

XXIII. Martinský bioptický seminár SD-IAP

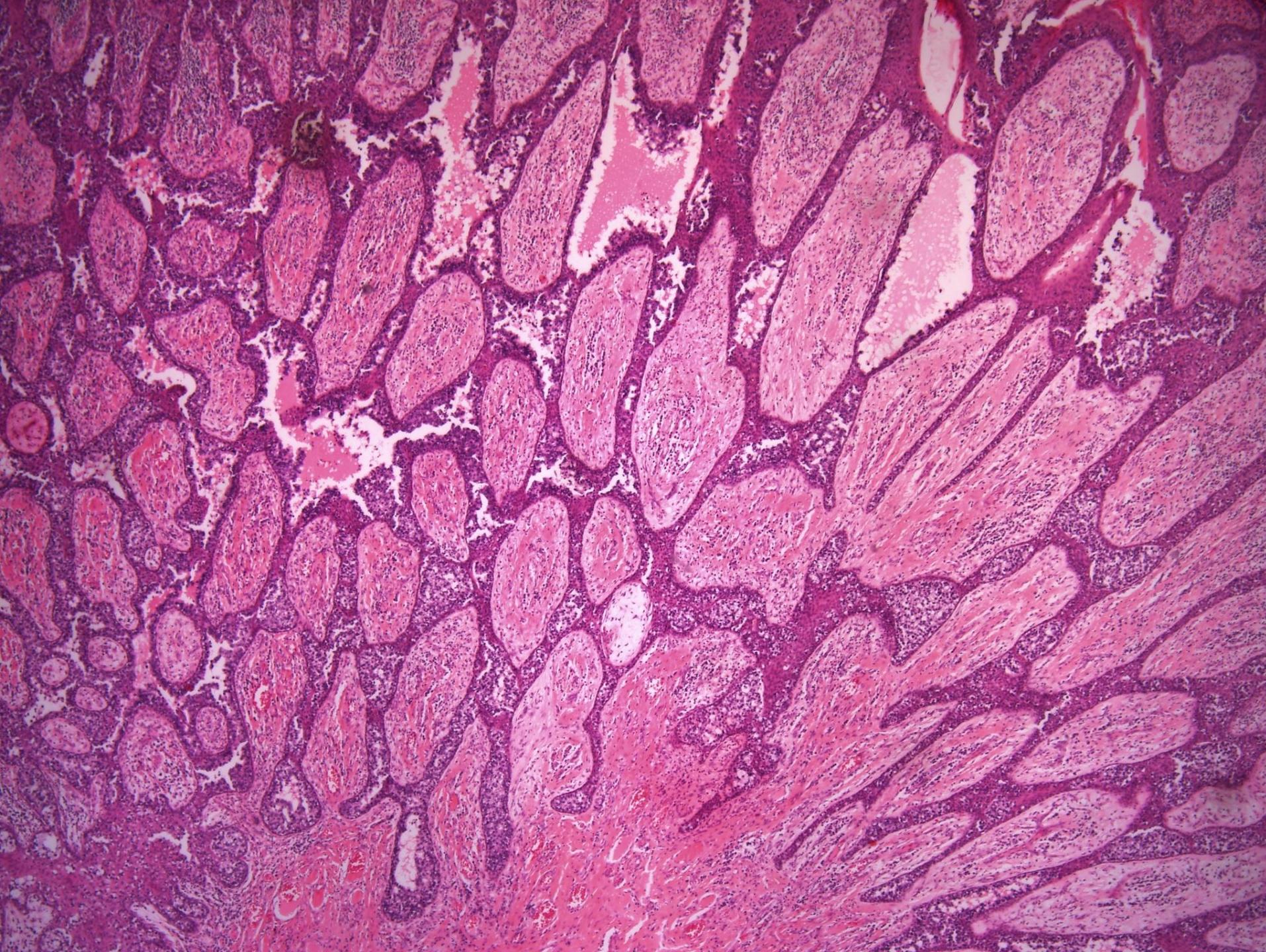
Lúčky, 10.-11.11.2017

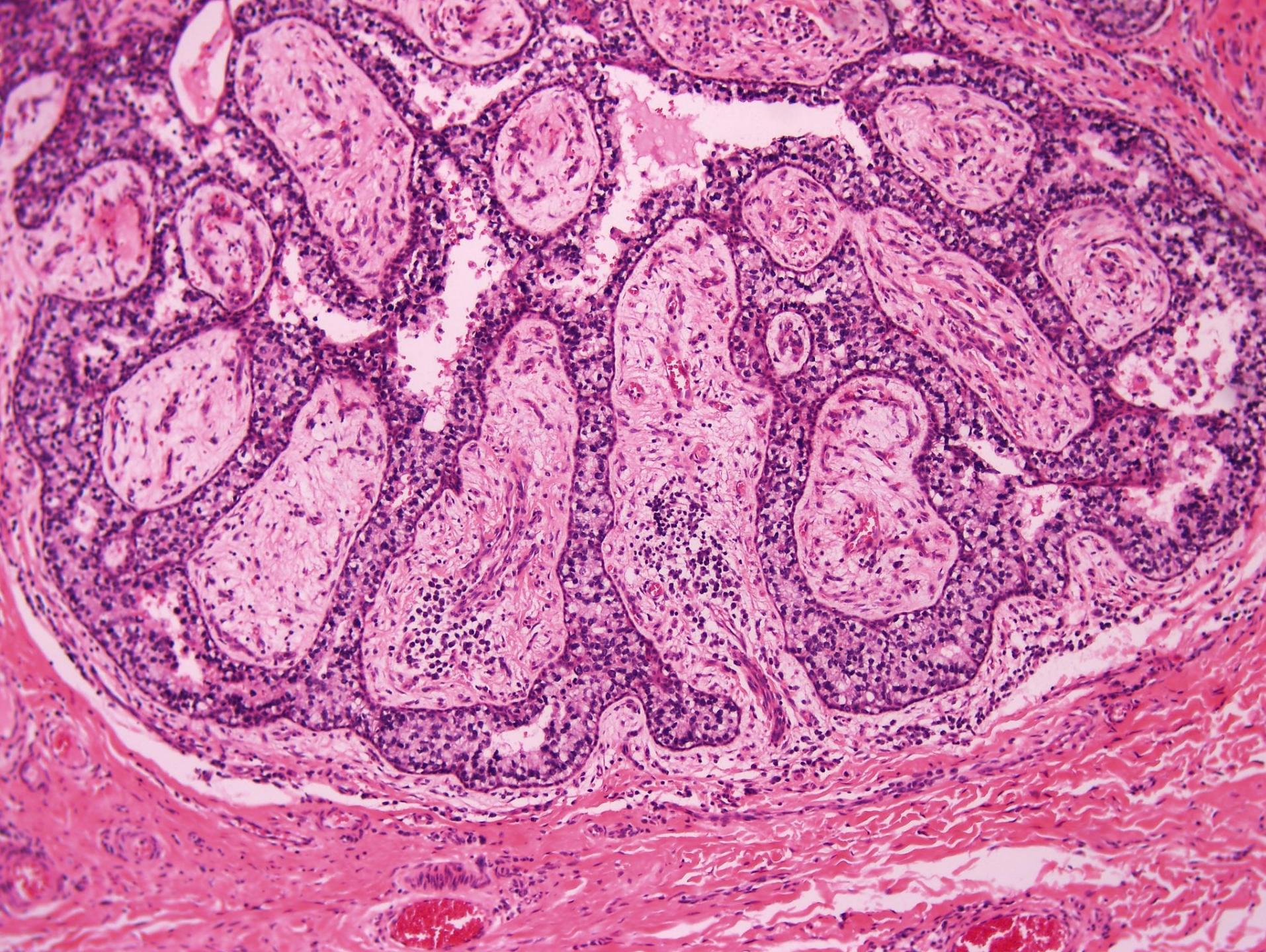
Prípad č. 8

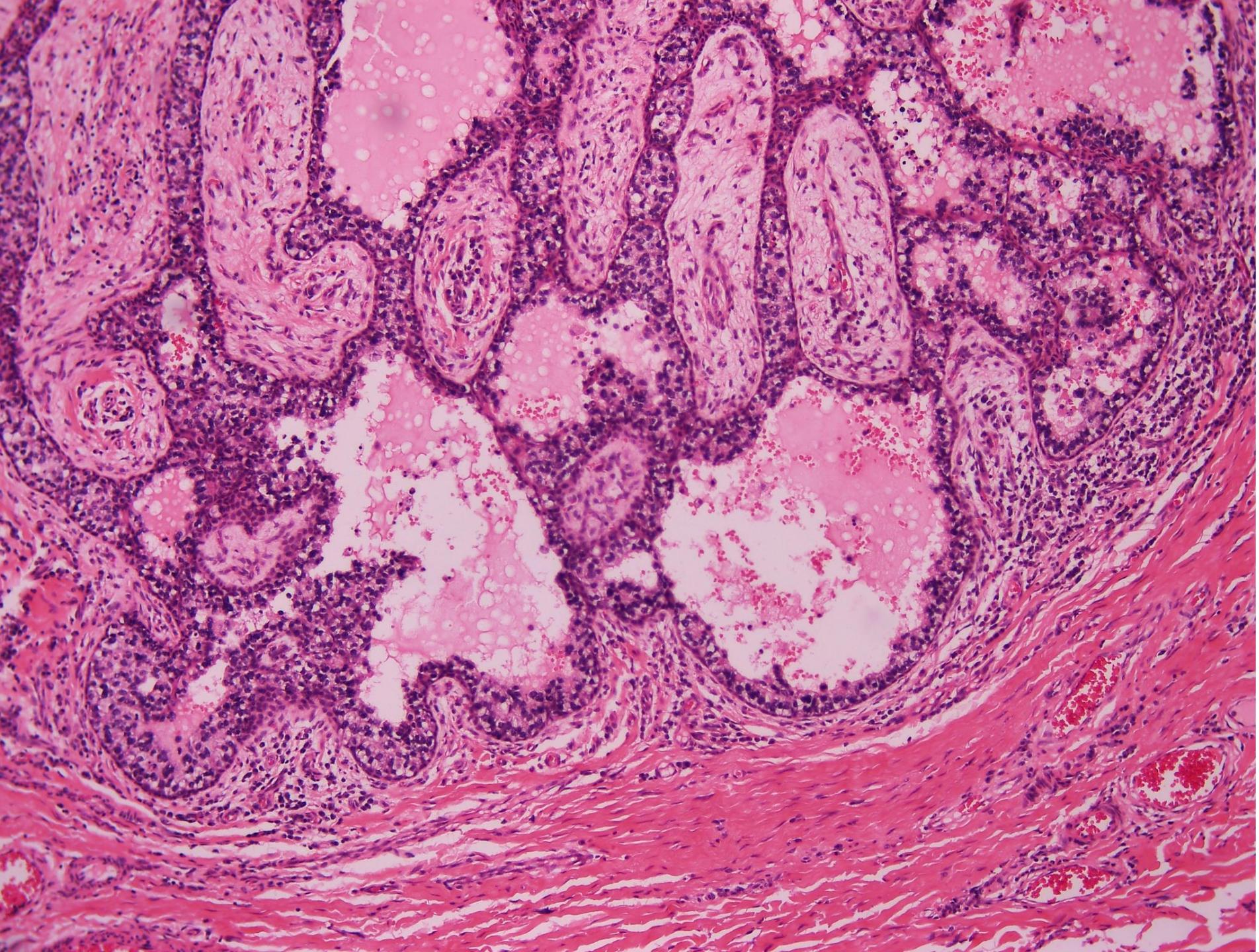
Martina Bobrovská
ÚPA JLF UK a UN Martin

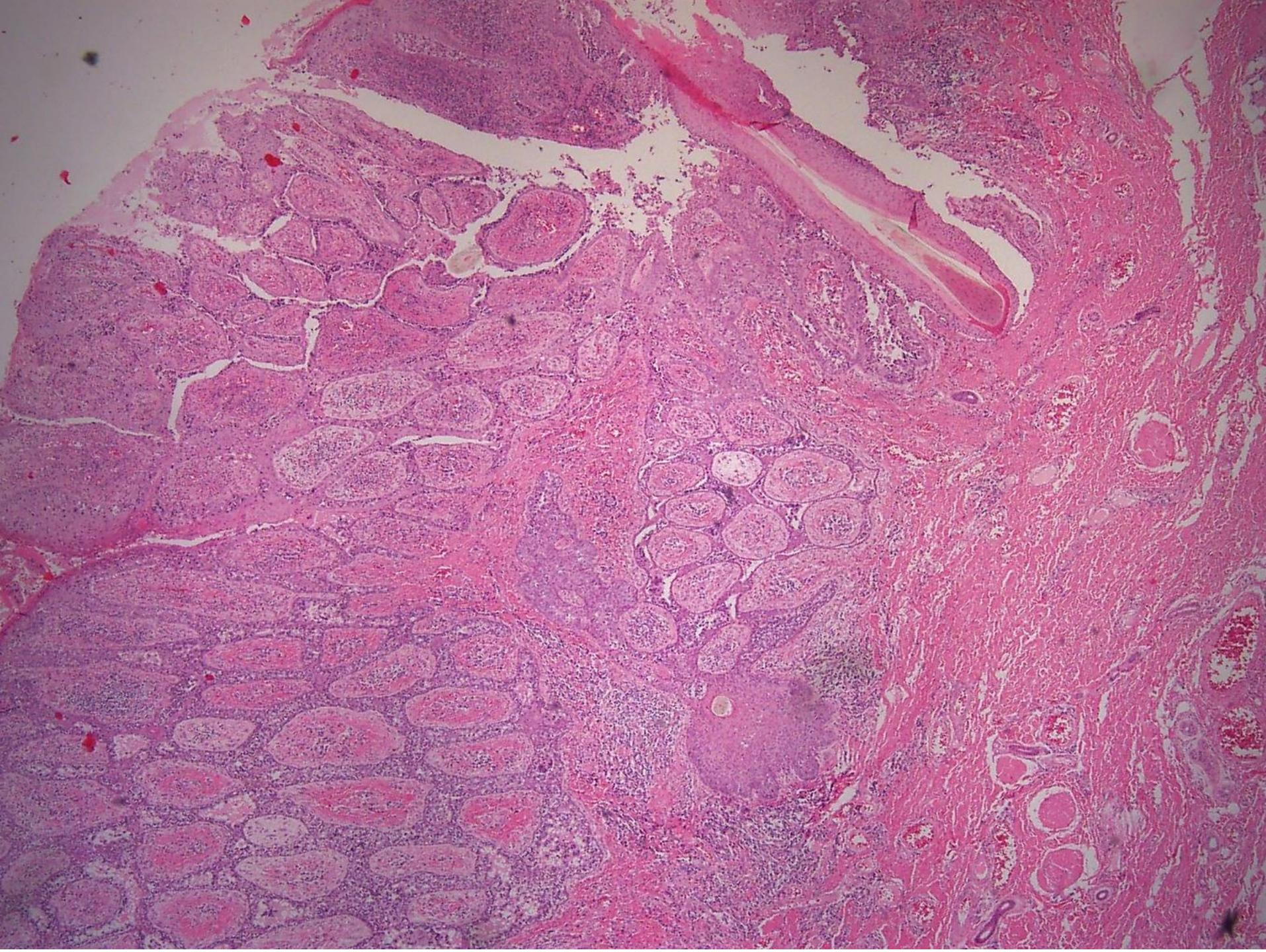
Klinické údaje

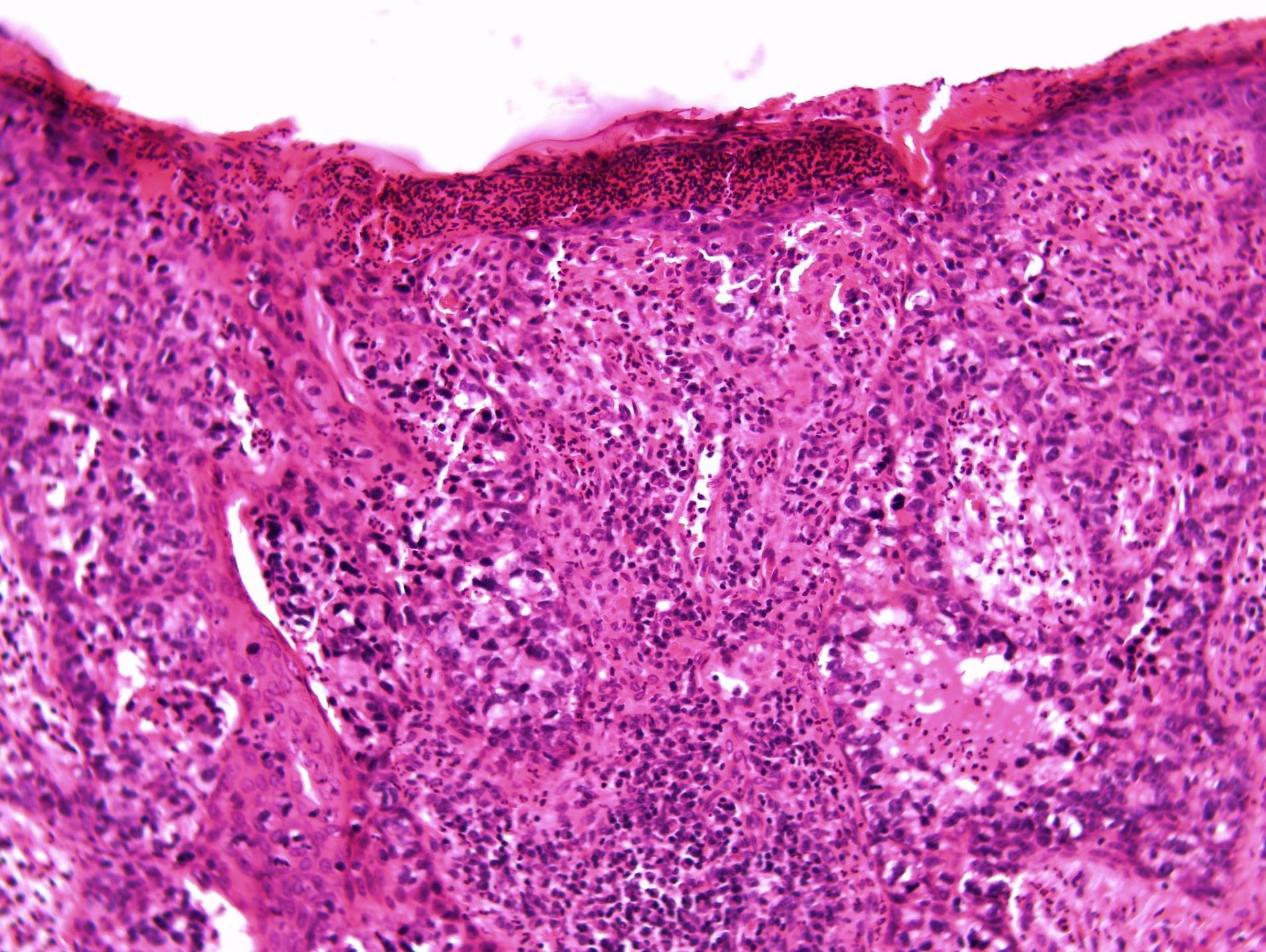
- 72 ročný muž
- predmet vyšetrenia: kožný tumor z ľavej slabiny
- klinická diagnóza: kožný tumor
- makropopis: excízia kože veľkosti 5,2x4x1,3 cm, v centre ktorej je na povrchu mierne prominujúci, granulovitý hrboľatý útvar nepravidelných okrajov, tuhej konzistencie, na reze žltkastobelavej farby
- konzultácia z PAO Komárno

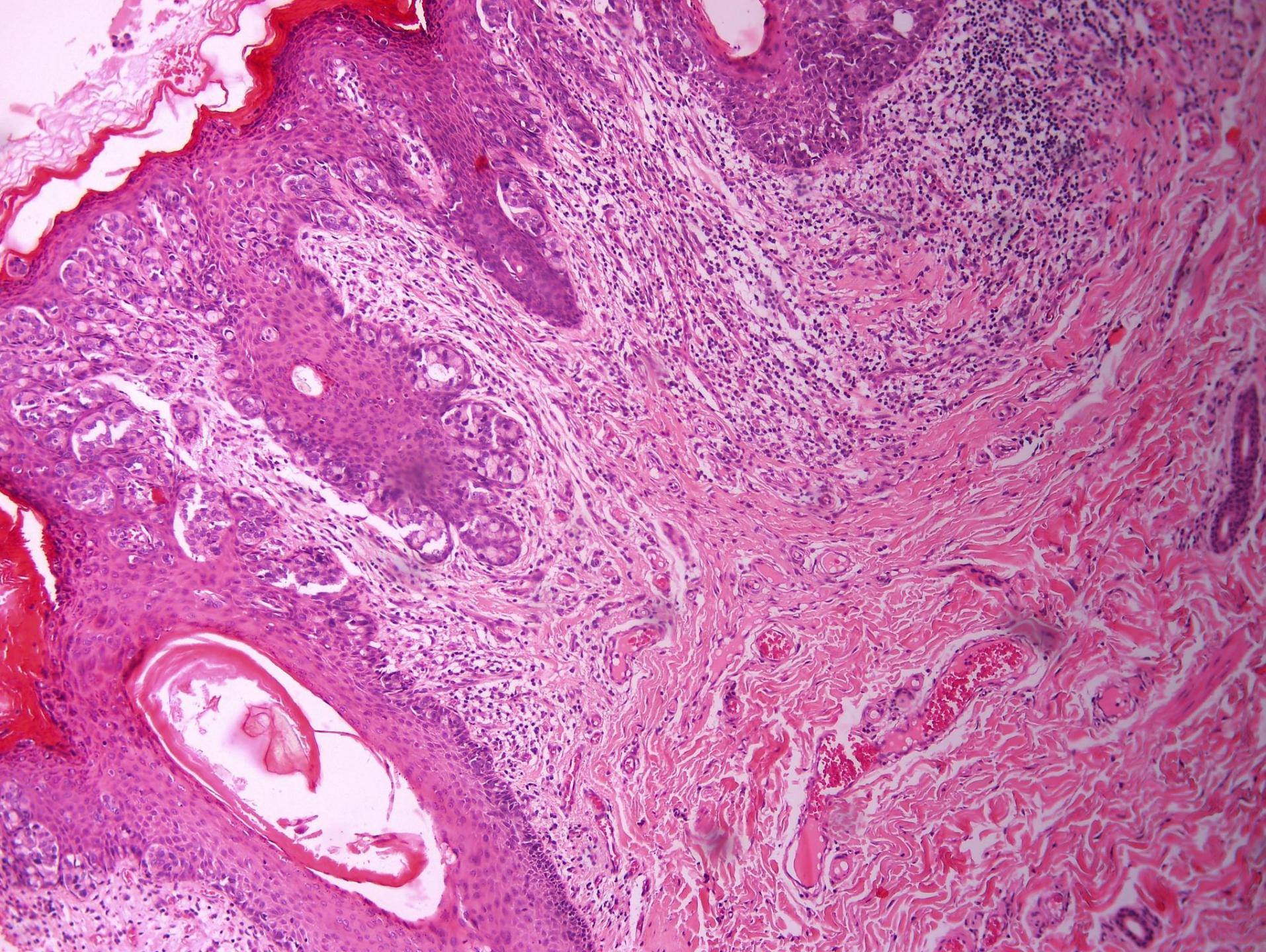


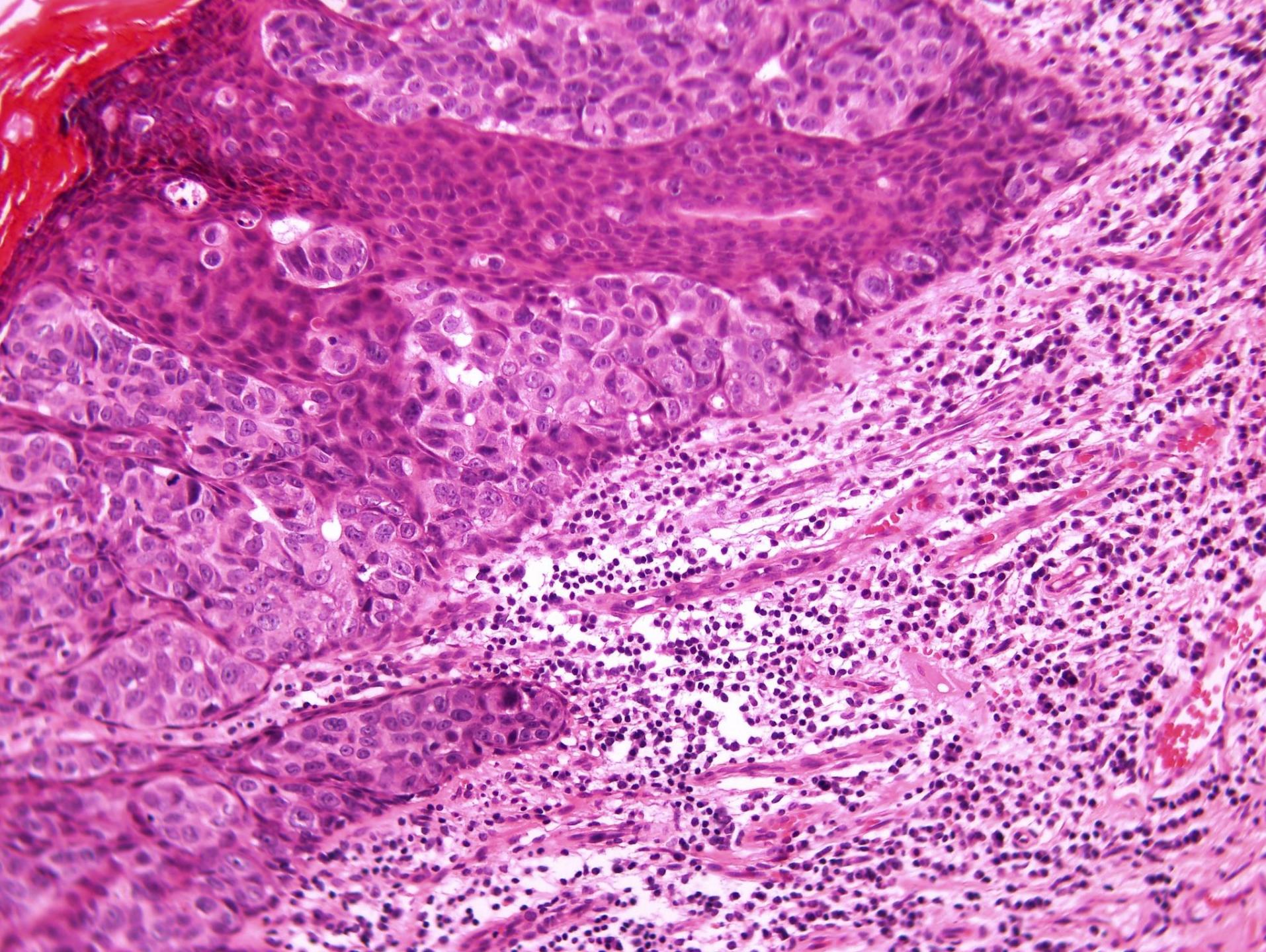


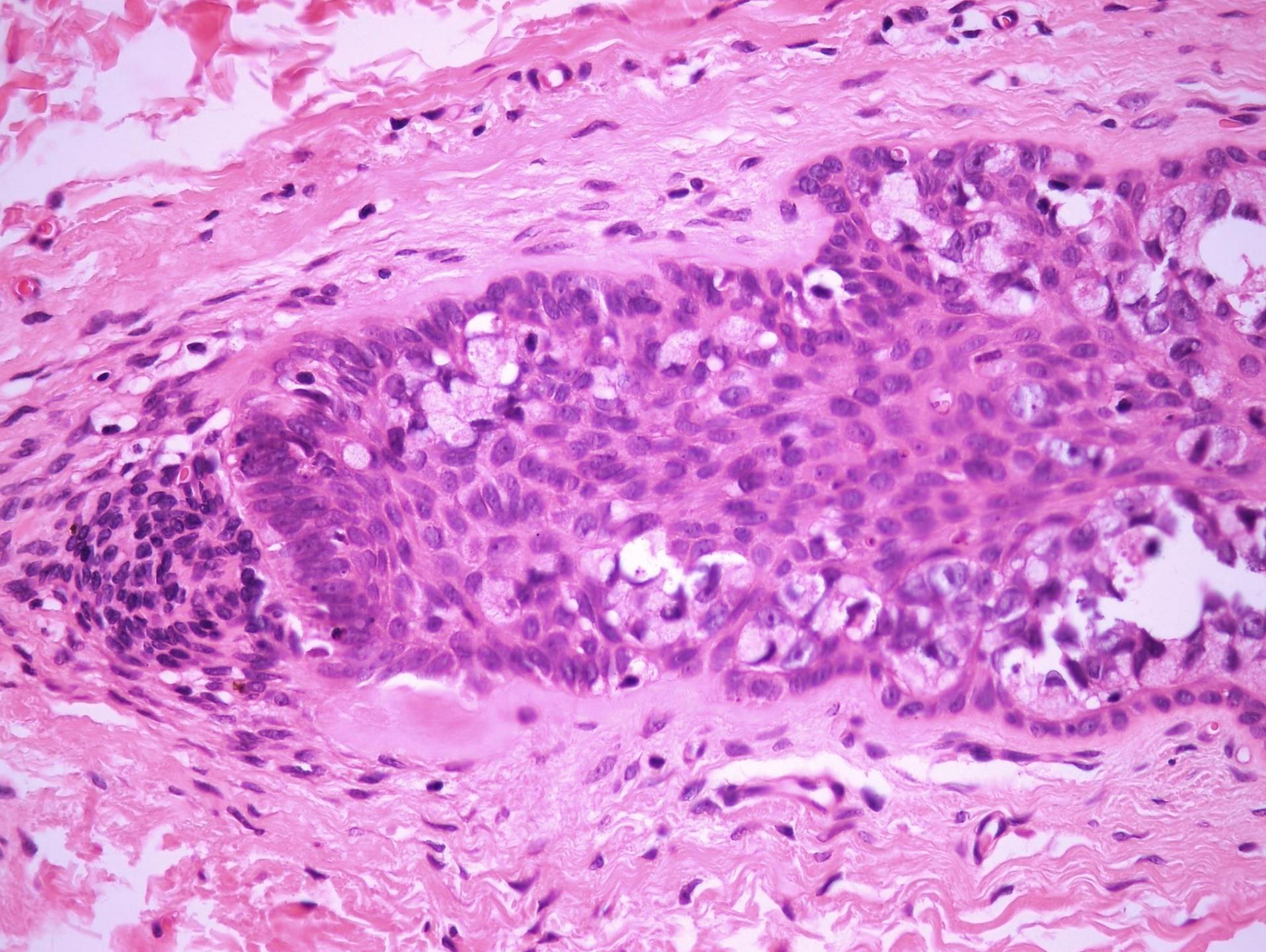


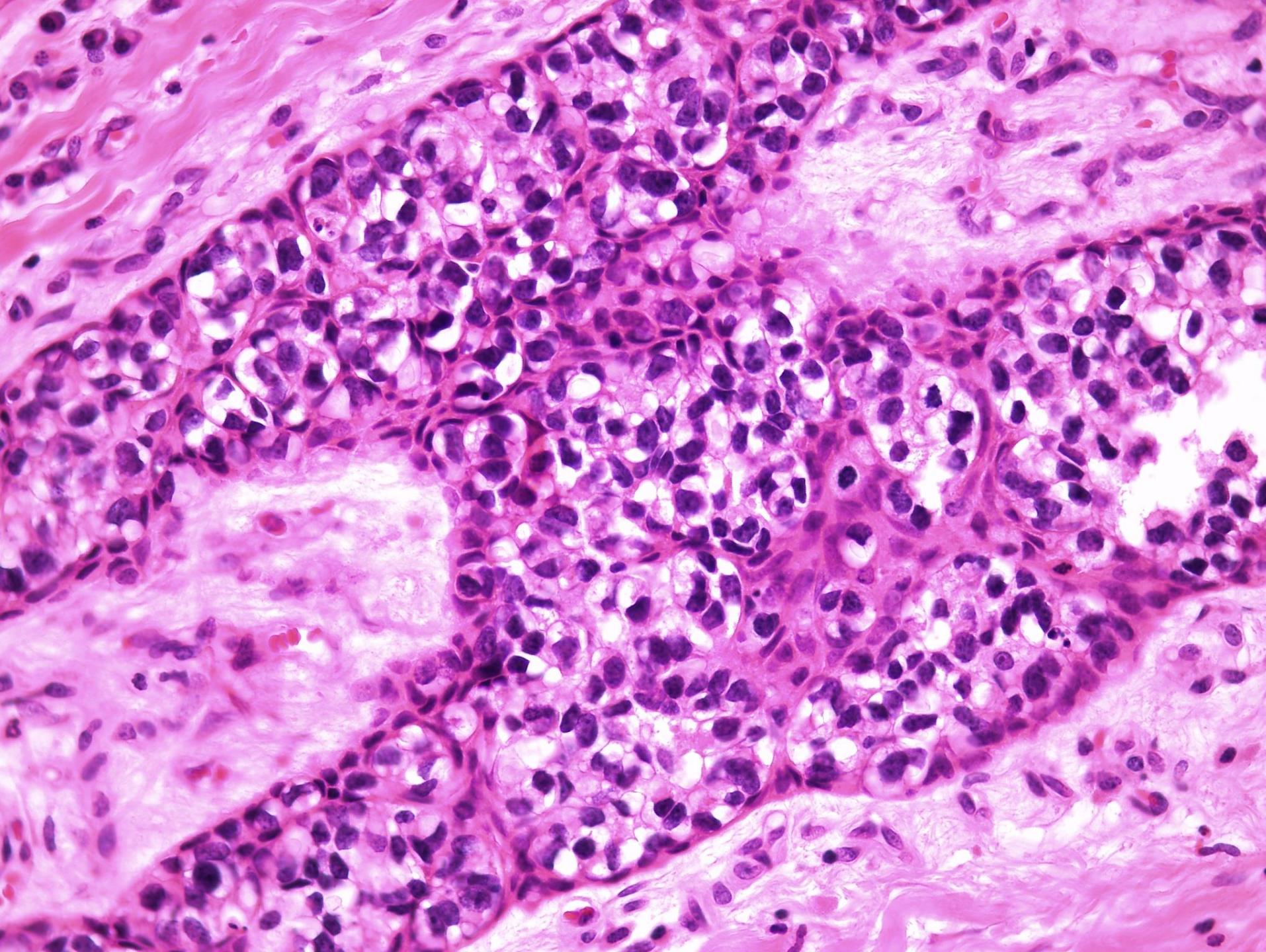


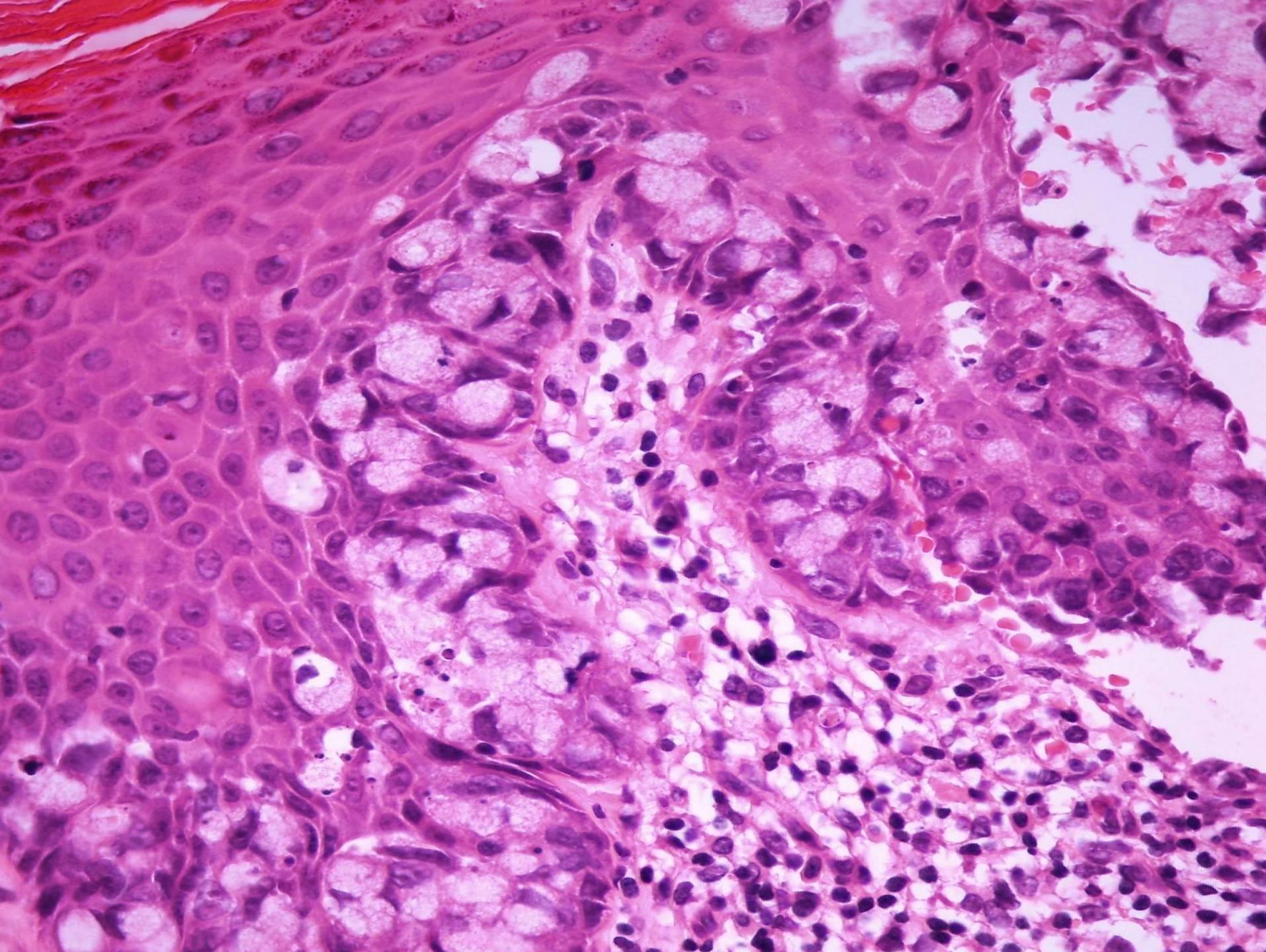


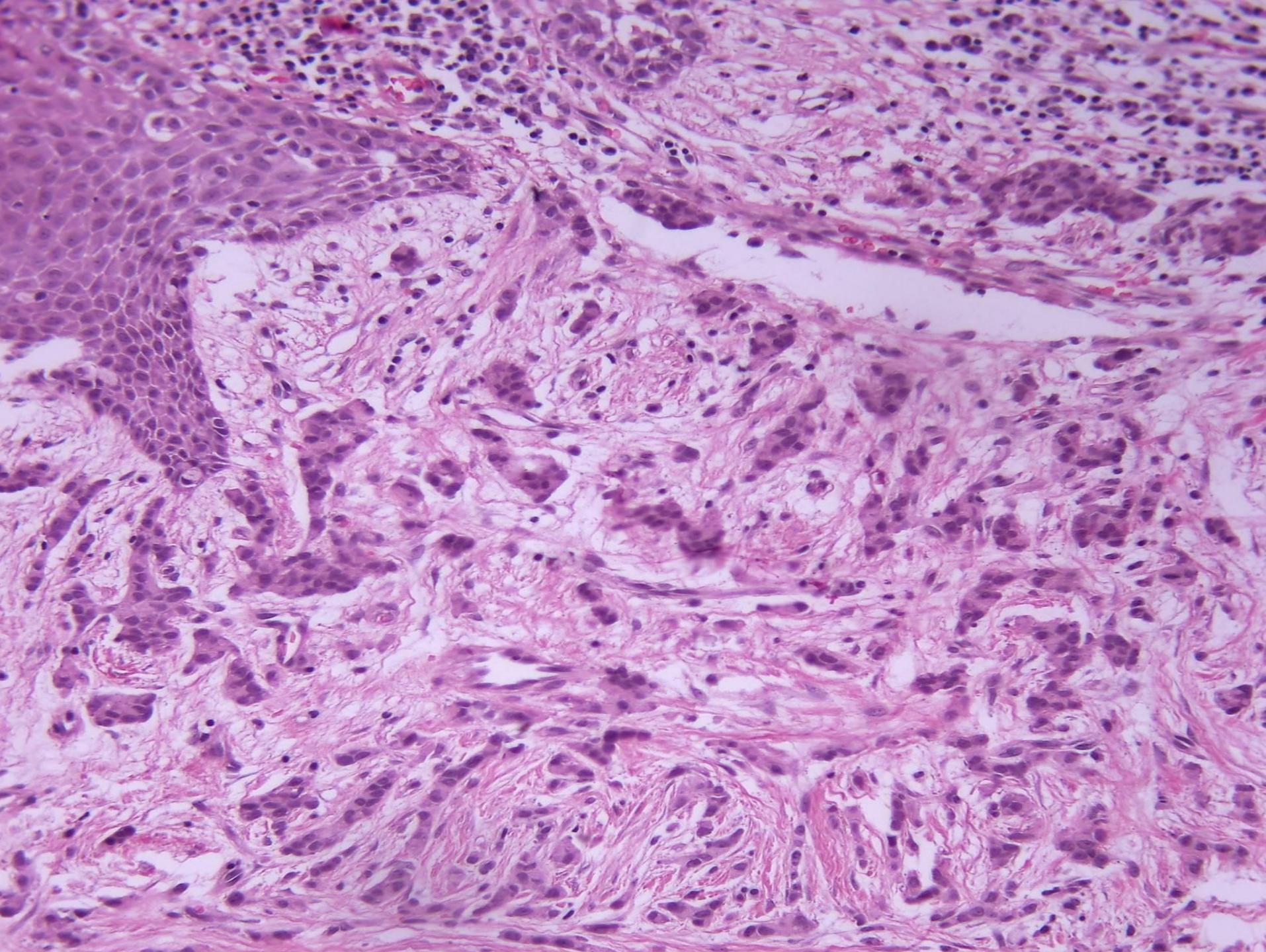


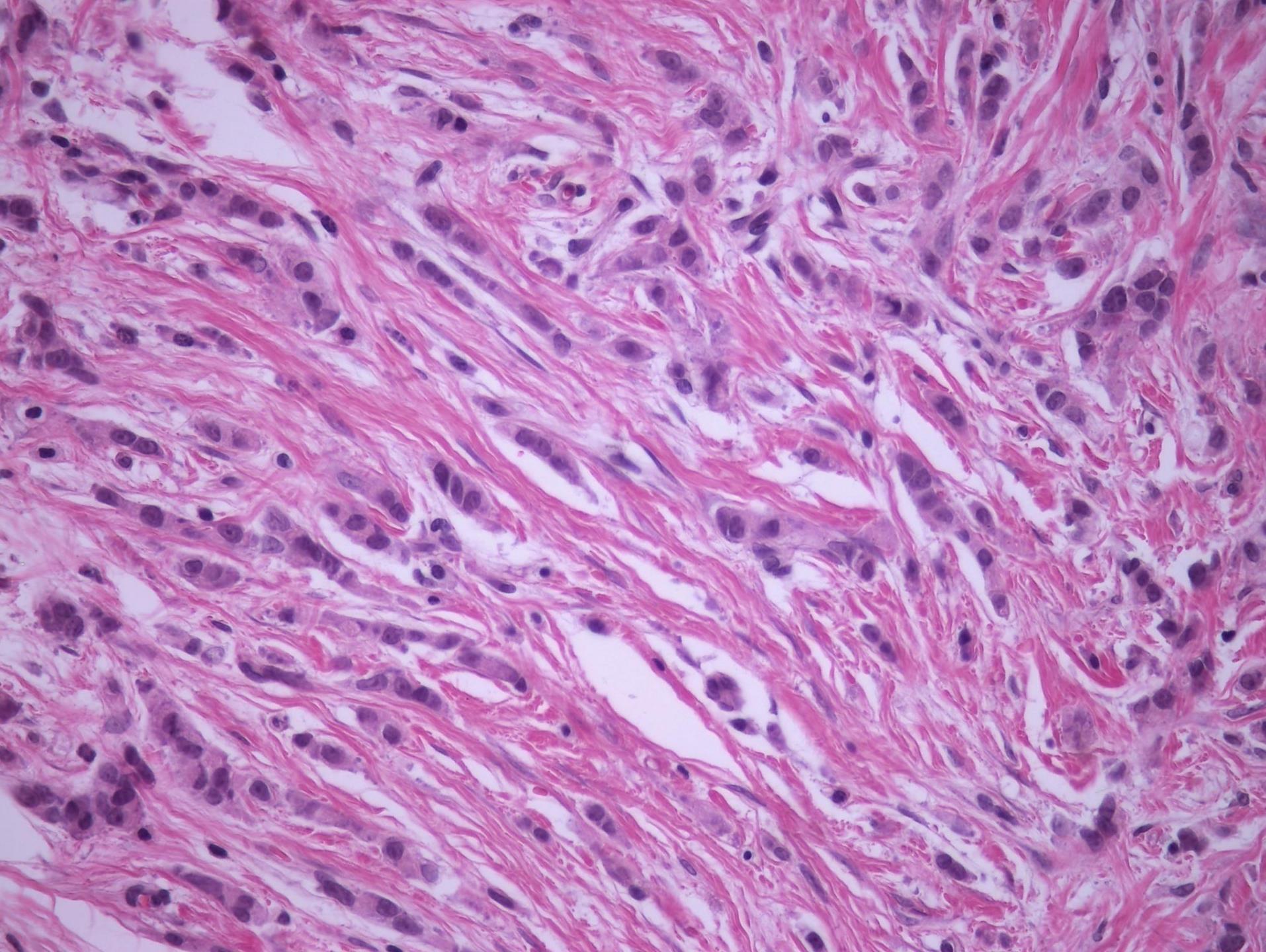






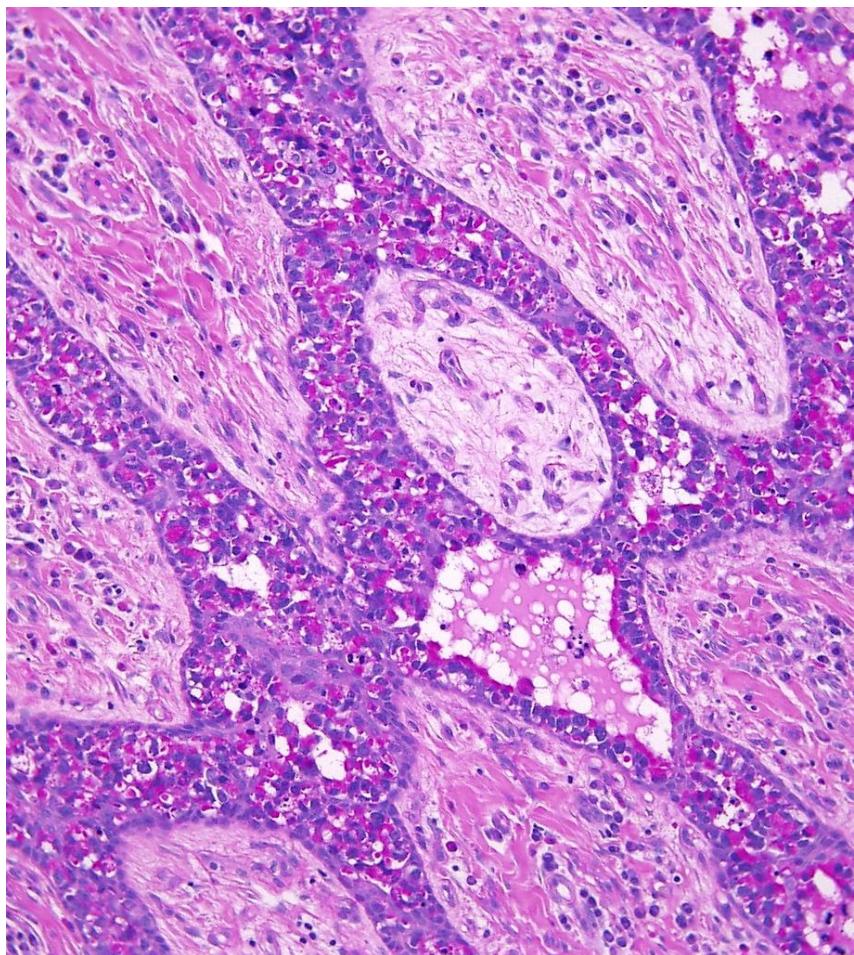




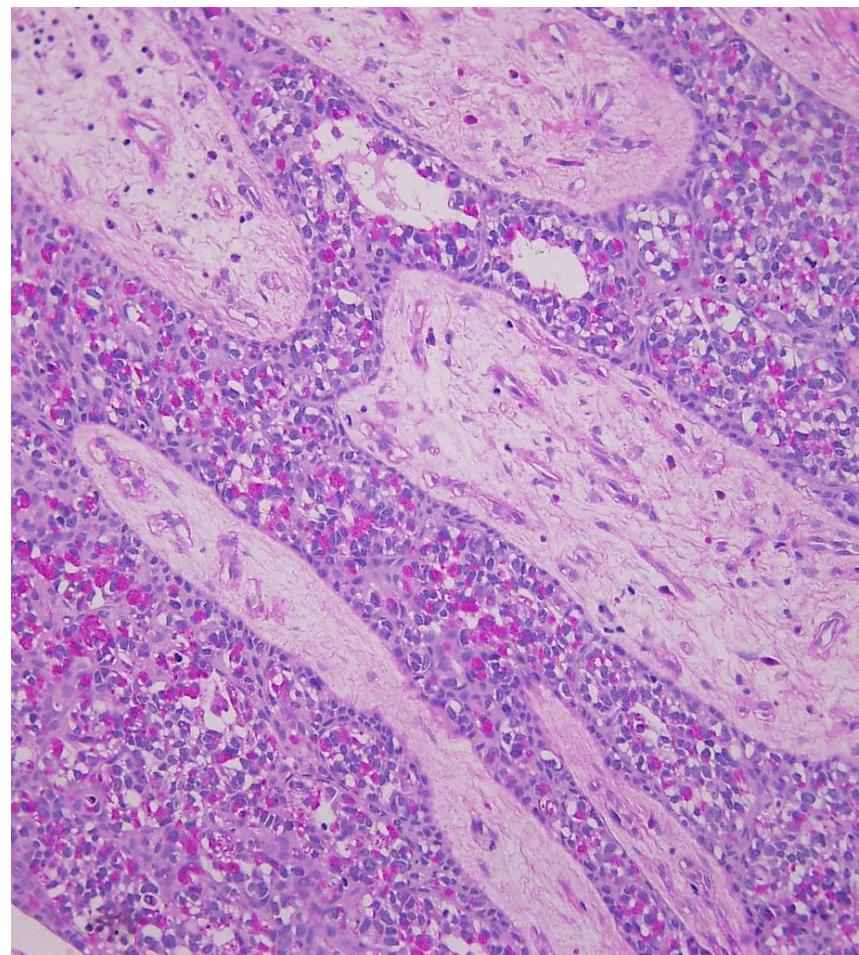




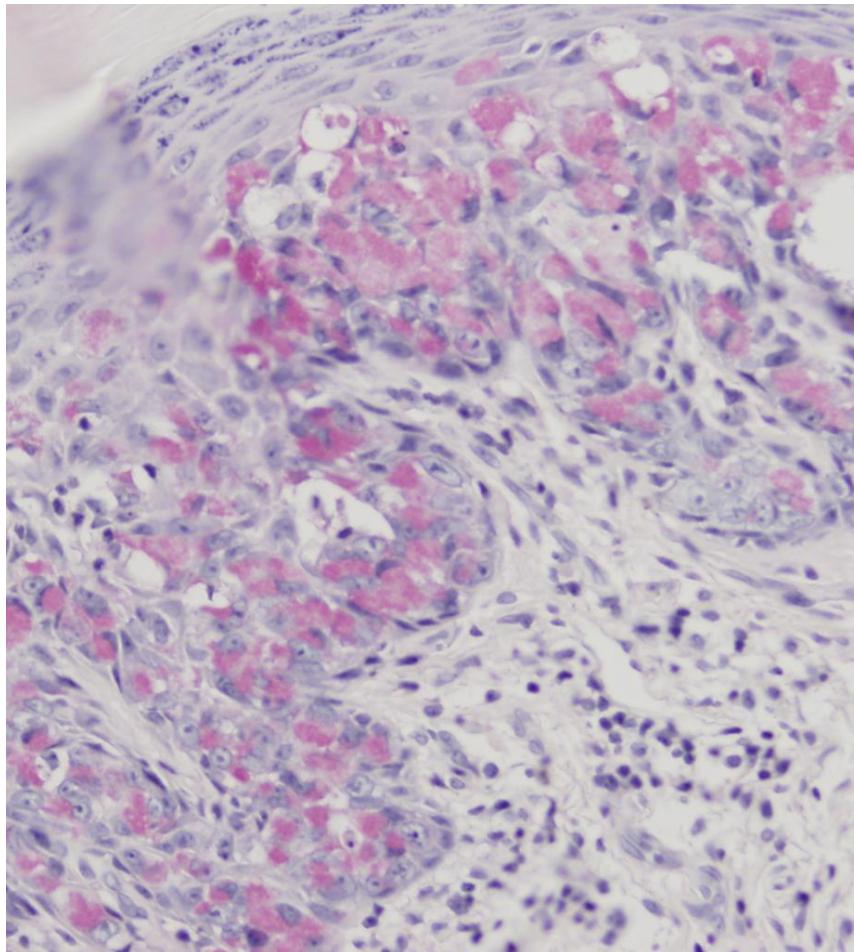
PAS



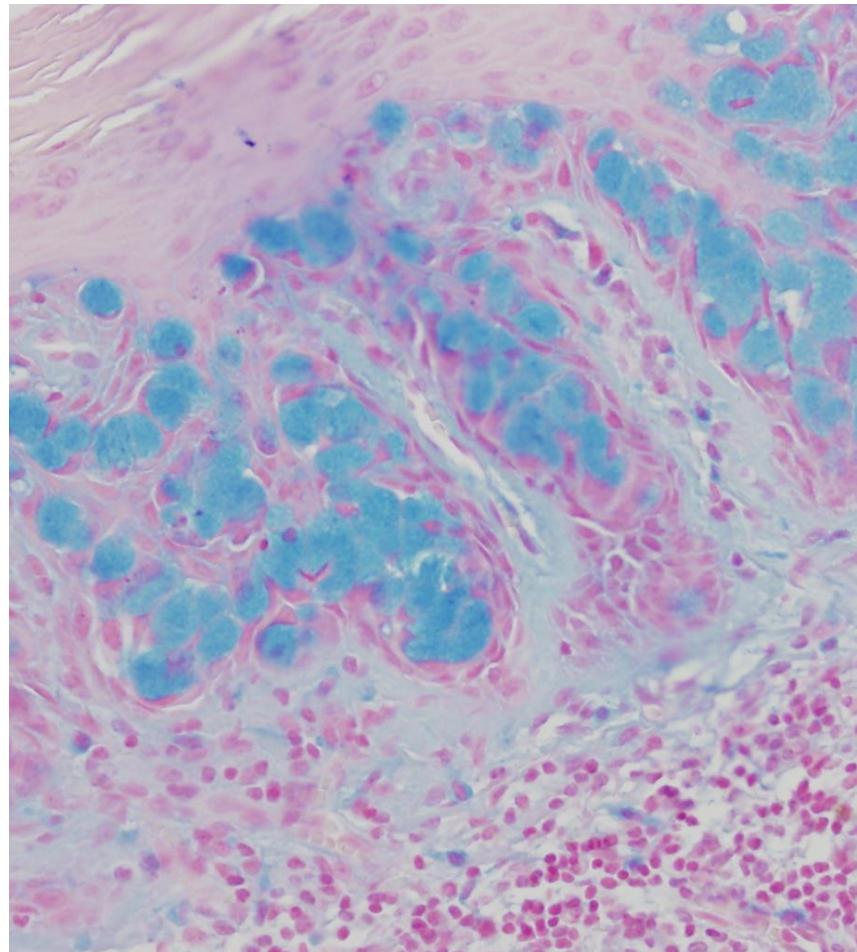
PAS kontr.



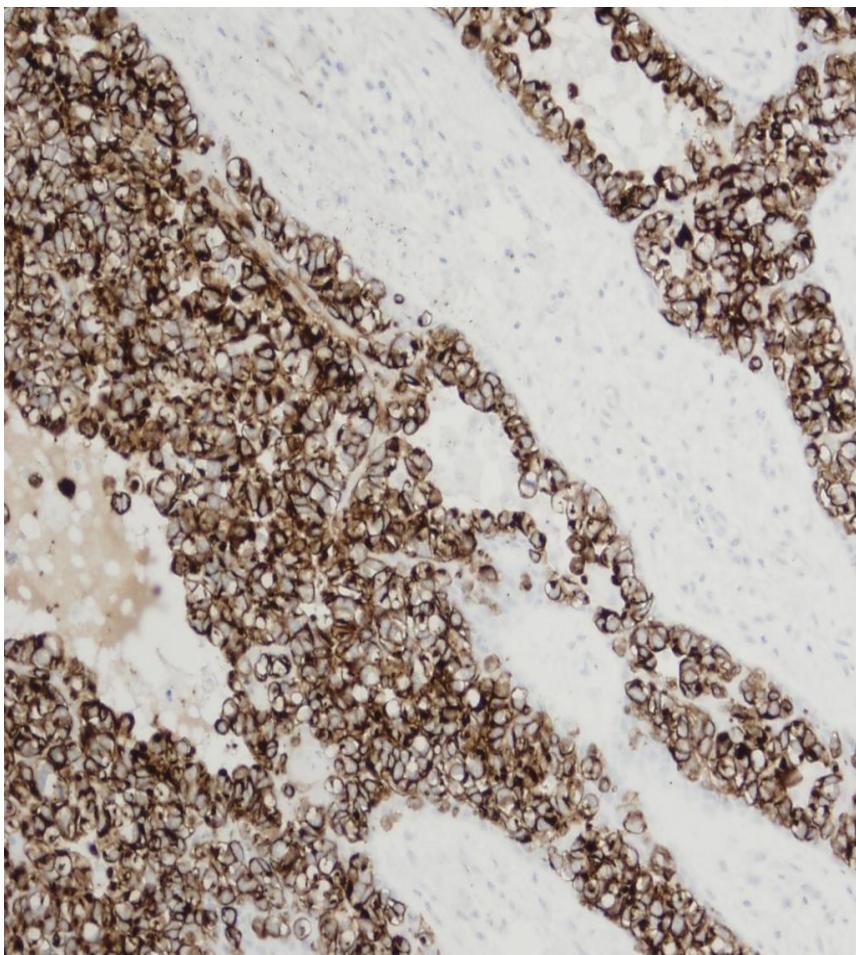
Mucikarmín



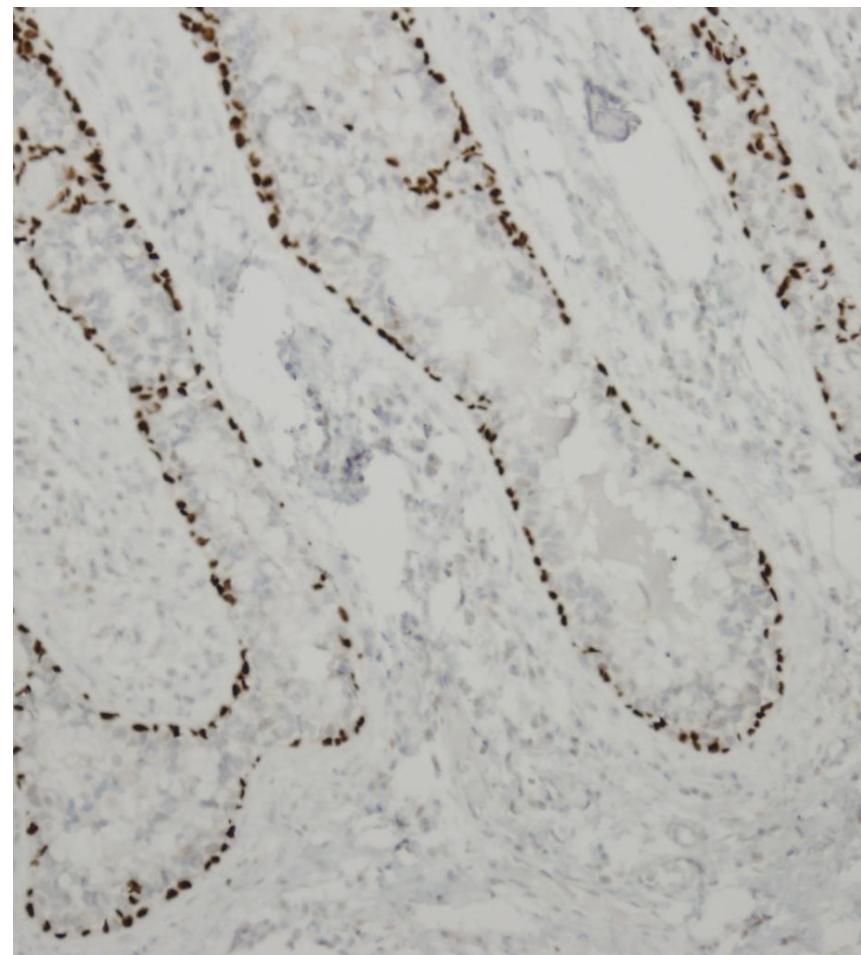
AM



CK7

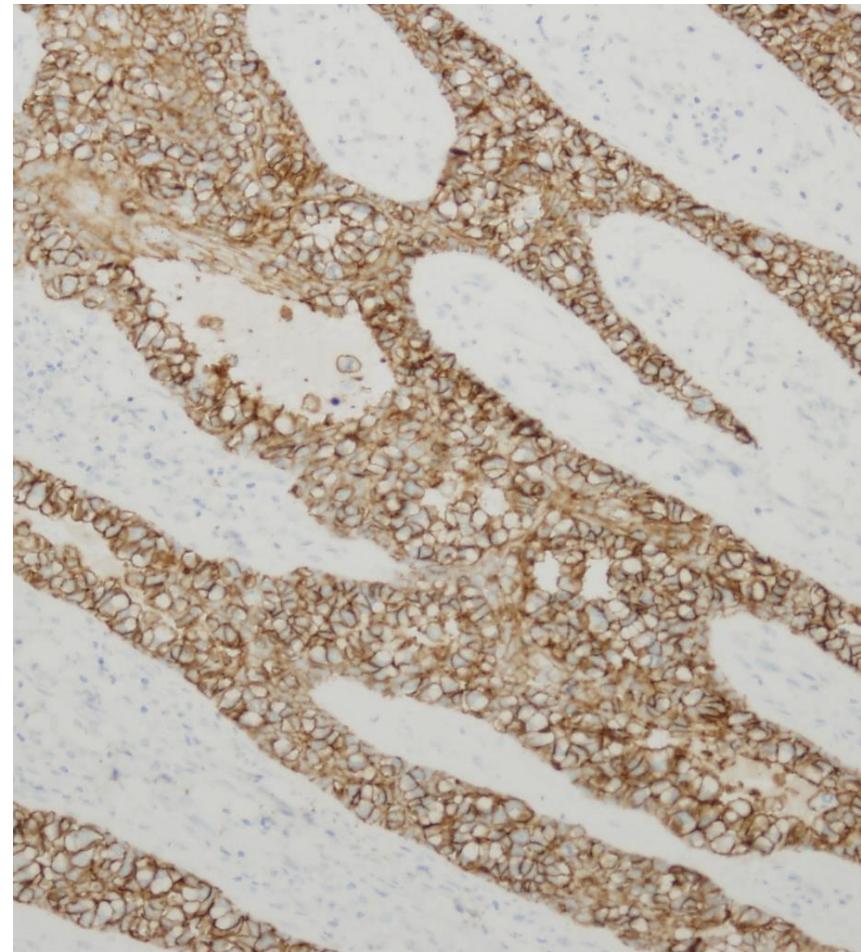
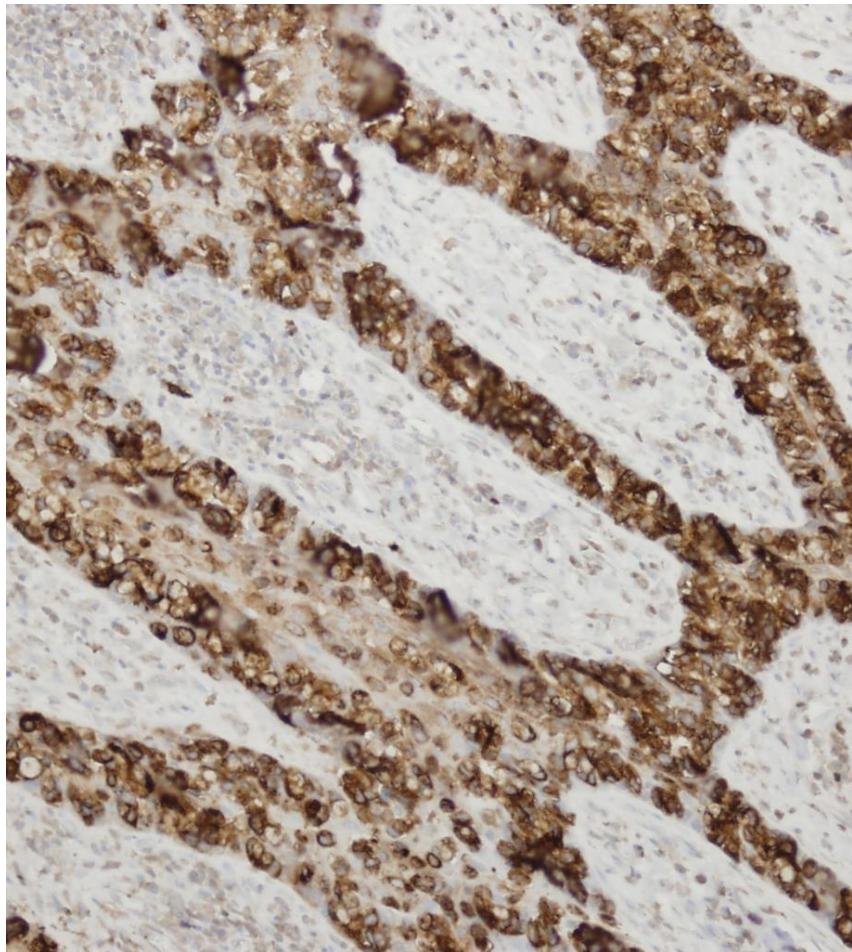


p63

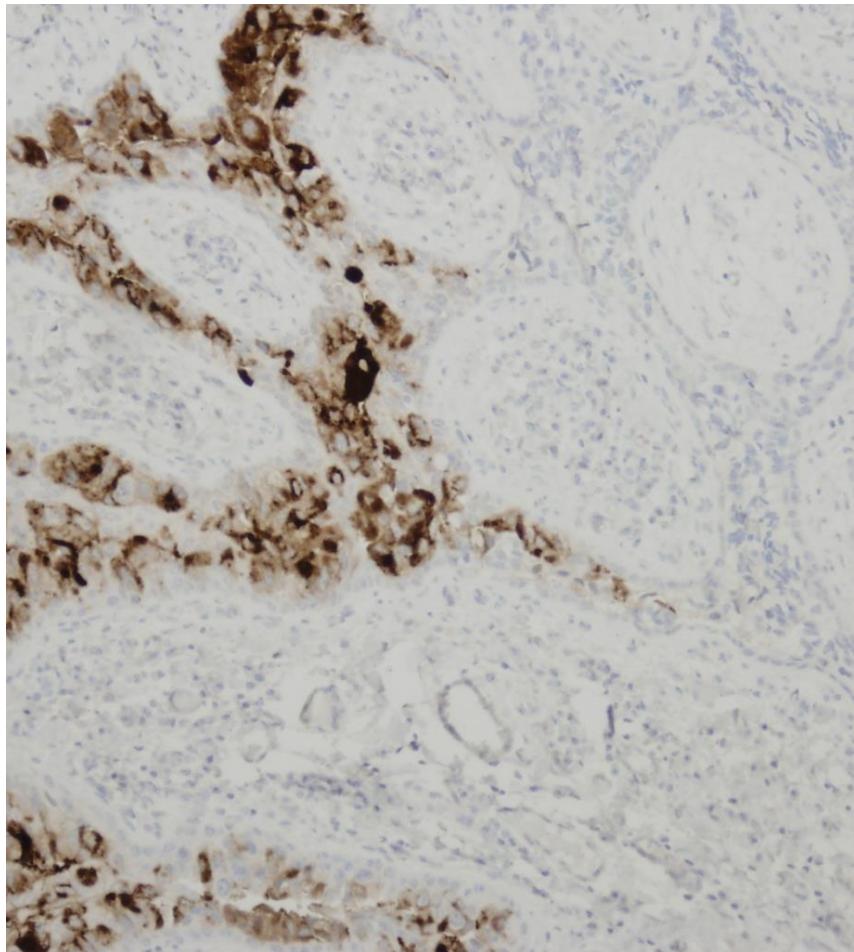


CEA

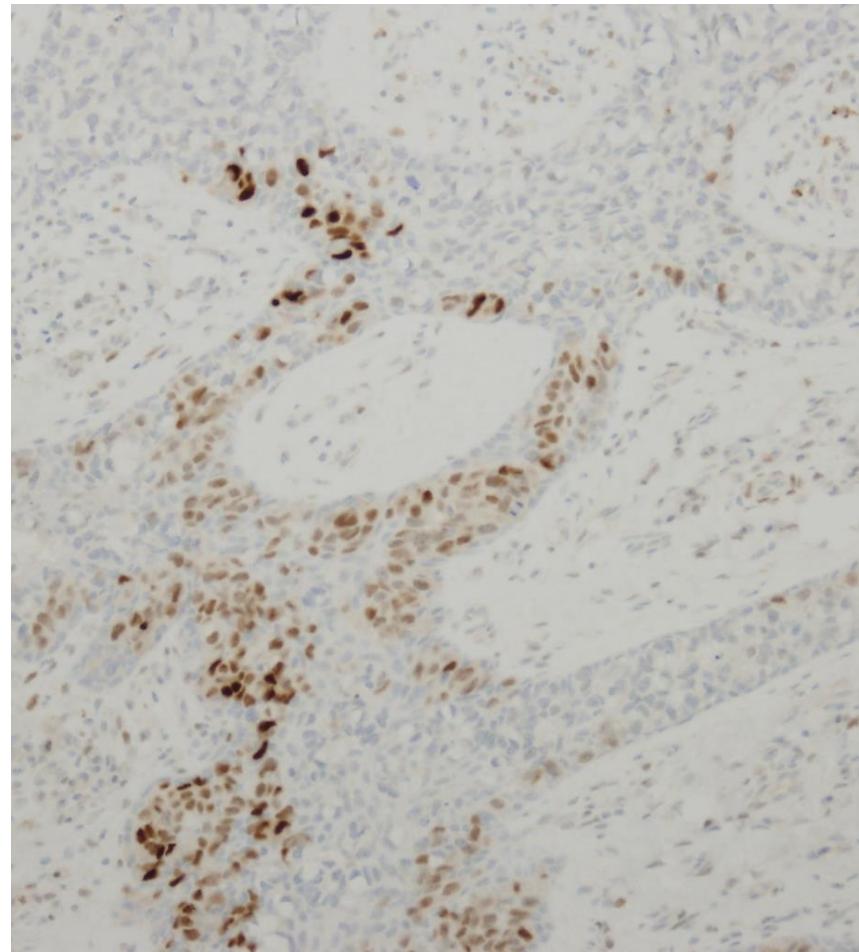
e-cadherín



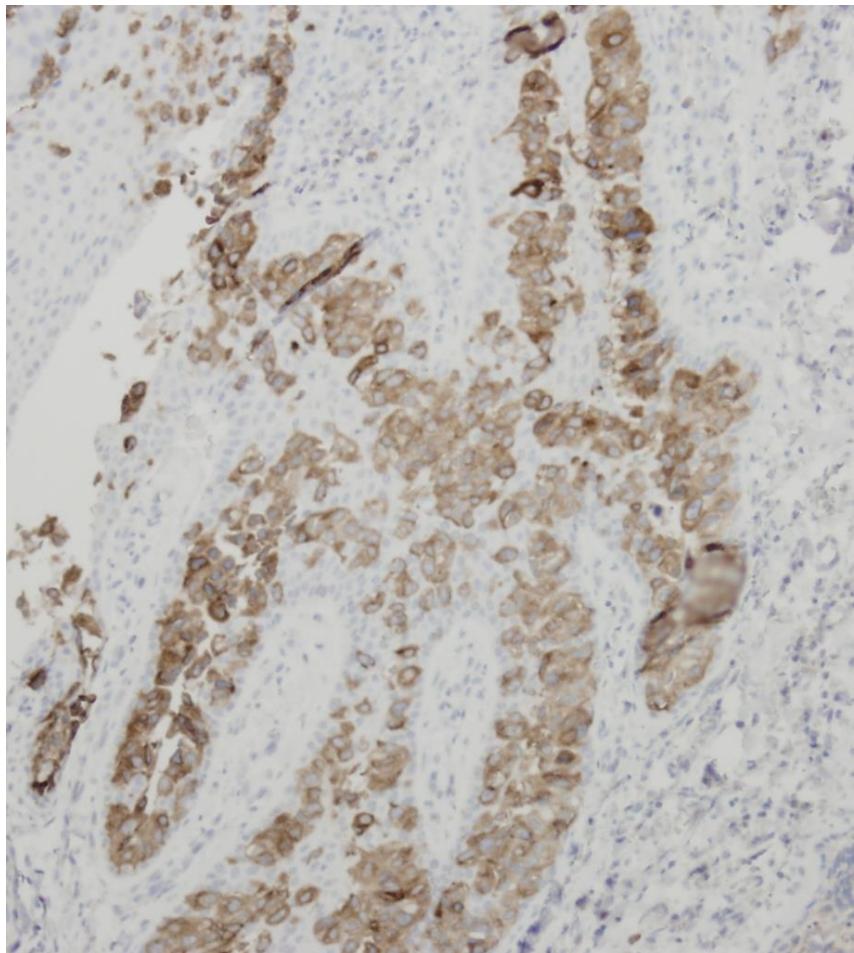
GCDFP-15



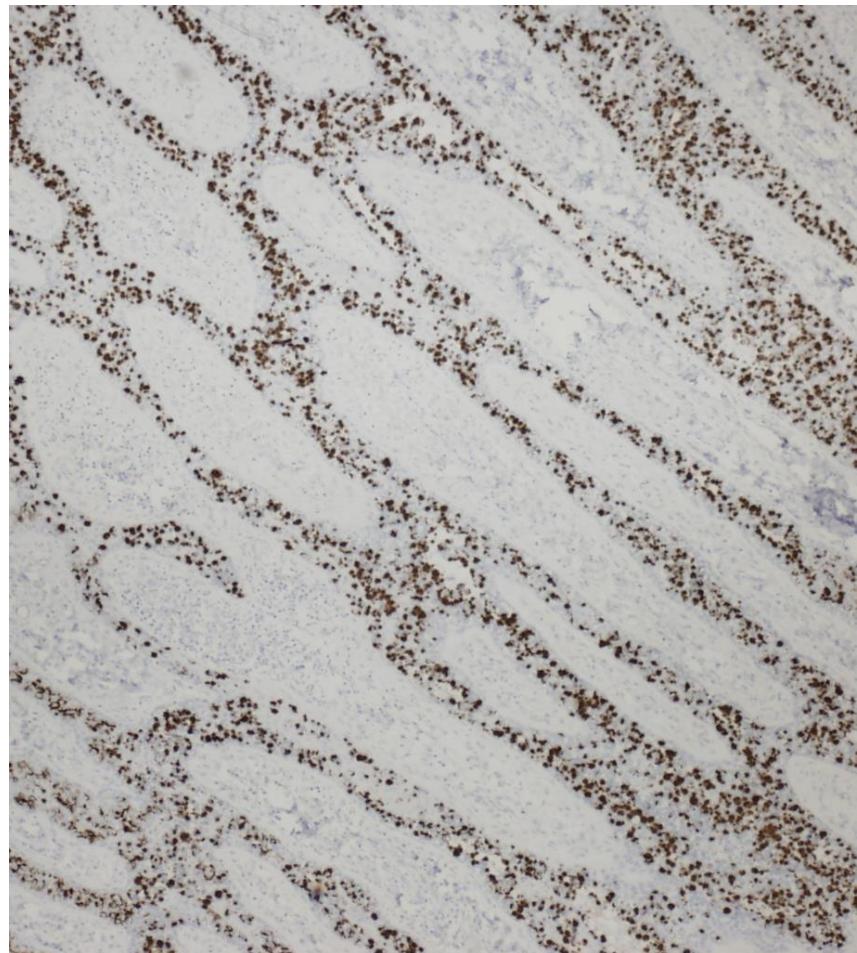
ER



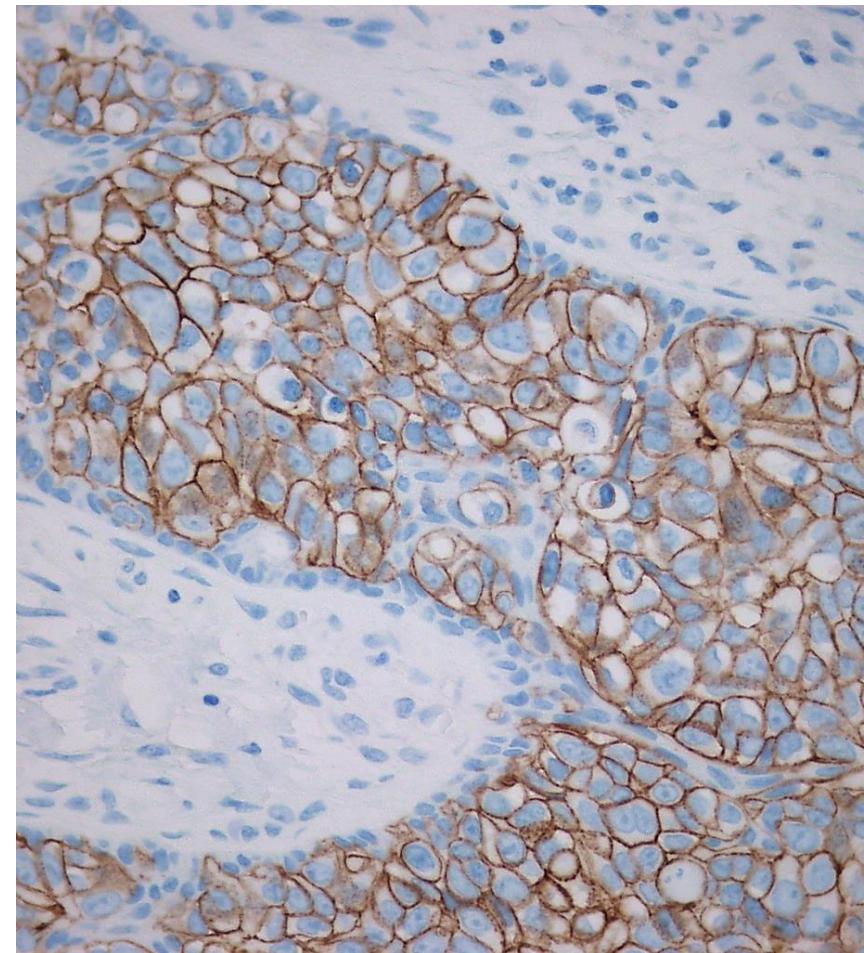
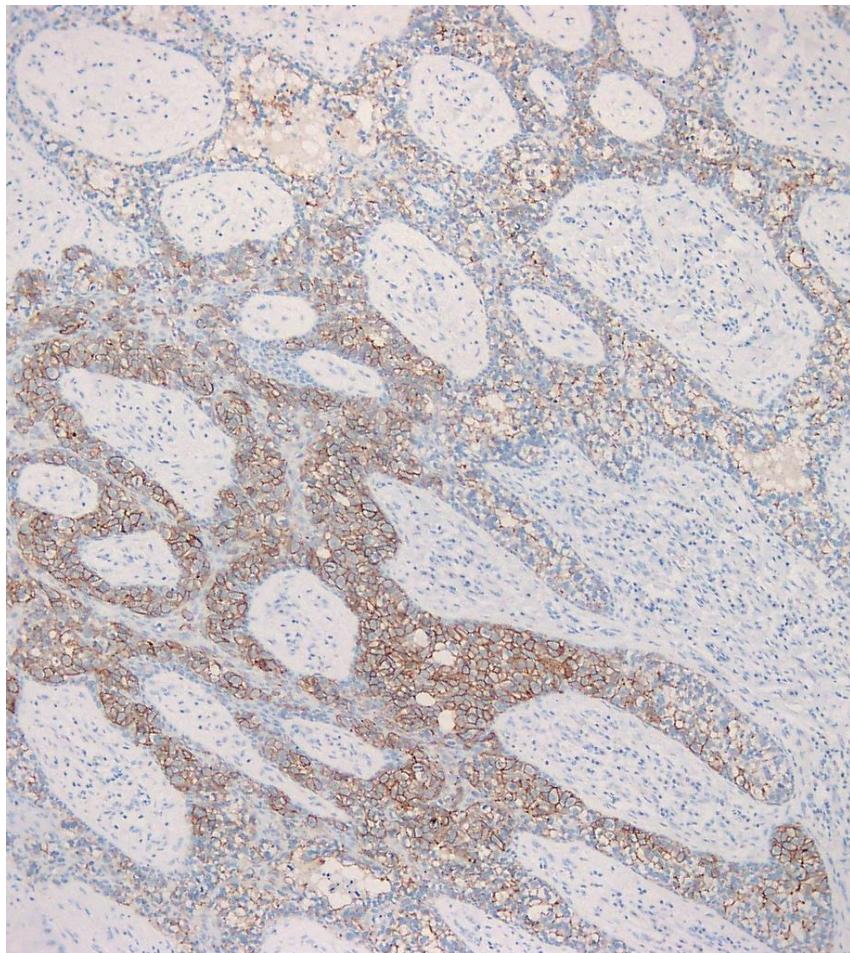
MUC1



MUC5 AC



HER2



Sumarizácia IHC analýzy

- CK7+
- CEA+
- e-cadherín+
- MUC1+
- MUC5AC+
- GCDFP-15+ fokálne
- ER+ fokálne ojed.
- HER2+
- S100mo-
- Melan A-
- CK20-
- CDX2-
- MUC2-
- p16-
- Uroplakín III-
- PSAP-
- p53-
- p63-



*Extramammárna Pagetova choroba s
hyperpláziou karcinómových buniek
imitujúcou syringocystadenocarcinoma
in situ, primárna pri vylúčení internej
malignity.*

Syringocystadenocarcinoma Papilliferum In Situ-Like Changes in Extramammary Paget Disease: A Report of 11 Cases.

Konstantinova AM¹, Kacerovska D, Stewart CJ, Szepe P, Pitha J, Sulc M,
Bencik V, Michal M, Shideler B, Kerl K, Kazakov DV.

Abstract

The authors report 11 cases of extramammary Paget disease (EMPD), all of which also demonstrated a combination of histological changes highly reminiscent of syringocystadenocarcinoma papilliferum in situ. In addition to the classical features of EMPD, characterized by the intraepidermal spread of individually dispersed neoplastic cells with ample cytoplasm, many of which contained mucin, there were areas of acanthosis with the substitution of spinous layer keratinocytes by neoplastic cells, whereas the native basal cell layer was intact. In addition to acanthosis (and sometimes papillomatosis), the dermal papillae showed a prominent infiltrate of plasma cells, completing the resemblance to syringocystadenocarcinoma papilliferum in situ; this similarity was further enhanced in 2 cases, which showed conspicuous gland formation. One additional case showed multifocal dermal proliferations compatible with eccrine syringofibroadenoma (syringofibroadenomatous hyperplasia). The changes described herein seem to be relatively rare in EMPD, and they can represent a diagnostic pitfall, as evidenced by 2 cases that were originally misinterpreted as syringocystadenocarcinoma papilliferum in situ. Clinically, these microscopic changes sometimes corresponded to nodular lesions, which were specifically noted to have a papillated erosive surface.

Extramammárna Pagetova choroba (EMPD)

1% nádorov anogenitálnej oblasti

- primárna: origo v koži
- sekundárna: origo malignity v dolnom GITe a urogenitálnom trakte, 5-30%

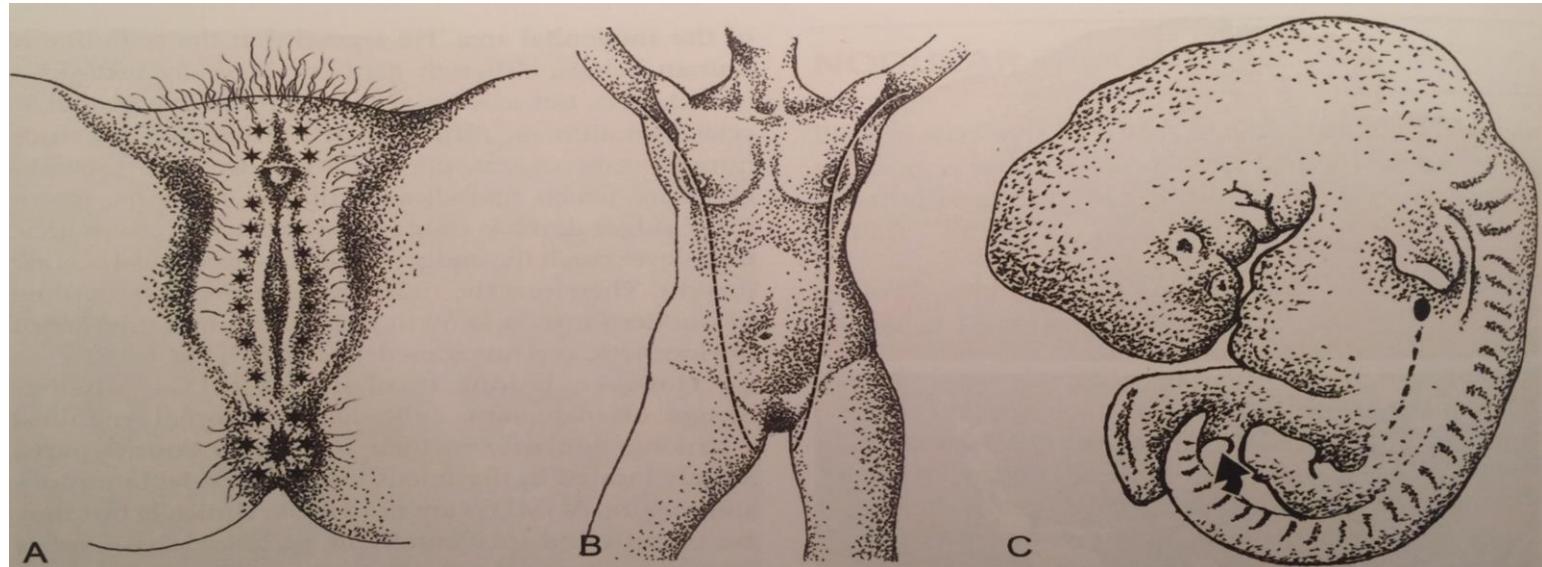
Primárna EMPD

Histogenéza

- Kožné adnexá (ekrinné a apokrinné žľazy)
- Anogenitálne mammary-like žľazy (AGMLGs)
- Vulvárne Tokerove bunky
- Pluripotentné germinatívne bunky epidermy

Anogenitálne mammary-like žľazy (AGMLGs)

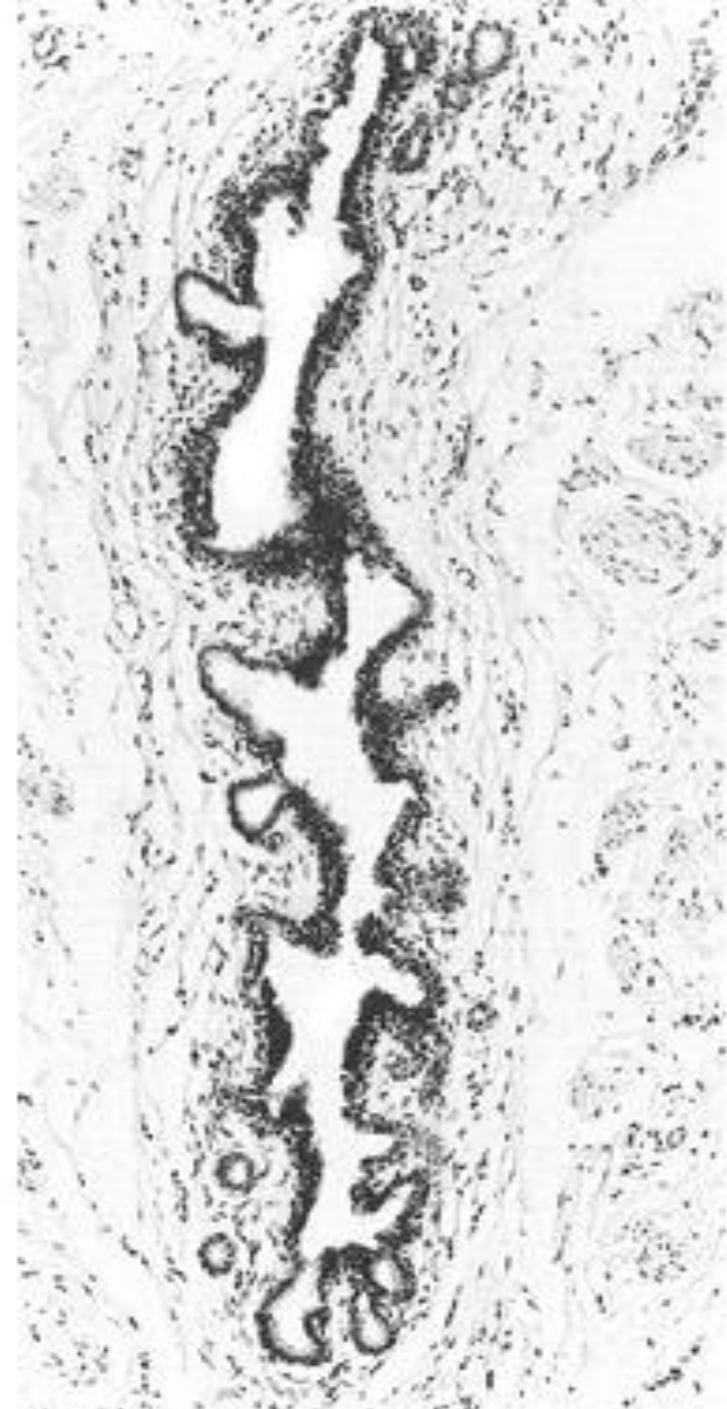
- Hartung, 1872, tkanivo mammárneho typu na vulve, ektopický prsník v kaudálnom zvyšku mliečnej lišty
- van der Putte, 1991-94, tkanivo mammárneho typu v anogenitálnej oblasti označil za fyziologické štruktúry , argument: u ľudských embryí mammárne línie prítomné v axilárno-pektorálnej oblasti, nedosahujú anogenitálnu oblasť



AGMLGs

Histológia:

- jednoduché gl. štruktúry s okrúhlym lumenom (muži)
- komplexné gl. jednotky (ženy)
- stróma riedka al. denzná fibrotická
- periférna myoepitelová vrstva, lumenálne kolumnárny epitel, často so známkami apokrinnej sekrécie



A

B

AGMLGs

AGMLGs

Benígne tu

- Hidradenoma papilliferum
- Laktačný adenóm
- Tubulárny adenóm
- Fibroadénom, aj juvenilný typ
- Phyllodes tu, benígny

Malígne tu

- Phyllodes tu, malígny
- **EMPD**
- Mammárny typ DIC , DCIS
- Mammárny typ LIC
- Mucinózny karcinóm

Prsník

Benígne tu

- Intraduktálny papilóm
- Laktačný adenóm
- Tubulárny adenóm
- Fibroadénom, aj juvenilný typ
- Phyllodes tu, benígny

Malígne tu

- Phyllodes tu, malígny
- **MPD**
- DIC, DCIS
- LIC
- Mucinózny karcinóm

Molecular alterations in lesions of anogenital mammary-like glands and their mammary counterparts including hidradenoma papilliferum, intraductal papilloma, fibroadenoma and phyllodes tumor

Anastasia M. Konstantinova, Tomas Vanecek, Petr Martinek, Liubov Kyrpychova, Dominic V. Spagnolo, Colin J.R. Stewart, Francesca Portelli, Michal Michal, Dmitry V. Kazakov

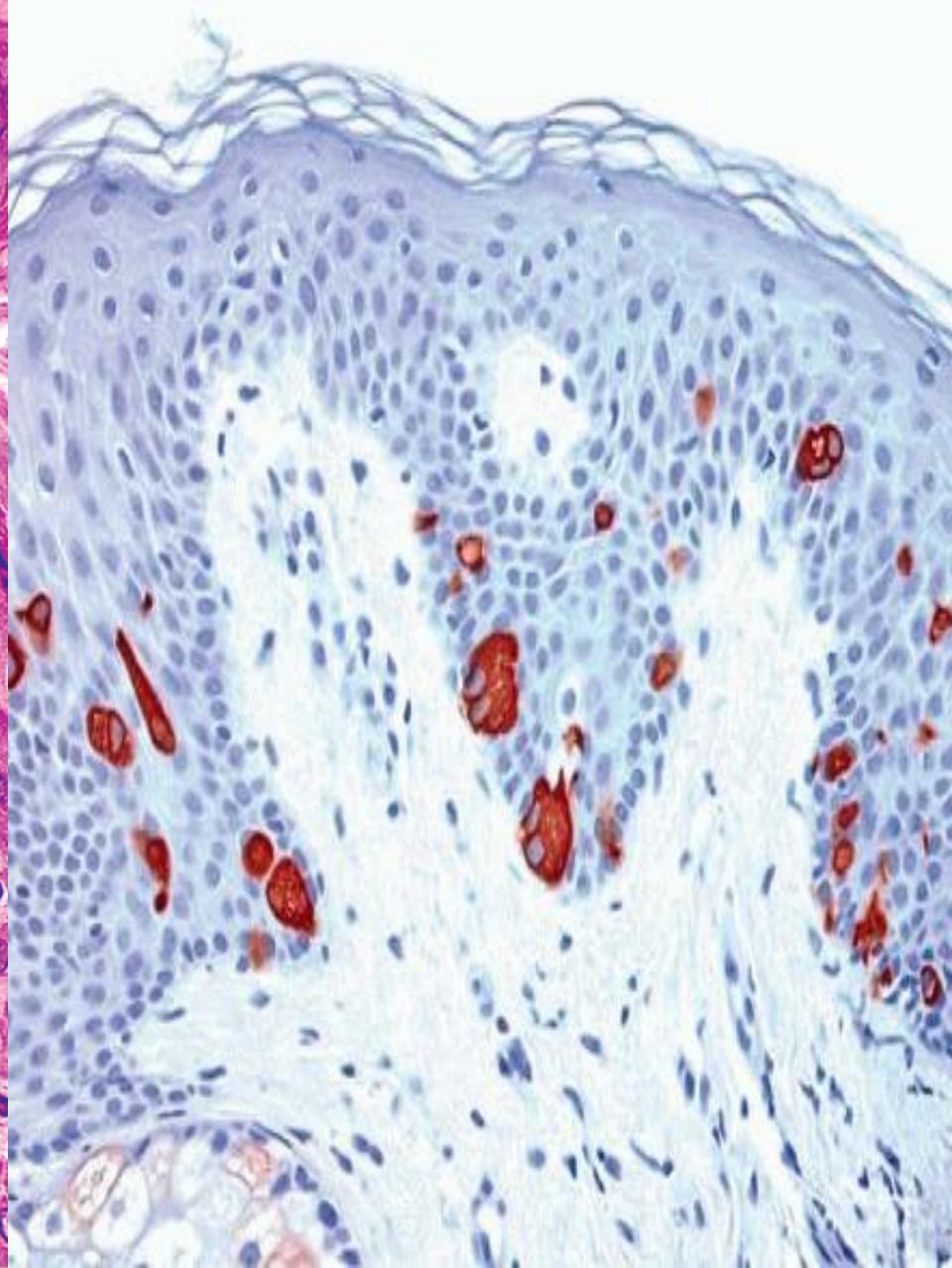
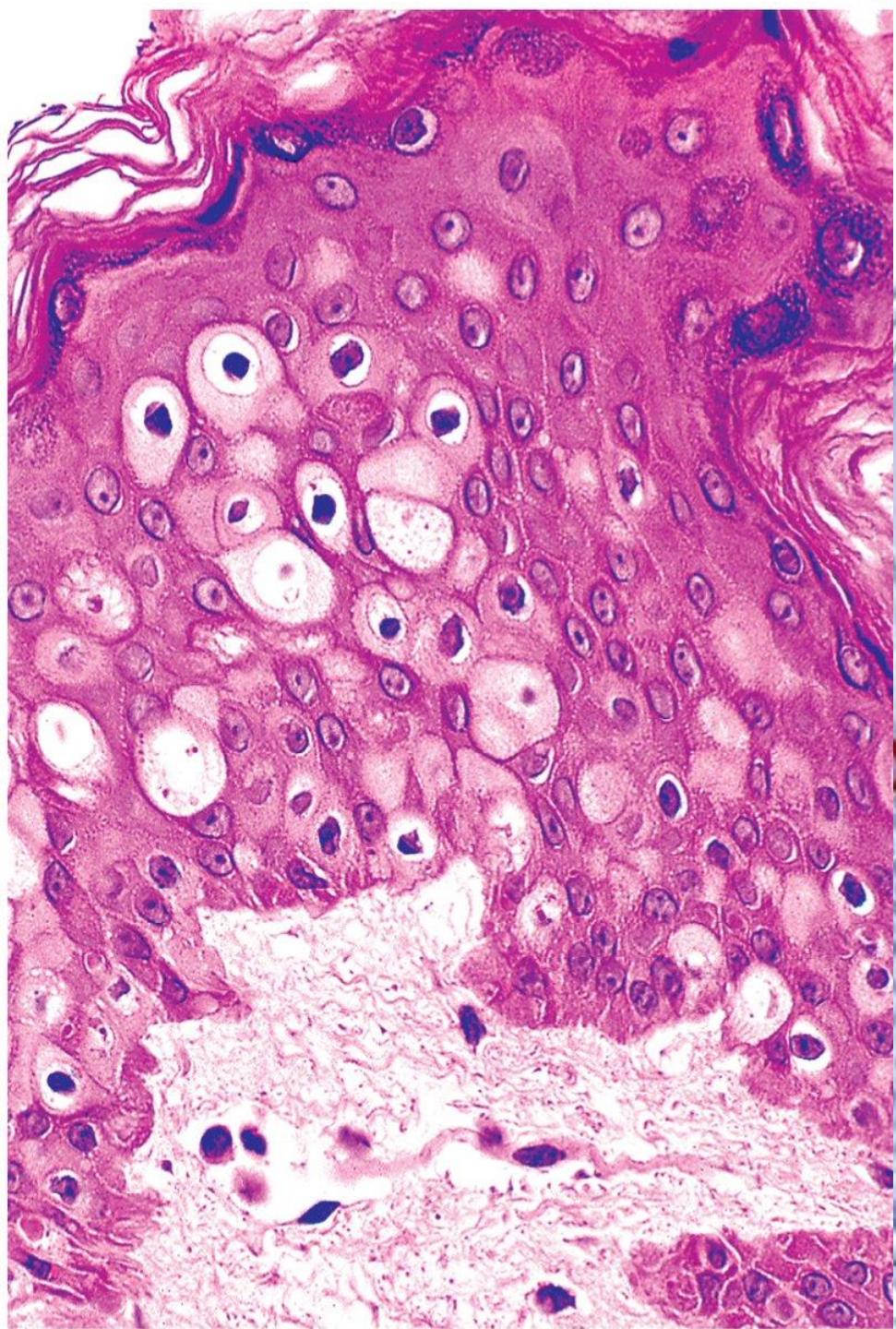
Abstract

Lesions affecting anogenital mammary-like glands (AGMLG) are histopathologically very similar to those seen in the breast but whether this morphological similarity is also reflected at the genetic level is unknown. To compare the underlying molecular mechanisms in lesions of AGMLG and their mammary counterparts, we analyzed the mutational profile of 16 anogenital neoplasms including 5 hidradenomas papilliferum (HP), 1 lesion with features of HP and fibroadenoma (FA), 7 FA, 3 phyllodes tumors (PhT) and 18 analogous breast lesions (6 intraductal papillomas (IDP), 9 FA, and 3 PhT) by high-coverage next generation sequencing (NGS) using a panel comprising 50 cancer-related genes. Additionally, all cases were analyzed for the presence of a mutation in the *MED12* gene. All detected mutations with allele frequencies over 20% were independently validated by Sanger sequencing (concordance: 100%). Mutations in *PIK3CA*, *AKT1*, *MET*, *ABL1* and *TP53* genes were found in lesions of AGMLG and also their mammary counterparts. The PI3K-AKT cascade plays a role in tumors arising at both sites. It appears that some histopathologically similar anogenital and breast lesions develop along similar molecular pathways.

Presented in part at the 2017 annual meeting of the United States and Canadian Academy of Pathology, San Antonio, TX, USA.

Tokerove bunky

- lokalizácia: dolná časť epidermy
- usporiadanie: jednotlivo al. v klastroch, v okolí vývodov AGMLG duktov, zriedkavo ductoidné štruktúry pozdĺž bazálnej vrstvy epidermy
- cytológia: blandné okrúhle jadrá, svetlá cytoplazma
- IHC: CK7+



Primárna EMPD

Klinická prezentácia:

- postmenopauzálné ženy, 70-75 r., muži menej
- vulva (labium majus, minus, klitoris), perineum, perianálna oblast, skrótum, penis, podbruško, inguiny
- dobre ohraňičená plochá, vyvýšená, erytematózna lézia s exkoriáciami/krustou
- hyper, hypo, depigmentácia
- multicentrické ochorenie: genit.+bilat. axily “triple EMPD”

EMPD



Primárna EMPD

Histopatologické črty

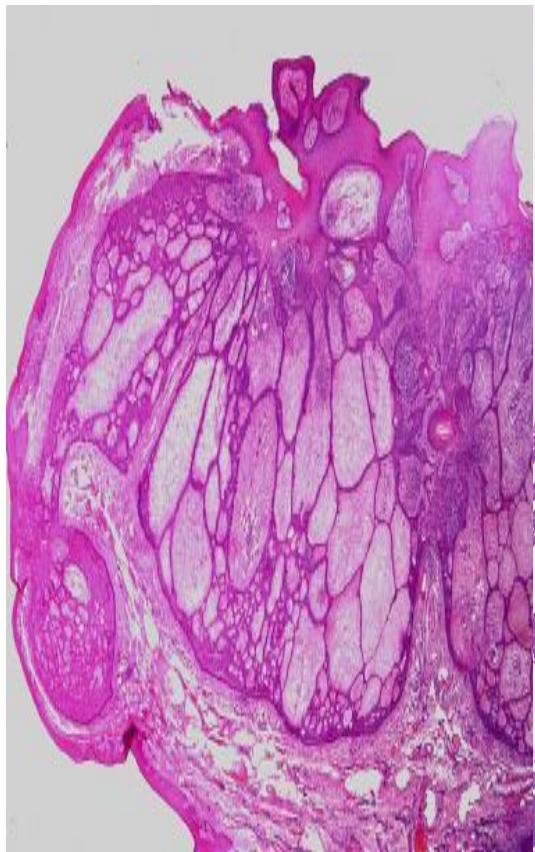
- cytológia: vezikulárne jadrá, jadierka, hojná svetlá, amfofilná, bazofilná cytoplazma, kvapôčky intracytoplazmatického mucínu, variácie: hyperchromázia, viacjadrové elementy
- rast: solitárne, v hniezdach, žľazoidných štruktúrach
- adnexotropizmus: vlasové folikuly, ekrinné dukty

Primárna EMPD

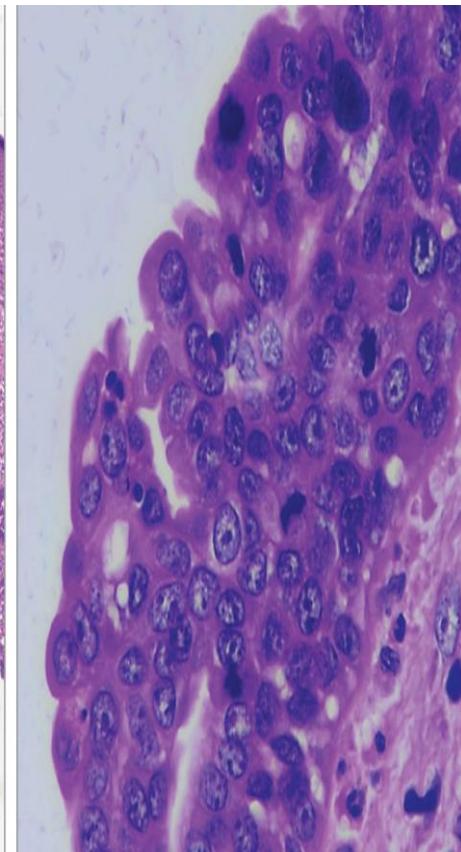
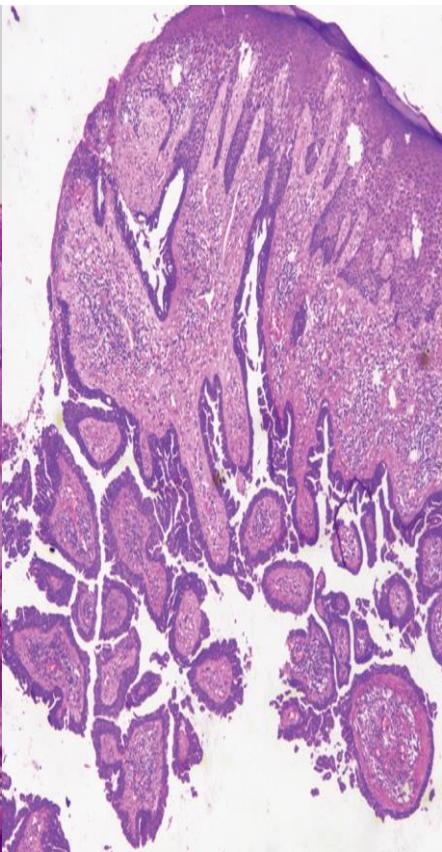
Morfologické variácie:

- asociácia s mammárnym typom karcinómu a mammárnym typom zmien v AGMLGs
- proliferatívne epidermálne lézie (*fibroepitelioma-like (A)*, papilomatázna hyperplázia, skvamózna hyperplázia, psoriaziformná hyperplázia)
- *syringocystadenocarcinoma papilliferum in situ-like arey (B)*
- syringoma-like štruktúry
- hyperpigmentované formy
- “skip” arey

A)



B)



Primárna EMPD

Histochemické a IHC črty:

- + mucikarmín, aldehyd fuchsín, AM, PAS k.
- + CK7, CEA, GCDFP-15

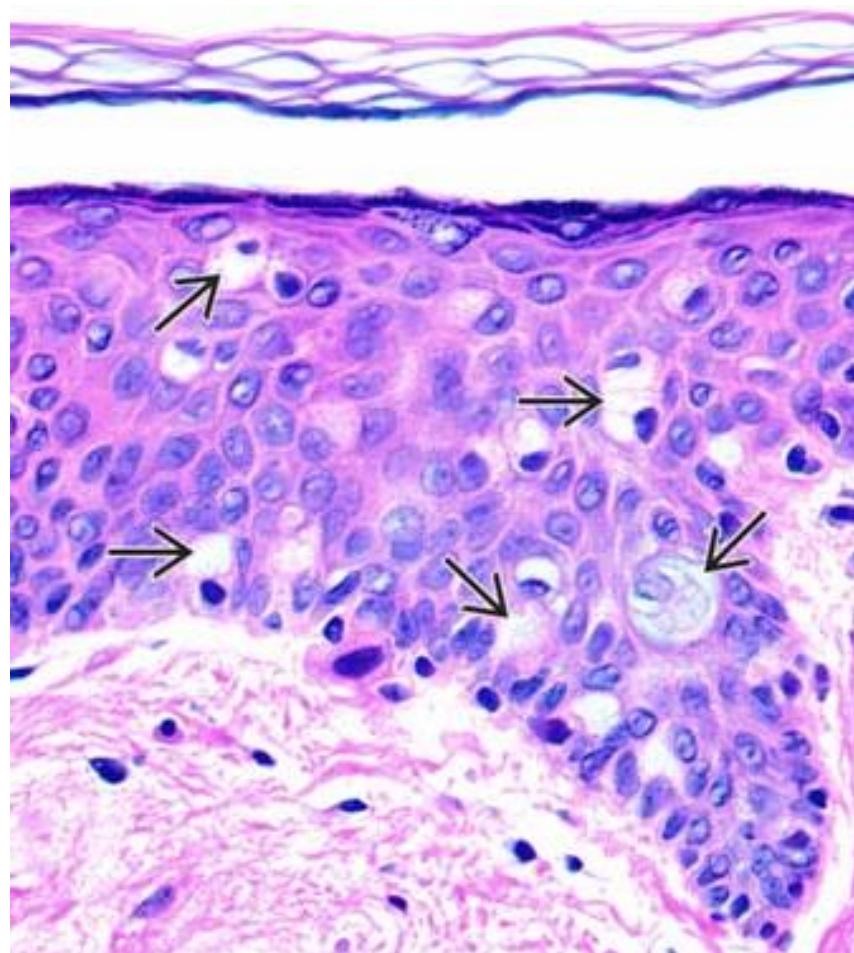
Molekulová biológia:

- amplifikácie chromozómu X, q21 a 19
- strata heterozygozity v niekoľkých lokusoch ako v iných humánnych malignitách (3p, 9p, 9q, 13q, 16q, 17p a 17q)

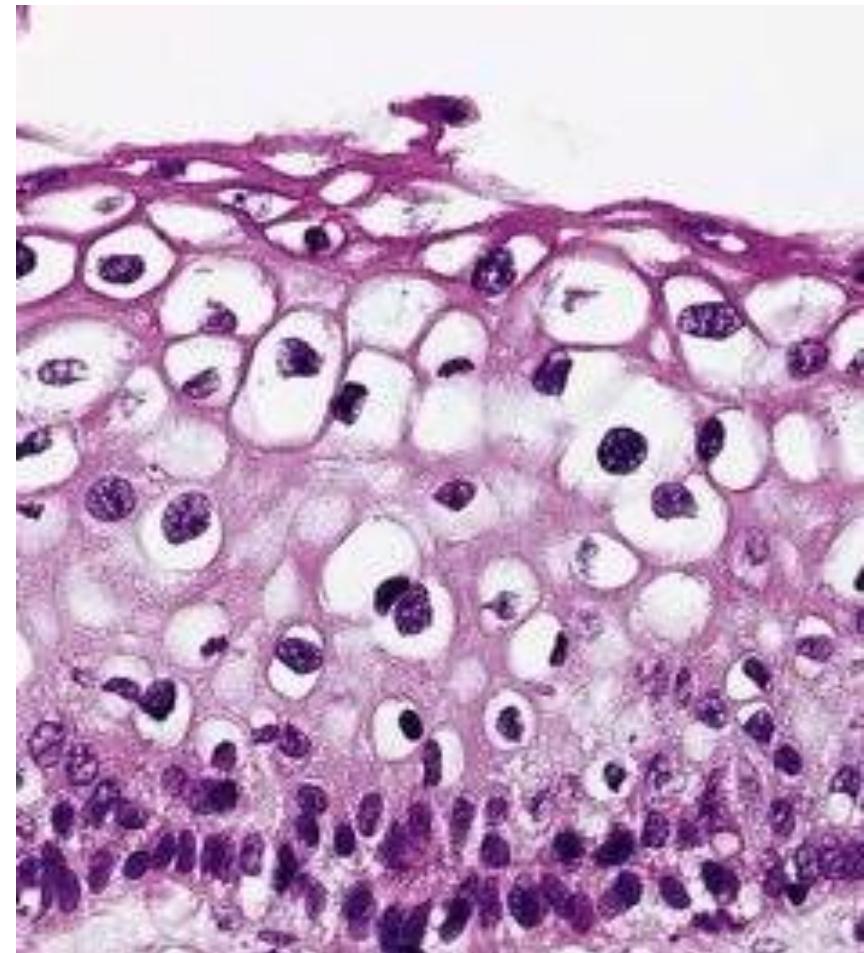
Primárna EMPD dif. dg.

- hyperplázia Tokerových bb.
- VIN3/ca in situ
- SSM
- kožný lymfóm s epidermotropizmom
- Pagetoidná dyskeratóza
- lézie asociované s HPV
- syringocystadenoma/ca papilliferum in situ
- periokulárny sebaceózny ca
- CK7+, MIB1 nízke, asociácia s iným ochorením
- CK7-, Ber-EP4-, p16+
- CK7-, S100+, Melan A+...
- CK7-, LCA+, CD3+...
- CK7-, reaktívny proces
- CK7-, HPV +
- CK7+, EMA+...
- CK7+, EMA+, p53, bcl-2...

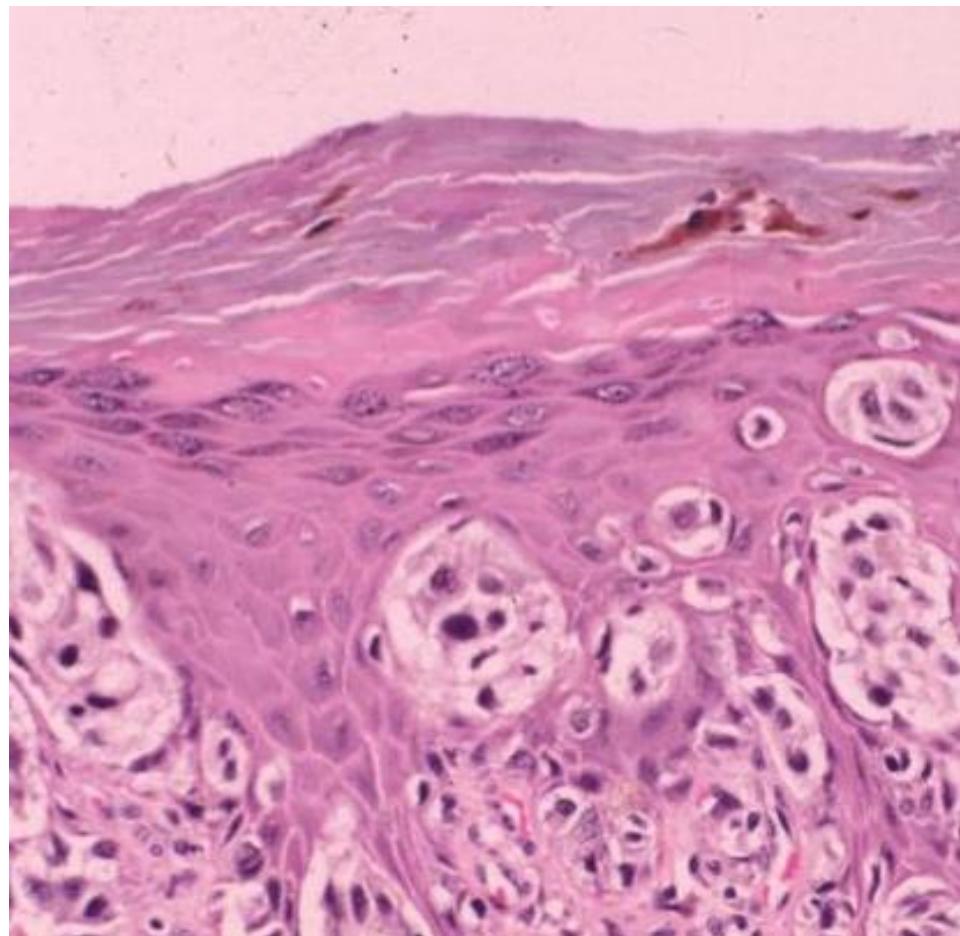
Hyperplázia Tokerových bb.



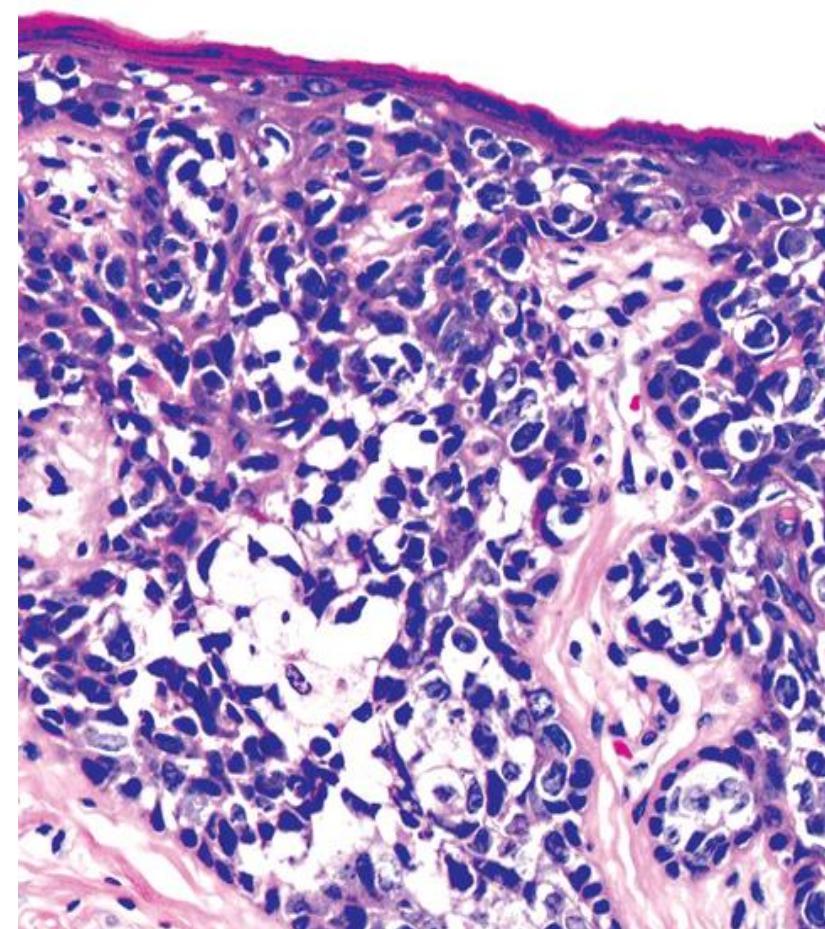
Koilocytóza



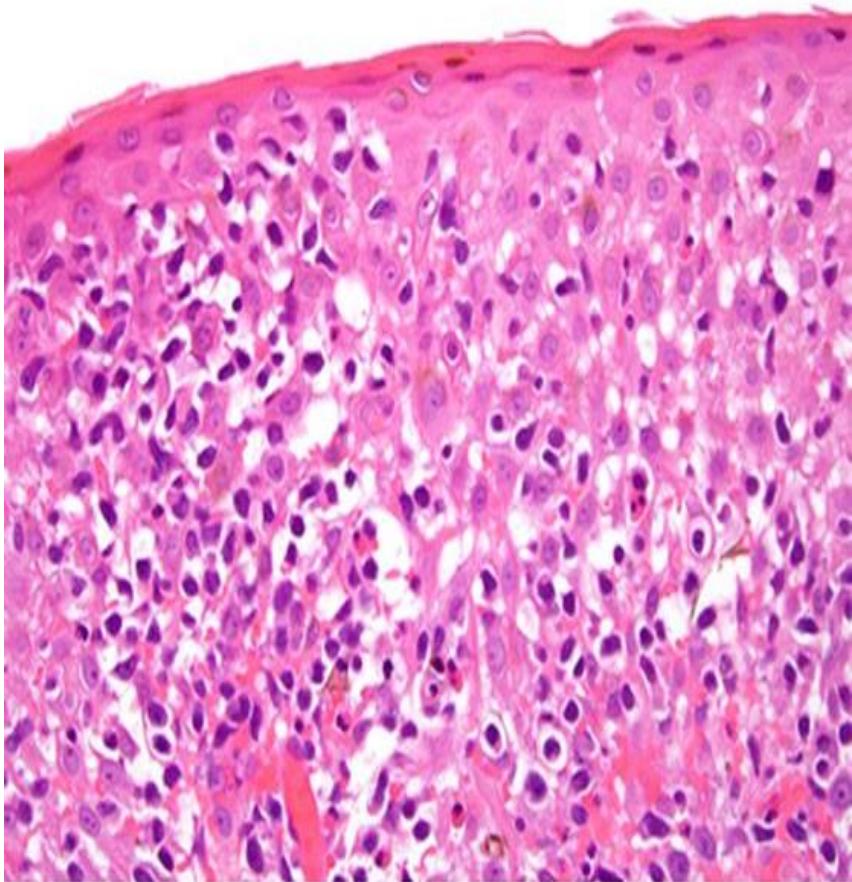
SSM



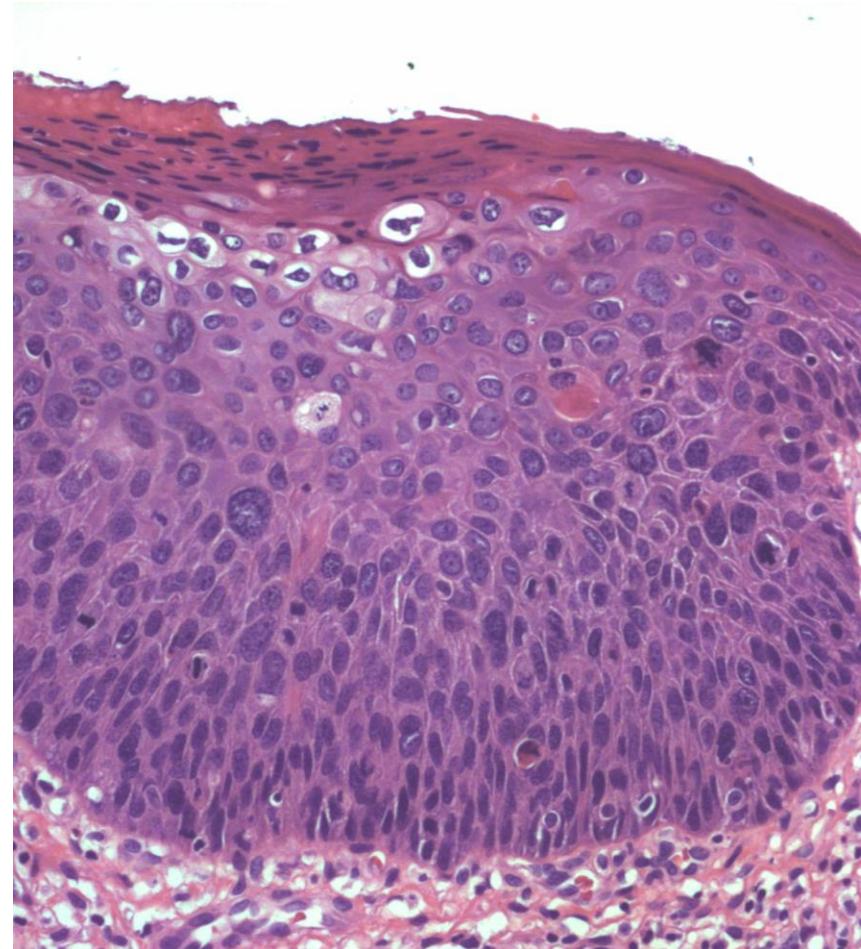
Sebaceózny ca



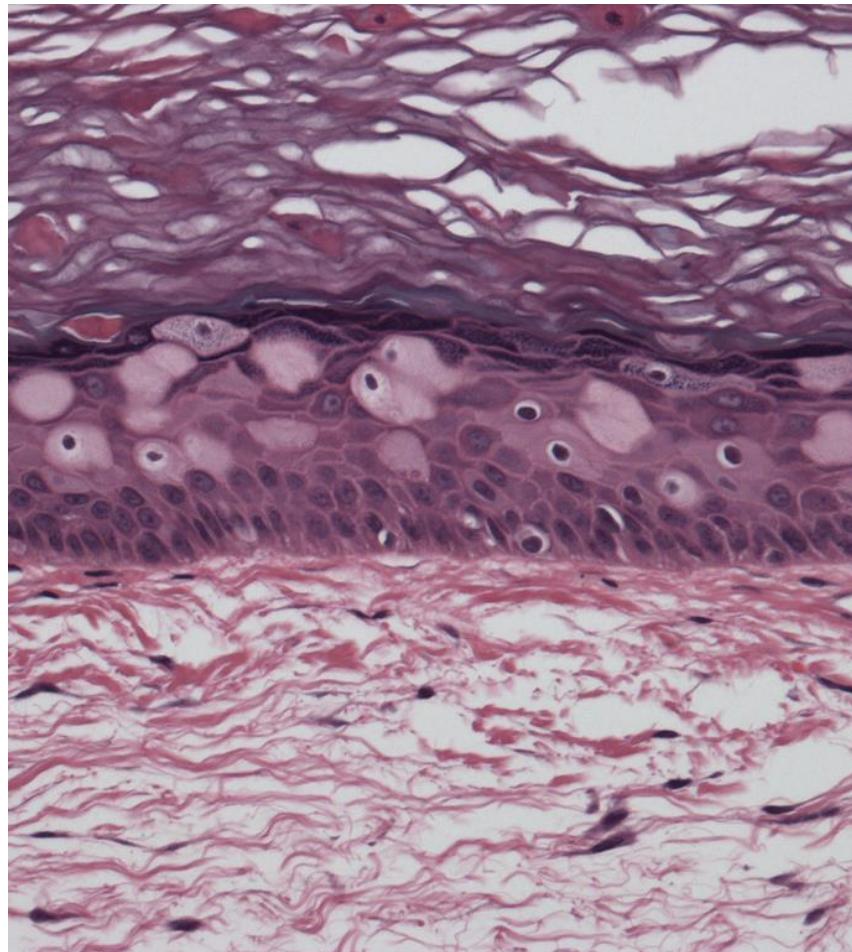
Kožný T bunkový lymfóm



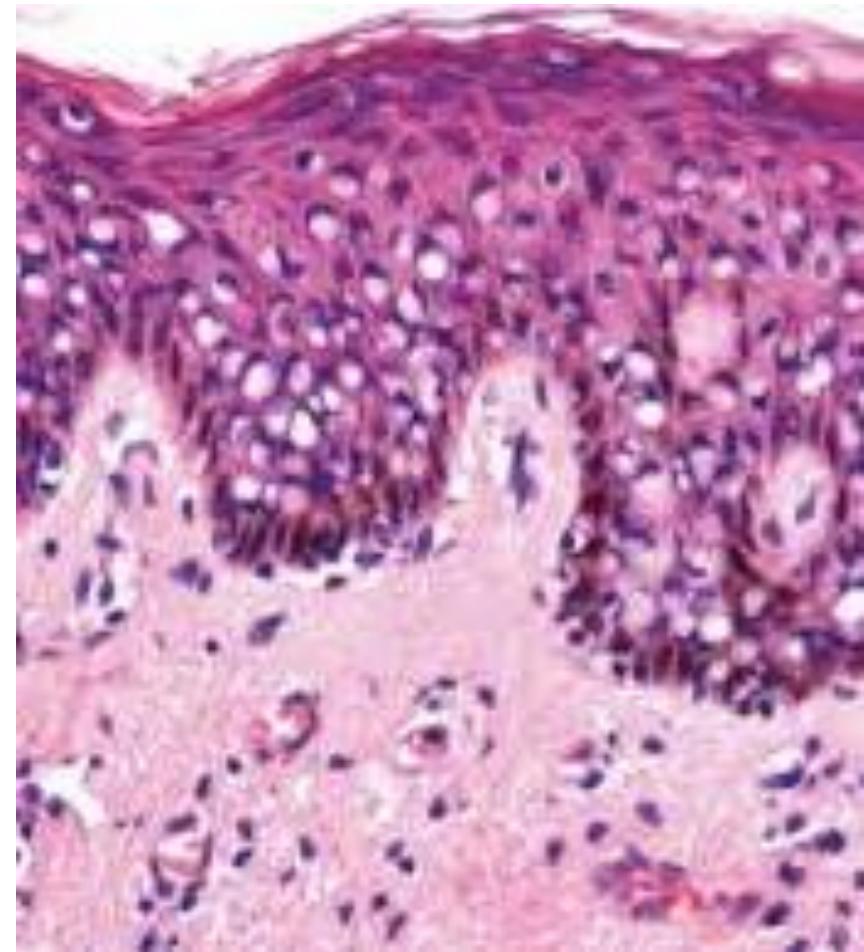
VIN3



Pagetoidná dyskeratóza



Fixačný artefakt



Primárna EMPD

Prognóza:

- non-rekurentné lézie
- rekurentné lézie, 32-33% (pozit. okraj, negat. okraj – “skip” arey a multicentrický pôvod, epidermálna akantolýza, dermálna a LV invázia)
- negatívne prognostické IHC črty – HER2+, p53+, strata e-cadherínu, lokalita: klitoris

Sekundárna EMPD dif.dg.

- dolný GIT- ca kolorekta
- urotheliálny ca
- prostatický ca
- ca gl. Bartholini
- CD20+, CDX2+
- Uroplakin III
- PSA, PSAP (! 50% PSA+ bez ca prostaty)



Záverom

EMPD

- pohlavie ♂
- lokalita
- morfologické variácie
- široká dif.dg.
- vylúčenie internej malignity

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