8. Východoslovenský bioptický seminár
Košice 2018

Prípad SD-IAP č. 667

Magdaléna Puchertová
Boris Rychlý

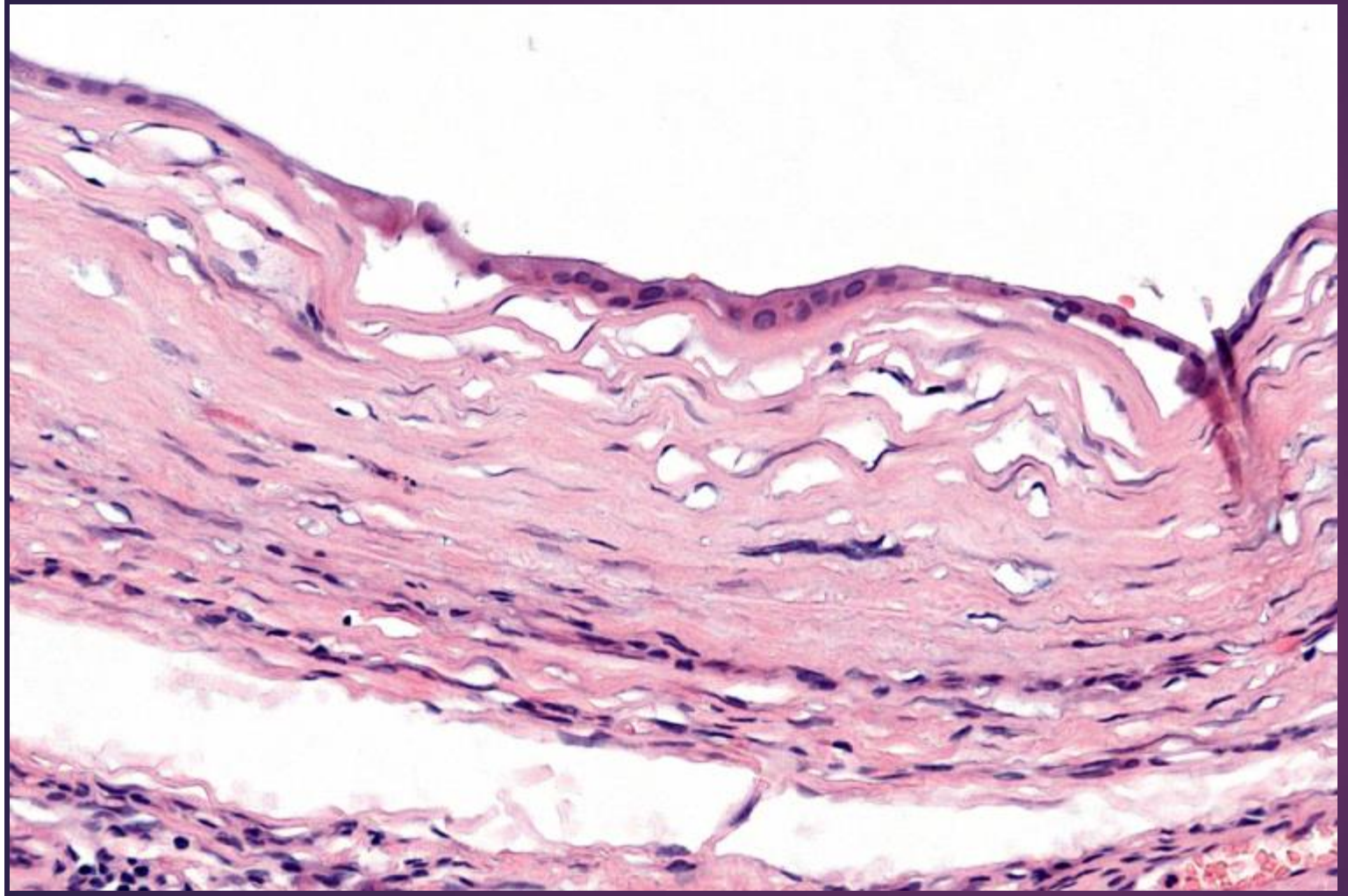
Slovenská Zdravotnícka Univerzita
cyto pathos United Qualities of Pathology

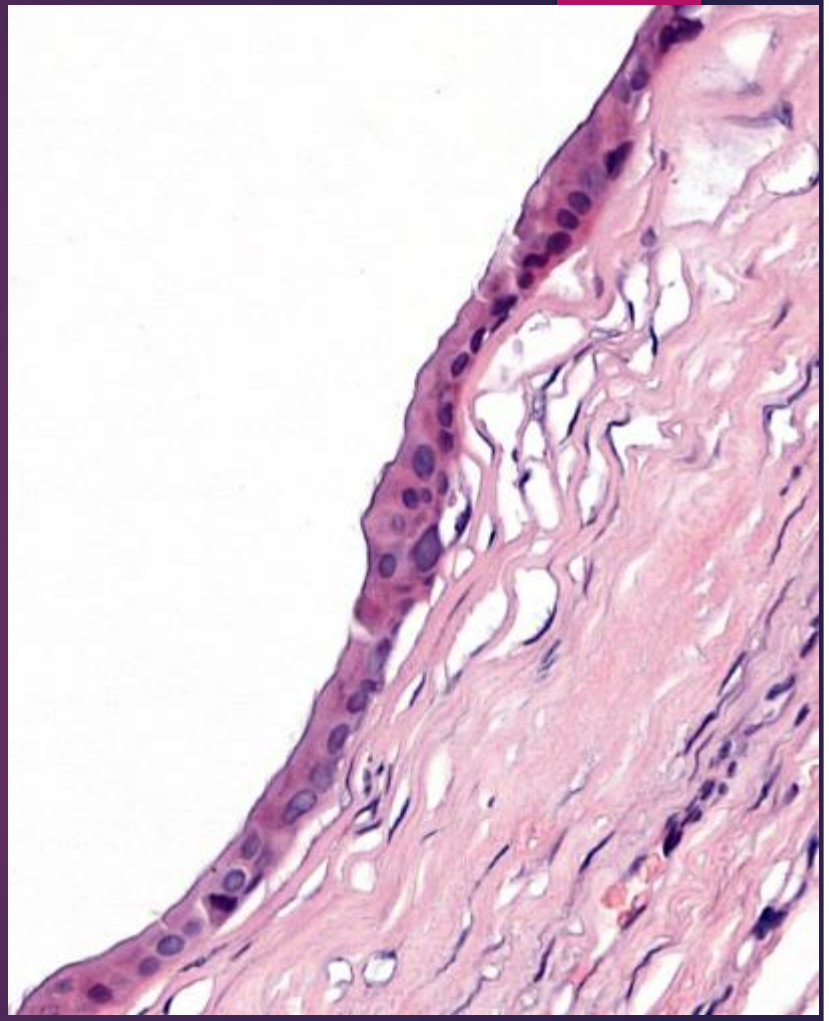
Prípad SD-IAP č. 667

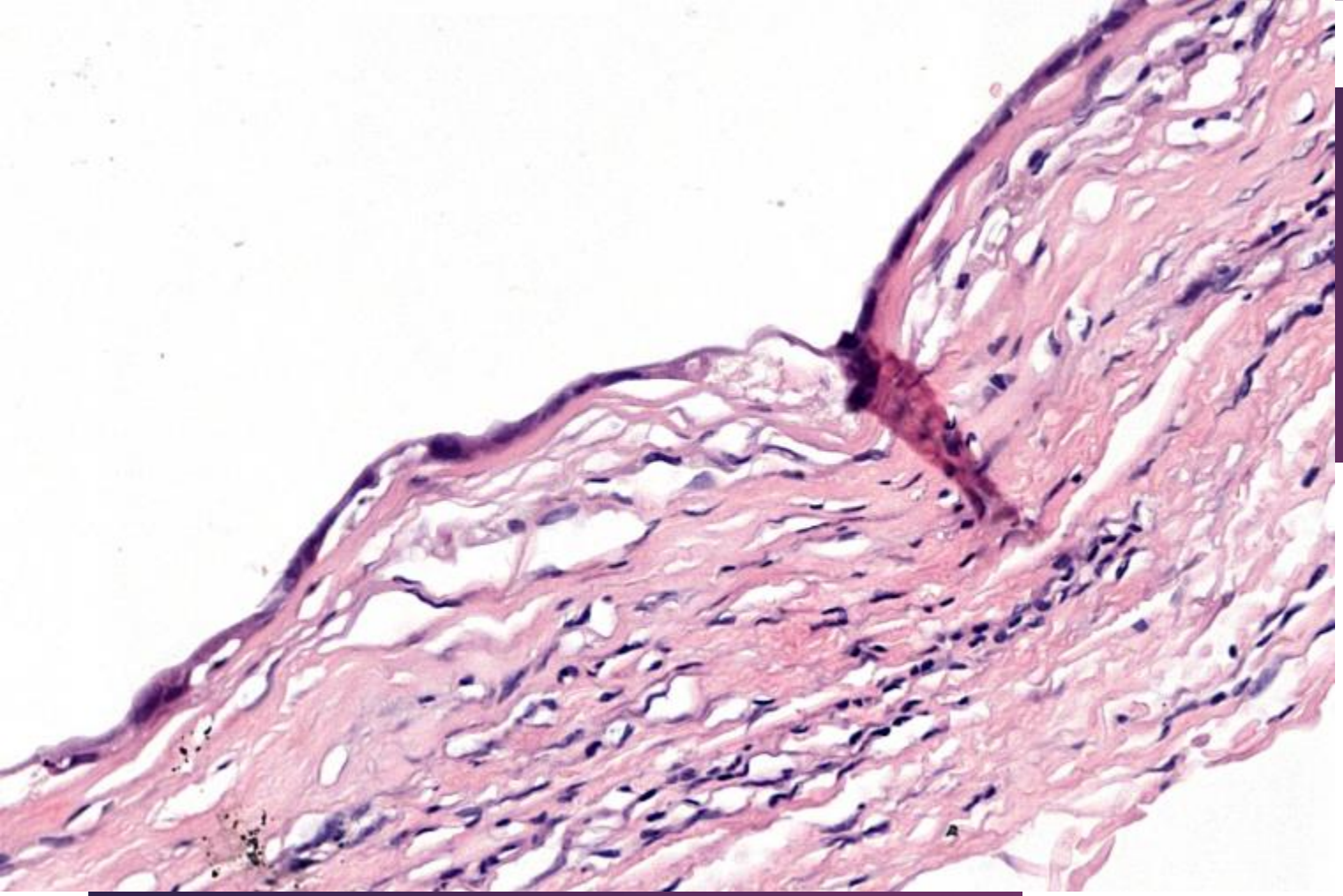
43 ročná žena

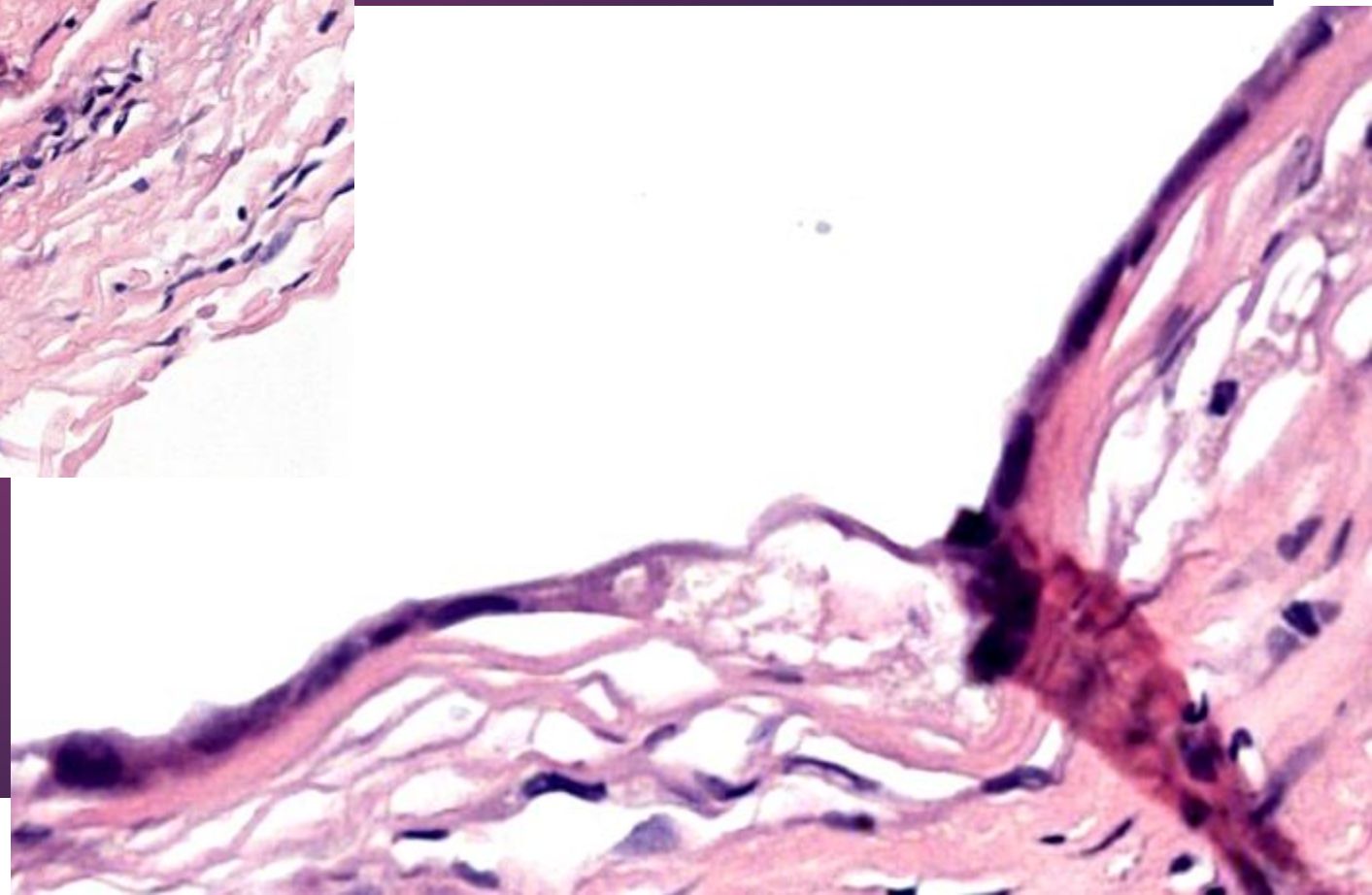
Klin. dg.: susp. atheroma reg. mesogastrii l. sin.

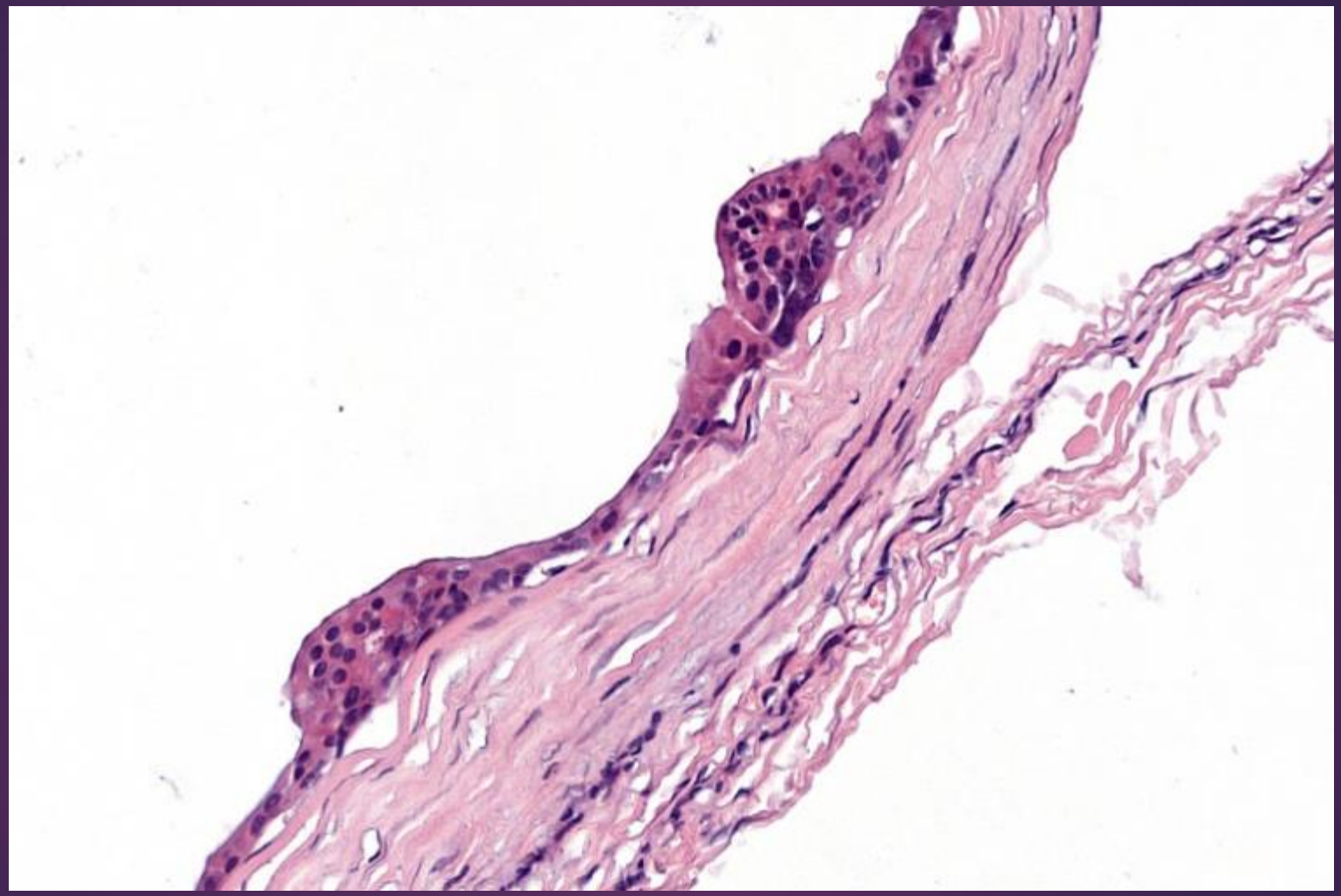
Kožná excízia s podkožím veľkosti 7 cm x 5 cm x 4 cm, na reze centrálne dutina max. priemeru 4,5 cm vyplnená svetlohnedou želatinóznou hmotou

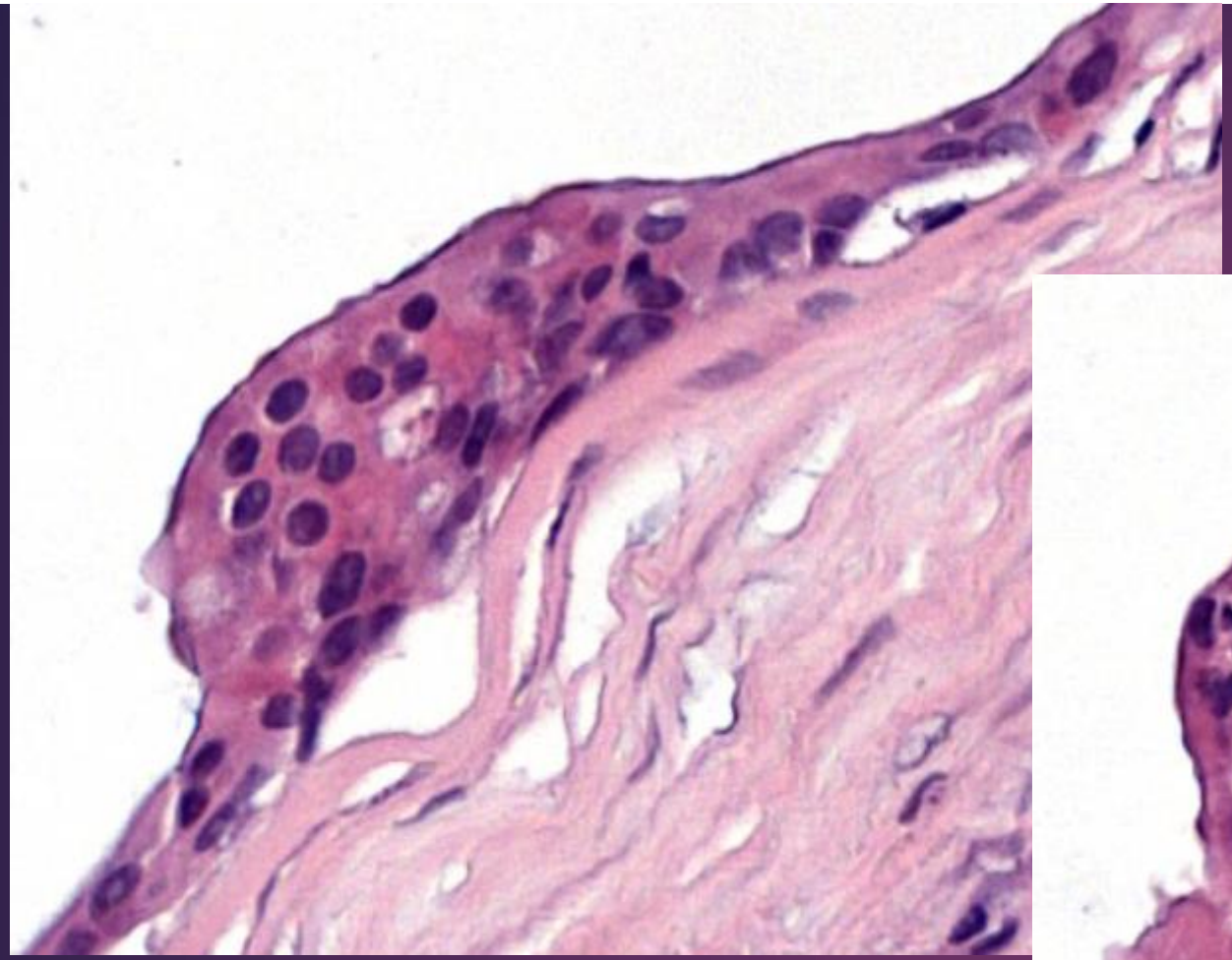


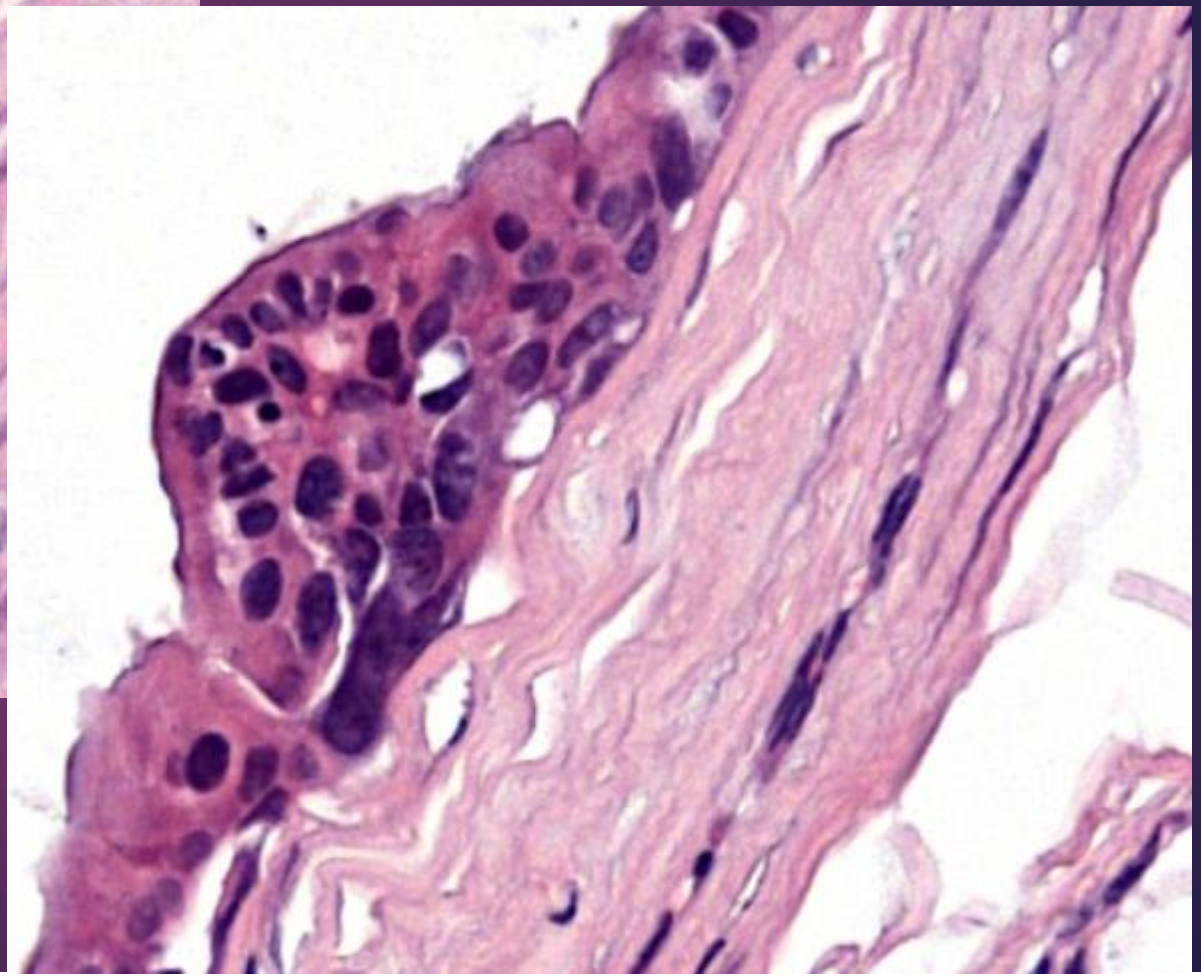




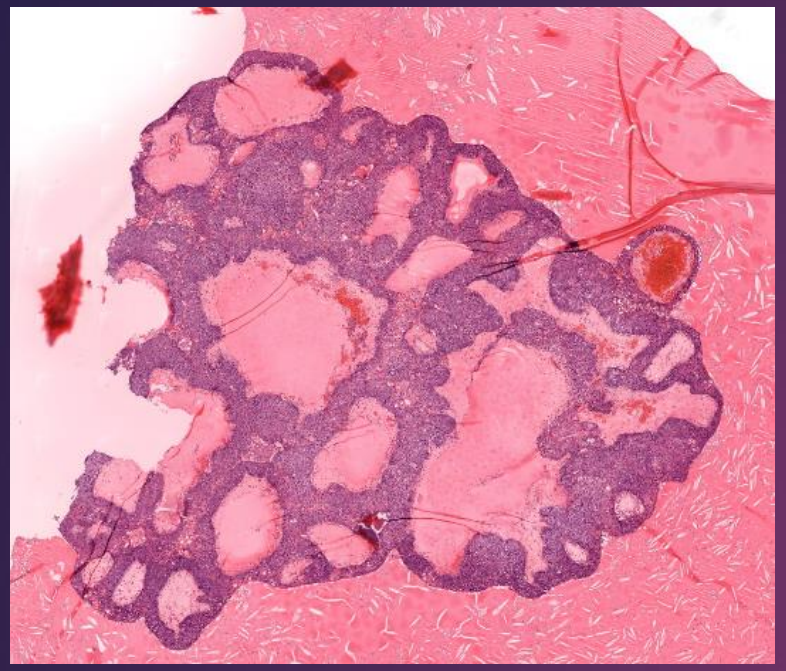


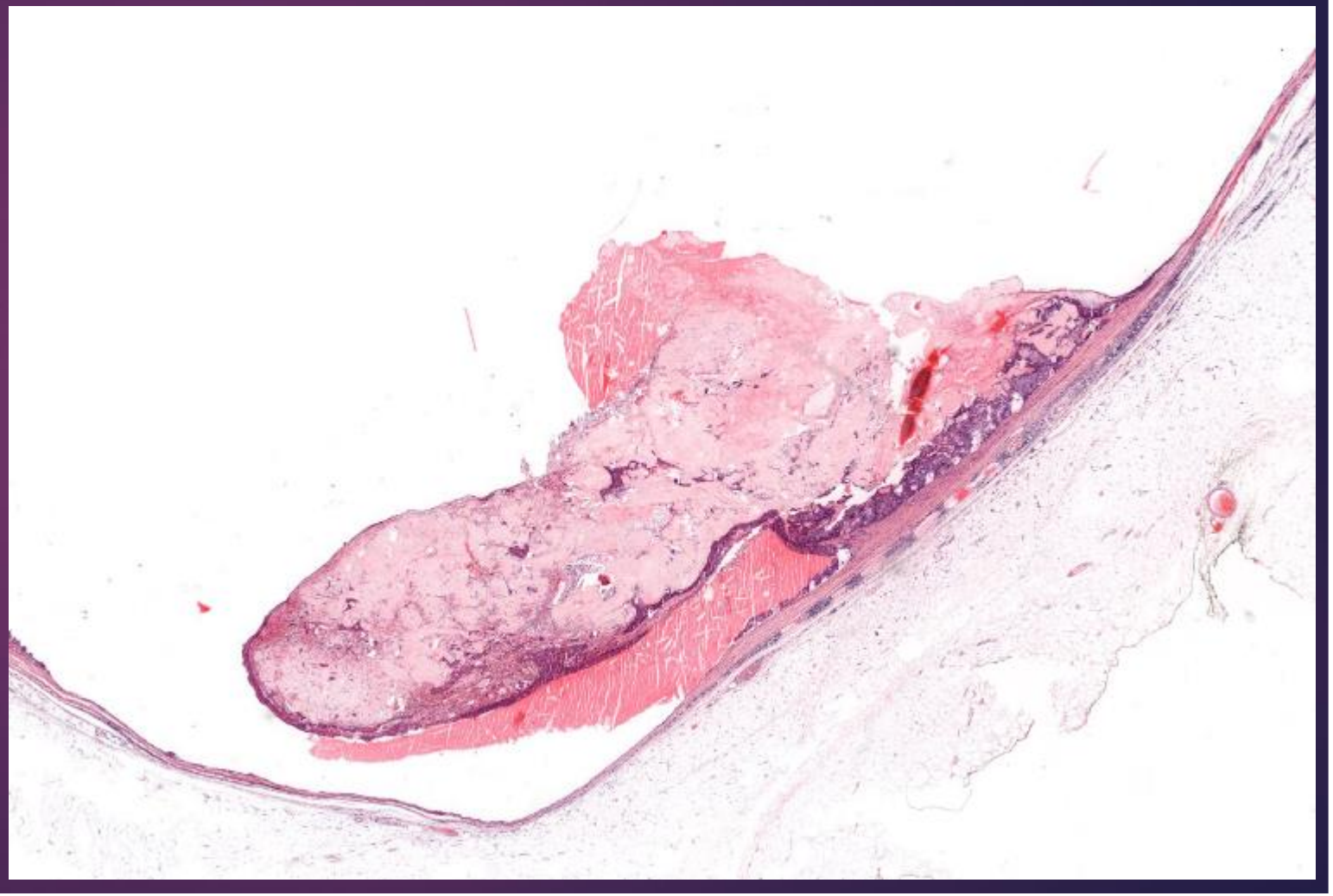


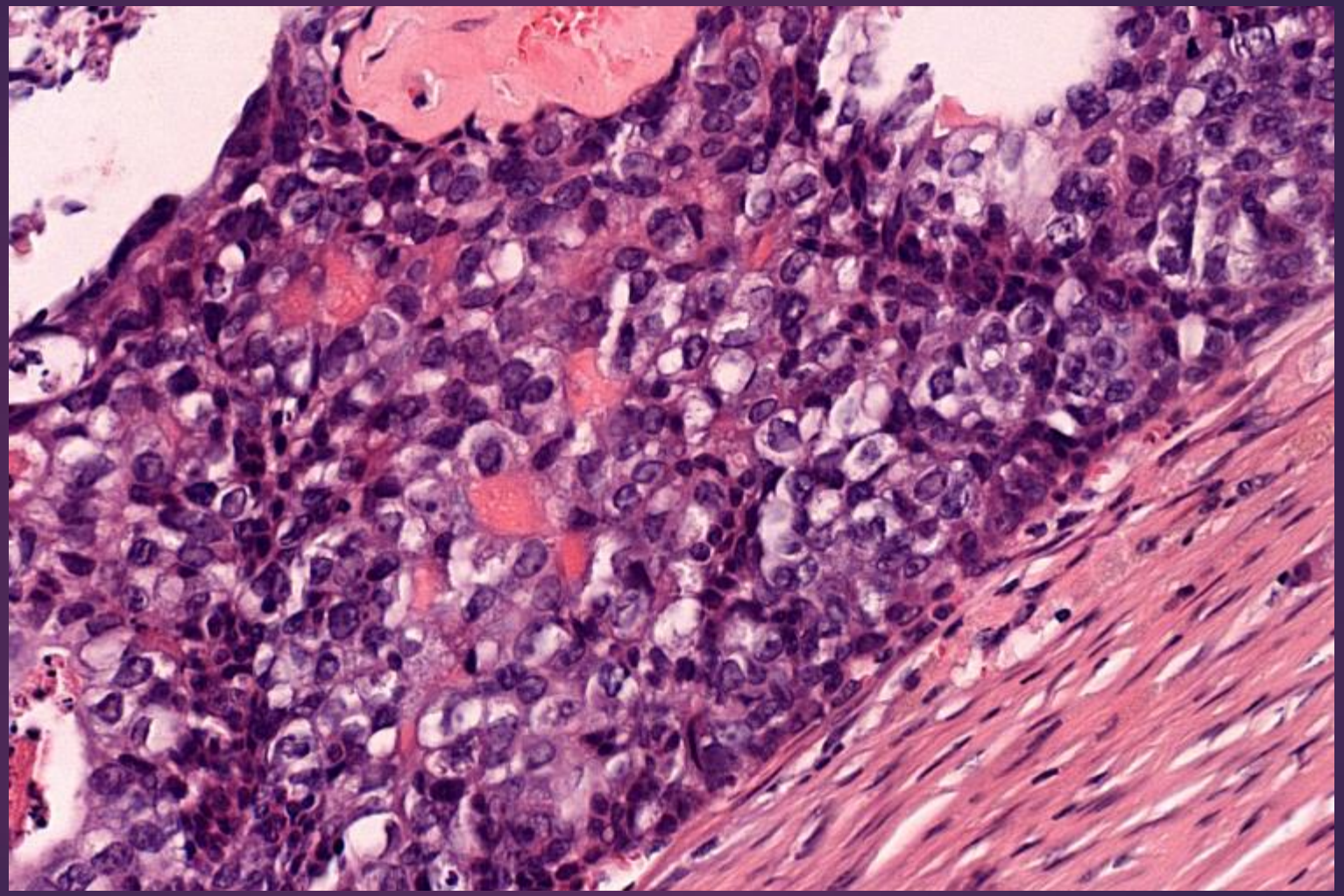


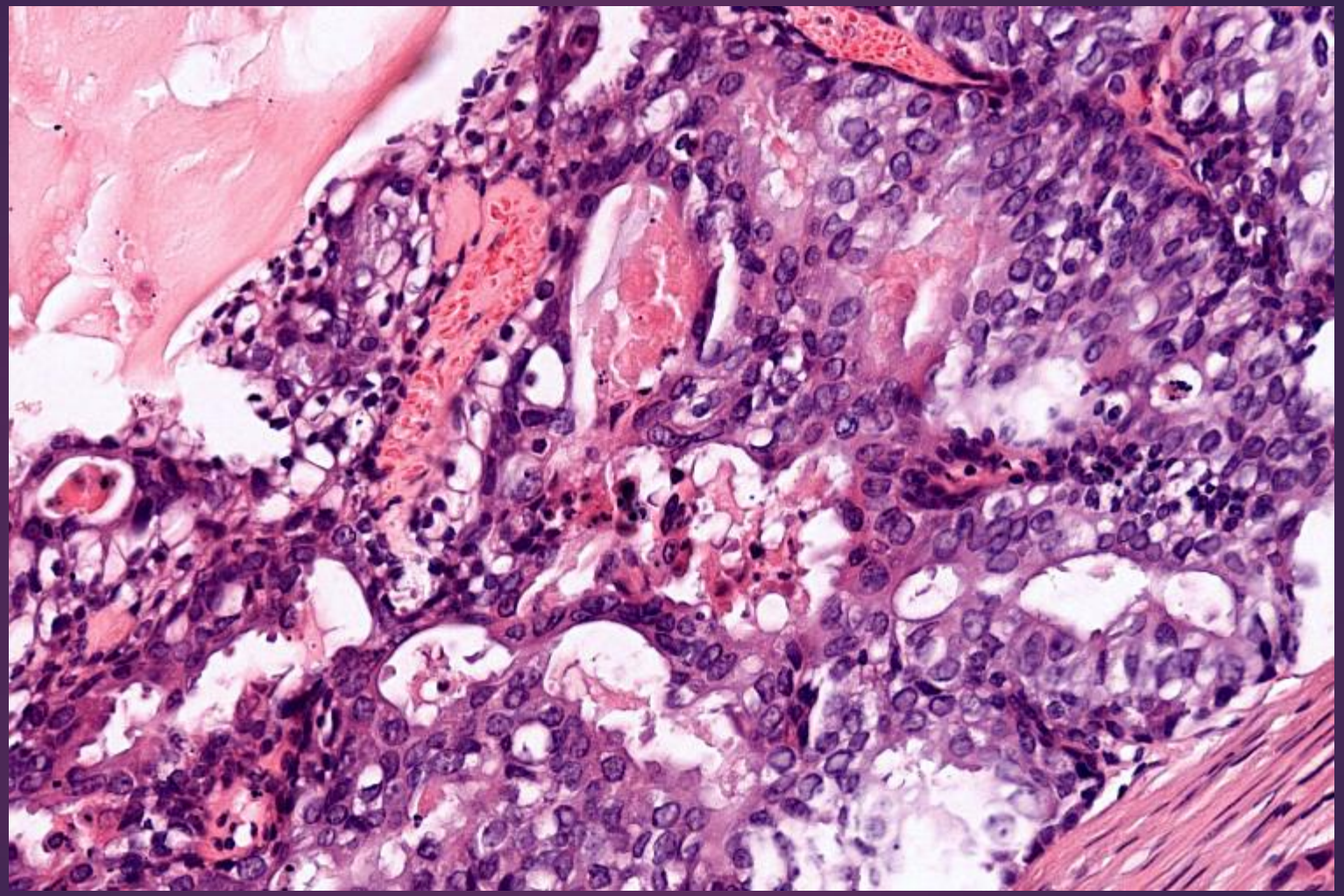


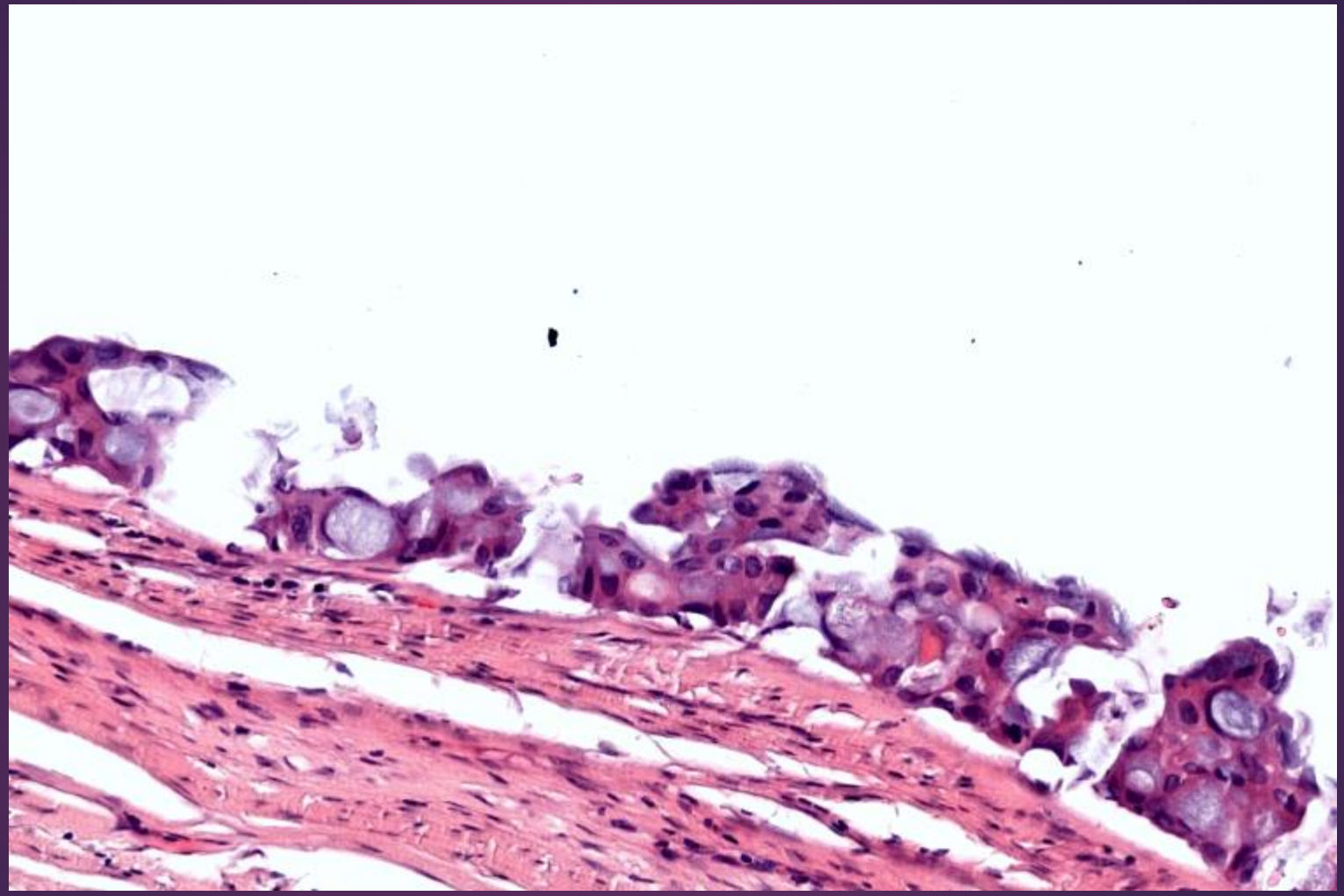
?

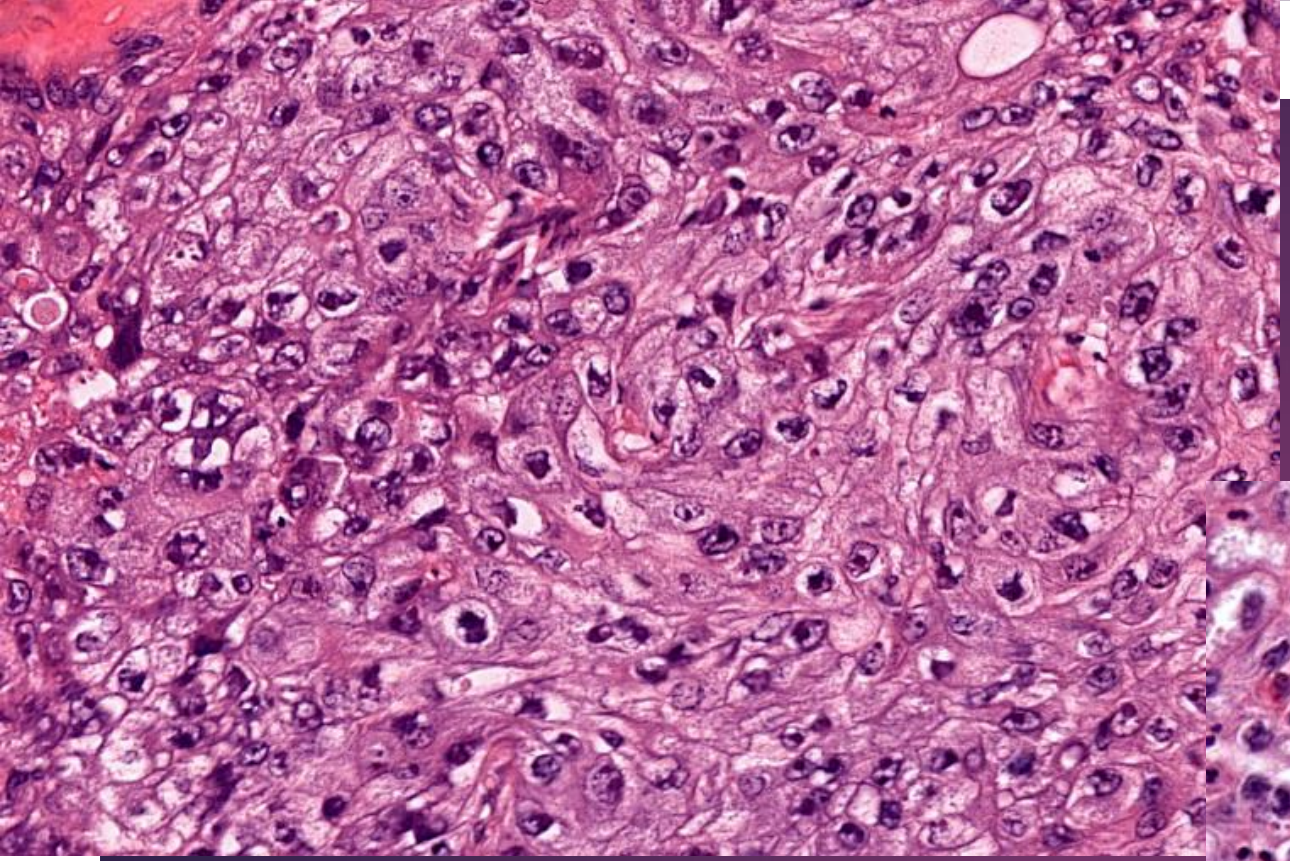


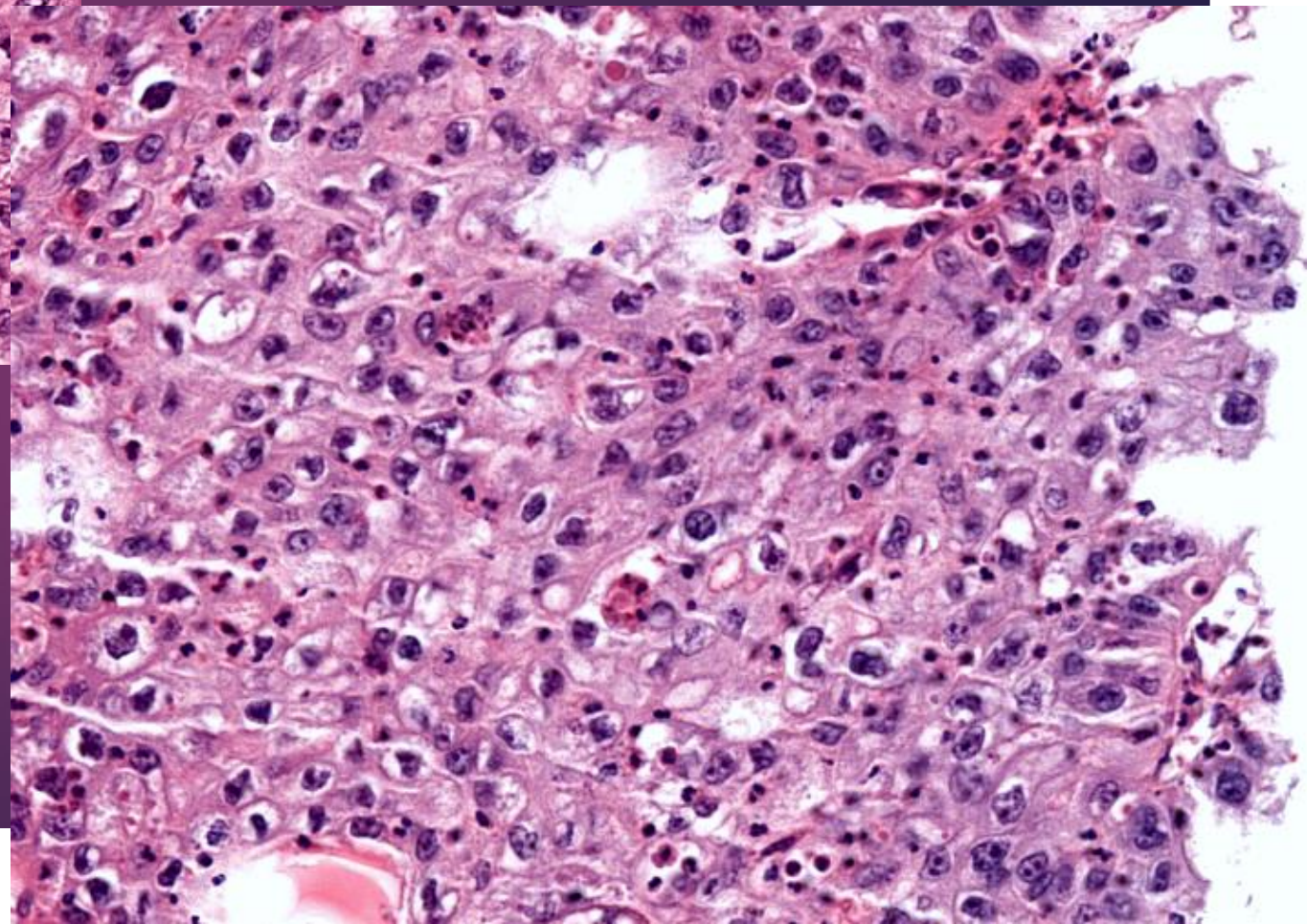


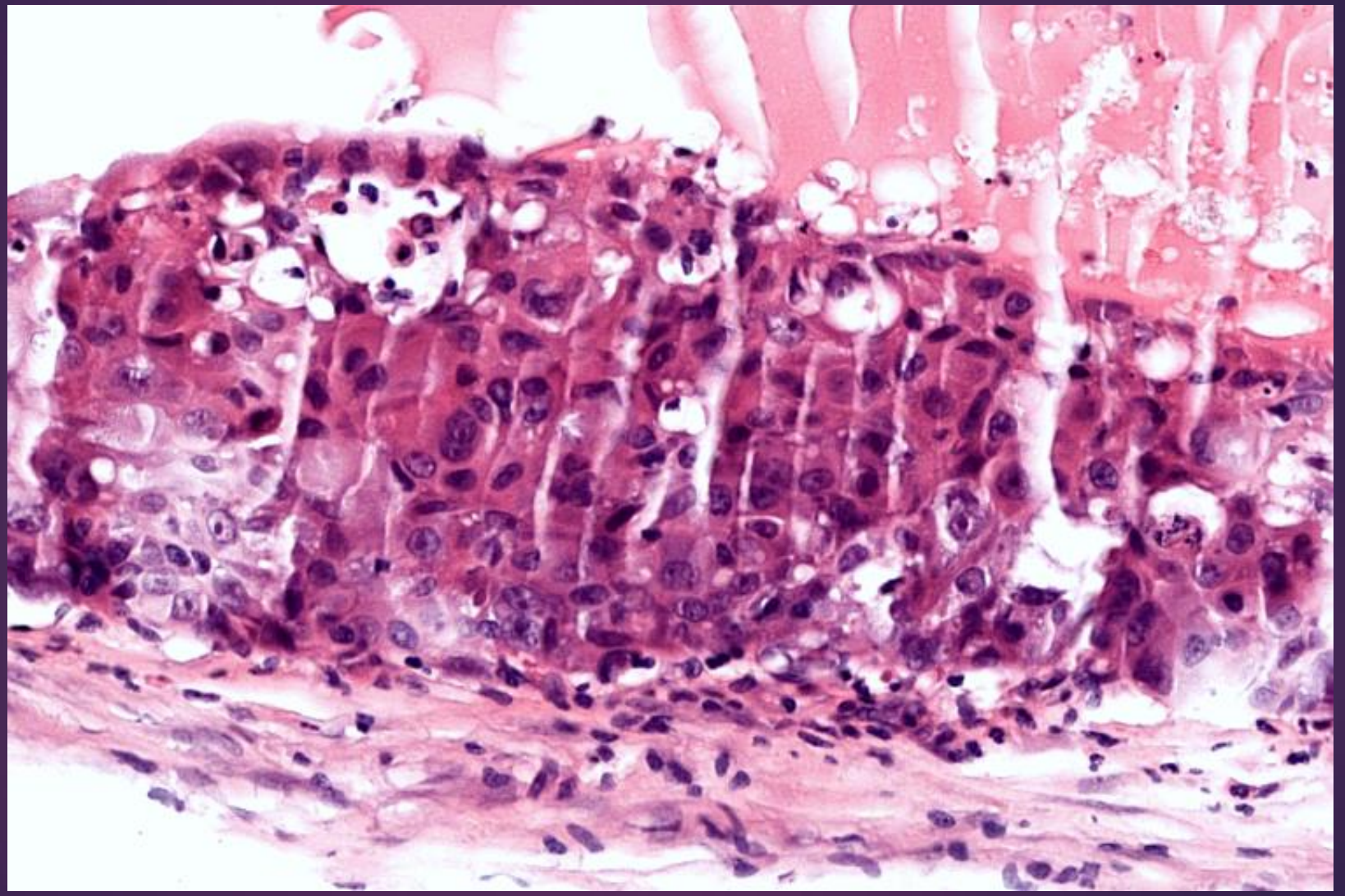


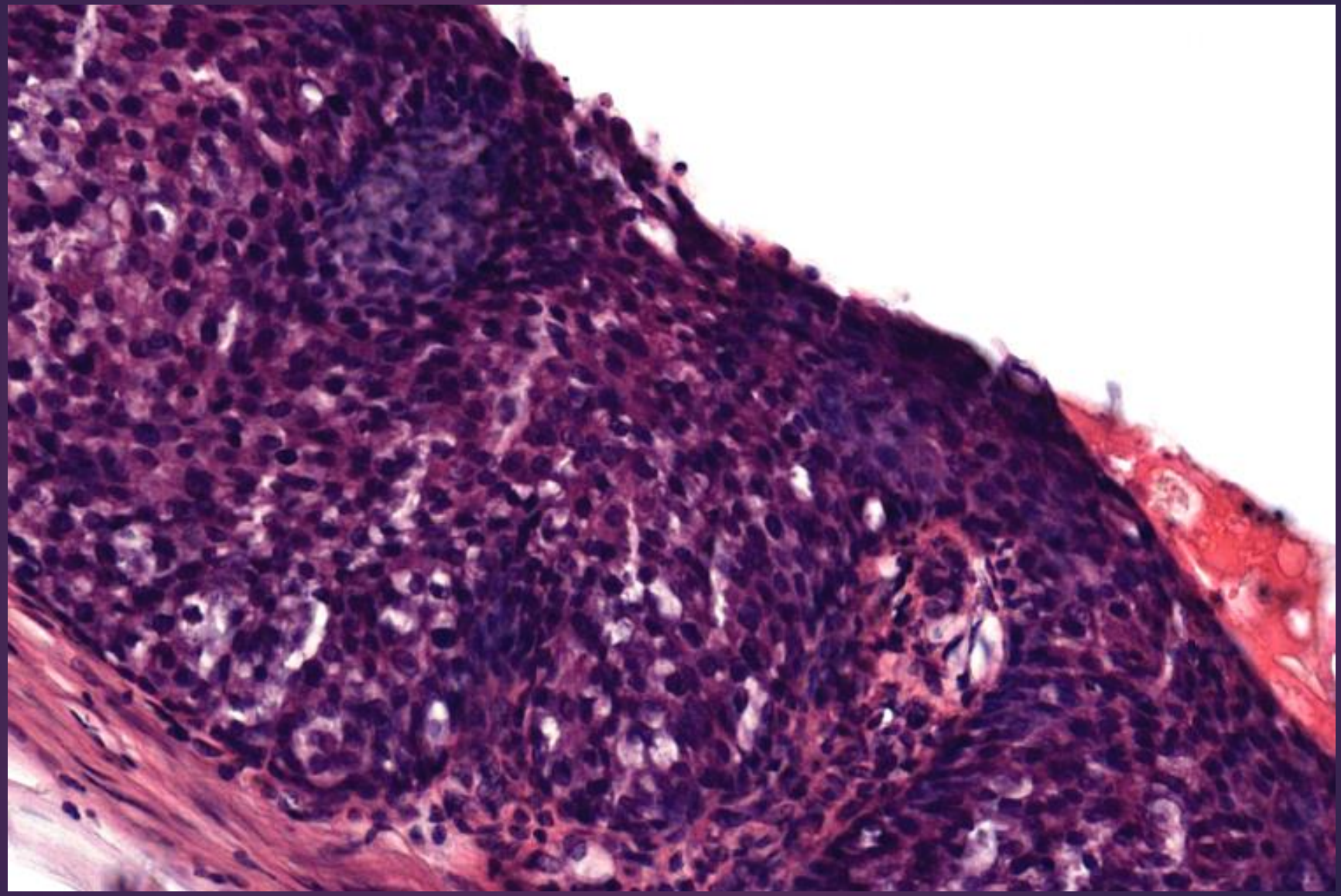


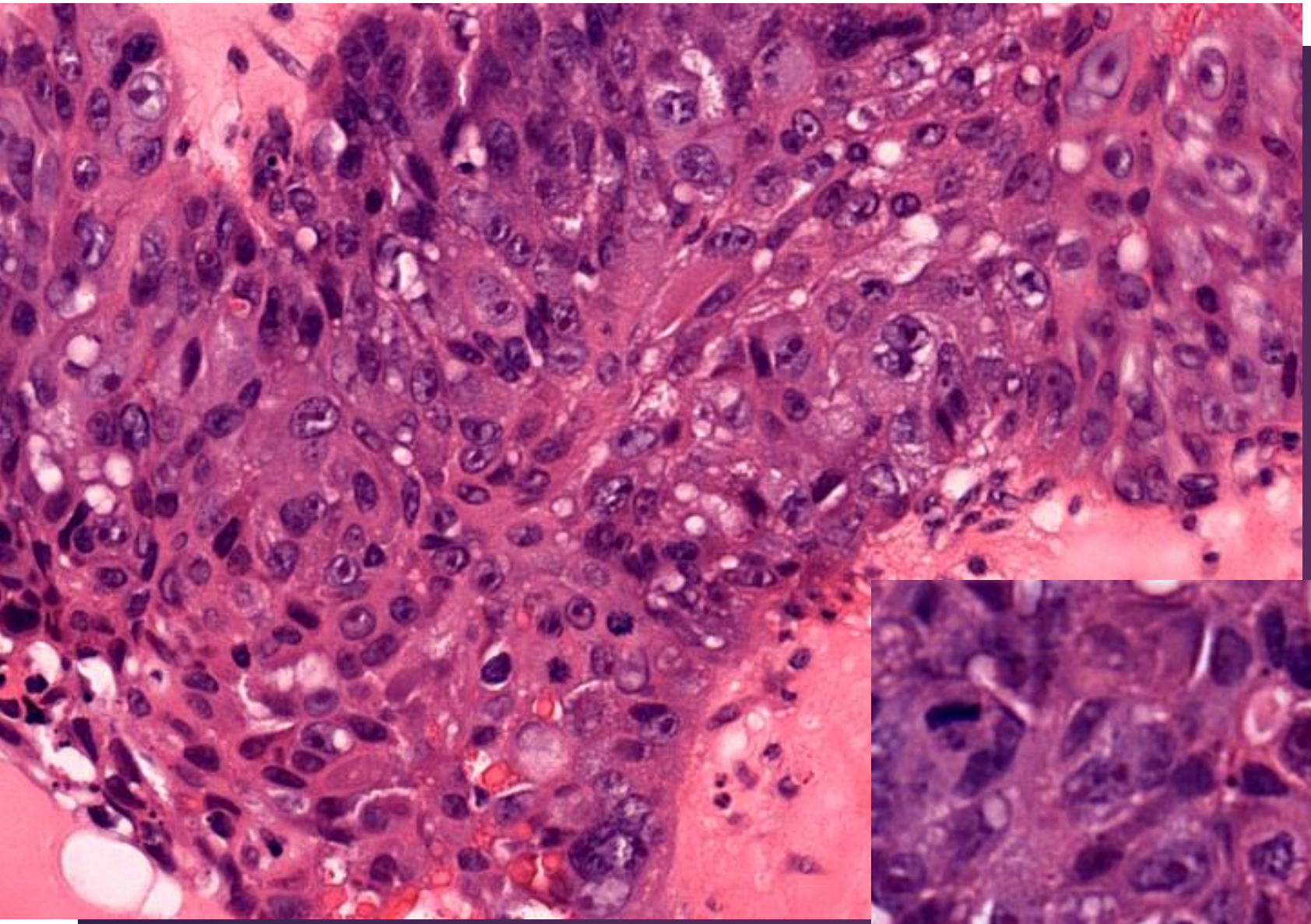


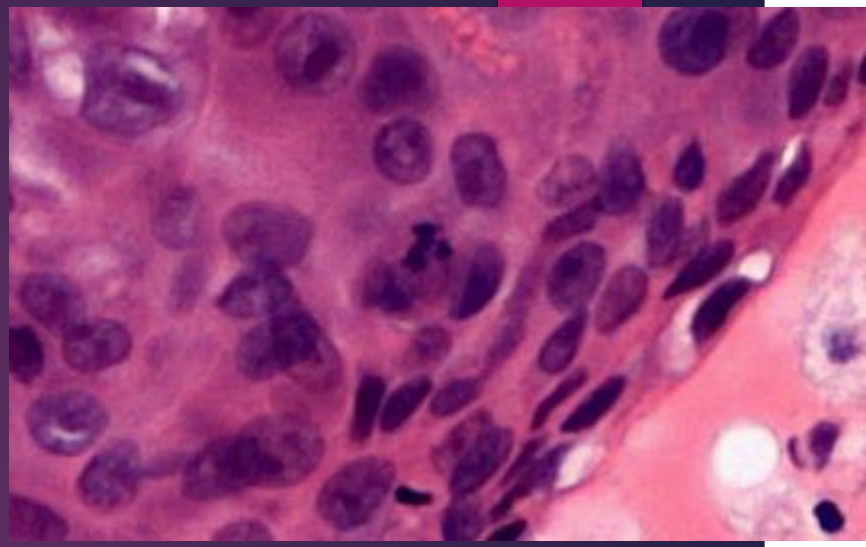


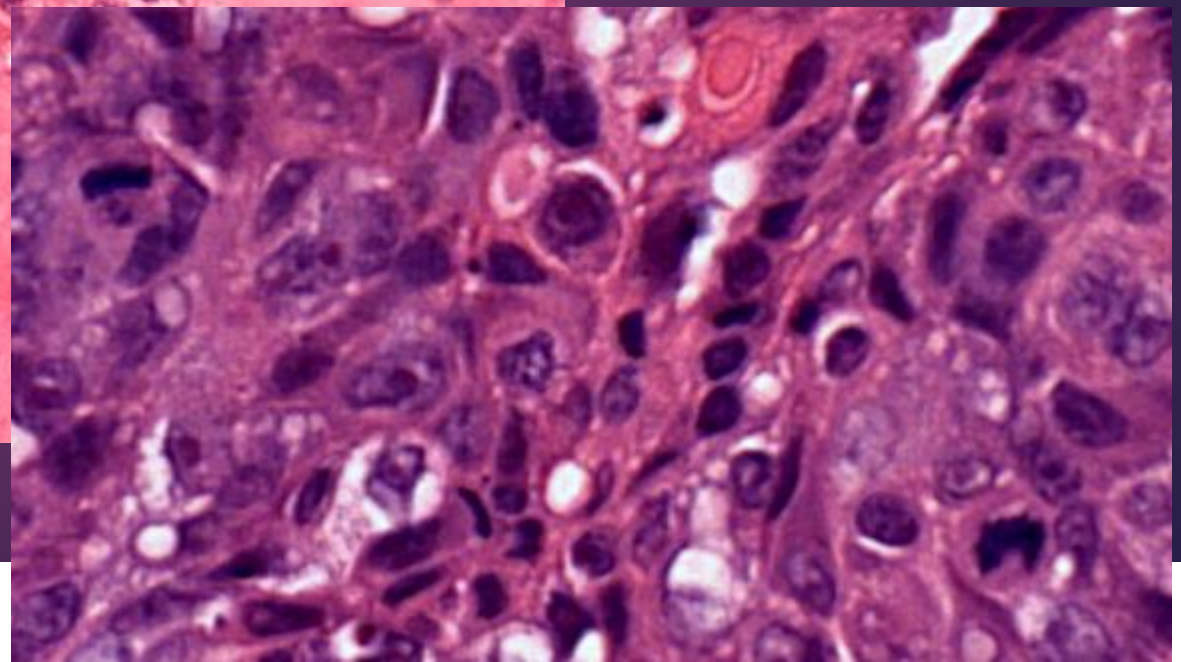




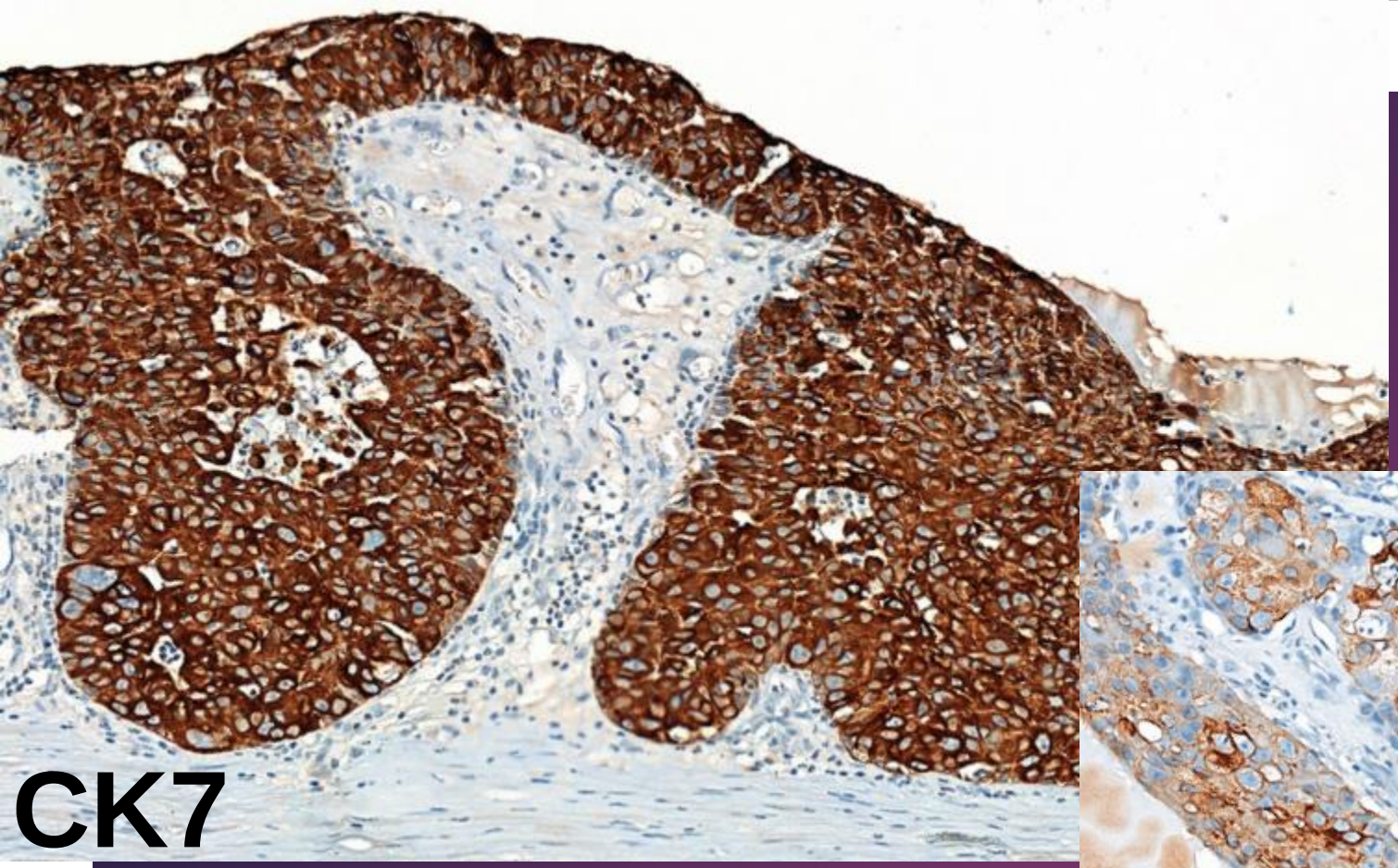


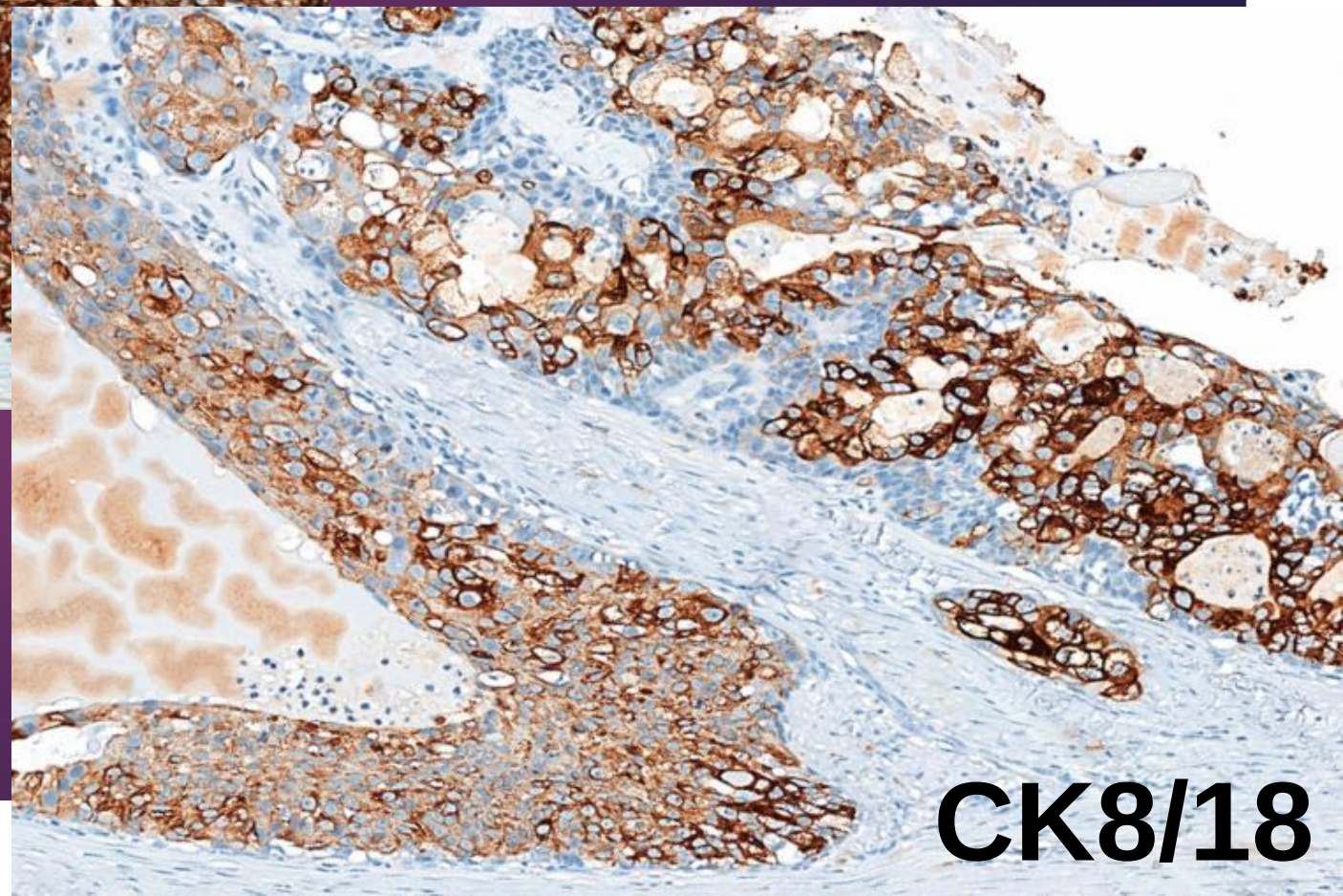


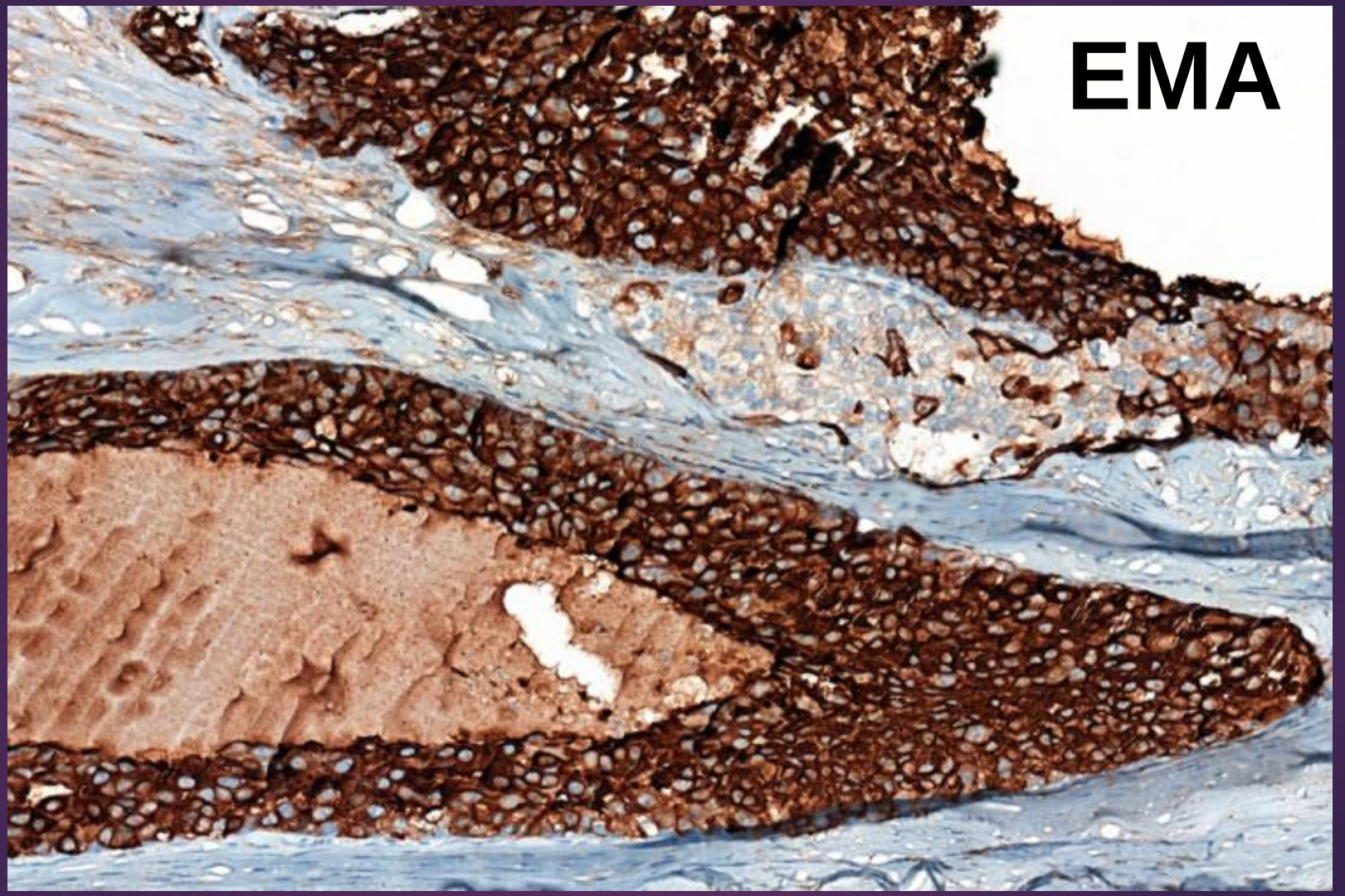


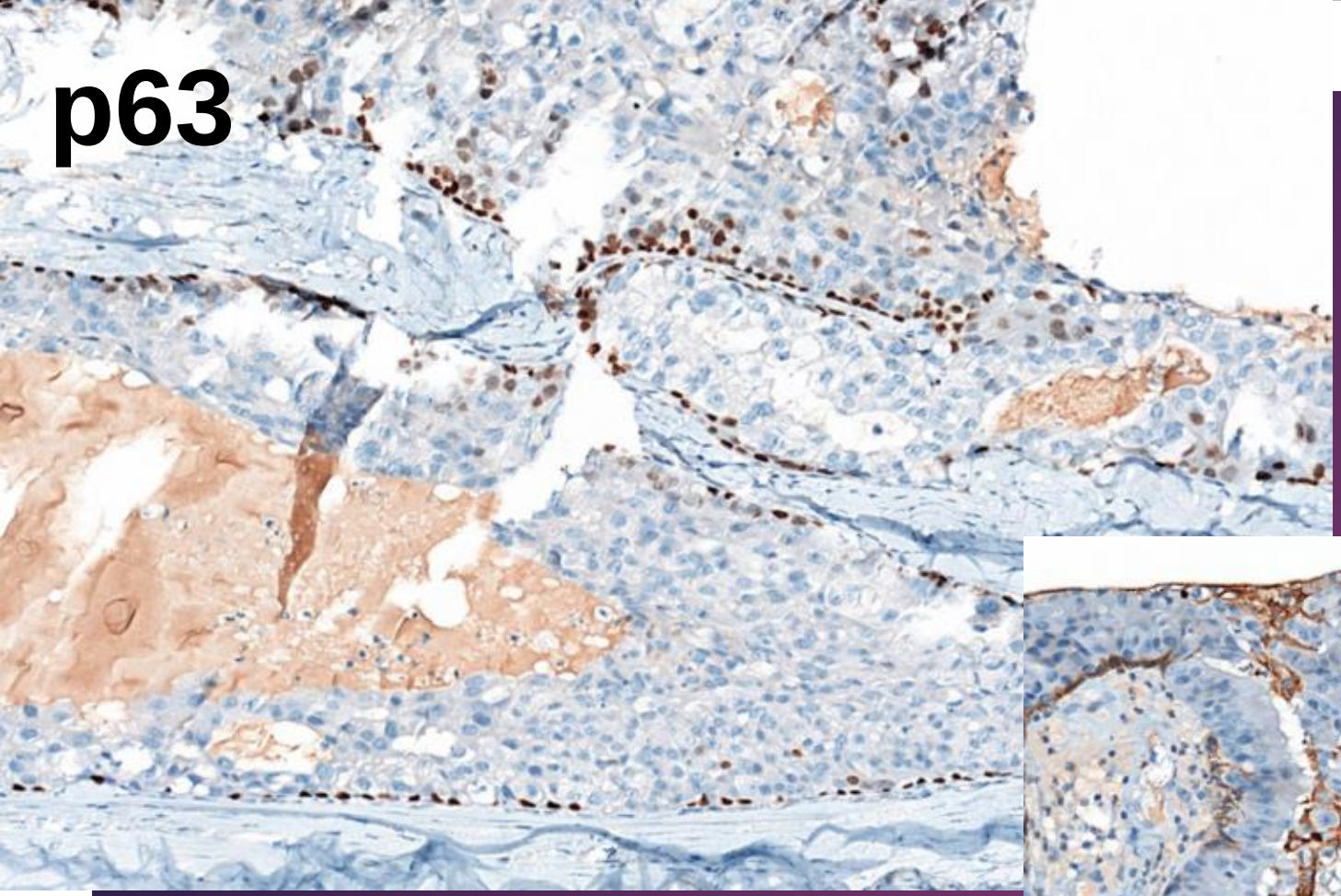


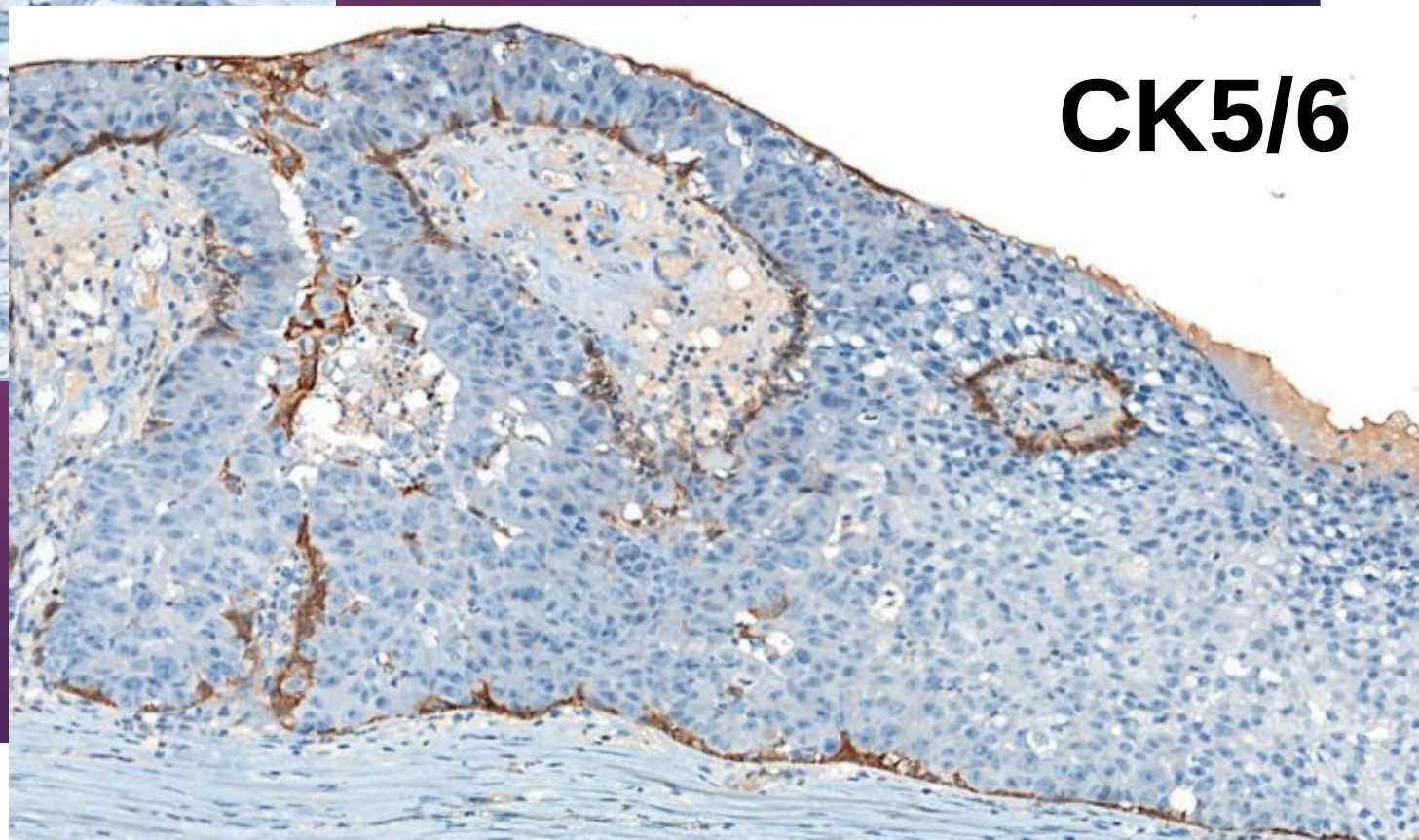
?

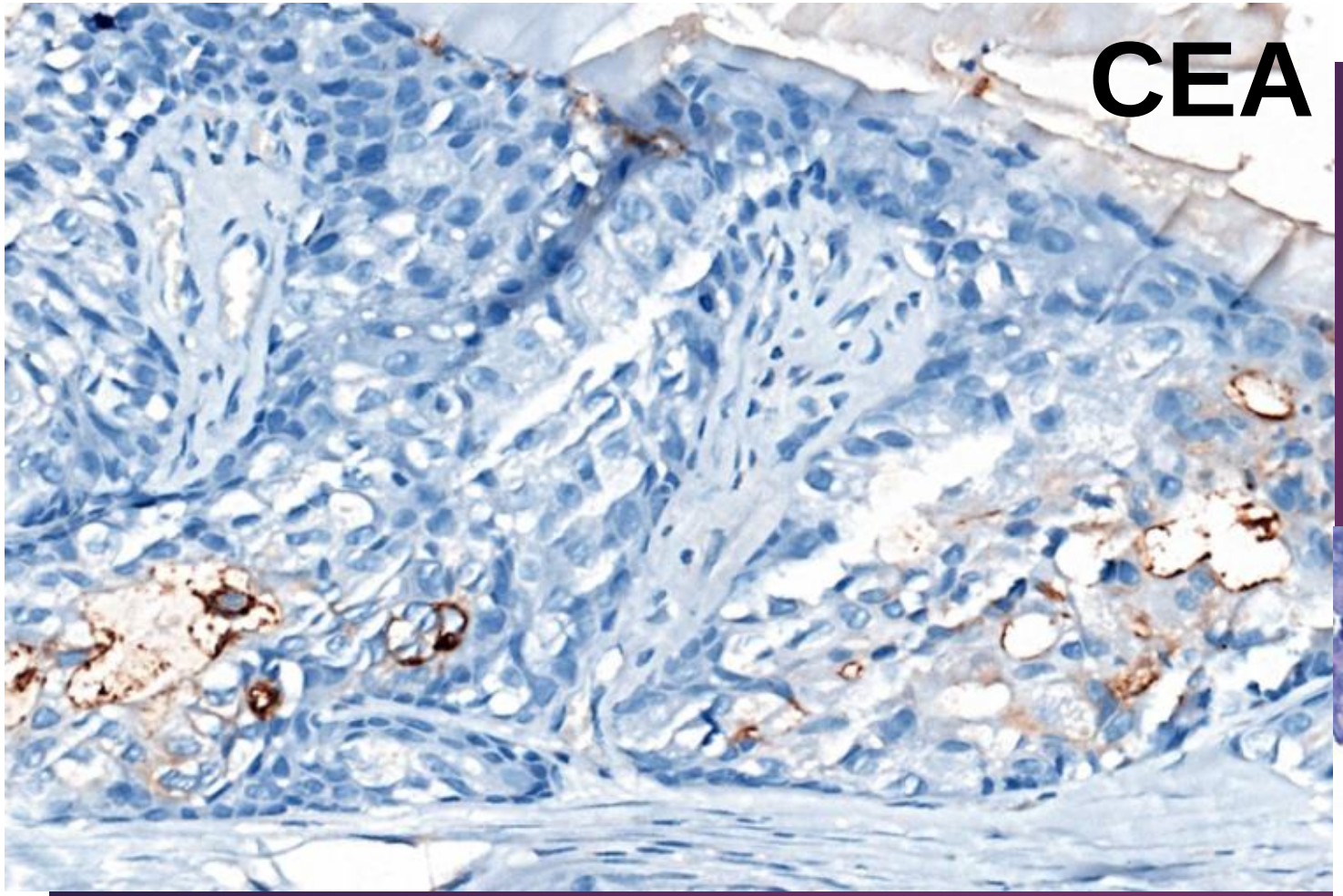

CK7

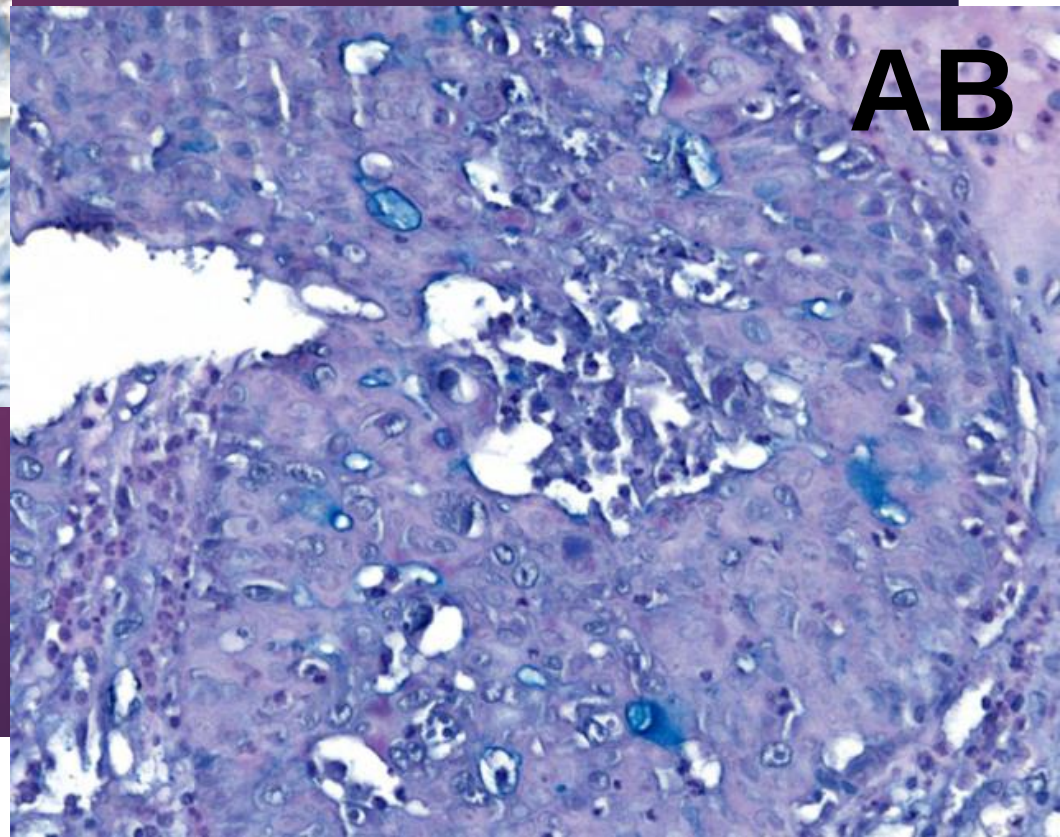

CK8/18


EMA


p63


CK5/6


CEA


AB

IHC

POZITÍVNE

- CK7, EMA difúzne
- CK8/18 vo väčšine
- p63 a CK5/6 v bazálnych bb. diskontinuálne
- CEA fok.luminálne
- PR slabo pozit.

NEGATÍVNE

- CK20
- WT1
- ER
- p16
- SATB2
- S100, SMA, GFAP, dezmin
- CD117


?
WHICH
WAY
NEXT

Bližšie nešpecifikovateľný adenokarcinóm

Adnexálny karcinóm – hidradenokarcinóm

(prof.MUDr.Dmitry Kazakov,PhD.)

Bioptická laboratoř, Plzeň

Detekcia zlomu génu MAML2 (FISH) **– pozitívna**

Detekcia t(11;19) (CRTC1/MAML2) (RT-PCR) - negatívna
Detekcia t(11;15) (CRTC3/MAML2) (RT-PCR) - negatívna

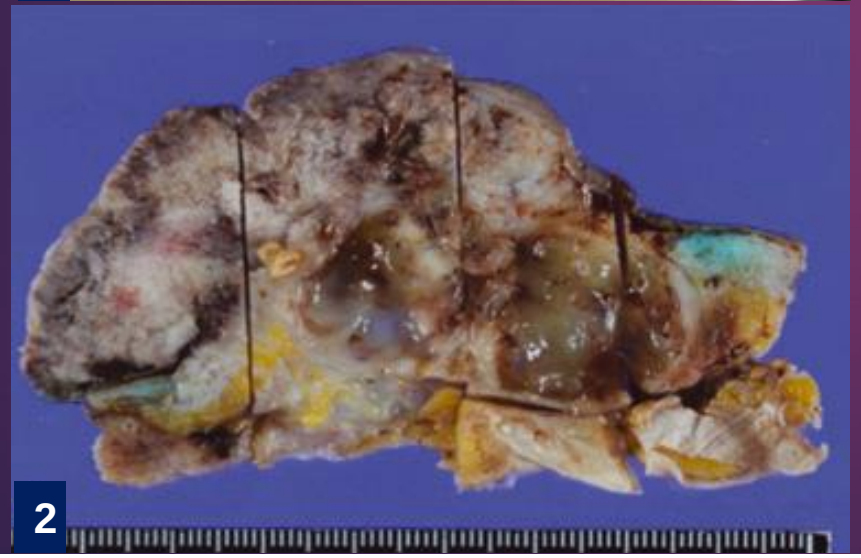
Detekcia zlomu génu ETV6 (FISH) - negatívna
Detekcia translokácie t(12;15) (ETV6/NTRK3) (RT-PCR) - negatívna

Zlom génu MAML2 (FISH), i keď bez dokázaného fúzneho partnera (PCR), podporuje dg. hidradenokarcinómu.

Hidradenokarcinóm

- malígny tumor potných žliaz
- zriedkavý výskyt (2,6 / 1 mil. SEER data)
- 5.-7. dec., M≥Ž
- oblasť hlavy a krku, končatiny
- de novo / malígnou transformáciou hidradenómu
- prognóza zlá
- LG - lokálne rekurencie; HG - mts LU aj vzdialene


1


2


3

1 Yoshimi K Translocation of the MAML2 gene in hidradenocarcinoma. J Dermatol 2017

2 Honda Y Hidradenocarcinoma showing prominent mucinous and squamous differentiation and associated pagetoid cells. J Cutan Pathol. 2013

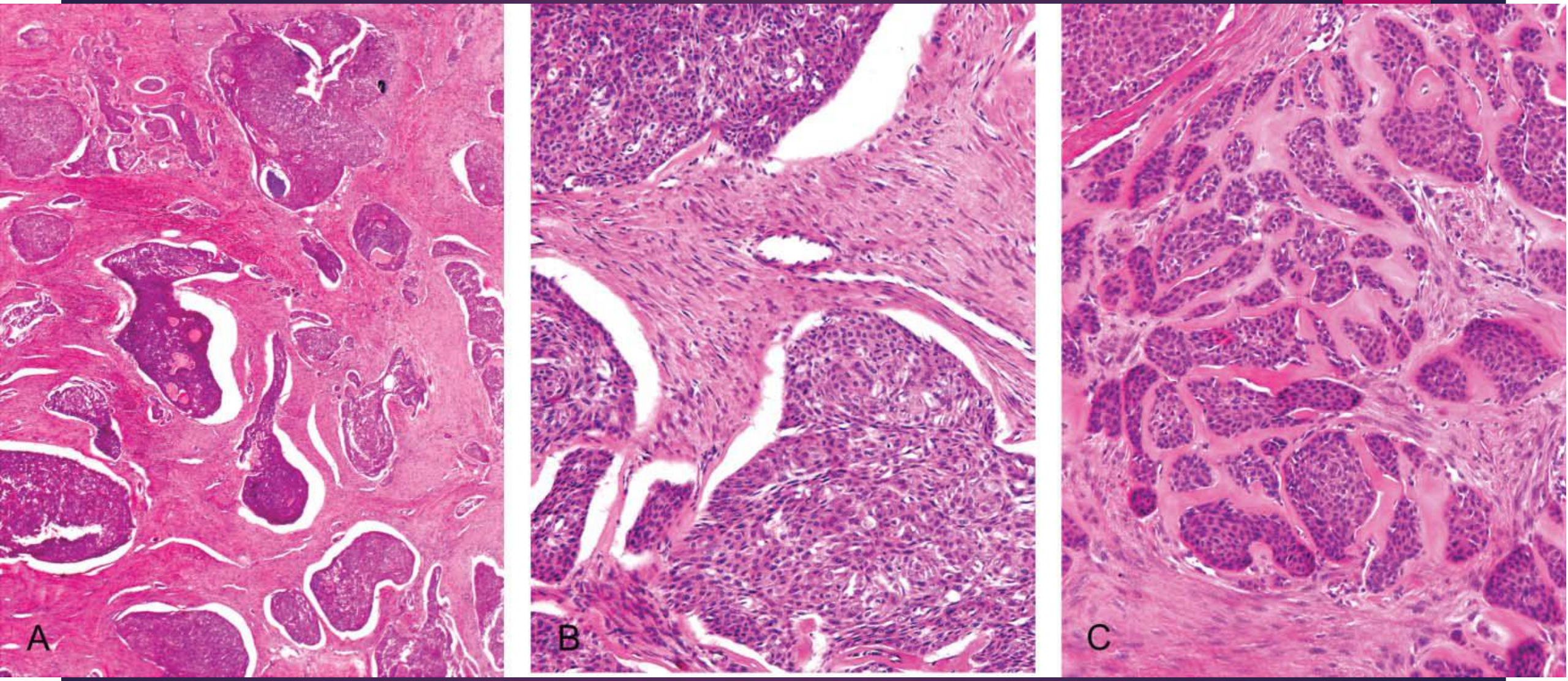
3 Cohen M Apocrine Hidradenocarcinoma of the Scalp: A Classification Conundrum. Head and Neck Pathol 2009

Hidradenokarcinóm

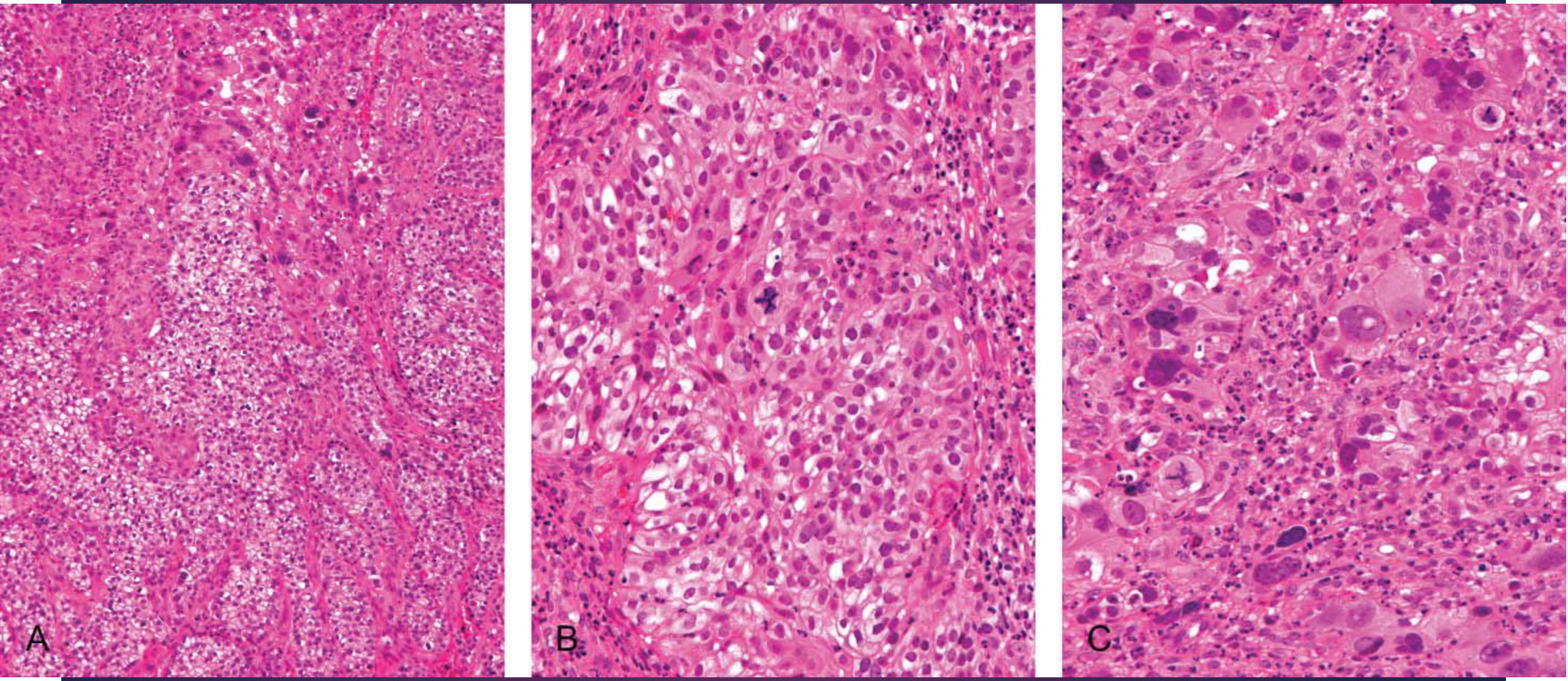
Mikroskopicky – heterogenita

- viaceré typy buniek – svetlé, eozinofilné, skvamoidné, onkocytoidné, mucinózne a transitionálne (+ skvamózna, mucinózna metaplázia)
- noduly + duktálna diferenciácia

Rast - solídny, solídne cystický



Kazakov D Am J Dermatopathol 2009



Kazakov D Am J Dermatopathol 2009

Hidradenokarcinóm IHC

Žiadne špecifické imuno pre stanovenie dg.

AE1/3, CK5/6, EMA
Cam5.2, CEA, CK7 (luminálne)
p53
Ki67

Hidradenokarcinóm - genetika

MAML2 - zlom génu
- translokácia t(11;19) CRTC1/MAML2

mutácie P53

amplifikácia HER2/neu terapeutický význam?

Genes Chromosomes Cancer. 2005 Jun;43(2):202-5.

Clear cell hidradenoma of the skin-a third tumor type with a t(11;19)--associated TORC1-MAML2 gene fusion.

Behboudi A[1], Winnes M, Gorunova L, van den Oord JJ, Mertens F, Enlund F, Stenman G.

Genes Chromosomes Cancer. 2007 Jun;46(6):559-63.

Frequent fusion of the CRTC1 and MAML2 genes in clear cell variants of cutaneous hidradenomas.

Winnes M[1], Mölne L, Suurküla M, Andrén Y, Persson F, Enlund F, Stenman G.

Ann Diagn Pathol. 2016 Aug;23:8-13. doi: 10.1016/j.anndiagpath.2016.04.006. Epub 2016 Apr 16.

Cutaneous hidradenoma: a study of 21 neoplasms revealing neither correlation between the cellular composition and CRTC1-MAML2 fusions nor presence of CRTC3-MAML2 fusions.

Kyrpychova L[1], Kacerovska D[2], Vanecek T[2], Grossmann P[2], Michal M[2], Kerl K[3], Kazakov DV[4].

Am J Dermatopathol. 2009 May;31(3):236-47. doi: 10.1097/DAD.0b013e3181984f10.

Cutaneous hidradenocarcinoma: a clinicopathological, immunohistochemical, and molecular biologic study of 14 cases, including Her2/neu gene expression/amplification, TP53 gene mutation analysis, and t(11;19) translocation.

Kazakov DV[1], Ivan D, Kutzner H, Spagnolo DV, Grossmann P, Vanecek T, Sima R, Kacerovska D, Shelekhova KV, Denisjuk N, Hillen U, Kuroda N, Mukensnabl P, Danis D, Michal M.

J Dermatol. 2017 Aug;44(8):e190-e191. doi: 10.1111/1346-8138.13830. Epub 2017 Mar 11.

Translocation of the MAML2 gene in hidradenocarcinoma.

Yoshimi K[1], Goto H[2], Otsuka M[1], Yoshikawa S[1], Omodaka T[3], Kiyohara Y[1].

Hum Pathol. 2017 Dec;70:55-61. doi: 10.1016/j.humpath.2017.10.004. Epub 2017 Oct 24.

A novel fusion gene CRTC3-MAML2 in hidradenoma: histopathological significance.

Kuma Y[1], Yamada Y[2], Yamamoto H[2], Kohashi K[2], Ito T[1], Furue M[3], Oda Y[4].

cases by fluorescence in situ hybridization. Moreover, neither the fusion genes nor gene rearrangement was detected in prominent cystic tumors and poroid hidradenomas. We conclude that CRTC1/3-MAML2 fusion gene analysis can be a useful method for diagnosing hidradenoma. Considering the histological and genetic similarity to mucoepidermoid carcinoma, hidradenoma may be a cutaneous counterpart of salivary gland mucoepidermoid carcinoma.

Kožný analóg mukoepidermoidného karcinómu slinných žliaz?

Rare Tumors. 2015 Feb 25;7(1):5719. doi: 10.4081/rt.2015.5719. eCollection 2015 Feb 11.

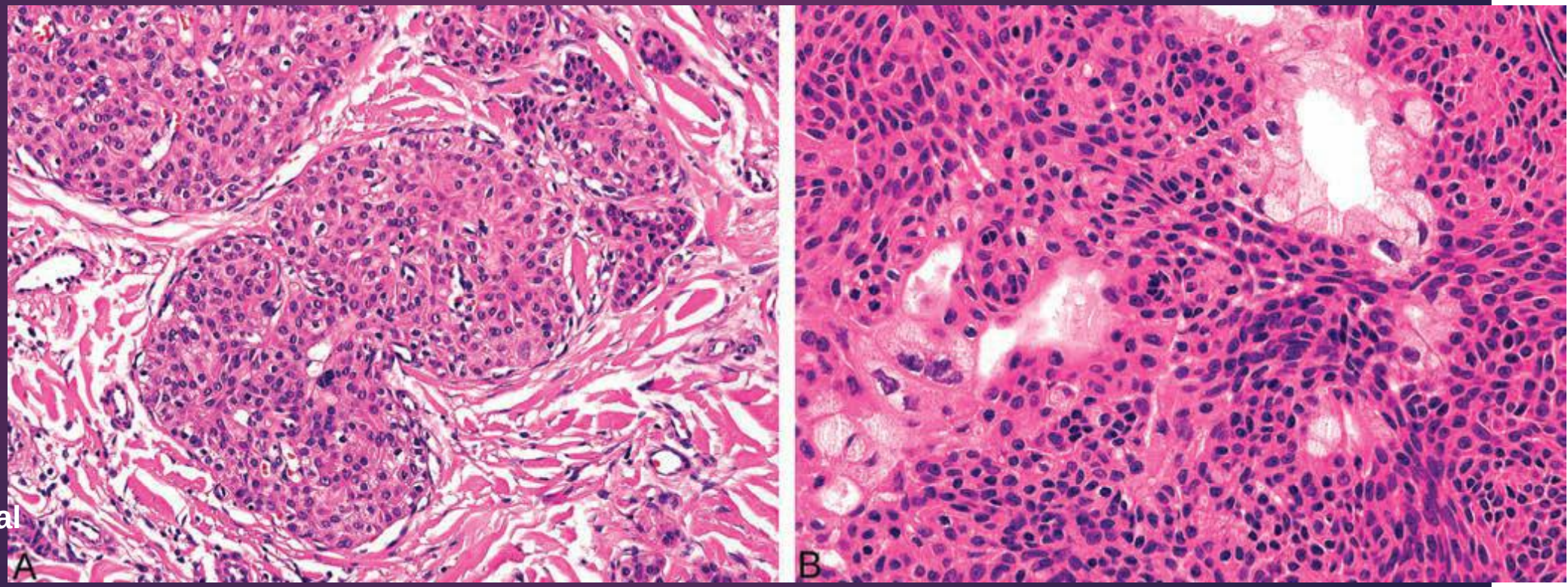
Whole exome sequencing of a patient with metastatic hidradenocarcinoma and review of the literature.

Gupta E[1], Guthrie KJ[2], Krishna M[3], Asmann Y[4], Parker AS[5], Joseph RW[1].

Gene	Gene product name	Genomic event	Gene product	Potential impact of mutation
FGFR1	Fibroblast growth factor receptor 1	Amplification	Tyrosine Kinase Receptor	Increased expression could allow for increased activation of MAPK pathway and cell growth.
CDH1	E-cadherin	c.2439+1G>C	Cell adhesion	Loss of function mutations in CDH1 could allow cells to grow even in the presence of cell to cell contact
MYST3	MYST histone acetyltransferase (monocytic leukemia) 3	Amplification	Histone acetyl transferase	Increased expression could lead towards dysregulated epigenetic changes.
ZNF703	Zinc Finger 703	Amplification	Transcription Factor	Transcriptional corepressor which does notbind directly to DNA and may regulate transcription through recruitment of histone deacetylases to gene promoters
PTCH1	c.C3641T	Missense	p.T1214M	Hedgehog signaling pathway
TCF7L1	c.C710T	Missense	p.S237F	WNT/Hippo signaling pathways
ARID1A	c.G4468T	Nonsense	p.E1490X	Chromatin Remodeling
CDH1	c.2439+1G>C	Splicing	p.E1490X	Cadherin C
FBX011	c.G1993C	Missense	p.D665H	Ubiquitin protein ligase complex
FNBP1	NM_025133	Nonsense	cG1783T	Formin binding protein family
IL6ST	NM_002184	Missense	c.T2532G	Jak-Stat pathway
MYC	NM_002467	Missense	c.C459G	MYC amino terminal region

Hidradenokarcinóm DDx

LG – hidradenóm - v 10% fokálne mierne atypie bb.



Kazakov et al. Cutaneous adnexal tumors 2009

Hidradenokarcinóm DDx

LG – hidradenóm

Znaky malignity: asymetria, infiltratívny rast, zvýšená mitotická aktivita, prominentný clefting medzi strómou a nádorovými hniezdami, výrazná dezmoplastická stromálna reakcia

Hidradenokarcinóm DDx

LG – hidradenóm

Návrh pre klasifikovanie tumoru ako malígneho
- prítomnosť 3 a viac znakov: strata ohraničenia, infiltratívny rast, hlboká extenzia, nekróza, perineur. invázia, vaskulárna invázia, pleomorfia jadier a 4+ mitózy /10 HPF
(+ atypické mitózy pri tumoroch s 1 - 2 znakmi)

Hidradenokarcinóm DDx

HG –
dg HG adnexálneho tumoru ako hidradenoca aspoň fokálne partie napodobňujúce hidradenóm (nižší grade, typické bunkové zloženie alebo sklerotická hyalinizovaná stróma)

Hidradenokarcinóm DDx

Podľa prevažujúceho typu buniek - **skvamoidné**

- Porokarcinóm (asociovaný poróm, početné spojenia s epidermou, ihc: p63...)
- SCC - pseudoglandulárny/akantolytický variant (intraepidermový prekurzor ako in situ SCC, -Cam5.2)

Hidradenokarcinóm DDx

Podľa prevažujúceho typu buniek - **clear cells**

- spektrum primárnych a mts tumorov (CCRCC)
- Trichilemálny karcinóm (asociácia s folikulom, benígnym prekurzorom, trich.keratinizácia)
- SCC

Hidradenokarcinóm DDx

Podľa prevažujúceho typu buniek - **clear cells**

- Bazalióm - clear cell variant (rastový vzor a cytológia BCC; +Ber-EP4)
- Sebaceózny karcinóm (sebaceózna difer., -glykogén, -Cam5.2)
- Balloon cell melanoma (-Cam5.2; +S100 a melanocytové markery)

Záver

1. Aj „ateróm“ môže prekvapiť...
2. Sampling
3. Vylúčiť mts

Literatúra

- Kazakov DV et al. Cutaneous adnexal tumors 2009
- Busam KJ ed. Dermatopathology 2nd ed. (Foundations in diagnostic pathology) 2016
- Nazarian RM et al. Atypical and malignant hidradenomas: a histological and immunohistochemical study. Mod Pathol. 2009 Apr;22(4):600-10.
- Gauerke S, Driscoll JJ. Hidradenocarcinomas: a brief review and future directions. Arch Pathol Lab Med. 2010 May;134(5):781-5.
- Nash JW et al. Metastatic hidradenocarcinoma with demonstration of Her-2/neu gene amplification by fluorescence in situ hybridization: potential treatment implications. J Cutan Pathol 2007: 34: 49–54

Ďakujem za pozornosť