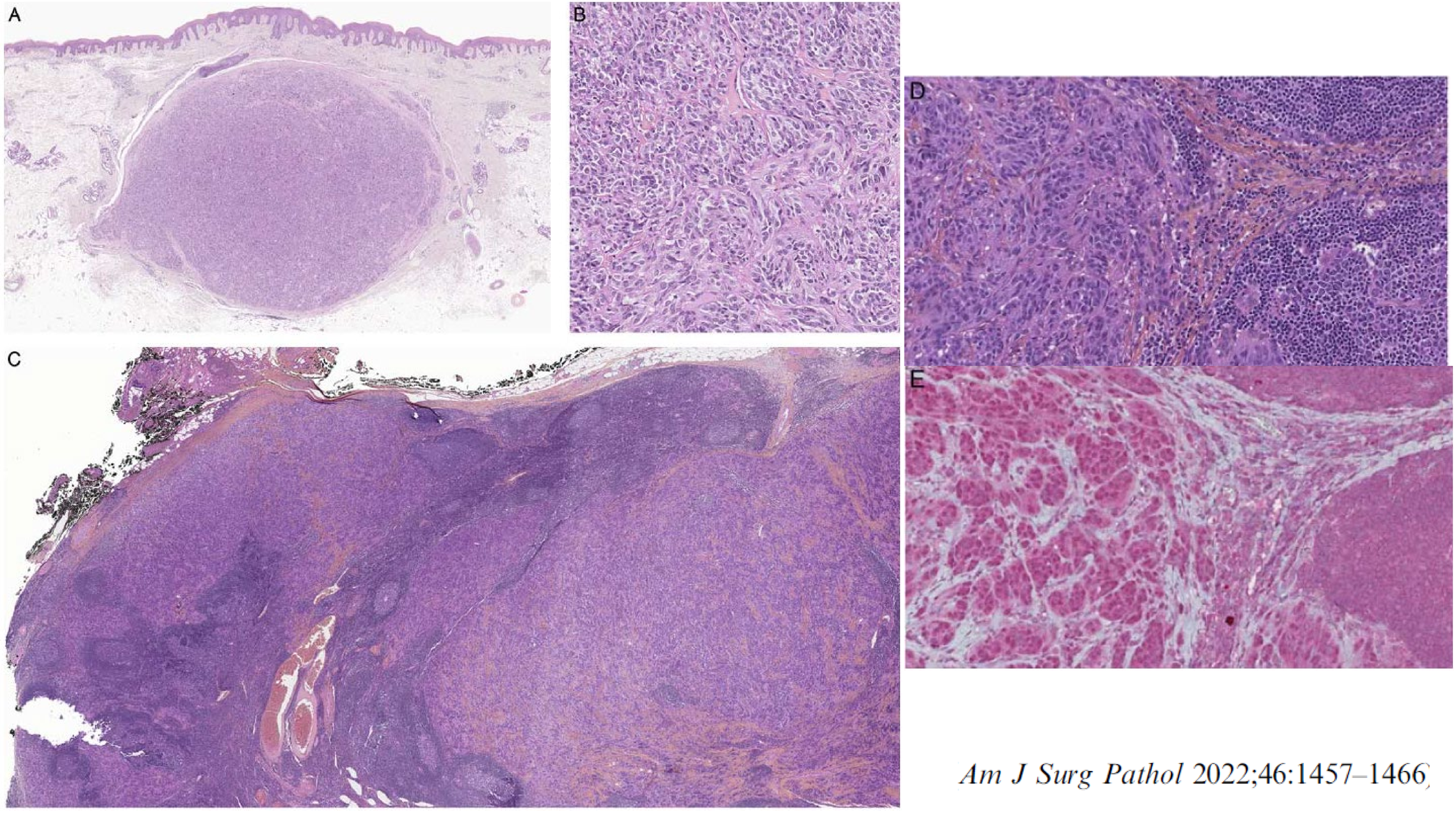


Am J Surg Pathol 2022;46:1457–1466



Immunostain	n/N (%) Diffusely Positive	Multifocally/Focally Positive	Negative
SOX10	17/17 (100)	0	0
S100	11/25 (44)	9/25 (36)	5/25 (20)
Melan-A/Mart-1	2/23 (9)	12/23 (52)	9/23 (39)
HMB-45	1/27 (4)	14/27 (52)	12/27 (44)
Pan-TRK	8/14 (57)	5/14 (36)	1/14 (7)
Trim11	17/18 (94)	0	1/18 (6)

Am J Surg Pathol 2022;46:1457–1466

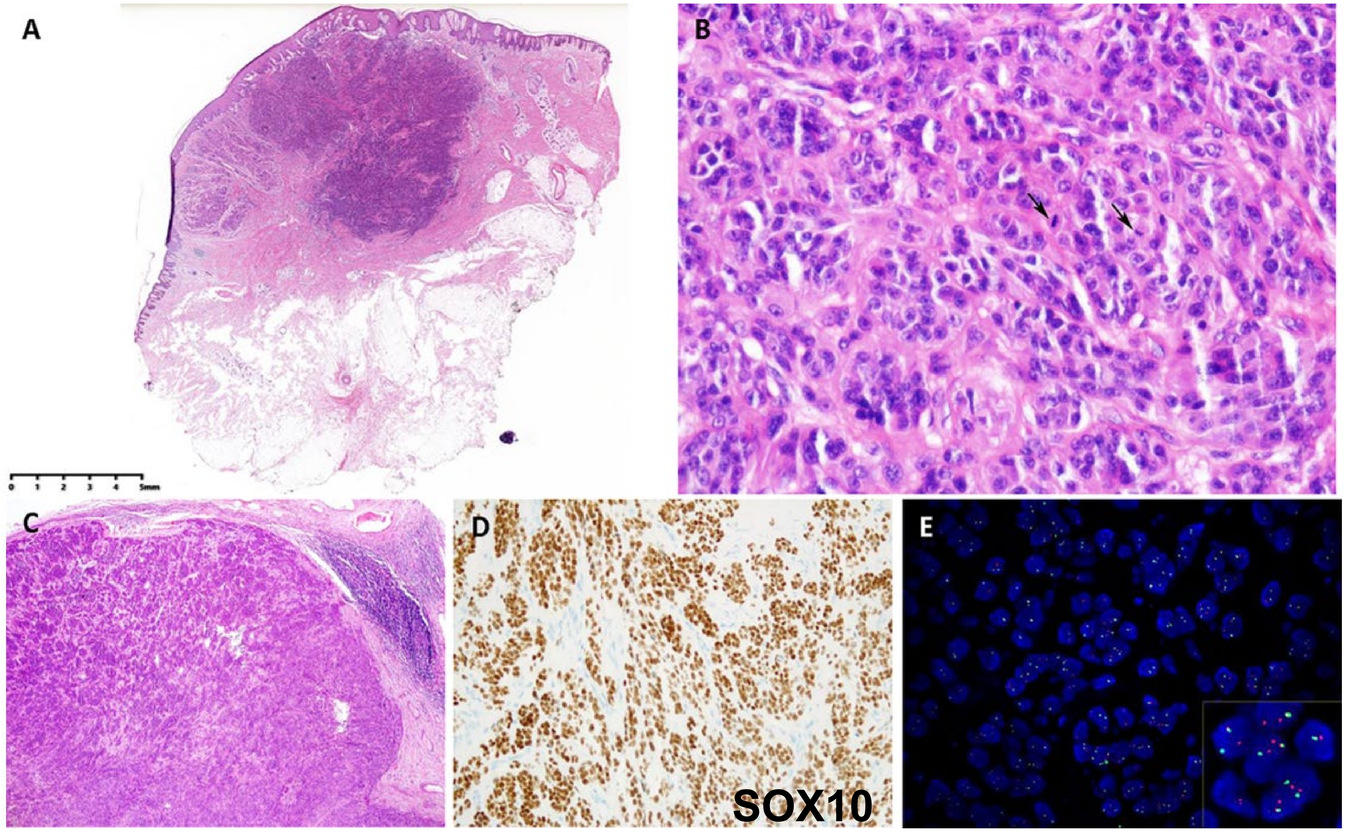


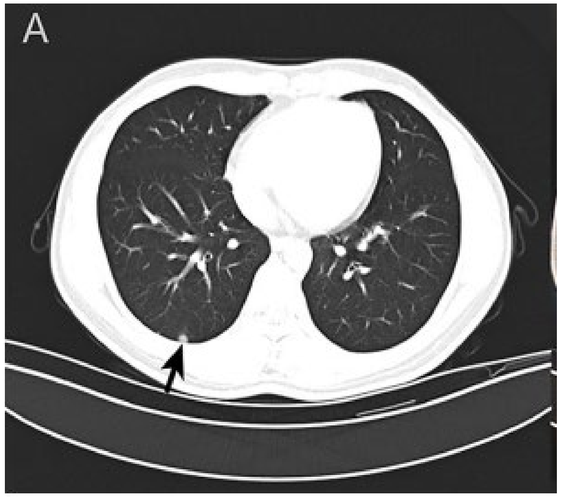
Am J Surg Pathol 2022;46:1457–1466

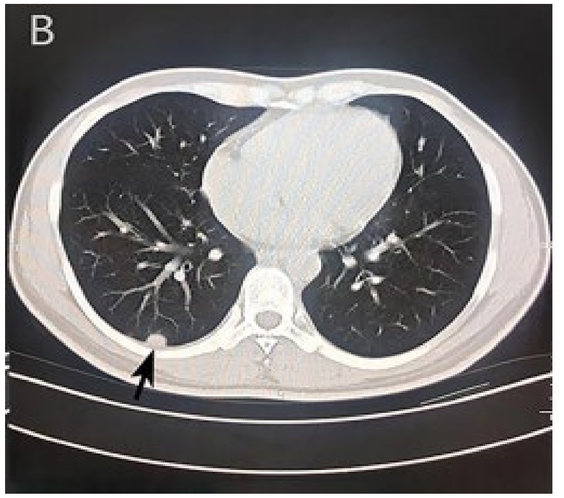
Histopathology. 2022 Sep 29. doi: 10.1111/his.14812. Online ahead of print.

Cutaneous melanocytic tumor with CRTC1::TRIM11 fusion in a case with recurrent local lymph node and distant pulmonary metastases at early stage: aggressive rather than indolent?

Li Yang [#1], Zhiyong Yin [#2], Jie Wei [1], Jia Chai [1], Danhui Zhao [1], Yixiong Liu [1], Yongqiang Tang [3], Hong Cheng [1], Wang Zhe [1], Linni Fan [1]





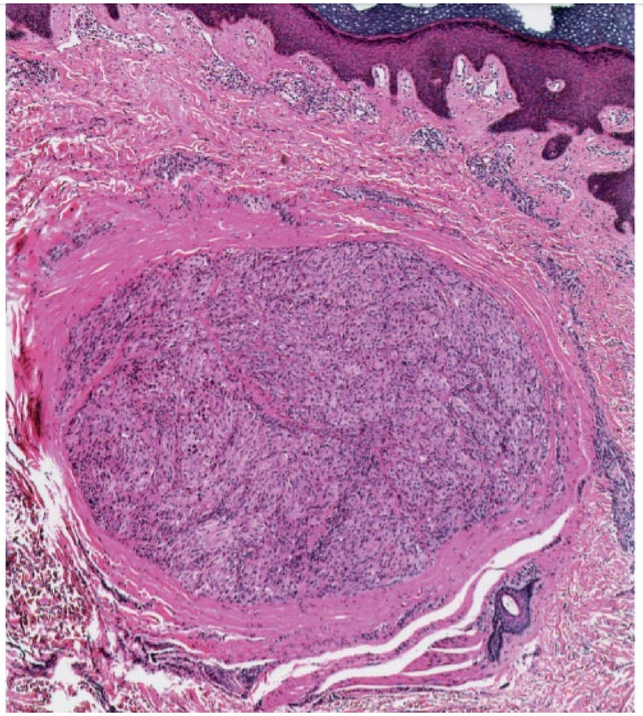


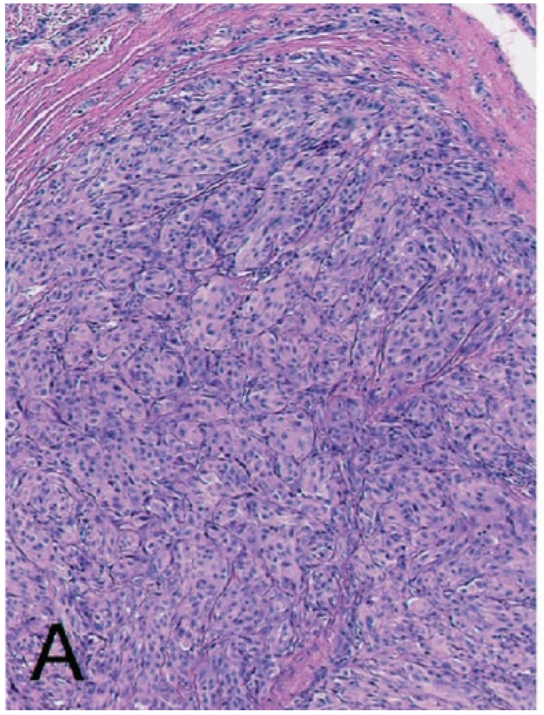
Paraganglioma-like Dermal Melanocytic Tumor

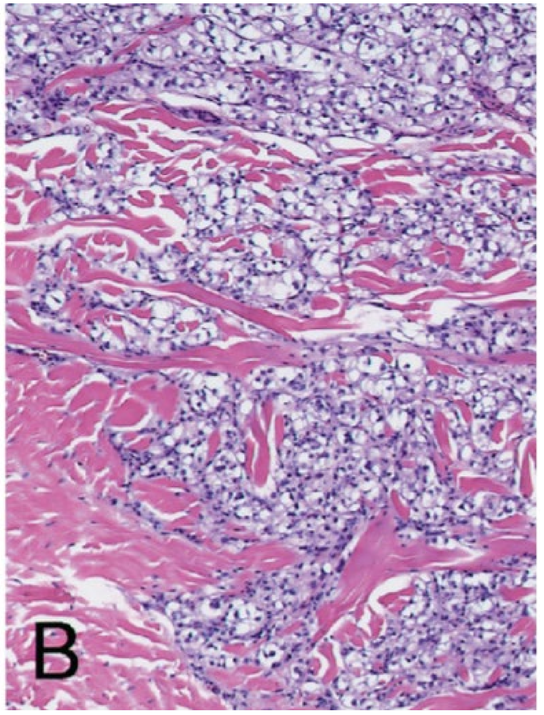
A Unique Entity Distinct From Cellular Blue Nevus, Clear Cell Sarcoma, and Cutaneous Melanoma

Andrea T. Deyrup, MD, PhD, Pamela Althof, BA,† Ming Zhou, BS,† Michael Morgan, MD,‡ Alvin R. Solomon, MD,* Julia A. Bridge, MD,† and Sharon W. Weiss, MD**

(*Am J Surg Pathol* 2004;28:1579–1586)

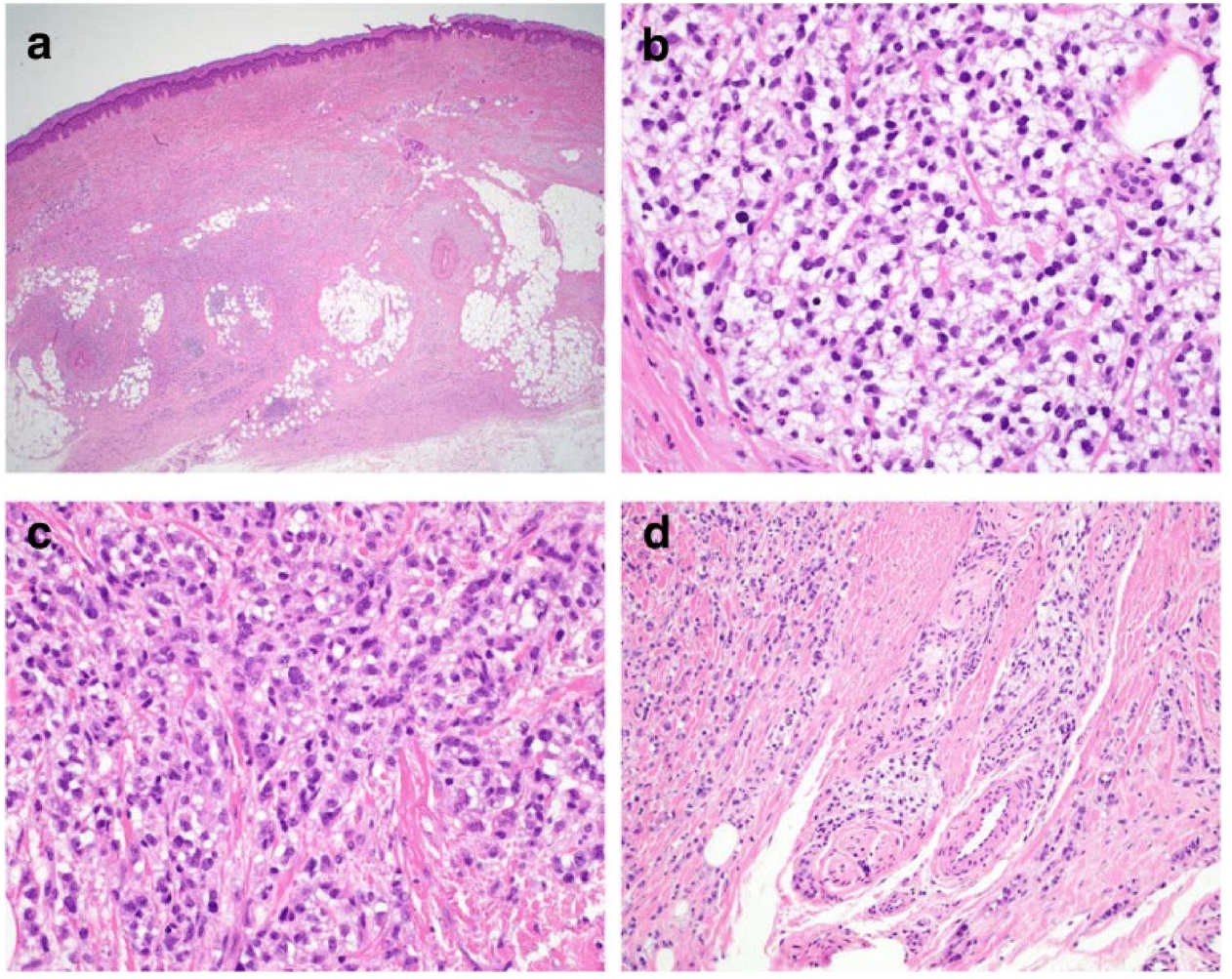




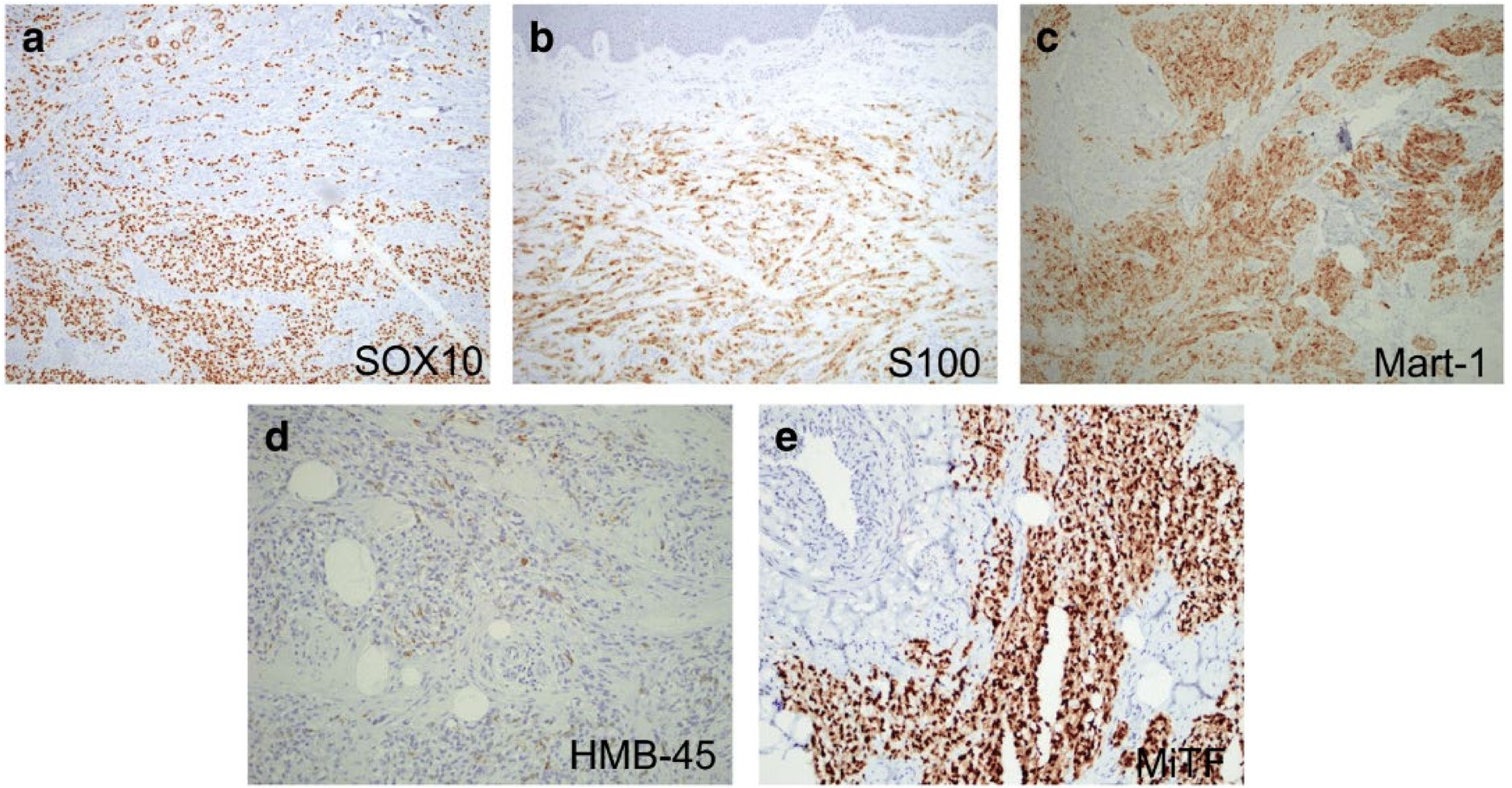


Clear cell tumor with melanocytic differentiation and MITF-CREM translocation: a novel entity similar to clear cell sarcoma

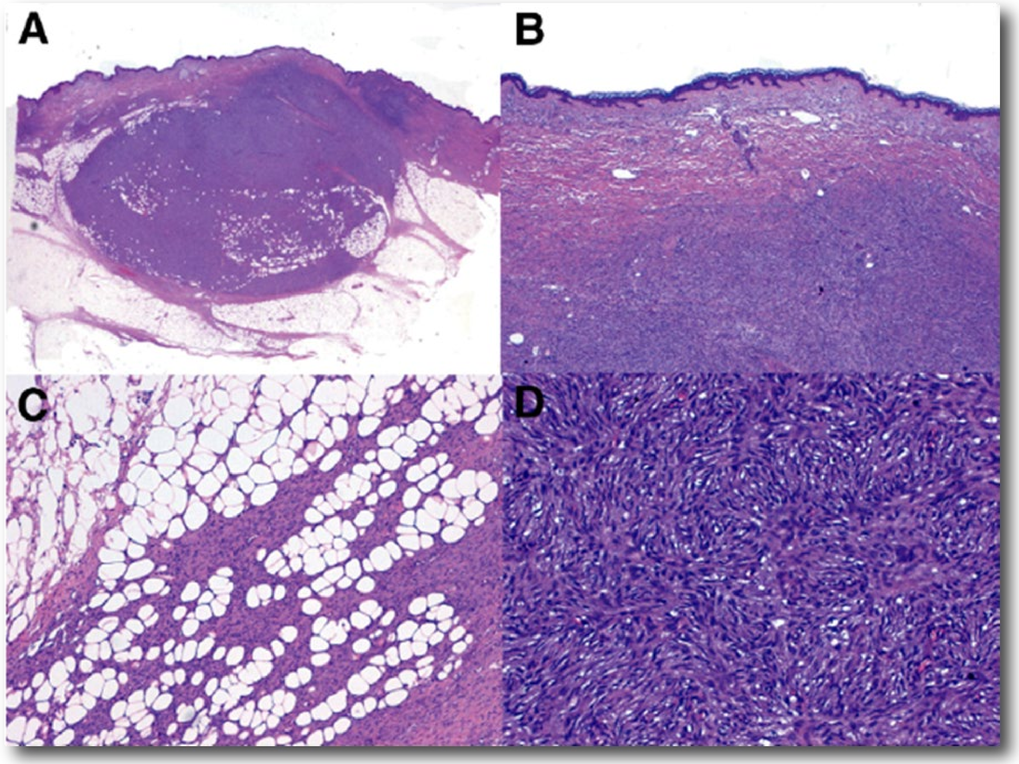
Arnaud de la Fouchardiere[1] · Daniel Pissaloux[1] · Franck Tirode[1] · John Hanna[2]



Virchows Archiv
https://doi.org/10.1007/s00428-021-03027-3


a
SOX10
b
S100
c
Mart-1
d
HMB-45
e
MiTF

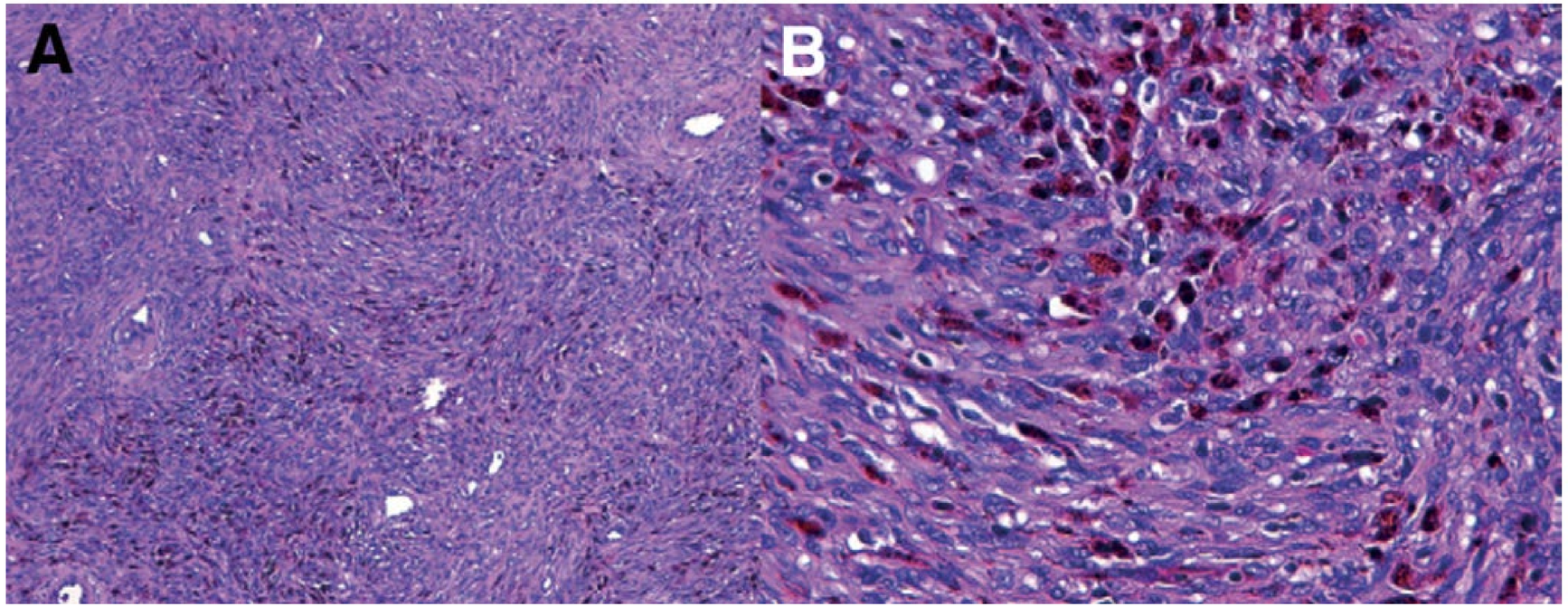
Dermatofibrosarcoma Protuberans (DFSP)



- Giant cell fibroblastoma
- **Pigmented DFSP**
- DFSP with myoid nodules
- Fibrosarcomatous DFSP
- Myxoid DFSP

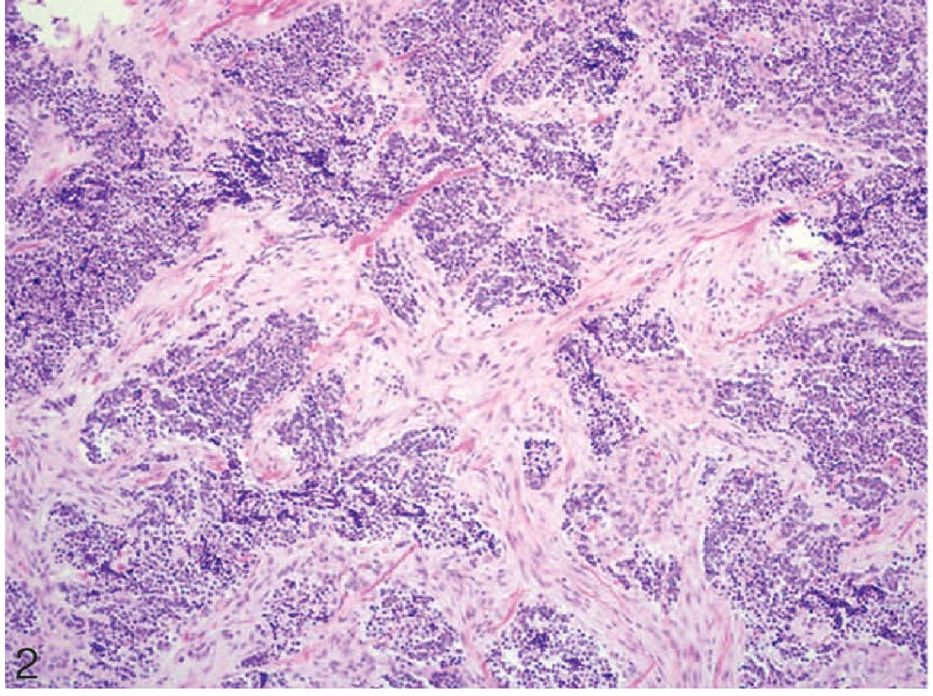
Seminars in Diagnostic Pathology (2013) 30, 13-28

Pigmented DFSP (Bednar Tumor)



Melanotic Neuroectodermal Tumor of Infancy

- Rapidly growing pigmented neoplasm
- Typically in infants <1 year-old
- Predominantly involves craniofacial sites
- Biphasic population of **melanocytic** and **primitive neuroectodermal cells**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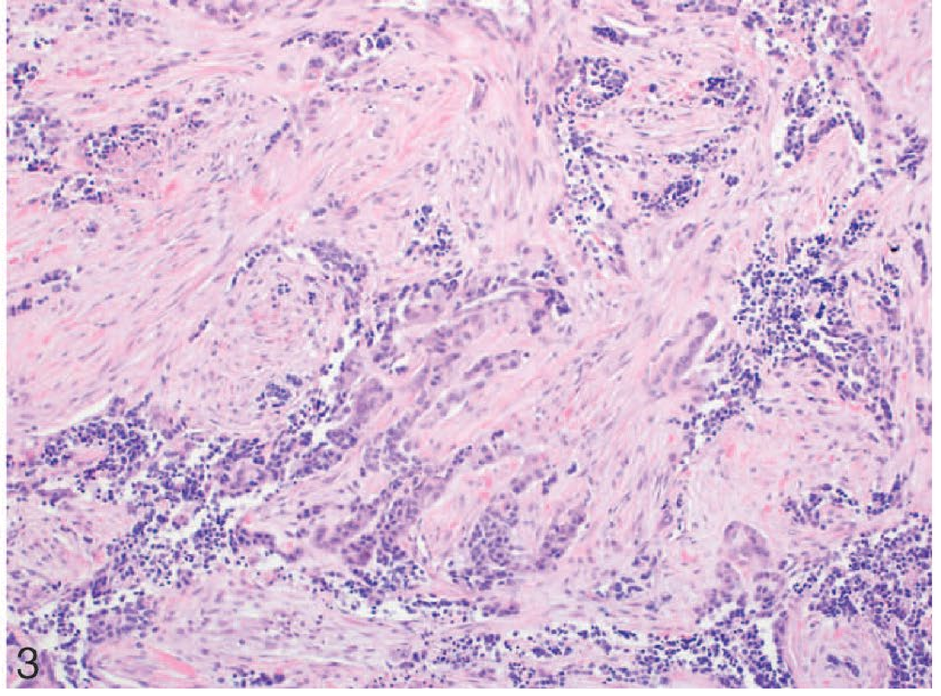
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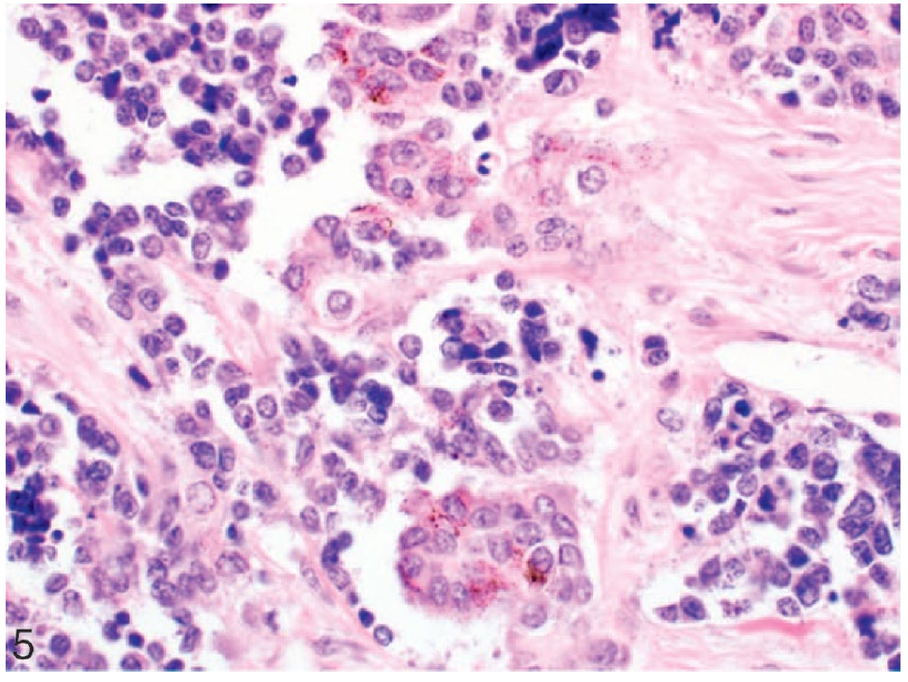
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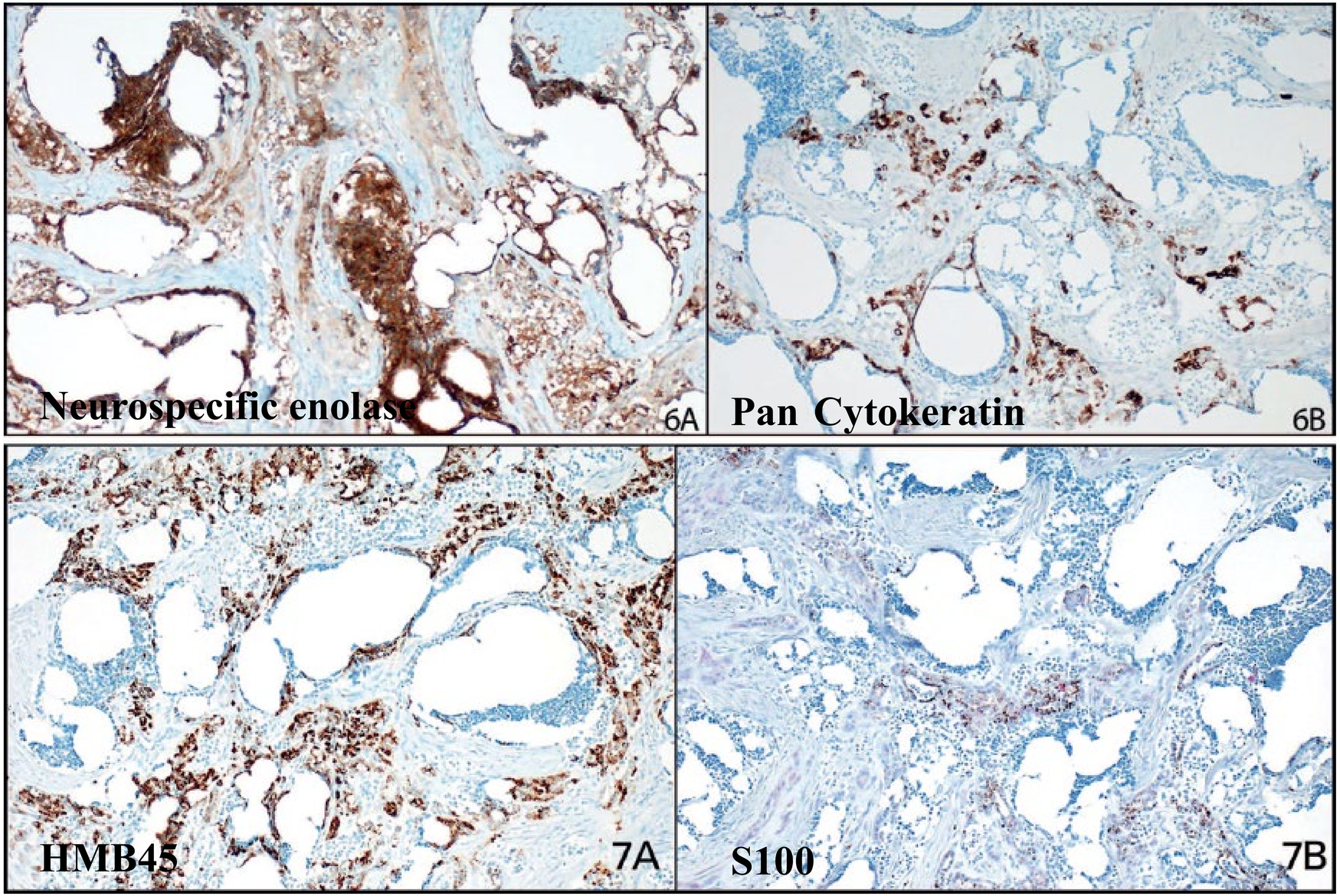
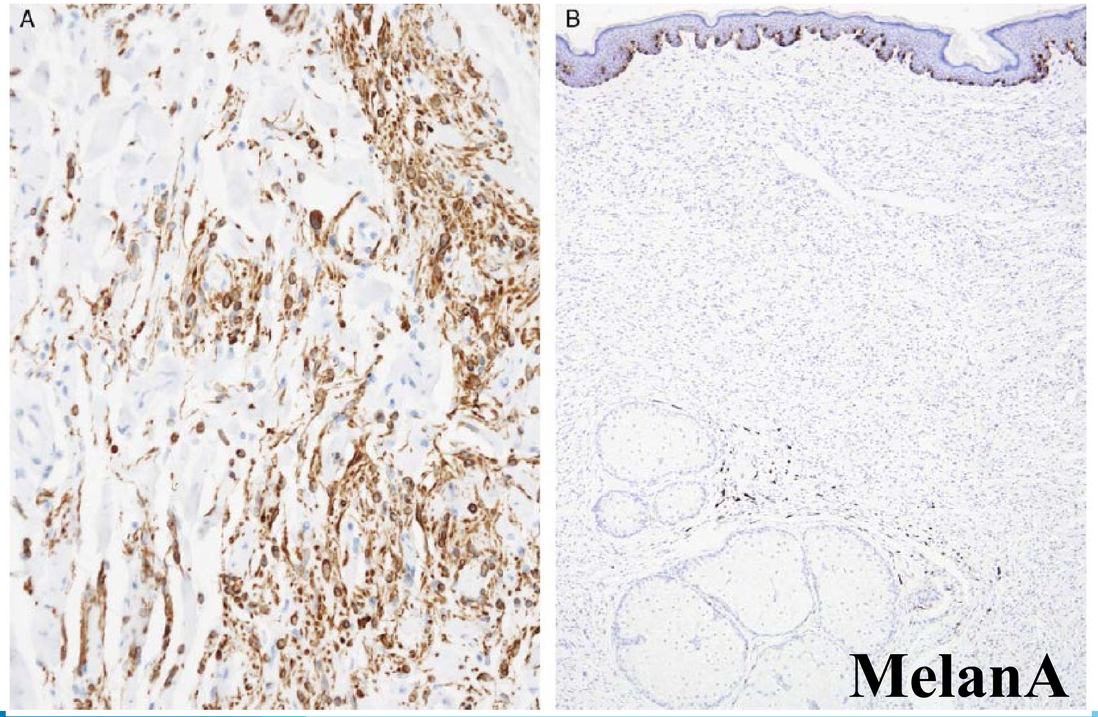

Neurospecific enolase
6A
Pan Cytokeratin
6B
HMB45
7A
S100
7B

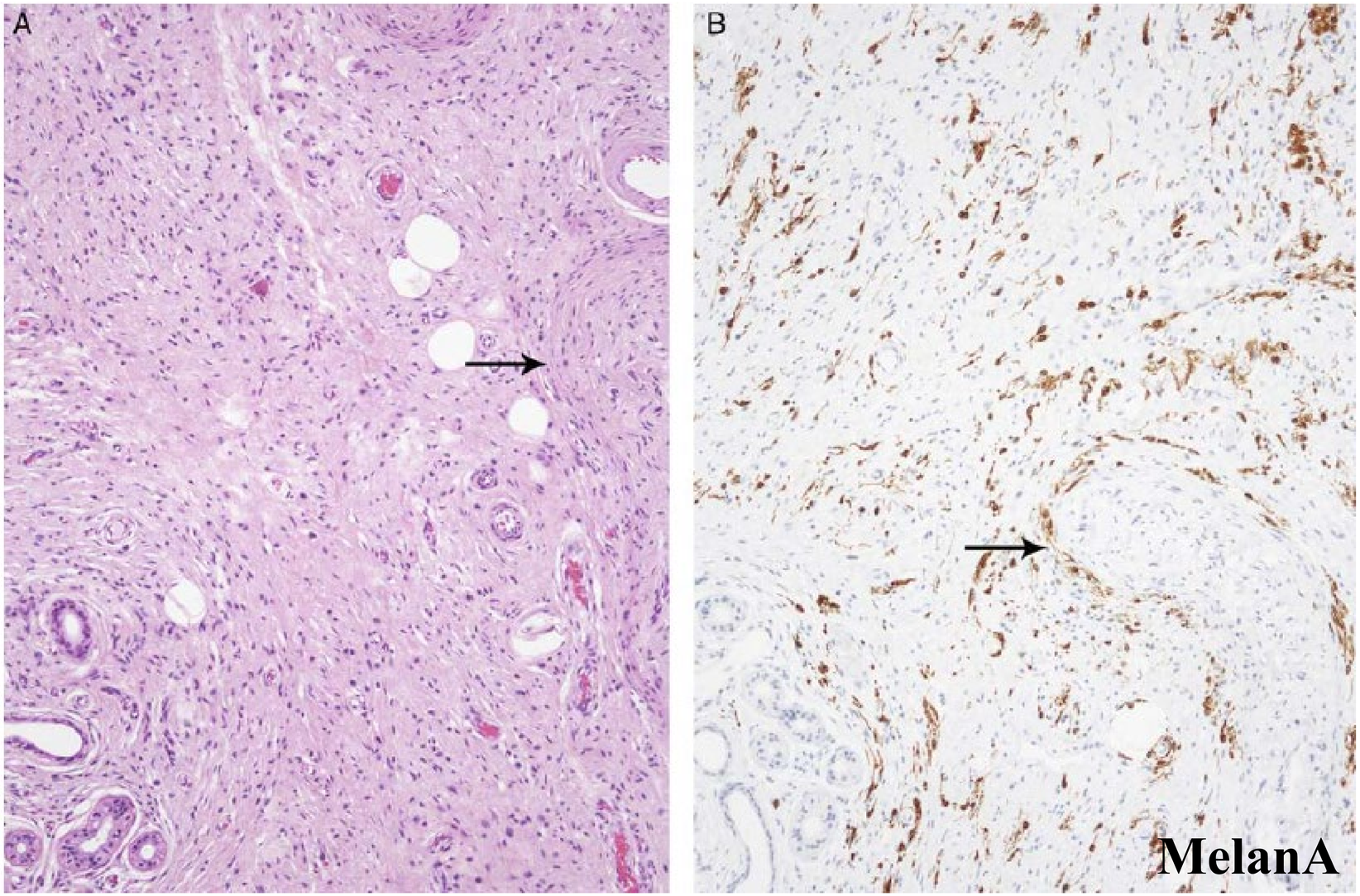
Melanocytic Differentiation Is Present in a Significant Proportion of Nonpigmented Diffuse Neurofibromas

A Potential Diagnostic Pitfall

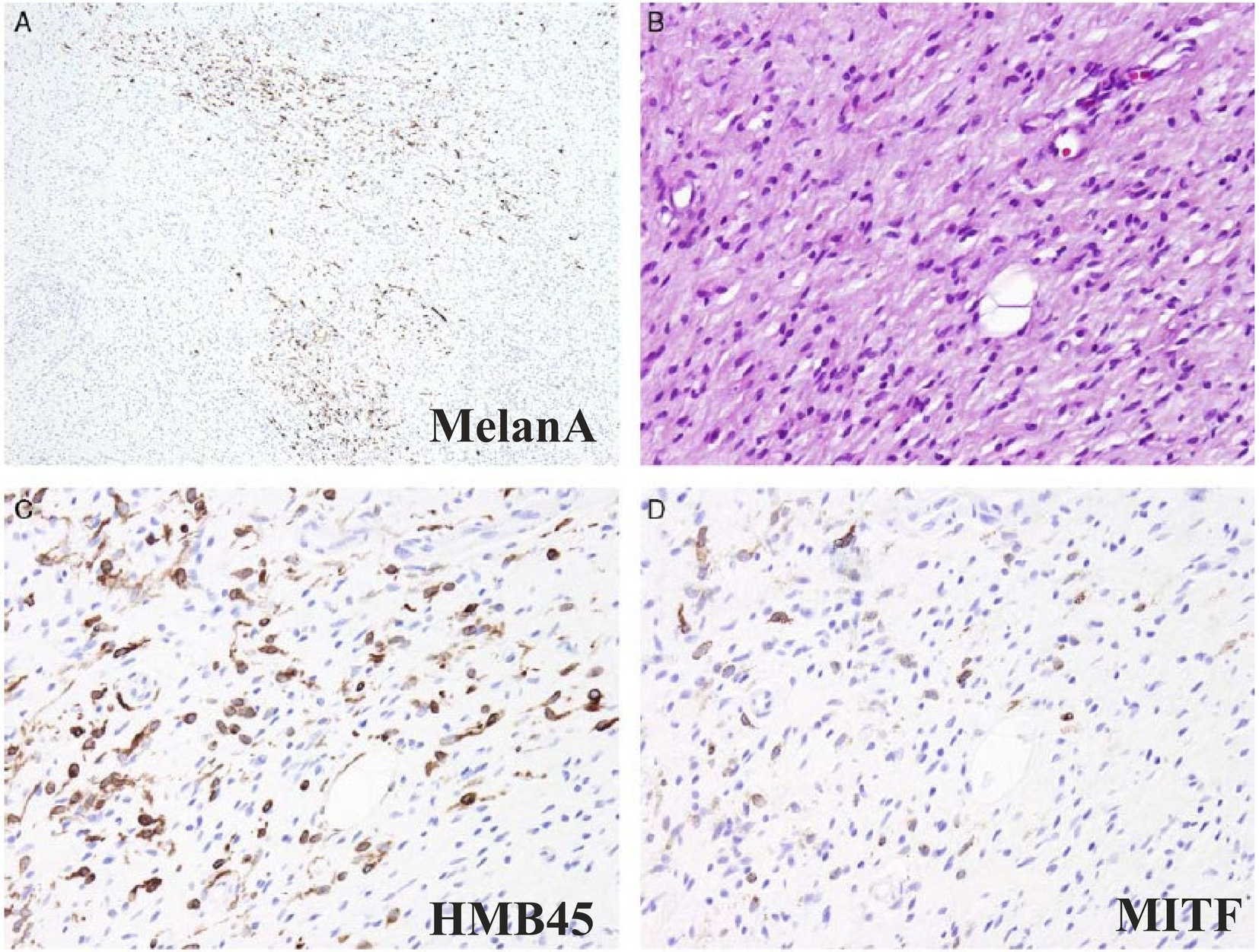
Jože Pižem, MD, PhD, Kimberly M. Nicholson, MD,† Jerica Mraz, BSc Microbiol,* and Victor G. Prieto, MD, PhD‡*



(*Am J Surg Pathol* 2013;37:1182–1191)



(*Am J Surg Pathol* 2013;37:1182–1191)


A
MelanA
B
C
HMB45
D
MITF

DOI: 10.1111/cup.14232

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REVIEW

Nevus, melanoma, or something else? Mesenchymal neoplasms with melanocytic differentiation

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Abstract

The overwhelming majority of cutaneous neoplasms with melanocytic differentiation are nevi, melanomas, or less commonly melanocytomas. Nevertheless, there is also a group of mesenchymal neoplasms with genuine melanocytic differentiation which can create diagnostic difficulties with significant repercussions. These can rarely present as primary or metastatic cutaneous lesions. The ones that are relevant to a dermatopathologist include malignant melanotic nerve sheath tumor, perivascular epithelioid cell neoplasm, and clear cell sarcoma. This work will provide a thorough review of clinical presentation, morphologic and immunohistochemical features as well as molecular pathogenesis of these tumors. We hope to familiarize the general dermatopathology readership with a group of neoplasms of mesenchymal lineage exhibiting melanocytic differentiation and ultimately avoid diagnostic misadventures.

KEYWORDS
clear cell sarcoma, differentiation, malignant melanotic nerve sheath tumor, melanocytic, mesenchymal, PEComa

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Thank you

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