Případ 767

Zdeněk K I N K O R

XXVII. Martinský bioptický seminář

2021

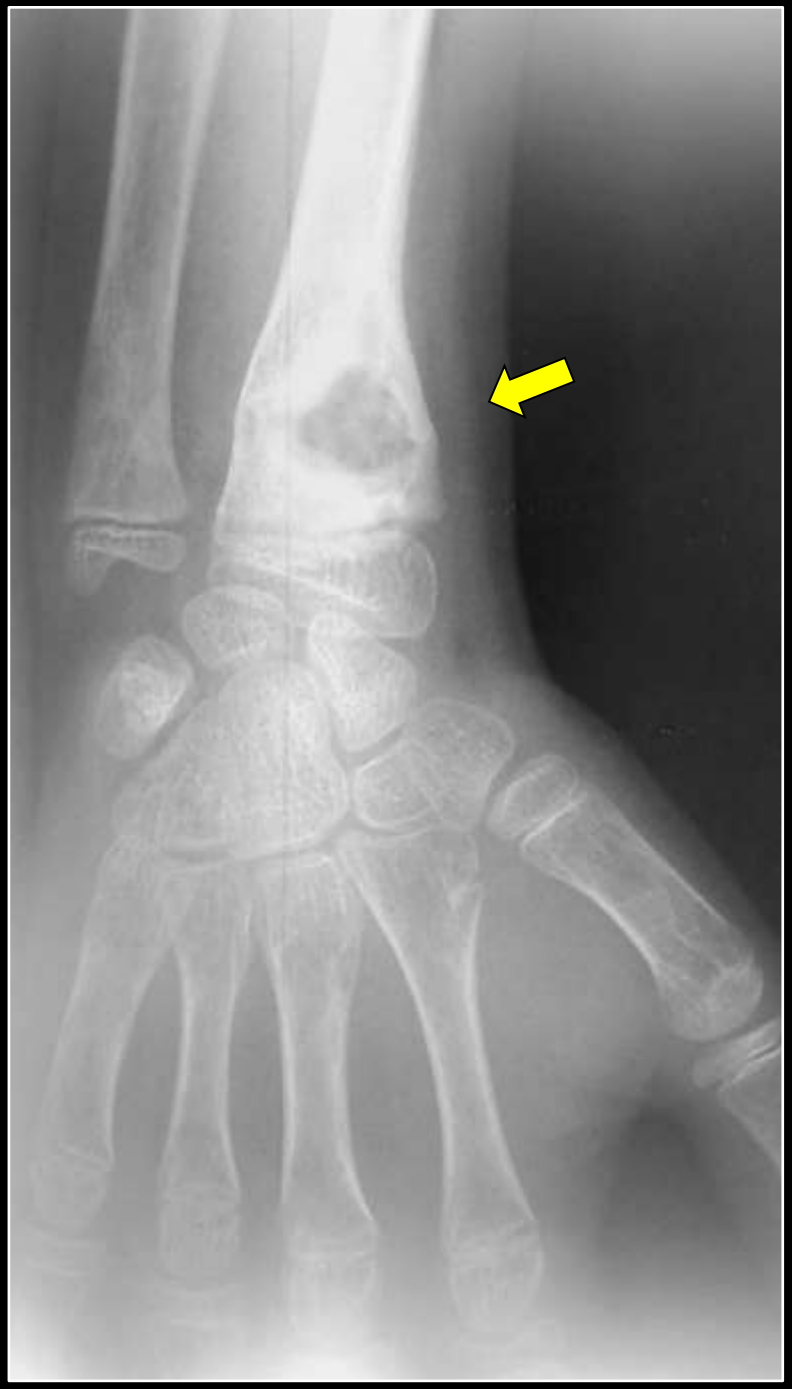
Pozadí případu

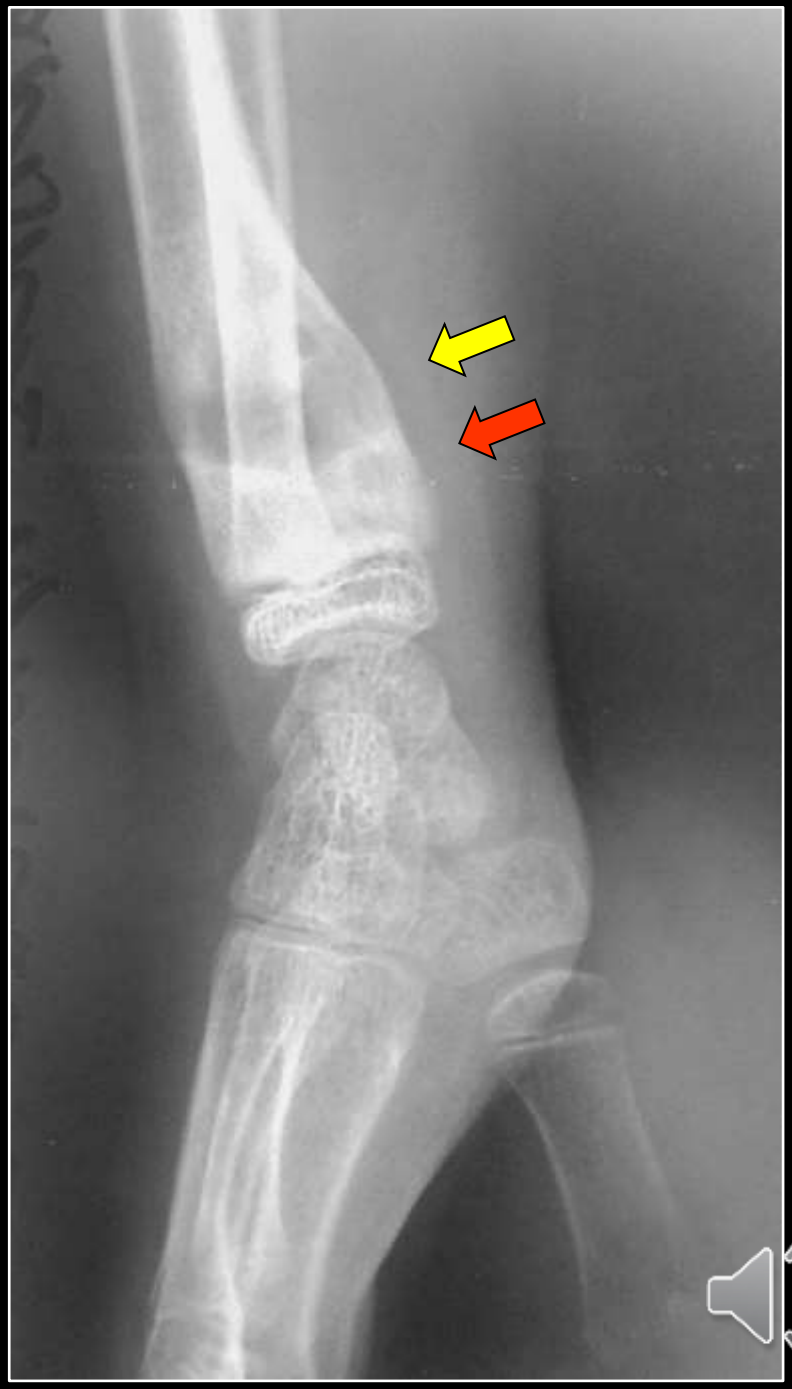
- chlapec **12** let
  bolesti zápěstí, klin. dg. cystický **enchondrom** dist. radia
  - **dvě** ložiska → část RTG dokumentace se ztratila …**?**

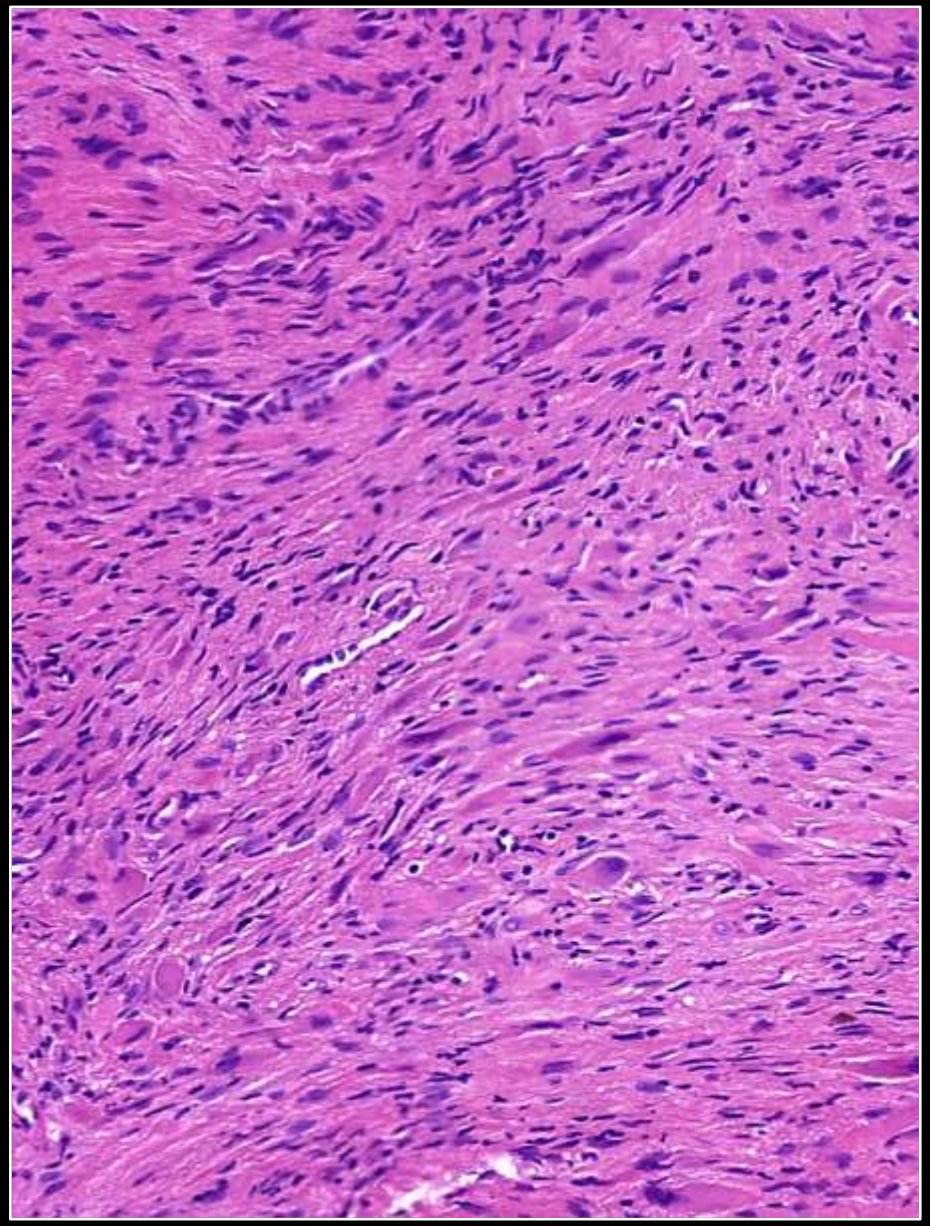
- Dg. vyšetřujícího patologa - osteoblastom vs. osteosarkom?
  II. čtení - s rozpaky **epiteloidní hemangioendoteliom …**

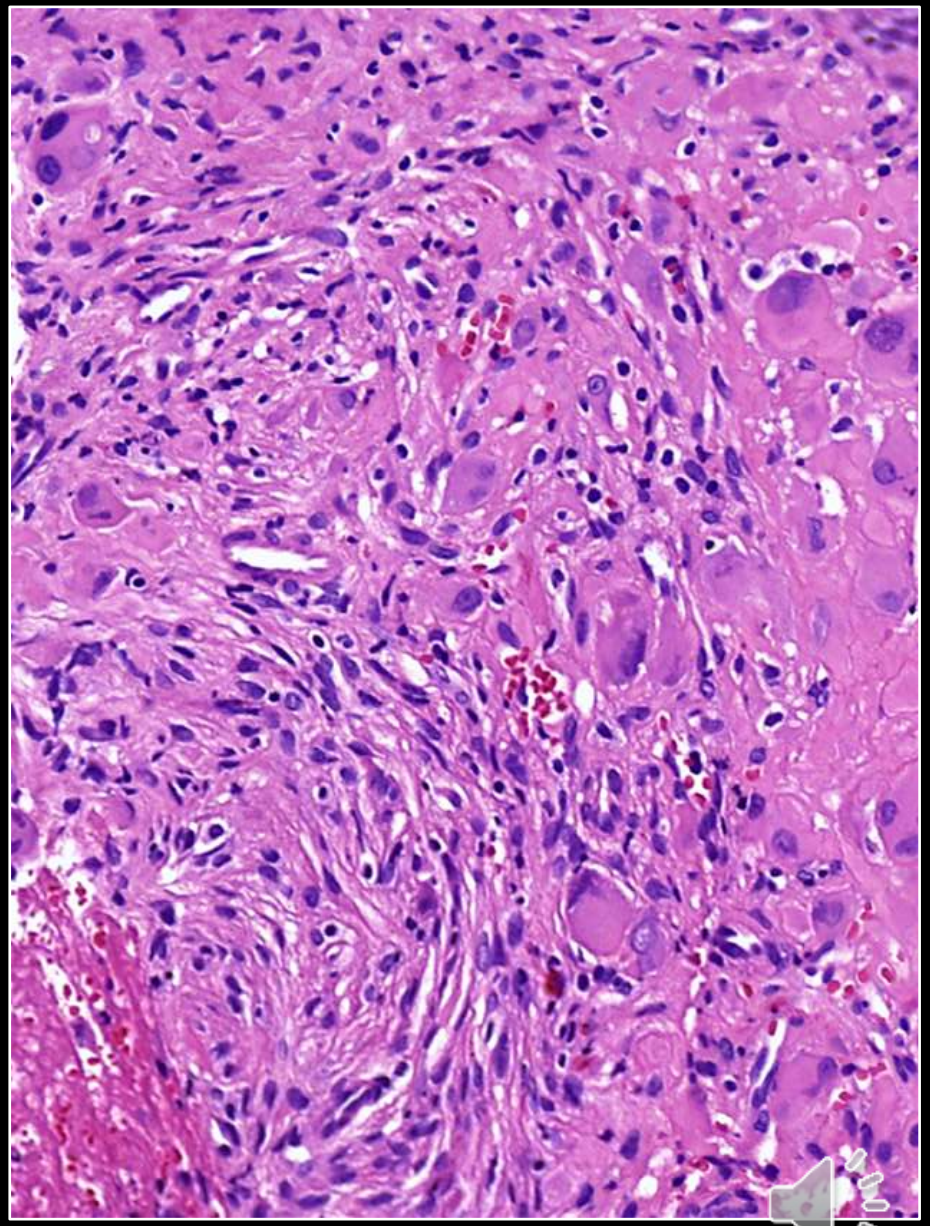
- předneseno na fóru patologů - dg. **nebyla všeobecně přijata ?**

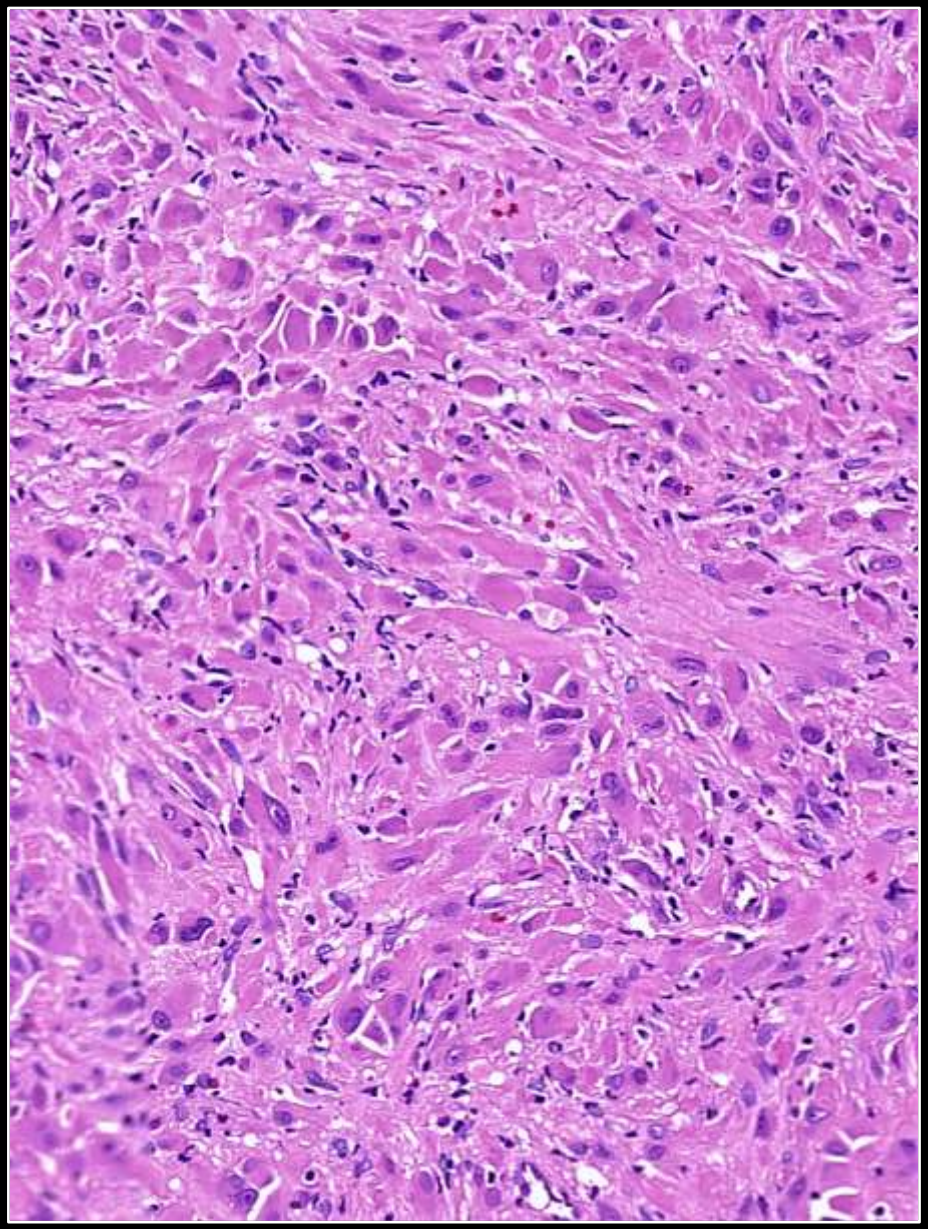
- po **4** letech revize diagnózy **…**

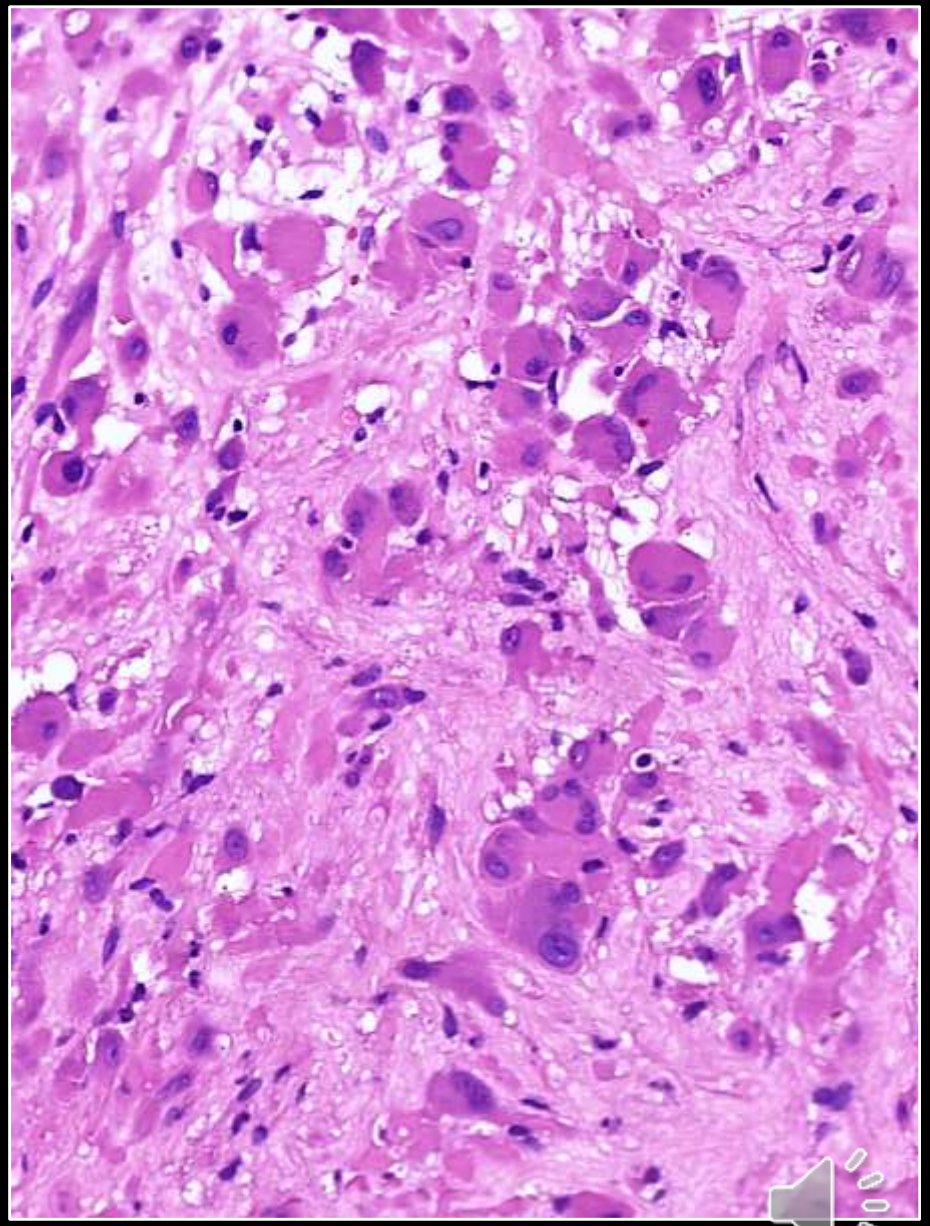


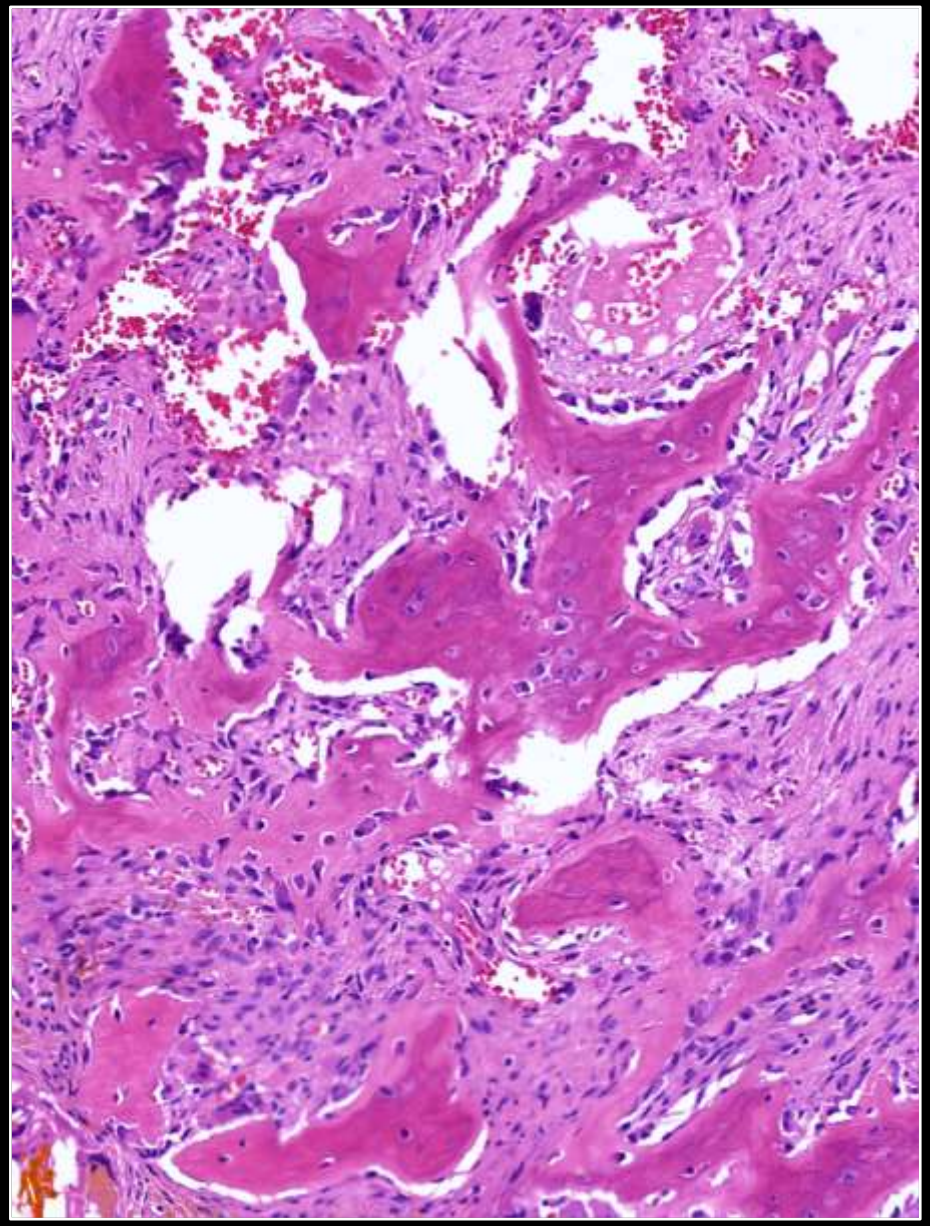


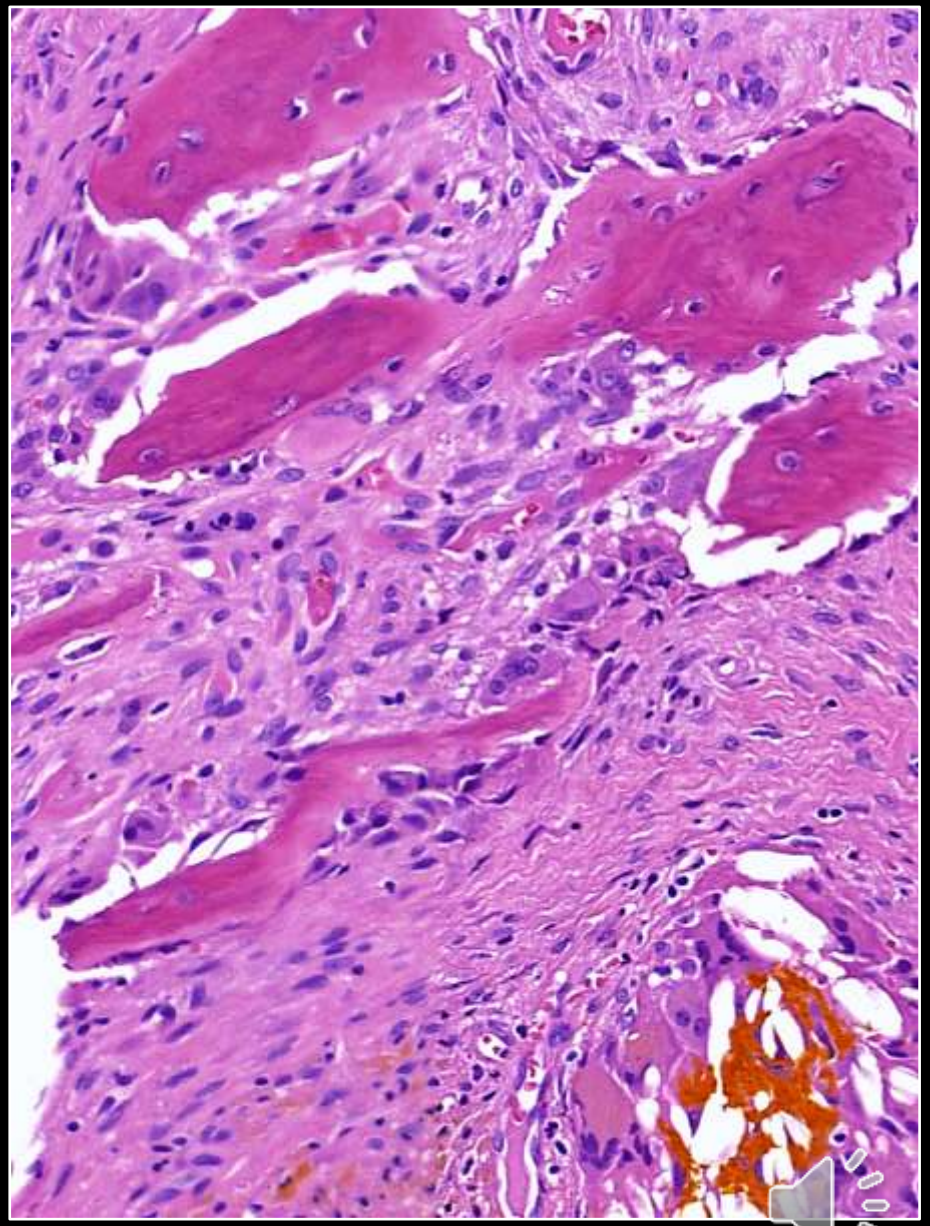


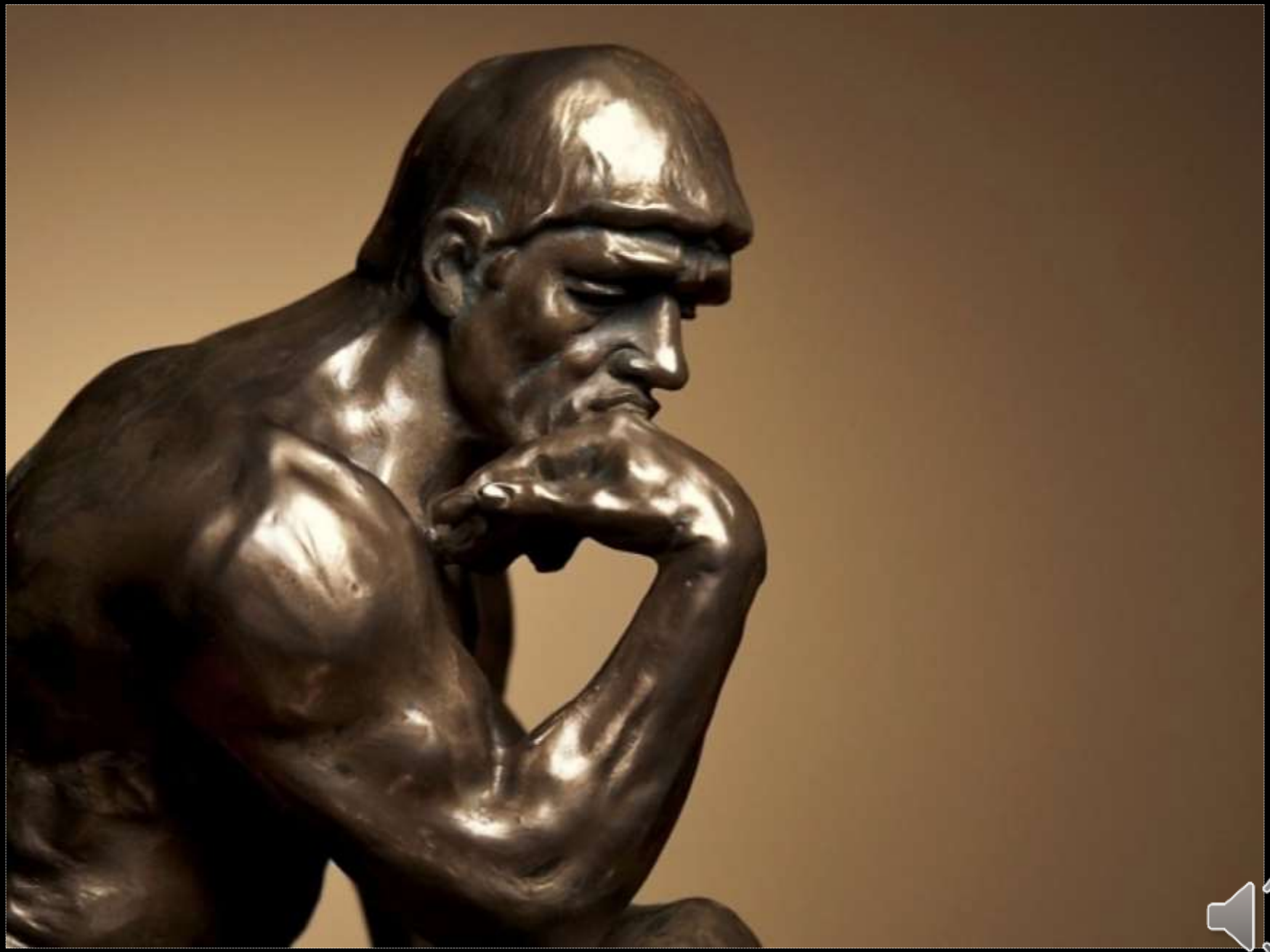


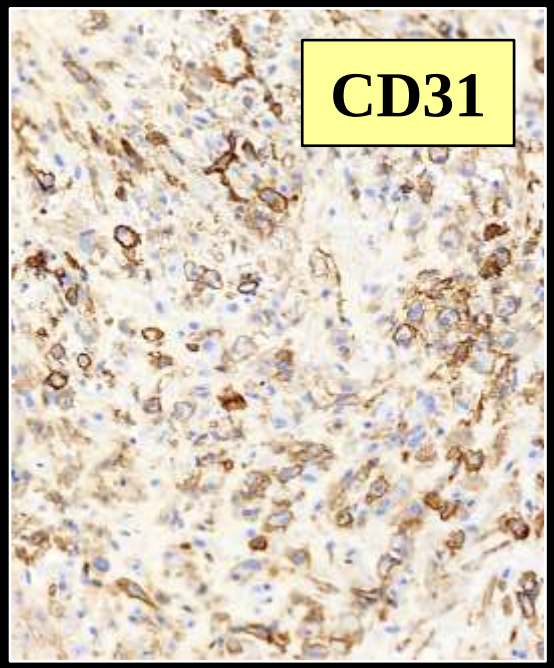


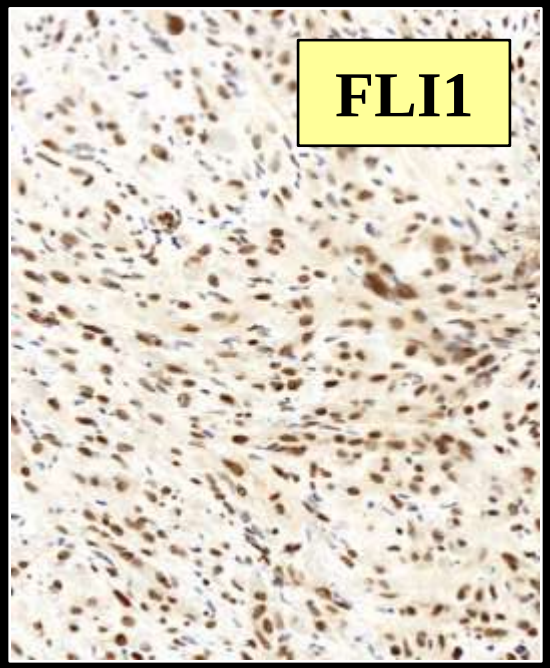


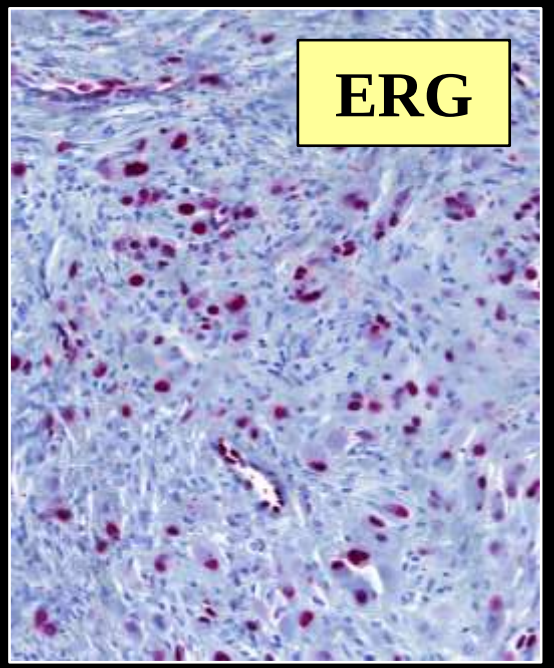


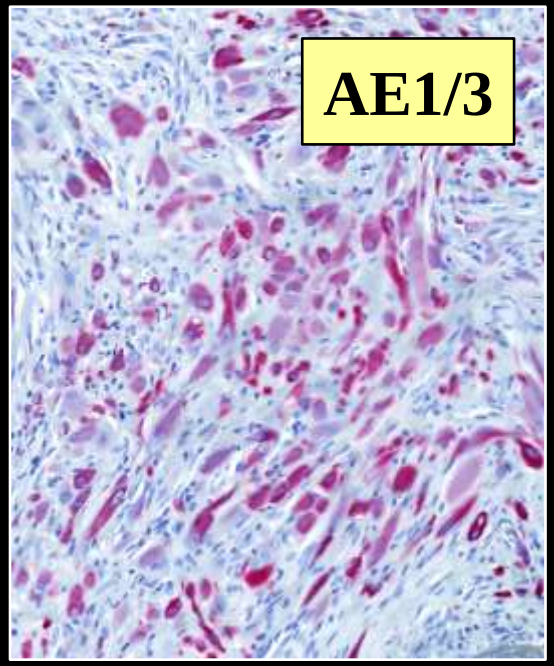




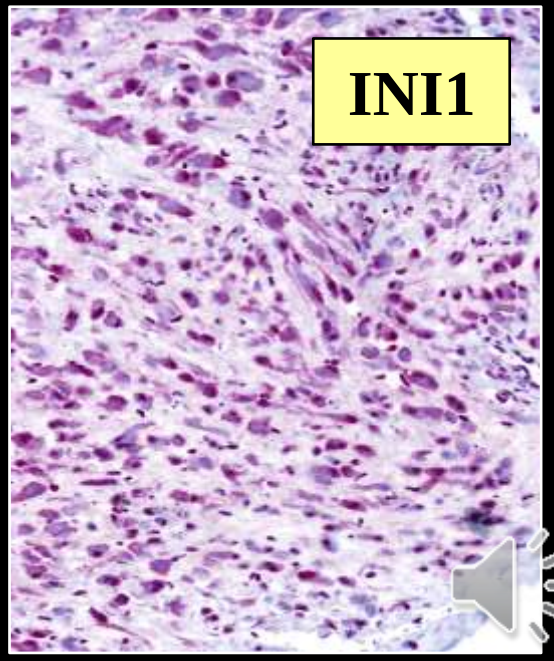

CD31

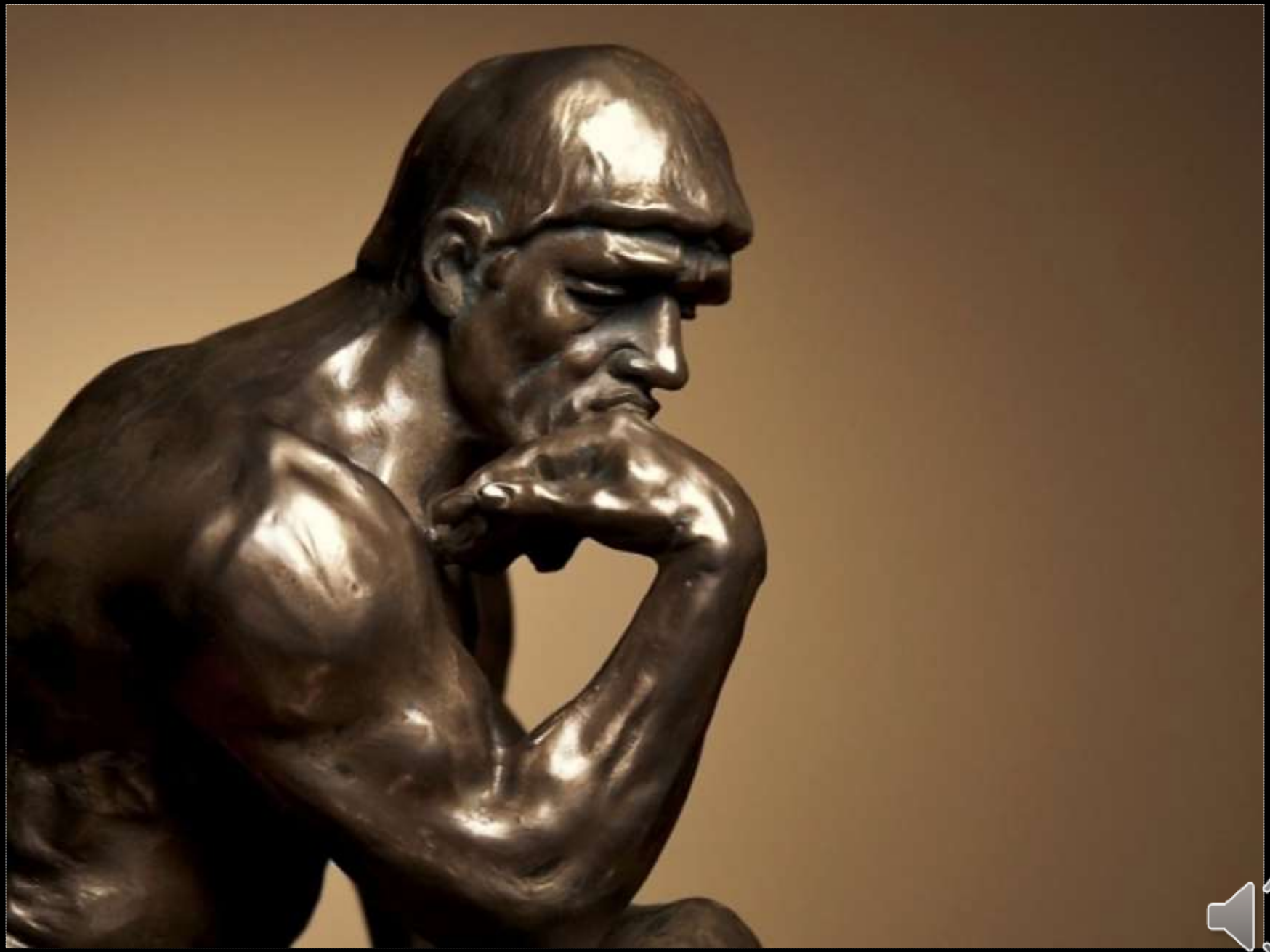

FLI1


ERG

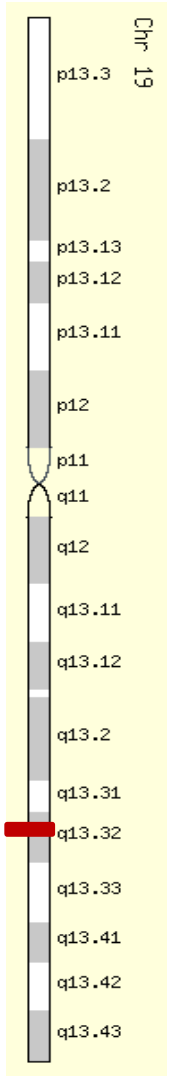

AE1/3


CK OSKAR

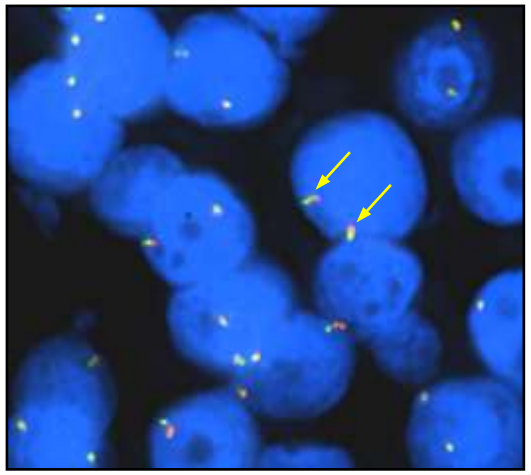

INI1



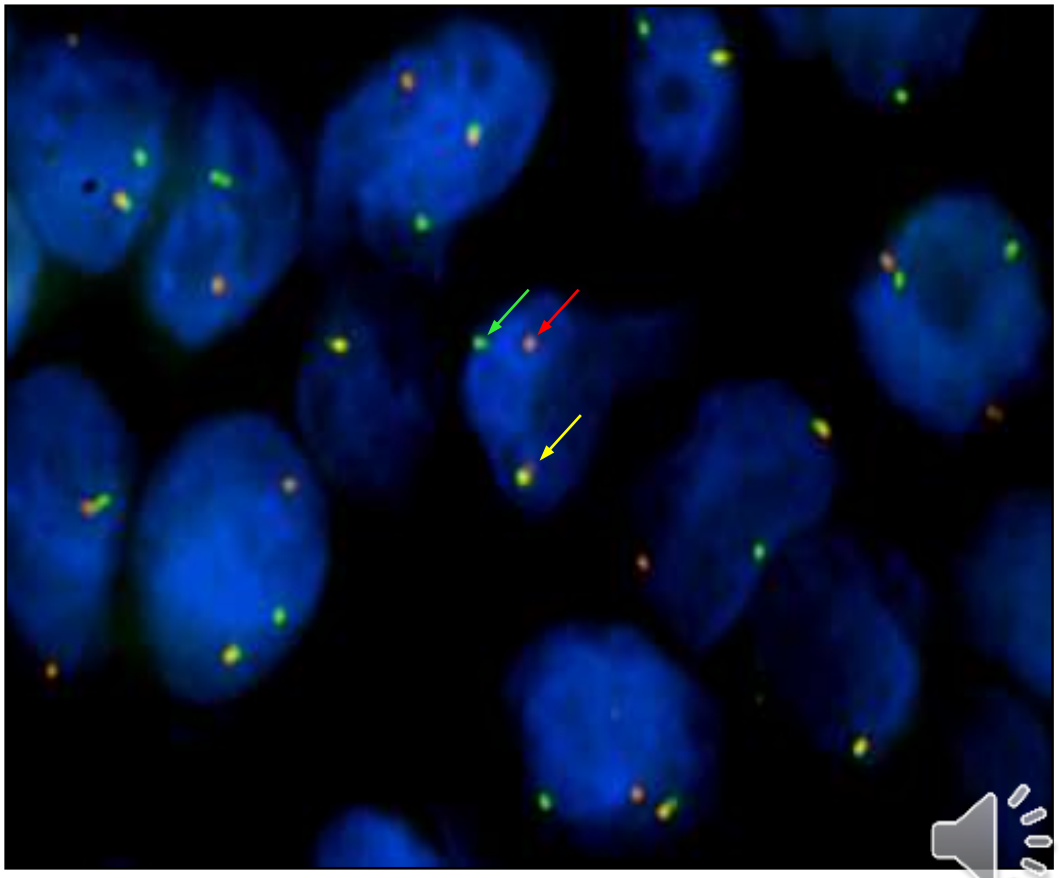
FISH (break apart) **analýza zlomu genu *FOSB*** *(19q13.32)*

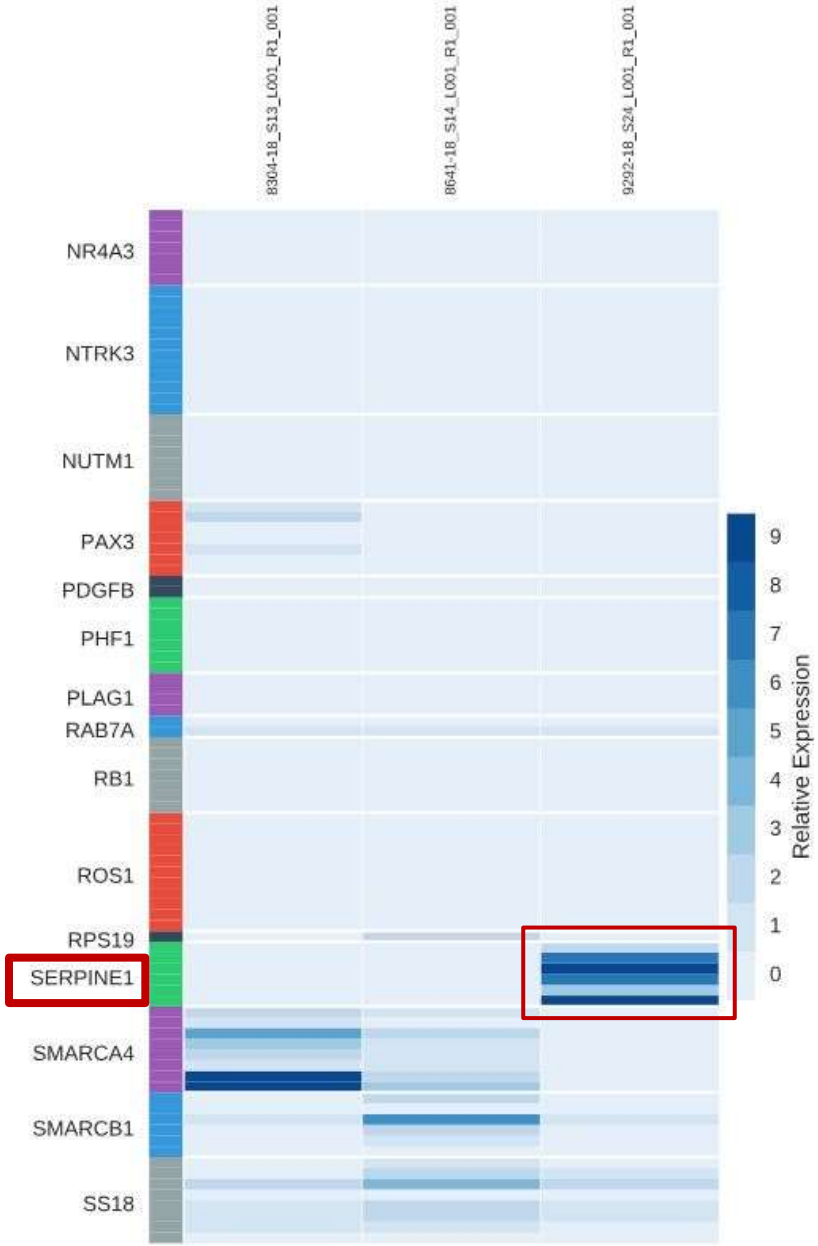


kontrola



tumor

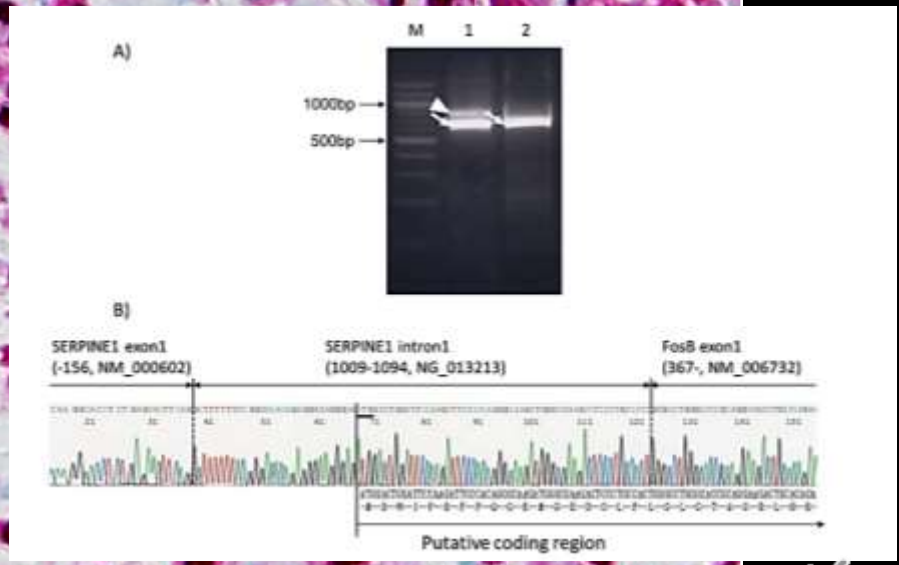




NGS

Archer FusionPlex
SAR5 panel

RT-PCR / Sanger seq.



Definitivní diagnóza

Pseudomyogenní hemangioendoteliom

Diferenciální diagnóza

Epiteloidní sarkom

Leiomyosarkom

Osteoblastom

Neosifikující fibrom

Metastáza karcinomu

Jiné vaskulární léze

ORIGINAL ARTICLE

Mirra JM et al.

The fibroma-like variant of epithelioid sarcoma: a fibrohistiocytic/myoid cell lesion often confused with benign and malignant spindle cell tumors.

Cancer 1992; 9: 1382-1395.

incompletely characterized. We examined 50 cases of this distinctive tumor to evaluate histologic, immunophenotypic, and clinical features. There was a 4.6:1 male predominance (mean age, 31 y; 82% ≤40 y). Half of the patients presented with

1 patient was alive with unknown disease status, 2 patients were alive with recurrent disease, and 1 patient died of the disease. In summary, we describe a distinctive type of rarely metastasizing ("intermediate") tumor affecting mainly young men and usually

ORIGINAL ARTICLE

Billings SD et al.

Epithelioid sarcoma-like hemangioendothelioma.

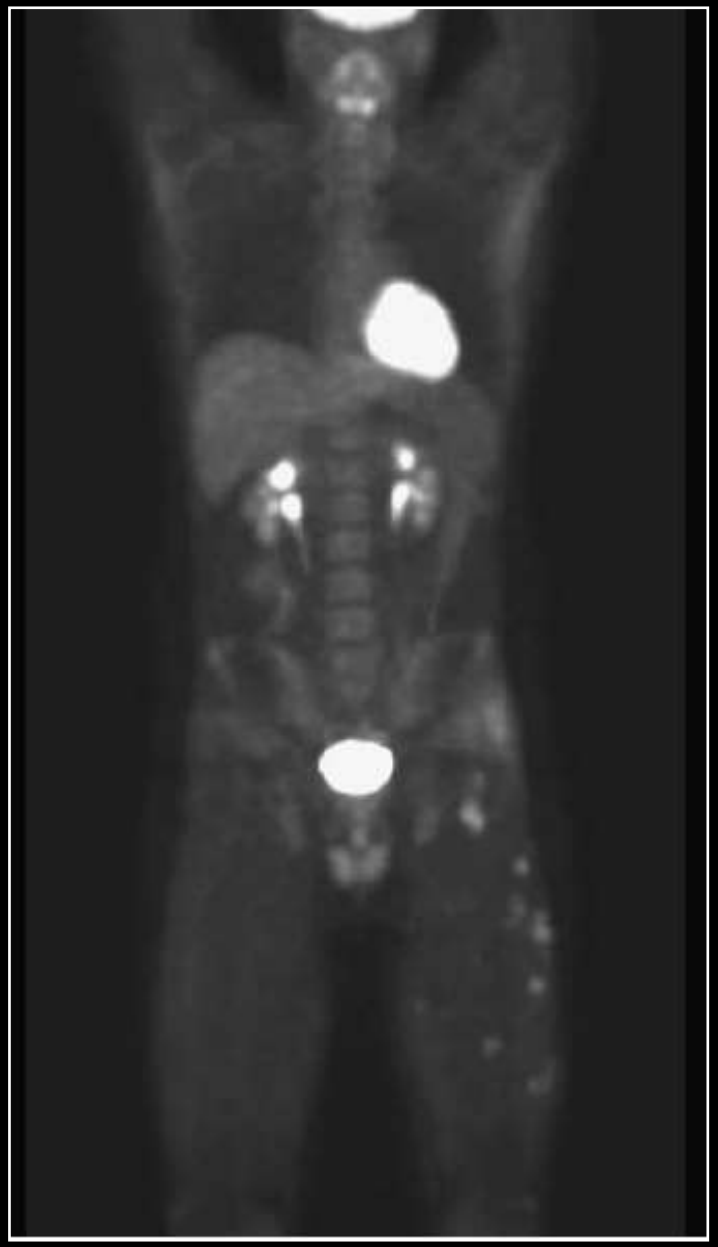
Am J Surg Pathol 2003; 27: 48-57.

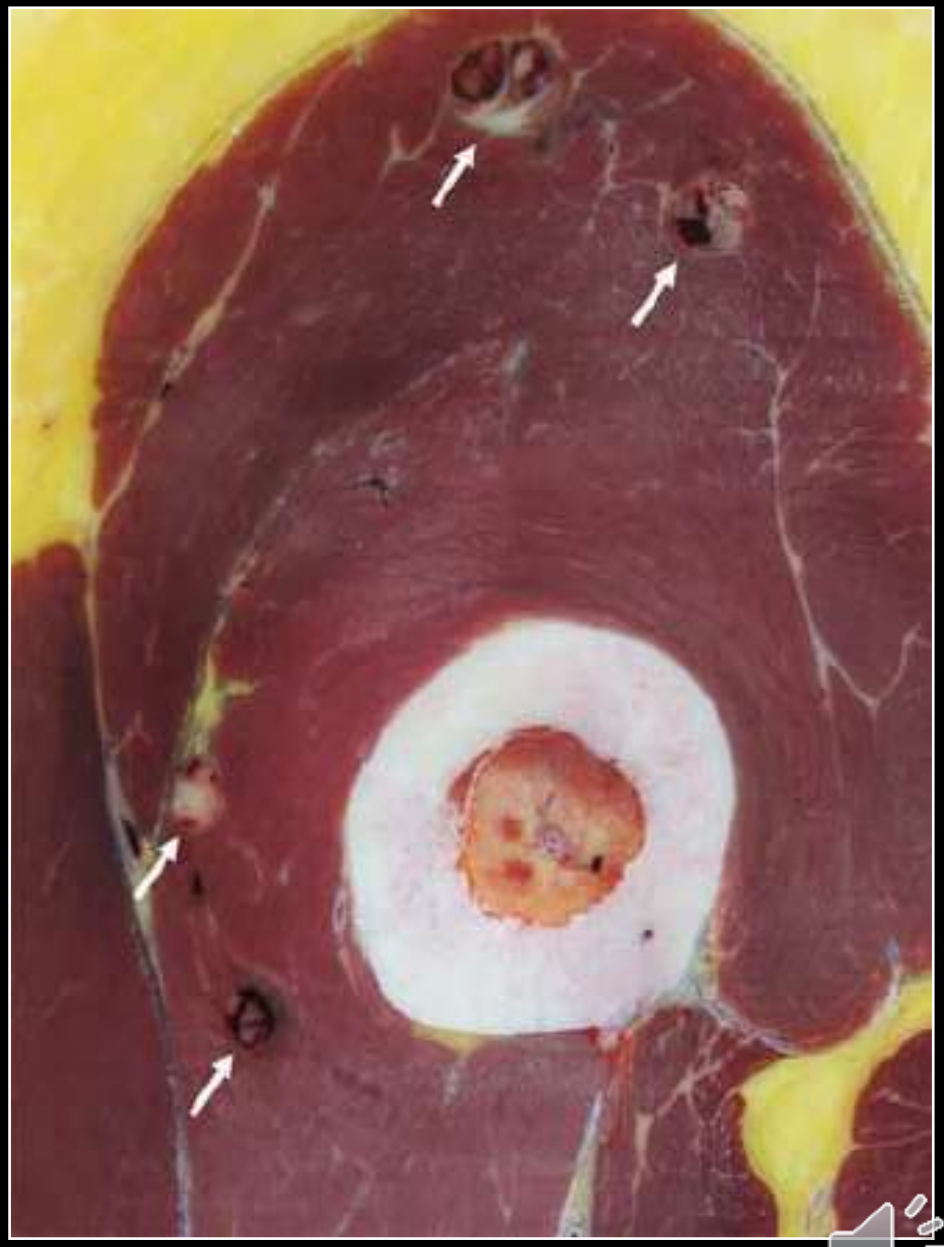
Abstract: Pseudomyogenic hemangioendothelioma (PMH) is a well-recognized neoplasm that usually arises in the soft tissue; concurrent bone involvement occurs in 24% of cases. PMH of bone without soft tissue involvement is rare. We describe the clinicopathologic findings of 10 such cases, the largest series reported to date. The study included 9 male and 1 female pa-

static carcinoma. Because of its rarity, unusual presentation, and morphology, accurate diagnosis can be challenging.

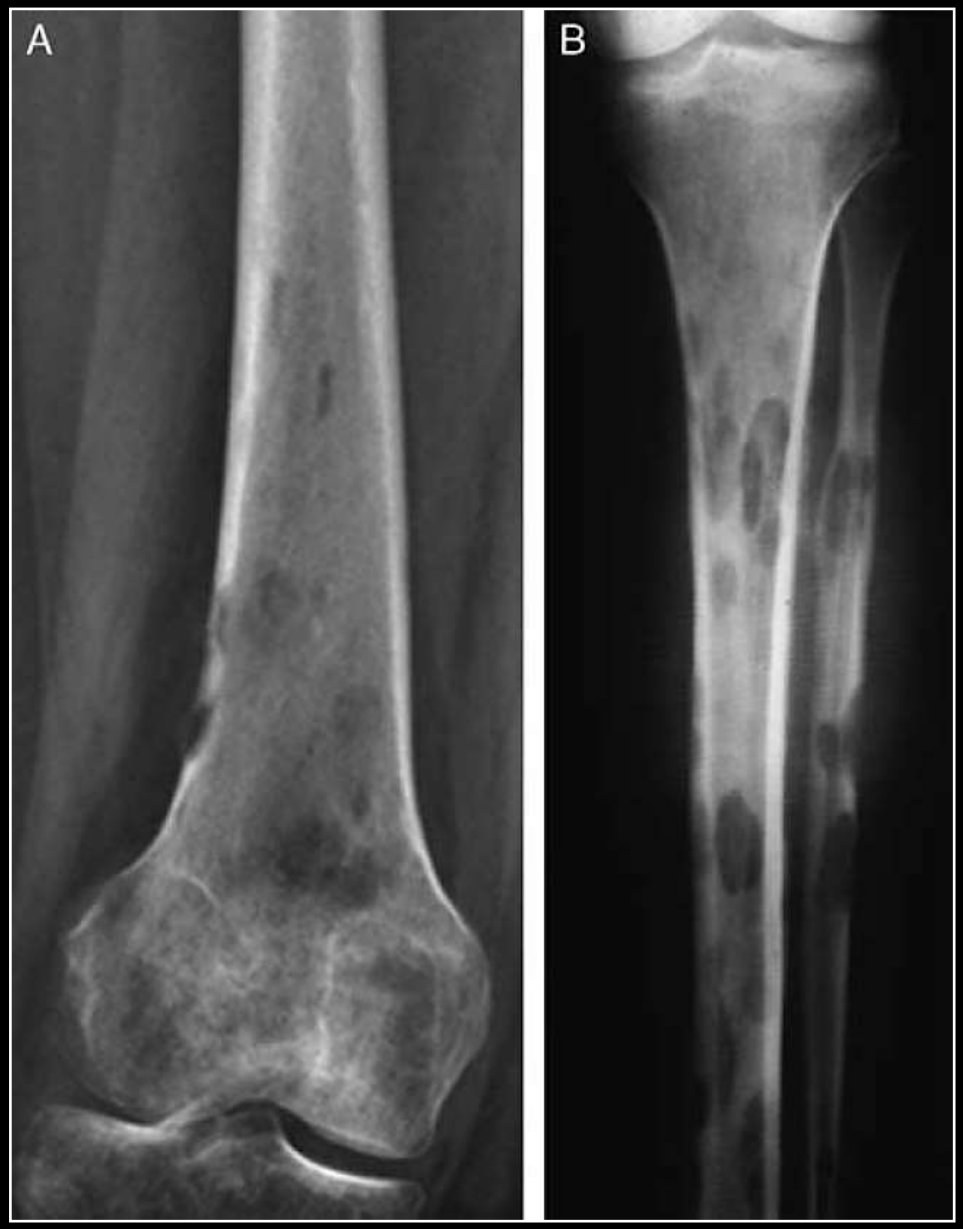
Key Words: pseudomyogenic hemangioendothelioma, vascular tumor, bone

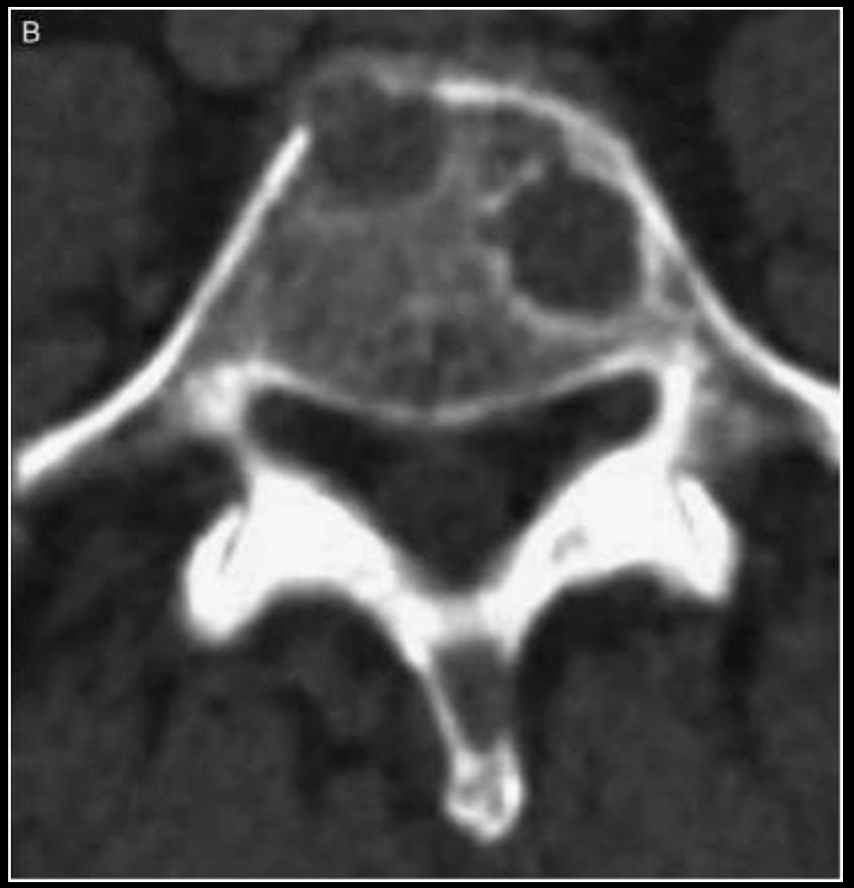
(*Am J Surg Pathol* 2016;40:587–598)



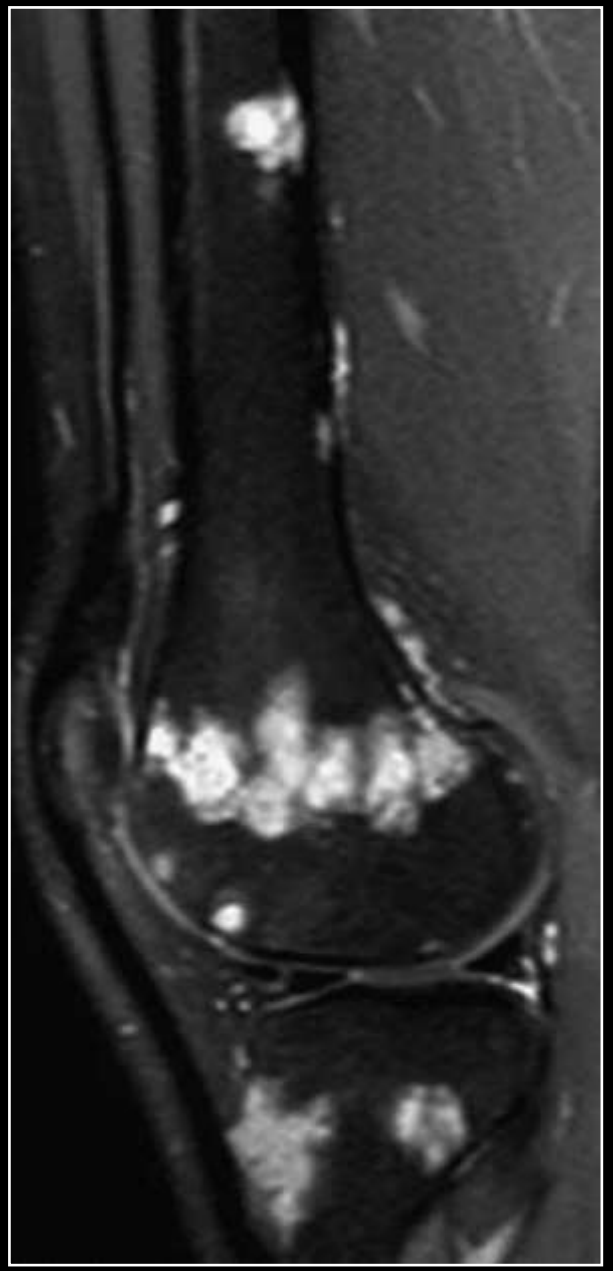


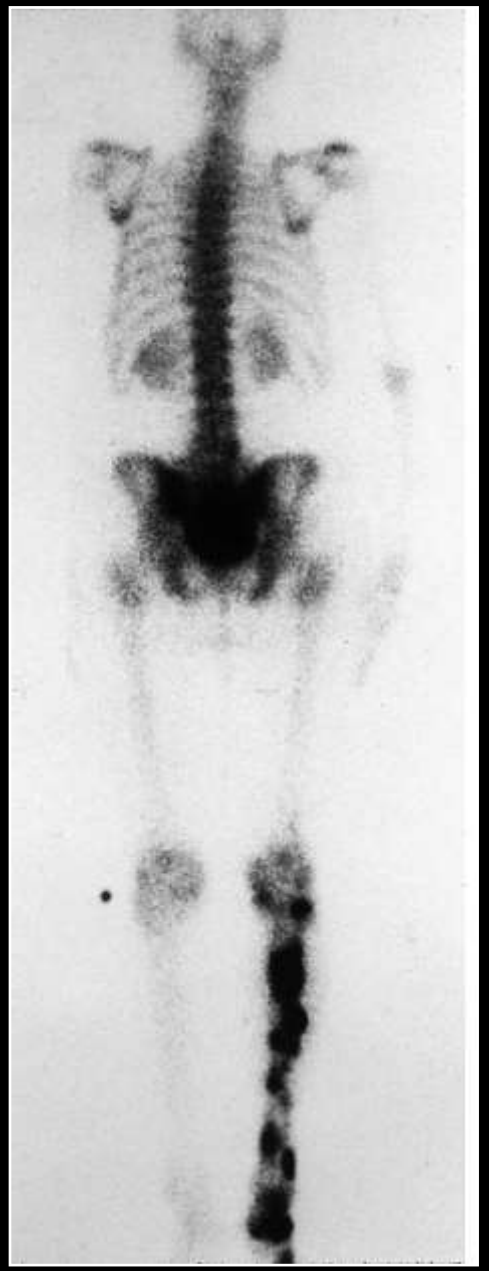
Inyang A et al. AJSAP 2016



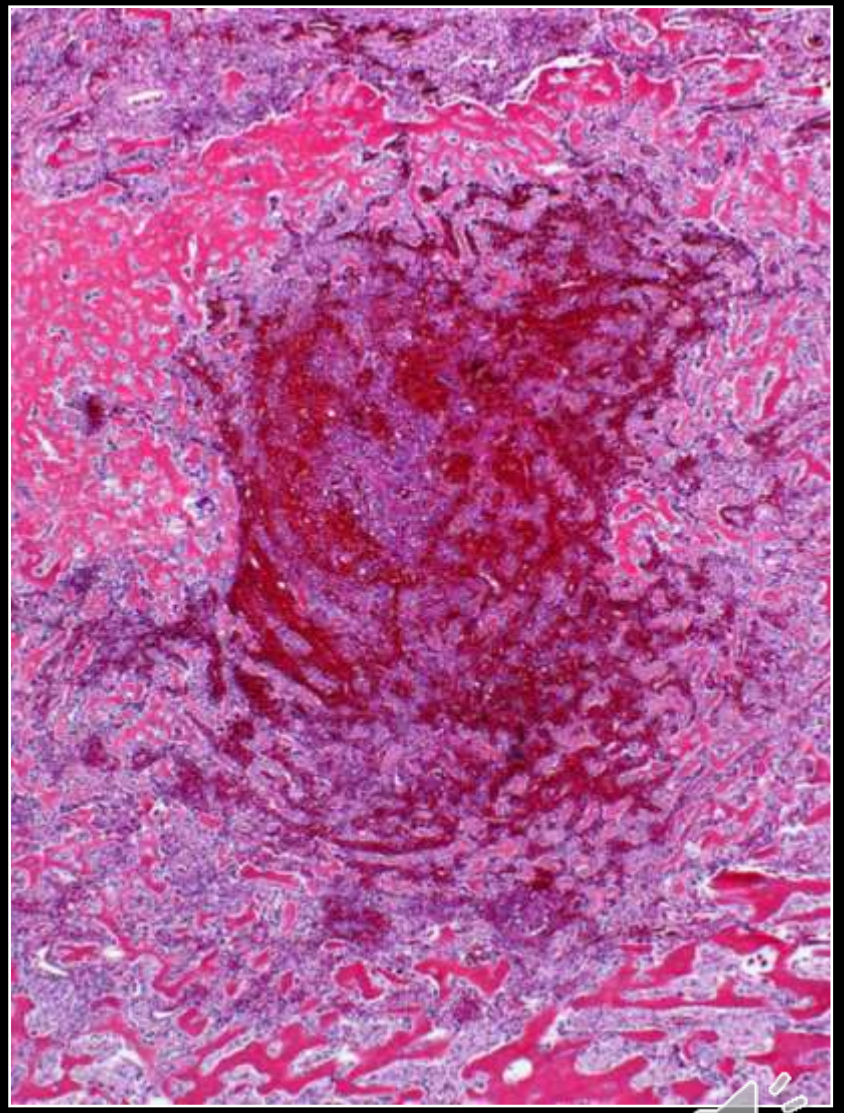


Inyang A et al. AJSAP 2016



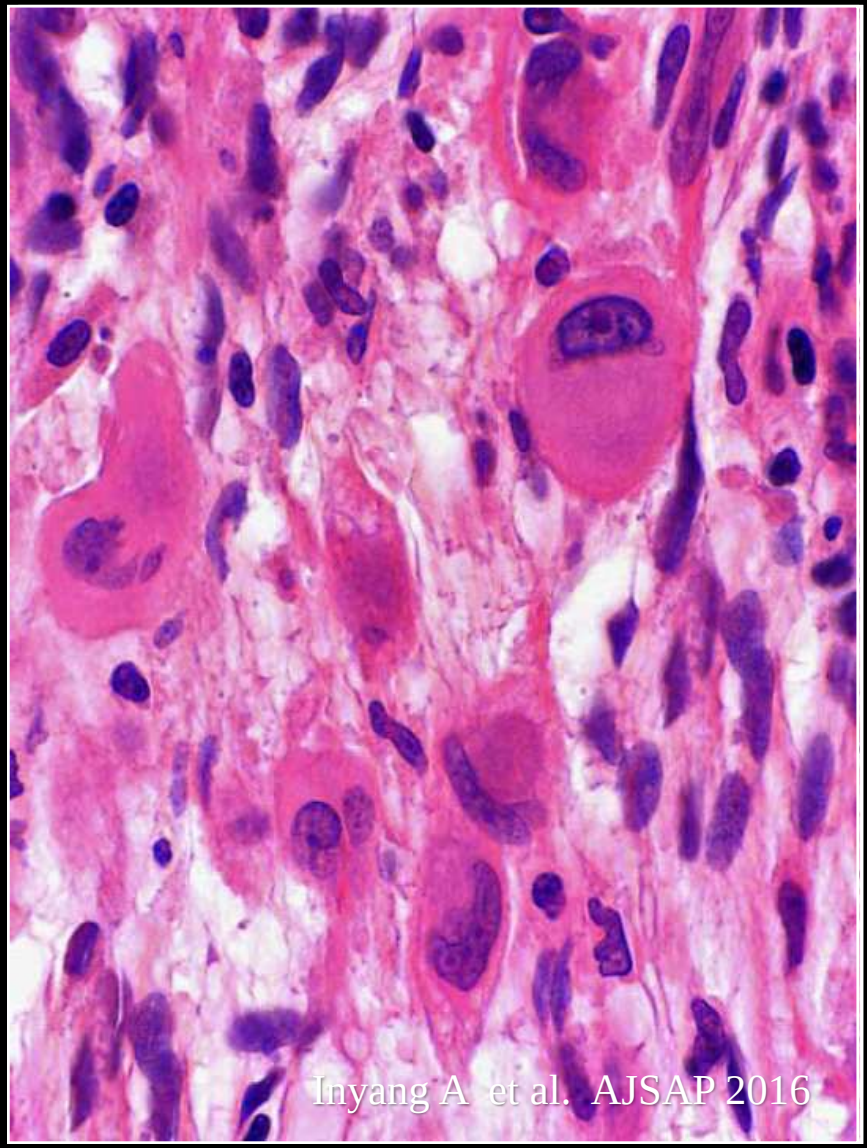


Inyang A et al. AJSAP 2016



Inyang A et al. AJSAP 2016

Pseudomyogenní hemangioendoteliom (PMH)



- **indolentní, ale recidivuje; 1x meta**
- **t(7;19) *SERPINE1* - *FOSB***
  ACTB* - *FOSB
- **Dif. Dg.: EH, EHE, angioSA, epithelioid sarcoma, carcinoma, rhabdomyoSA, melanoma, osteoSA, PEComa, leiomyosarcoma, IMT, osteoblastoma ...**
- **jde a priori o vaskulární lézi**

Histopathology

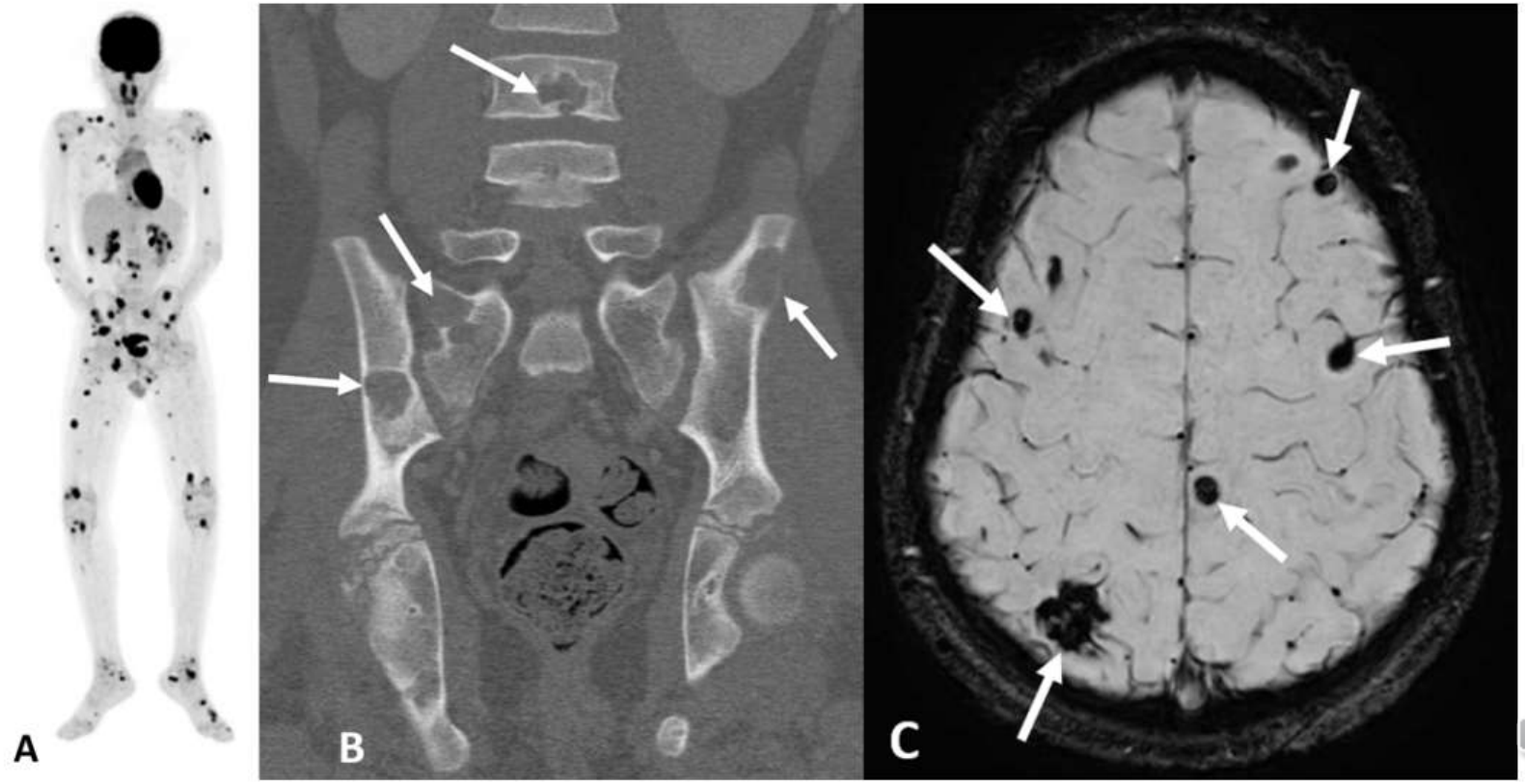
Volume 79, Issue 5
November 2021
Pages 888-891

Correspondence

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

Melanie H Hakar, Kevin White, Barry G Hansford, Jeff Swensen, Jessica L Davis

First published: 07 February 2021 | https://doi.org/10.1111/his.14349



BIOLOGIE

Epiteloidní hemangiom

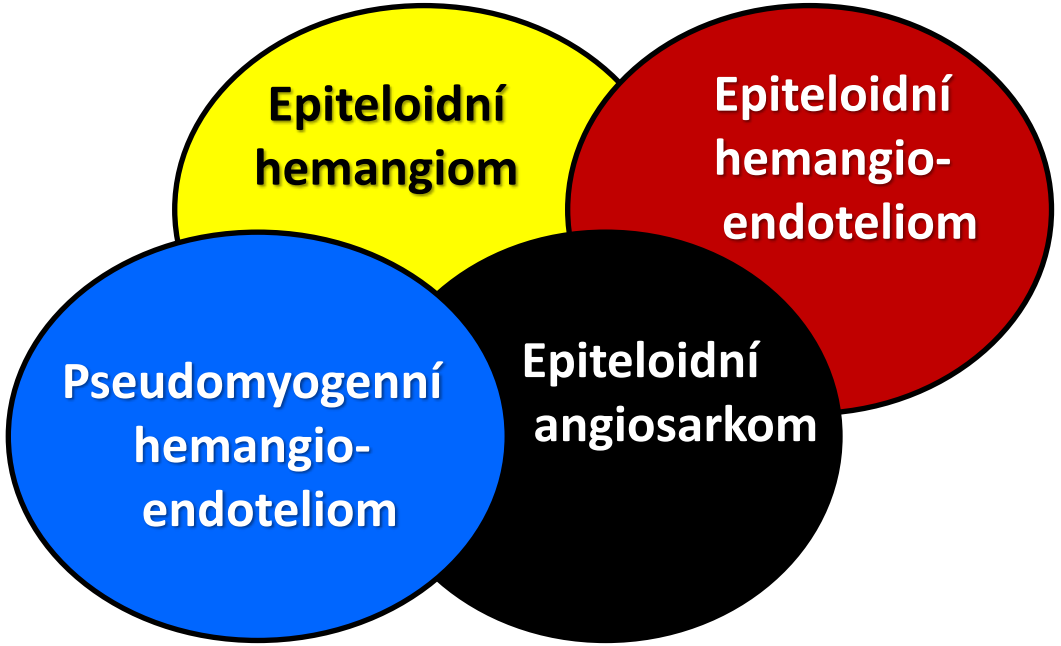
Pseudomyogenní hemangio-endoteliom

Epiteloidní hemangio-endoteliom

Epiteloidní angiosarkom

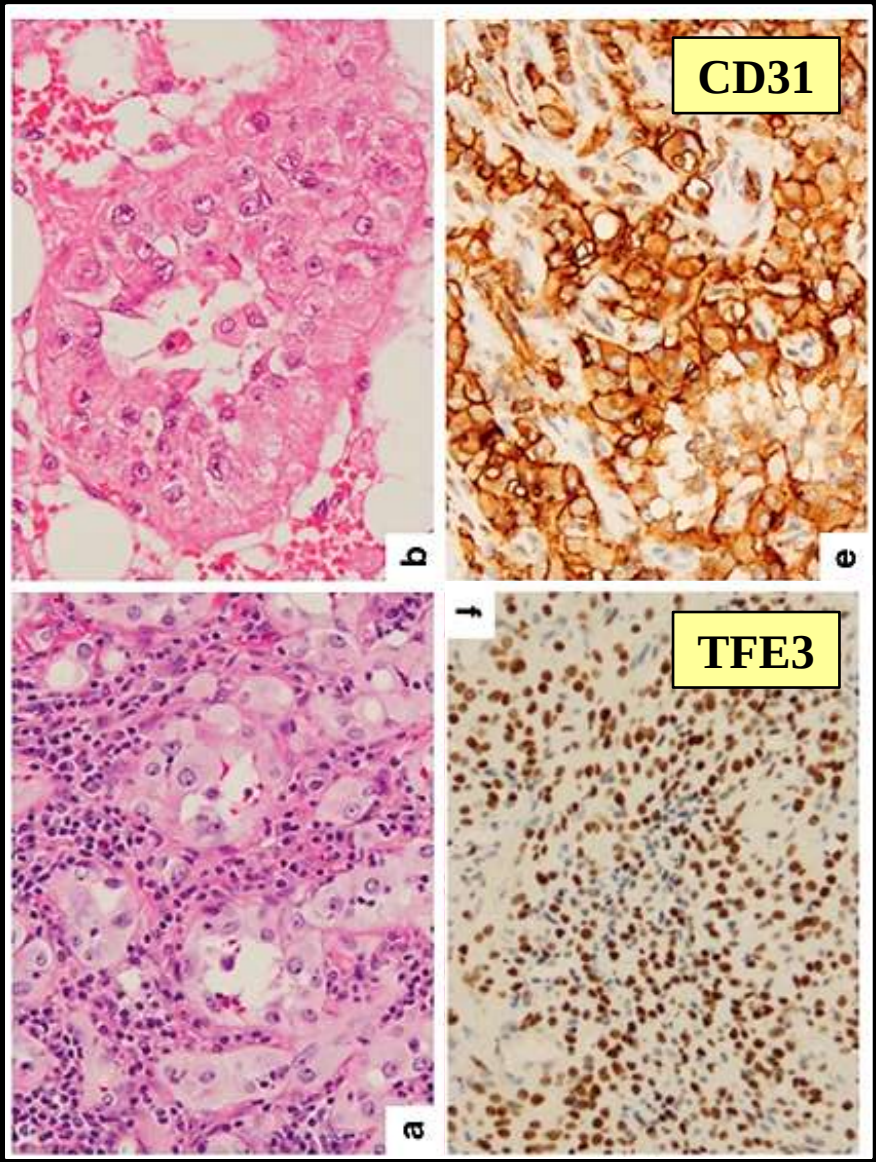
MORFOLOGIE

značný překryv !



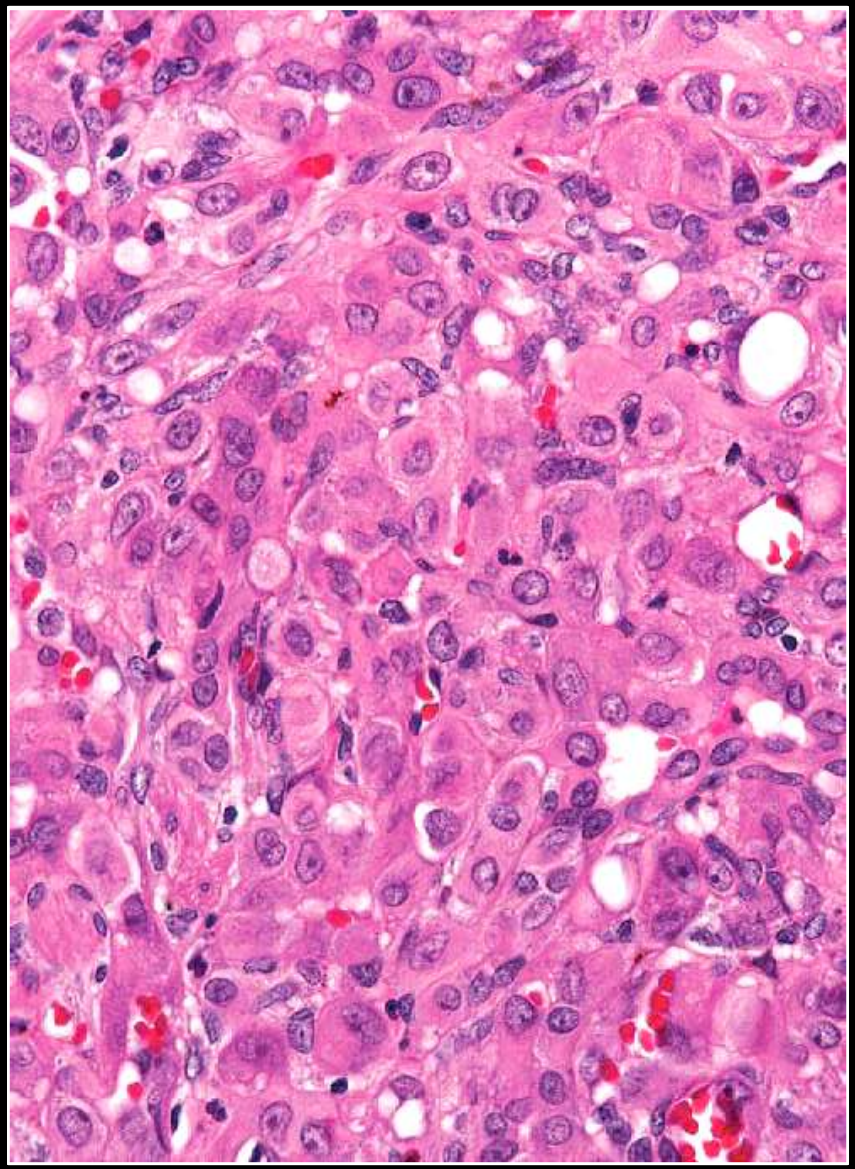
GENETIKA

Epiteloidní hemangioendoteliom (EHE)



- **bez cévních formací**
- **<35% metastazuje** (**maligní** léze)
- **měkké tkáně/kosti, játra, plíce**
- IHC - CAMTA1, exprese **CK**
  - ***WWTR1 - CAMTA1*** (95%)
  - ***YAP1 - TFE3*** (indolentní **?**)
- **Dif.Dg. - EH, EAS, karcinom mezoteliom…**

Epiteloidní hemangiom (atypický/buněčný) (EH)



- multifokální, biologicky **benigní**

ORIGINAL ARTICLE

Frequent *FOS* Gene Rearrangements in Epithelioid Hemangioma

A Molecular Study of 58 Cases With Morphologic Reappraisal

Shih-Chiang Huang, MD,† Lei Zhang, MD,† Yun-Shao Sung, MSc,† Chun-Liang Chen, MSc,† Thomas Krausz, MD,‡ Brendan C. Dickson, MD,§ Yu-Chien Kao, MD,‖ Narasimhan P. Agaram, MBBS,† Christopher D.M. Fletcher, MD, FRCPath,¶ and Cristina R. Antonescu, MD†*

- **atypie, nekróza, zánětlivá**

GENES, CHROMOSOMES & CANCER 53:951–959 (2014)

***ZFP36-FOSB* Fusion Defines a Subset of Epithelioid Hemangioma with Atypical Features**

Cristina R Antonescu,[1]* Hsiao-Wei Chen,[1] Lei Zhang,[1] Yun-Shao Sung,[1] David Panicek,[2] Narasimhan P Agaram,[1] Brendan C Dickson,[3] Thomas Krausz,[4] and Christopher D Fletcher[5]*

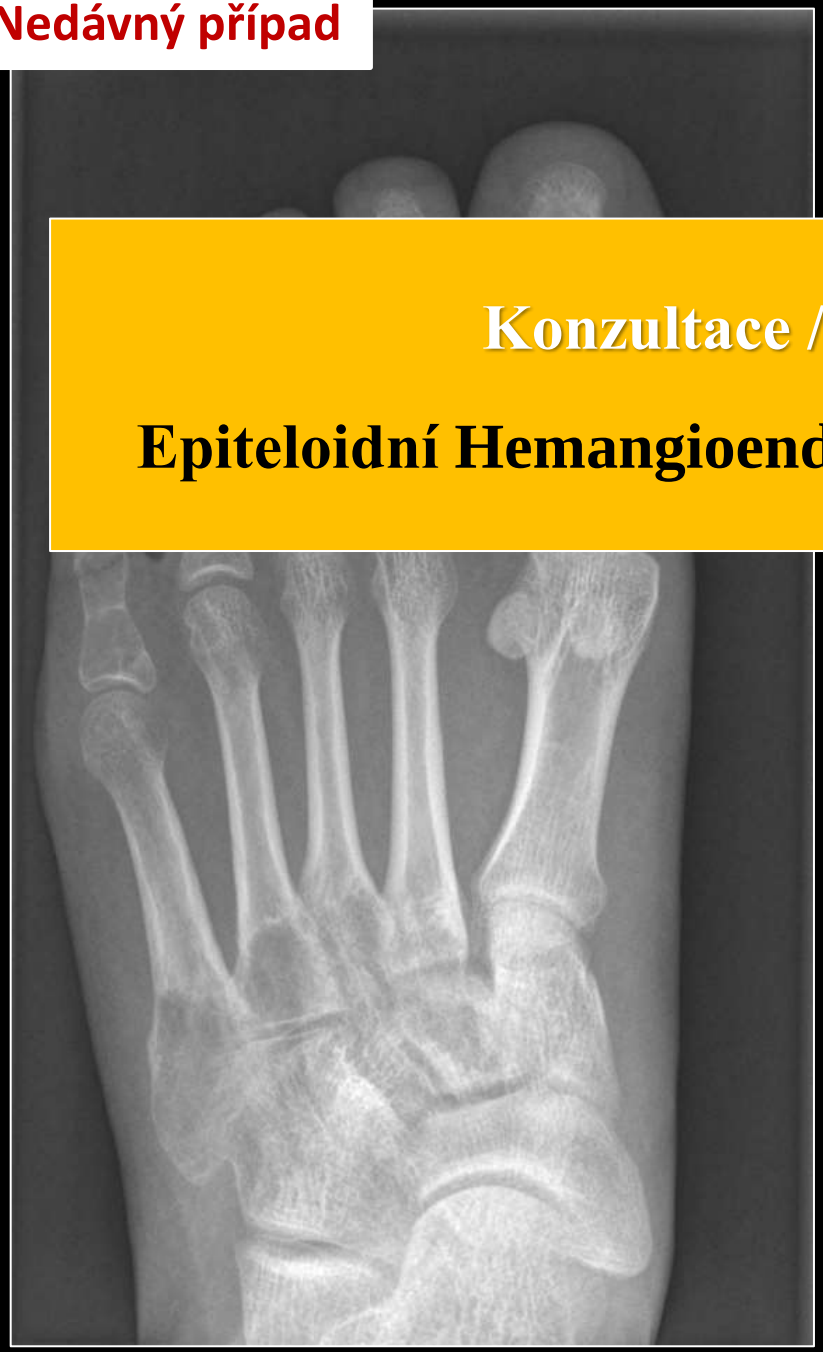
[1]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY
[2]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY
[3]Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada
[4]Department of Pathology, University of Chicago, Chicago, IL
[5]Department of Pathology, Brigham and Women's Hospital, Boston, MA

- ***WWTR1 – FOSB***

~ 50% bone soft tissue

Nedávný případ

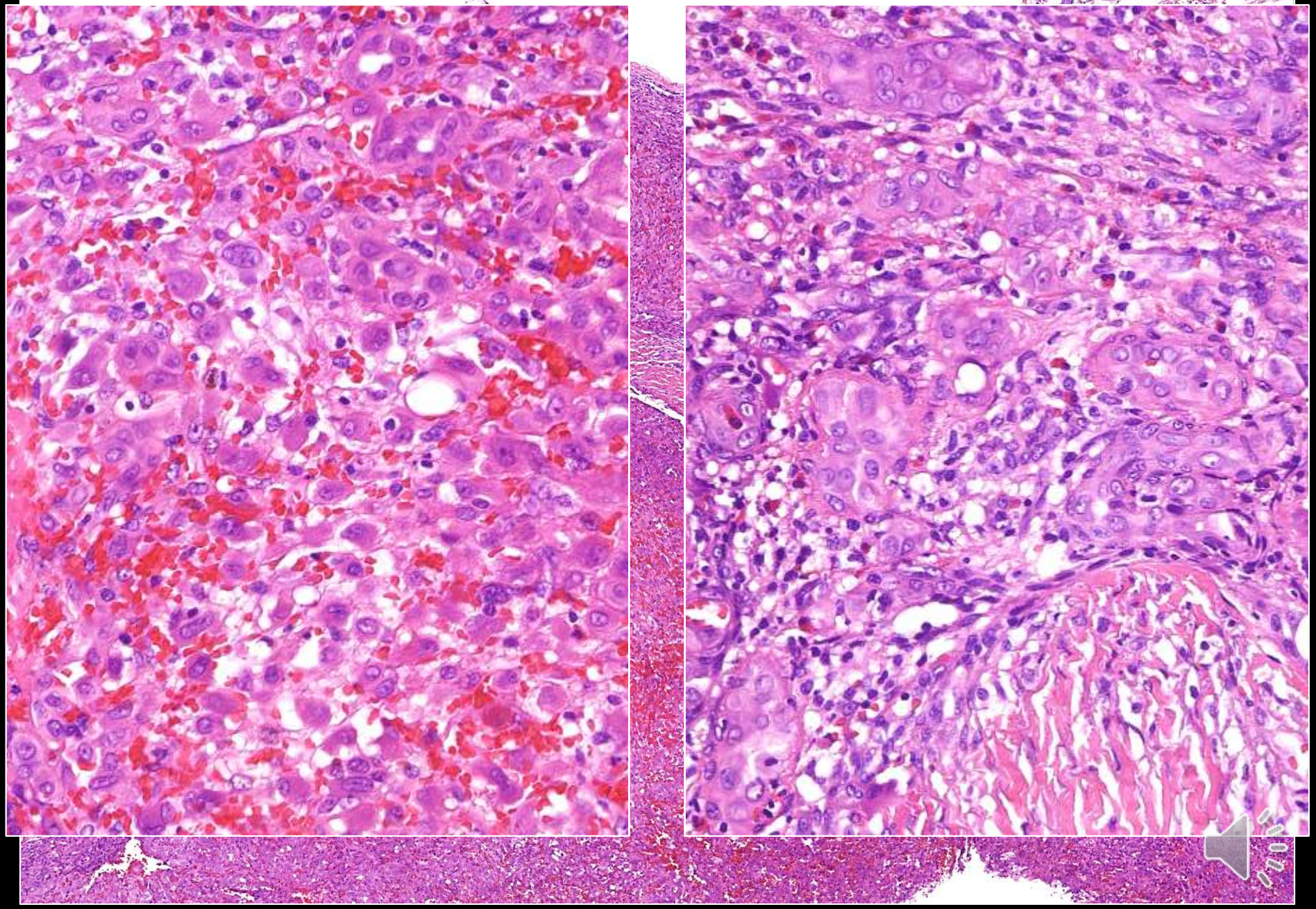
za 6 měsíců

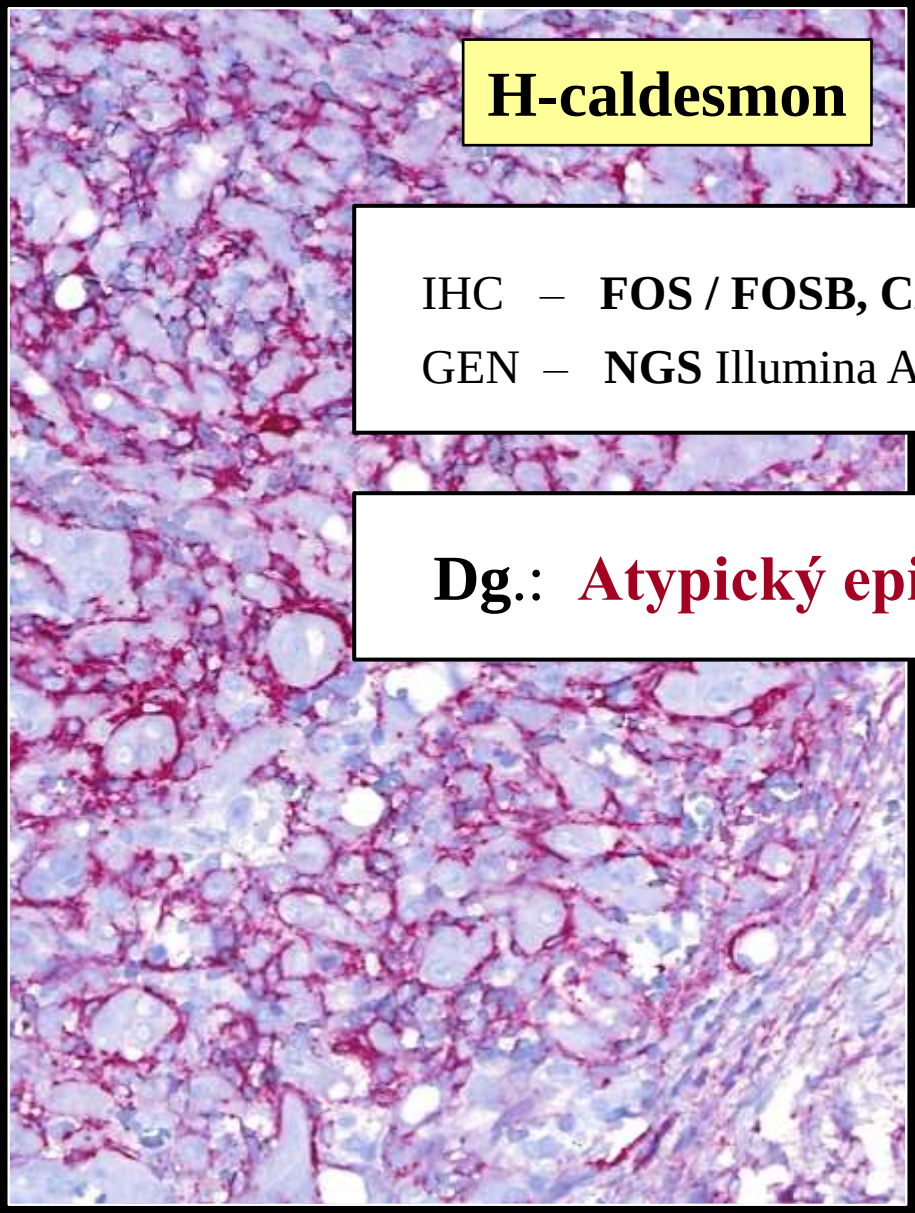


Konzultace / II. čtení biopsie:

Epiteloidní Hemangioendoteliom, susp. **Angiosarkom ?**


1241/21
6
7
8





IHC – **FOS / FOSB, CAMTA1** negativní

GEN – **NGS** Illumina ArcherPlex-**SAR6** - negativní

Dg.: Atypický epiteloidní hemangiom

Modern Pathology (2021) 34:934–941
https://doi.org/10.1038/s41379-020-00723-4

USCAP

ARTICLE

Novel *GATA6-FOXO1* fusions in a subset of epithelioid hemangioma

Cristina R. Antonescu[1] · Shih-Chiang Huang[2] · Yun-Shao Sung[1] · Lei Zhang[1] · Burkhard M. Helmke[3] · Martina Kirchner[4] · Albrecht Stenzinger[4] · Gunhild Mechtersheimer[4]

sekvenace

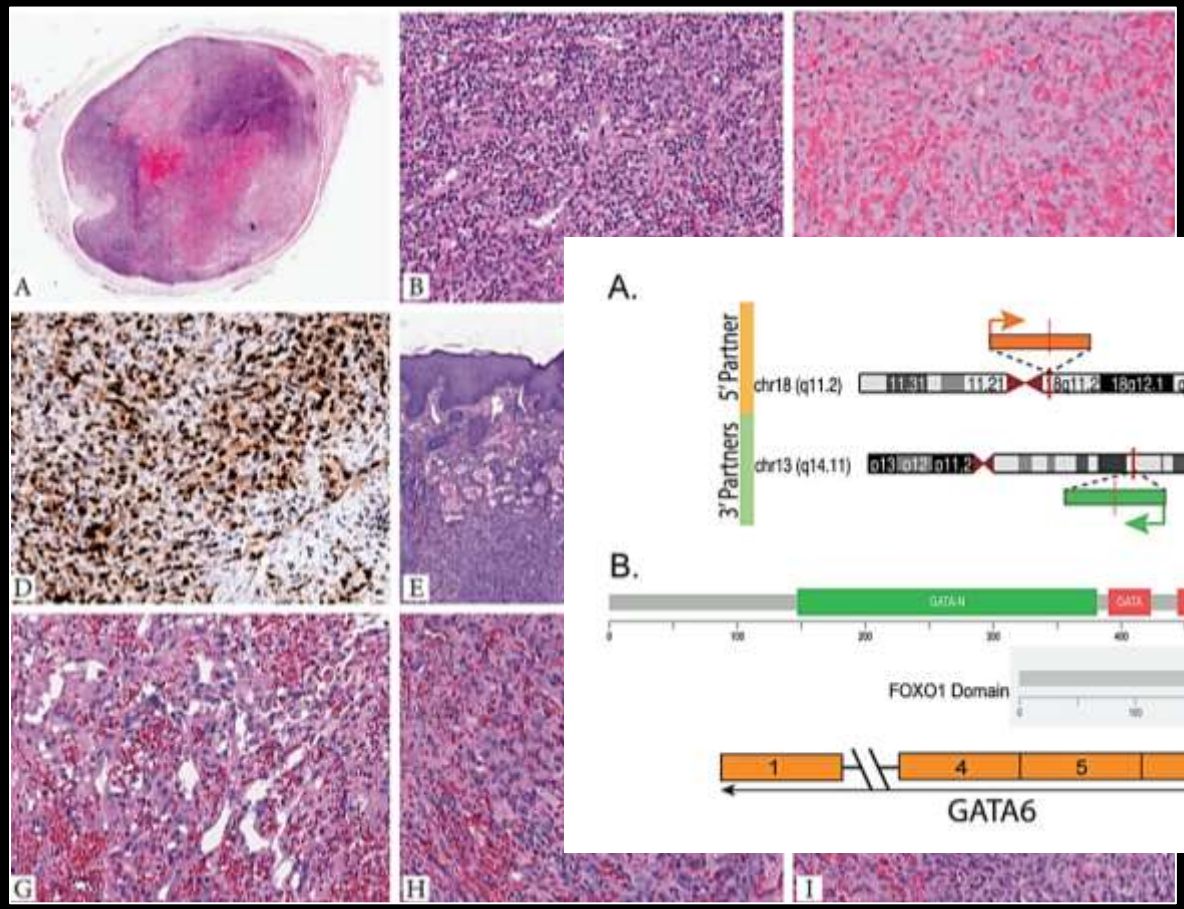
FOS/FOSB negativních

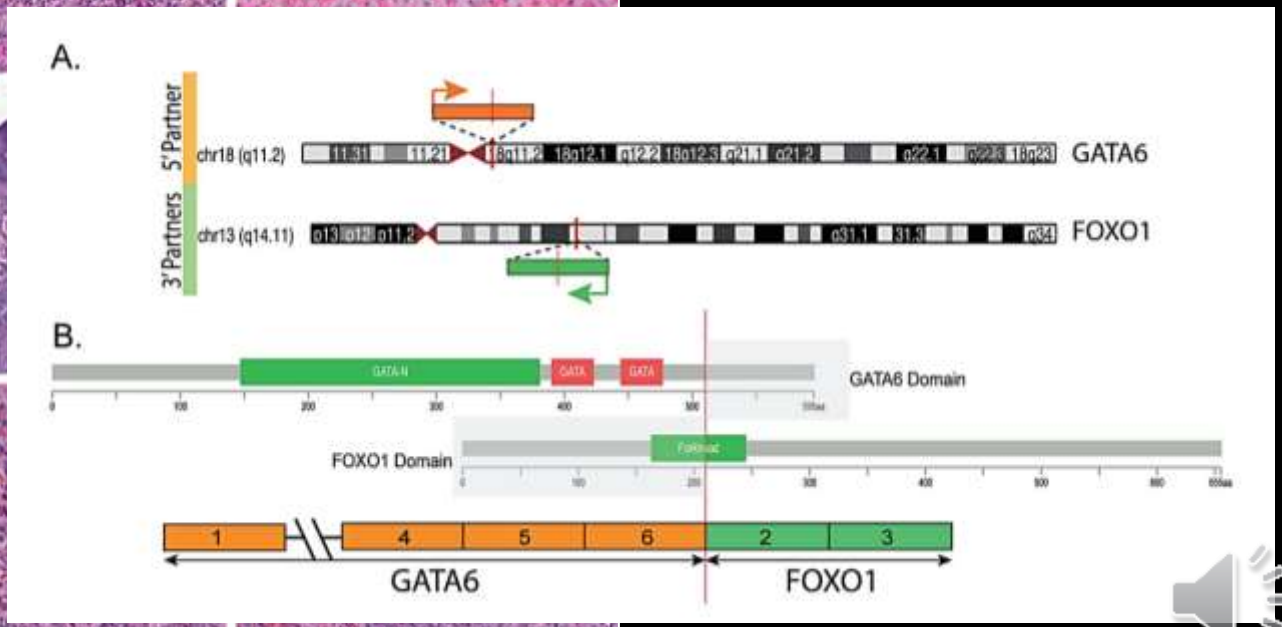
EH napodobujících EHE

kožní léze, hlava, krk

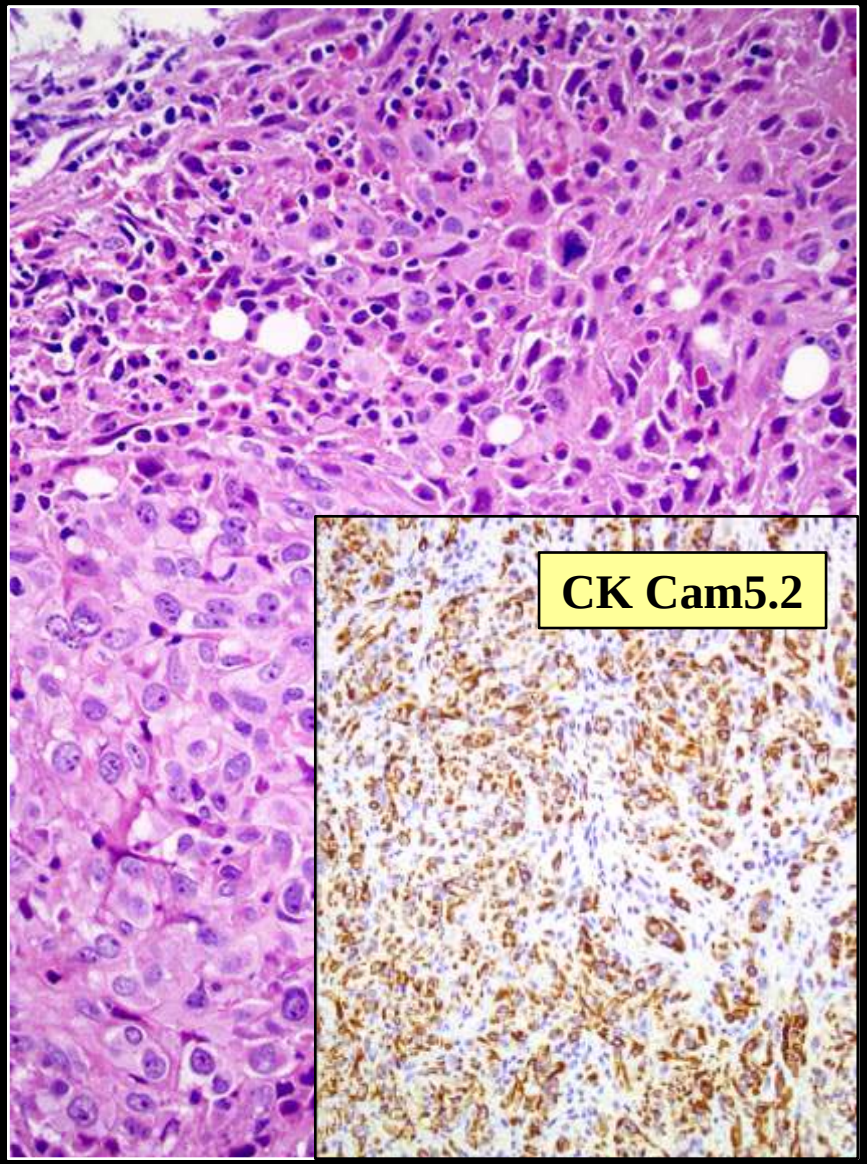
solidní, vasoformativní

indolentní průběh





Epiteloidní angiosarkom (EAS)



- **high-grade, nekrózy, prokrvácení solidní - není vazoformativní**
- **Dif. Dg.:** EH, EHE, **karcinom** (CK)…
- **primární** vs **sekundární**

  ampl. ***MYC, FLT4; PTPRB***

  mut. ***PLCG1/KDR***

- ***CIC-LEUTX ; CIC*** **mut. !**
  - mladí lidé, viscerálně, agresívní
  - solidní epiteloidní (vřetenité)
  - nejsou vazoformativní
  - genová exprese jako CIC-DUX4 small cell Ewing-like sarkomy

Epiteloidní vaskulární léze - SHRNUTÍ

- biologicky, morfologicky a geneticky heterogenní
- multifokální - kůže, měkké tkáně, přilehlá kost
- RTG nepříliš relevantní v predikci morfologie
- histologie však někdy nepříjemně PODOBNÁ

  EH - vřetenobuněčný, atypie, nekróza, destrukce kortikalis **!**
- genetika je užitečná - FOS/FOSB, CIC, CAMTA1, TFE3
- Dif.Dg. - CA, epiteloidní SA, melanom, PECom, mezoteliom

Genetika mnohdy klíčová; IHC užitečná pro základní triage

Table 1 Genetic alterations in vascular neoplasms and useful immunohistochemical markers

Neoplasm	Genetic alteration (prevalence)	Immunohistochemical markers (sensitivity)
Epithelioid hemangioma	*WWTR1-FOSB* } 20% cellular subtype *ZFP36-FOSB* *FOS-VIM* } 50% cellular subtype *FOS-MBLNI* *FOS-lincRNA* *FOS*-(unknown)	FOSB **FOS** } 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 } ? nearly 100% *GNA14* mutation *GNAQ* mutation	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

ALHE angiolymphoid hyperplasia with eosinophilia

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

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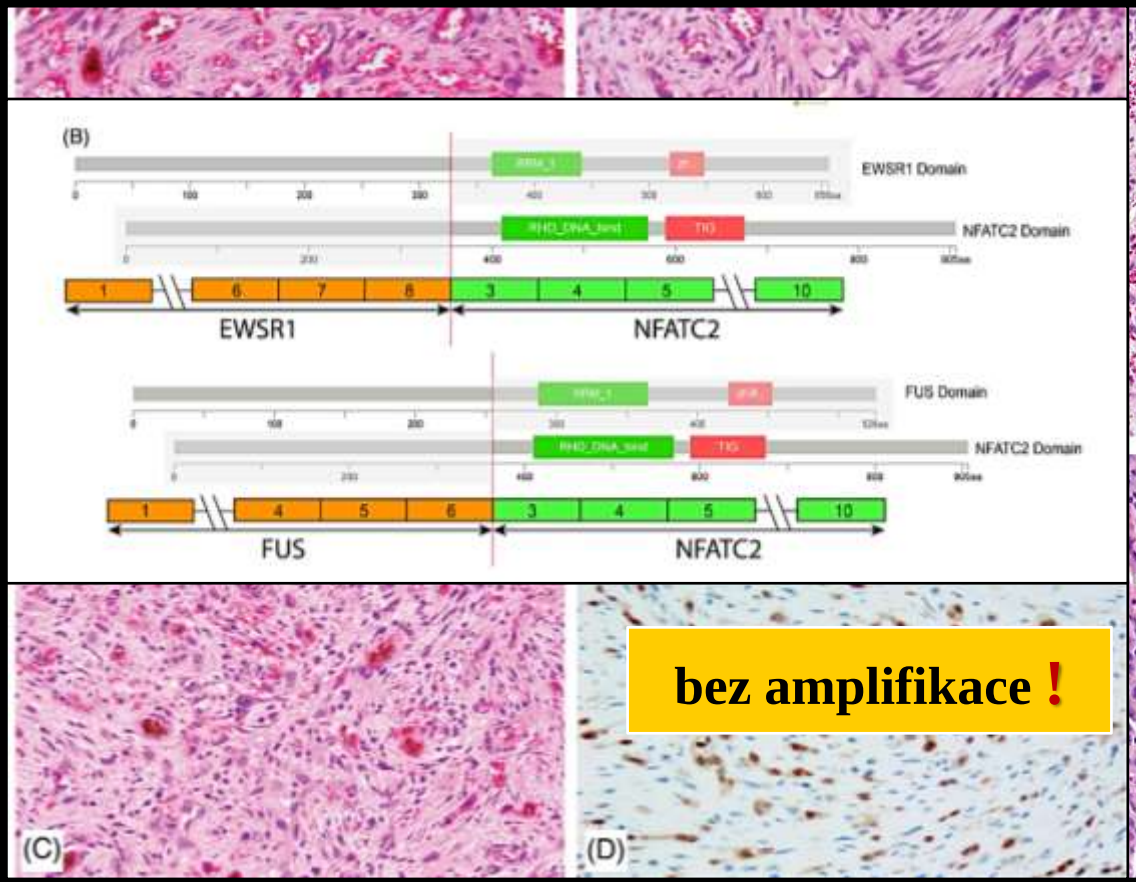
sekvenace fůzně negativních
(CAMTA1, WWTR1, TFE3, YAP1, FOS, FOSB)
epiteloidních cévních lézí



bez amplifikace !

skelet

destruktivní,
agresivně rostoucí

vazoformativní , solidní
atypie, rhabdoidní

napodobuje
EH, EHE, PMH, CHE, AS

recidivy, nemetastázuje

Děkuji za pozornost