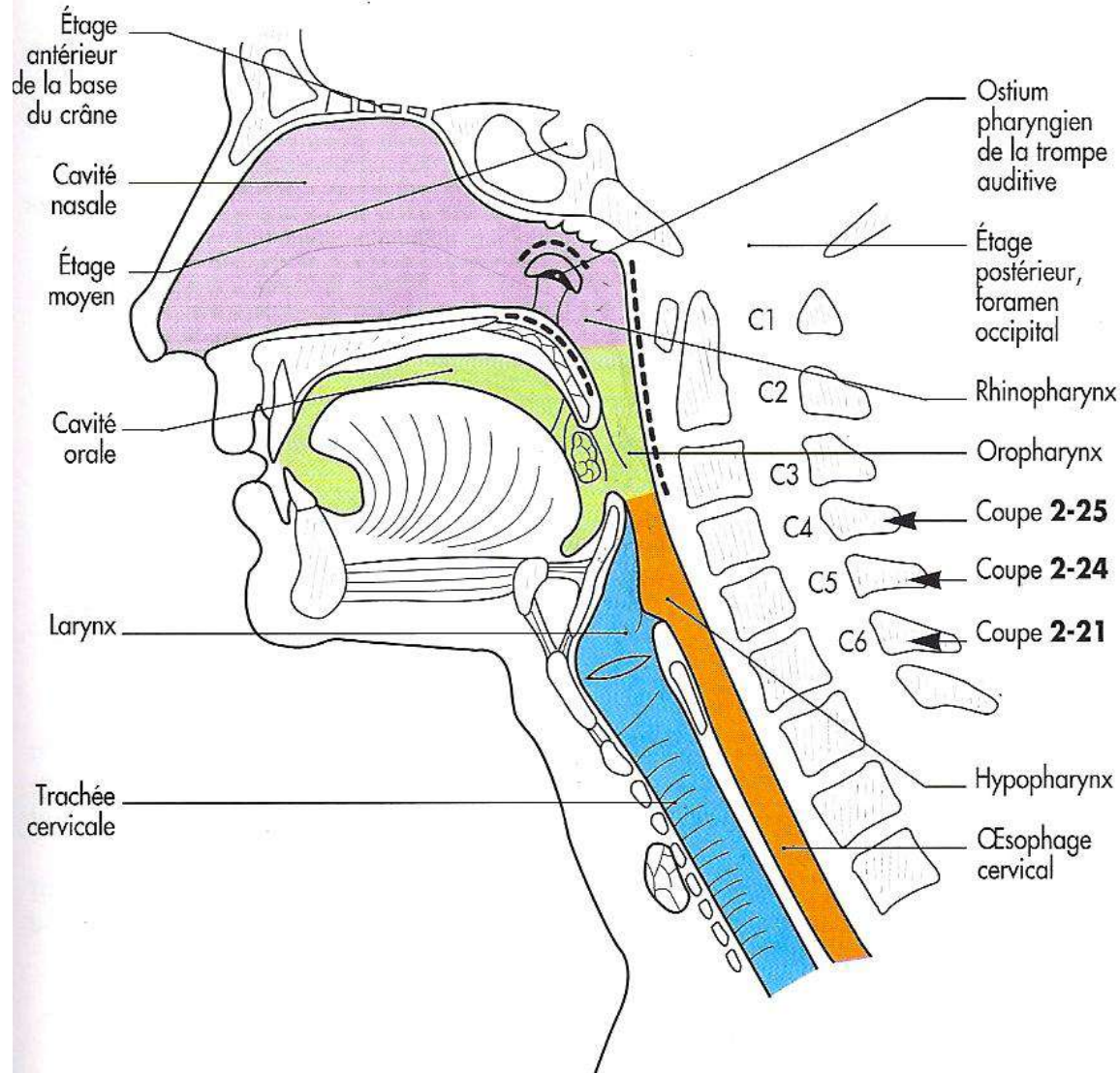


Head and Neck pathology



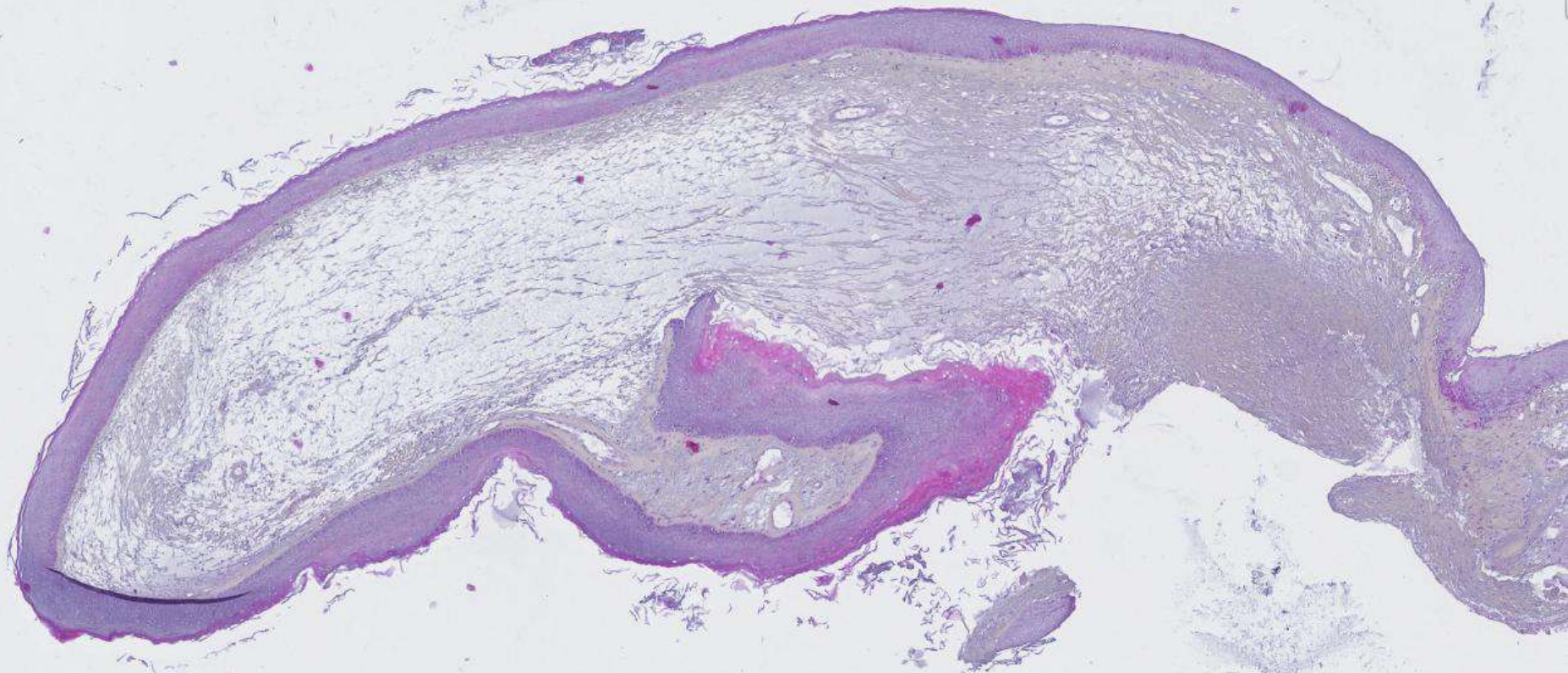
Pr Cécile Badoual
Service d'anatomo-pathologie
Hôpital Européen G Pompidou

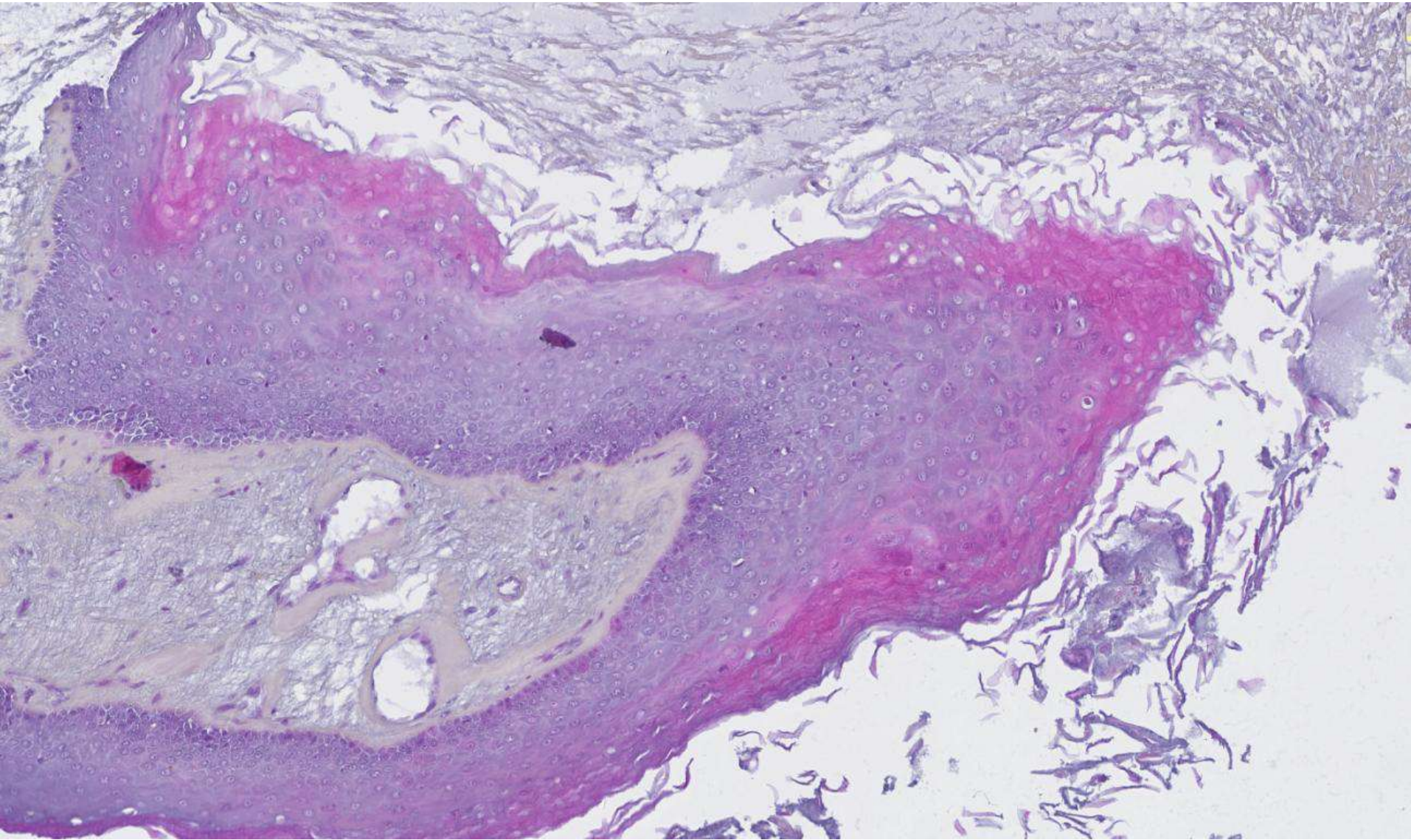
2-1 Coupe sagittale médiane tête et cou

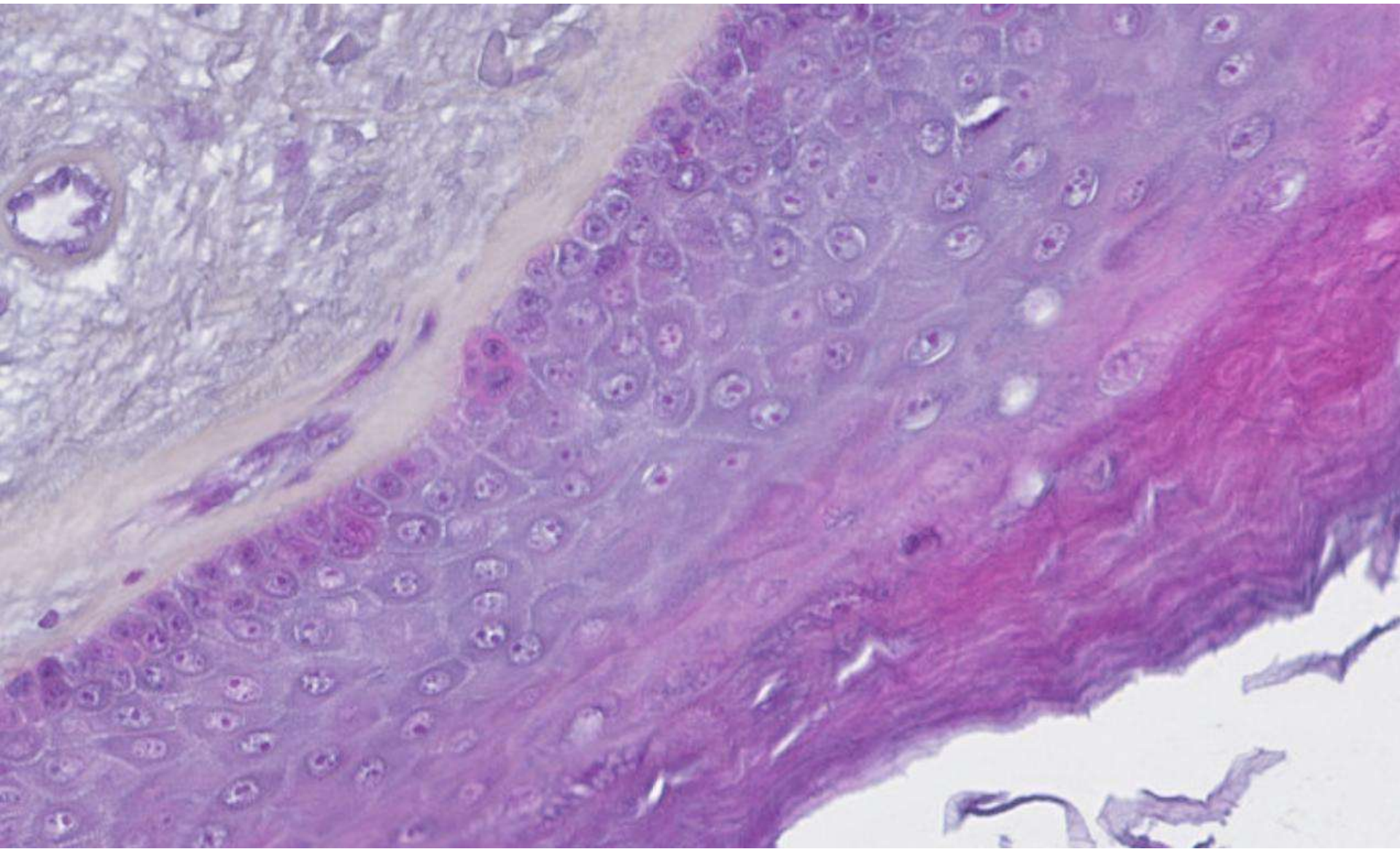


Case 1A

Man 56yo hard palate







Case 1B

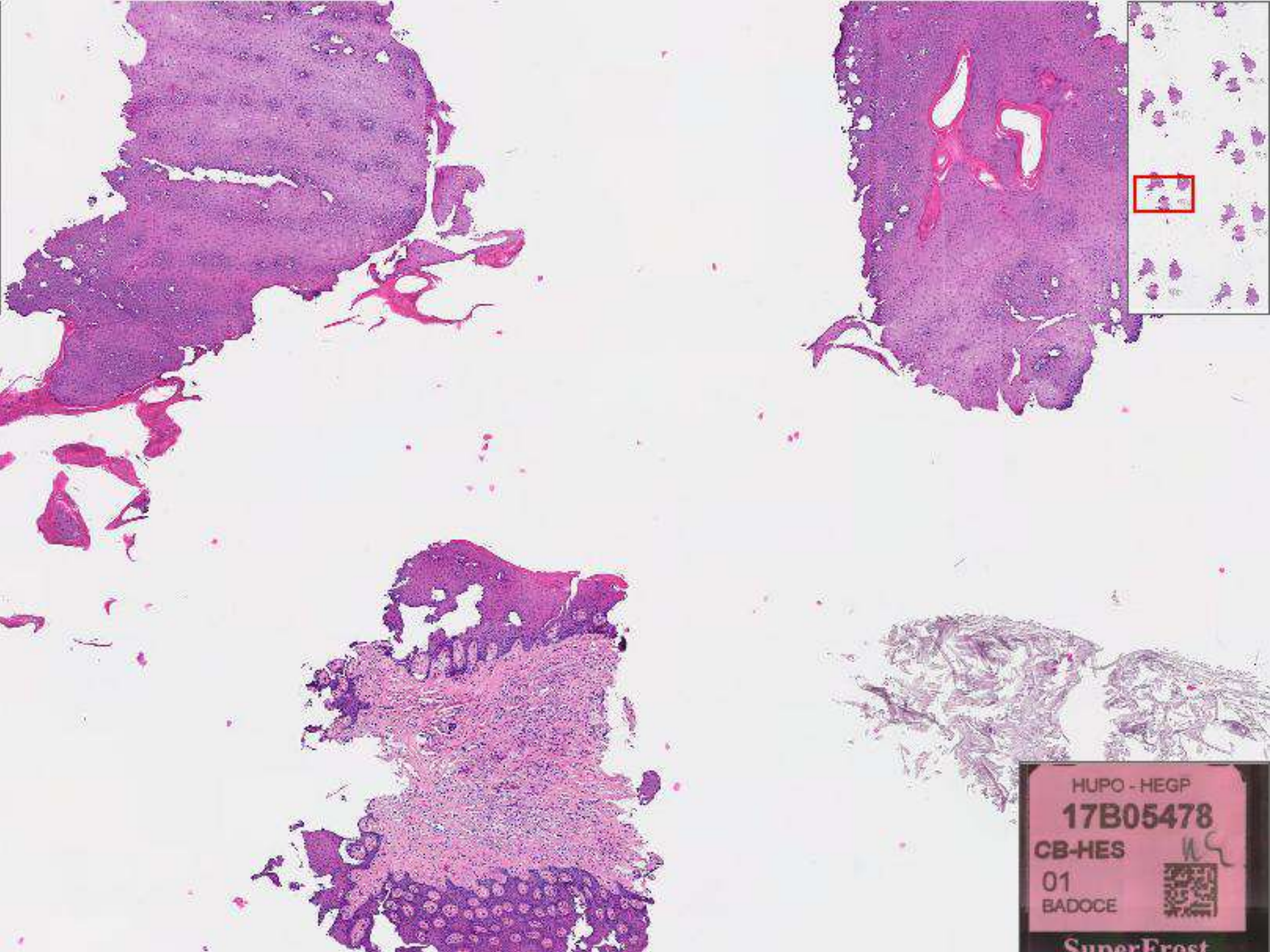
Man 72 yo smoker oral cavity biopsy

Oral epithelial disorder

Premalignant lesions	Premalignant conditions
Leukoplakia	Lichen planus
Erythroplakia	Discoid lupus erythematosus
Proliferative verrucous leukoplakia(PVL)	Epidermolysis bullosa
Viadent leukoplakia	Verruciform xanthoma
Candida leukoplakia	Graft-versus-host-disease
Reverse smokings' palate	Cheilitis glandularis
Verrucous hyperplasia	Xeroderma pigmentosum
Oral verrucous carcinoma	Syphilis (third stage)
Dyskeratosis congenita	Plummer-Vinson syndrome
Actinic cheilosis	Malnutrition
Keratoacanthoma	Vitamin A, B, C deficiency
Oral submucous fibrosis	Immunosuppressive diseases [AIDS]

Disorders	Clinical features	Locations	Risk of malignancy
Leukoplakia	White plaque	Cheeks, lips, gingivae	15.6–39.2%
Early (thin)			NA*
Homogenous			1–7%
Verruciform			4–15%
Speckled			18–47%
Erythroplakia	A predominantly red lesion	Mouth floor, tongue, retromolar pad, soft palate	51%
Proliferative verrucous leukoplakia (PVL)	Multifocal white patch or plaque + rough surface projections	Gingivae	63.3–100%
Viadent leukoplakia	White patch or plaque	Gingivae, buccal and labial vestibule	NA
Candida leukoplakia	Firm, white leathery plaques	Cheeks, lips, palate	4–5 times more common than leukoplakia
Smokeless tobacco keratosis	White plaque	Buccal or labial vestibule	NA
Palatal keratosis associated with reverse smoking	White patches and plaques	Palate, tongue	83.3% dysplasia 12.5% SCC
Verrucous hyperplasia	Extensive thick white plaque	Buccal mucosa	68% dysplasia
Oral verrucous carcinoma	Extensive thick white plaque	Buccal mucosa	20%
Dyskeratosis congenita	Oral leukoplakia	Buccal mucosa, tongue, oropharynx	NA
Actinic cheilosis	Diffuse, poorly defined atrophic, erosive, ulcerative or keratotic plaques	Lower lip	6–10%
Keratoacanthoma	Firm, sessile non tender nodule + a central plug of keratin	Lips, tongue, sublingual region	24%
Oral submucous fibrosis	Mucosal rigidity	Buccal mucosa, retromolar area, tongue, soft palate	7–26%
Lichen planus	Reticular, erosive, atrophic, bullous, ulcerative, papular, plaque like	Posterior buccal mucosa, tongue, gingivae, palate, vermilion border	0.4–3.7%
Discoid lupus erythematosus	White plaques with elevated borders, radiating white striae and telangiectasia	Cheeks, lips, palate	NA
Epidermolysis bullosa	Bullae and vesicle formation following mild trauma	Cheeks, tongue, palate	25%
Verruciform xanthoma	A well demarcated mass with a yellow-white or red color and a papillary or verruciform surface	Gingivae, tongue, buccal mucosa, vestibular mucosa, floor of the mouth	NA
Graft-versus host disease	Atrophy, erythema, erosions, ulcers, lichenoid lesions	Cheeks, tongue, lips, buccal & labial vestibule	NA

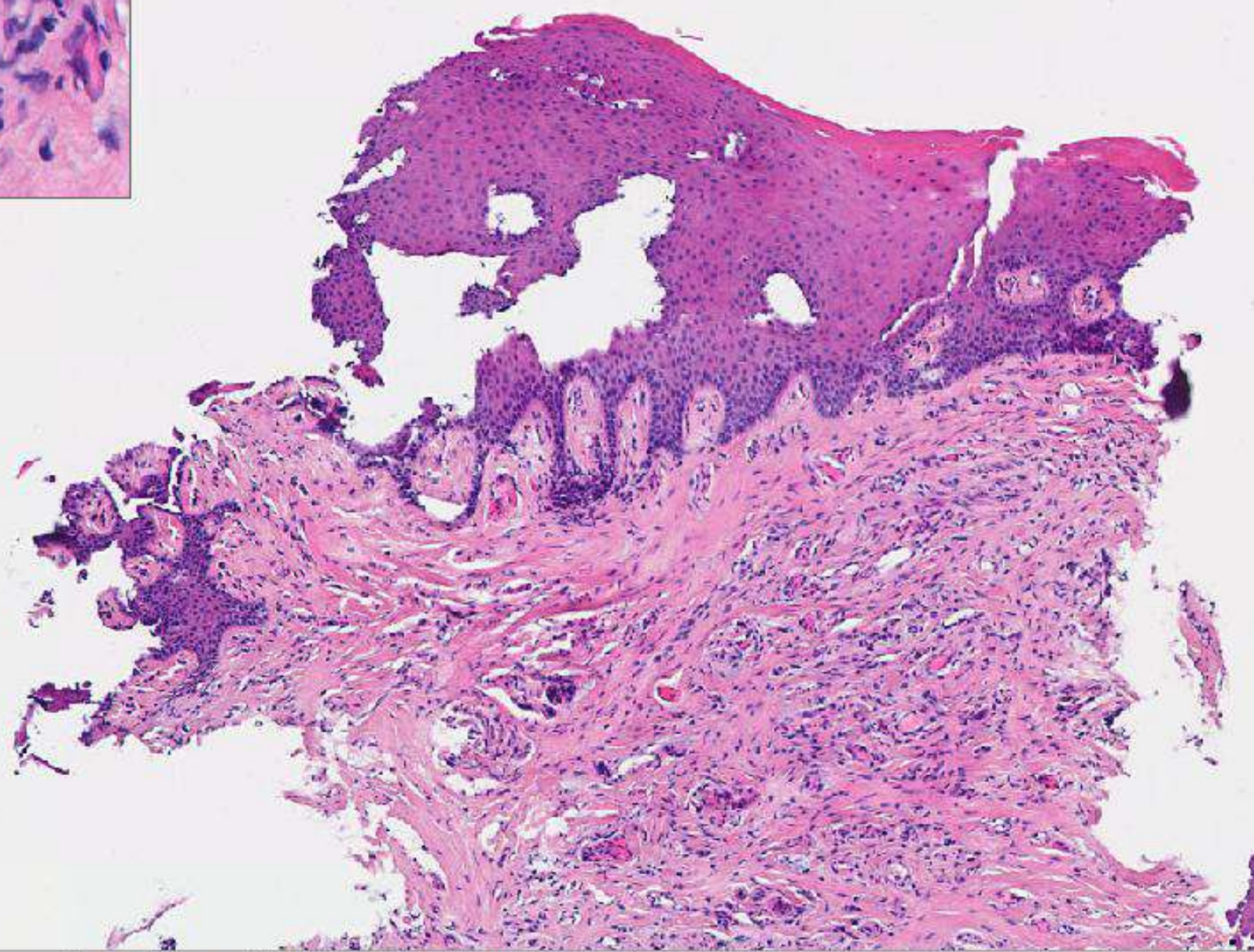
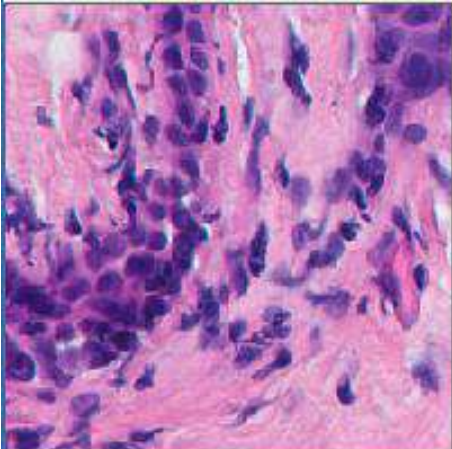
*NA: not assigned



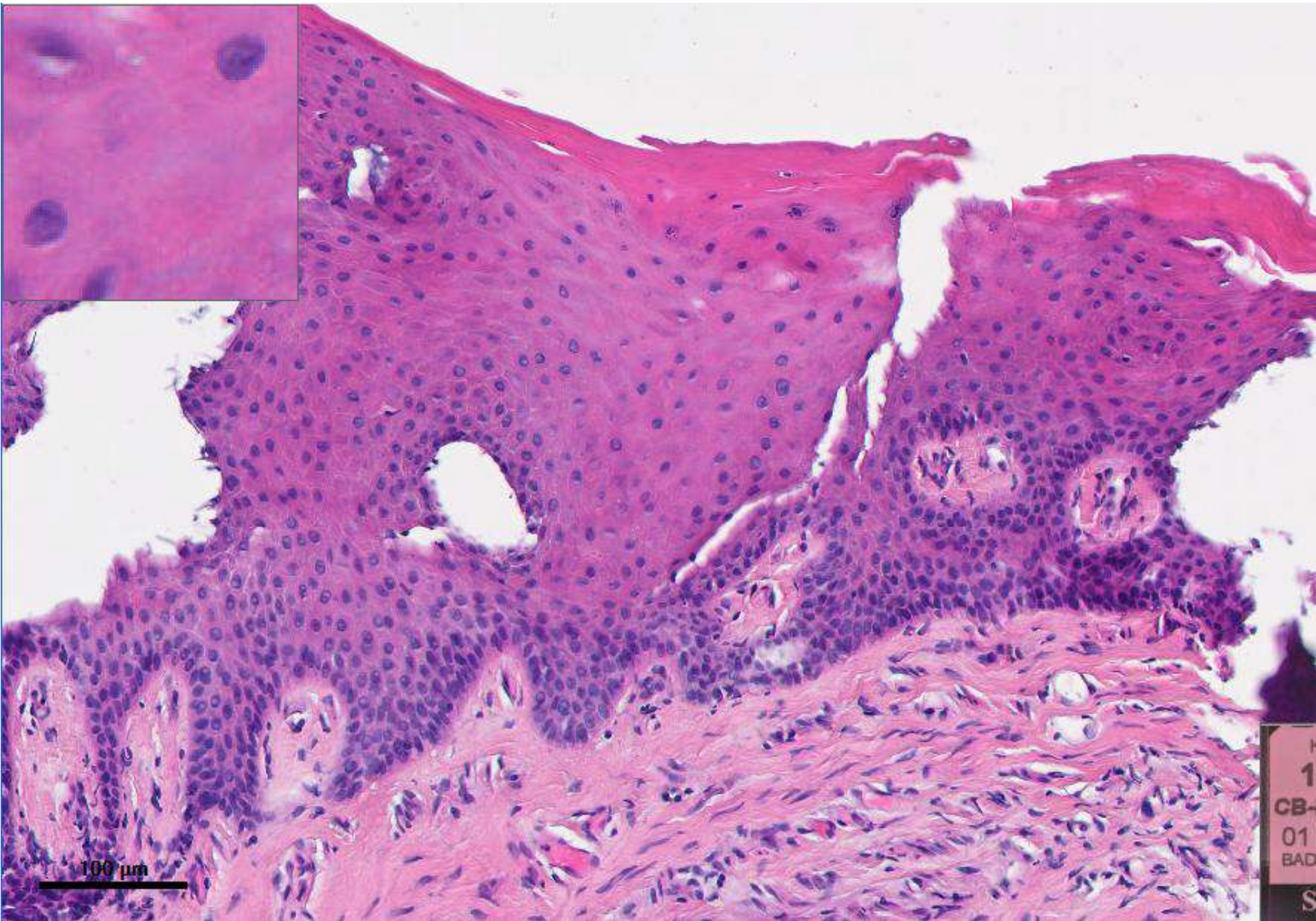
HUPO - HEGP
17B05478
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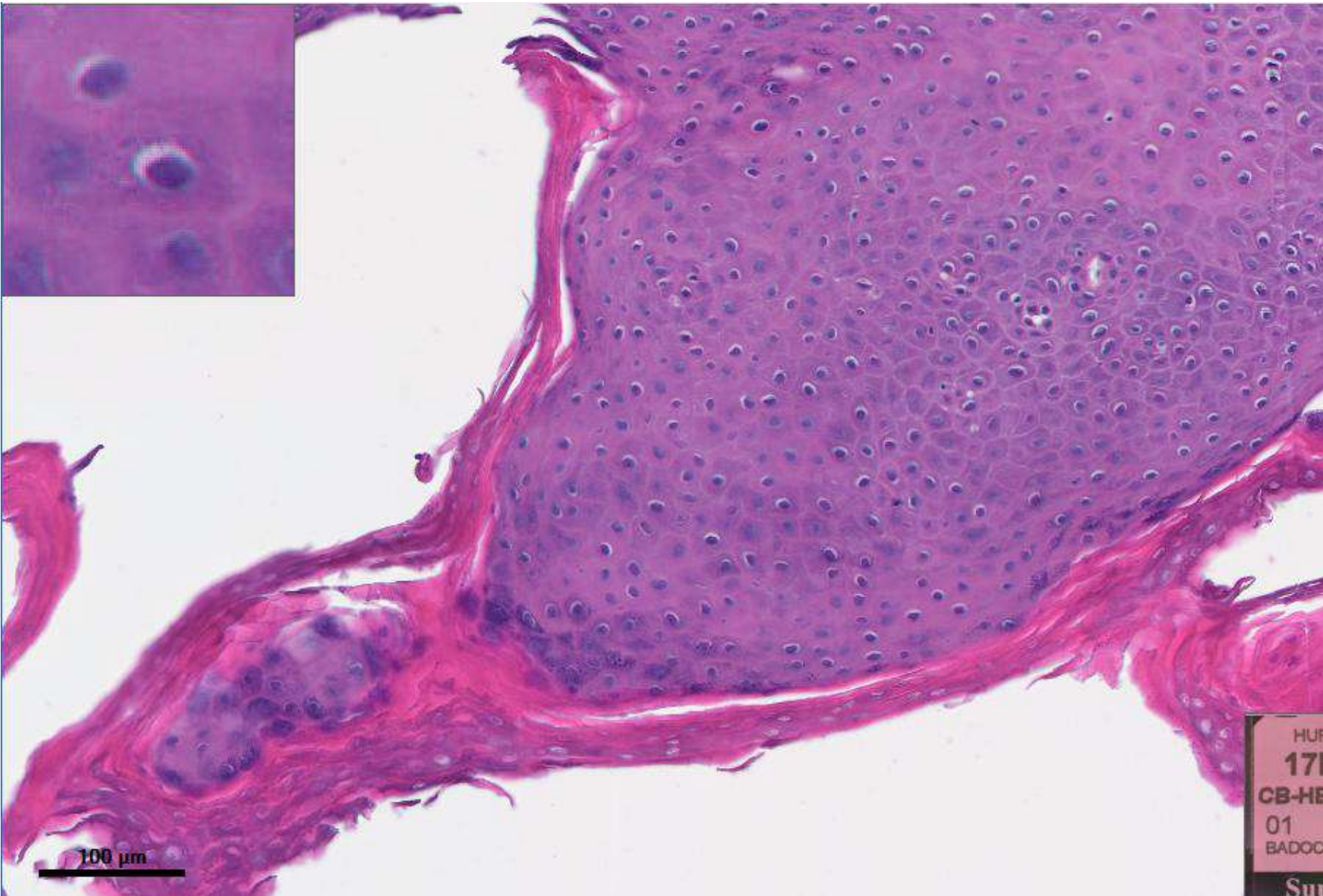


SuperFrost



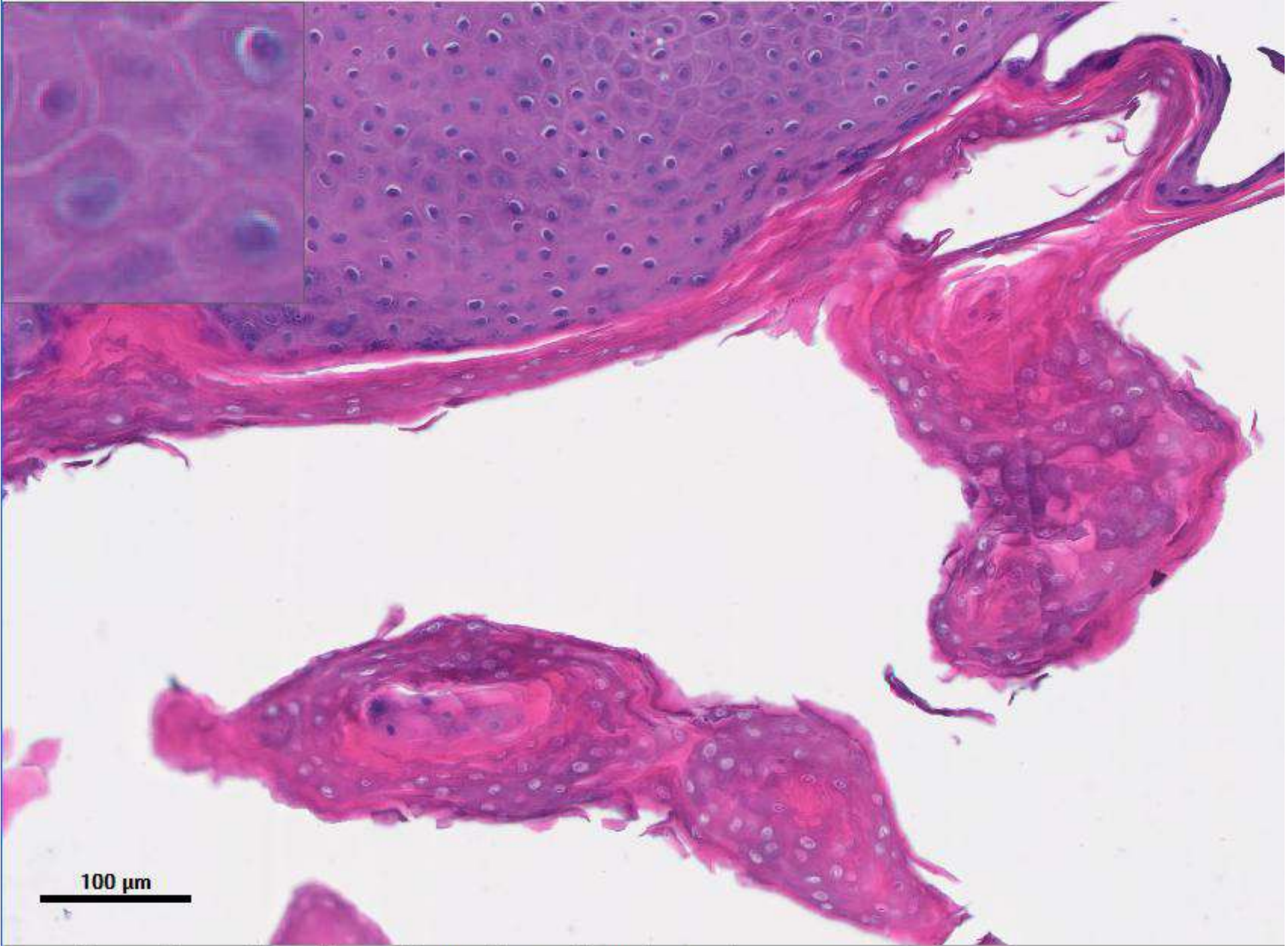
200 μ m





100 μ m

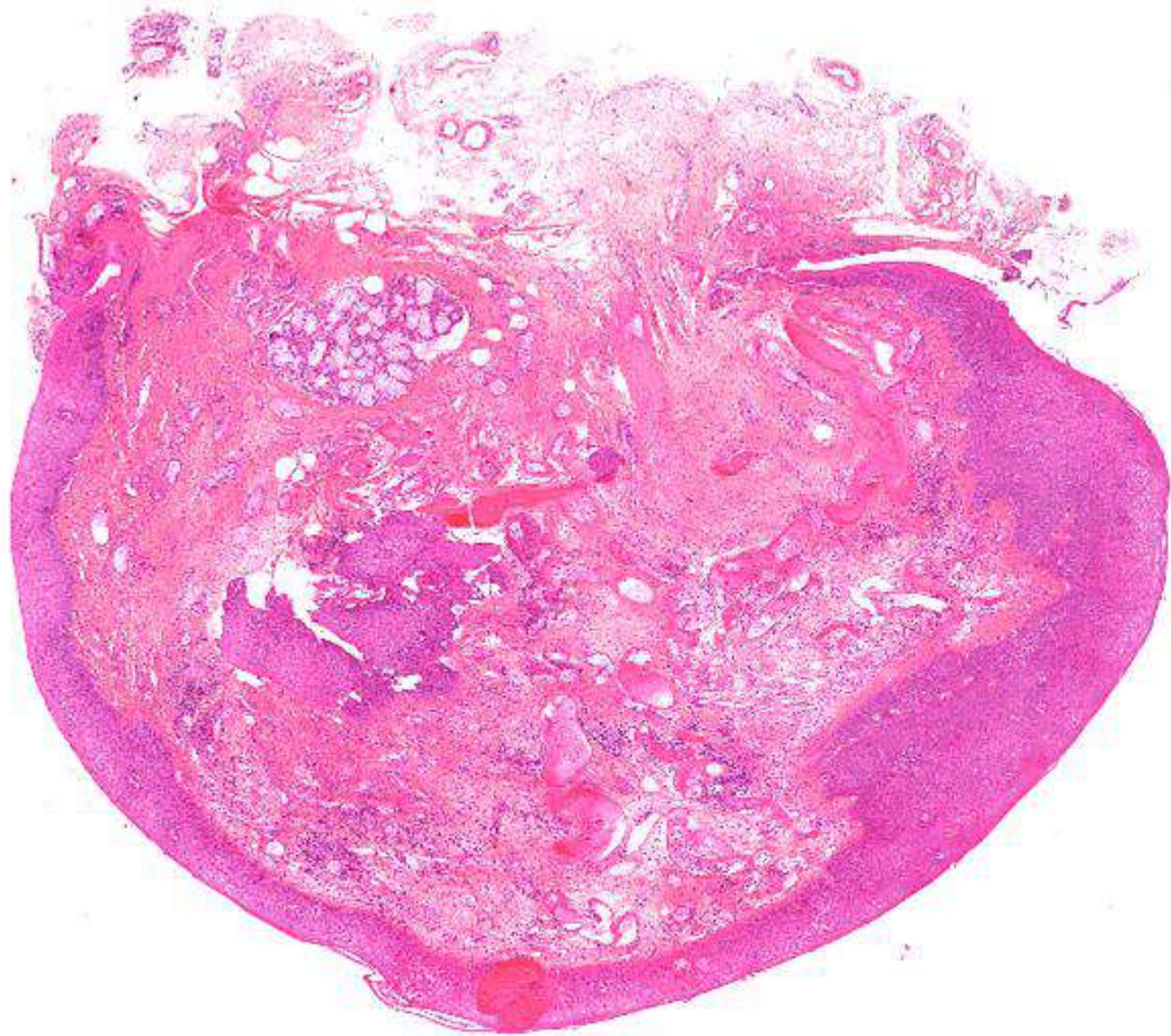
HU
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CB-HE
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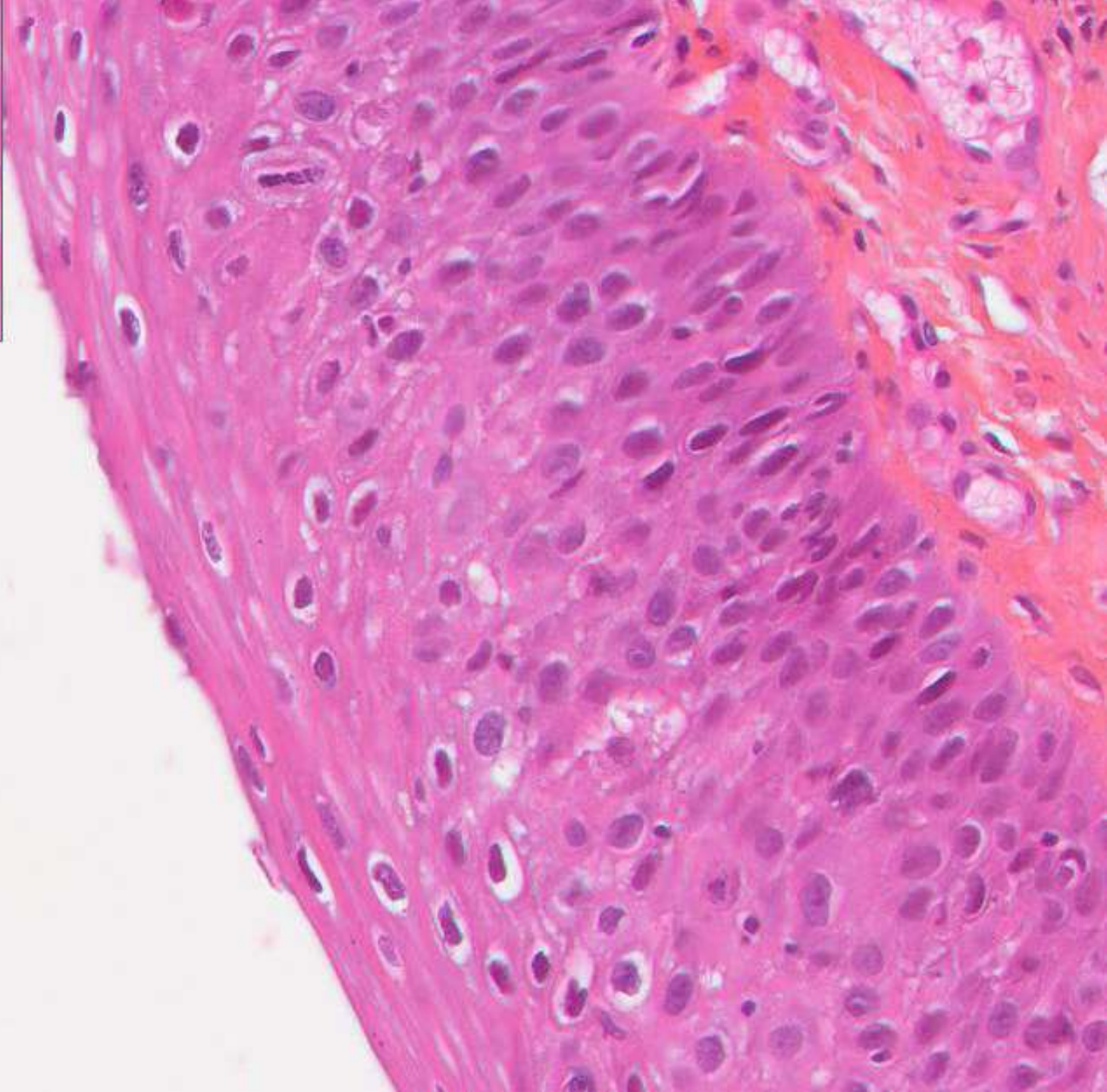


100 μm

Cas 10

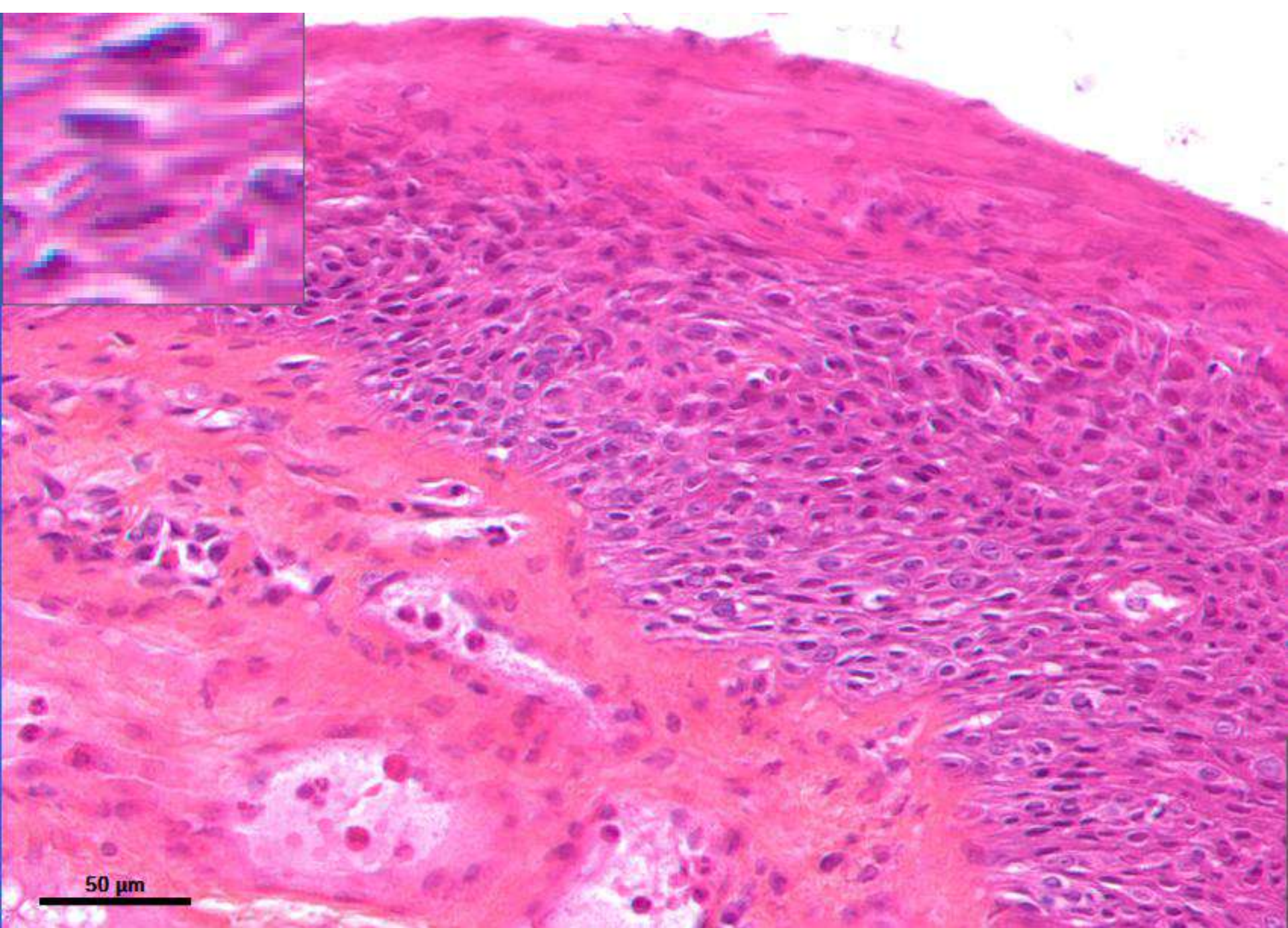
Man 42 yo smoker, oral cavity,
palate

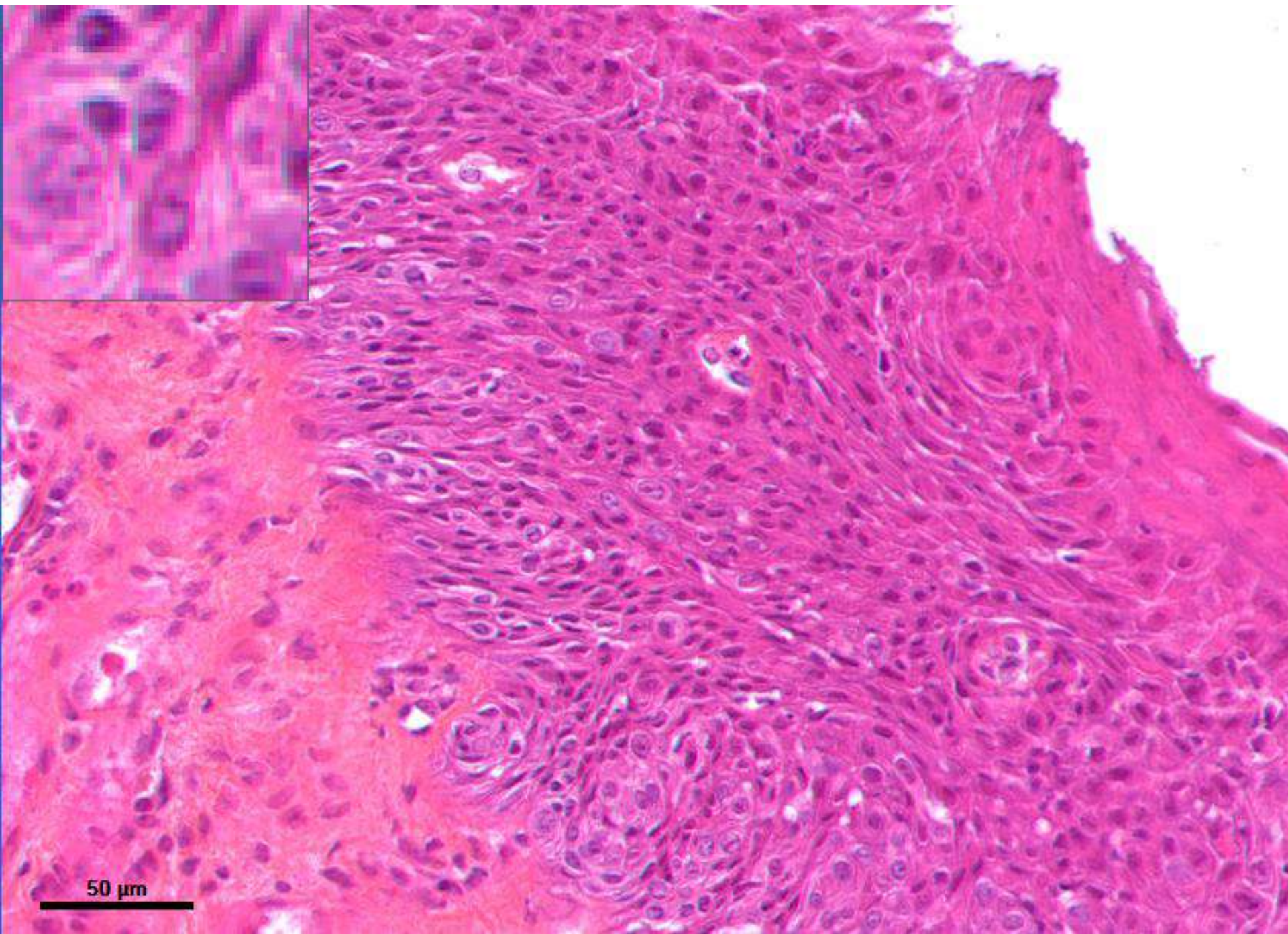




50 μ m







Diagnosis criteria for epithelial dysplasia,

adaped Barnes L

Architecture

Irregular epithelial stratification

Loss of polarity of basal cells

Drop-shaped rete ridges

Increased number of mitotic figures

Abnormally superficial mitoses

Premature keratinization in single cells
(dyskeratosis)

Keratin pearls within rete pegs

Cytology

Abnormal variation in nuclear size (anisonucleosis)

Abnormal variation in nuclear shape (nuclear
pleomorphism)

Abnormal variation in cell size (anisocytosis)

Abnormal variation in cell shape (cellular
pleomorphism)

Increased nuclear-cytoplasmic ratio

Increased nuclear size

Atypical mitotic figures

Increased number and size of nucleoli

Hyperchromasia



[International Journal of Clinical Oncology](#)

February 2011, Volume 16, Issue 1, pp 15-26 | [Cite as](#)

Oral premalignant lesions: from the pathological viewpoint

Authors

[Authors and affiliations](#)

Toshiyuki Izumo 

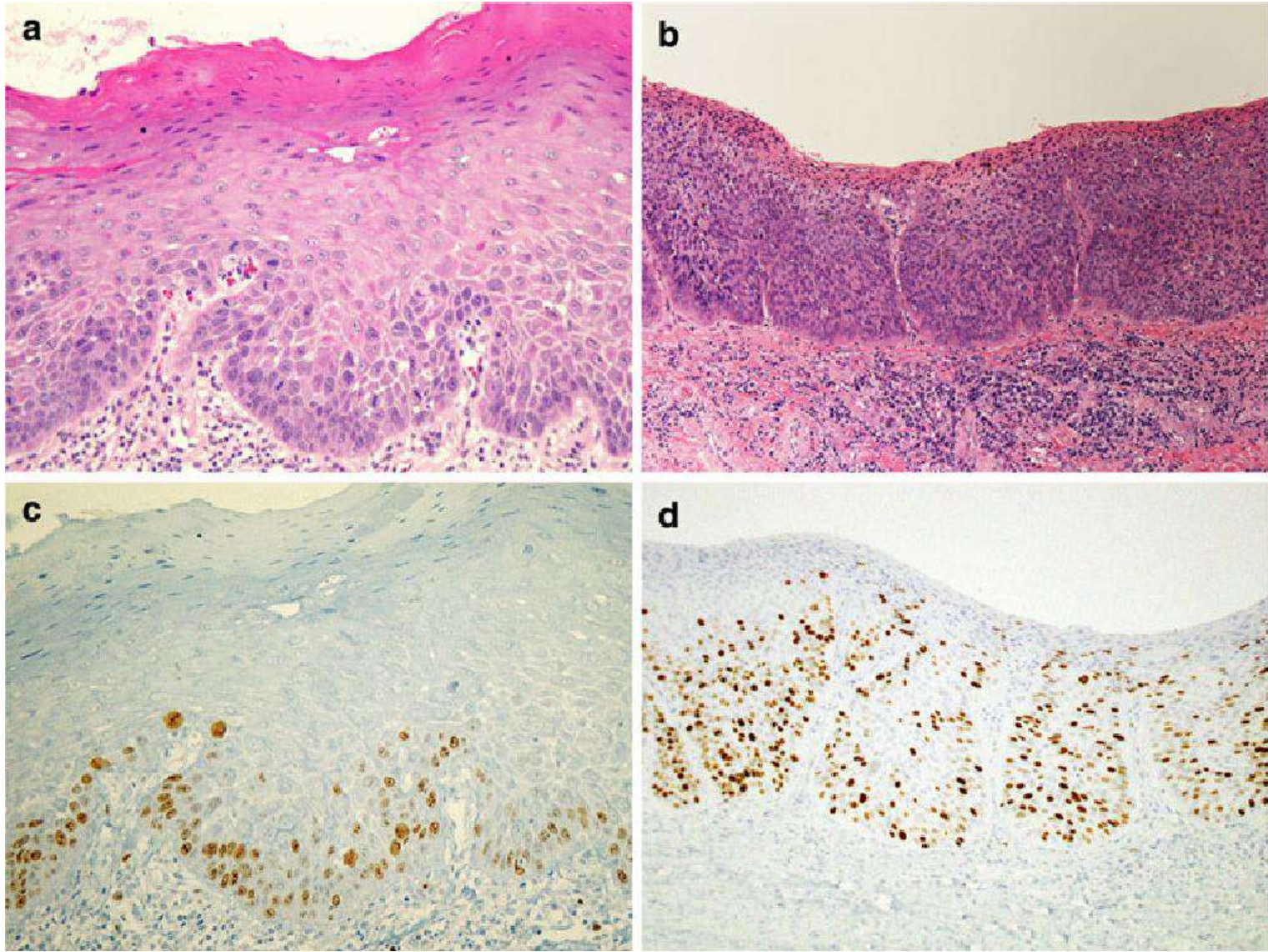


Fig. 1 a OIN/CIS (JSOP) differentiated type, c immunohistochemistry for Ki-67/MIB1 (differentiated type) [7]. b OIN/CIS (JSOP) basaloid type, d immunohistochemistry for Ki-67/MIB1 (basaloid type)

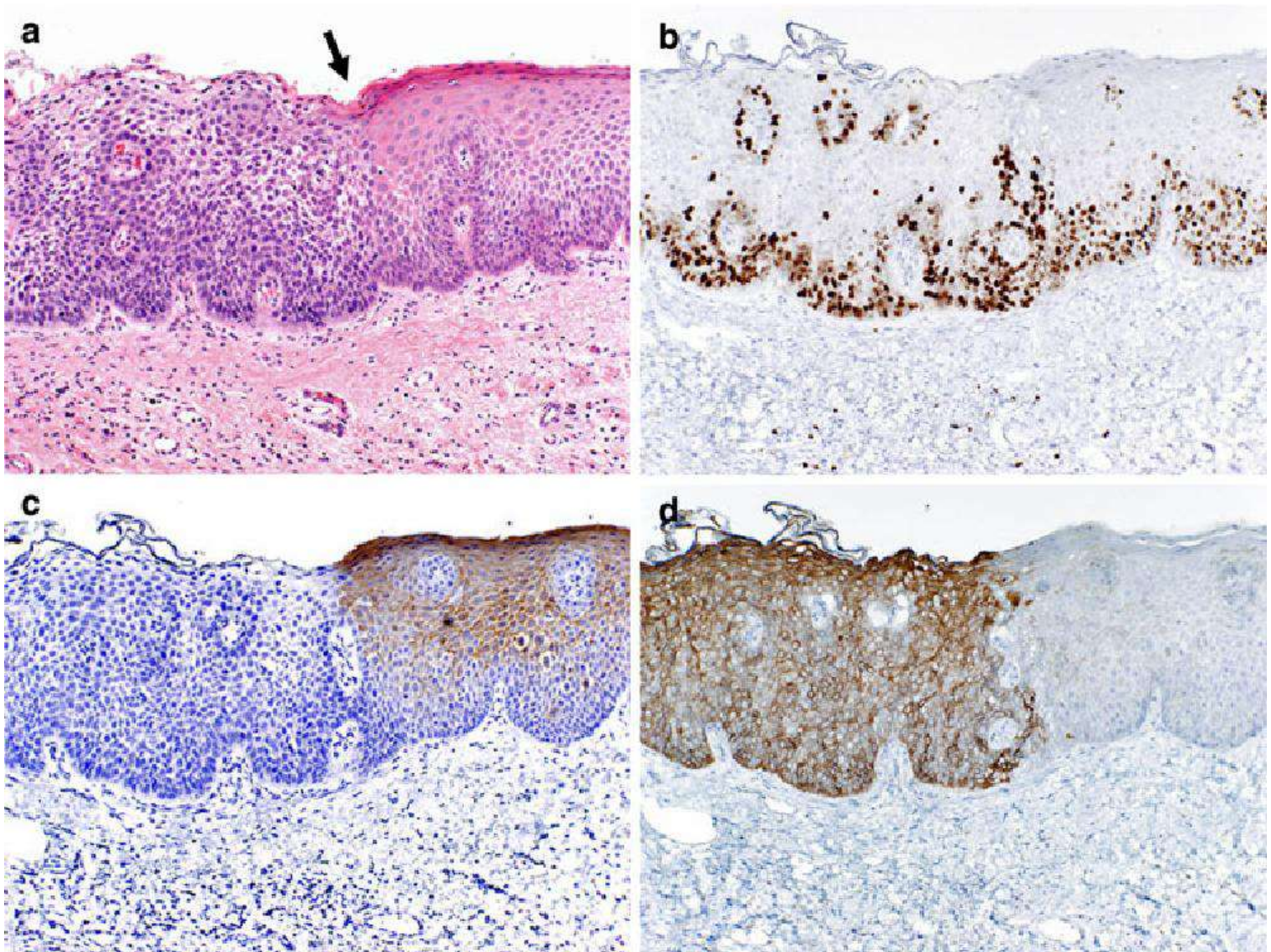
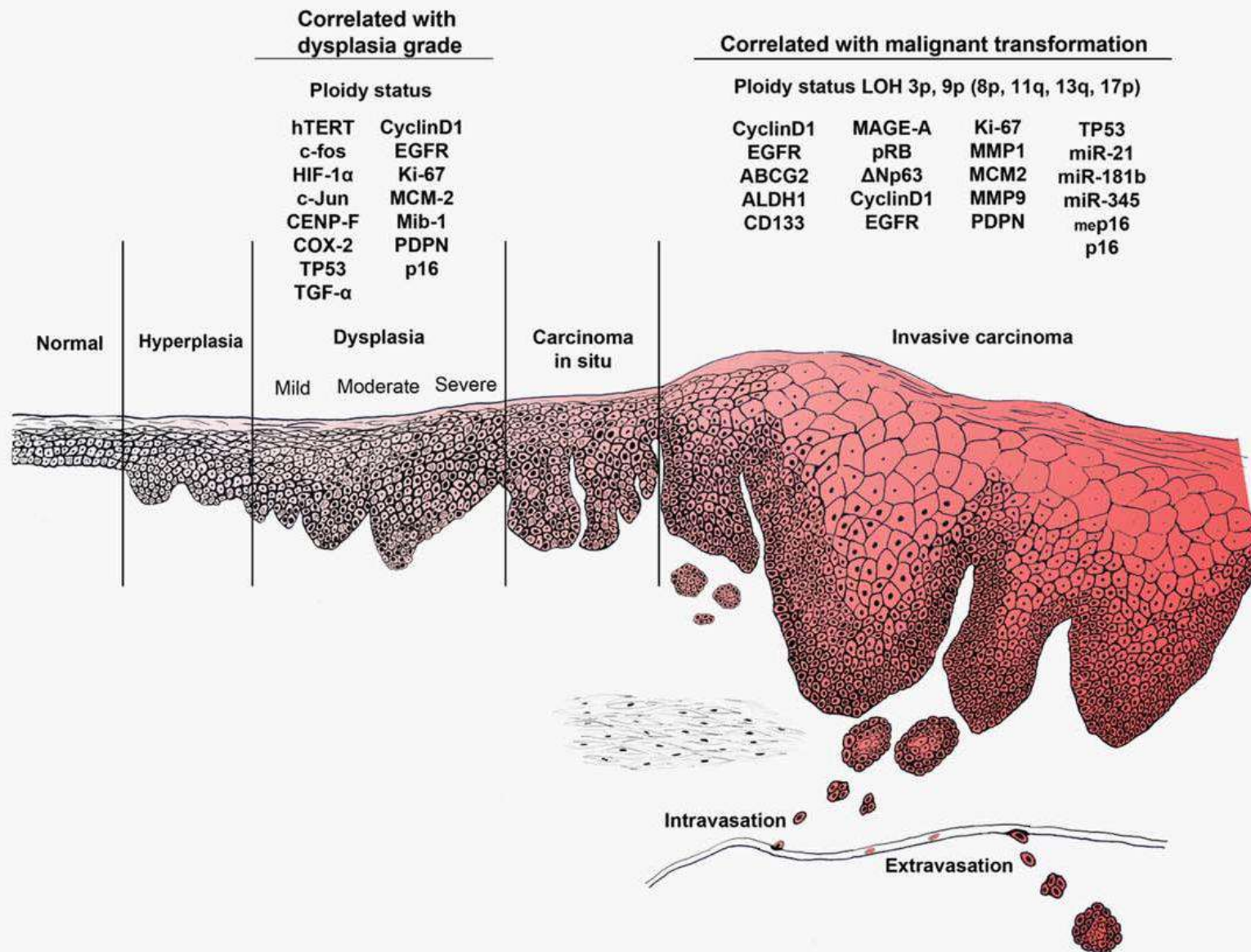


Fig. 2 a OIN/CIS(JSOP) differentiated type (left) (arrow shows the front line), b–c immunohistochemistry for Ki-67/MIB1 (b), cytokeratin 13 (c) and cytokeratin 17

WHO	SIN	SIL	OIN/CIS (JSOP) system		
		Hyperplasia /keratosis	Reactive atypical epithelium		
Mild dysplasia	SIN1	SIL I (low grade)	OED	→	Follow up
Moderate dysplasia	SIN2				
Severe dysplasia	SIN3	SIL II (high grade)	OIN/CIS (JSOP)	→	Mucosal resection
CIS					

WHO World Health Organization classification, *SIN* squamous intraepithelial neoplasia classification, *SIL* modified binary system of SIN [45, 55], *OIN/CIS (JSOP)* oral intraepithelial neoplasia/carcinoma in situ (Japanese Society for Oral Pathology), *OED* oral epithelial dysplasia, *CIS* carcinoma in situ



[Int J Cancer](#). 2015 Feb 1;136(3):503-15.

Potentially malignant disorders of the oral cavity: current practice and future directions in the clinic and laboratory.

[Dionne KR¹](#), [Warnakulasuriya S](#), [Zain RB](#), [Cheong SC](#).

WHO Classification of Head and Neck Tumours

Edited by

Adel K. El-Naggar, John K.C. Chan, Jennifer R. Grandis, Takashi Takata, Pieter J. Slootweg





Evaluation of a new grading system for laryngeal squamous intraepithelial lesions—a proposed unified classification

Nina Gale, Rok Blagus,¹ Samir K El-Mofty,² Tim Helliwell,³ Manju L Prasad,⁴

Ann Sandison,⁵ Metka Volavšek, Bruce M Wenig,⁶ Nina Zidar & Antonio Cardesa⁷

Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, ¹*Institute for Biostatistics and Medical Informatics, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia,* ²*Department of Pathology and Immunology, School of Medicine, Washington University, St Louis, MO, USA,* ³*Department of Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool, UK,* ⁴*Department of Pathology, Yale University School of Medicine, New Haven, CT, USA,* ⁵*Department of Histopathology, Charing Cross Hospital, London, UK,* ⁶*Department of Pathology, Beth Israel Medical Center, New York, NY, USA,* and ⁷*Department of Pathology, Hospital Clinic, University of Barcelona, Barcelona, Spain*

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TABLE 2 Classification of squamous intraepithelial neoplasia (SIN) [12]

Classification	Hyperplastic form	Atrophic form
Hyperplasia/ keratosis	Thickened, hyperplastic epithelium Rare mitosis confined to suprabasal layer Normal maturation Surface keratinization common No nuclear pleomorphism	Atrophy Thin mucosa Normal mucosal maturation No nuclear pleomorphism
SIN I (low grade)	Epithelial hyperplasia Increased mitoses common [1–2 per high power field (HPF)] Three or more layers of basal-like cells Minor nuclear pleomorphism	Some proliferation of basal-like cells Increased mitoses (1–2 per HPF) Minor nuclear pleomorphism Surface maturation still evident
SIN II (high grade)	Epithelial hyperplasia Mitoses in all layers common, including abnormal forms Marked epithelial maturation abnormalities with immature basal-like cells constituting inner and middle one third or in combination with premature keratinization, including presence of pearls Prominent nuclear pleomorphism Increased chromatin staining	Proliferation of basal-like cells involving the full thickness Prominent submucosal changes Numerous mitoses at all levels; may have abnormal mitotic forms Prominent nuclear pleomorphism Little or no evidence of maturation or keratinization

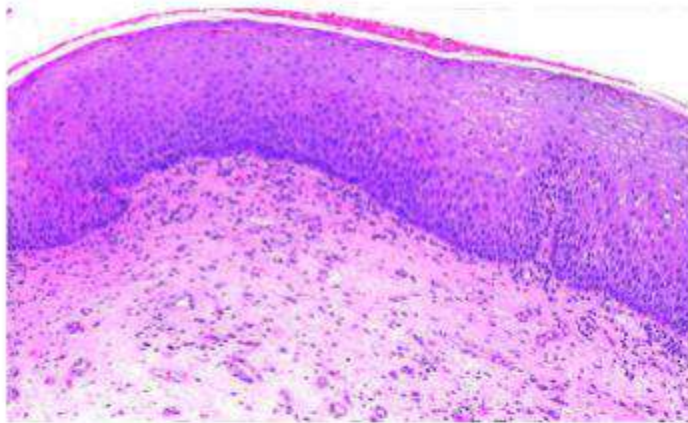


Figure 1. Low-grade squamous intraepithelial lesion. Hyperplastic squamous epithelium with augmented parabasal cells, oriented perpendicularly to the basement membrane, extends up to the middle of the epithelial thickness. The upper part of the epithelium is unchanged. There is no cytological atypia.

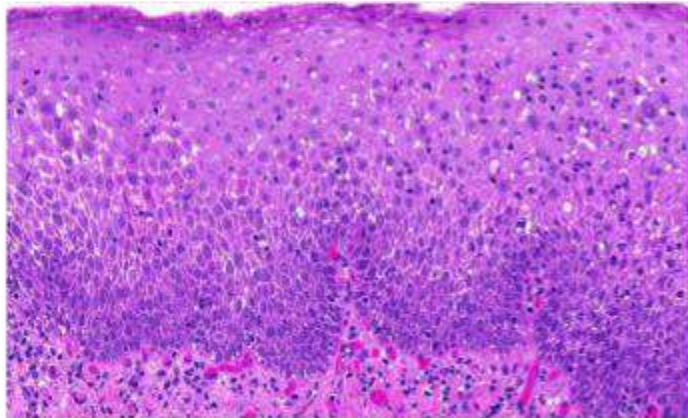


Figure 2. Low-grade squamous intraepithelial lesion. Augmented parabasal cells, oriented perpendicularly to the basement membrane, extends up to the one third of the epithelial thickness. The upper part of the epithelium is unchanged. There is no cytologic atypia.

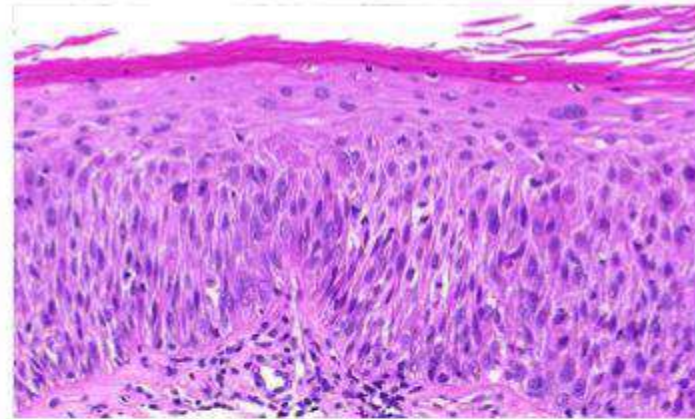


Figure 3. High-grade squamous intraepithelial lesion. Polymorphic epithelial cells occupy two-thirds of the epithelial thickness, and perpendicular orientation to the basement membrane is preserved.

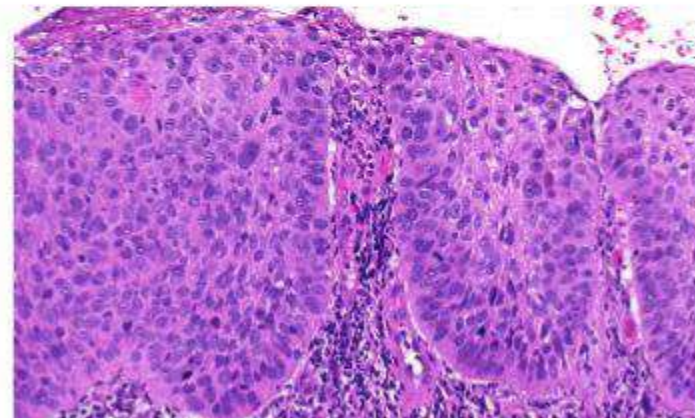
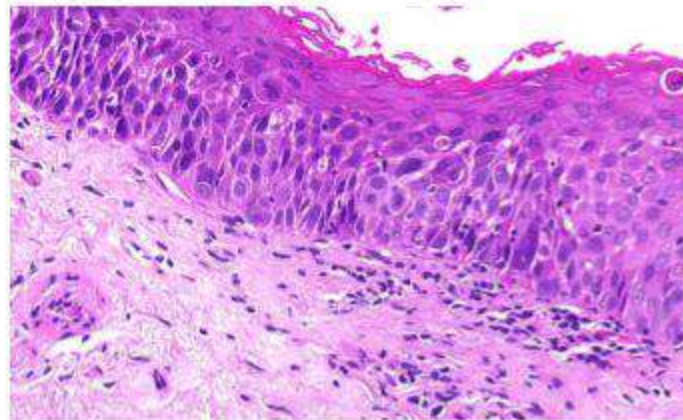


Figure 4. High-grade squamous intraepithelial lesion. The thickened epithelium is almost entirely occupied by moderately polymorphic epithelial cells, which show preserved perpendicular orientation to the basement membrane. Increased mitotic activity is evident.

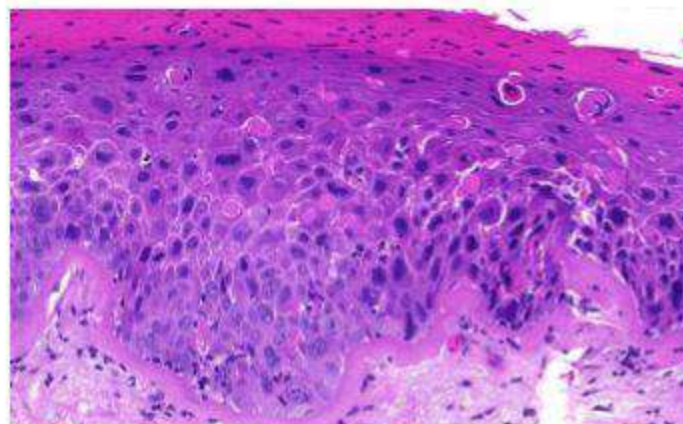
Evaluation of a new grading system for laryngeal squamous intraepithelial lesions—a proposed unified classification

Nina Gale,¹ Rok Blagus,² Samir K El-Mofly,² Tim Helliwell,³ Manjiv I Prasad,⁴ Ann Sandison,⁵ Metka Volavsek,⁶ Bruce M Wenig,⁷ Nina Zidar & Antonia Gerdan/⁸
 Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, ¹Institute for Biostatistics and Medical Informatics, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, ²Department of Pathology and Immunology, School of Medicine, Washington University, St Louis, MO, USA, ³Department of Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool, UK, ⁴Department of Pathology, Yale University School of Medicine, New Haven, CT, USA, ⁵Department of Histopathology, Charing Cross Hospital, London, UK, ⁶Department of Pathology, Beth Israel Medical Center, New York, NY, USA, and ⁷Department of Pathology, Hospital Clinic, University of Barcelona, Barcelona, Spain

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Figures 5. Carcinoma *in situ*. Pronounced architectural disorder of the epithelium with severe cellular and nuclear atypias and increased number of mitoses and dyskeratotic cells are evident.



Figures 6. Carcinoma *in situ*. All histological characteristics of carcinoma *in situ* are present: pronounced architectural disorder, severe cellular and nuclear atypias and increased number of mitoses. Minimally preserved epithelial maturation is seen in the upper layer.

Table 3.02 Morphological criteria for the classification of laryngeal precursor lesions (797)

Low-grade dysplasia (including previous category of mild dysplasia): Low malignant potential: a spectrum of morphological changes ranging from squamous hyperplasia to an augmentation of basal and parabasal cells occupying as much as the lower half of the epithelium, while the upper portion retains maturation	
Architectural criteria	<p>Stratification is preserved: transition of basal cells or augmented basal/parabasal cell layer with perpendicular orientation to the basement membrane to prickle cells horizontally oriented in the upper part</p> <p>Spinous layer: spectrum of changes ranging from increased spinous layer in the whole thickness up to changes in which prickle cells are seen only in the upper epithelial half</p> <p>Basal/parabasal layer: spectrum of changes, from 2-3 unchanged layers to augmentation of basal and parabasal cells in the lower half of the epithelium</p>
Cytological criteria	<p>At most minimal cellular atypia</p> <p>Parabasal cells: slightly increased cytoplasm compared to basal cells, enlarged nuclei, uniformly distributed chromatin, no intercellular bridges</p> <p>Rare regular mitoses in or near basal layer</p> <p>Few dyskeratotic cells present</p>

High-grade dysplasia (including previous categories of moderate dysplasia, severe dysplasia, and carcinoma in situ):

A premalignant lesion; a spectrum of changes including immature epithelial cells occupying at least the lower half of the epithelium and as much as the whole epithelial thickness

Architectural criteria^a	<p>Abnormal maturation</p> <p>Variable degrees of disordered stratification and polarity in as much as the whole epithelium</p> <p>Altered epithelial cells usually occupying from half to the entire epithelial thickness</p> <p>Two subtypes: keratinizing (spinous-cell type) and non-keratinizing (basal-cell type)</p> <p>Variable degree of irregularly shaped rete (bulbous, downwardly extending), with an intact basement membrane</p> <p>No stromal alterations</p>
Cytological criteria^a	<p>Easily identified to conspicuous cellular and nuclear atypia, including marked variation in size and shape, marked variation in staining intensity with frequent hyperchromasia, nucleoli increased in number and size</p> <p>Increased N:C ratio</p> <p>Increased mitoses at or above the suprabasal level, with or without atypical forms</p> <p>Dyskeratotic and apoptotic cells are frequent throughout the entire epithelium</p>

^aComplete loss of stratification and polarity and/or severe cytological atypia and atypical mitoses qualifies as carcinoma in situ if a three-tiered system is used

Level of abnormal maturation WHO 2005	WHO 2005 classification 92 832 2417 5 ISBN	SIN Classification 978 1 4160 2589 4 ISBN	Ljubljana classification 18752537	WHO 2017 classification 24689850
	Squamous hyperplasia	Squamous hyperplasia	Squamous hyperplasia	LG SIL
Lower 1/3	Mild dysplasia	SIN 1	Basal/parabasal hyperplasia	
1/3 to 1/2	Moderate	SIN 1? or SIN2	Atypical hyperplasia	HG-SIL
Upper 1/2-3/4	Moderate			
Full thickness	Severe dysplasia			
	CIS		CIS	CIS

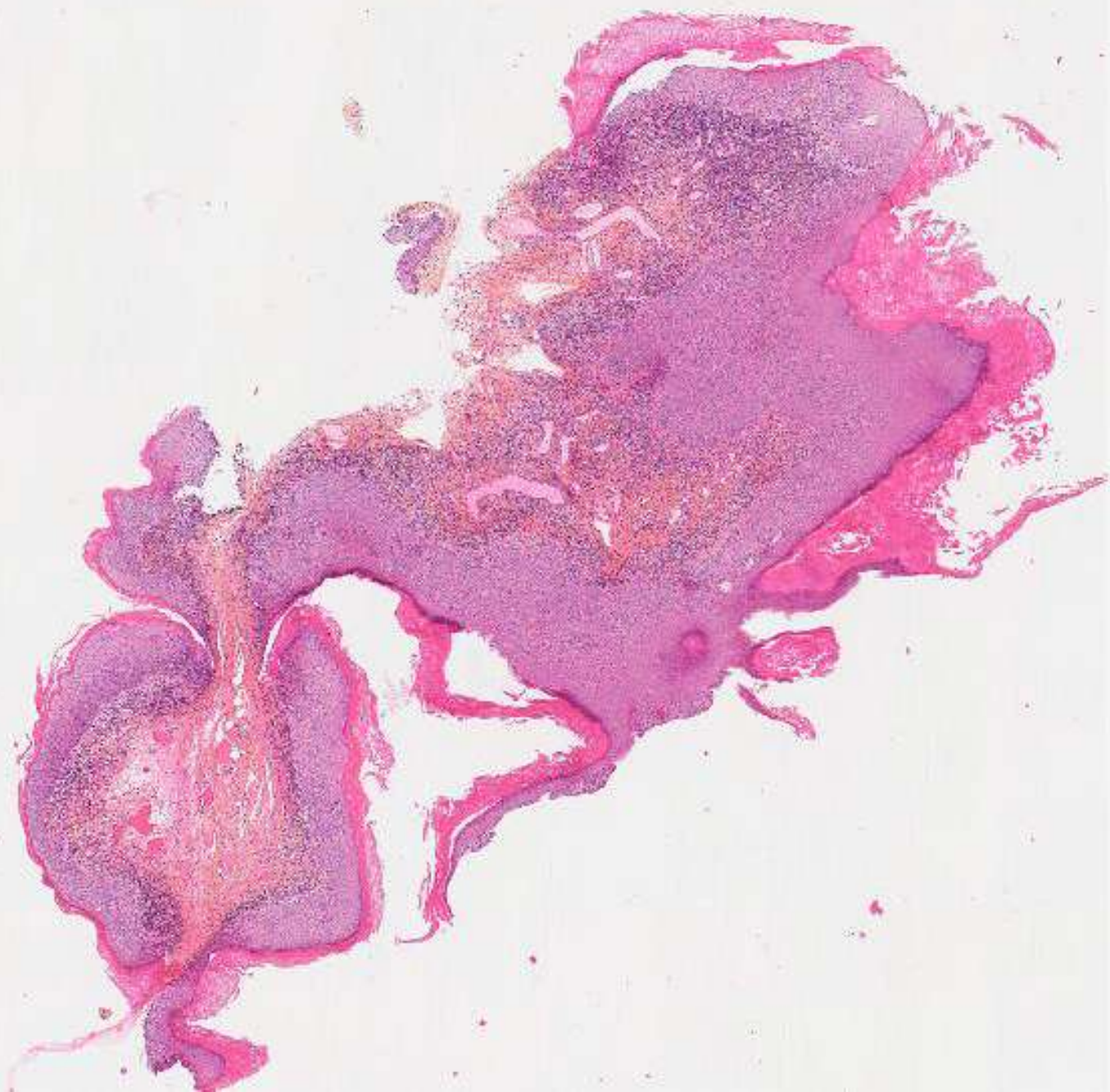
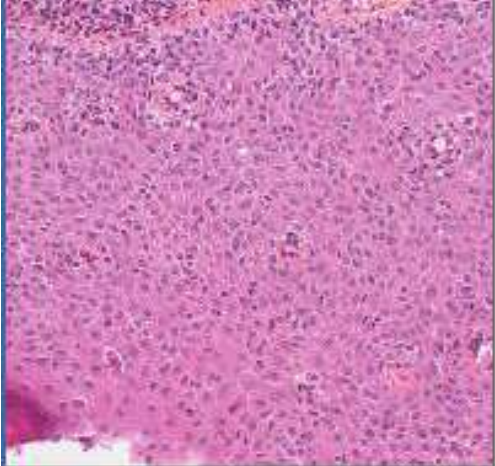
SIN = squamous intraepithelial neoplasia

LG SIL= low-grade intraepithelial lesion

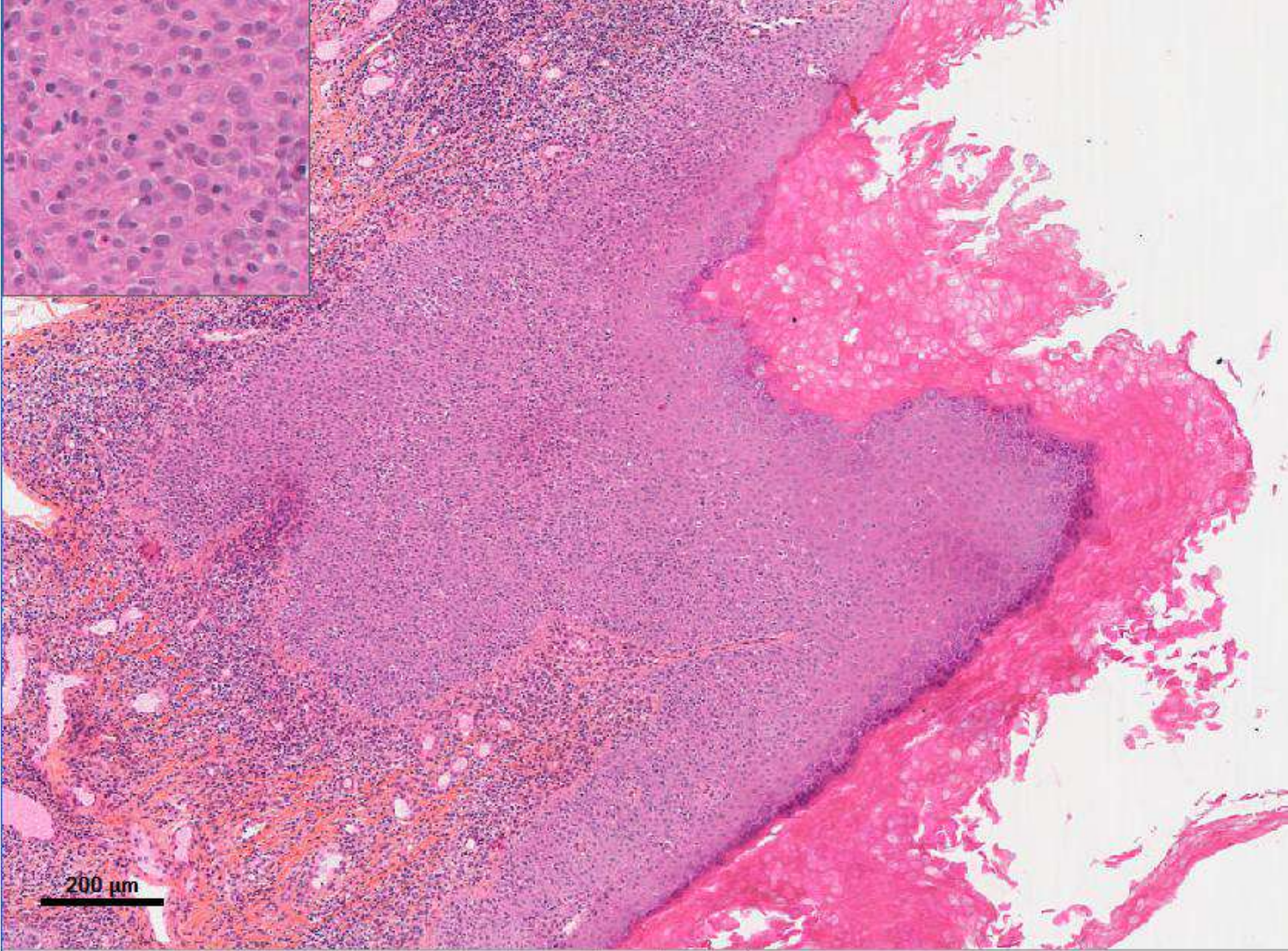
HG SIL = high-grade intraepithelial lesion

Case 1N

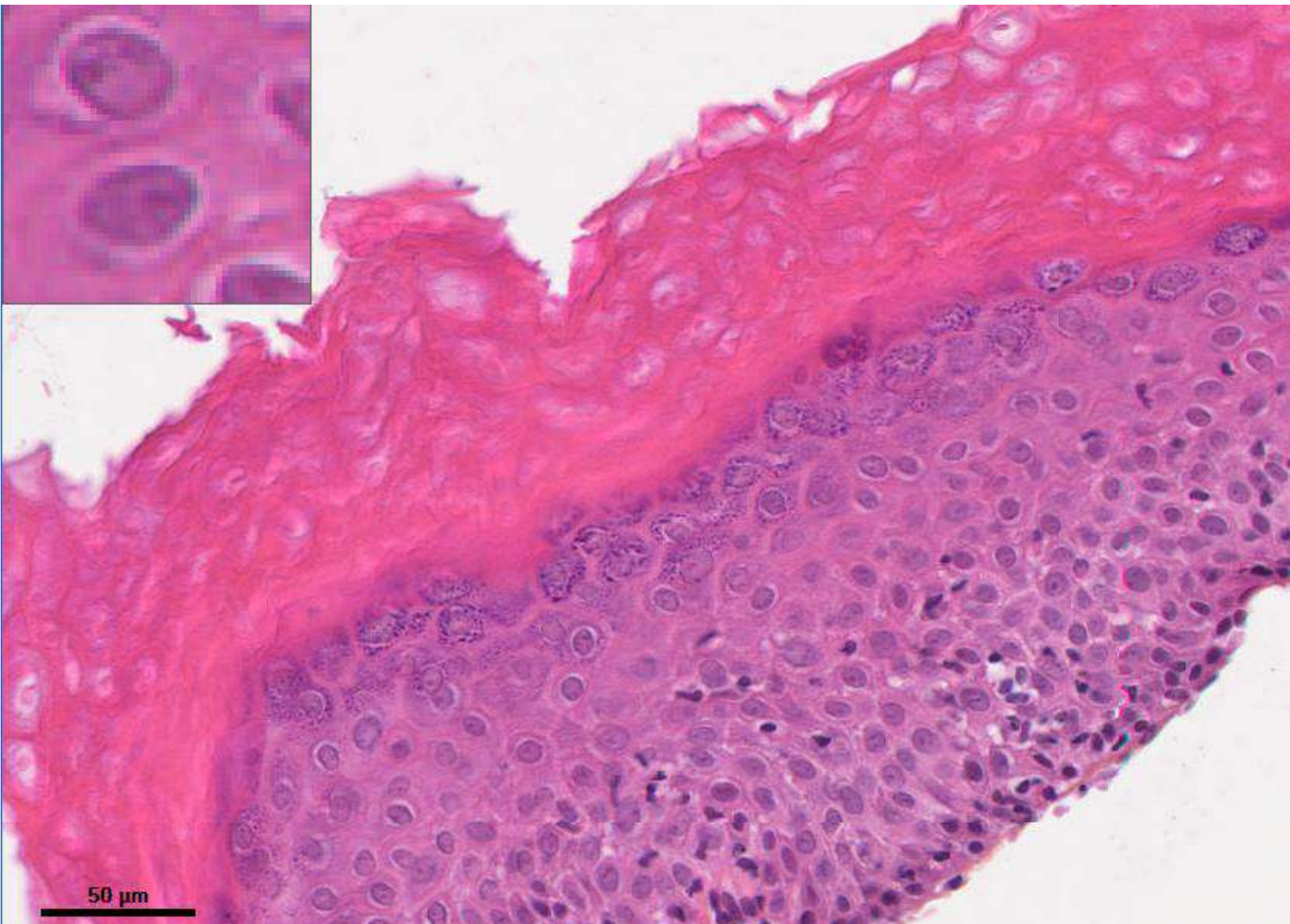
Woman 63 yo smoker oral cavity



800 μm

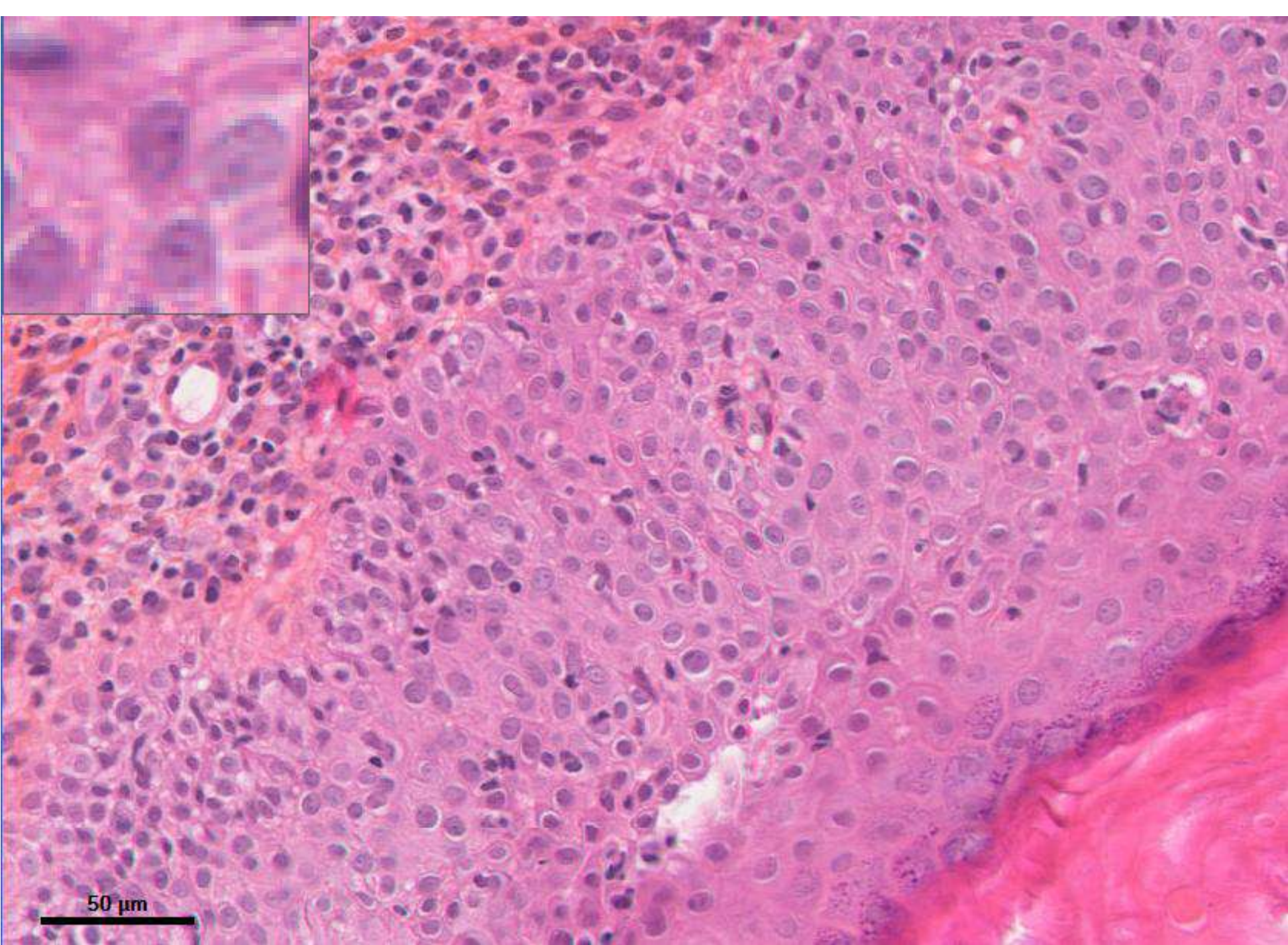


200 μ m



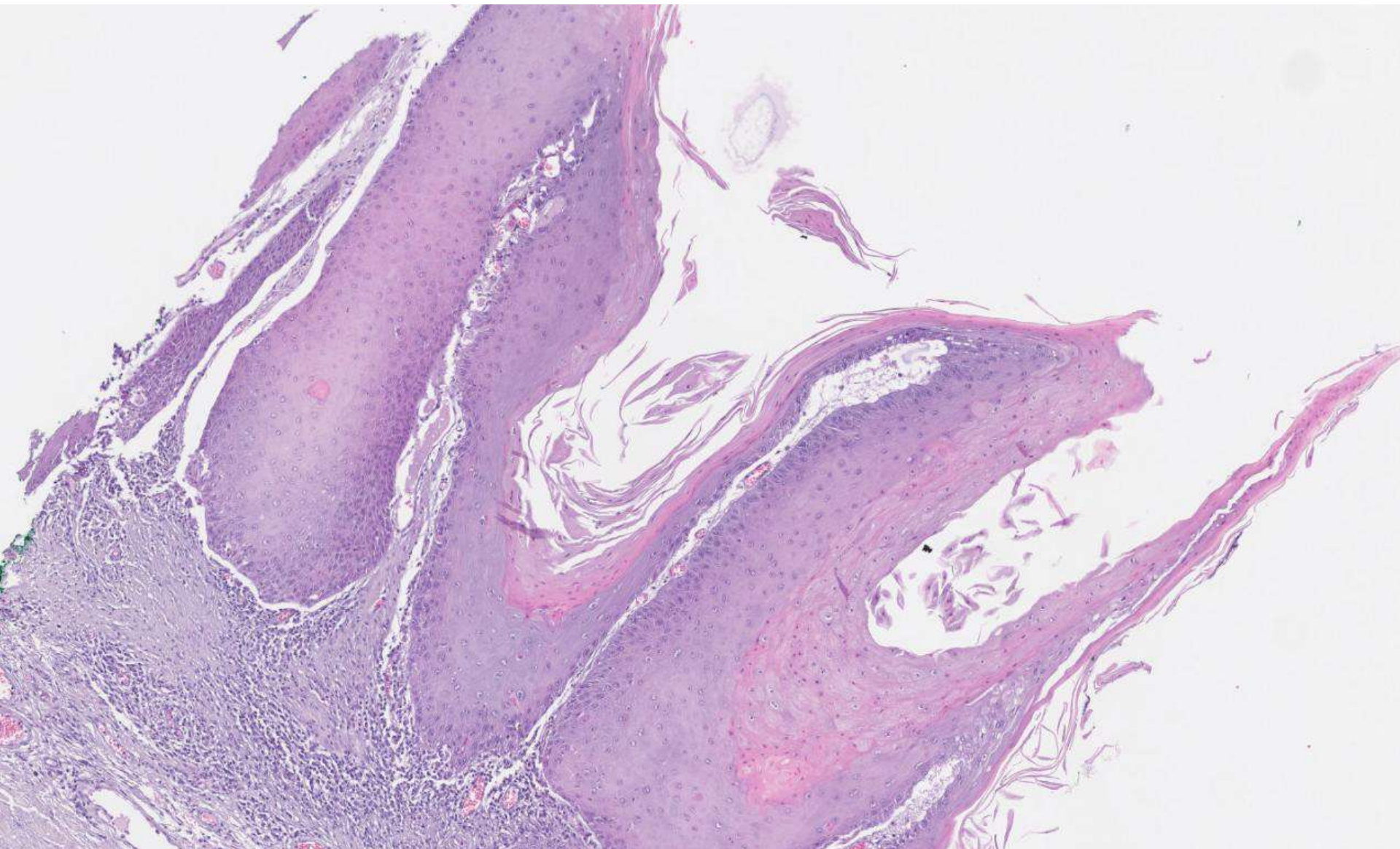
50 μ m

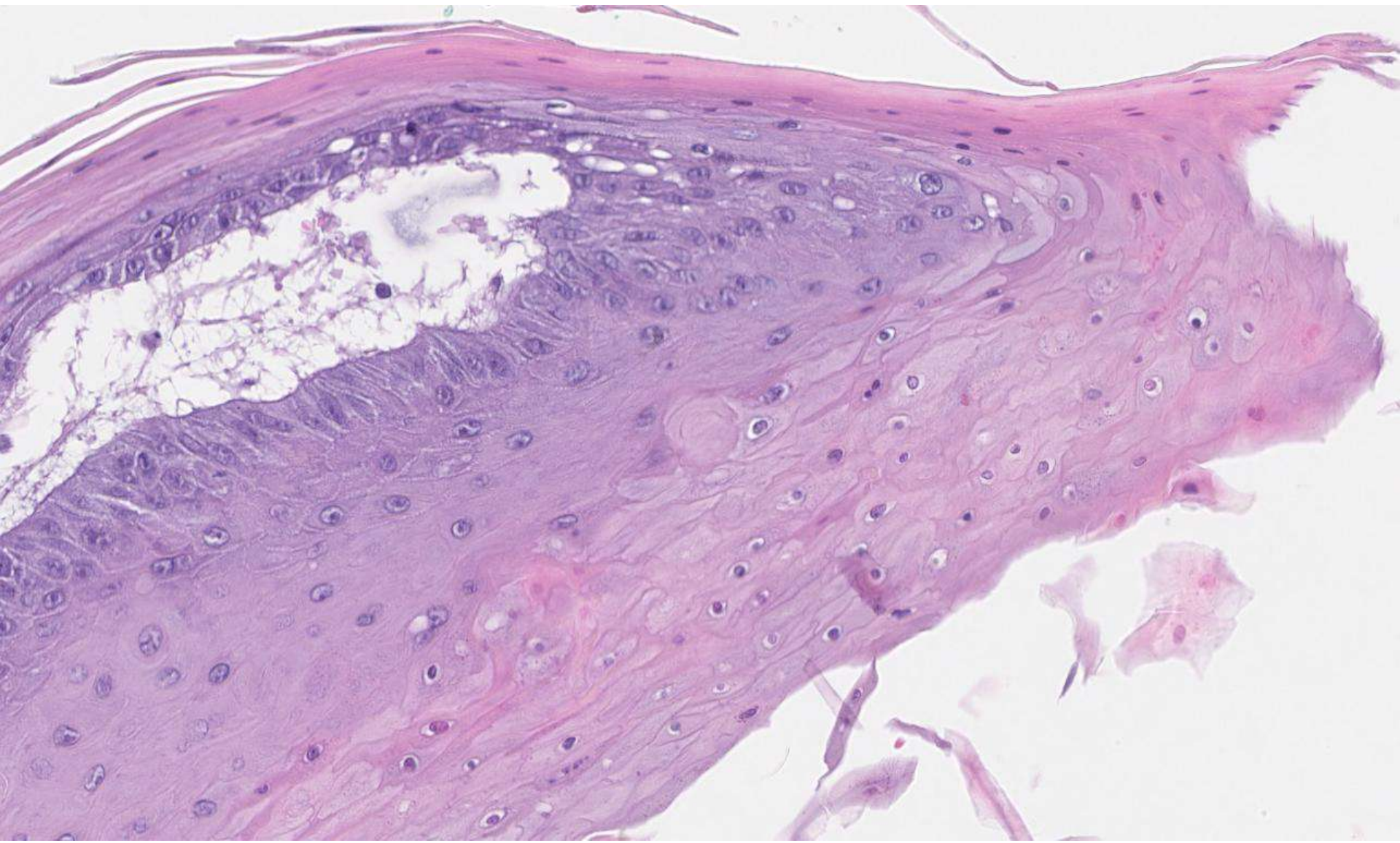


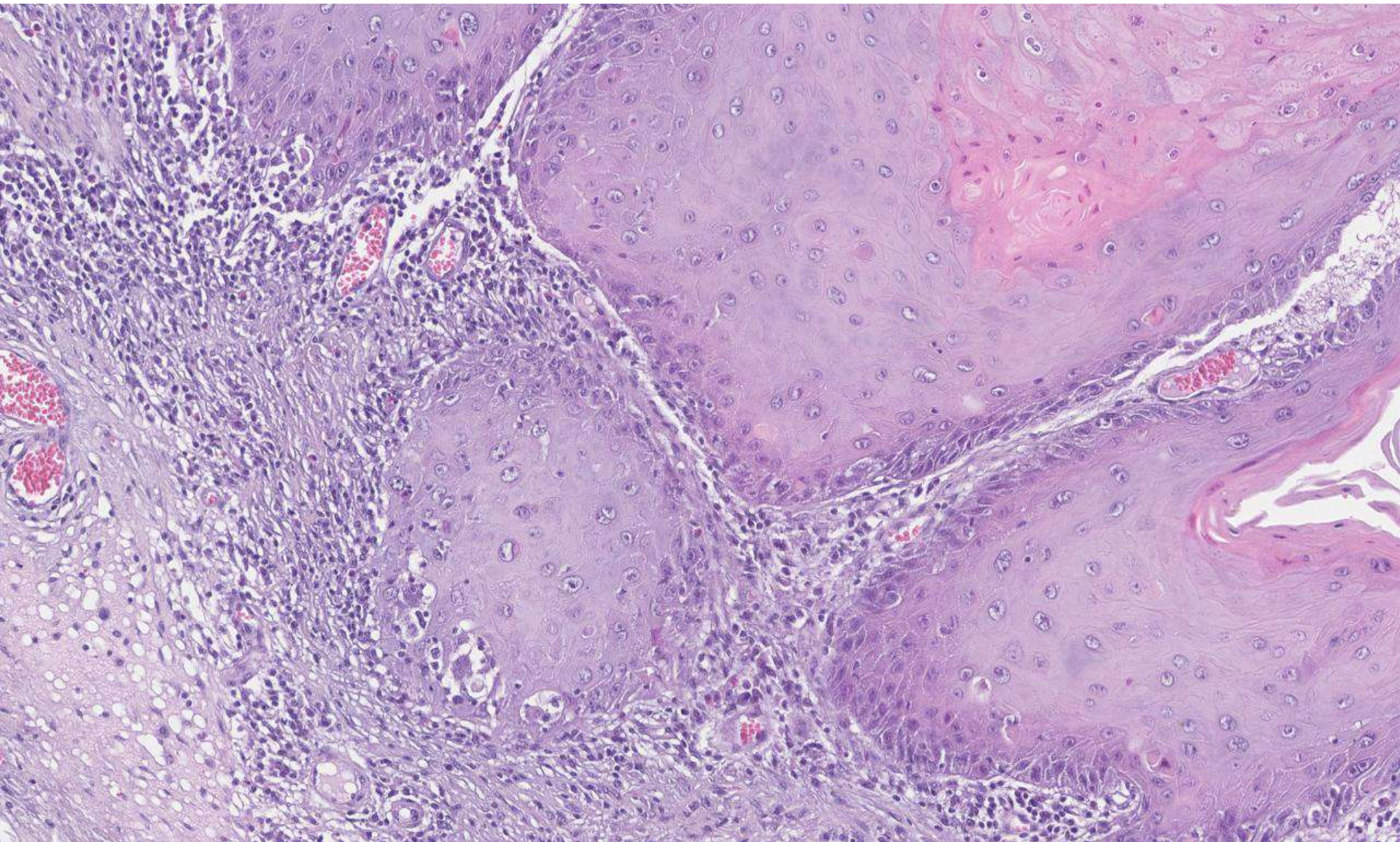


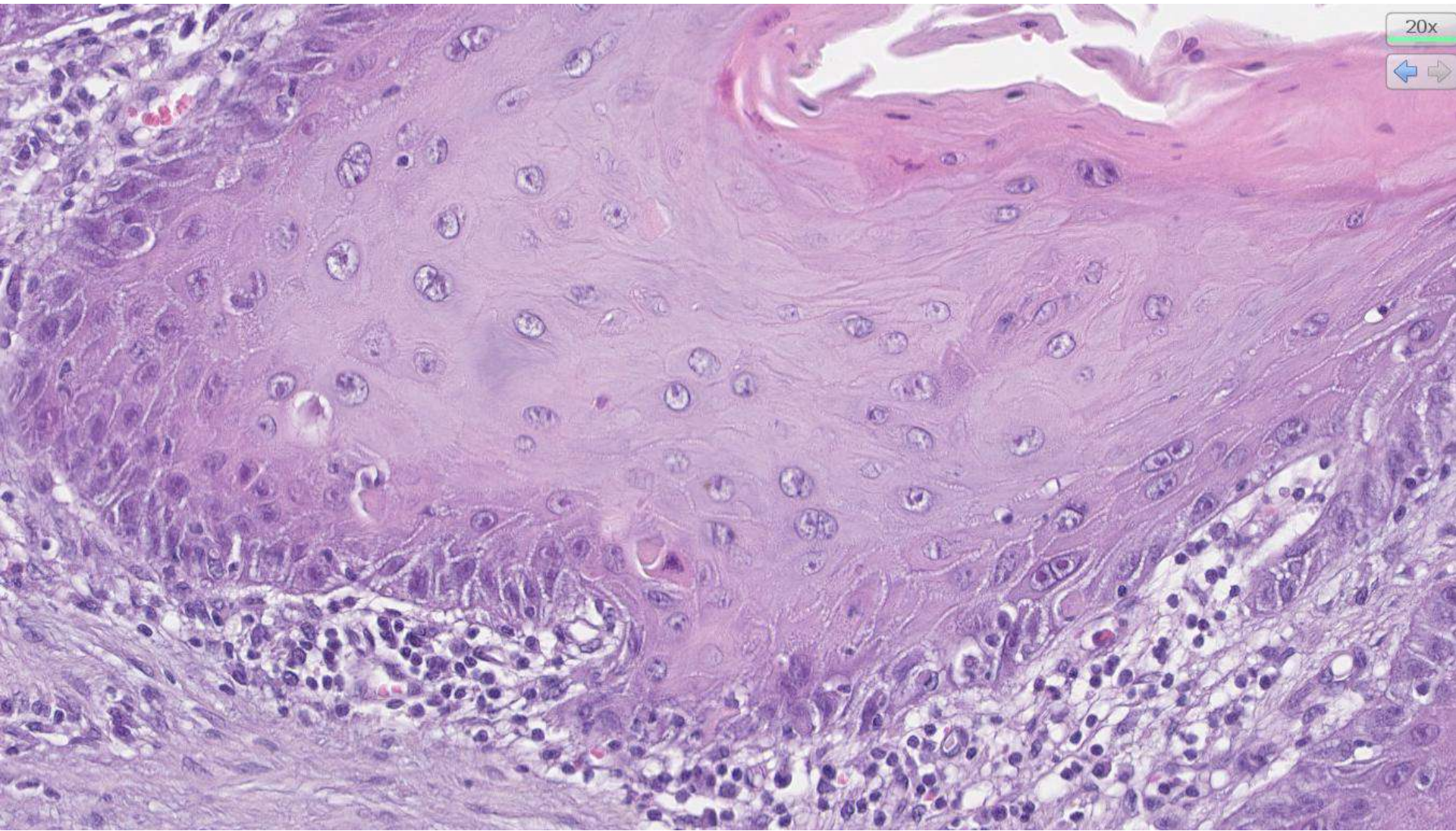
Case 1C
Man 61 yo











Verrucous carcinoma (Ackerman tumor, florid oral papillomatosis)

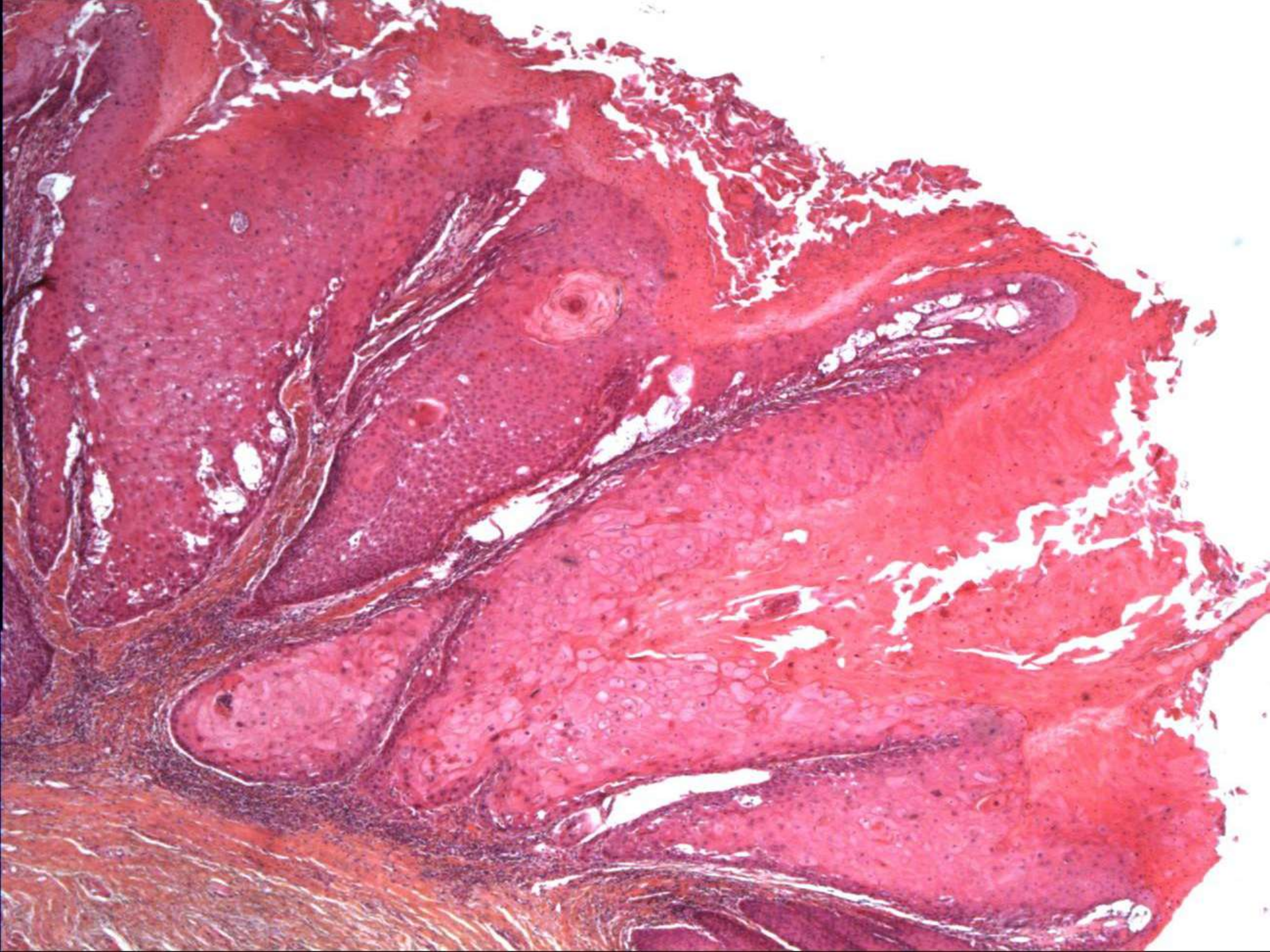
- Most often older man (70 yo), rare
- Very well differentiated squamous cell carcinoma with keratinisation without atypias.
- No “invasive” aspect but can be the origin of important local damage
- Oral cavity (15-35%) and larynx, mostly at the level of the true vocal cord (1-4%). Sometimes seen in the supraglottis, subglottis, trachea..
- Linked to tobacco smoking, no association with HPV

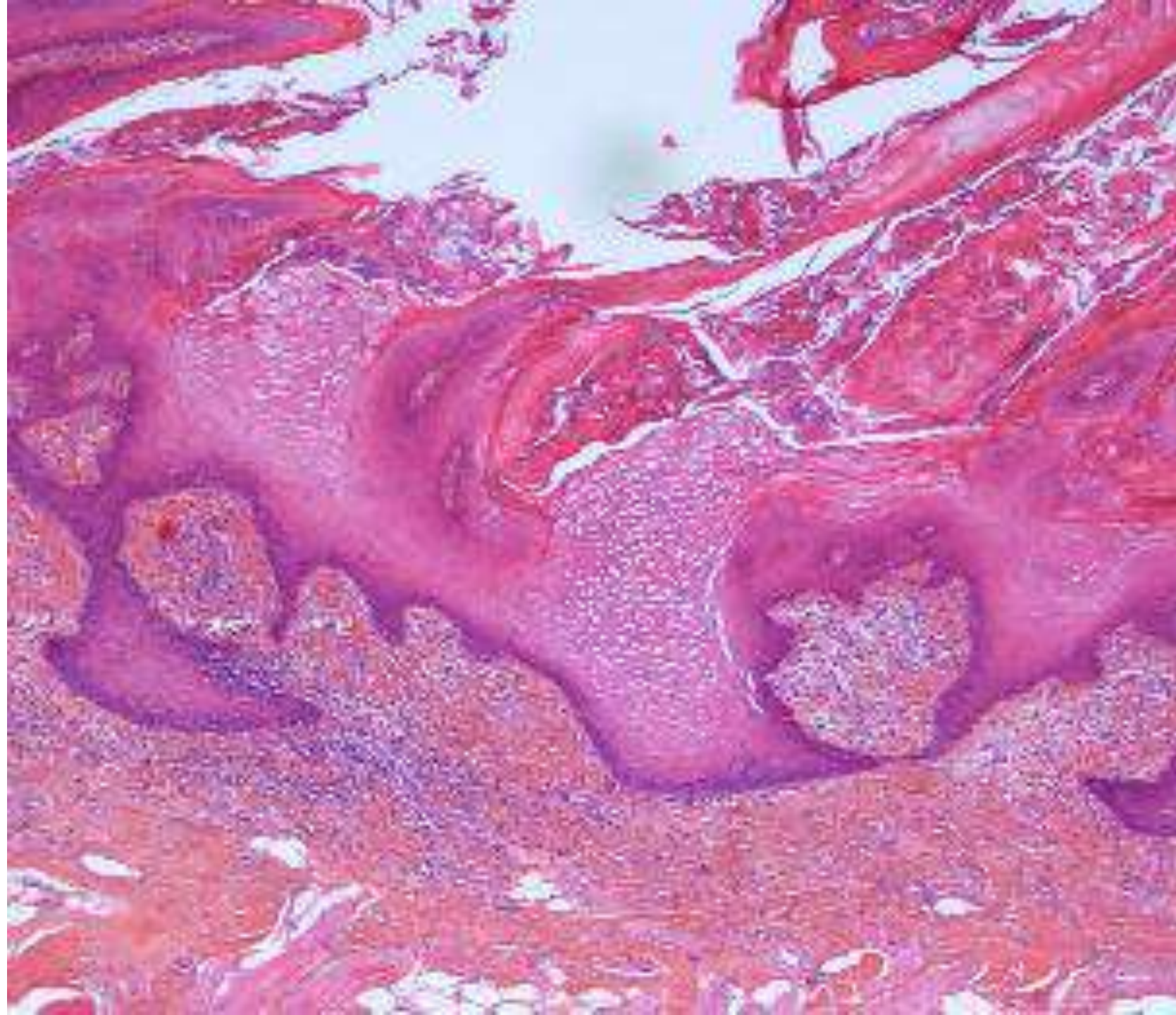
Verrucous carcinoma (Ackerman tumor, florid oral papillomatosis)

- Thickened, club-shaped projection and invaginations of well differentiated squamous epithelium.
- One or several basal layers. Rare mitosis, no abnormal mitosis.
- Invasion of the stroma with a well defined pushing border and invasion below the level of adjacent epithelium are usually difficult to be observed. **Be careful with the small biopsies**
- Lymphoplasmatic inflammation common
- Hybrid SCC/invasive SCC

Verrucous carcinoma (Ackerman tumor, florid oral papillomatosis)

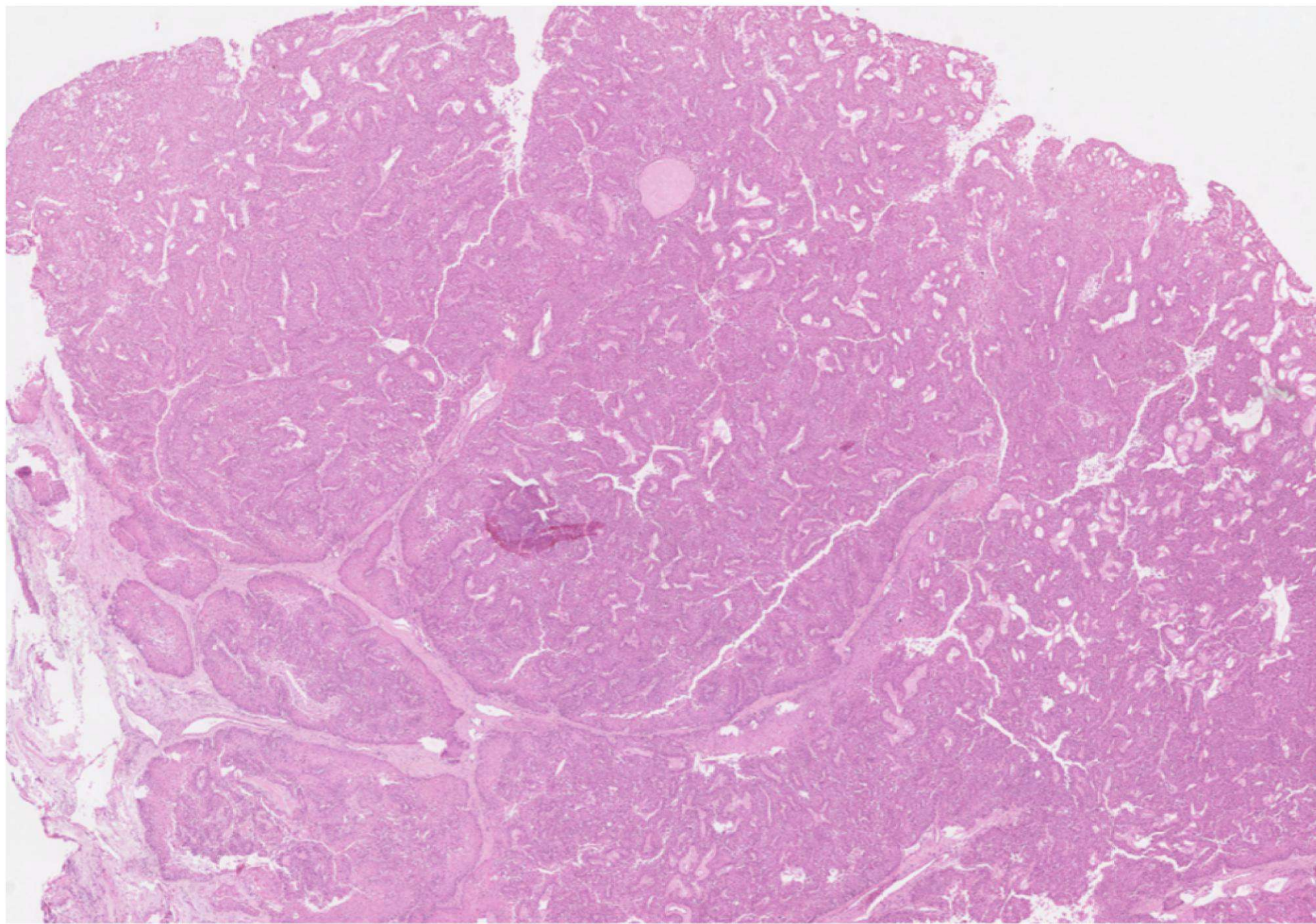
- No metastasis but possibility to transform in invasive SCC : conventional SCC with verrucous shape
- Numerous differential diagnosis : well differentiated squamous cell carcinoma , papillary SCC, warts, papilloma, inverted Schneiderian papilloma or atypical verrucous hyperplasia
- Surgery is the main treatment. Local control sometimes difficult
- Excellent prognosis if the surgery is complete. 5y survival rate >80%
- Radiotherapy is less recommended (transformation?)

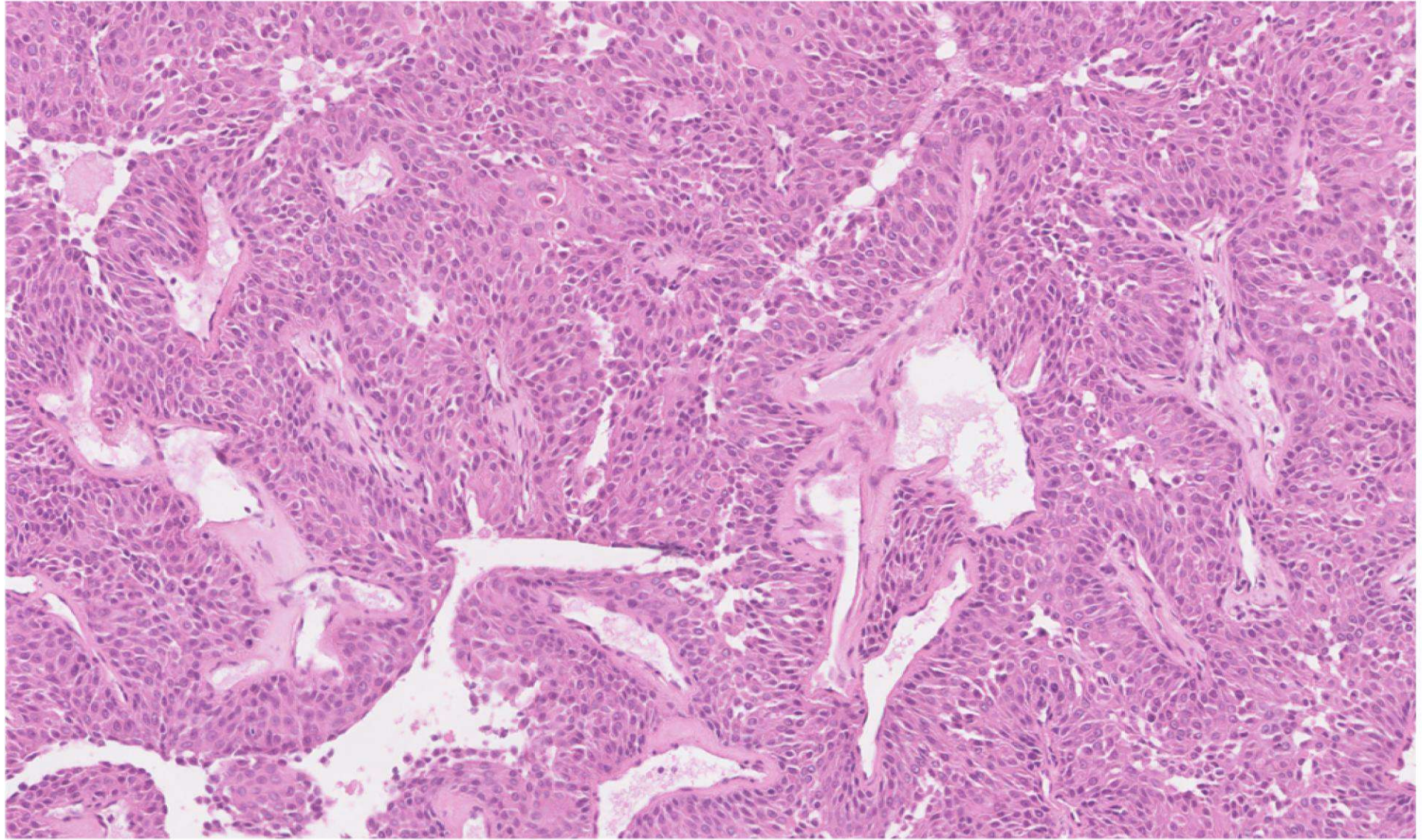




Case 1F

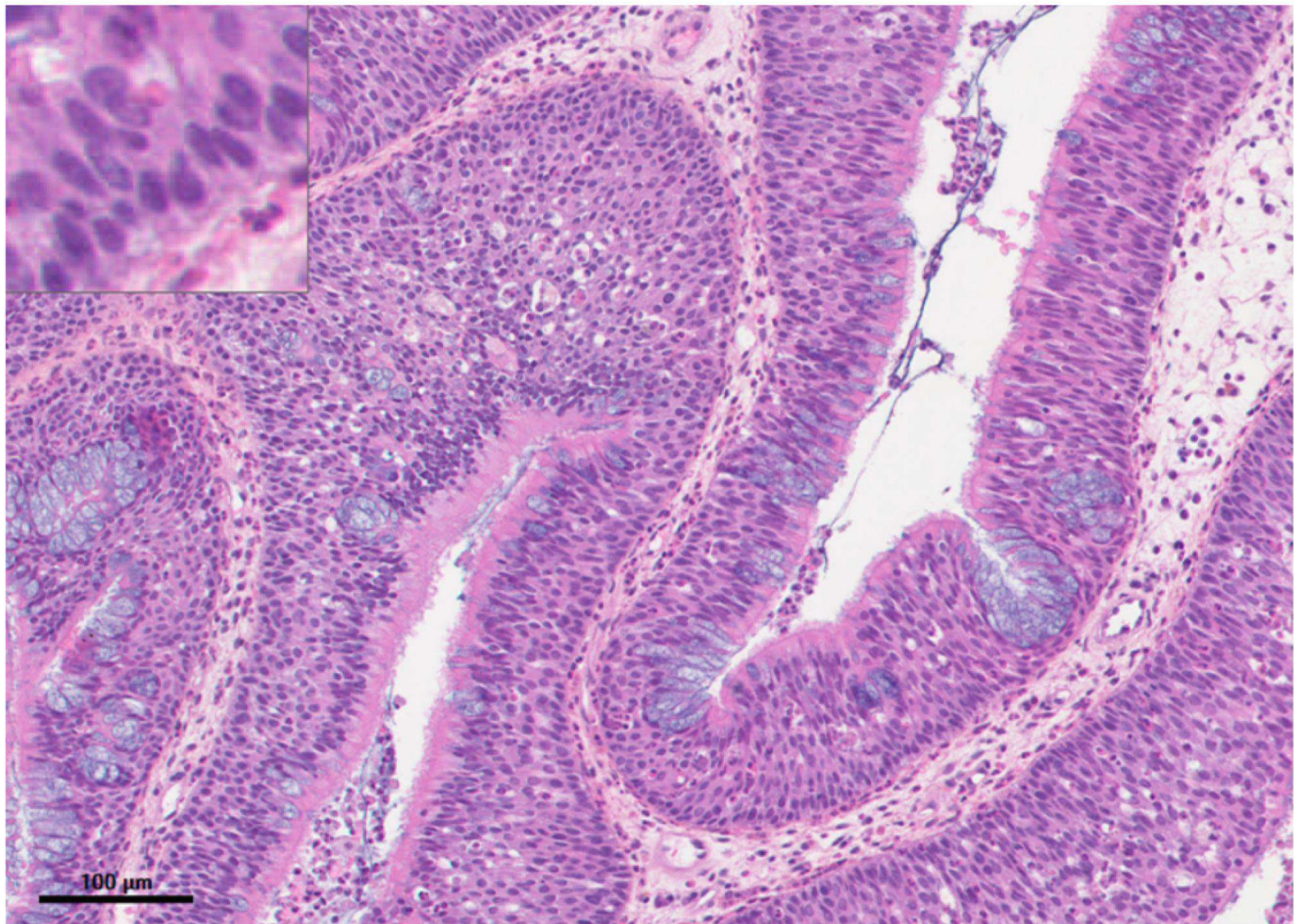
Homme 34 ans biopsies fosses
nasales

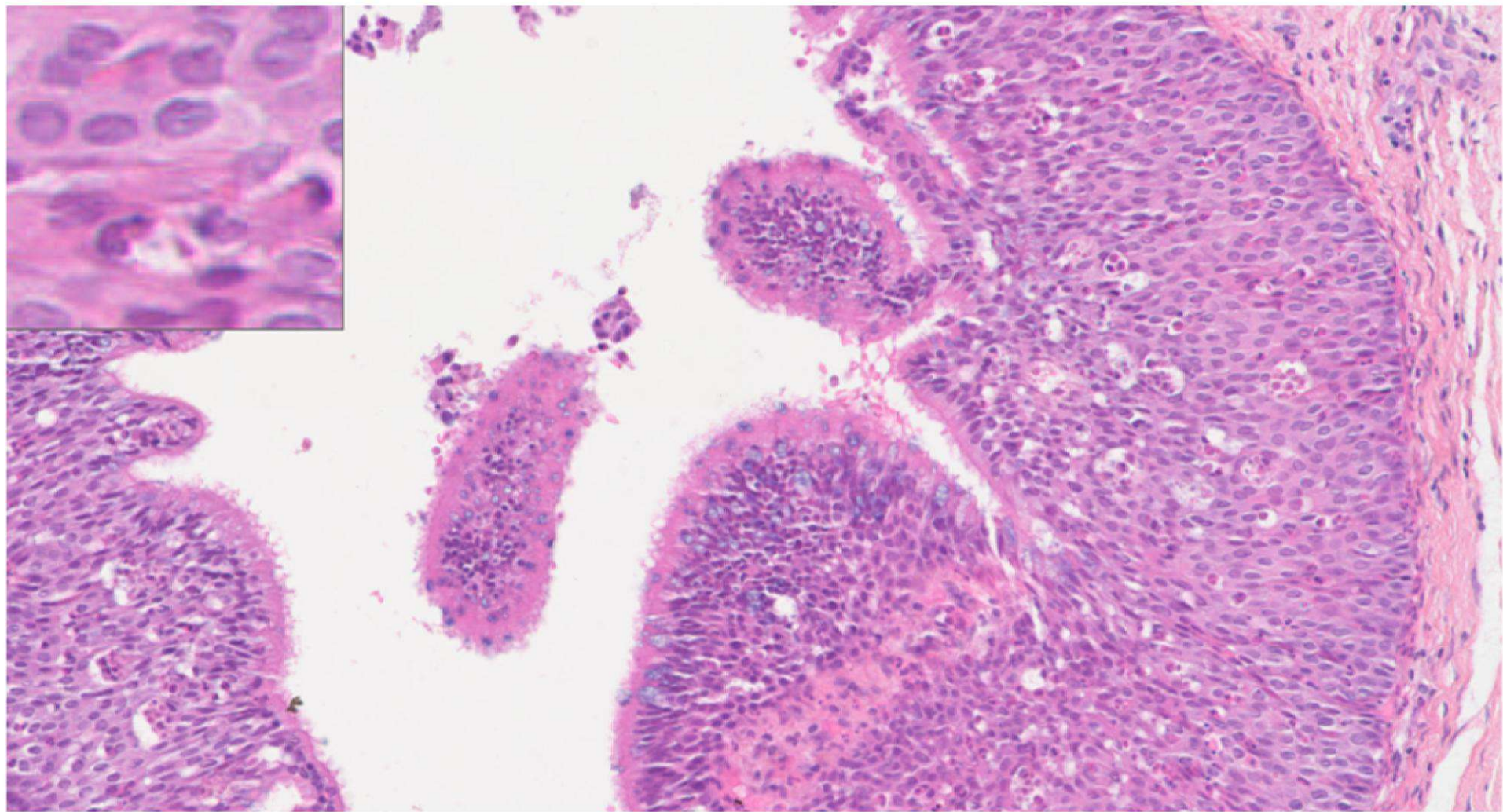


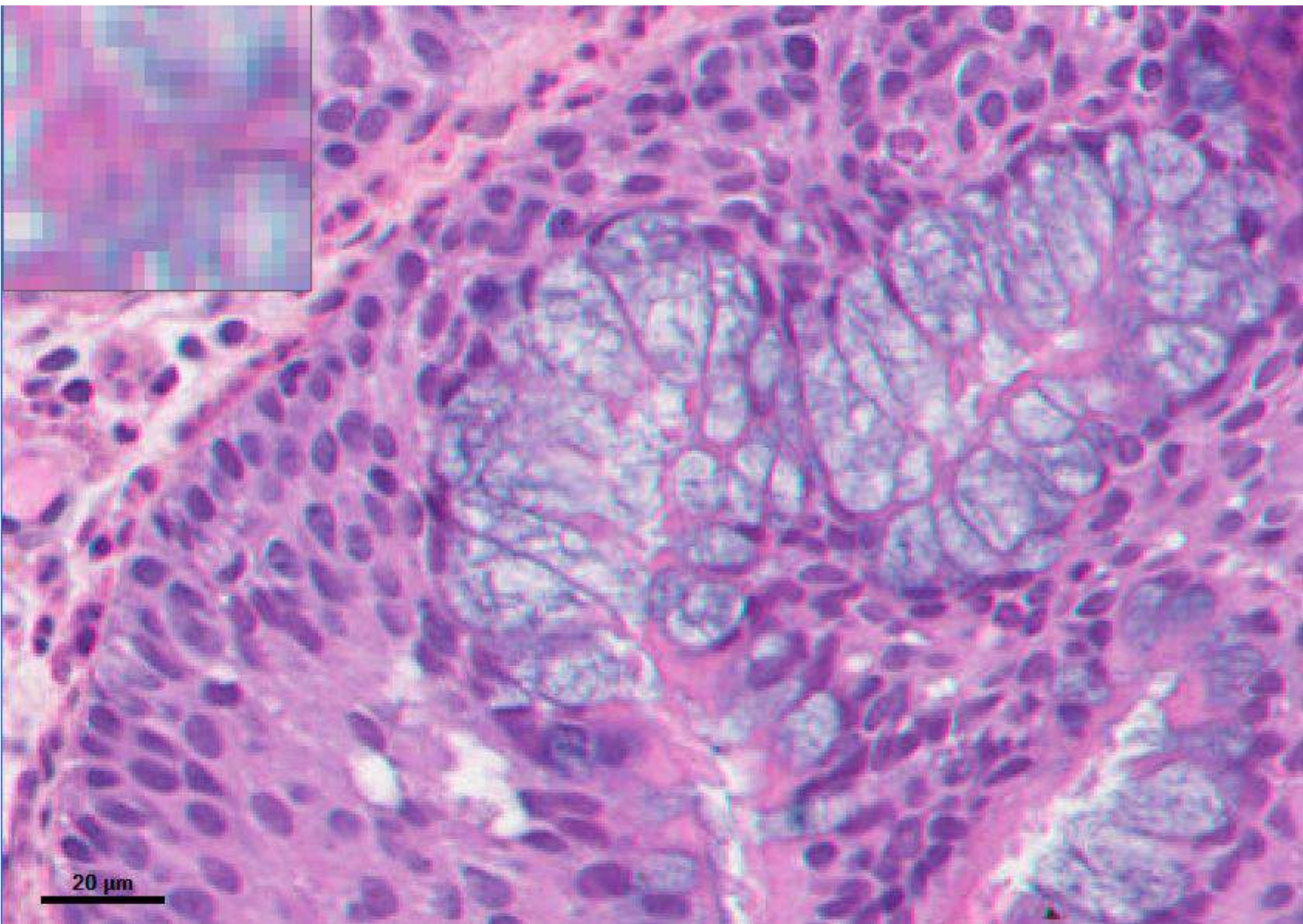


Case 1J

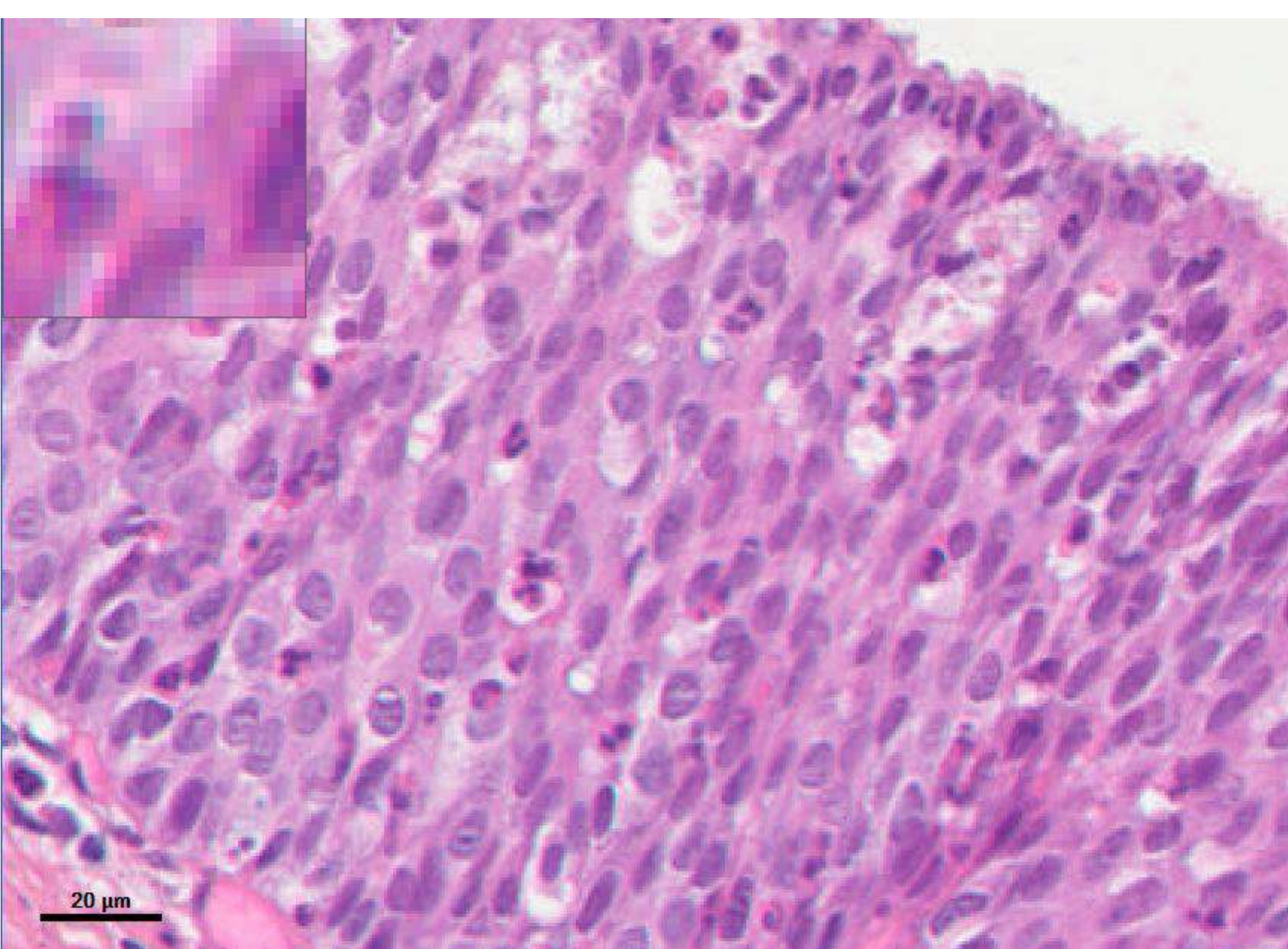
Man 54 yo sinus cavity biopsy







20 μ m



Sinonasal papilloma

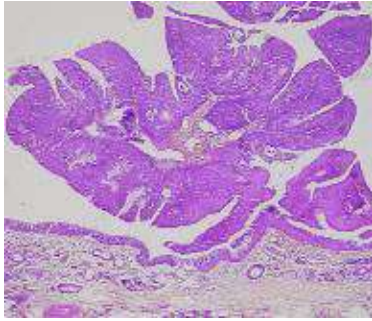

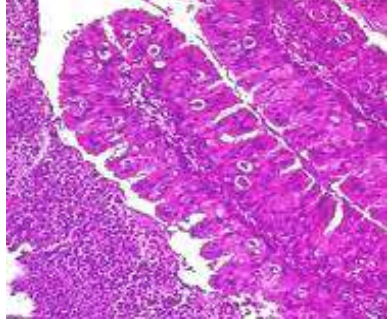
Squamous, transitional, mucinous, columnar

No grade for dysplasia

- **exophytic** Thin axillary, fibrous, recurrence 20%
- **inverted**: Multiple inversions of the surface epithelium into the underlying stroma edematous axes, exophytic papillary fringes and inverted aspects, "microabscess",
 - recurrence 30%
 - Association/transformation carcinoma (SCC, mucoepidermoid, adenocarcinoma or SNUC)
- **oncocytic** : rare, same architecture, mucous microcysts and "microabscess"
 - recurrence 40%.
 - Association with carcinoma (SCC, mucoepidermoid, adenok or SNUC)

Sinonasal papilloma

- Developed at the expense of the respiratory type epithelium, they represent 0.4 to 4.7% of nasosinus tumors.
- 2 to 5H / 1F, with a peak around 50 years old. Three histological types are described:

	Exophytique: 32%	Inverted: 62%	Oncocytic: 6%
HPV role	Perhaps important	discussed	no
Localisation	Anterior nasal septum	Nasal cavity and maxillary sinus	paroi latérale nasale
transformation	exceptional	11-15% (1,9-27)	4 à 17%
			

- For all the cases, **recurrence is the main evolution risk (30%)**

Sinonasal inverted papilloma: From diagnosis to treatment



Q. Lisan, O. Laccourreye, P. Bonfils*

Service d'ORL et de Chirurgie Cervico-Faciale, Hôpital Européen Georges Pompidou, Faculté de Médecine Paris Descartes, Université Paris V, 20 Rue Leblanc, 75015 Paris, France

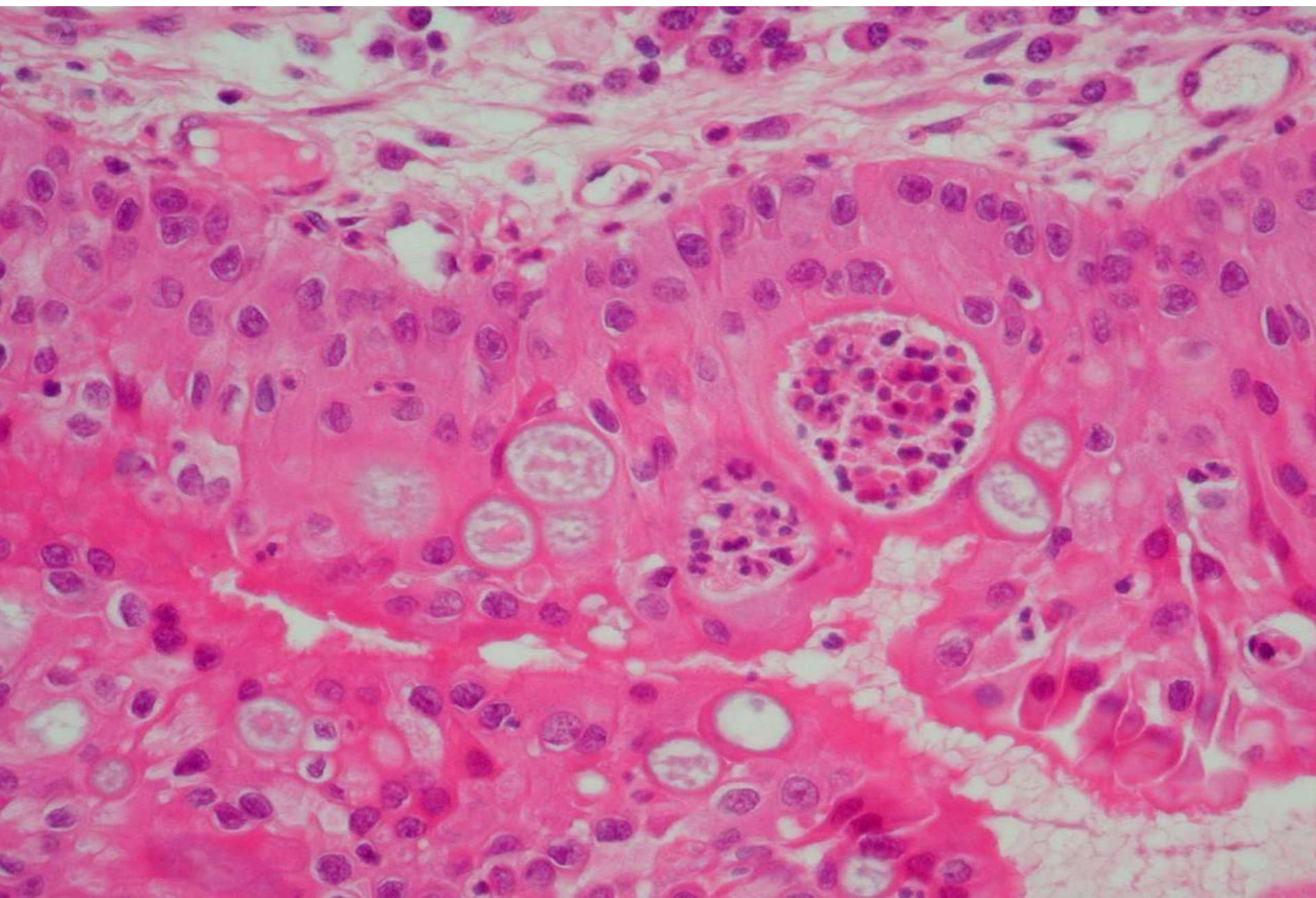
Table 1
Krouse classification, from [28].

Krouse staging system for inverted papilloma	
T1	Tumor totally confined to the nasal cavity, without extension into the sinuses. There must be no concurrent malignancy.
T2	Tumor involving the ostiomeatal complex, and ethmoid sinuses, and/or the medial portion of the maxillary sinus, with or without involvement of the nasal cavity. There must be no concurrent malignancy.
T3	Tumor involving the lateral, inferior, superior, anterior, or posterior walls of the maxillary sinus, the sphenoid sinus, and/or the frontal sinus, with or without involvement of the medial portion of the maxillary sinus, the ethmoid sinuses, or the nasal cavity. There must be no concurrent malignancy.
T4	All tumors with any extranasal/extrasinus extension to involve adjacent, contiguous structures such as the orbit, the intracranial compartment or the pterygomaxillary space. All tumors associated with malignancy.

Table 2
Surgical approach according to tumor extension, following [4,12–15,29,31–34,36].

Involvement	Suggested surgical approach
Septum Lateral wall of nasal cavity Anterior or posterior ethmoid Sphenoethmoid and sphenoid spaces Maxillary sinus (medial, superior or posterior wall) Frontal space and frontal sinus (limited medial involvement)	Endonasal endoscopic
Lateral wall of frontal sinus	Endonasal endoscopic + frontal osteoplastic flap (e.g., bicoronal approach)
Maxillary sinus (anterior, inferior or lateral wall)	Endonasal endoscopic + Caldwell-Luc approach
Extranasus extension Associated carcinoma	External (e.g., paralateronasal approach)





ORIGINAL PAPER

Transcriptionally Active High-Risk Human Papillomavirus is Not a Common Etiologic Agent in the Malignant Transformation of Inverted Schneiderian Papillomas

Lisa M. Rooper¹ · Justin A. Bishop^{1,2} · William H. Westra^{1,2,3} 

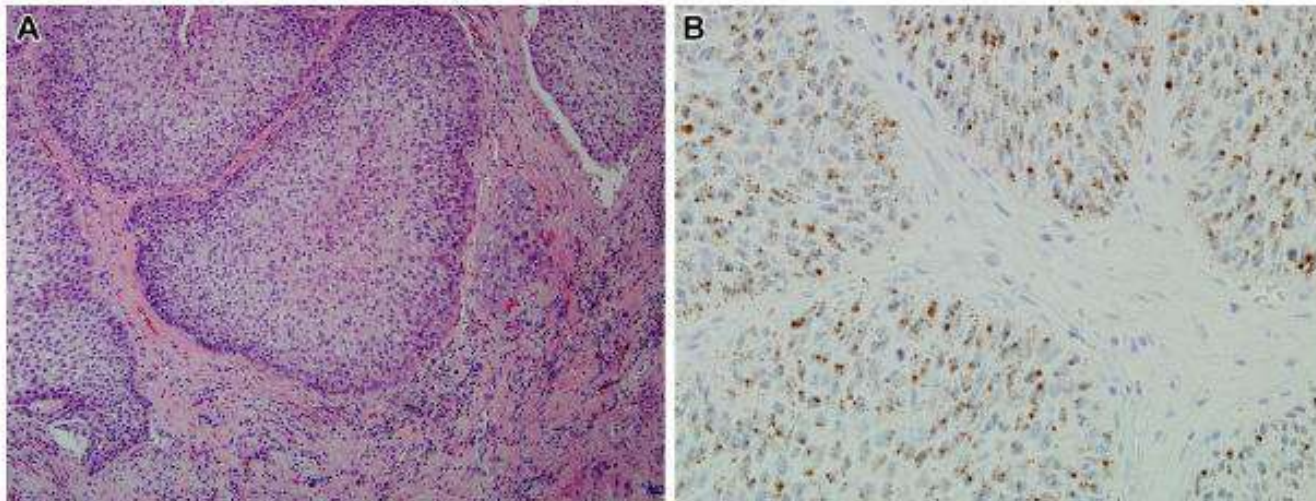


Fig. 3 Non-keratinizing SCC of the sinonasal tract with inverted growth characterized by lobules of tumor cells with smooth and rounded borders (a). Despite some morphologic similarities to inverted Schneiderian papilloma, a synchronous or metachronous

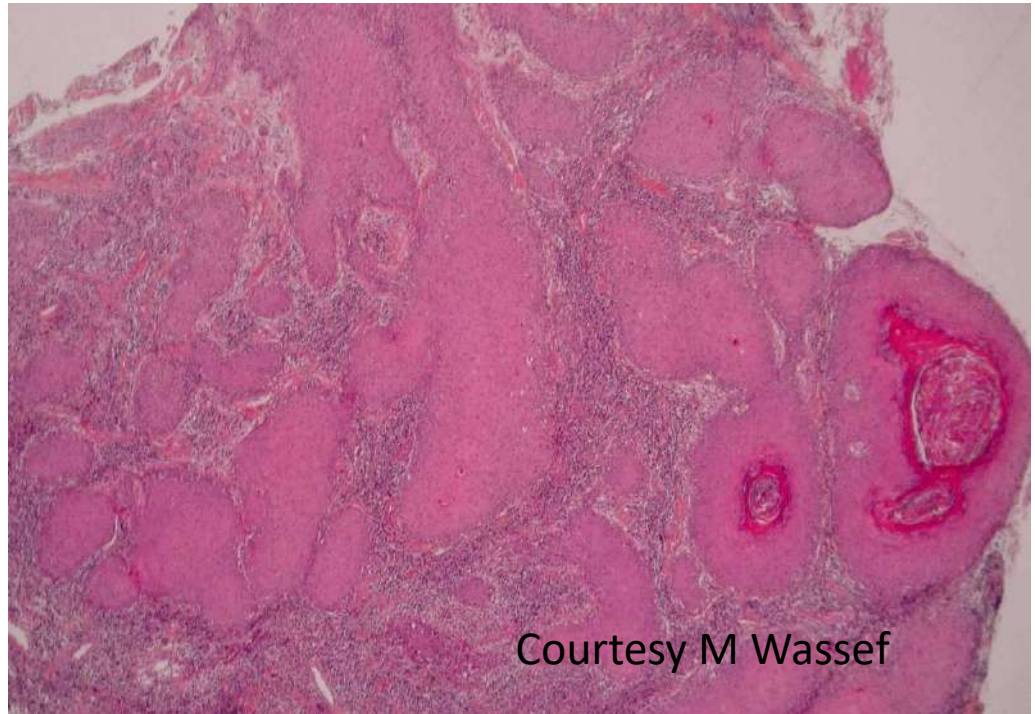
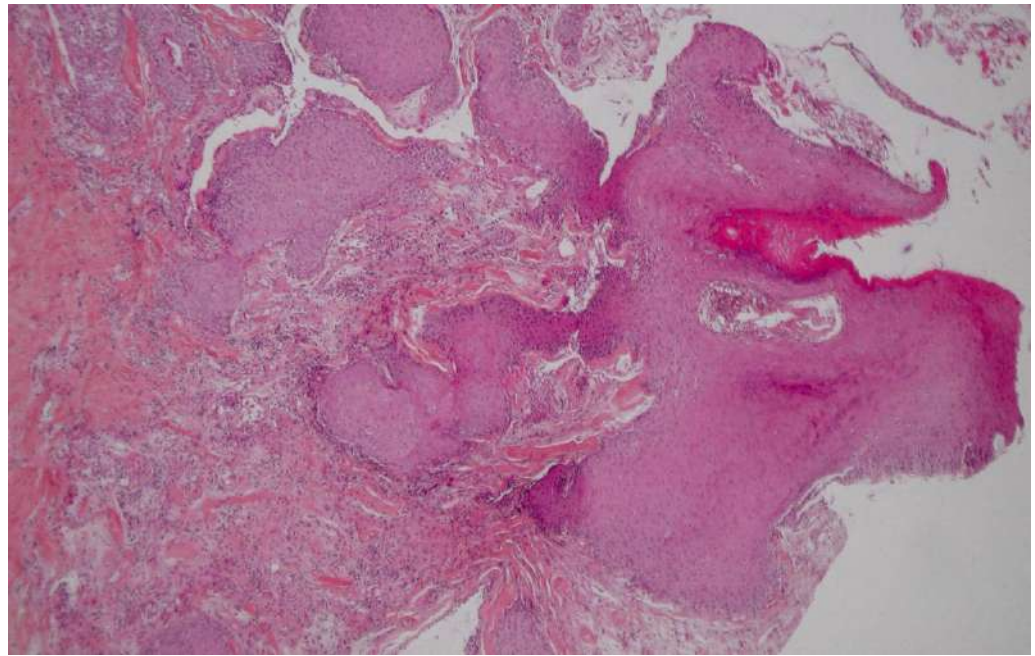
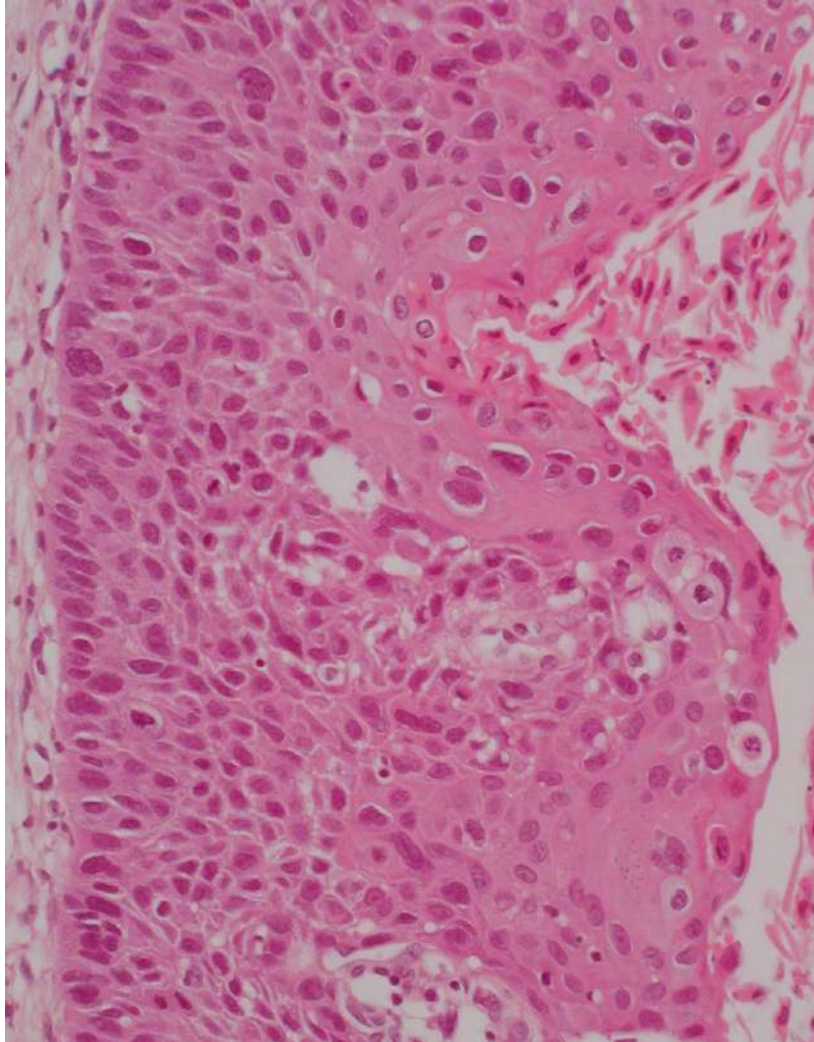
benign papilloma could not be histologically documented. Unlike the cases of Schneiderian papilloma with or without evidence of carcinomatous transformation, this carcinoma was positive for high-risk HPV (b) (high-risk HPV RNA in situ hybridization)

Be careful! Sometimes truly SCC can have “inverted sinonasal papilloma” shape

Sinonasal papilloma inverted type

- Most common form of sinonasal papillomas (schneiderian)
- Differential diagnosis: epithelial respiratory adenomatoid hamartoma
- Evolution:
 - recurrence in about 20-30%
 - Sampling ++ (inclusion if possible) due to possibility of transformation in transitional carcinoma or squamous cell carcinoma (10%)
- Role of HPV to be defined

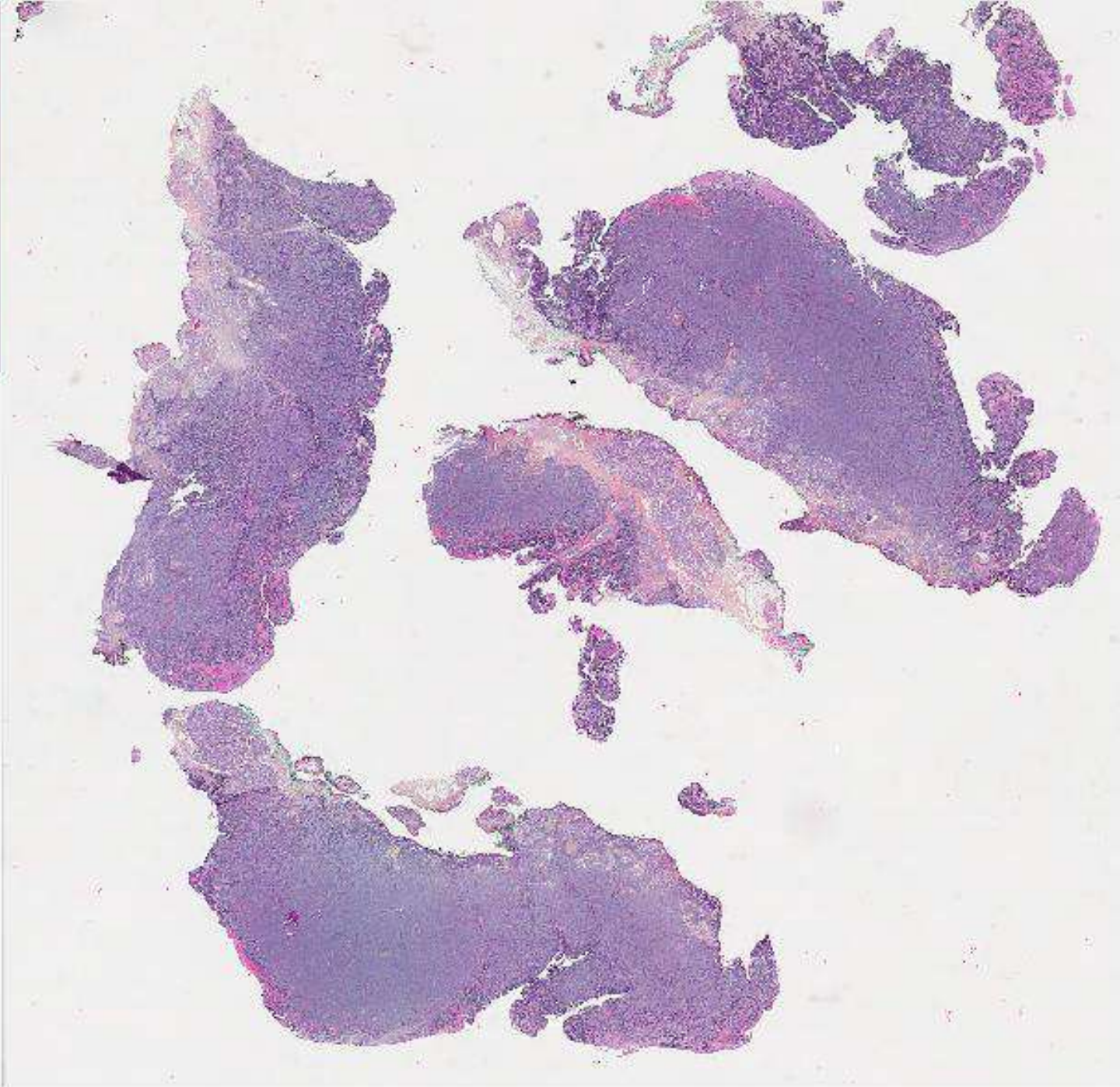
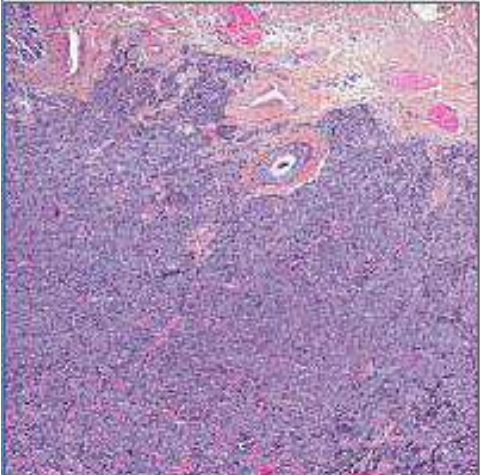
Transformed inverted papilloma.



Courtesy M Wassef

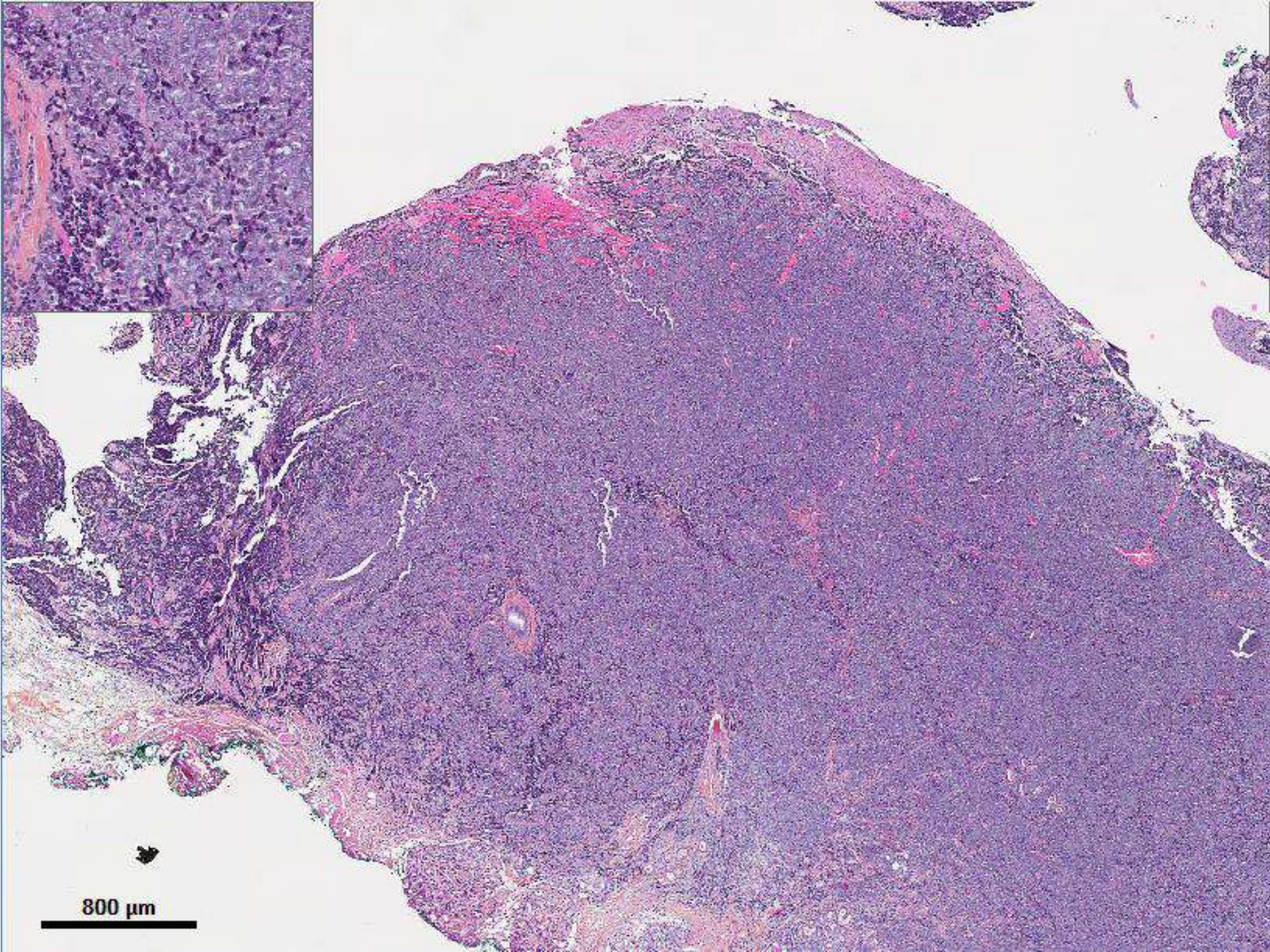
Case 1K

Man 51 yo nasal cavity lesion

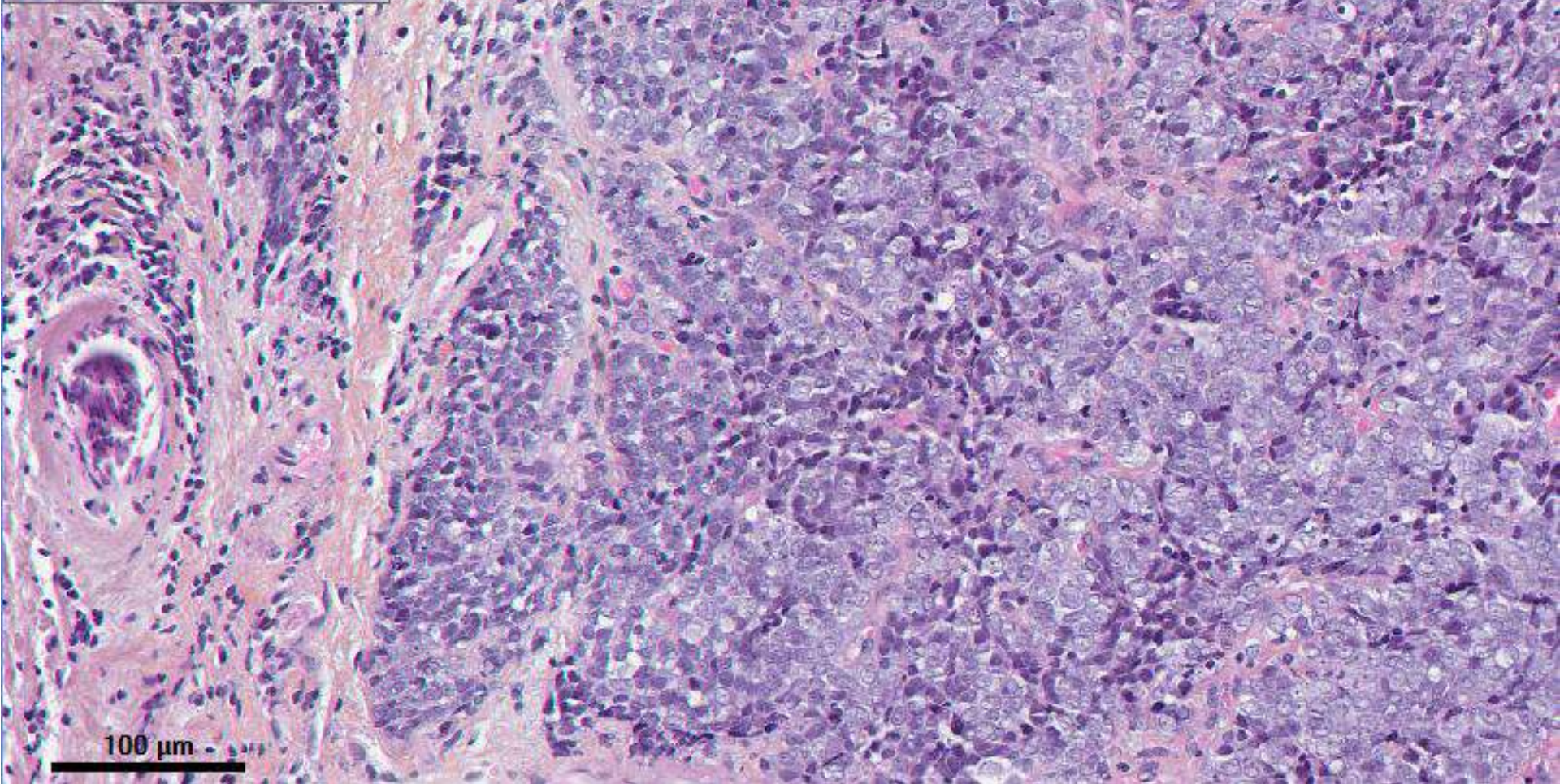
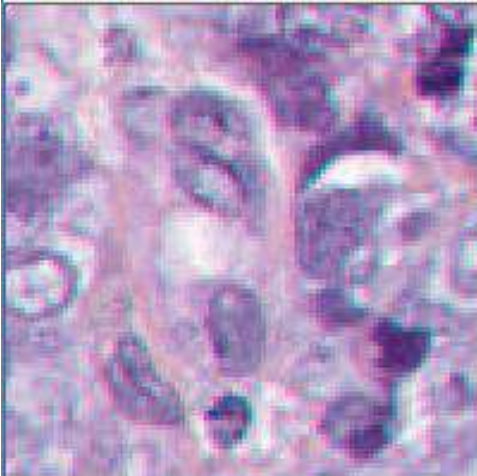


3 mm

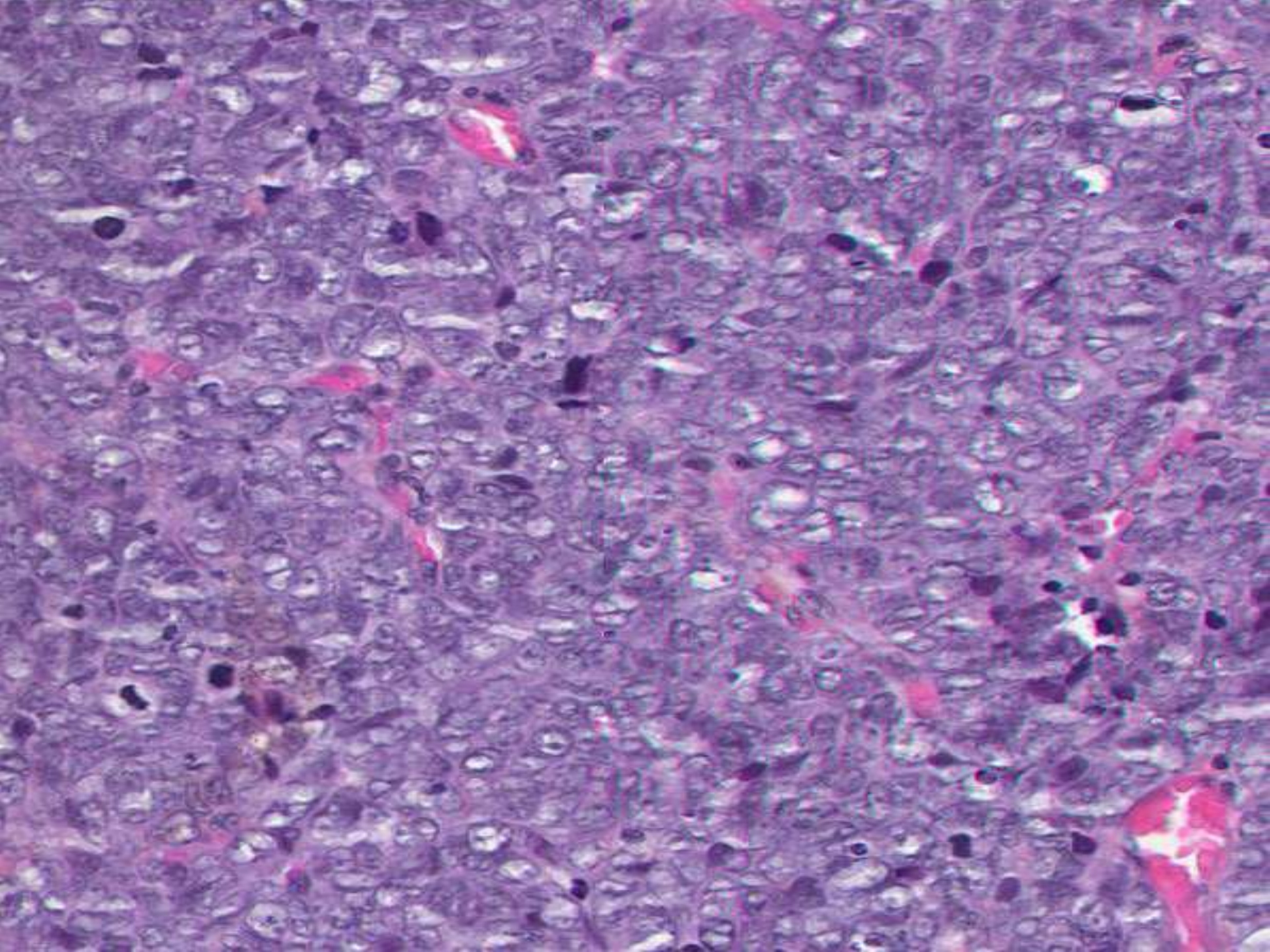


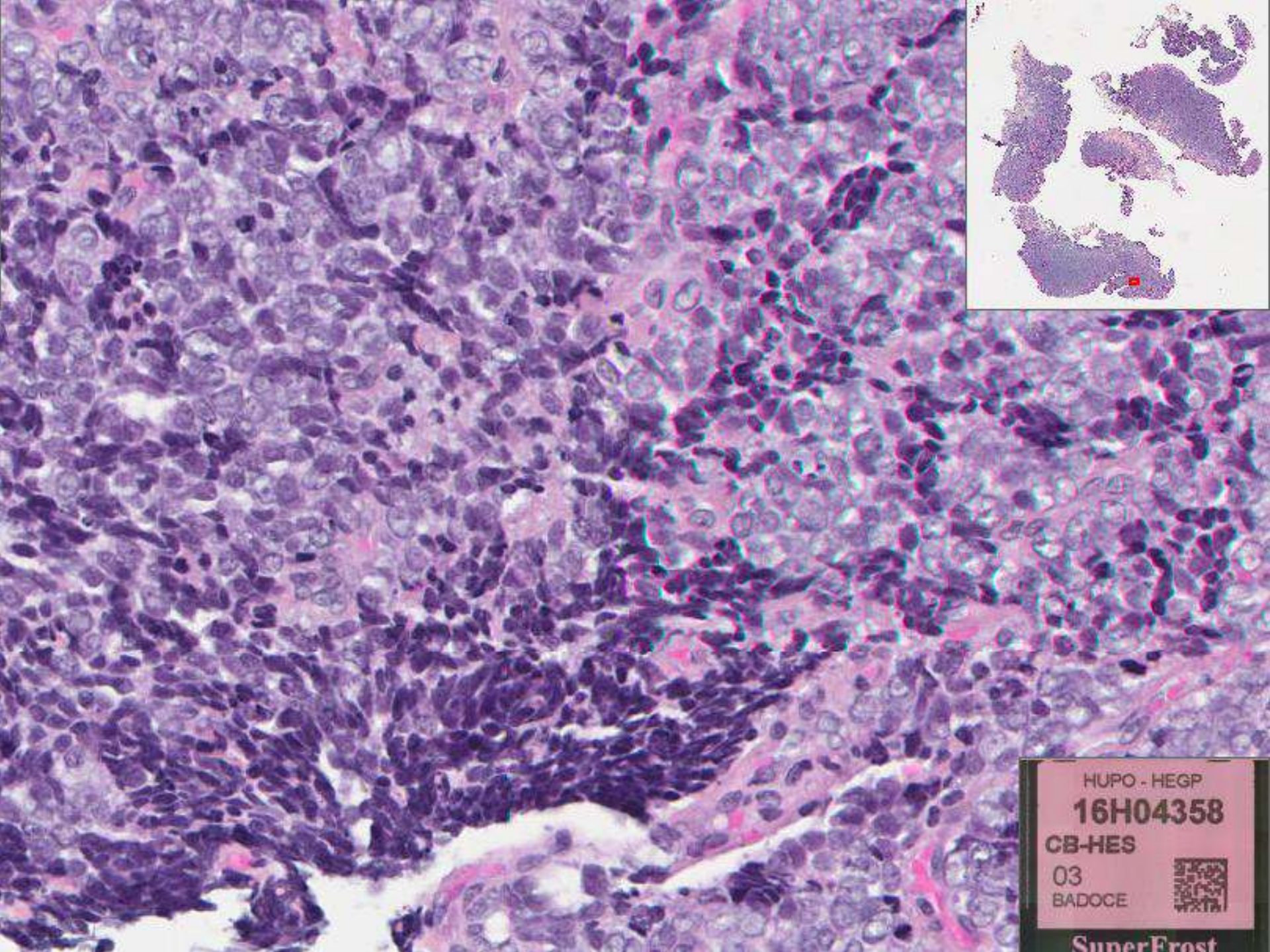


800 μm



100 μm





HUPO - HEGP

16H04358

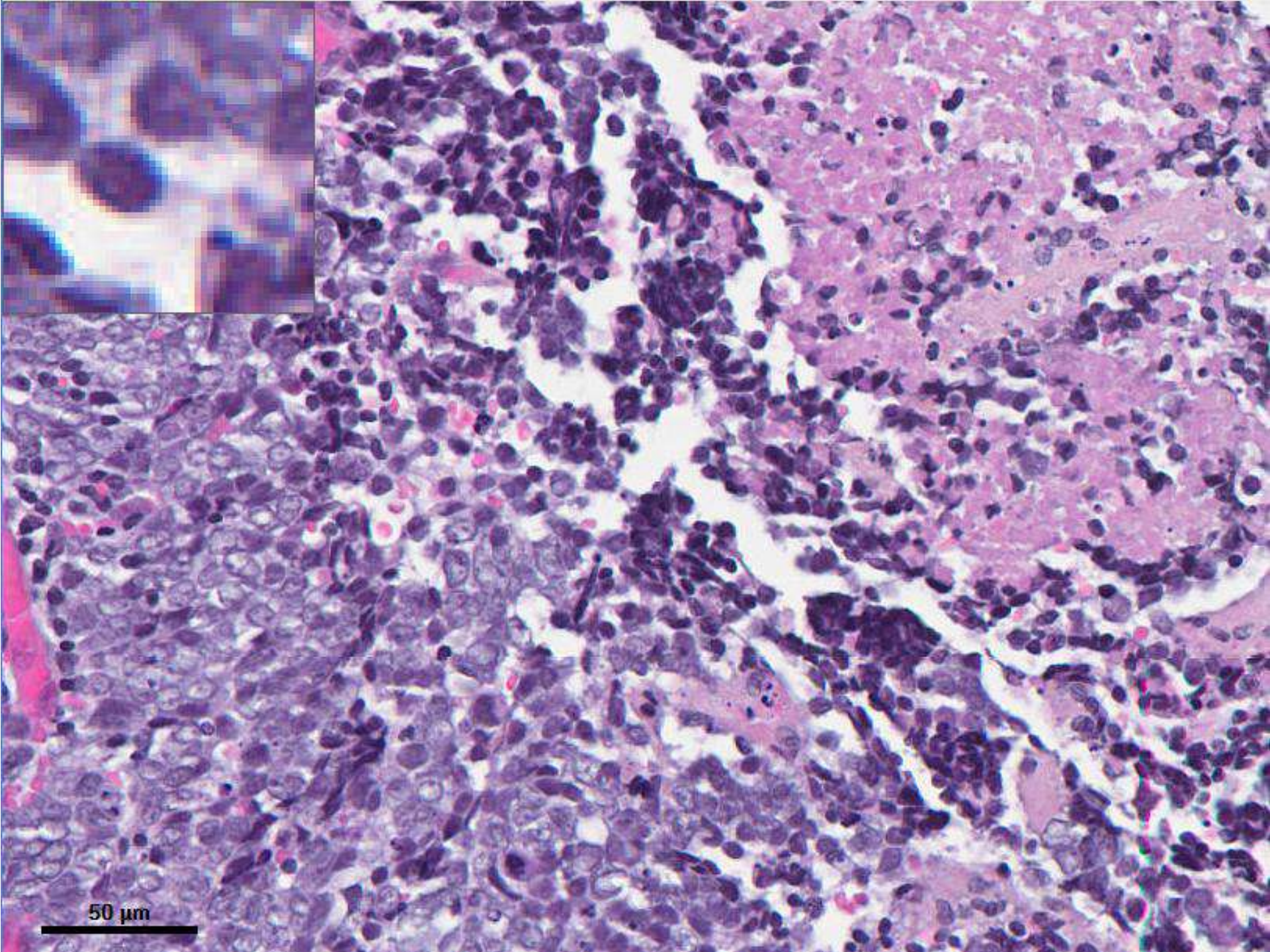
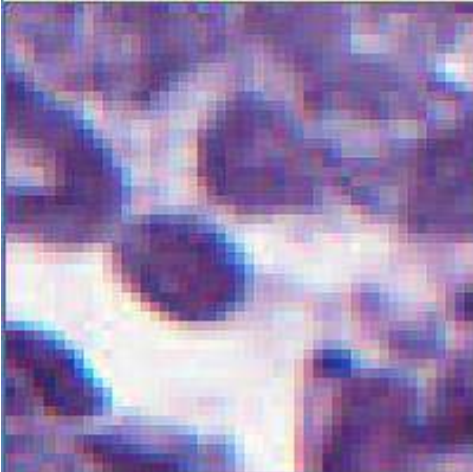
CB-HES

03

BADOCE



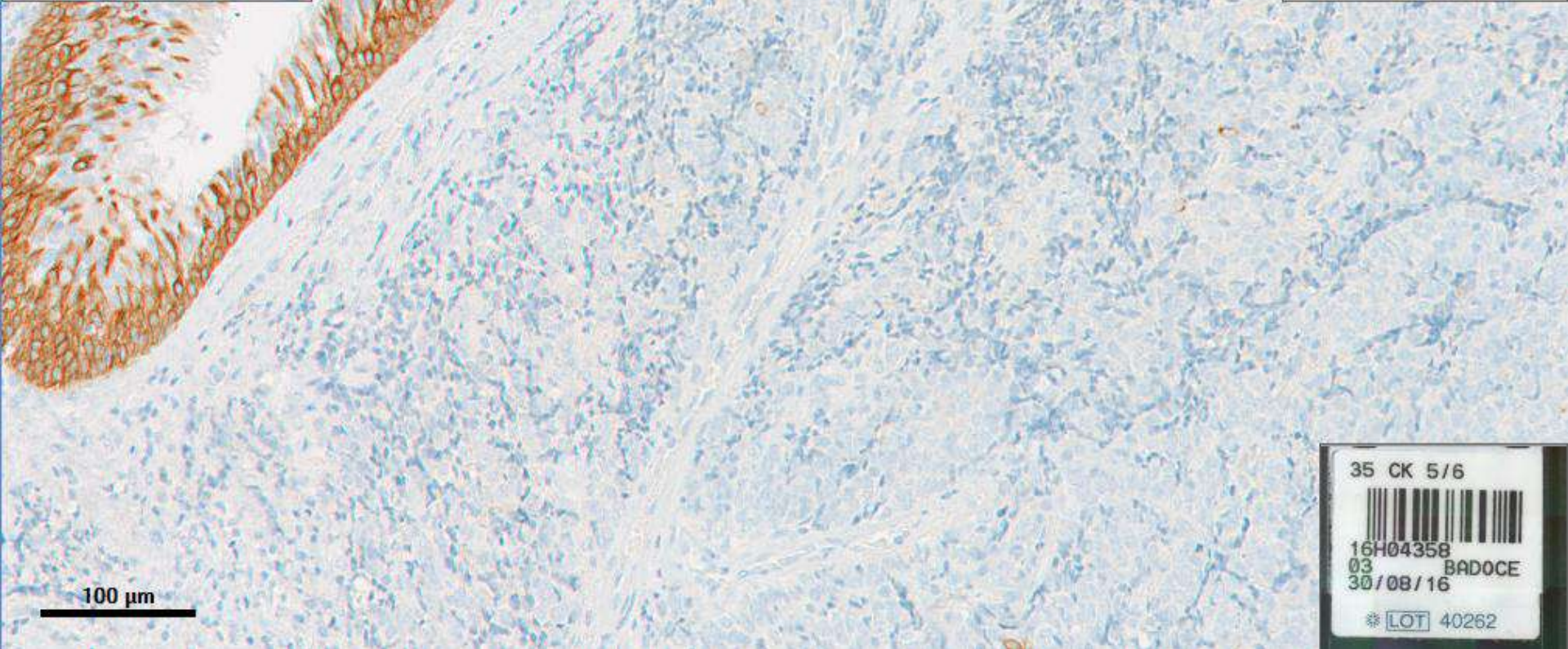
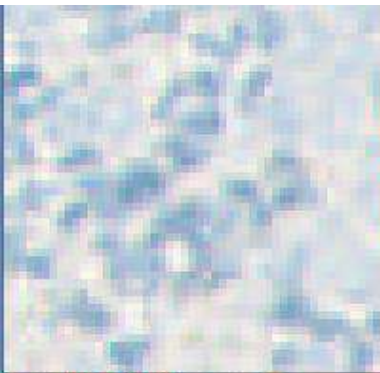
SuperFrost



50 μ m



?



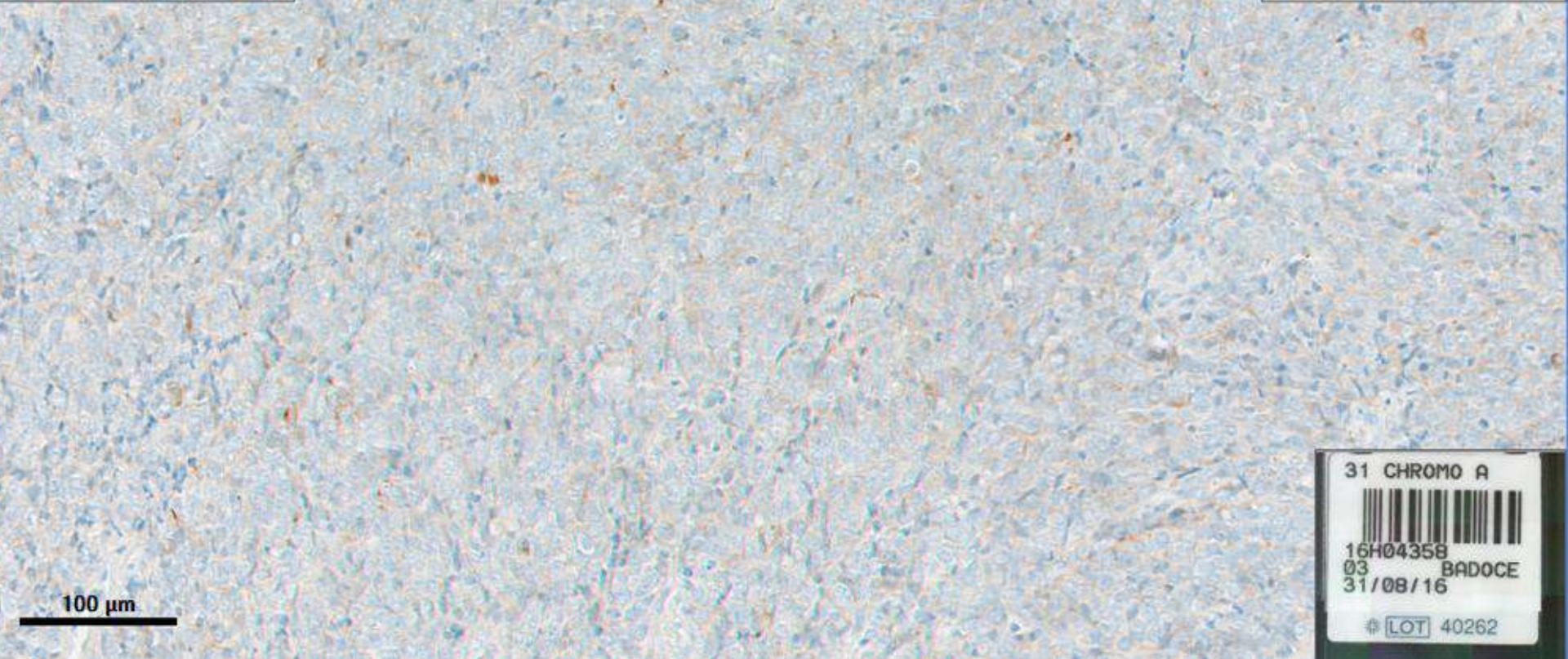
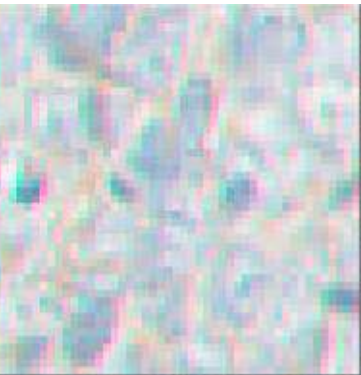
100 μ m

35 CK 5/6



16H04358
03 BADOCE
30/08/16

LOT 40262



100 μm

31 CHROMO A

16H04358
03 BADOCE
31/08/16
LOT 40262



100 μ m

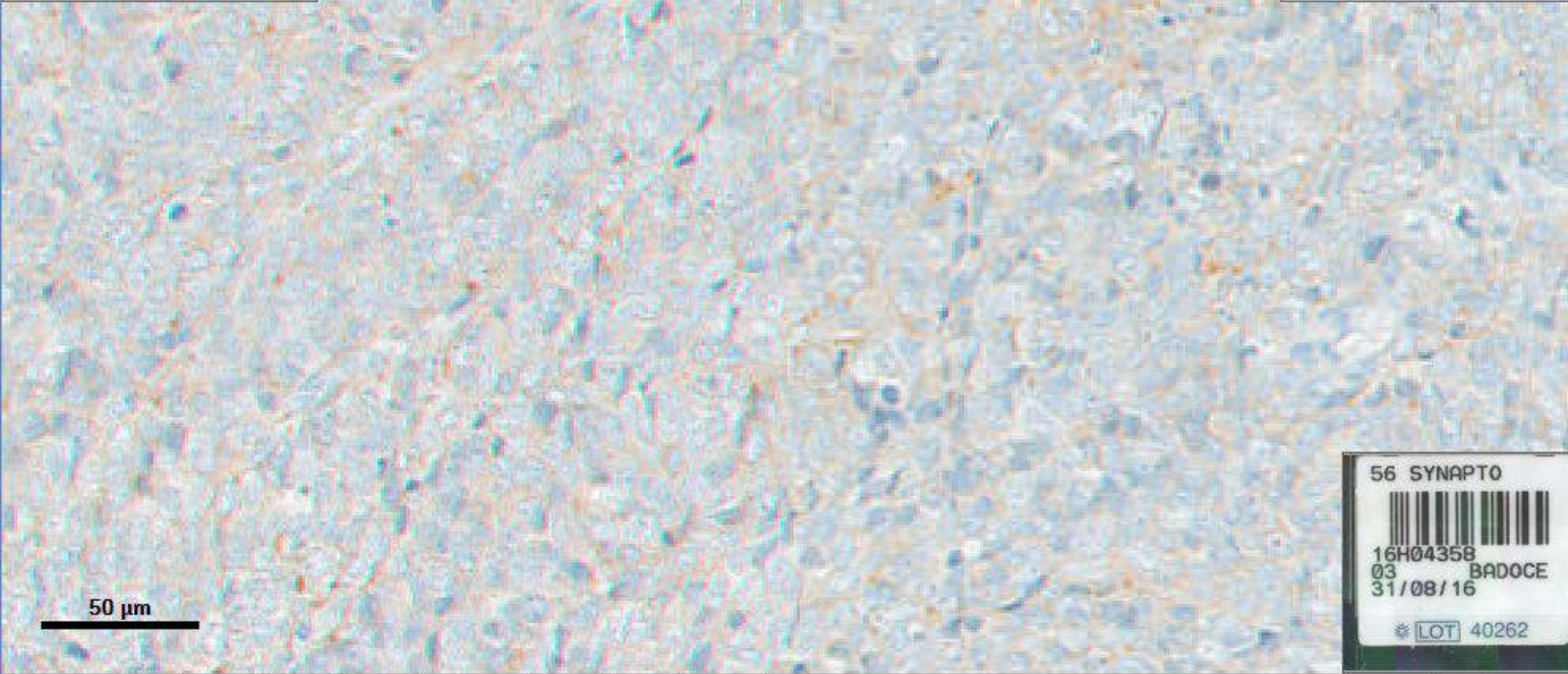
49 NCAM CD56



16H04358
03 BADOCE
05/09/16

LOT 40262

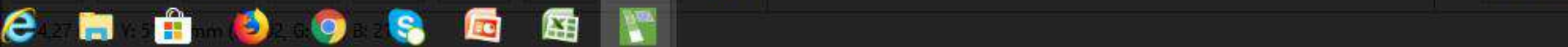




50 μm

56 SYNAPTO
16H04358
03 BADOCE
31/08/16
* LOT 40262

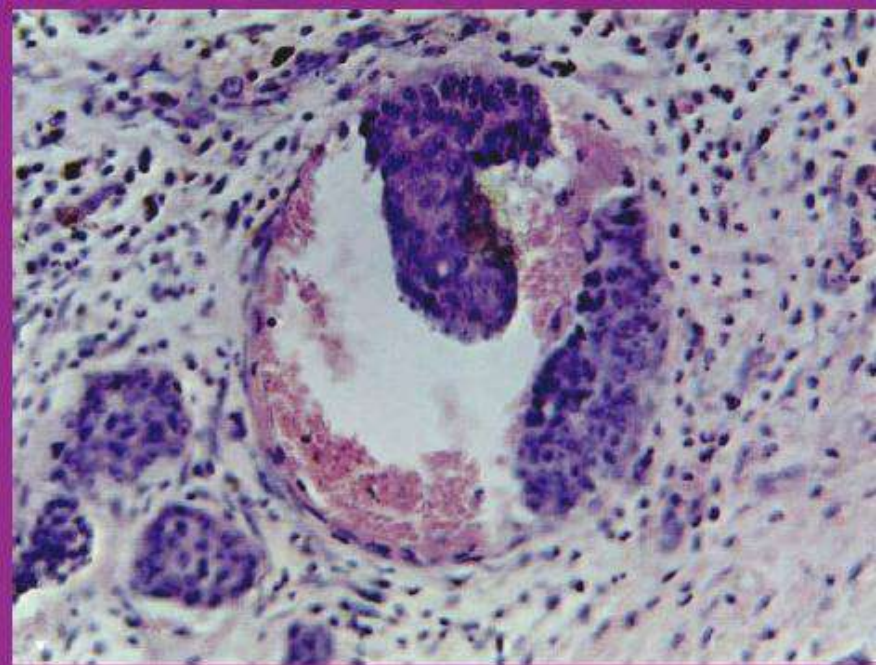
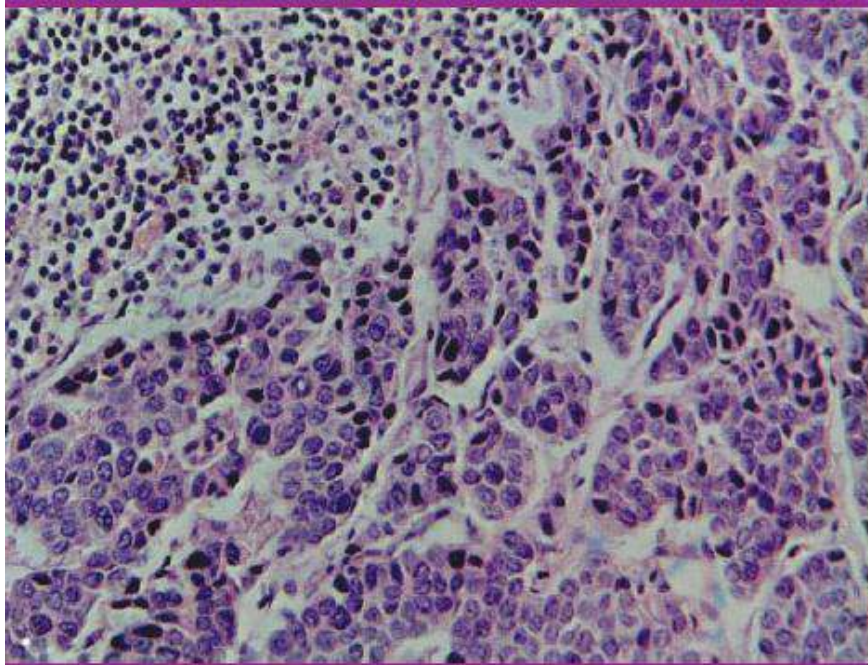
+ - Fit 1.25x 4x 10x 20x 40x 20.0x Snapshot



Carcinoid of the Larynx

Nelson C. Goldman, MD; C. Ian Hood, MD; and G. T. Singleton, MD, Gainesville, Fla

Arch Otolaryng—Vol 90, July 1969



James M. Woodruff, M.D.

Jatin P. Shah, M.D.

Andrew G. Huvos, M.D.

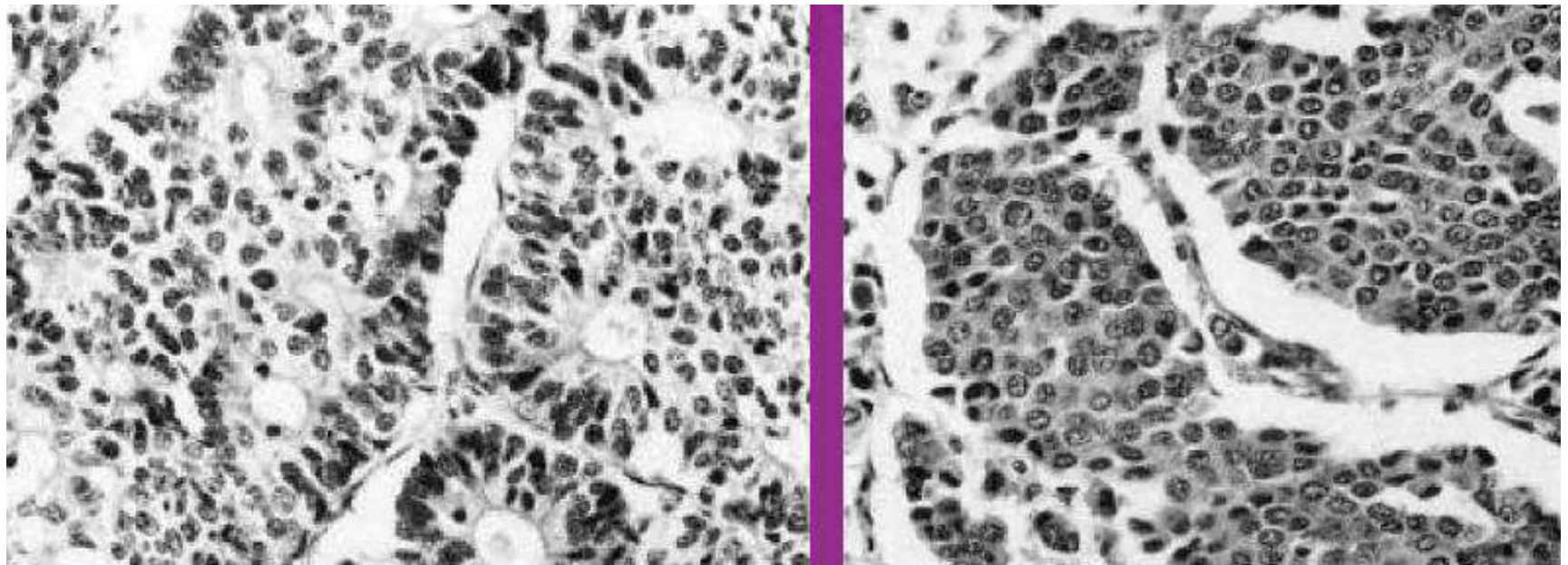
Frank P. Gerold, M.D.

Robert A. Erlandson, Ph.D.

Neuroendocrine carcinomas of the larynx

A study of two types, one of which mimics thyroid
medullary carcinoma

The American Journal of Surgical Pathology
9(11): 771-790, November
© 1985 Raven Press, New York



Neuroendocrine carcinomas

- Heterogeneous group of lesions, ranging just as in the lung, from benign tumors to high grade carcinomas
- The most common tumors are moderately differentiated carcinomas (atypical carcinoids) followed by poorly differentiated carcinomas (small cell carcinomas)
- Nests, cords, sheets, trabeculae +/- glands and / or rosettes.
- Tumors most often richly vascularisation. Cells have variable cytological aspects depending on the tumor subtype

(Modified) 2017 WHO Classification of Neuroendocrine carcinomas (NEC) of the Head and Neck

Classification		Criteria
Well-differentiated NEC		<ul style="list-style-type: none"> • Features of neuroendocrine differentiation • Minimal nuclear atypia • <2 mitoses/10HPFs
Moderately-differentiated NEC		<ul style="list-style-type: none"> • Necrosis and/or • 2-10 mitoses/10HPFs
Poorly-differentiated NEC	Small cell type	>10 mitoses/10 HPFs
	Large cell type	>10 mitoses/10 HPFs
Mixed neuroendocrine-non-neuroendocrine neoplasms		

2017 WHO Classification of Lung Neuroendocrine Neoplasms (Modified)

	Mitoses per 2mm ²	Necrosis	Ki-67 PI
Typical carcinoid	0-1	No	Up to 5%
Atypical carcinoid	2-10	Focal, if any	Up to 20%
Large cell NEC	>10 (median 70 MF/2mm ²)	yes	40-80%
Small cell NEC	>10 (median 80 MF/2mm ²)	yes	50-80%
Combined with non-small cell carcinoma			



Neuroendocrine Carcinomas of the Larynx and Head and Neck: Challenges in Classification and Grading

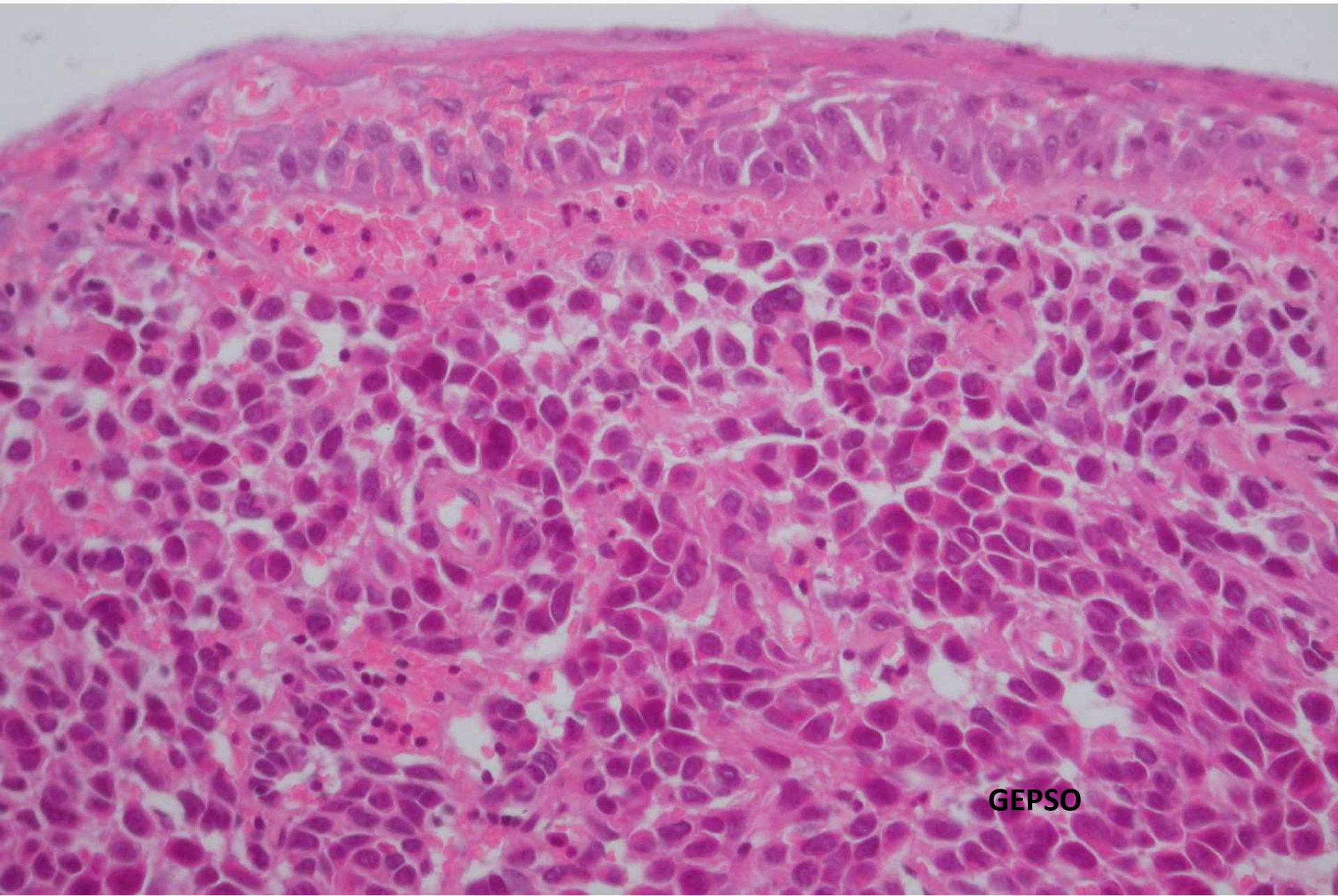
Table 4 Molecular alterations in NECs of the larynx and head and neck

Study	Tumor type	# of cases	Alterations	Methodology
Kao et al. [24] ^a	WD-NEC MD-NEC LC-NEC SC-NEC	23	p53 overexpression in LC- and SC-NEC No p53 overexpression in WD- and MD-NEC	IHC
Halmos et al. [29] ^b	WD-NEC MD-NEC LC-NEC SC-NEC	10	Negative p53 overexpression HPV 16 and HPV18 in one case each	IHC PCR
Alos et al. [30] ^a	LC-NEC SC-NEC	19	p53 overexpression p16 overexpression (73% of cases) Rb dysregulation (59% of cases) No HPV-DNA	IHC PCR
Franchi et al. [32] ^c	SC-NEC/SCC	1	Missense <i>TP53</i> exon 7 with p53 overexpression	IHC <i>TP53</i> sequencing
La Rosa et al. [33] ^d	SC-NEC/ITAC	1	Aberrant methylation of <i>APC</i> and <i>DAPK1</i> Gains and losses: 17p13 (<i>TP53</i>), 14q24 (<i>MLH3</i>) no <i>KRAS</i> , <i>BRAF</i> or p53 mutations	Methylation-specific PCR Mutation analysis <i>KRAS</i> , <i>BRAF</i> and <i>PT53</i>

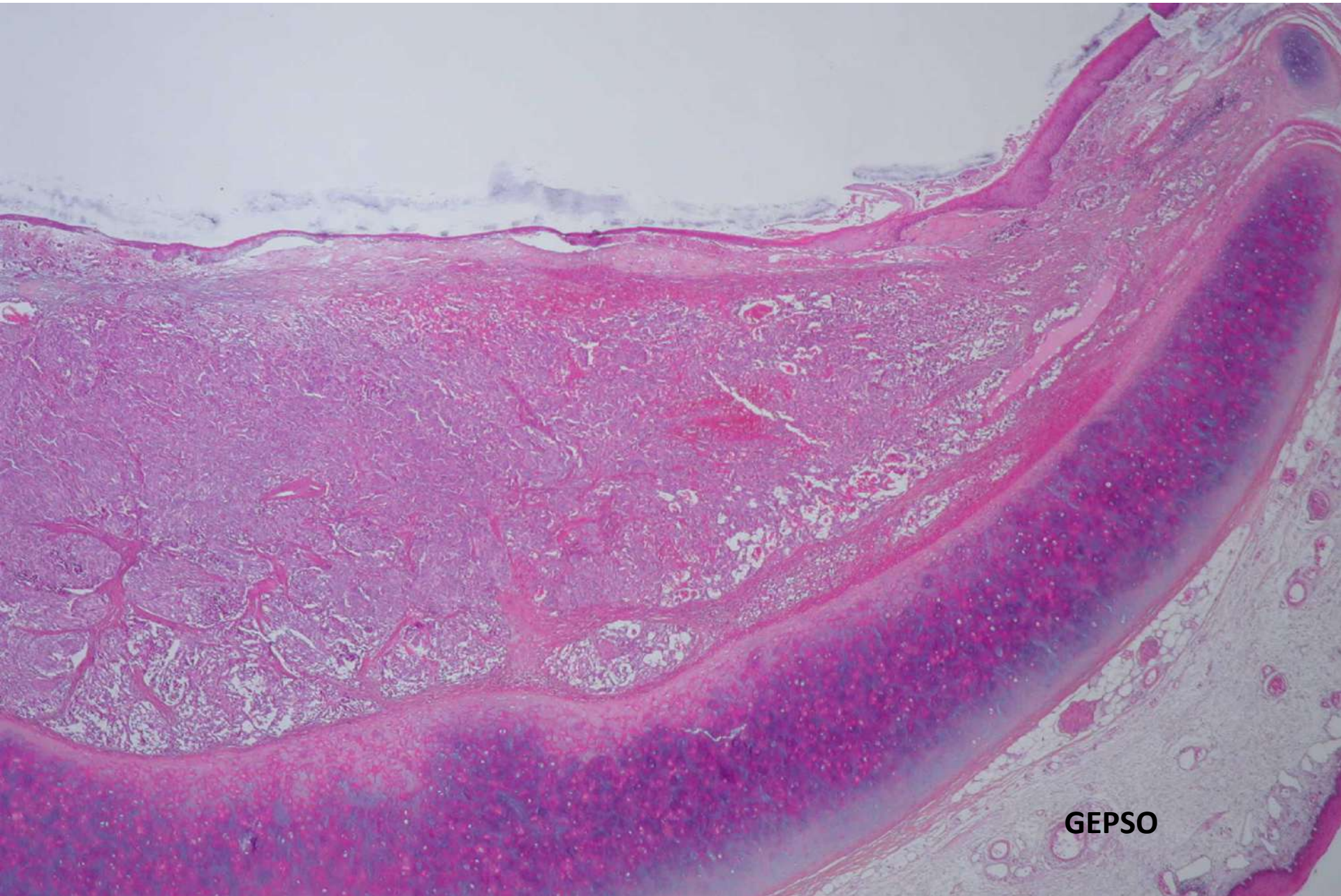
SCC squamous cell carcinoma, ITAC intestinal-type adenocarcinoma

Sites: ^ahead and neck; ^blarynx; ^cmaxillary sinus; ^dnasal cavity

OMS 2017	OMS 2005	Characteristics
<p>Well differentiated carcinoma</p> <p>60 yo</p> <p>Larynx</p>	<p>Carcinoid tumor, well differentiated neuroendocrine carcinoma.</p> <p>Synonyms: carcinoid, mature carcinoid</p>	<p>Round to slightly spindled cells with ample amphophilic to eosinophilic granular cytoplasm. Nuclei stippled or dispersed chromatin in salt and pepper pattern</p> <p>< 2 mitoses /10HPFs (/2mm²)</p>
<p>Moderately differentiated carcinoma</p> <p>Smokers</p> <p>Larynx</p>	<p>Atypical carcinoid, moderately atypical differentiated. Synonyms: atypical carcinoid tumor (grade II), neuroendocrine carcinoma moderately differentiated, malignant carcinoïde tumor, large cells neuroendocrine carcinoma</p>	<p>Morphology</p> <p>neuroendocrin/carcinoid</p> <p>2 to 10 mitoses /10 HPFs (/2mm²) and /or necrosis</p>



GEP SO

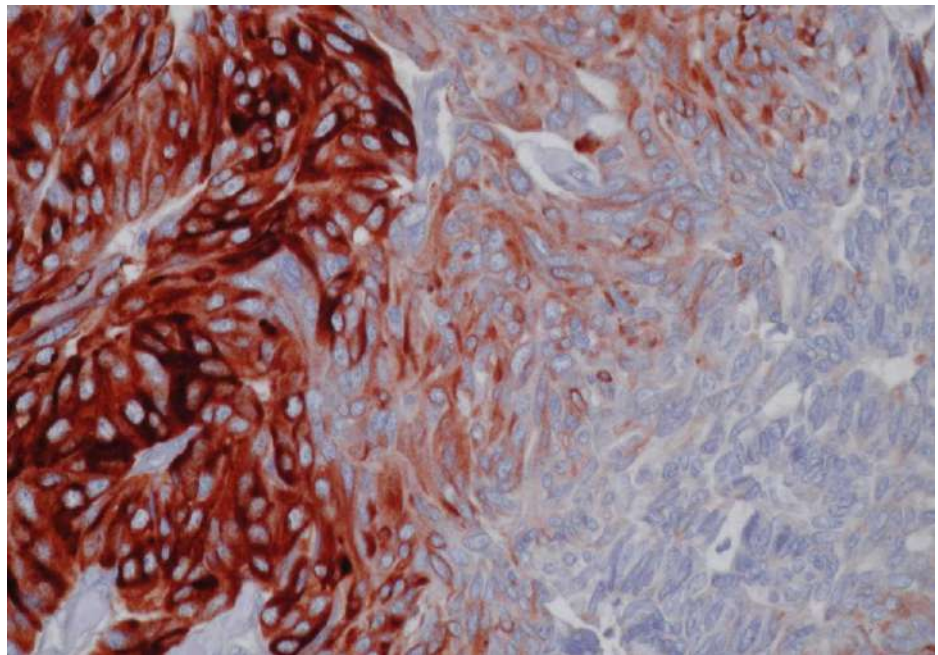
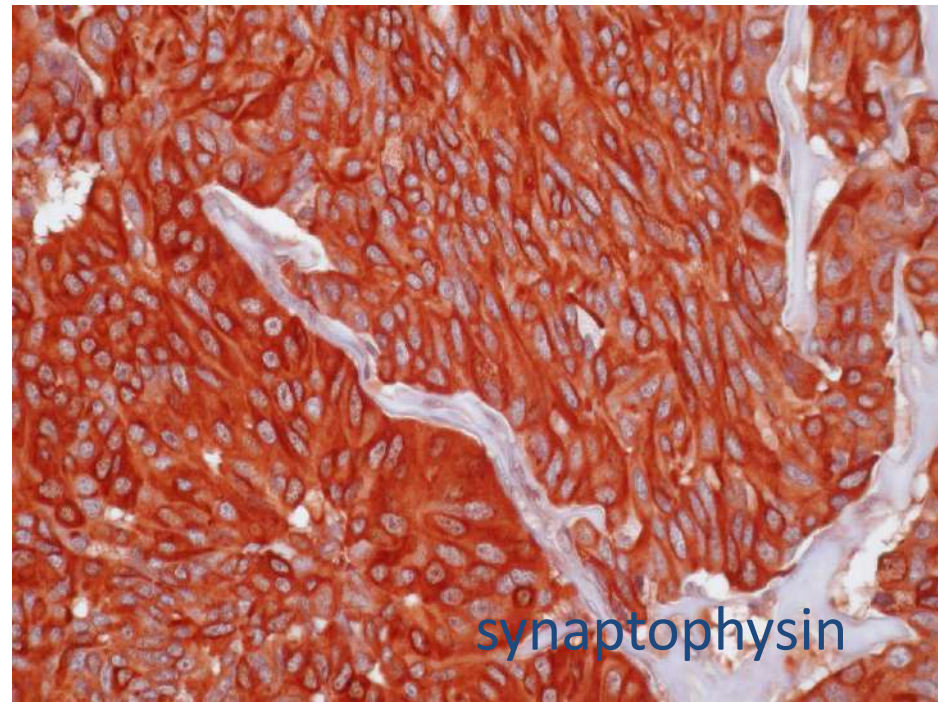
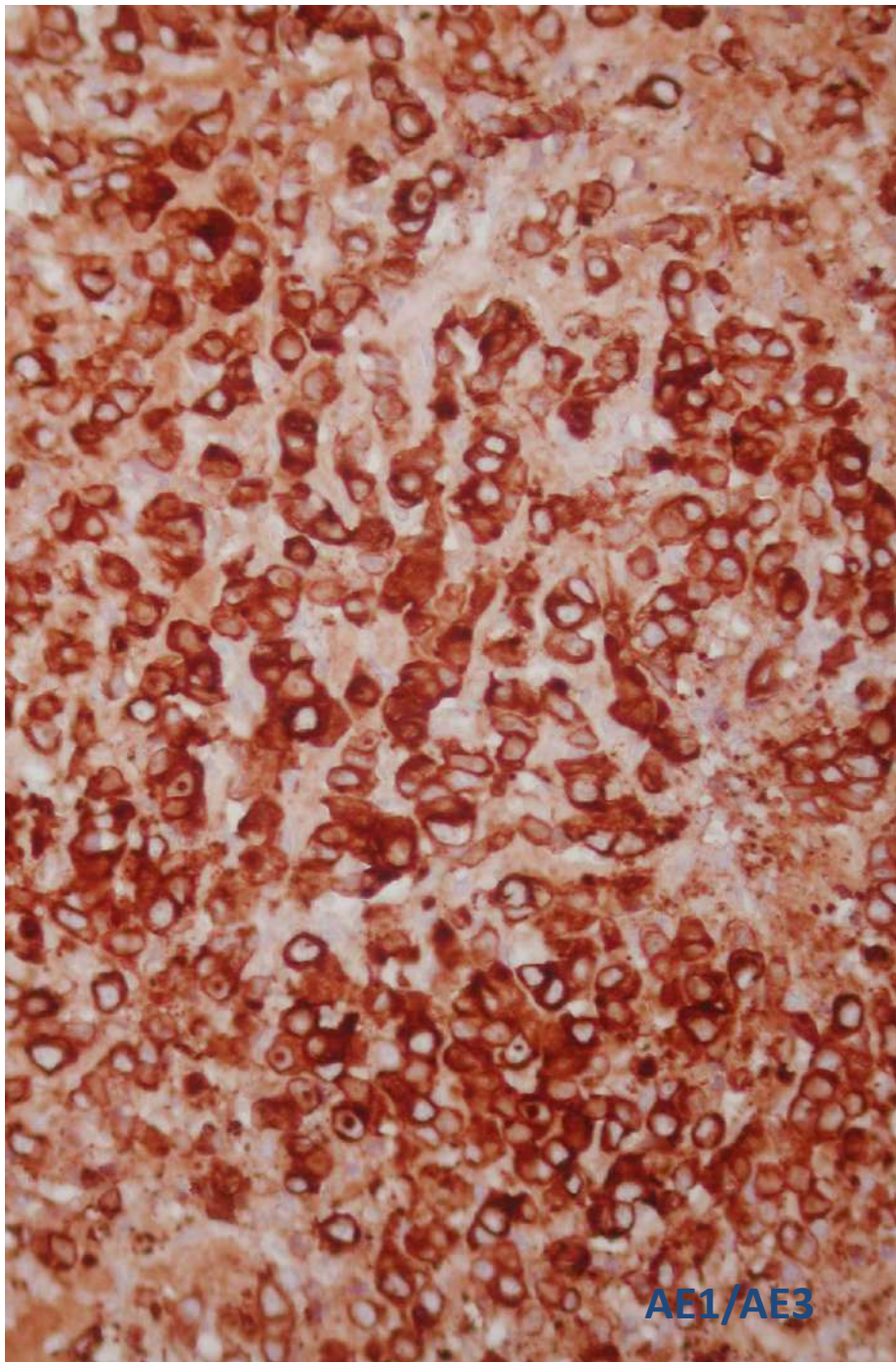


GEP SO

OMS 2017	OMS 2005	Characteristic
<p>Poorly differentiated neuroendocrine carcinoma</p> <p>Men >60</p> <p>90% smokers</p>	<p>Large cells poorly differentiated neuroendocrine carcinoma</p>	<p>Morphology : neuroendocrine differentiation.</p> <p>Small to medium size cells with hyperchromatic nuclei finely granular chromatin, indistinct nuclei. Crush artefacts.</p> <p>Large cell carcinoma cytological aspects</p>
		<p>≥ 11 mitoses /10 HPFs (/2mm²), mean 70</p>
		<p>Necrosis, apoptosis</p>
		<p>At least 1 neuroendocrine marker and/or neuroendocrine granules in electronic microscopy</p>
<p>Combined neuroendocrine carcinoma</p>	<p>Poorly differentiated neuroendocrine small cell carcinoma.</p> <p>Synonyms: small cells neuroendocrine carcinoma (grade III), poorly small cells neuroendocrine carcinoma</p>	<p>Small cells</p>
		<p>≥ 11 mitoses /10 HPFs (/2mm²), mean</p>
		<p>necrosis frequent</p>
	<p>Small cell neuroendocrine carcinoma neuroendocrine + non small cell carcinoma (SCC or adenocarcinoma..)</p>	

Neuroendocrine carcinoma

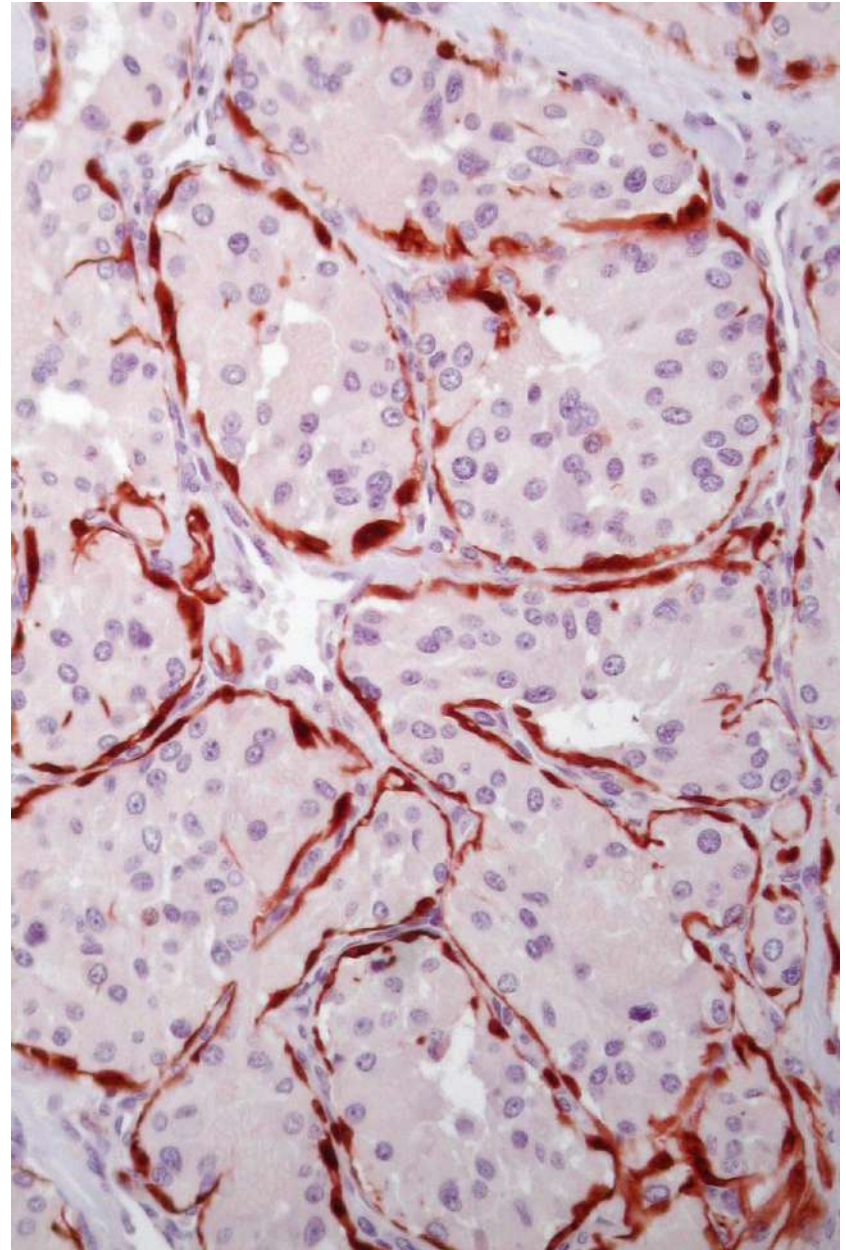
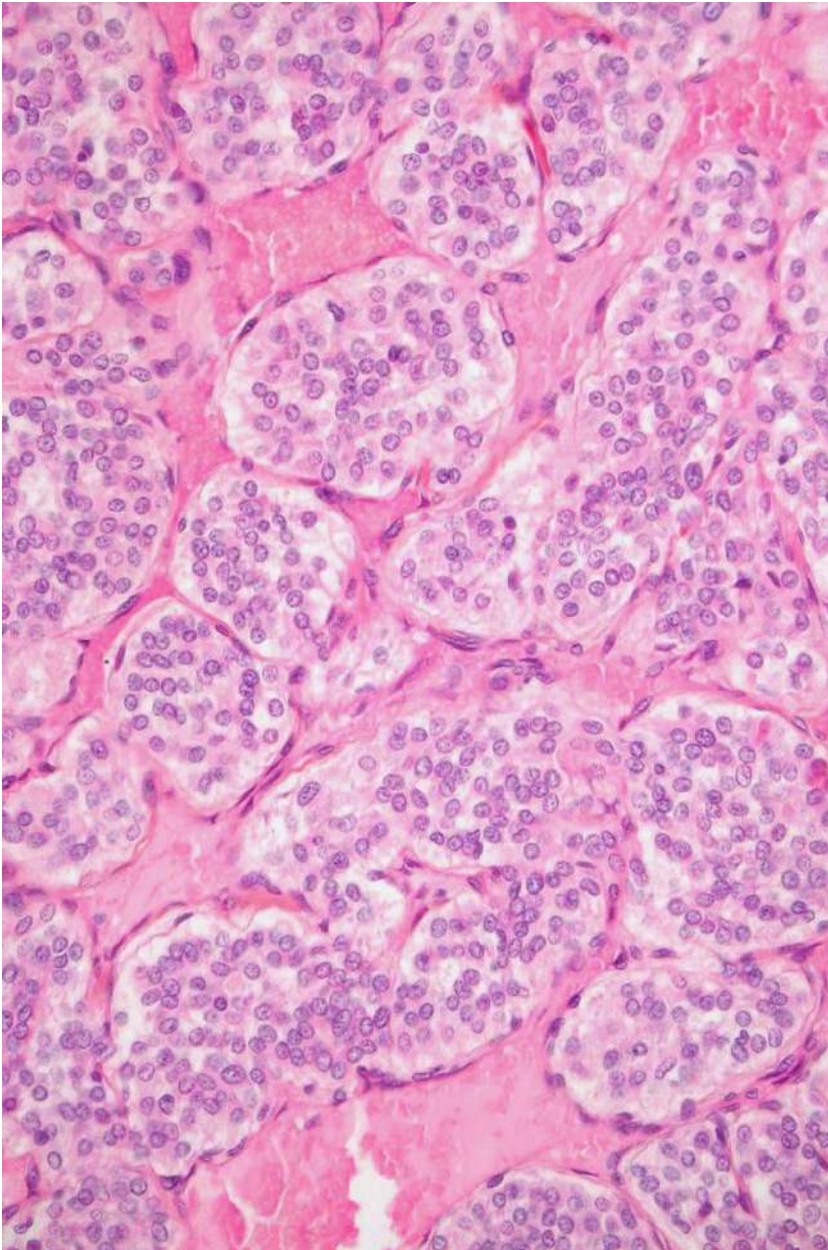
- Immunohistochemistry: pancytokeratin (AE1 / AE3) + cells, synaptophysin +, chromogranin +, NSE +, NCAM +, neuroendocrine differentiation.
- The tumor cells are sometimes labeled with antibodies to serotonin, calcitonin, bombesin and somatostatin.
- Neuro-endocrine carcinomas can be confused with poorly differentiated squamous cell carcinomas, especially basaloid



INSM1 staining in neuroendocrine tumors of the Head and Neck

Diagnosis	INSM1 n (%)	SYN n (%)	Chromo n (%)	CD56 n (%)
Parathyroid Adenoma	0/7 (0)	1/7 (14.3)	6/7 (85.7)	1/7 (14.3)
Middle Ear Adenoma	6/6 (100)	6/6 (100)	2/6 (33.3)	3/6 (50)
Paraganglioma	19/19 (100)	19/19 (100)	18/18 (100)	18/18 (100)
Parathyroid Carcinoma	0/16 (0)	5/16 (31.25)	7/16 (43.75)	3/15 (20)
Medullary Thyroid Carcinoma	24/24 (100)	22/22 (100)	22/22 (100)	22/22 (100)
Olfactory Neuroblastoma	15/15 (100)	15/15 (100)	9/11 (81.8)	11/11 (100)
Sinonasal Teratocarcinosarcoma	2/2 (100)	1/1 (100)	0/1 (0)	1/1 (100)
Large Cell Neuroendocrine Carcinoma	6/6 (100)	5/6 (83.3)	5/6 (83.3)	3/6 (50)
Small Cell Carcinoma	14/15 (93.3)	9/14 (64.3)	6/14 (42.9)	9/12 (75)

Differential diagnostic : paraganglioma



Neuroendocrine carcinomas treatment, pronostic

- well-differentiated neuroendocrine carcinoma
 - Surgery
 - Extended survival C.
- Moderately differentiated neuroendocrine
 - Surgery
 - 50% 5 years
 - 30% 10 years
- Poorly differentiated ,euroendocrine
 - Chemotherapy - radiotherapy
 - 15% 2 years
 - 5% 5 years

Case 1D

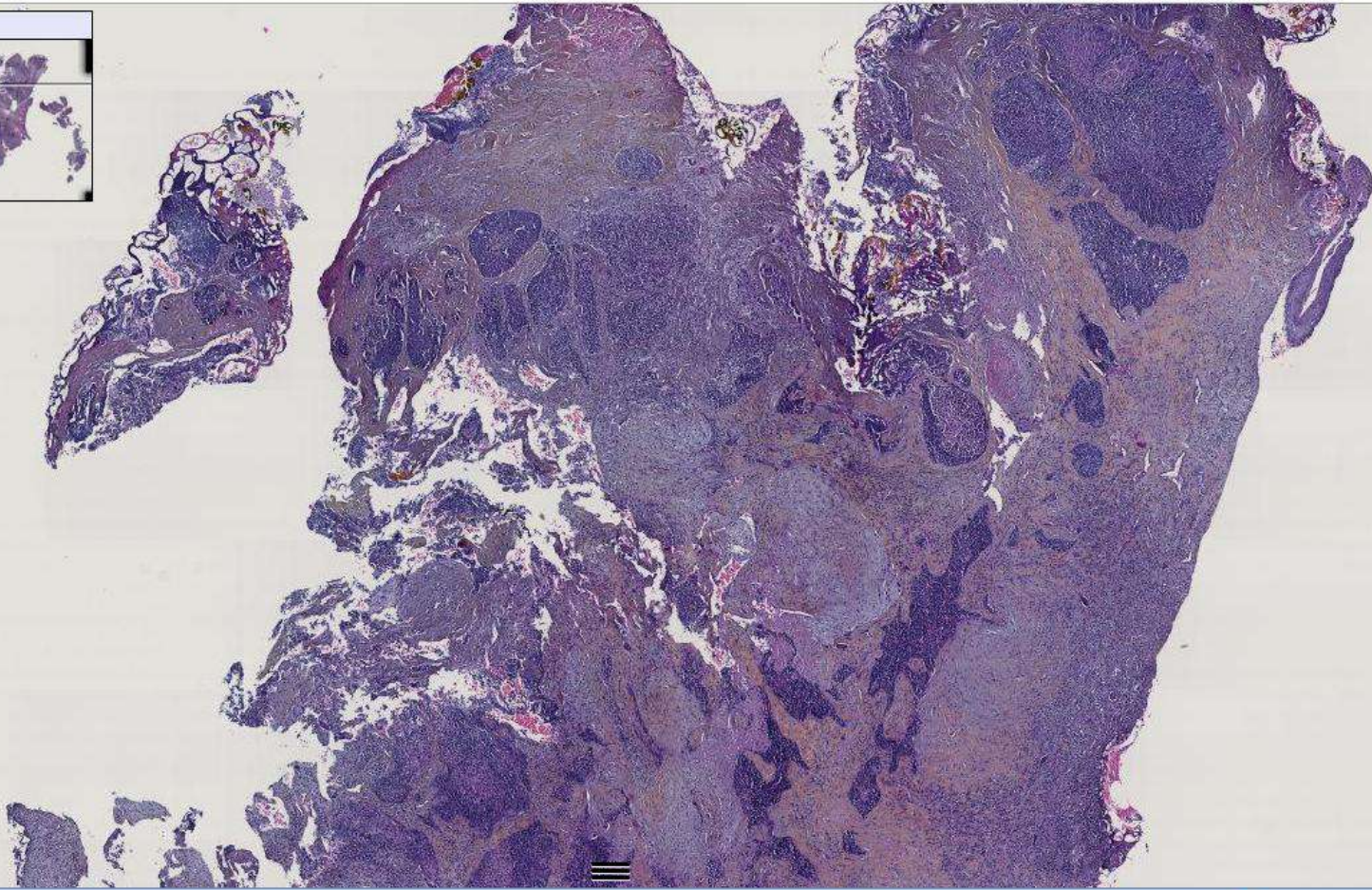
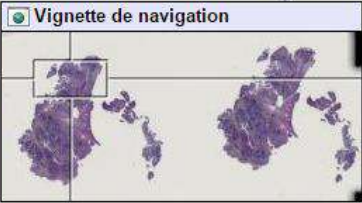
woman 45 yo laryngeal lesion

Clinical history

- 30 year old woman
- Antecedent : cyst of the left ovary.
- No alcohol-toxic intoxication.
- Late 2012 dysphonia: squamous cell carcinoma of the right vocal cord and right ventricular band, p16 +.
- 2013 laser resection T3N0 lesion: radiotherapy + cisplatin.

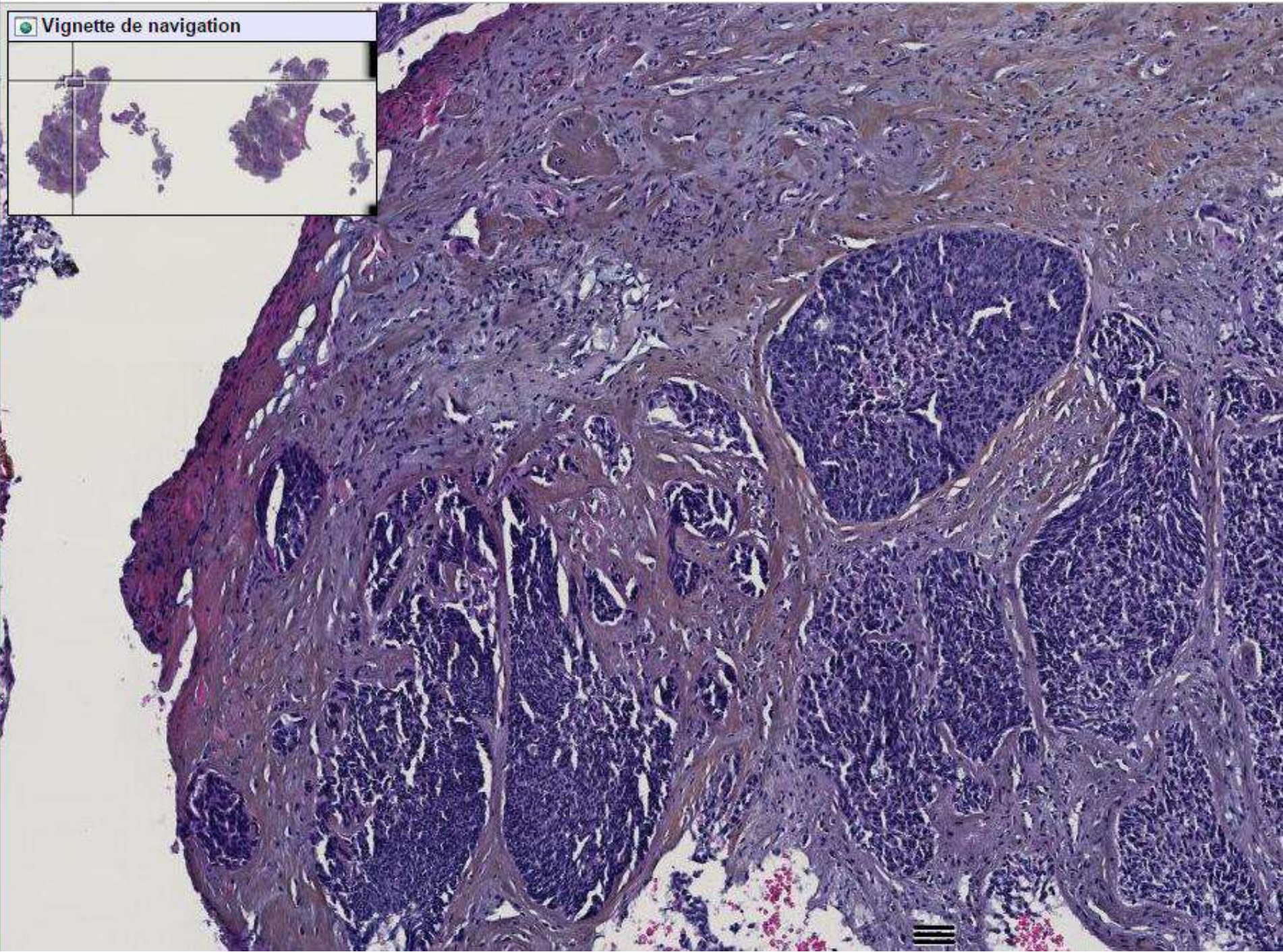
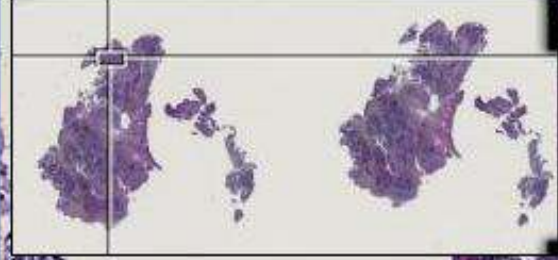
Clinical history

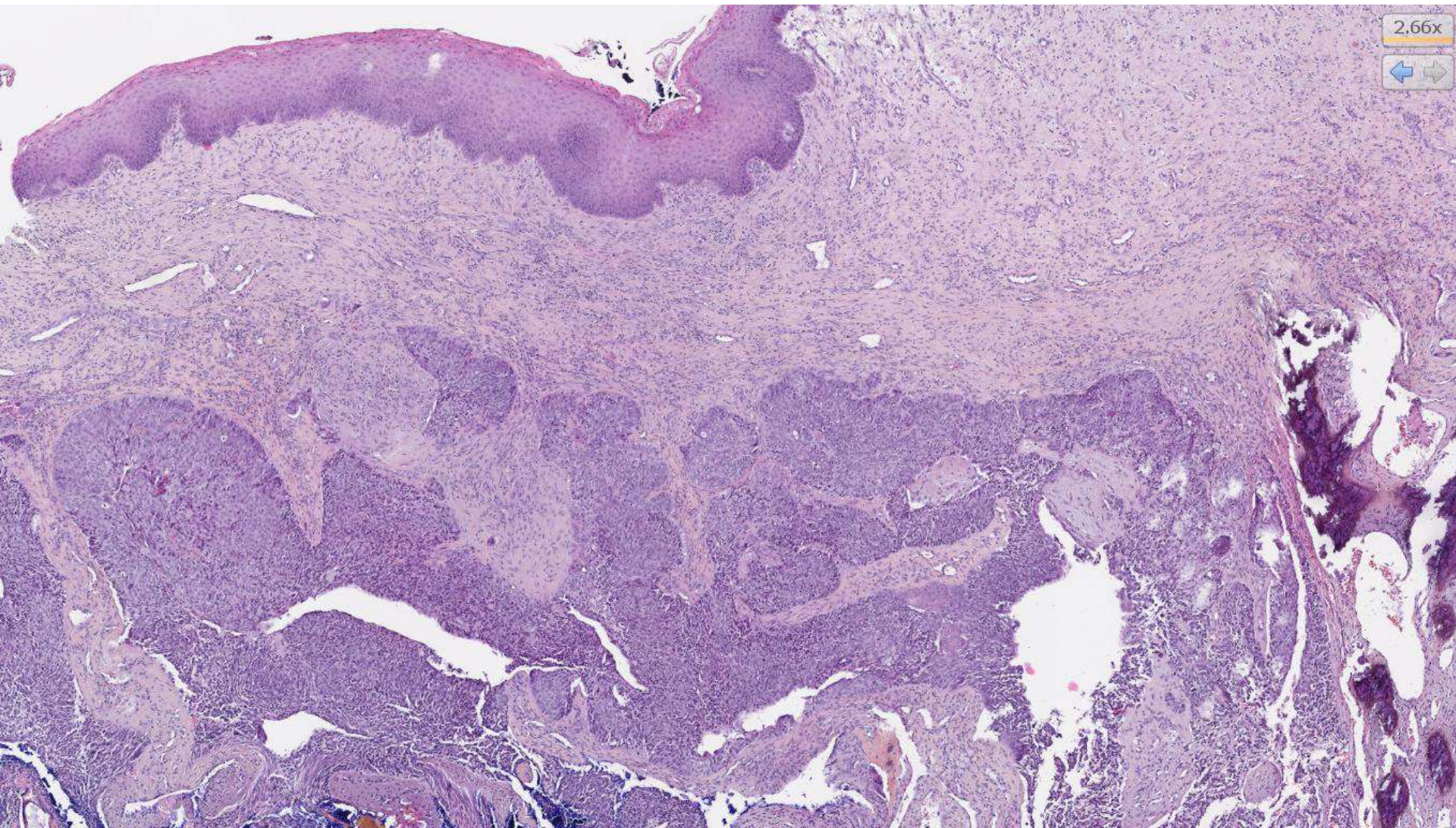
- Recurrence of the laryngeal tumor with progressive dyspnea.
- In September 2014, PET-scan local laryngeal recurrence with bilateral subclinical suspicious cervical lymphadenopathy in the context and a pulmonary nodule of the left lower lobe.
- Fibroscopic examination: voluminous anterior glotto-subglottic tumor bud treated by laser endolaryngeal disobstruction.



- 40,0X
- 20,0X
- 10,0X
- 5,0X
- 2,5X
- 1,25X
- 0,63X



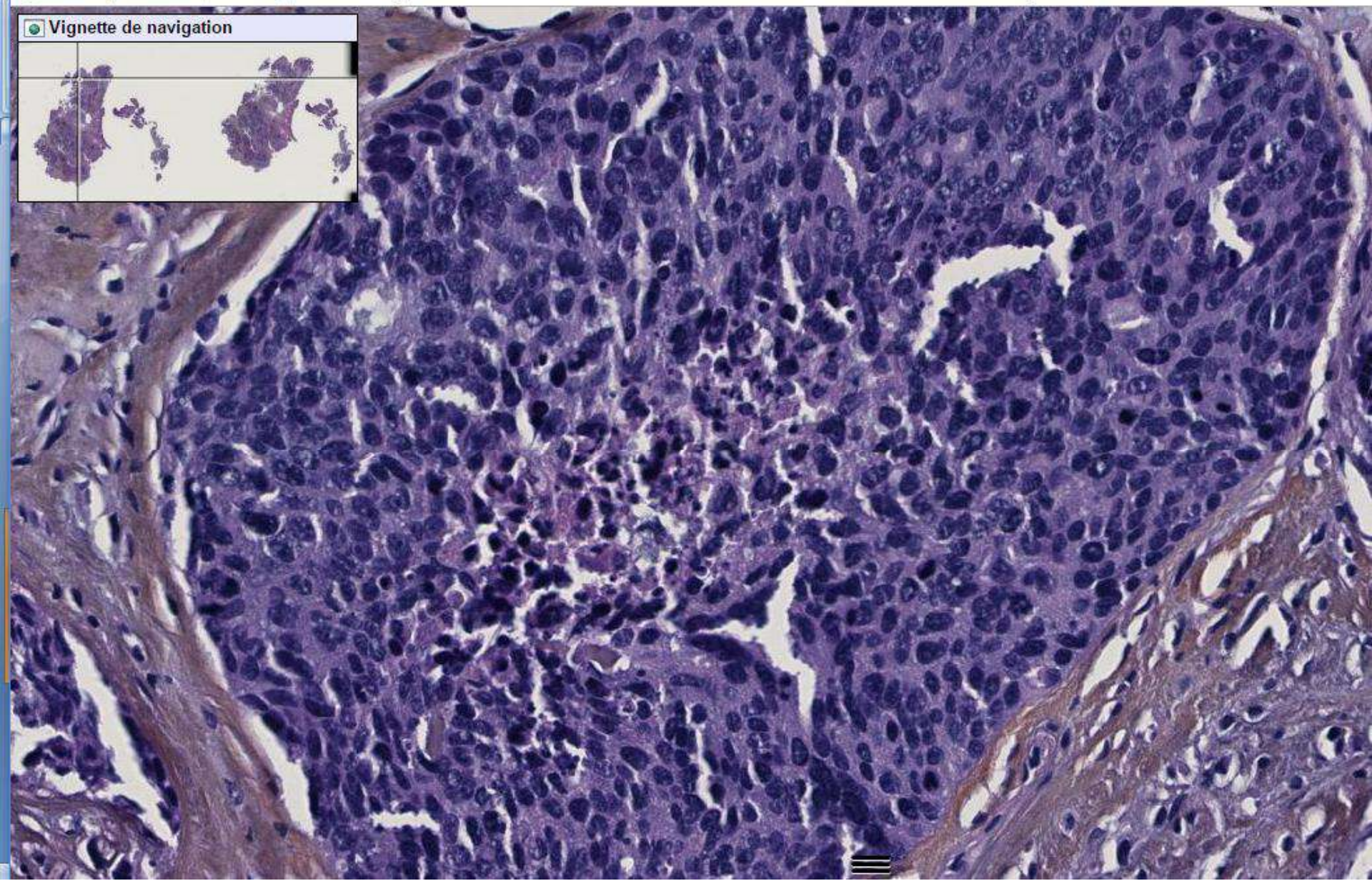


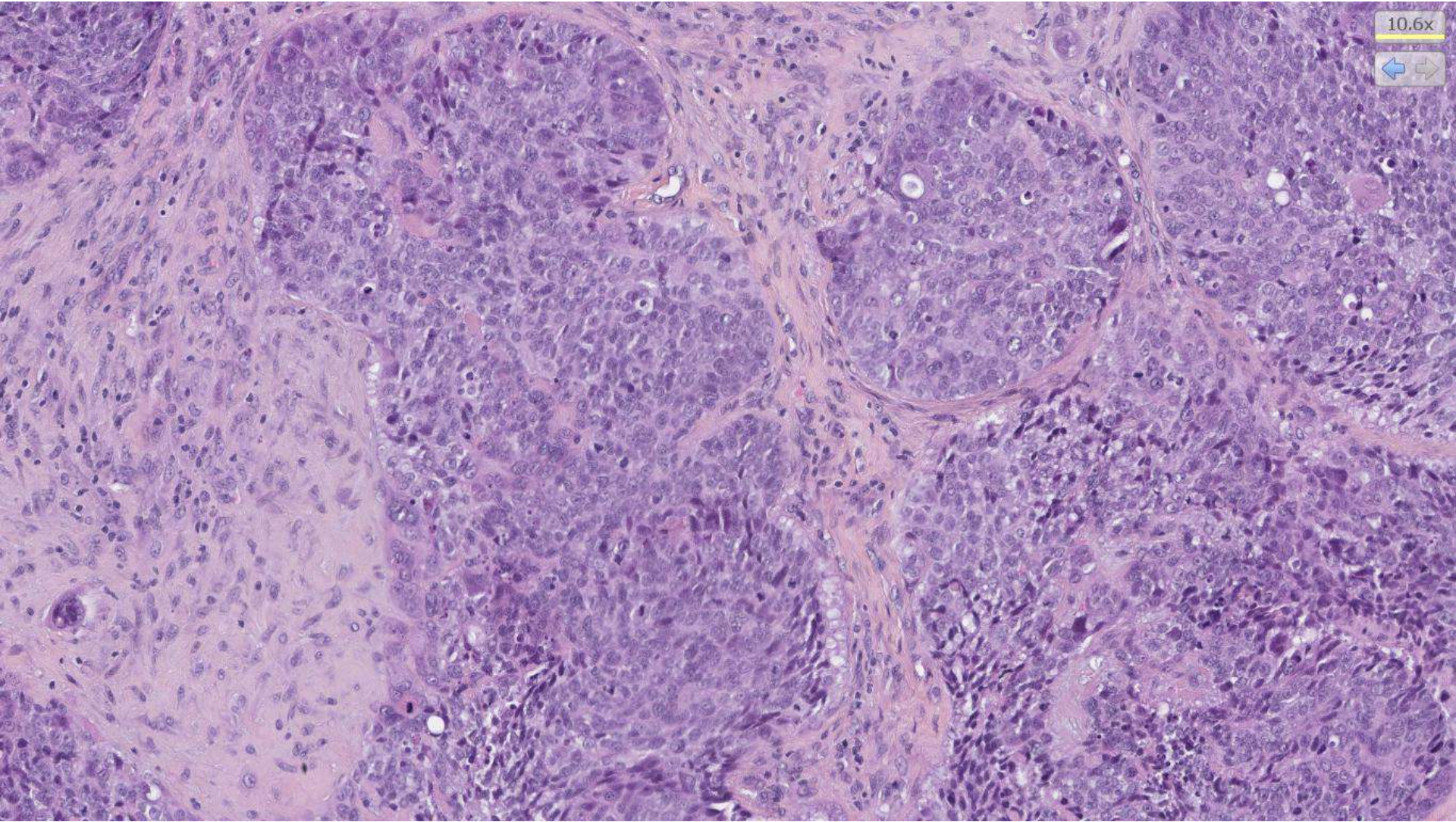


2.66x



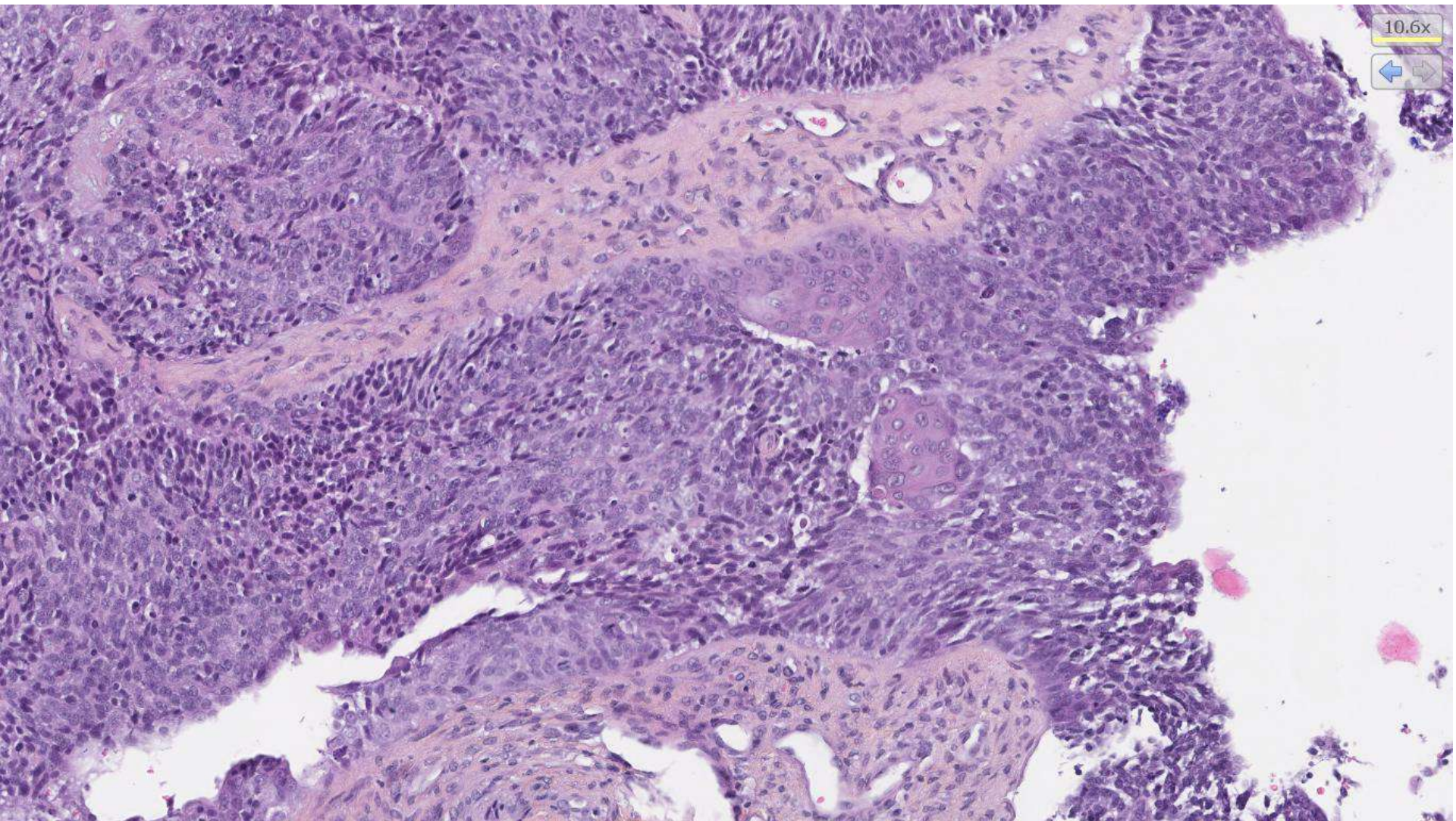
Vignette de navigation





10.6x

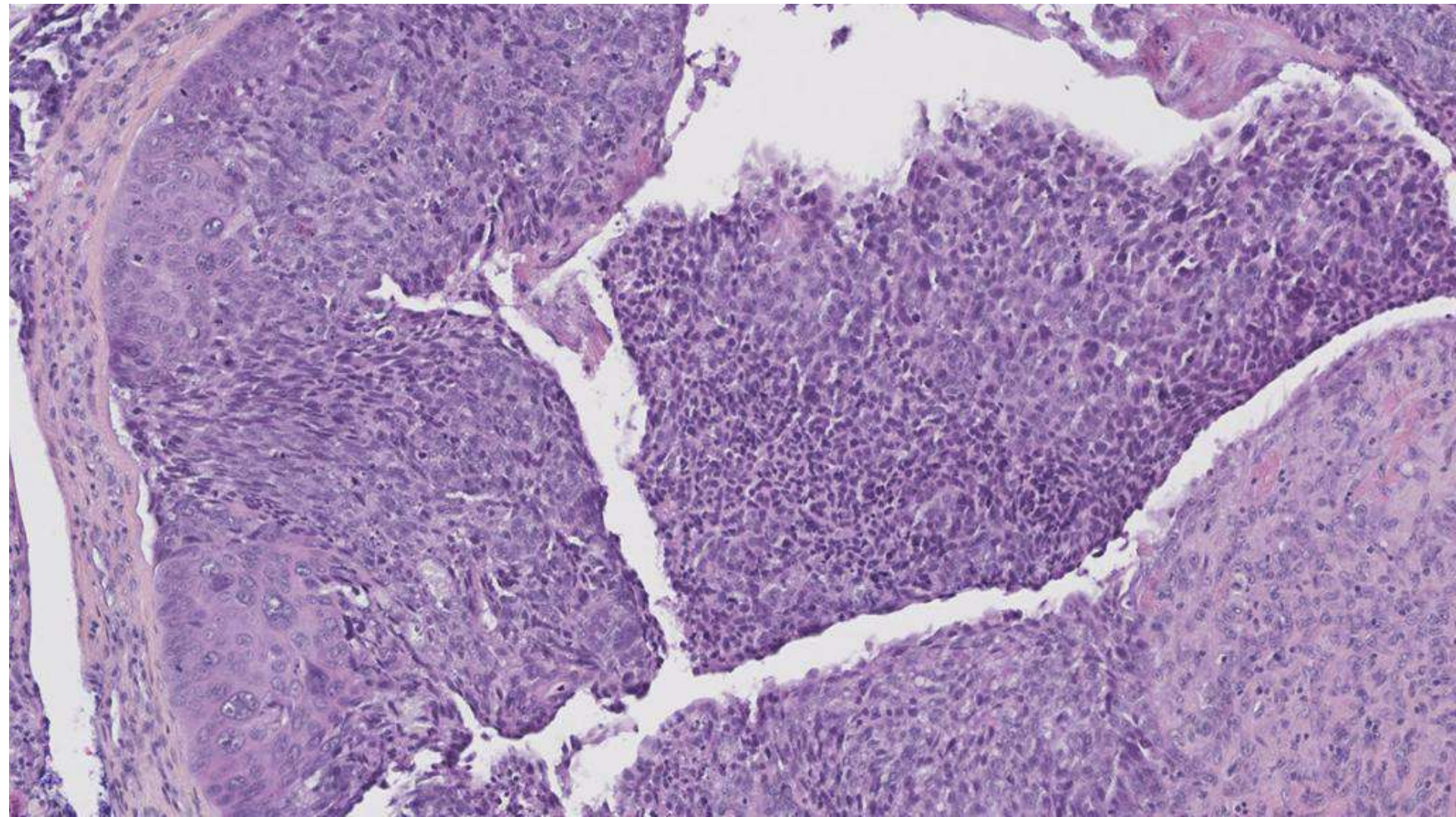


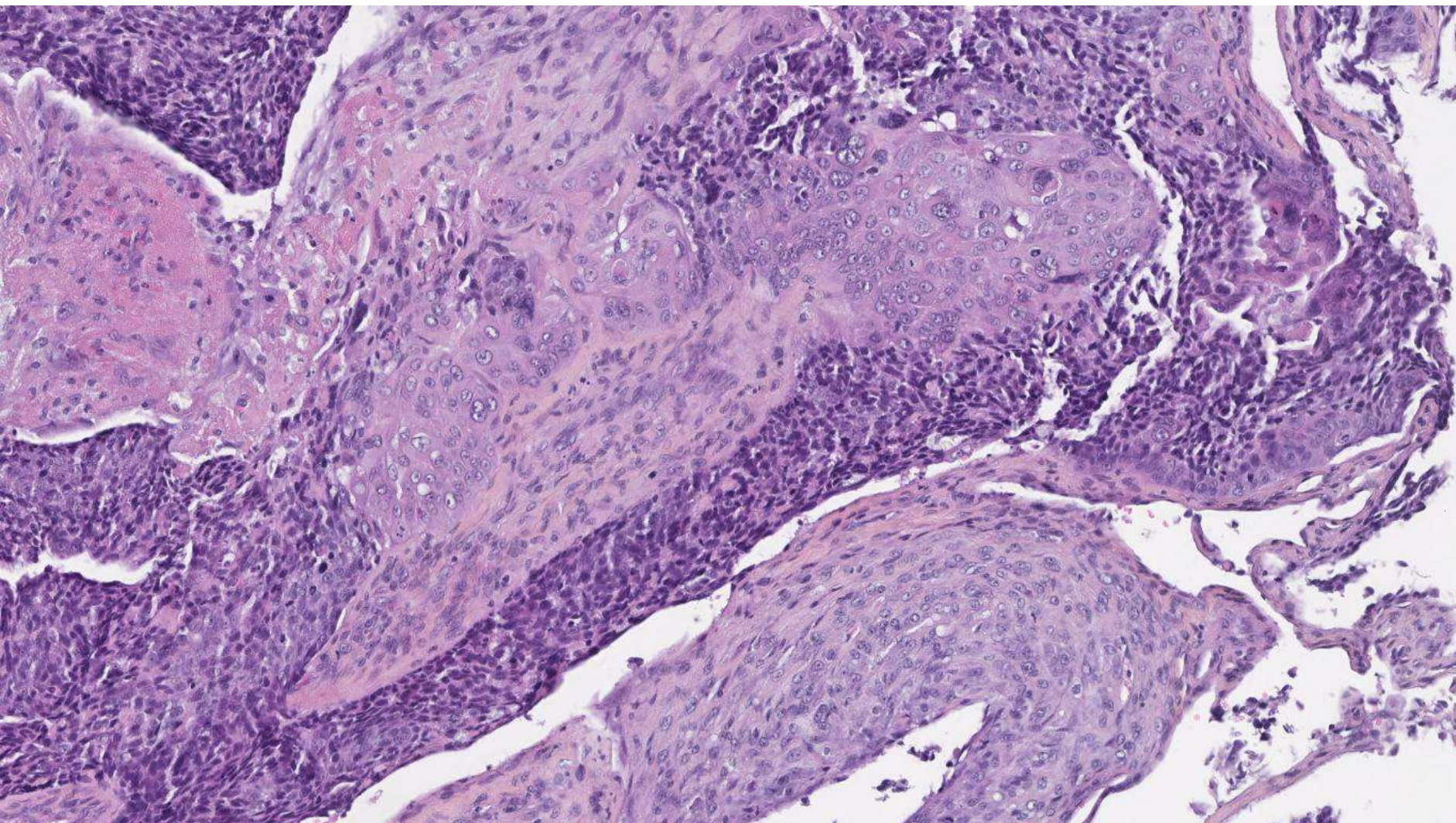


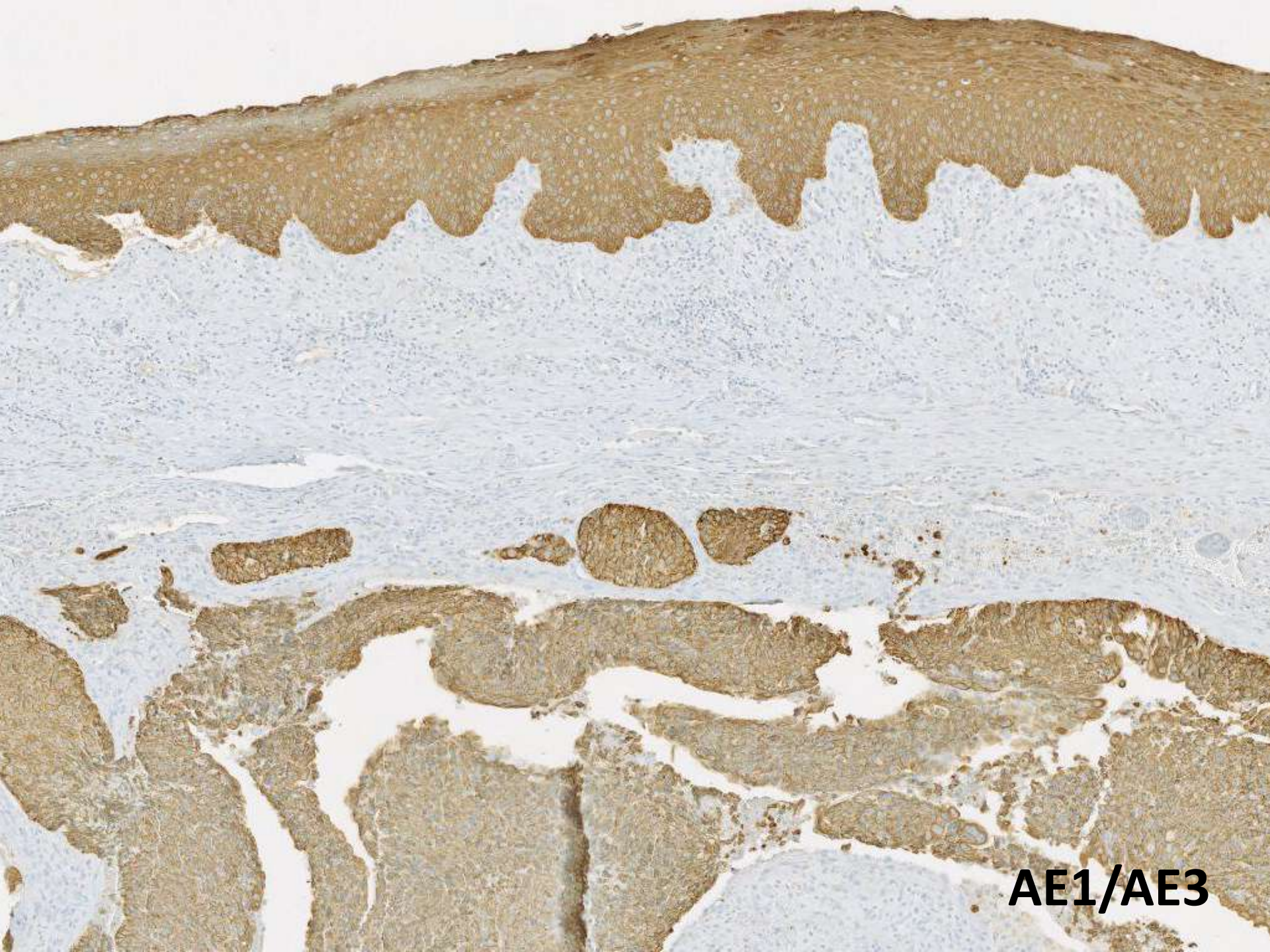
10.6x



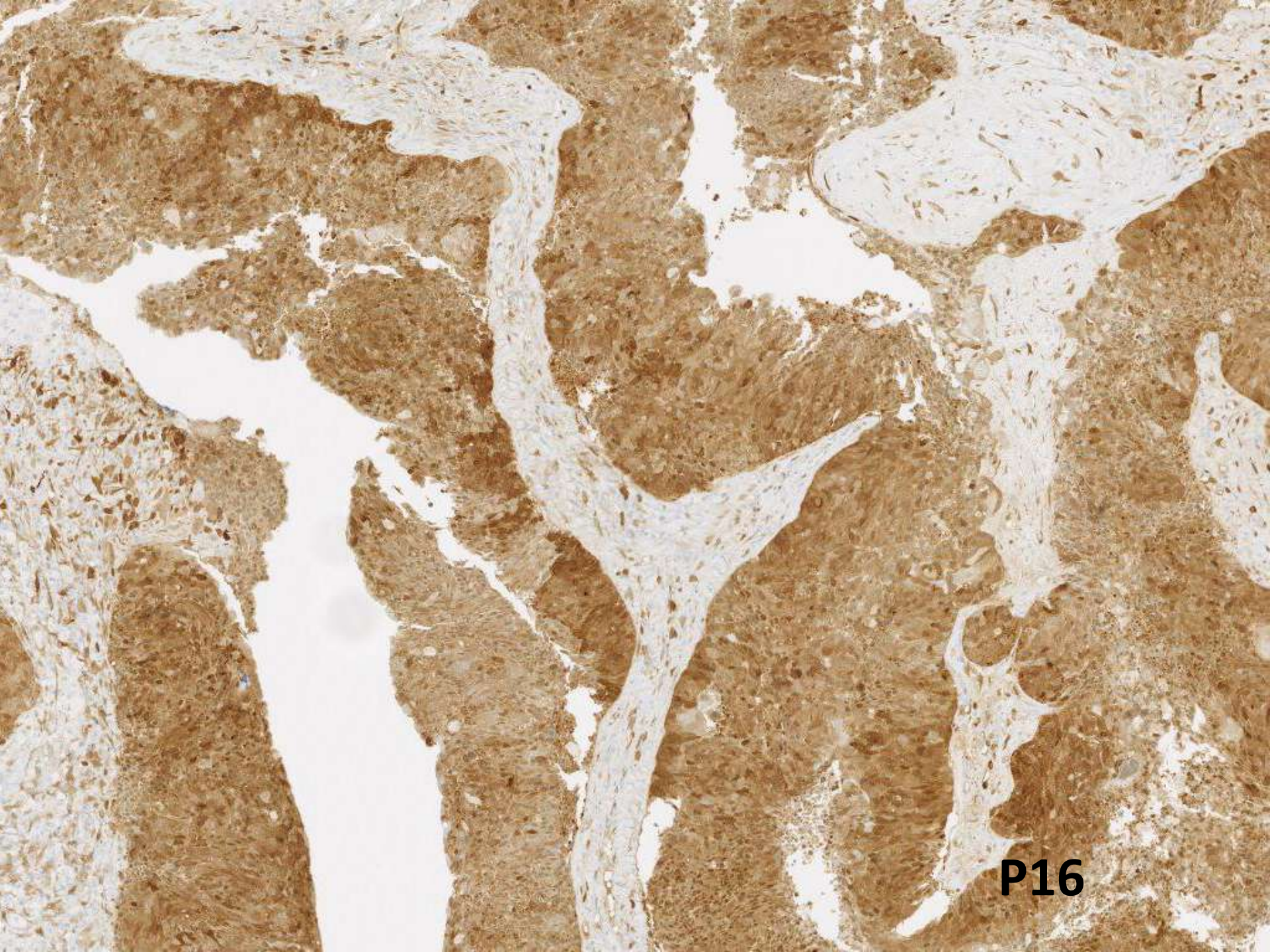
First biopsies







AE1/AE3



P16

Prescription du : 26/09/16
Prélèvement du : Non renseignée
Références labo : 1639004815 (1192709)

Enregistrement du : 27/09/16 12:51
Edition du : 07/11/16 18:02

N° Valise / Pneu :
complète en prévisualisation

RECHERCHE DE PAPILLOMAVIRUS HUMAINS (HPV)

Localisation : ORL
Localisation : ORL
Mode de prélèvement : Biopsie paraffinée
Méthode : Inno-Lipa HPV Genotyping extra II

Recherche d'HPV

Résultat : Positif

Détection d'HPV à haut risque

Résultat : Positif

Liste de HPV à haut risque détectés

HPV HR1 : 16

Détection d'HPV à bas risque

Résultat : Négatif

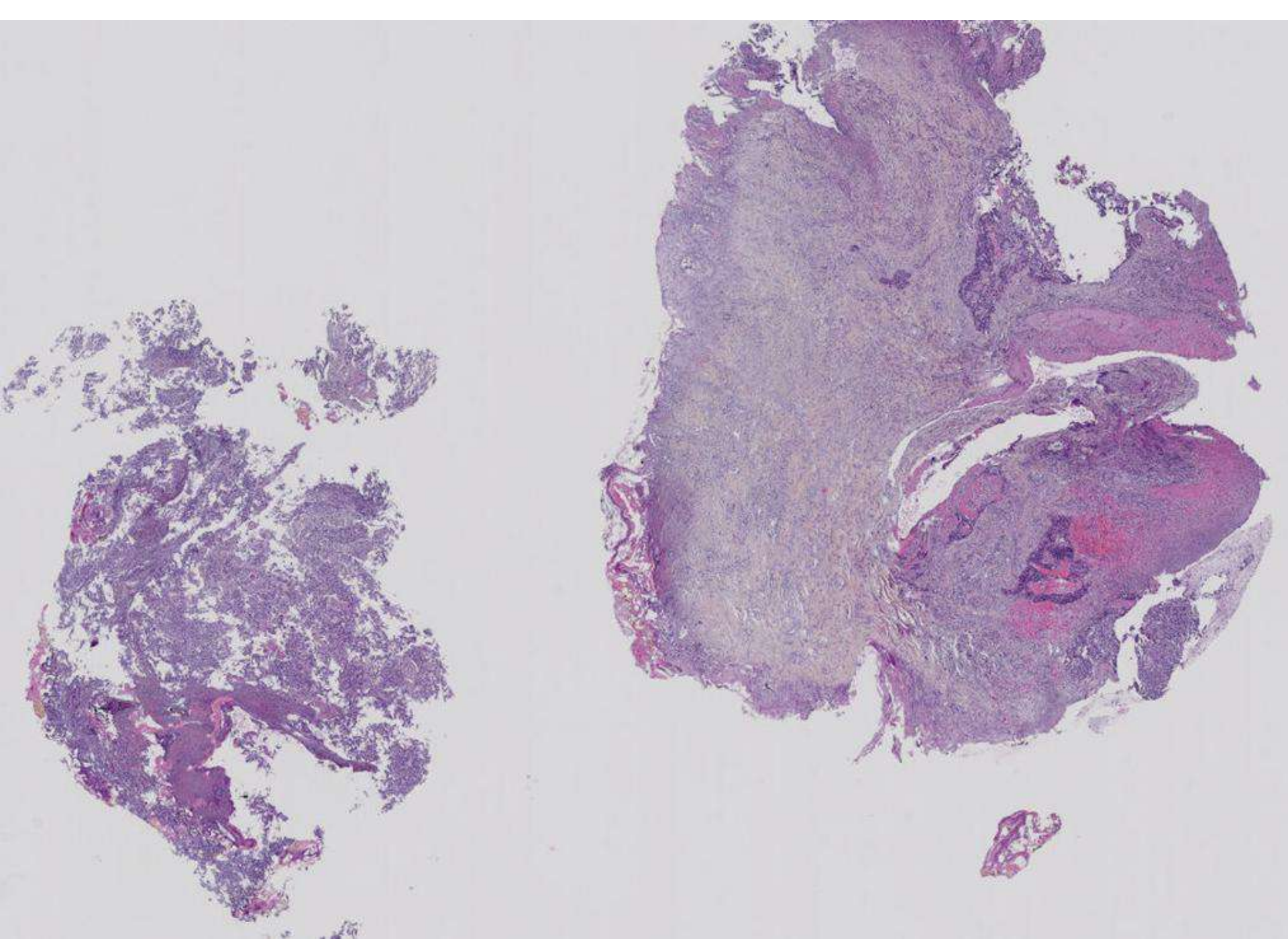
CONCLUSION

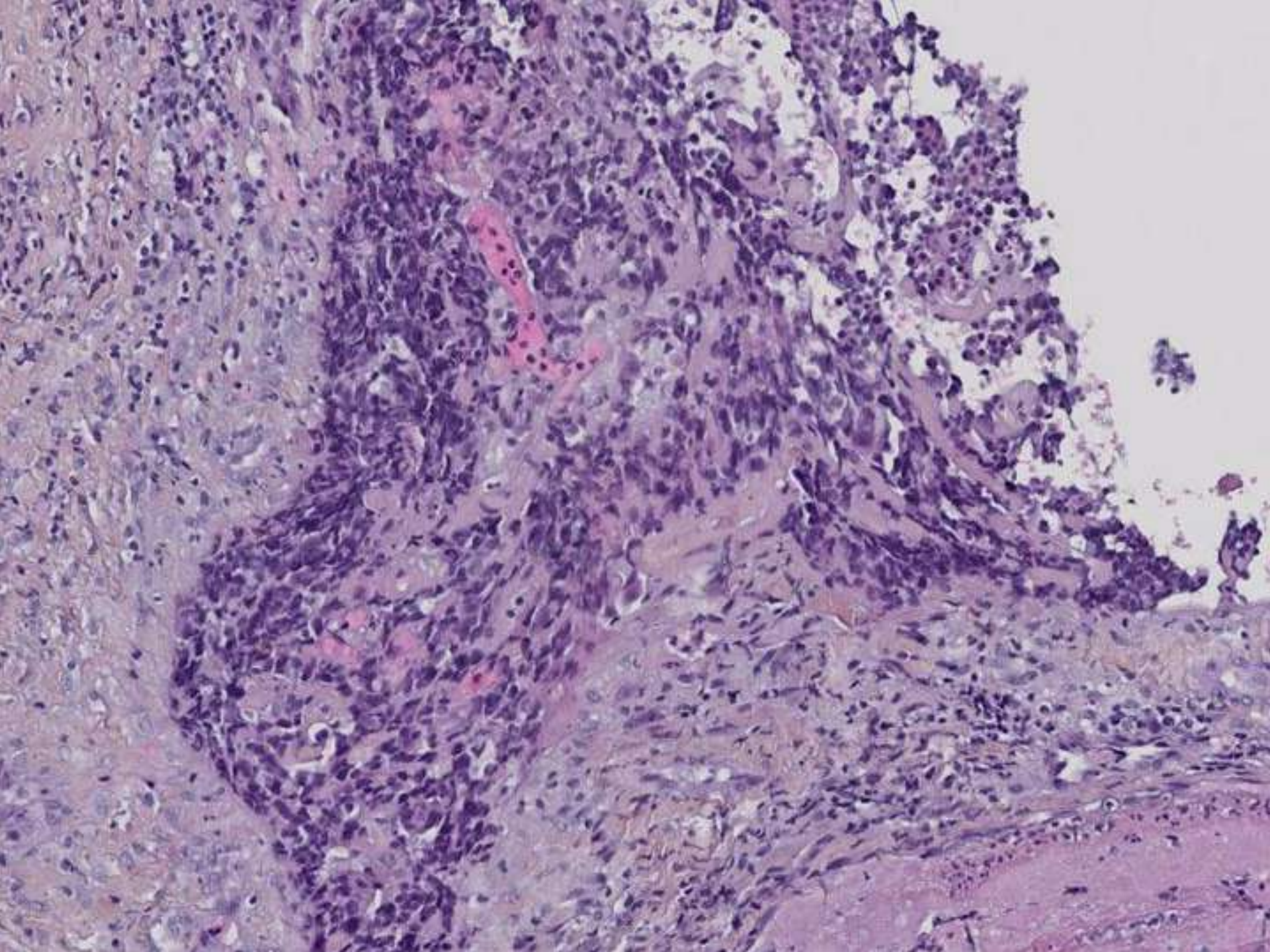
Infection simple par : HPV-16

HPV à haut risque recherchés
HPV à bas risque recherchés

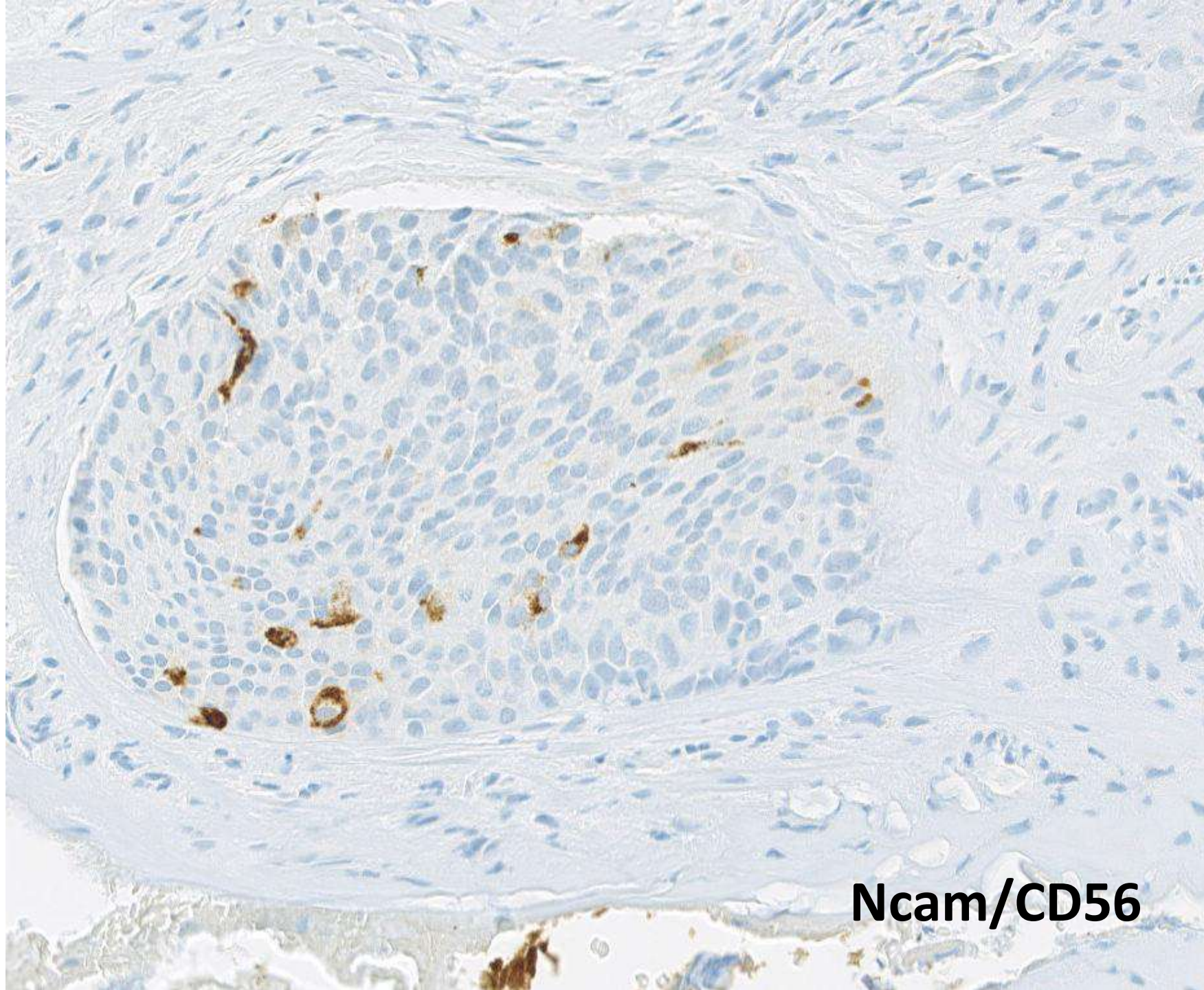
16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 73, 82, 83,
6, 11, 40, 42, 43, 44, 54, 61, 62, 70, 81, 89

Pulmonary biopsies

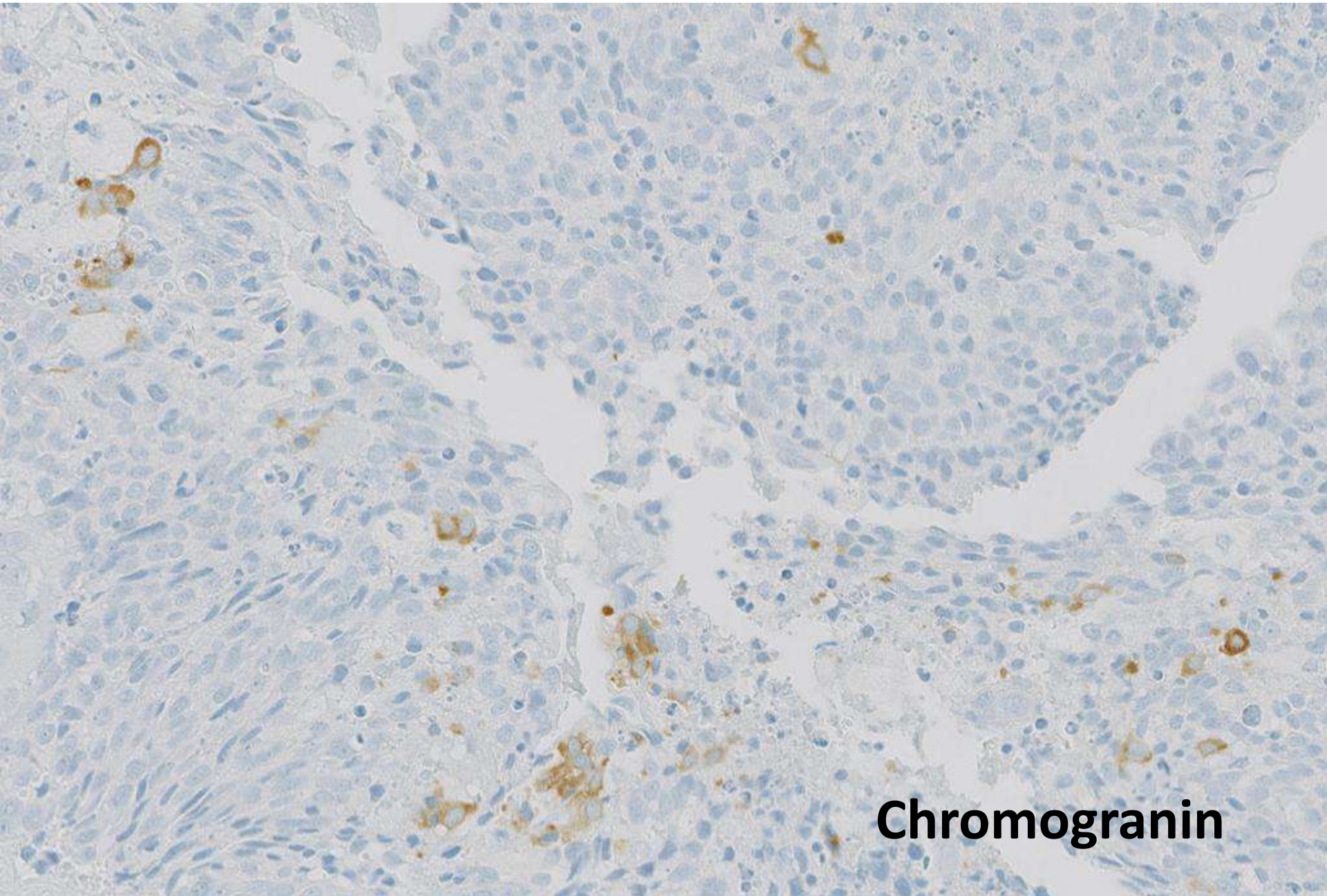




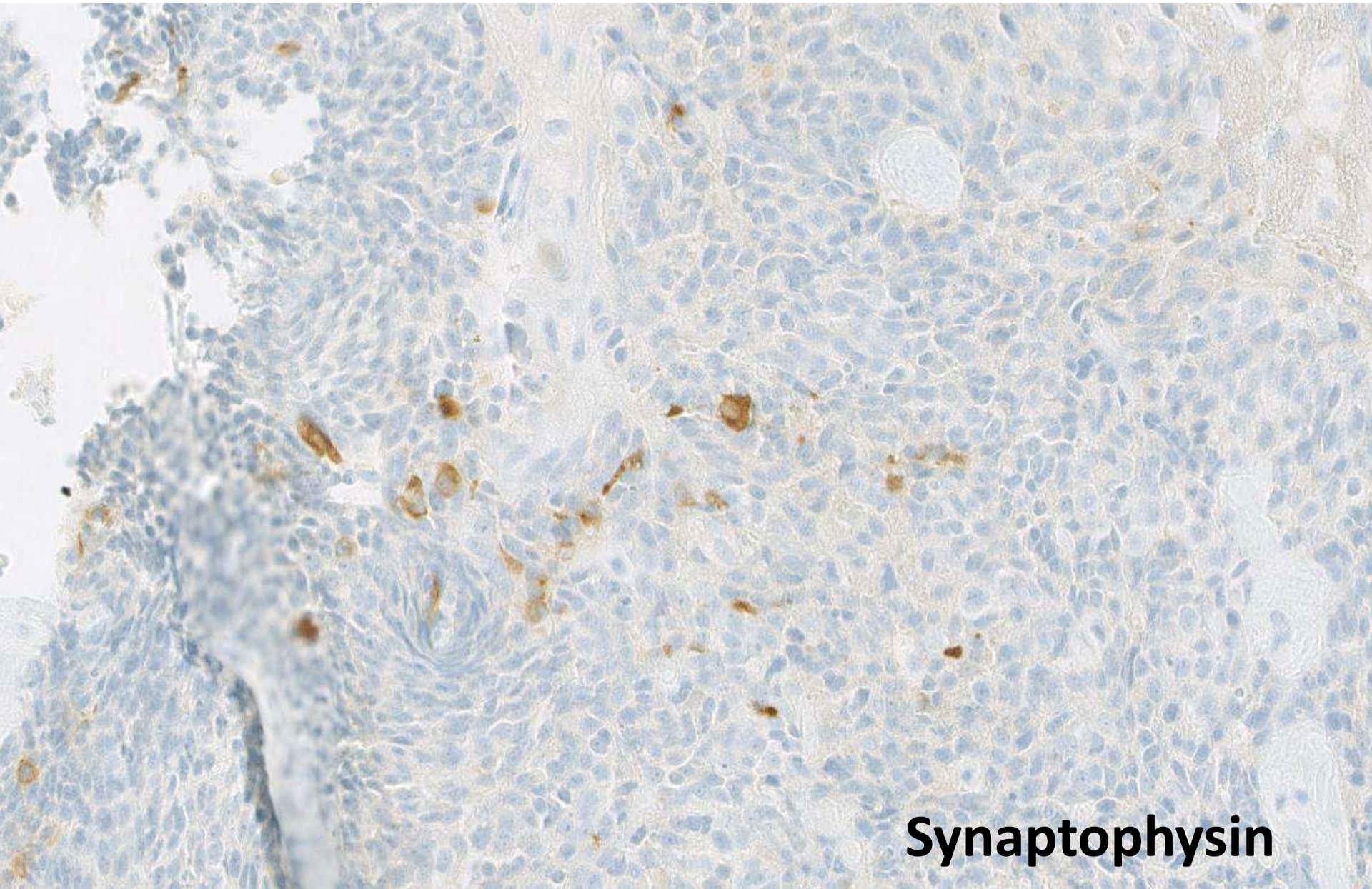
Reevaluation and complementary immunohistochemistry



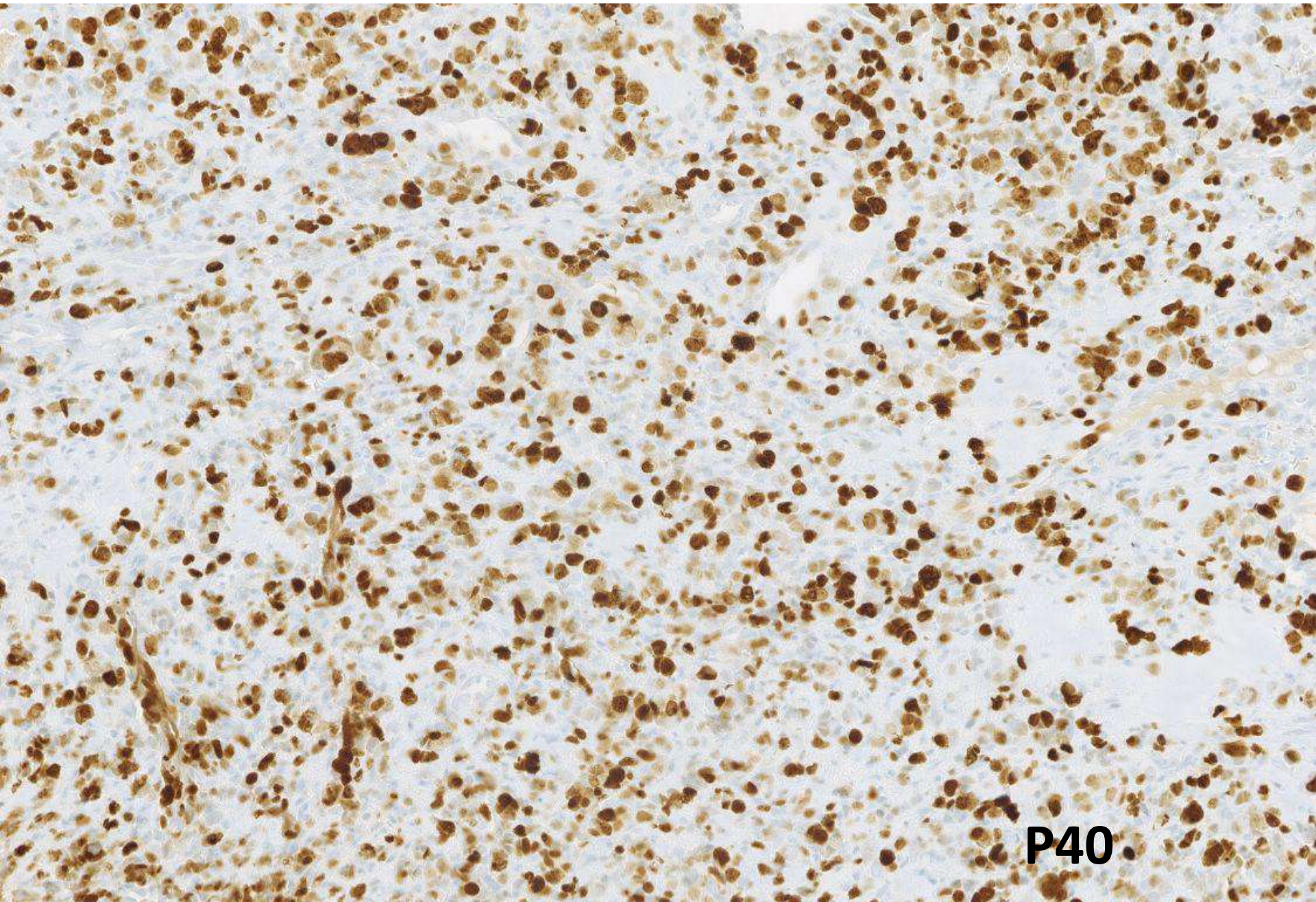
Ncam/CD56



Chromogranin

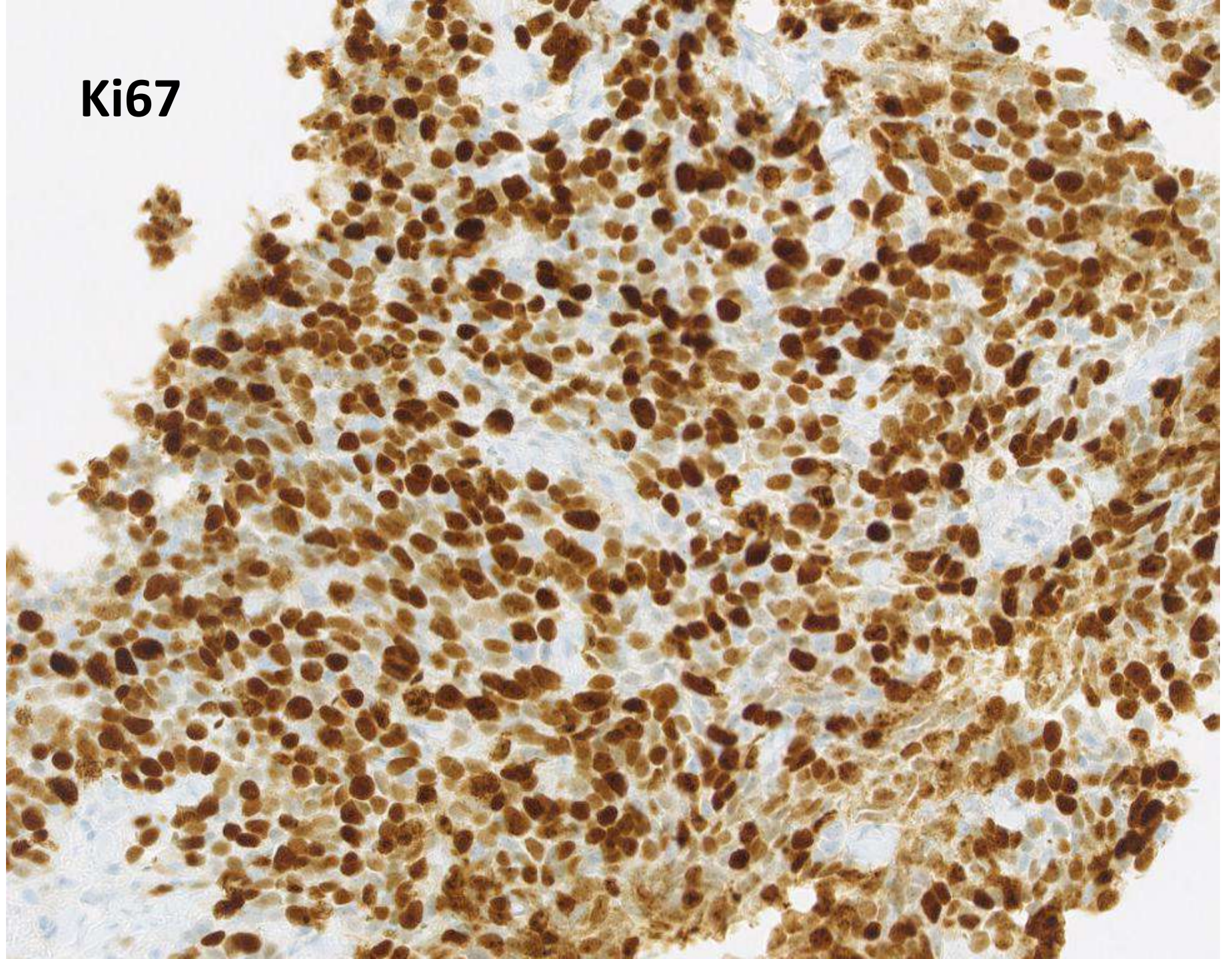


Synaptophysin



P40

Ki67



Terminology

Synonyms

A. Typical carcinoid

Carcinoid, well differentiated (Grade I)
neuroendocrine carcinoma

B. Atypical carcinoid¹

Malignant carcinoid, moderately differentiated
(Grade II) neuroendocrine carcinoma, large cell
neuroendocrine carcinoma¹

C. Small cell carcinoma,
neuroendocrine type²

Small cell neuroendocrine carcinoma,
poorly differentiated (Grade III)
neuroendocrine carcinoma

D. Combined small cell
carcinoma, neuroendocrine
type, with non-small cell
carcinoma (squamous cell
carcinoma, adenocarcinoma, etc.)

Combined small cell carcinoma,
composite small cell carcinoma

E. Paraganglioma

Non-chromaffin paraganglioma

¹Some atypical carcinomas may fulfill the diagnostic criteria of large cell neuroendocrine carcinoma of lung

²Not all small cell carcinomas of the larynx will show neuroendocrine differentiation

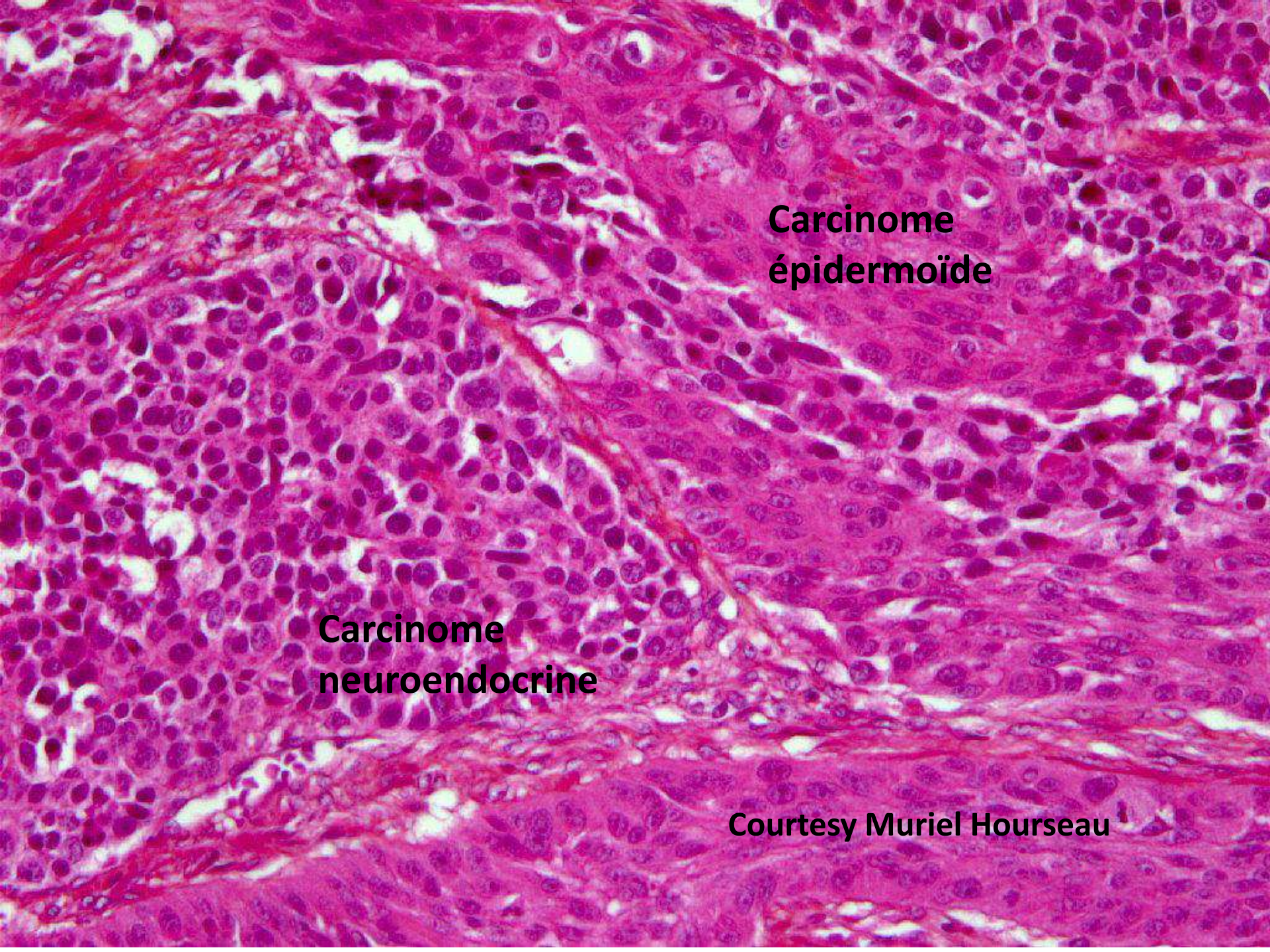
Mixed neuroendocrine-non-neuroendocrine neoplasms

Primary Combined Neuroendocrine and Squamous Cell Carcinoma of the Maxillary Sinus: Report of a Case with Immunohistochemical and Molecular Characterization

Alessandro Franchi • Davide Rocchetta •
Annarita Palomba • Duccio Rossi Degli Innocenti •
Francesca Castiglione • Giuseppe Spinelli

Composite intestinal-type adenocarcinoma and small cell carcinoma of sinonasal tract

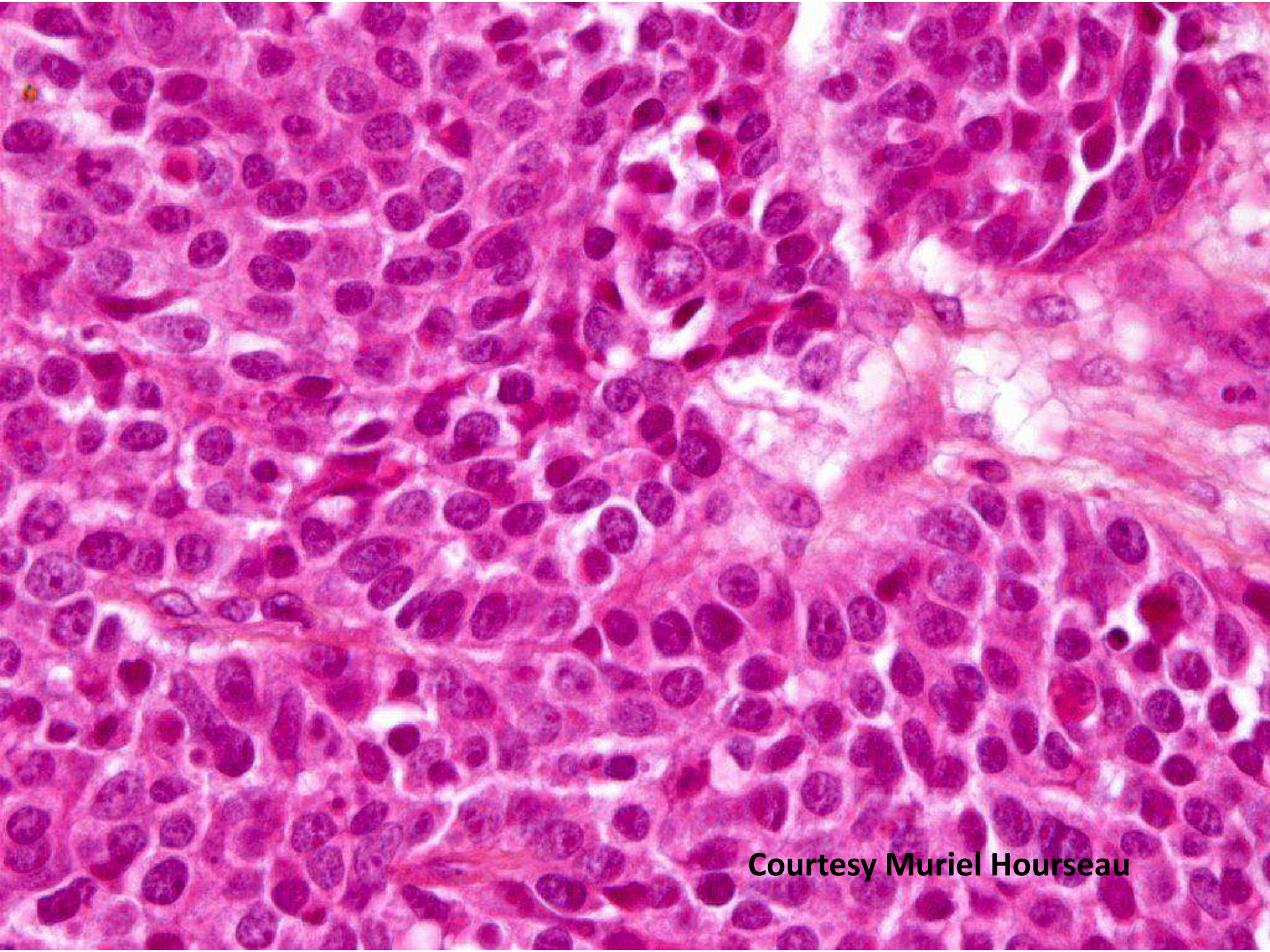
R Jain,¹ V Gramigna,² R Sanchez-Marull,² B Perez-Ordoñez^{1,3}



**Carcinome
épidermoïde**

**Carcinome
neuroendocrine**

Courtesy Muriel Hourseau



Courtesy Muriel Hourseau

HPV and HN carcinomas

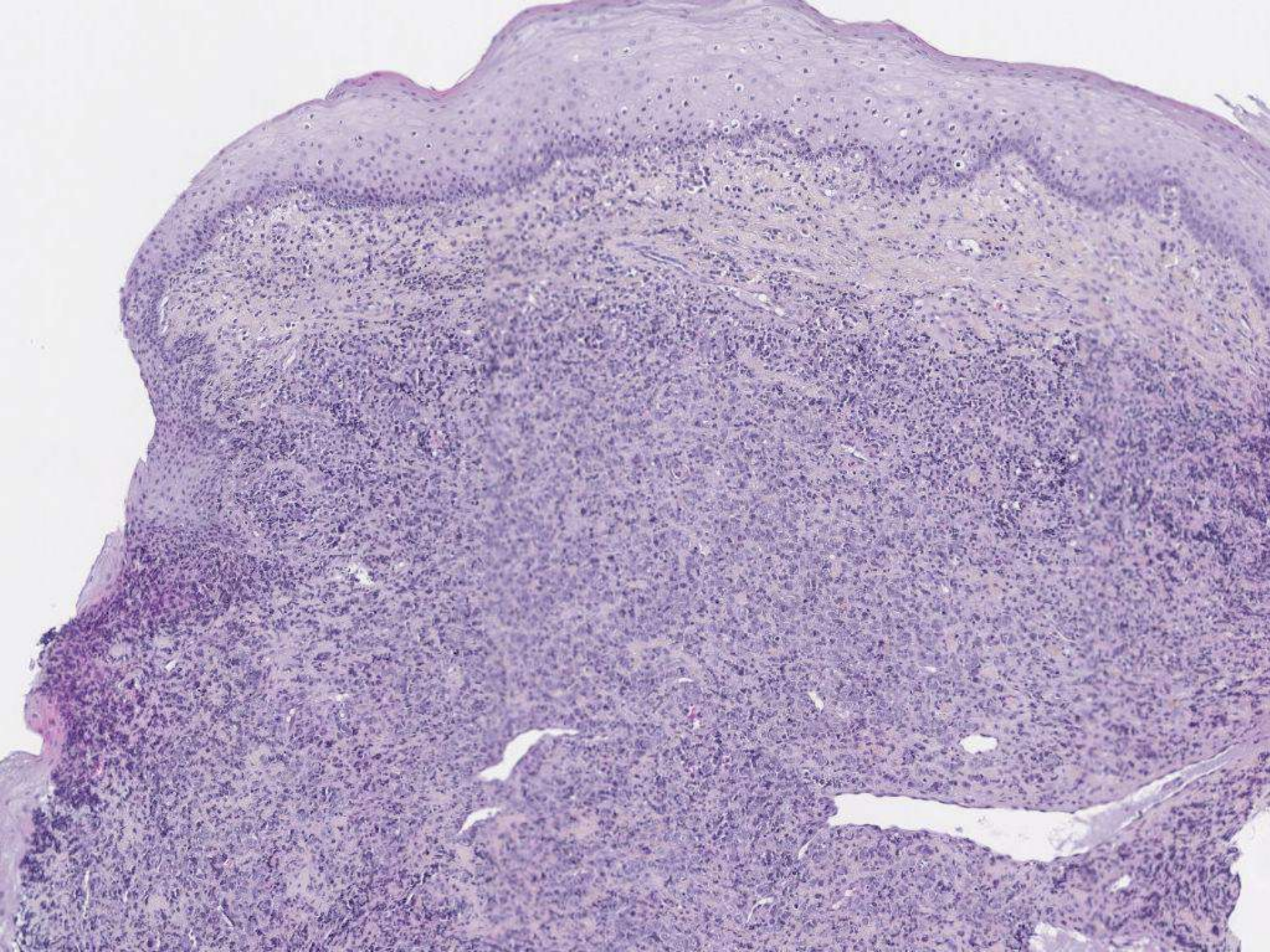
- HPV infection is also found in various sub types of oropharyngeal squamous cell carcinoma such as lymphoepithelial, adenosquamous, papillary ...
- HPV possibly found in other locations than oropharyngeal cancer (5-20%)

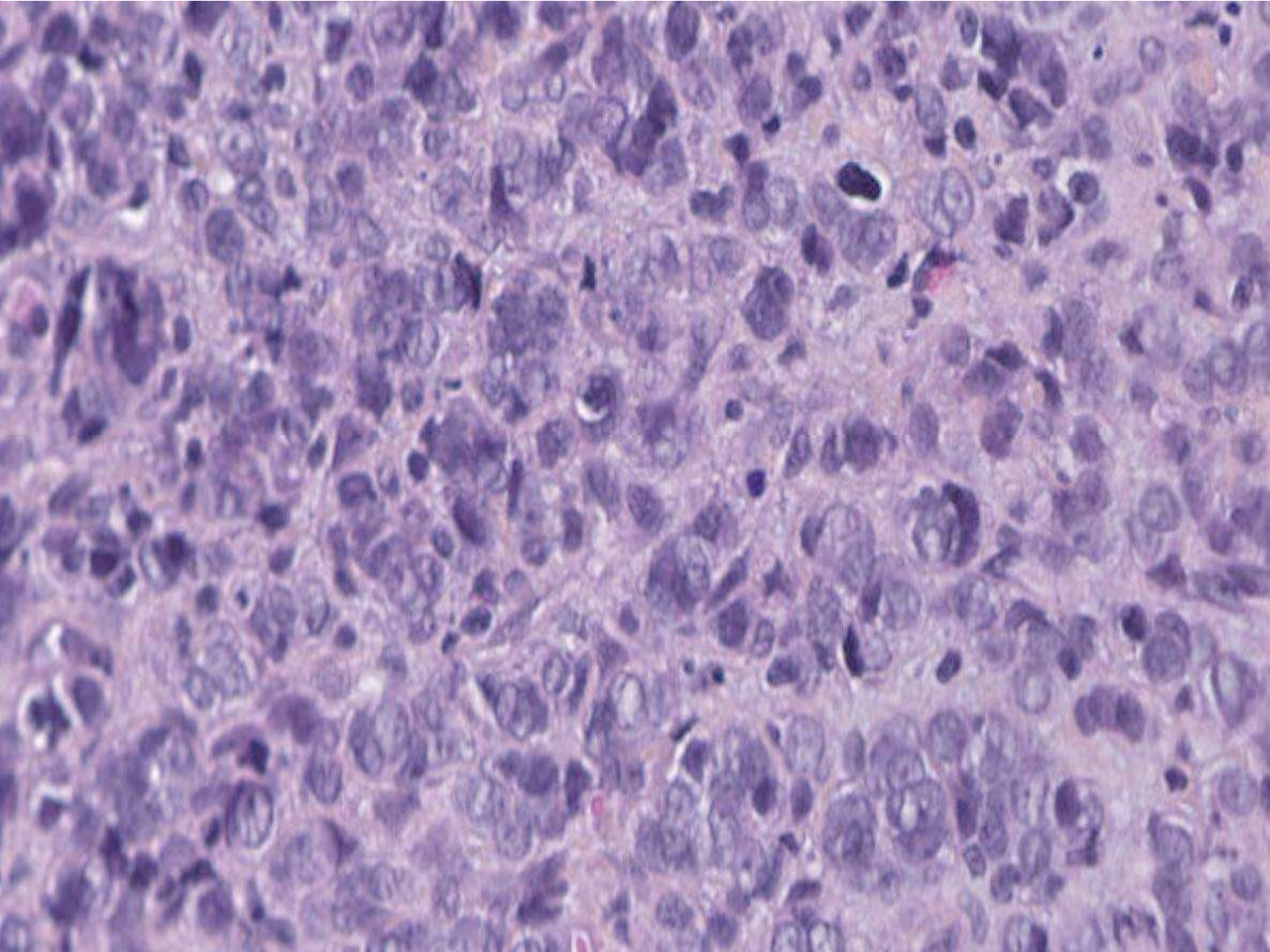


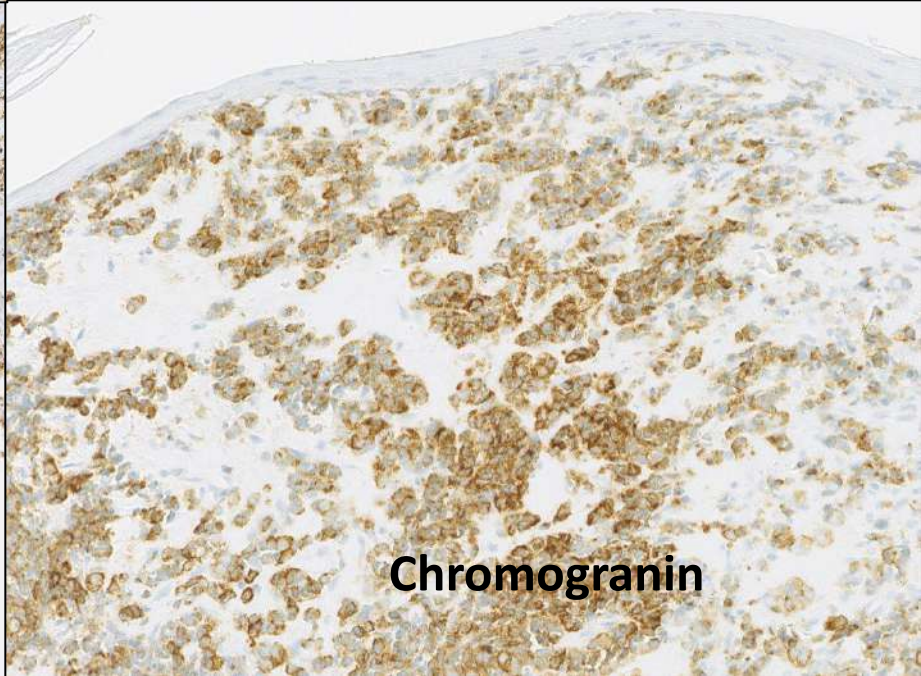
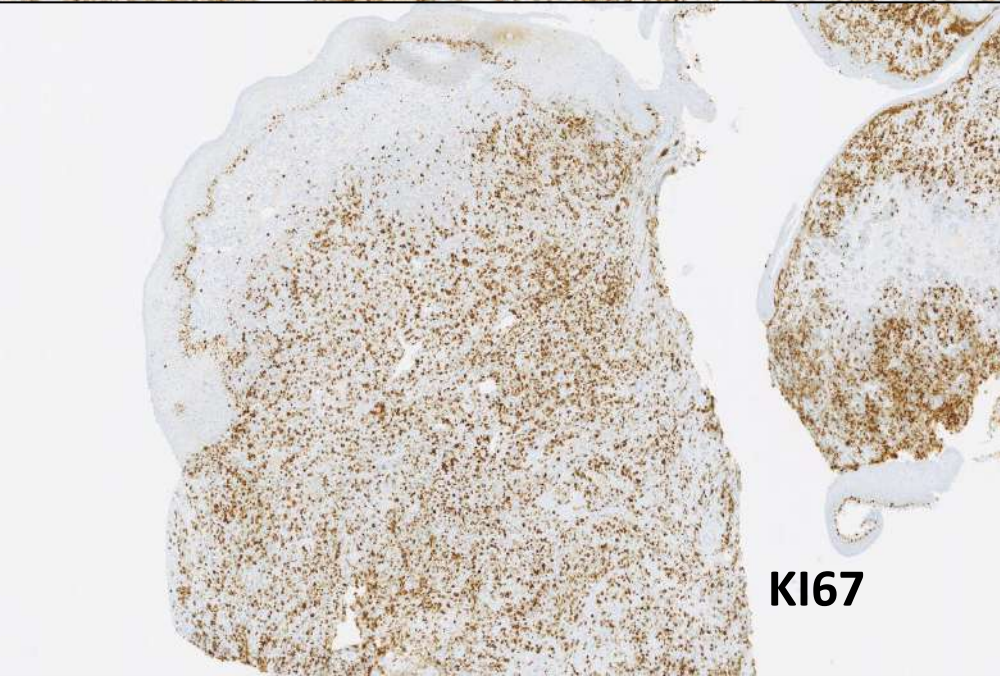
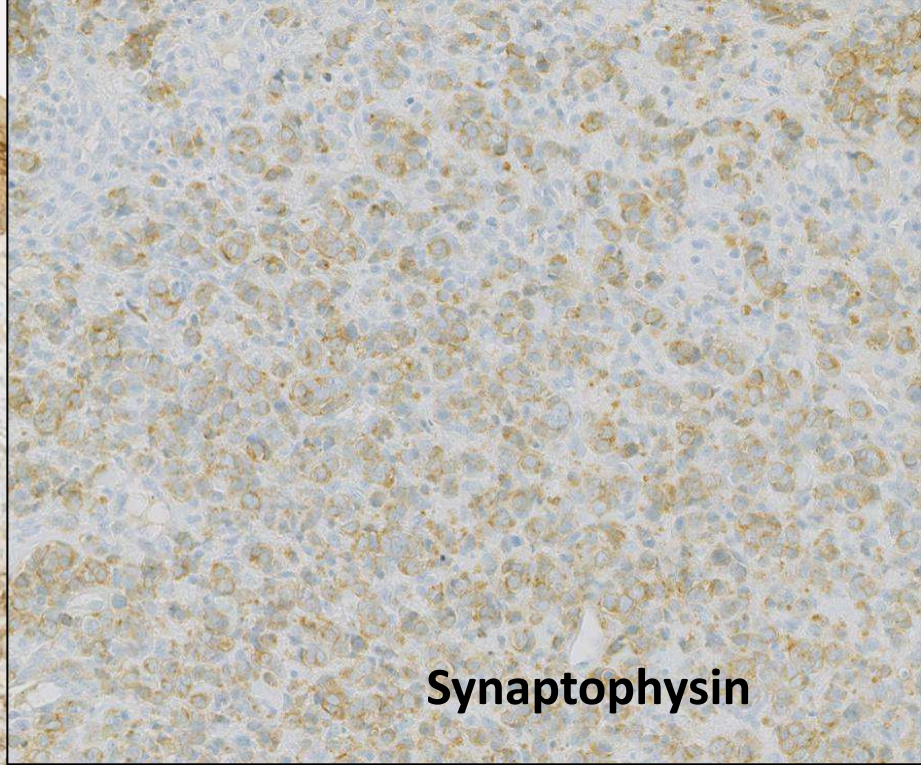
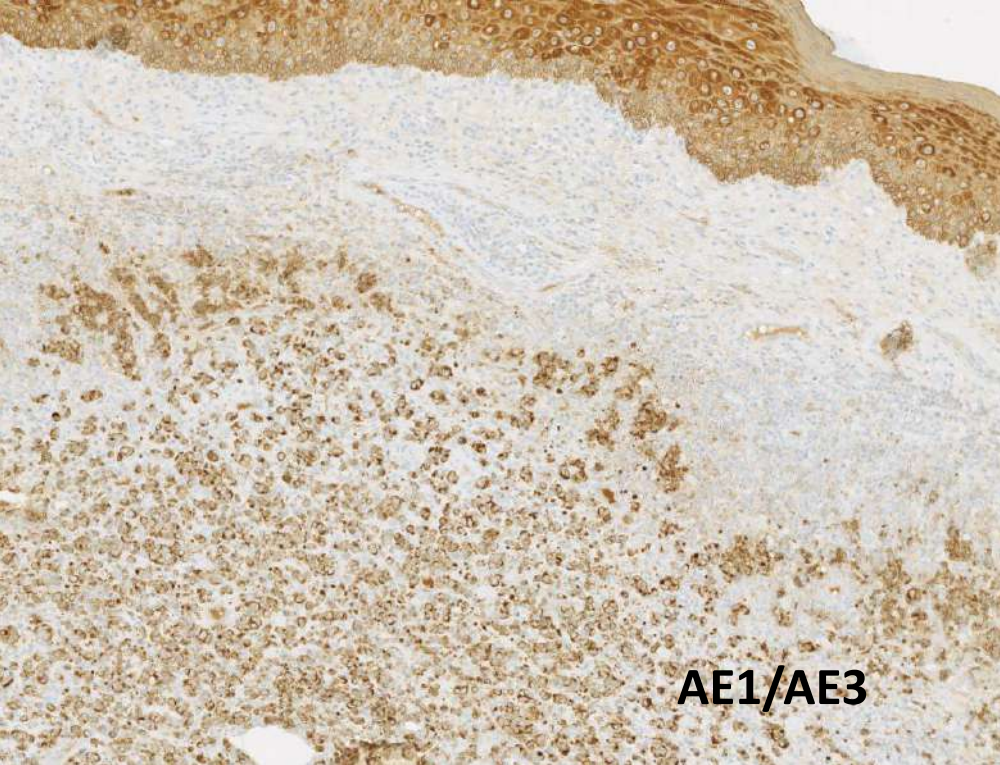
**Carrefour
Pathologie
2016**
Palais des Congrès de Paris

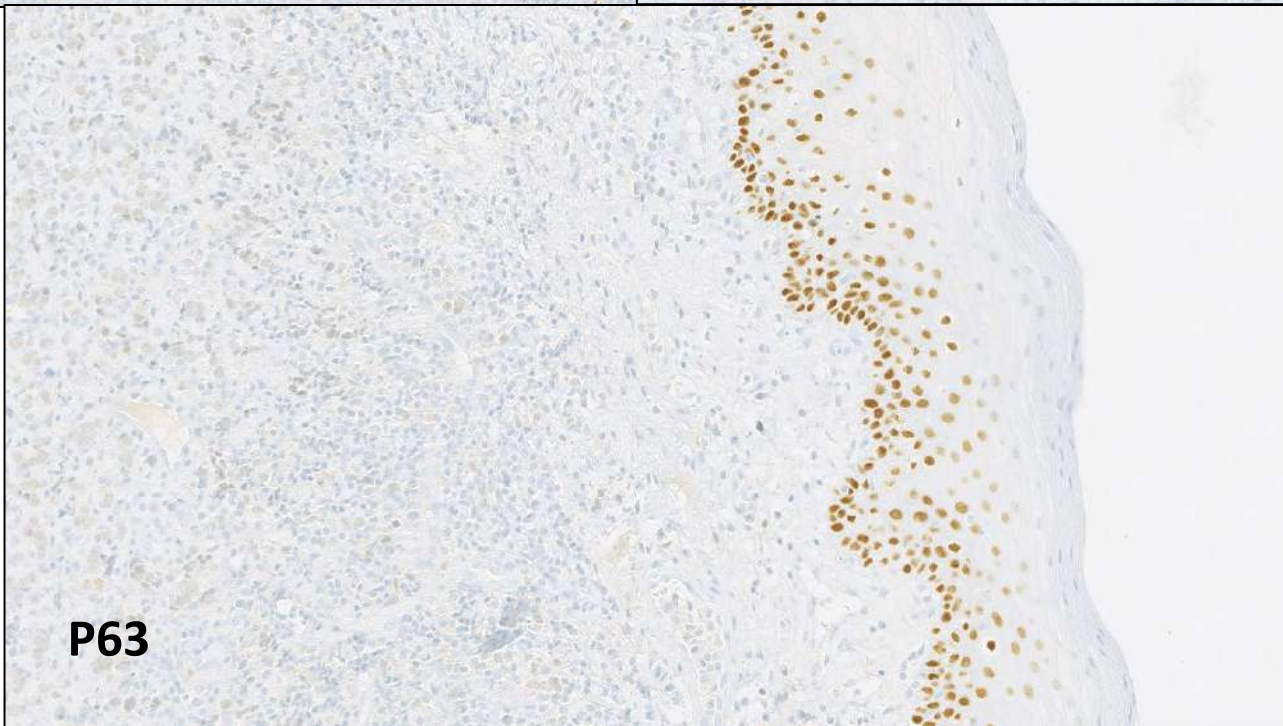
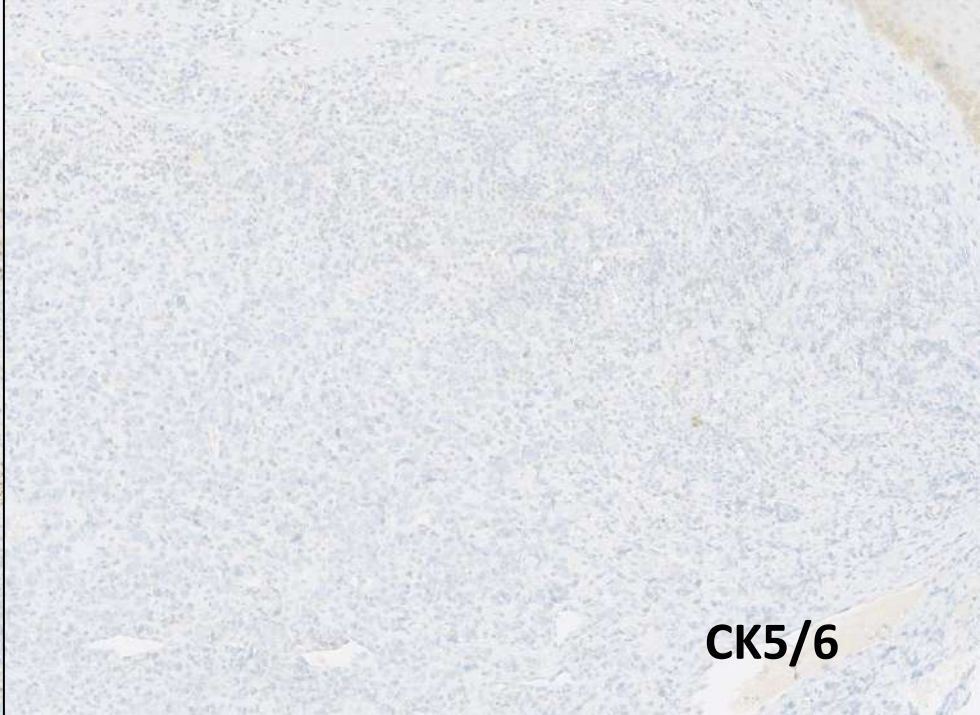
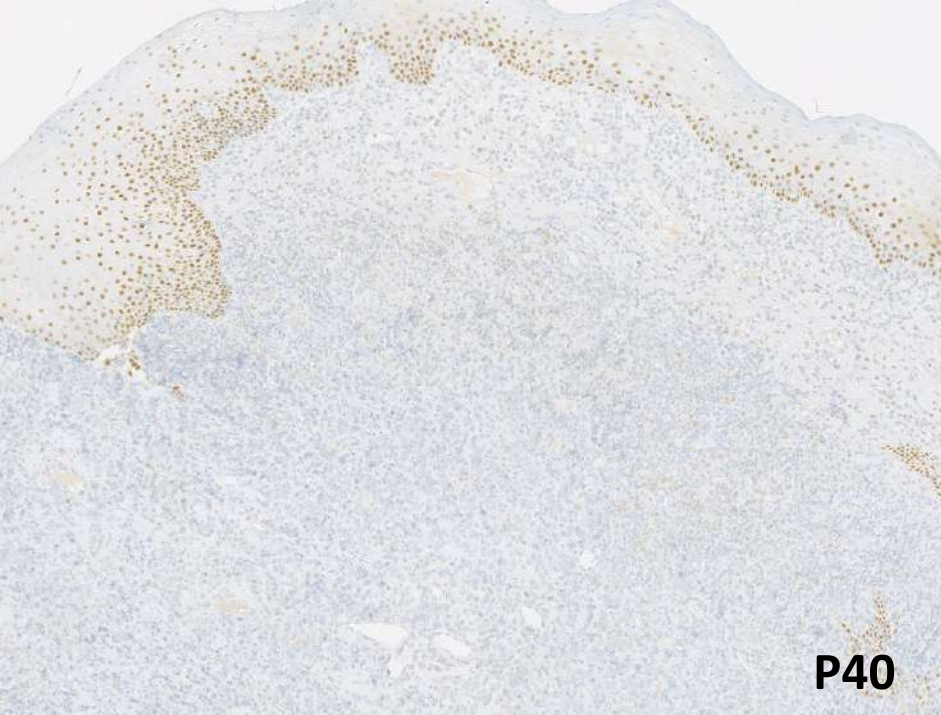


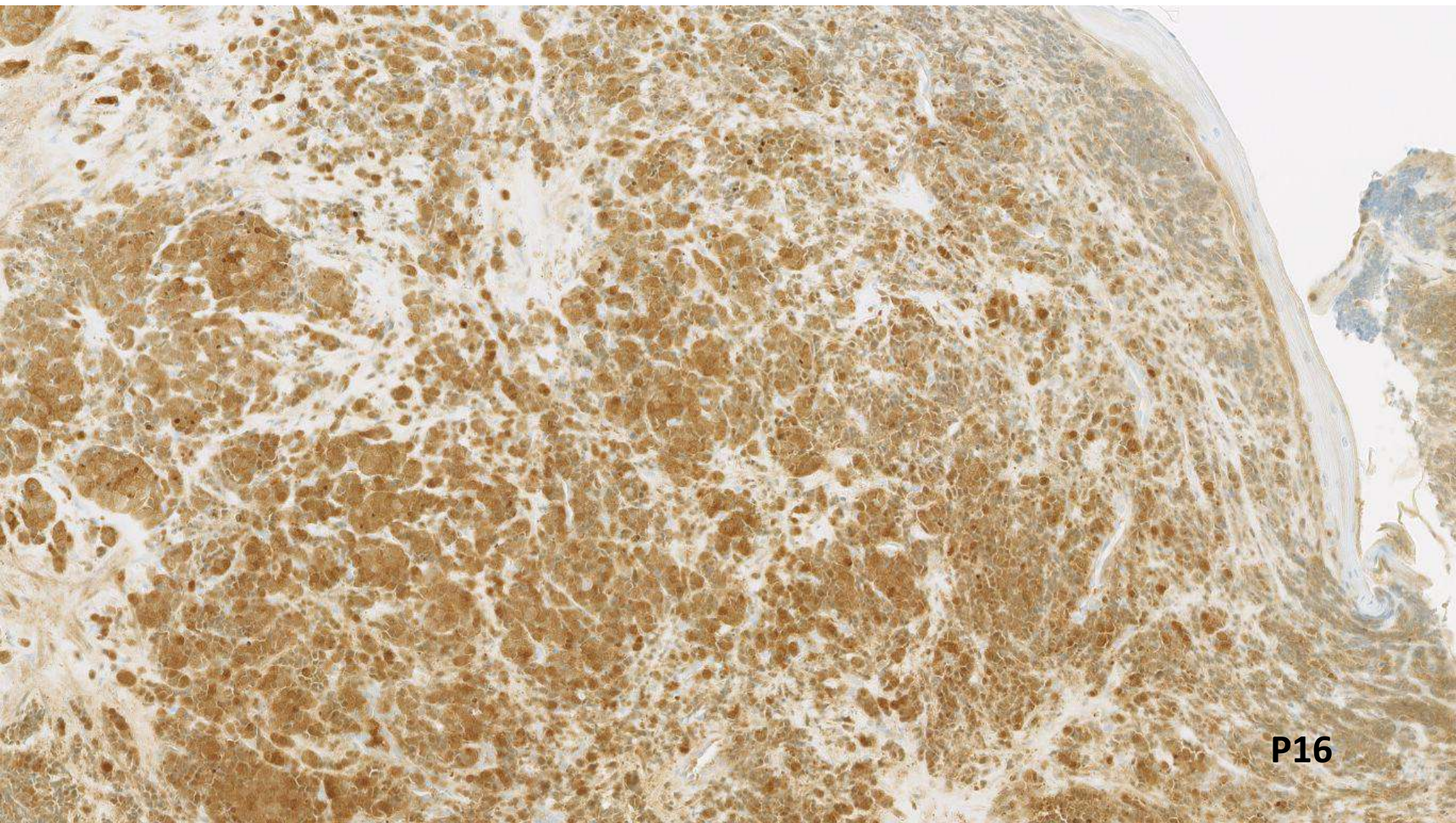
Neuroendocrine carcinoma and HPV?











P16

PCR HPV Innolipa négative

(Am J Surg Pathol 2011;35:1679-1684)

Human Papillomavirus-Related Small Cell Carcinoma of the Oropharynx

Justin A. Bishop, MD and William H. Westra, MD*†*

(Am J Surg Pathol 2012;36:321-330)

HPV-associated Neuroendocrine Carcinoma of the Oropharynx: A Rare New Entity With Potentially Aggressive Clinical Behavior

Stefan Kraft, MD,† William C. Faquin, MD, PhD,* and Jeffrey F. Krane, MD, PhD†*

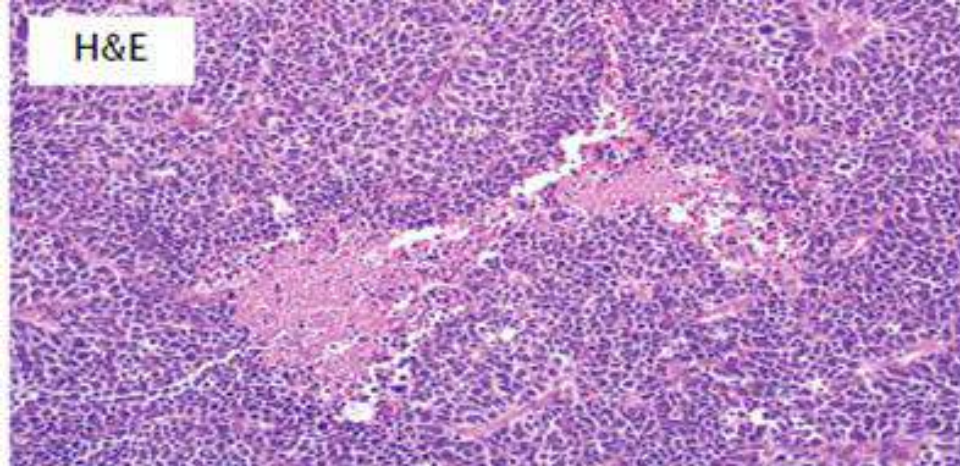
(Am J Surg Pathol 2016;40:471-478)

Large Cell Neuroendocrine Carcinoma of the Head and Neck

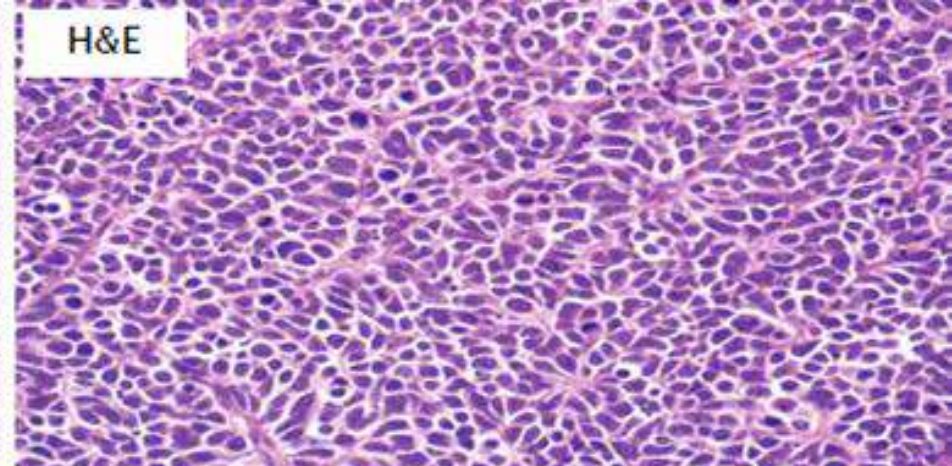
A Clinicopathologic Series of 10 Cases With an Emphasis on HPV Status

Elizabeth D. Thompson, MD, PhD, Edward B. Stelow, MD,† Stacey E. Mills, MD,† William H. Westra, MD,*‡§ and Justin A. Bishop, MD*‡§*

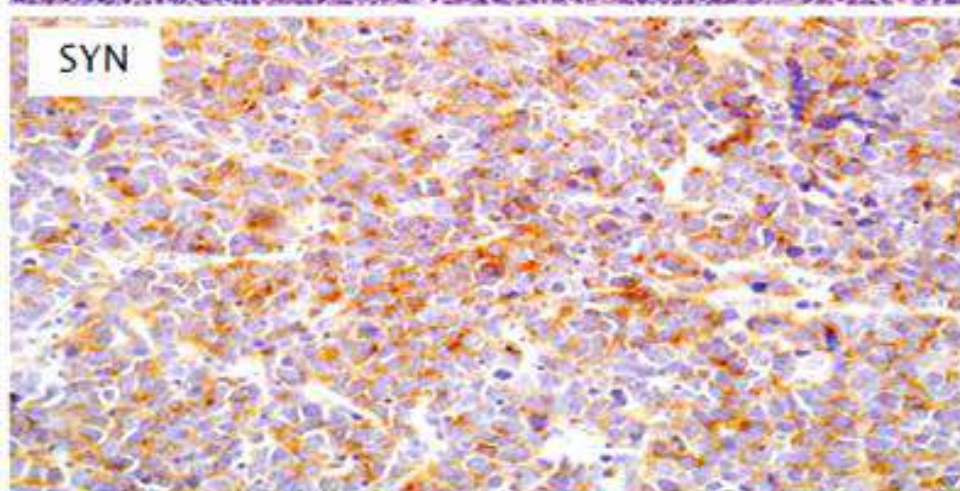
H&E



H&E



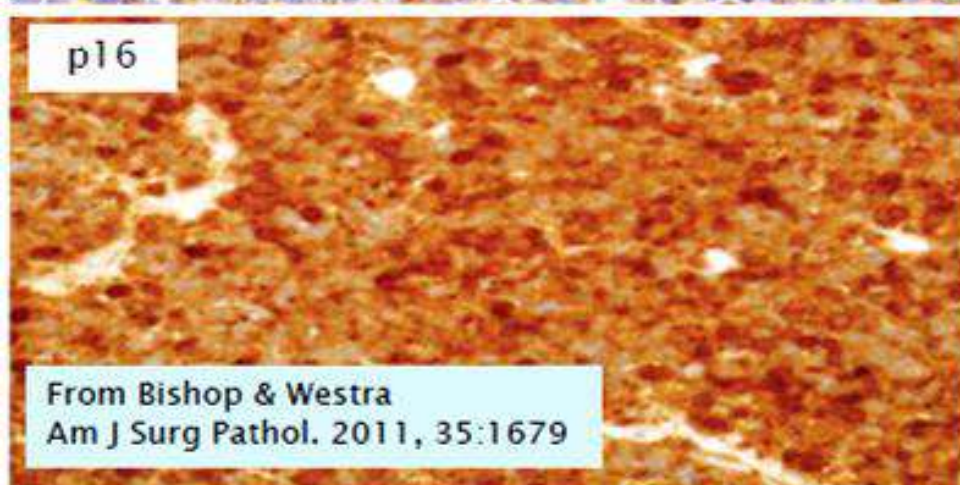
SYN



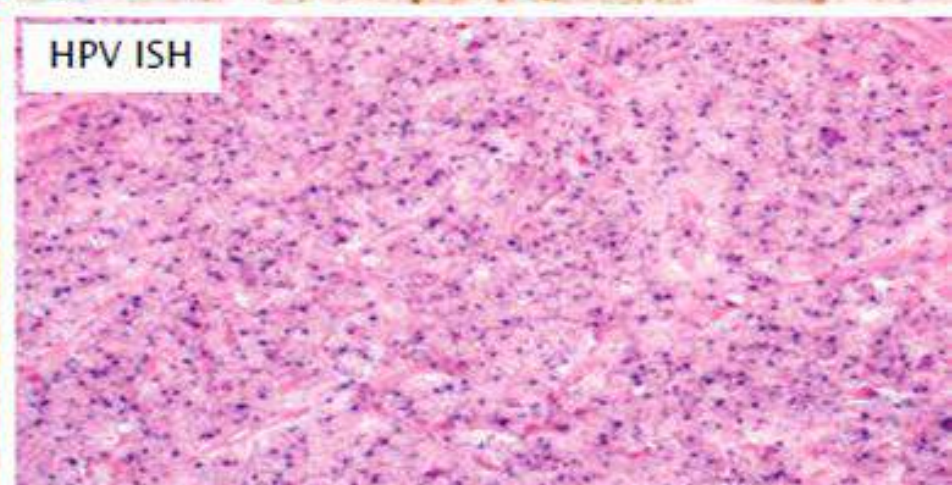
CAM5.2



p16



HPV ISH



From Bishop & Westra
Am J Surg Pathol. 2011, 35:1679

HPV and neuroendocrine carcinomas

- HPV found in cases of small oropharyngeal small cell neuroendocrine carcinoma T Bates, Head and Neck 2014; C Hojilla, Diag histopathology 2013; Bishop J, Am J Surg Pathol 2011; Kraft S, Am J Surg Pathol 2012
- But also in large cell neuroendocrine carcinomas

TABLE 2. In Situ Hybridization and Immunohistochemical Findings in HPV-related LCNECs of the Head and Neck

Case No	CK	p63	CK5/6	Synaptophysin	Chromogranin	TTF-1	CD56	p16	HPV ISH
1	+	-	-	+	-	-	+	+	+
2	+	-	-	+	-	-	-	+	+
3	+	-	+	+	+	-	ND	+	+
4	+	-	-	Focal +	-	-	+	-	ND
5	+	+ (in SqCC)	+ (in SqCC)	+	+	-	Focal +	-	ND
6	+	+ (in SqCC)	+ (in SqCC)	-	-	-	+	+	-
7	+	-	-	+	-	-	-	+	-
8	+	Focal +	ND	+	-	-	+	-	ND
9	+	Focal +	-	+	-	-	-	-	-
10	+	-	ND	+	+	-	ND	+	-

CK indicates cytokeratin; focal, immunostaining in $\leq 5\%$ of cells; ISH, in situ hybridization; ND, not done; SqCC, squamous cell carcinoma.

Table 1 Immunophenotype of high-grade neuroendocrine carcinomas of the head and neck

Case	Tumor site	Cell type	Cytokeratins			Neuroendocrine markers			Cell cycle proteins						
			AE1/AE3	CK7	CK20	Chro	Syn	NF	CD56	p63	Ki67	p53	p16	Rb	CyD1
1	Oropharynx	SC	+++	-	+++	-	+++	-	+++	-	+++	+++	+++	-	-
2	Larynx	LC	+++	+++	+	+	-	+++	+++	-	+++	+++	+++	++	-
3	Larynx	LC	+++	+++	-	+++	+++	-	-	-	+++	+++	+	++	+++
4	Larynx	LC	+++	-	-	+++	+++	-	+++	-	+++	+++	+	++	++
5	Larynx	SC	+++	-	-	+++	+++	-	+++	-	+++	+++	+++	-	-
6	Larynx	LC	+++	+++	+++	+++	+++	+	+++	+	+++	+++	+++	+	-
7	Larynx	SC + SCC	+++	+	+++	+++	+++	-	++	-	+++	+++	+	++	+++
8	Larynx	SC + SCC	+++	+	++	+	++	-	++	+++	+++	+++	++	+++	+++
9	Frontal sinus	LC	+++	+	+++	+++	+++	-	+++	+++	+++	+++	++	++	+++
10	Nasal Cavity	SC	+++	-	-	+++	-	-	+++	-	+++	+++	+++	-	+
11	Nasal Cavity	SC	+++	-	-	+	+	-	++	-	+++	+++	+++	++	+
12	Nasal Cavity	SC	+++	-	-	+++	+++	-	+++	-	+++	+++	+++	++	+
13	Nasal Cavity	SC	+++	-	-	+	+++	-	+++	-	+++	+++	+++	-	-
14	Parotid gland	SC	+++	-	-	-	+++	+	+++	+++	+++	+++	+++	-	-
15	Parotid gland	SC	+++	+++	-	+++	+++	+++	+++	-	+++	+++	+++	-	-
16	Parotid gland	SC	+++	-	+++	-	+++	+++	+++	-	+++	+++	+++	-	-
17	Parotid gland	SC	+++	-	+++	+++	+++	+++	+++	-	+++	+++	+++	-	-
18	Parotid gland	SC	+++	-	+++	-	+	+++	+++	-	+++	+++	+++	-	-
19	Parotid gland	SC	+++	-	-	+++	+++	-	+++	-	+++	+++	+++	-	-

LC large cell, SC small cell, SCC squamous cell carcinoma, Chro chromogranin, Syn synaptophysin, NF neurofilaments, Rb retinoblastoma, CyD1 cyclin D1

High grade neuroendocrine carcinoma of the head and neck

```
graph TD; A[High grade neuroendocrine carcinoma of the head and neck] --> B[Small cell carcinoma]; A --> C[Large cell neuroendocrine carcinoma];
```

Small cell carcinoma

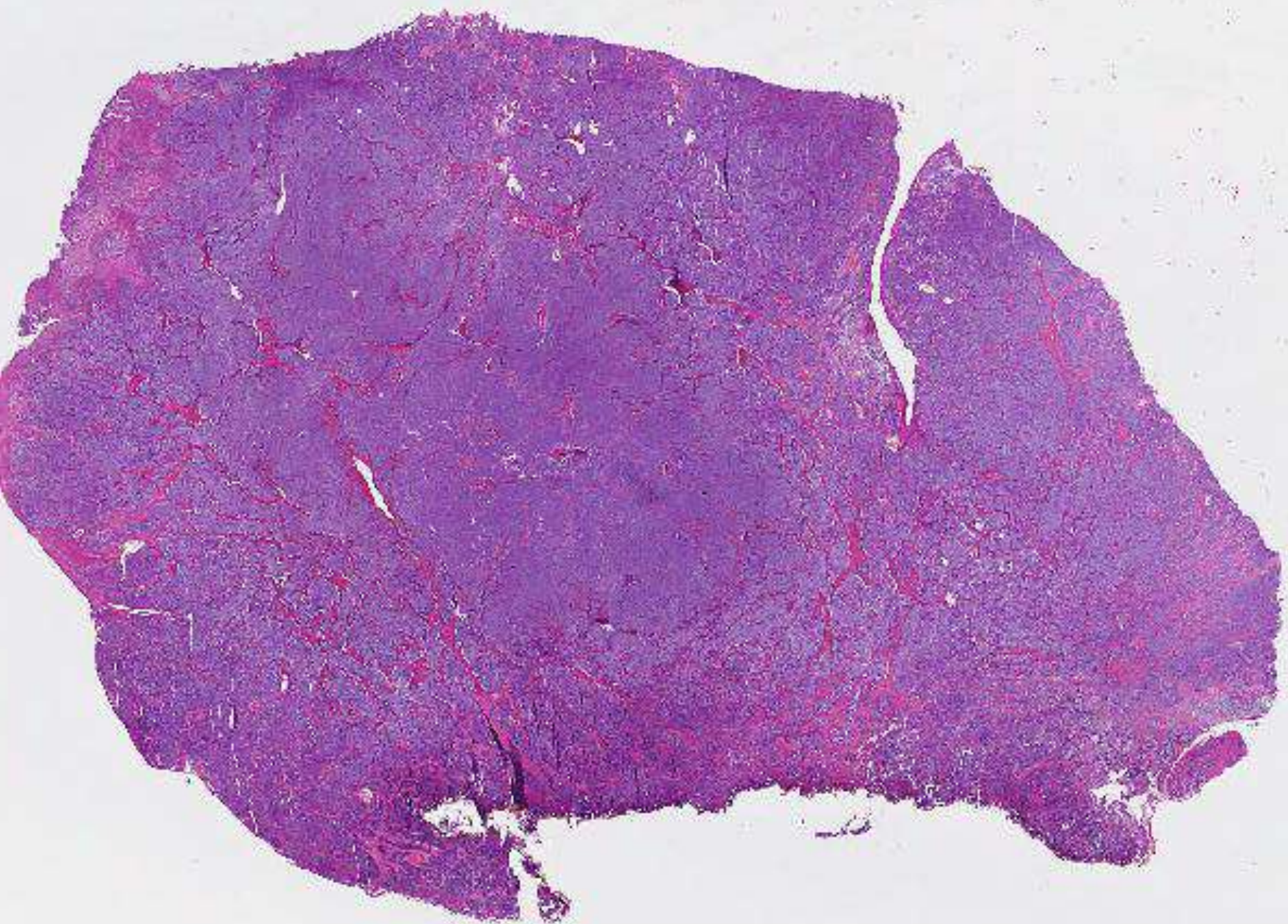
- Usually arise in larynx, but can occur in sinonasal tract, oral cavity and oropharynx
- Morphologically identical to counterpart in the lung
- Express markers of neuroendocrine differentiation
- Highly aggressive with rapid disease progression
- *Can be HPV positive when arising in the oropharynx or sinonasal tract*

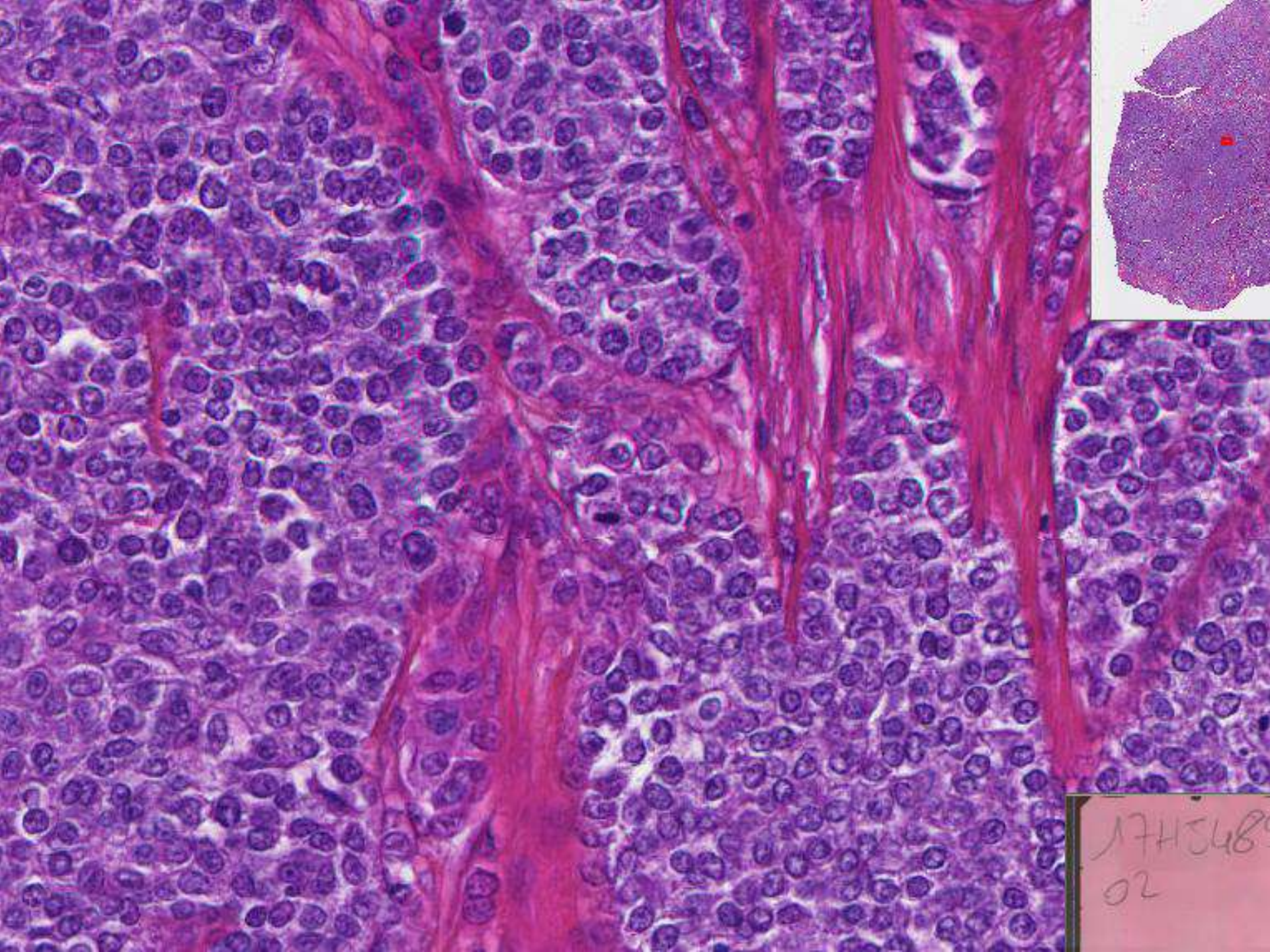
Large cell neuroendocrine carcinoma

- Usually arise in the larynx, but can occur in sinonasal tract, oral cavity and oropharynx
- Morphologically identical to counterpart in the lung
- Express markers of neuroendocrine differentiation
- Highly aggressive with rapid disease progression
- *Can be HPV positive when arising in the oropharynx or sinonasal tract*

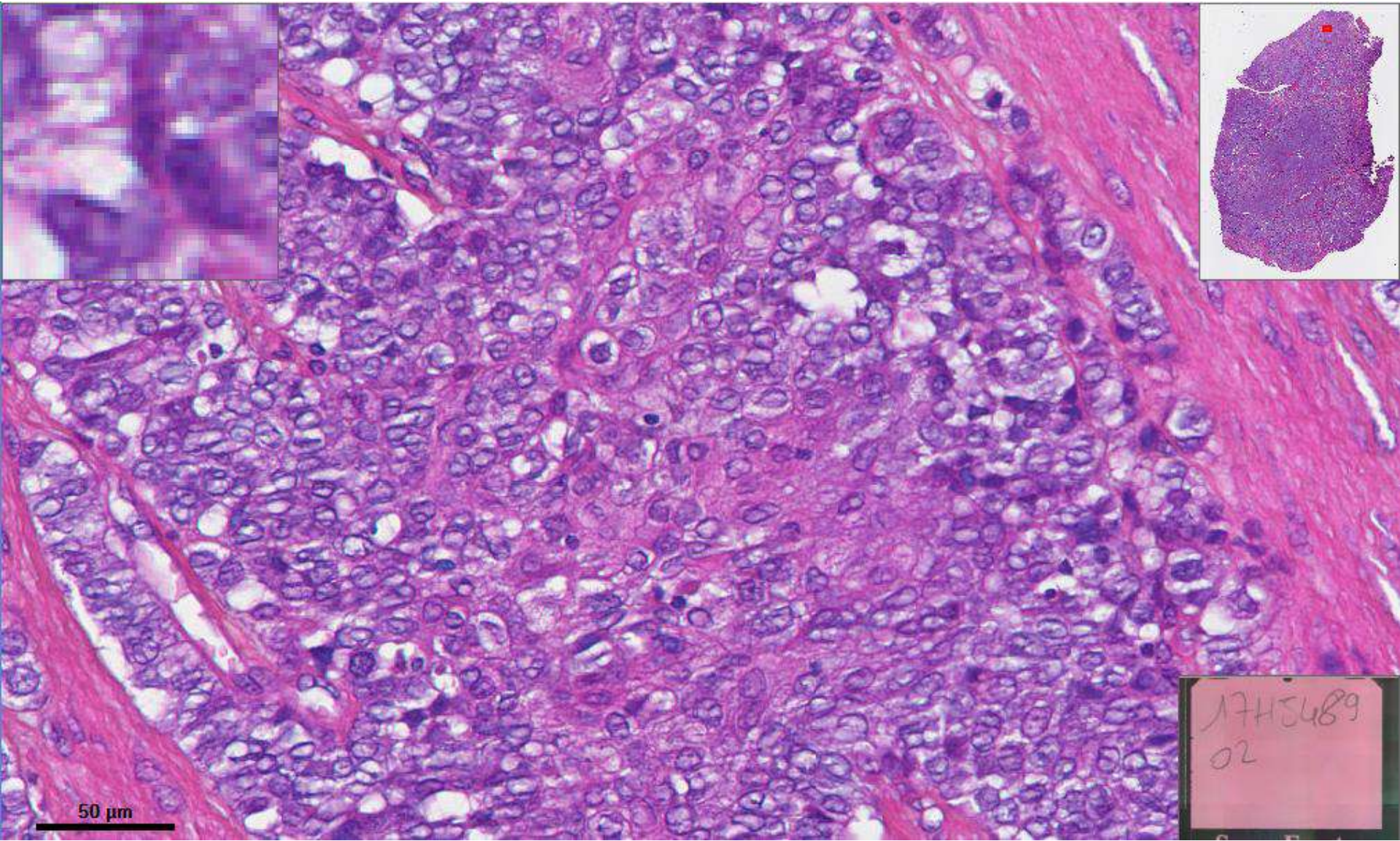
Case 1E

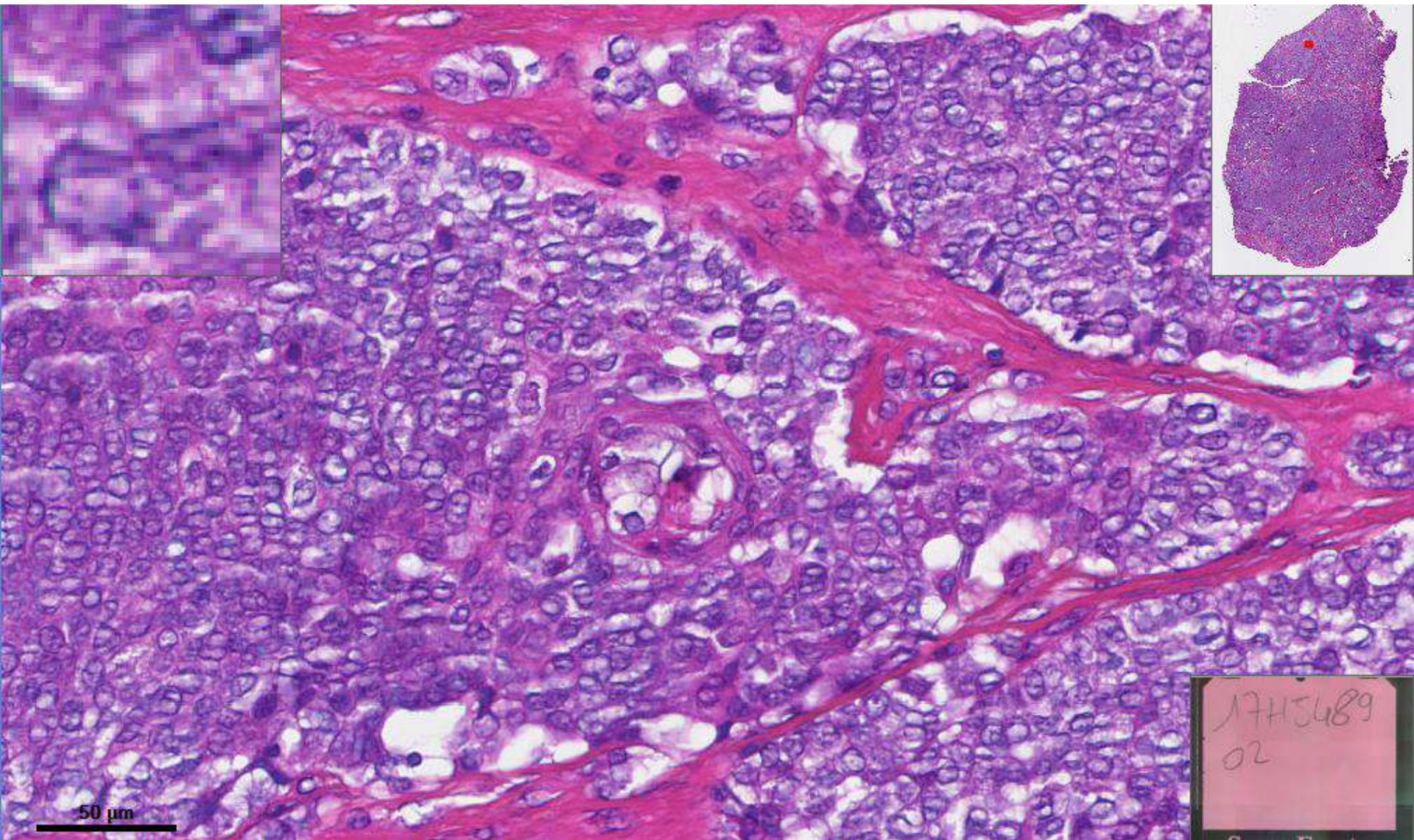
Woman 49 yo nasal cavity





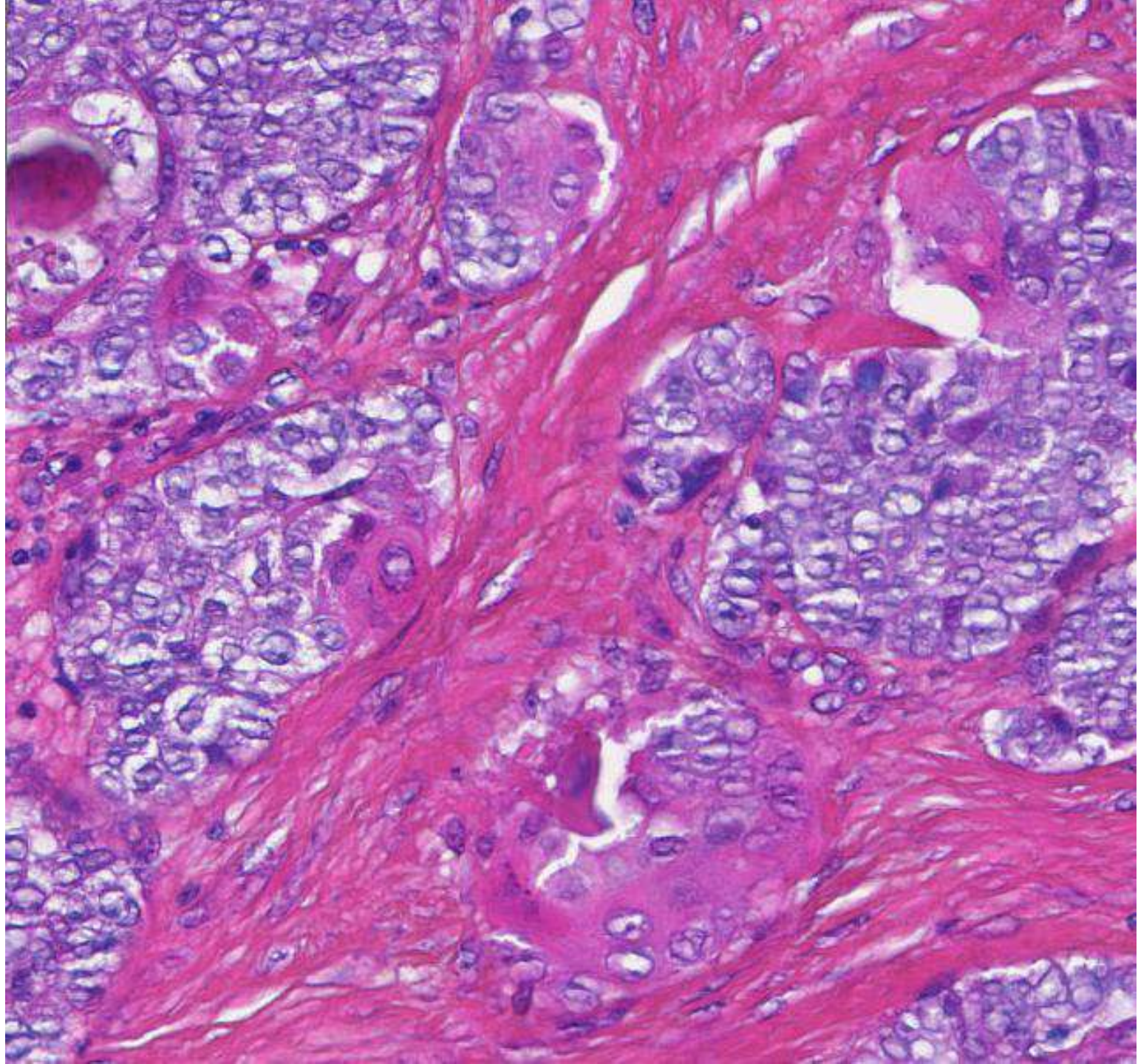
17H548
02





50 μ m

17H5689
02



NUT carcinomas

- Represents a rare subset of highly aggressive poorly differentiated carcinomas
- Characterized by rearrangement of the NUT (aka NUTM1, nuclear protein in testis) gene, most commonly fused to BRD4.
- Originally described as a mediastinal/thymic malignancy, NC has been reported in the upper and lower aerodigestive tract and rarely in intra-abdominal organs.
- Patients are mainly young adults but the age range varies from the new-born to the elderly.
- Originally considered strictly a neoplasm related to midline structures, recent case reports described this rare disease in lateralized organs (lungs and parotid gland).
- WHO has changed the name from NUTmidline carcinoma to NC

RESEARCH ARTICLE

NSD3-NUT Fusion Oncoprotein in NUT Midline Carcinoma: Implications for a Novel Oncogenic Mechanism

Christopher A. French¹, Shaila Rahman², Erica M. Walsh¹, Simone Kühnle², Adlai R. Grayson¹, Madeleine E. Lemieux⁹, Noam Grunfeld¹, Brian P. Rubin^{3,4,5}, Cristina R. Antonescu⁶, Songlin Zhang⁷, Rajkumar Venkatramani⁸, Paola Dal Cin¹, and Peter M. Howley²

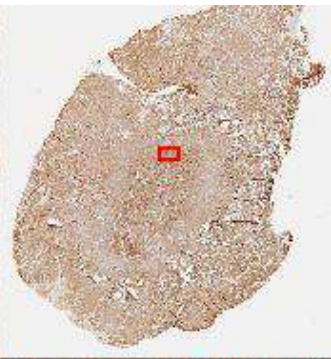
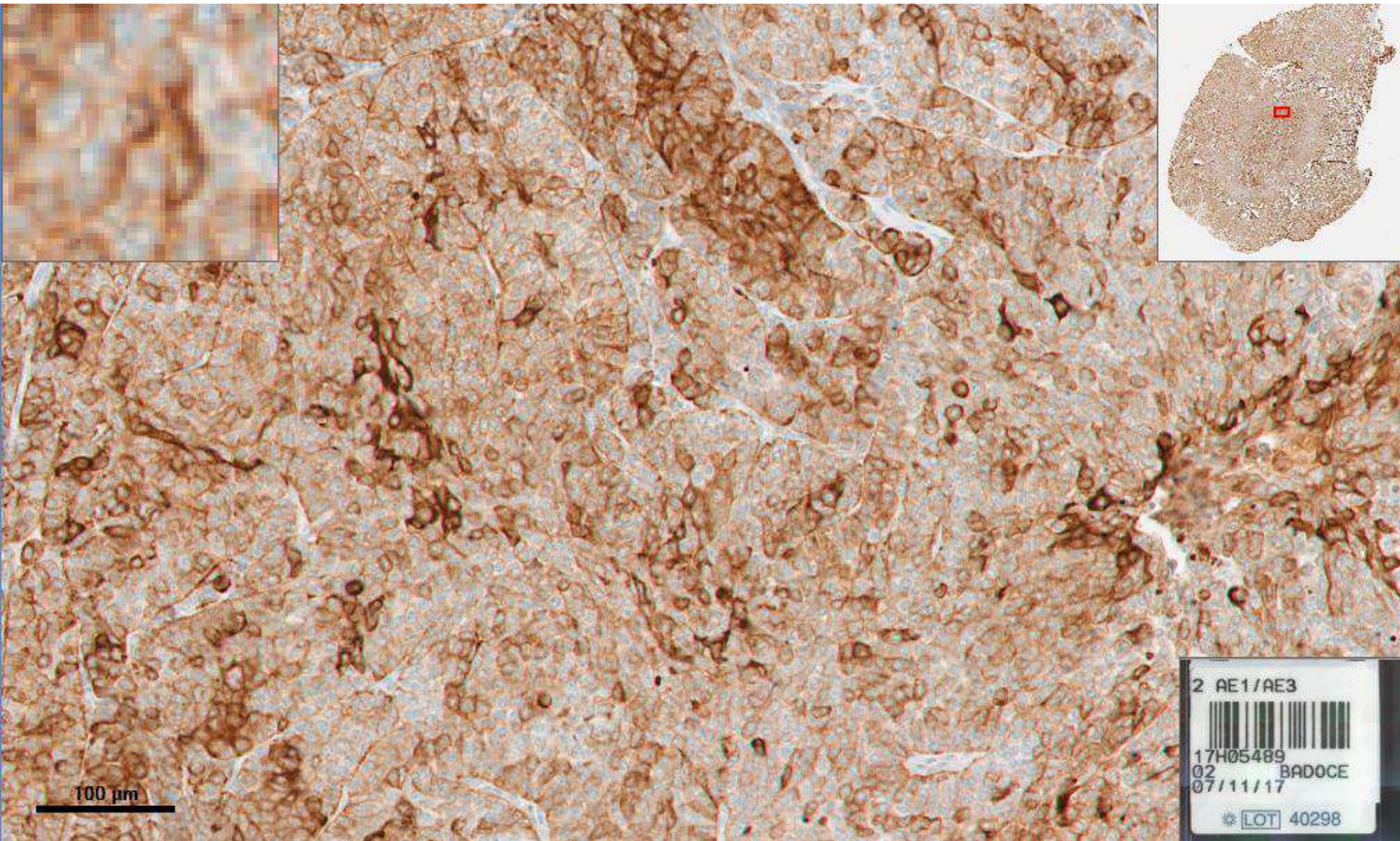
NUT Carcinoma of the Salivary Glands

Clinicopathologic and Molecular Analysis of 3 Cases and a Survey of NUT Expression in Salivary Gland Carcinomas

Abbas Agaimy, MD, Isabel Fonseca, MD,†‡ Carmo Martins, BSc, PhD,§ Khin Thway, MD,|| Ryan Barrette, BSc,¶ Kevin J. Harrington, BSc, MBBS, FRCP, FRCR, PhD,#** Arndt Hartmann, MD,* Christopher A. French, MD,¶ and Cyril Fisher, MD||*

Histologic examination

- Poorly differentiated neoplasms composed of poorly cohesive small sized to medium-sized cells with variable squamoid cell component that is focal and abrupt
- Immunohistochemistry :uniform expression of p63 and distinctive punctate expression of the NUT antigen in the tumor cell nuclei.

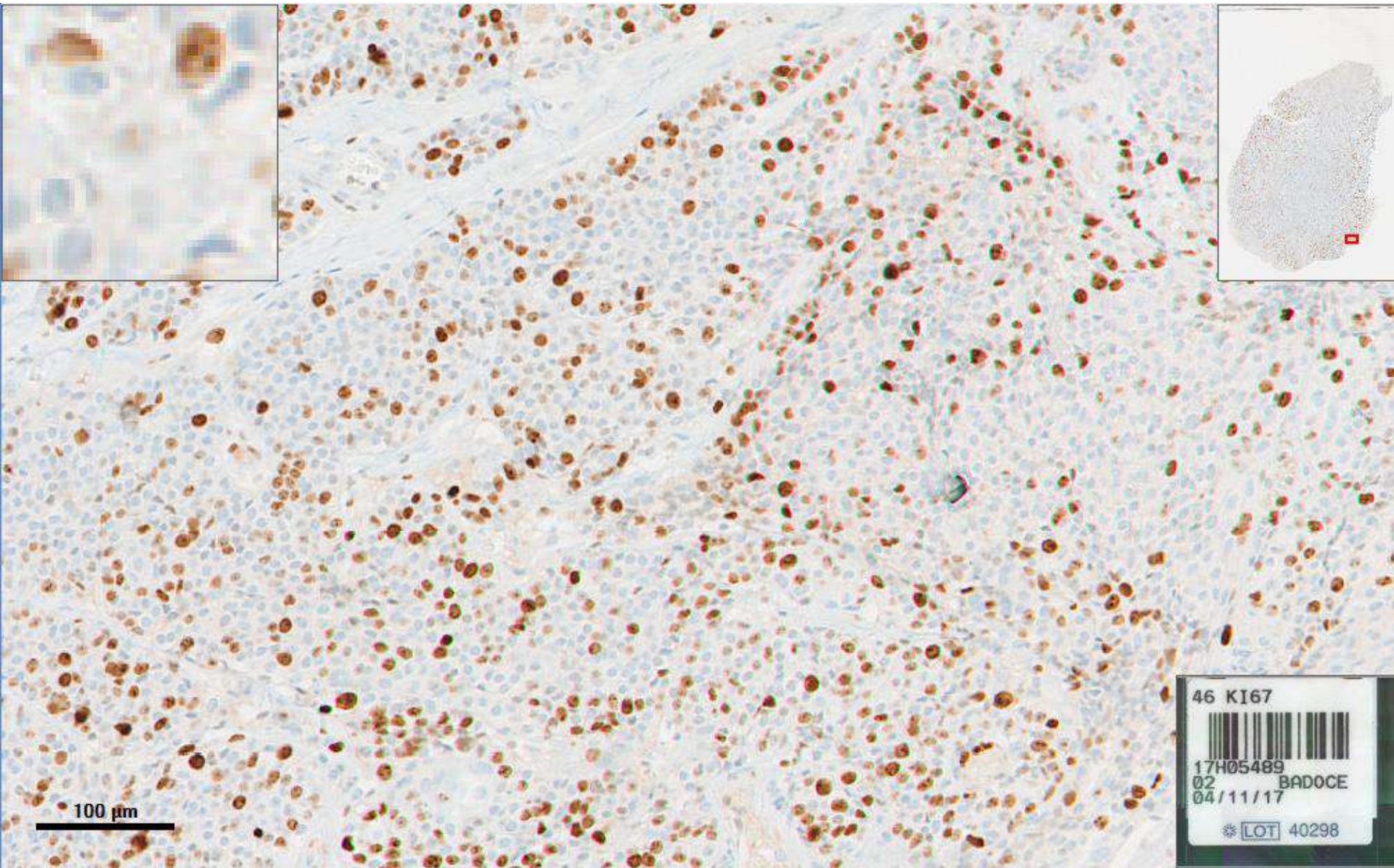


2 AE1/AE3



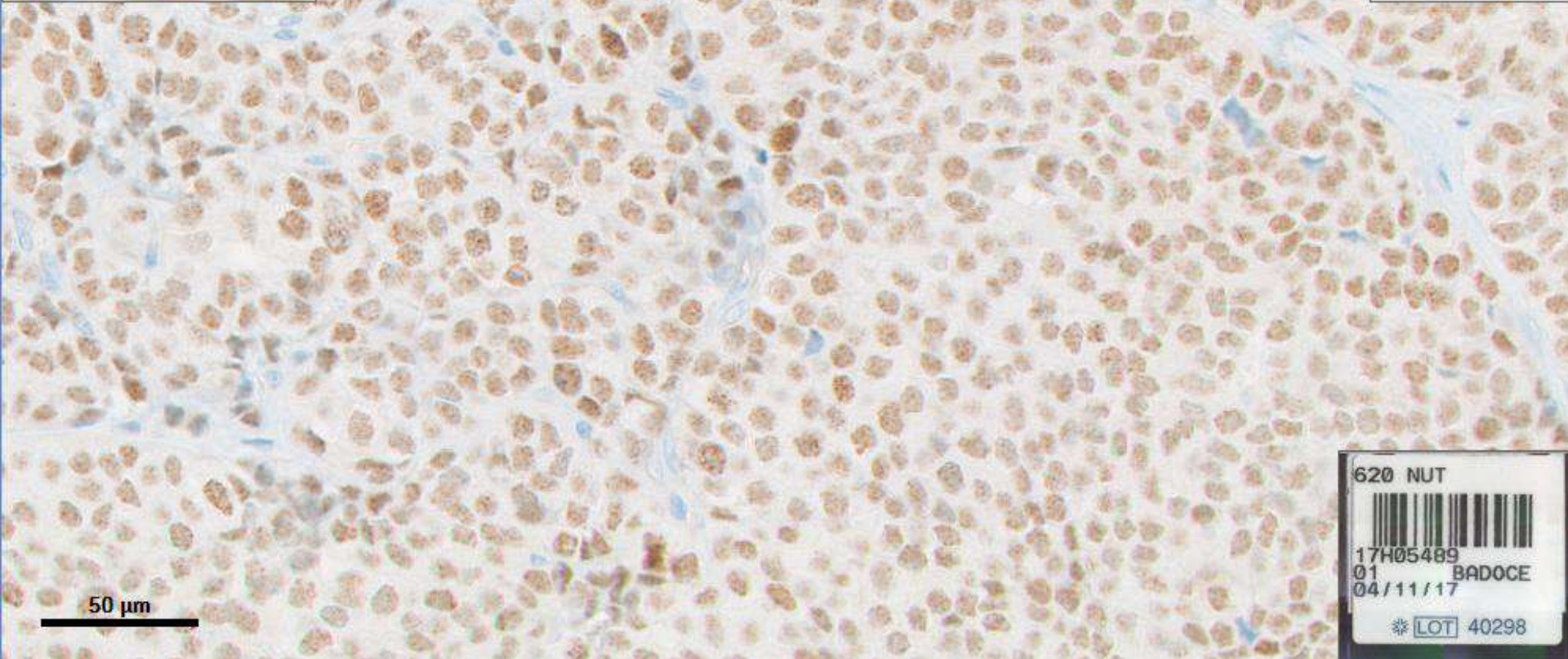
17H05489
02 BADOCE
07/11/17

* LOT 40298



100 μm

46 KI67
17H05489
02 BADOCE
04/11/17
LOT 40298

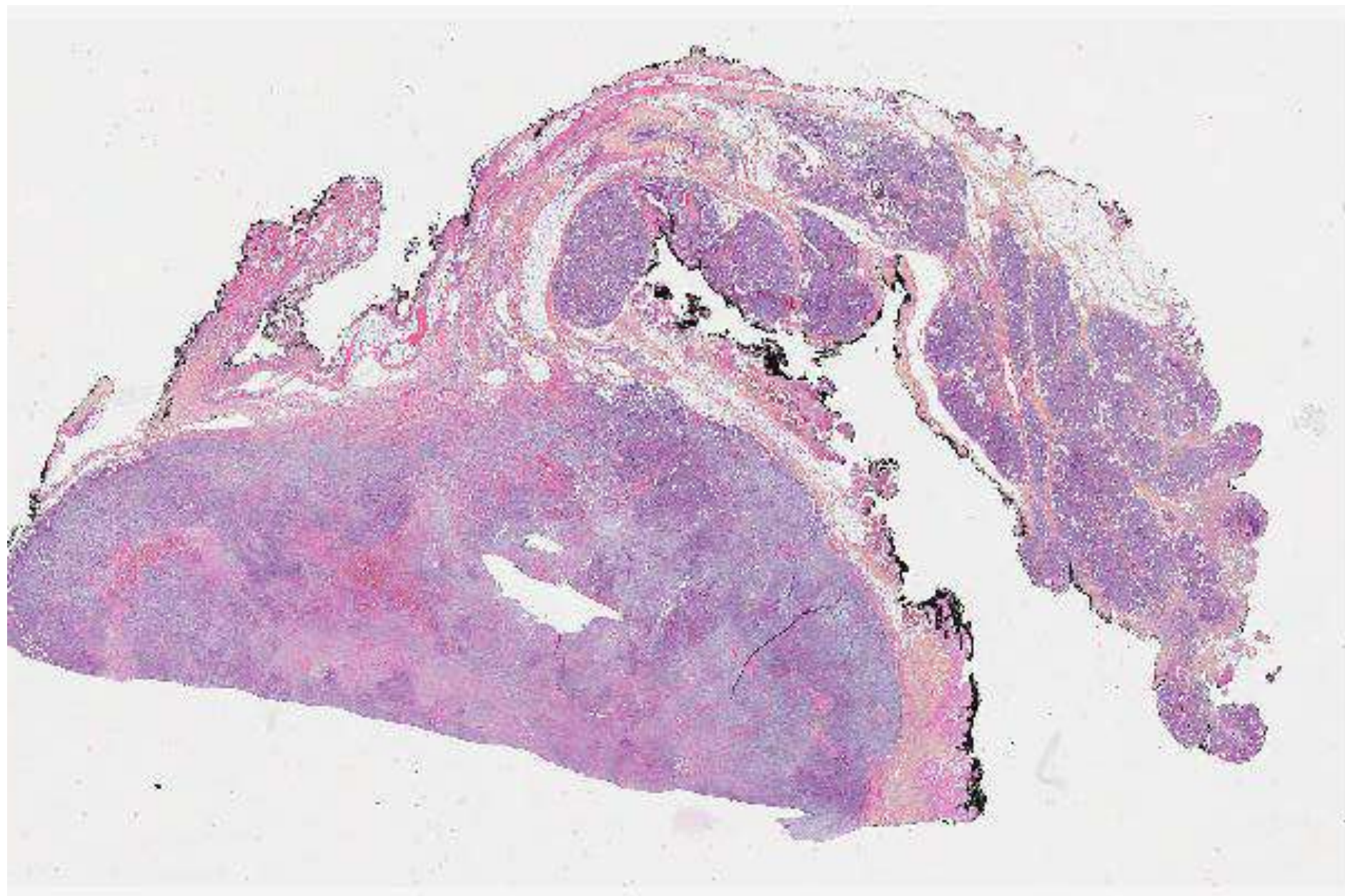


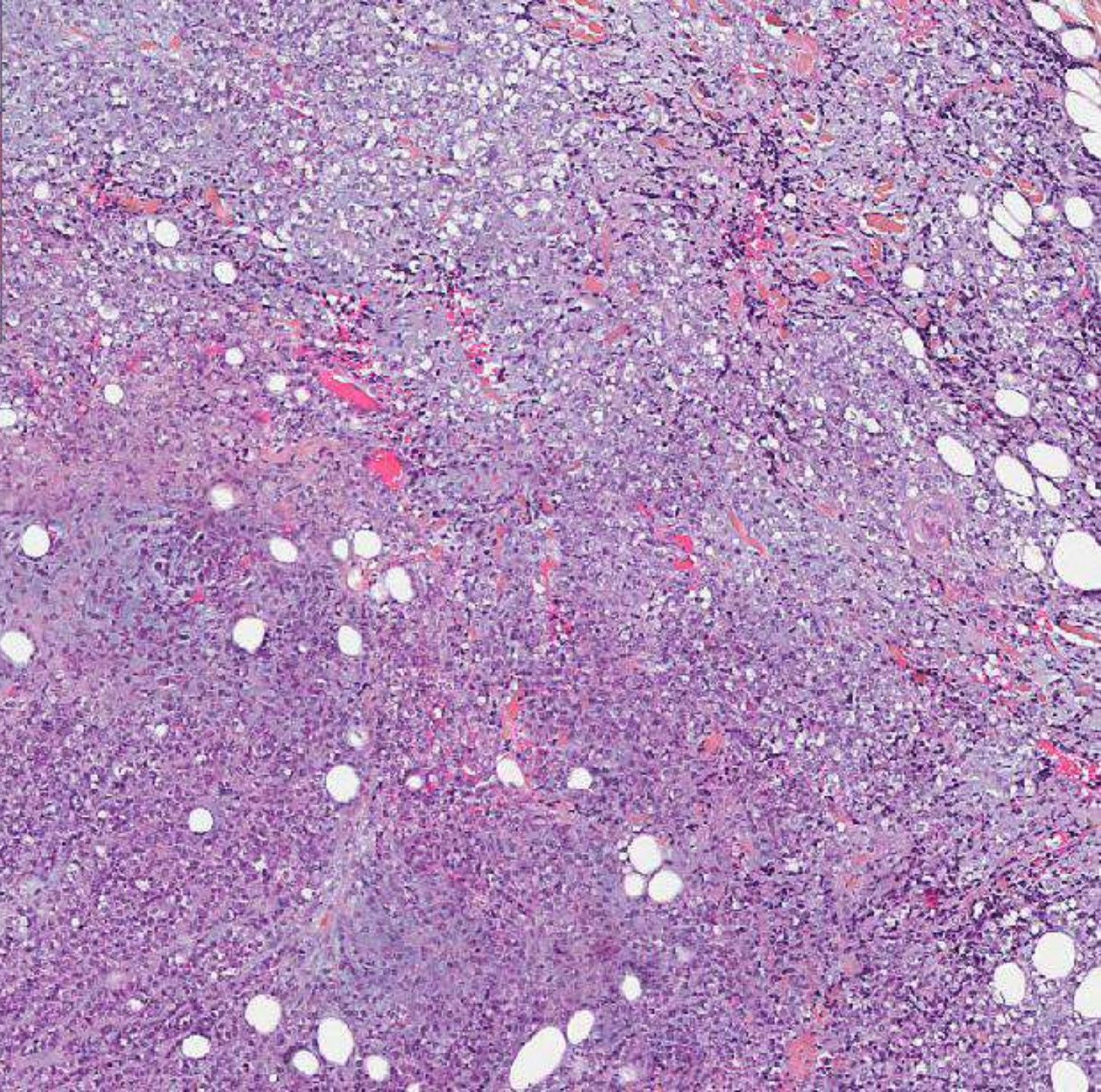
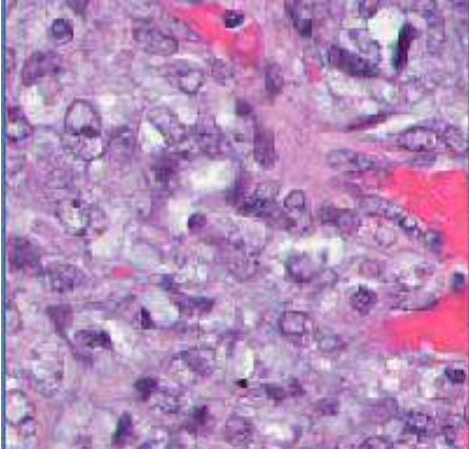
50 μ m

620 NUT
17H05489
01 BADOCE
04/11/17
* LOT 40298

Case 11

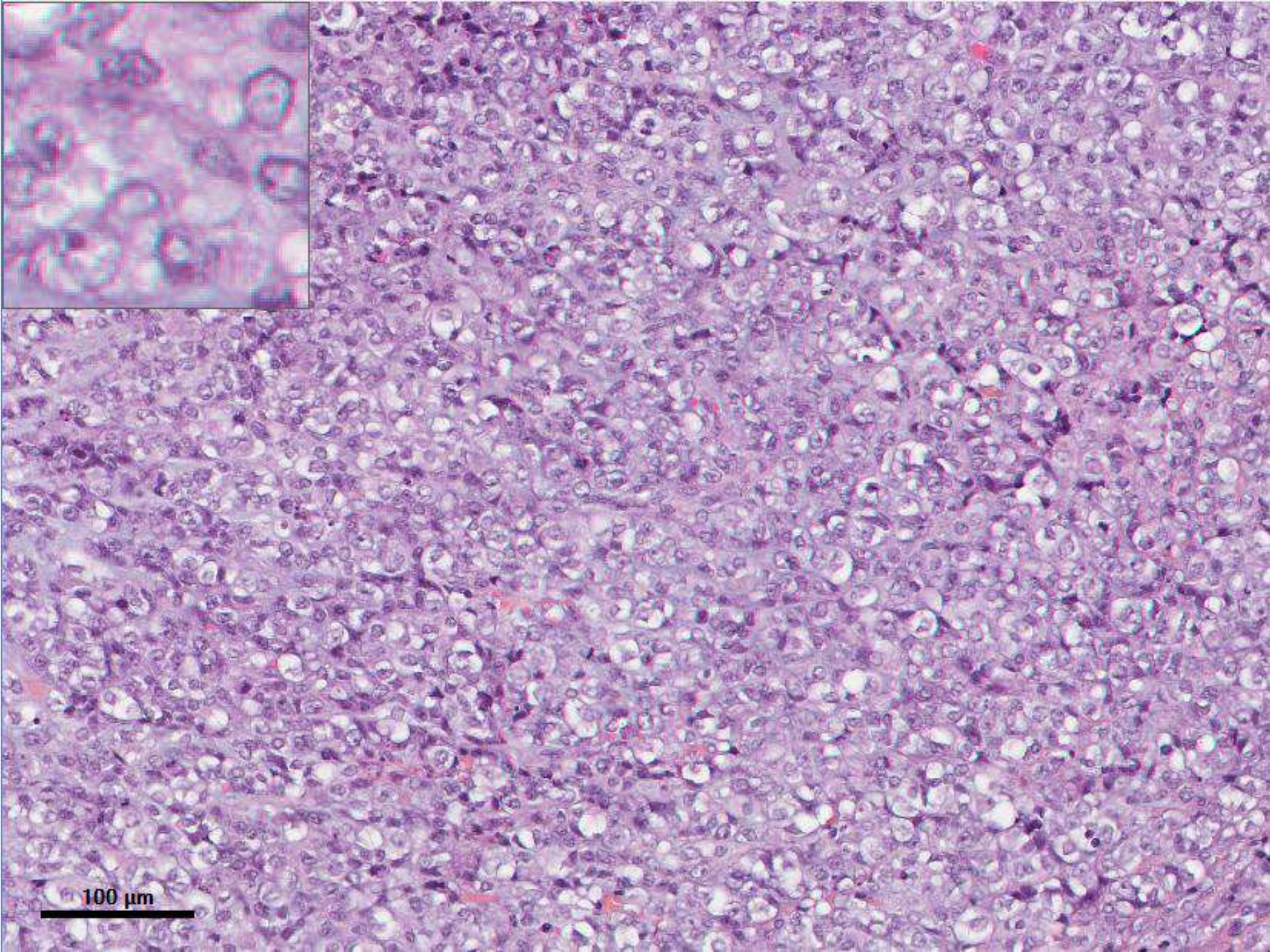
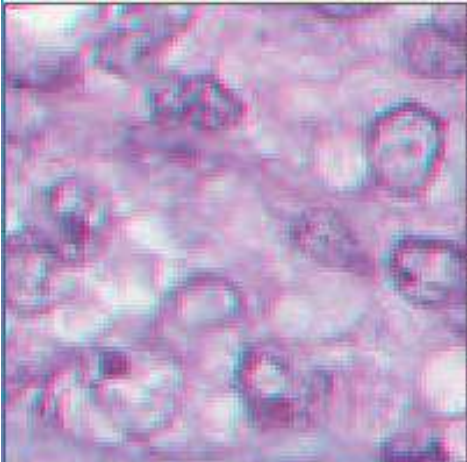
woman 19 yo right parotid lesion
with rapid growth





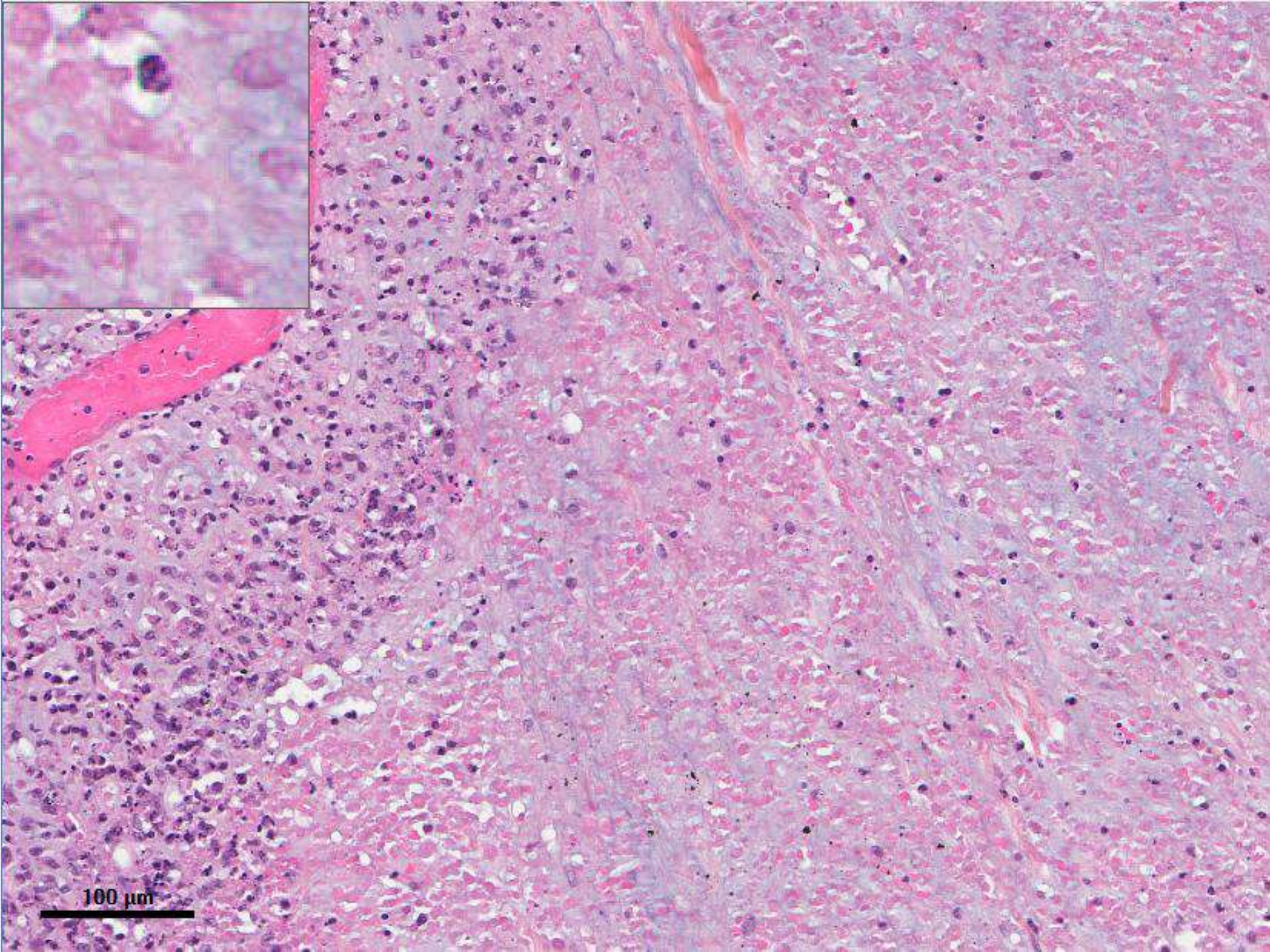
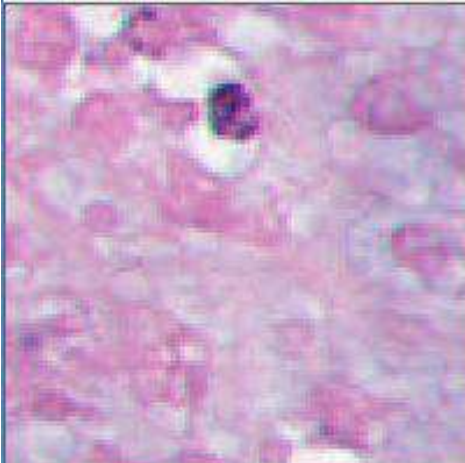
200 μ m





100 μm





100 μ m

NUT Carcinoma of the Salivary Glands

Clinicopathologic and Molecular Analysis of 3 Cases and a Survey of NUT Expression in Salivary Gland Carcinomas

Abbas Agaimy, MD, Isabel Fonseca, MD,†‡ Carmo Martins, BSc, PhD,§ Khin Thway, MD,||
Ryan Barrette, BSc,¶ Kevin J. Harrington, BSc, MBBS, FRCP, FRCR, PhD,#**
Arndt Hartmann, MD,* Christopher A. French, MD,¶ and Cyril Fisher, MD||*

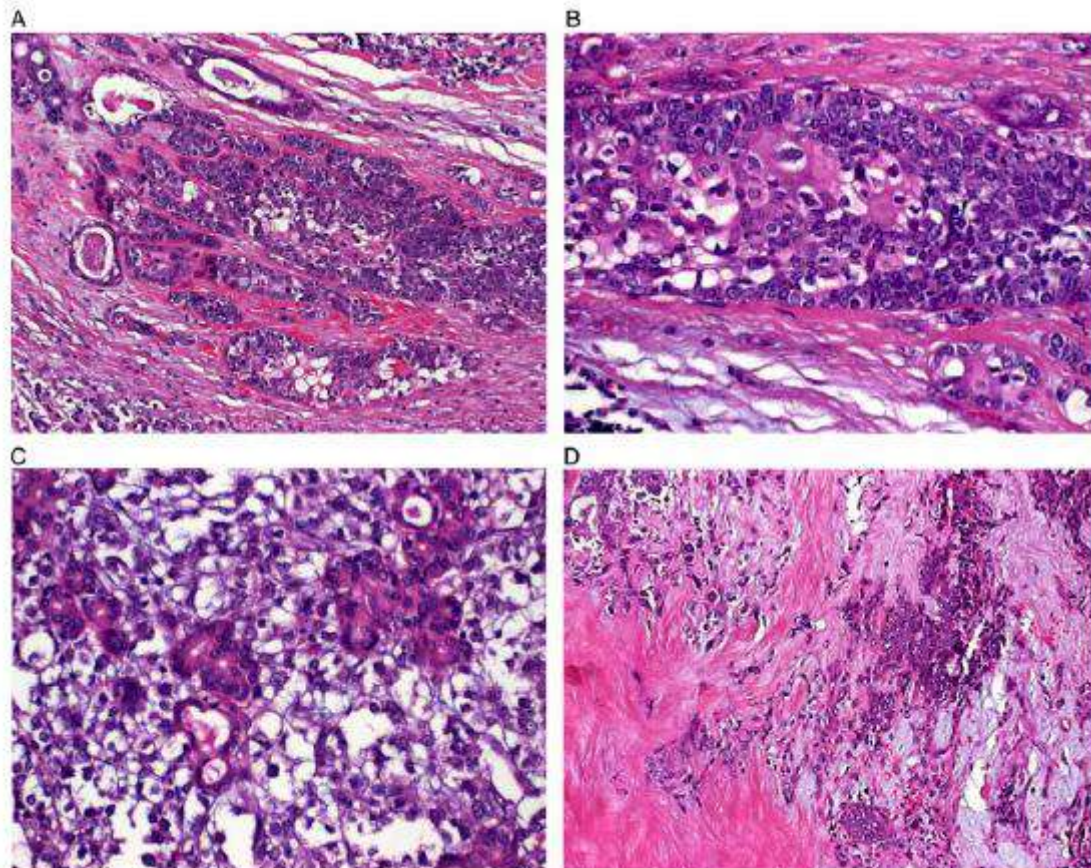


FIGURE 2. Foci of abrupt (clear cell) keratinization were seen in all 3 cases. Potentially misleading features included florid ductular proliferations (A, C) with entrapped or rare goblet cells (A, midlower field) and myxohyaline stromal changes reminiscent of pleomorphic adenoma (D). A to D from case 3.

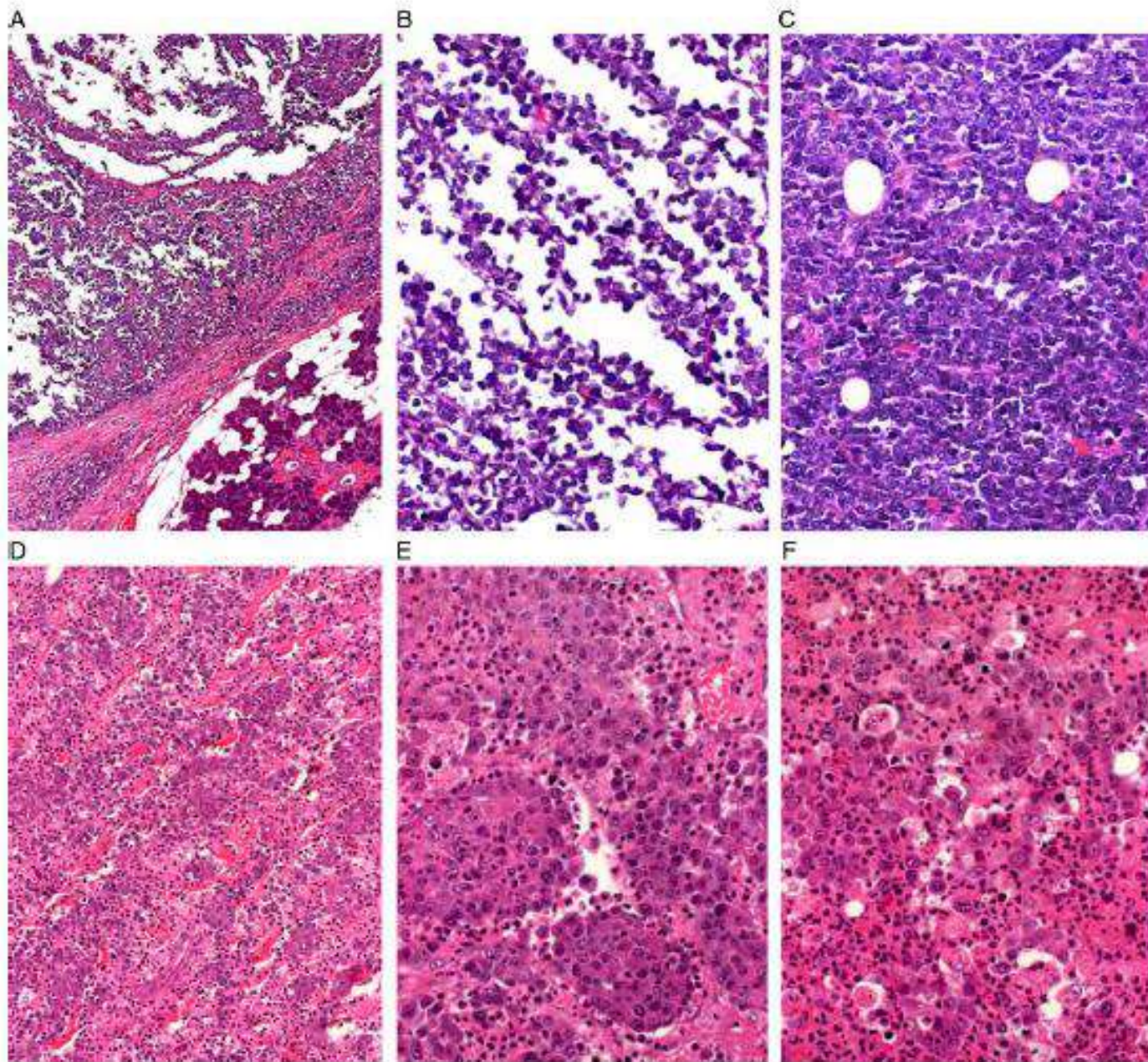


FIGURE 1. Salivary NCs were centered within salivary parenchyma (A) and displayed poorly cohesive sheets of small-sized to medium-sized cells arranged into pseudoalveolar (B), solid (C), corded (D), or nested (E) pattern. The nucleoli ranged from inconspicuous (C) to prominent (F), note extensive granulocytosis in F (A, B, C from case 3; D, E, F from case 1).

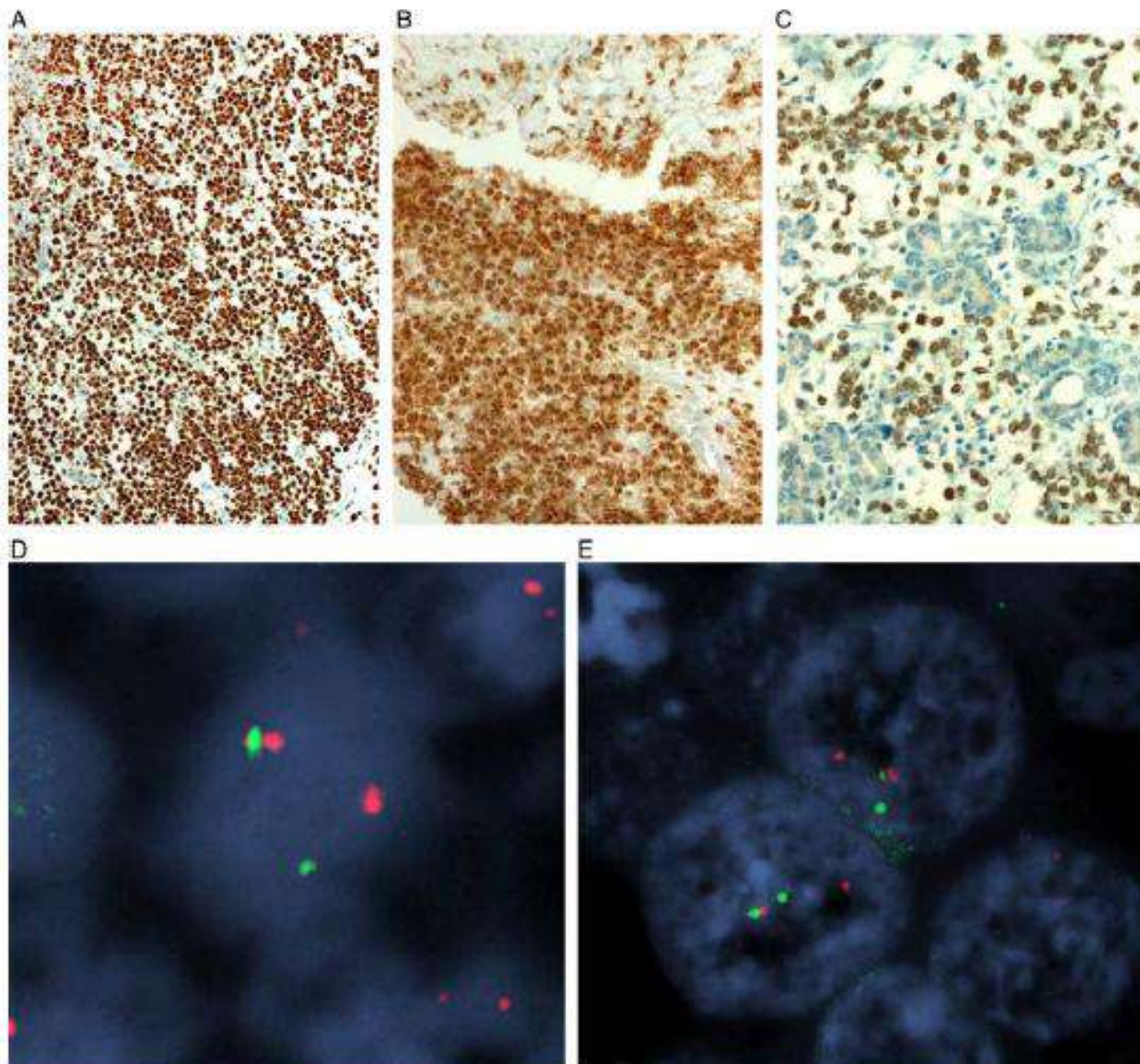
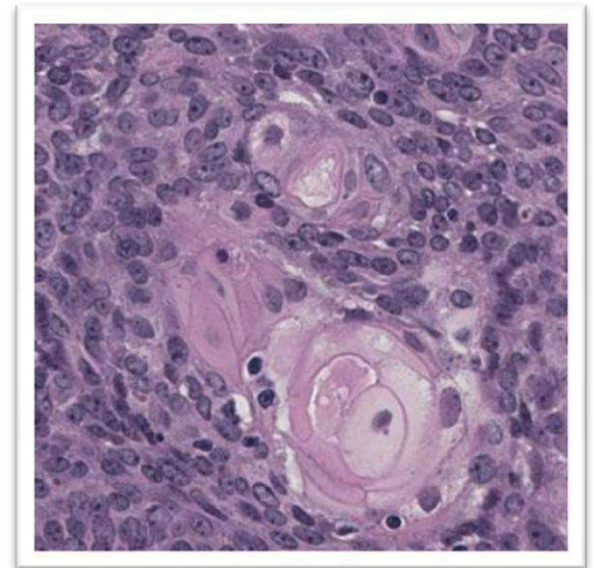


FIGURE 3. IHC showed consistent expression of p63 (A, case 3) and NUT protein (B, case 2). The NUT immunostain highlighted the neoplastic cells amid native salivary tissue (C, case 3). FISH analysis using the *NUT* probe (D) and *BRD4* probe (E) showed break-apart signals indicating a *NUT/BRD4* translocation (image from case 1).

NUT Carcinoma

- New entity
- Rare but certainly under diagnosed
- Due to translocation t (15; 19)
- Can be seen at any age but median age about 20 years old
- Think about it in front of a very monotonous AE1 / AE3 proliferation with abrupt keratinization (or large clear cells)
- **Anti-NUT immunochemistry**
- Very aggressive
- Targeted therapy
- Register patients in the database:
www.nmcregistry.org



Courtesy V Costes

Am J Surg Pathol. 2017 April ; 41(4): 458–471. doi:10.1097/PAS.0000000000000797.

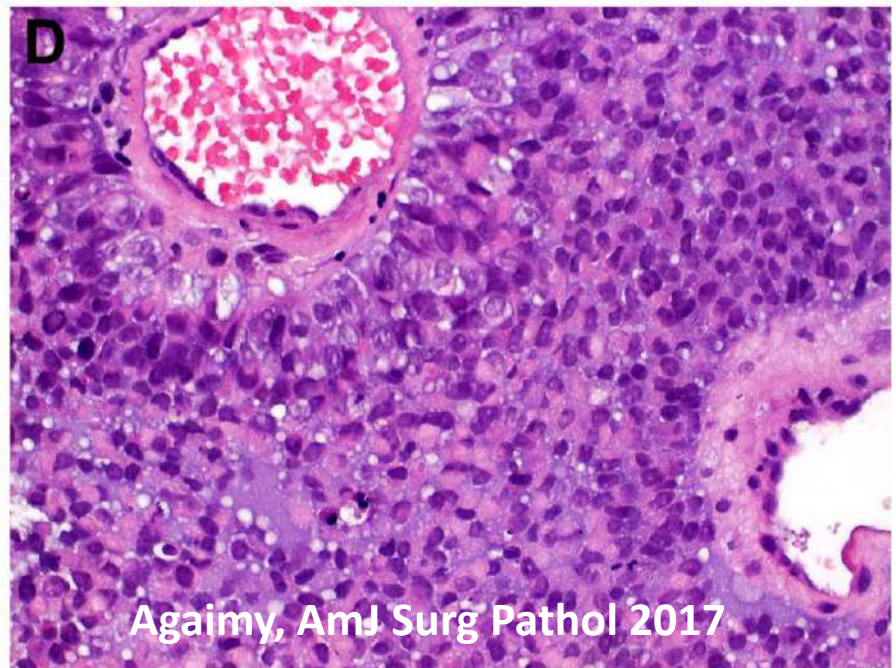
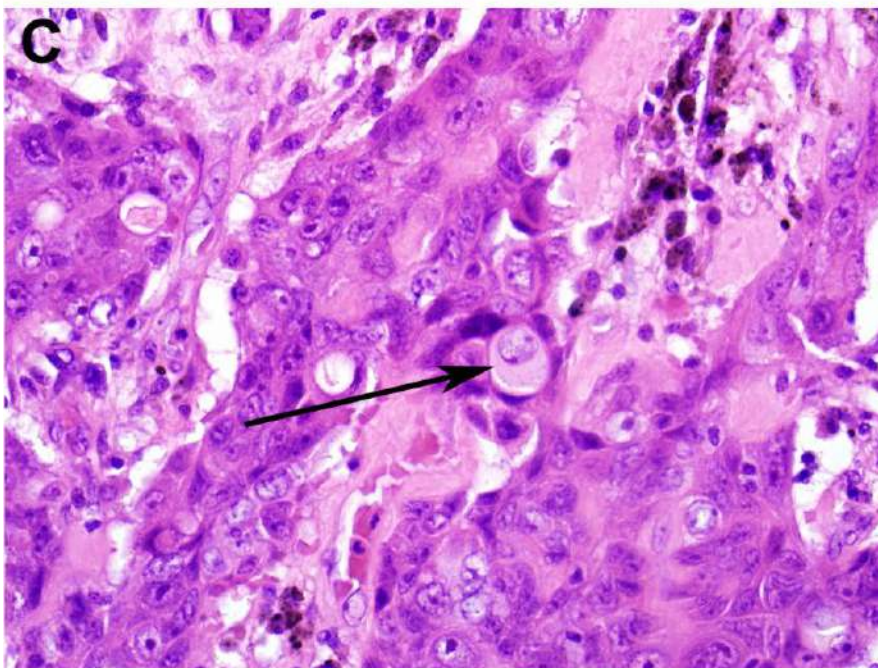
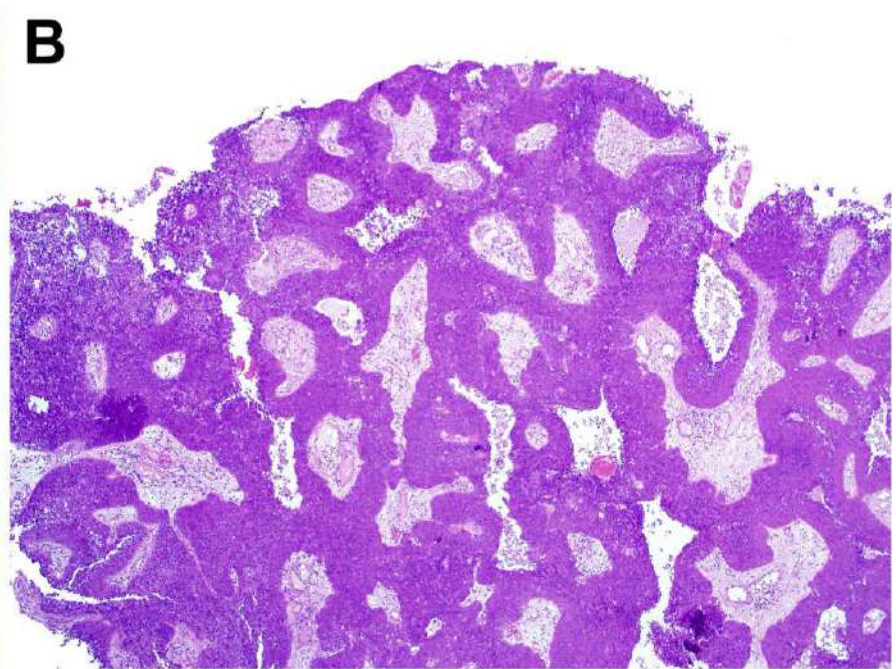
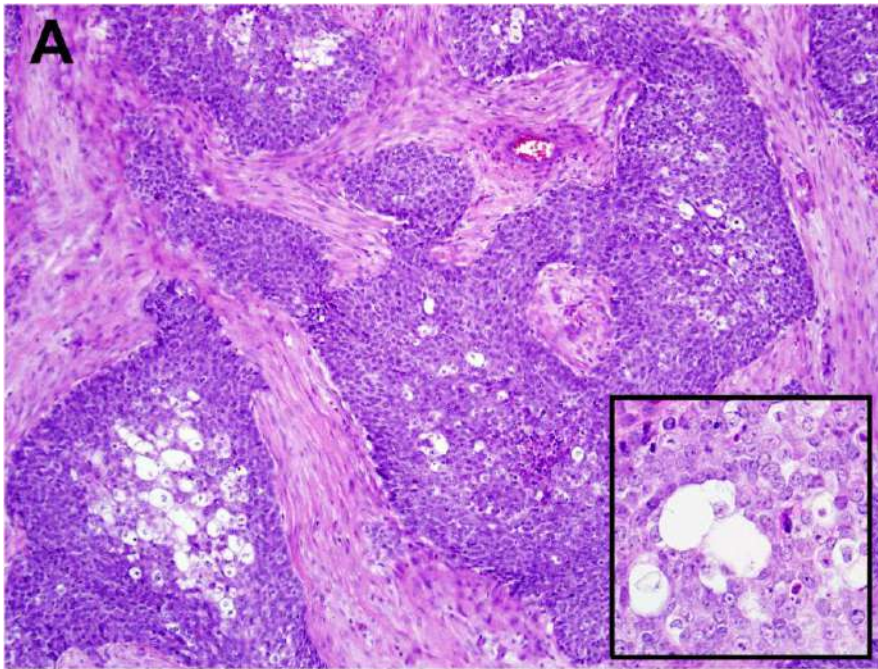
SMARCB1 (INI-1)-deficient Sinonasal Carcinoma: A Series of 39 Cases Expanding the Morphological and Clinicopathological Spectrum of a Recently Described Entity

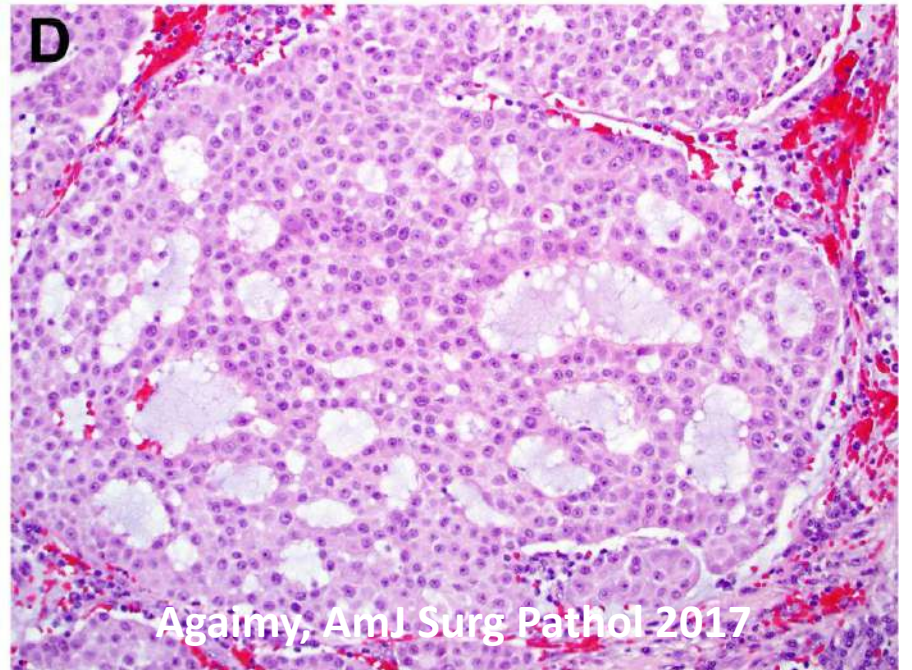
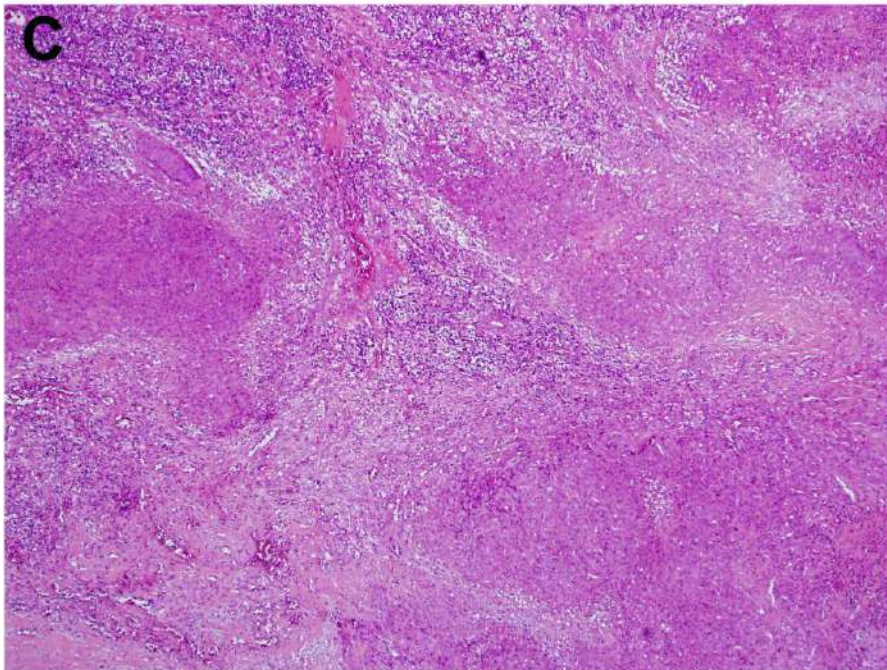
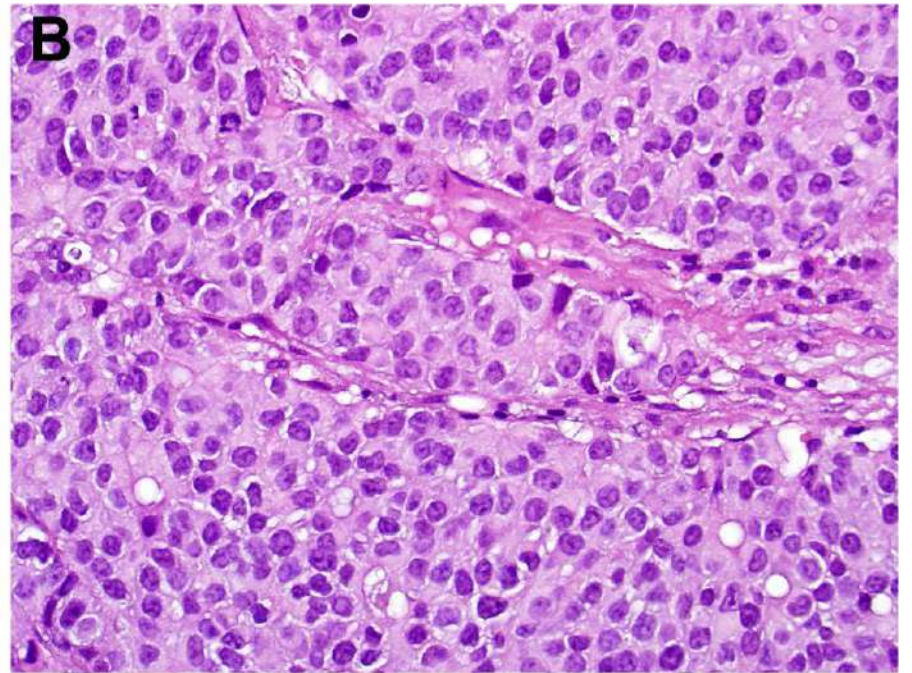
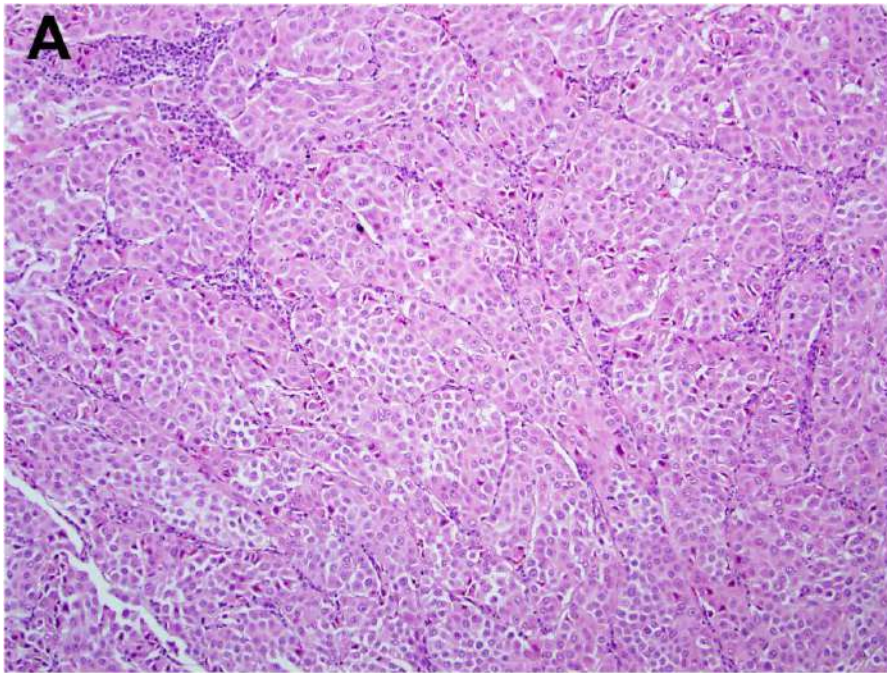
Abbas Agaimy, MD¹, Arndt Hartmann, MD¹, Cristina R. Antonescu, MD², Simion I. Chiosea, MD³, Samir K. El-Mofty, MD⁴, Helene Geddert, MD⁵, Heinrich Iro, MD⁶, James S. Lewis Jr., MD⁷, Bruno Märkl, MD⁸, Stacey E. Mills, MD⁹, Marc-Oliver Riener, MD¹⁰, Thomas Robertson, MD¹¹, Ann Sandison, MB, ChB, FRCPath¹², Sabine Semrau, MD¹³, Roderick H. W. Simpson, MB, ChB, FRCPath¹⁴, Edward Stelow, MD⁹, William H. Westra, MD¹⁵, and Justin A. Bishop, MD¹⁵

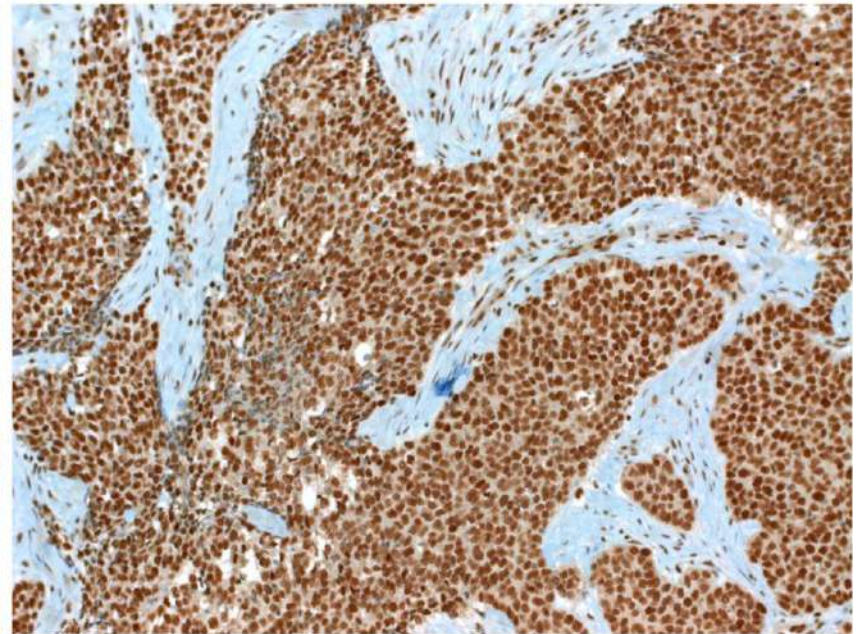
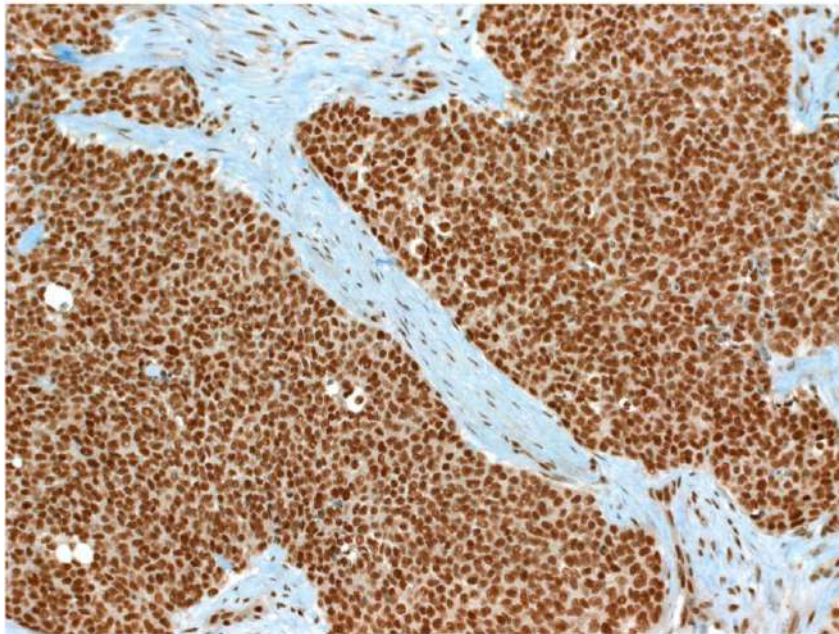
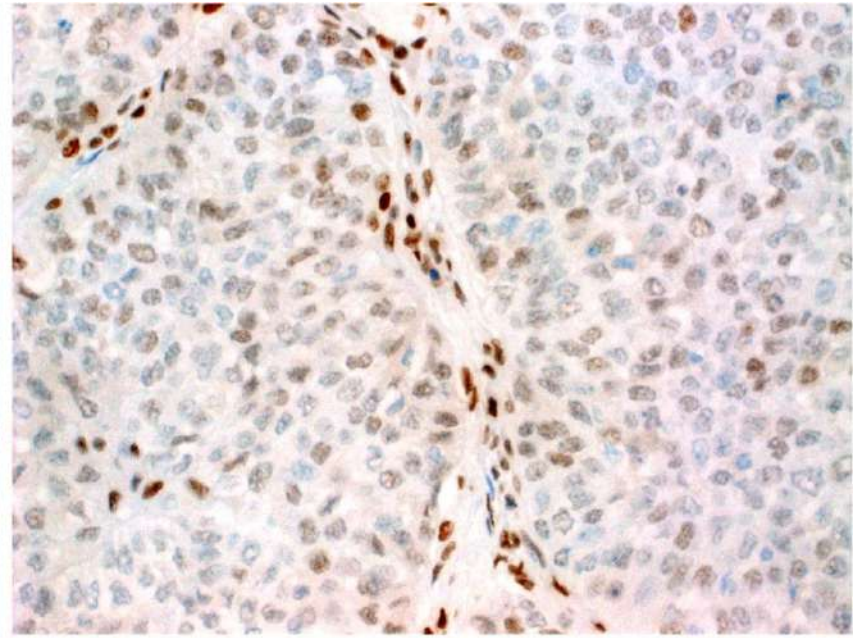
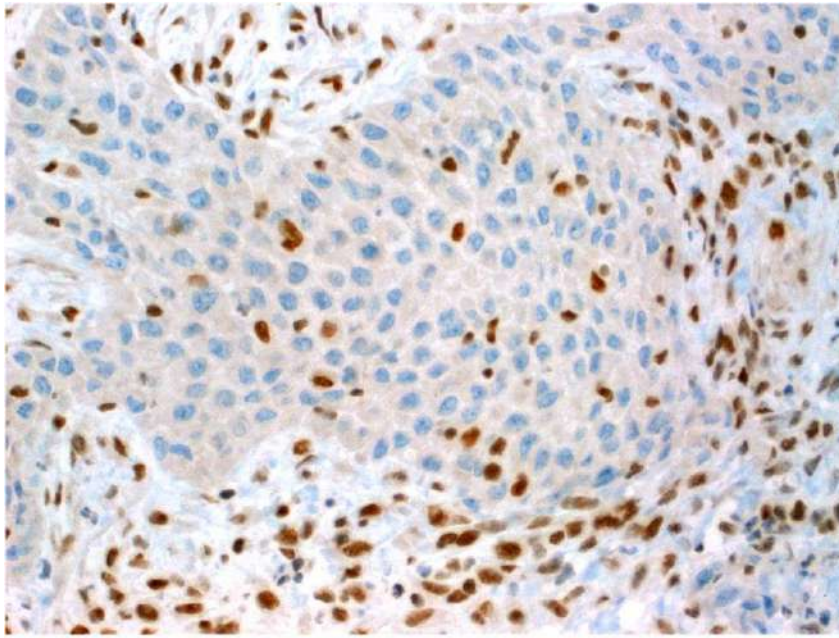
- Sinonasal tract malignancies are uncommon, representing no more than 5% of all head and neck cancers.
- Several recent studies and reviews have emphasized the propensity of this relatively small anatomic area of the body to develop a plethora of histogenetically and biologically distinctive, but morphologically highly overlapping neoplasms
- **sinonasal undifferentiated carcinoma (SNUC) as a distinctive and highly aggressive sinonasal carcinoma**
- Consequently, the group of SNUCs has been diminishing as new specific entities have emerged including **NUT-rearranged carcinoma**
- **HPV-related adenoid cystic-like carcinoma**
- **Adamantinoma-like Ewing sarcoma**
- Variant of sinonasal carcinoma characterized **by loss of nuclear SMARCB1 expression.**

Histological examination

- Cellular monotony with relatively monomorphic small-to-medium sized rounded nuclei
- Dispersed chromatin, variably prominent nucleoli and indistinctive cytoplasmic borders.
- Mitotic rates are uniformly high, and necrosis is common.
- **Conventional squamous dysplasia/carcinoma in situ was not seen.**
- **Presence of non-specific, clear, “empty” cytoplasmic vacuoles**



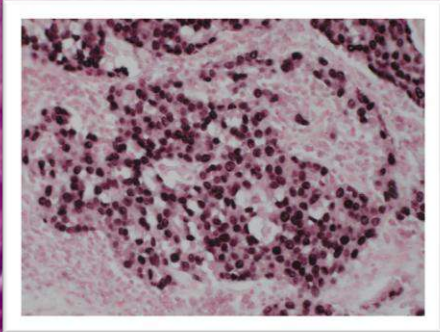
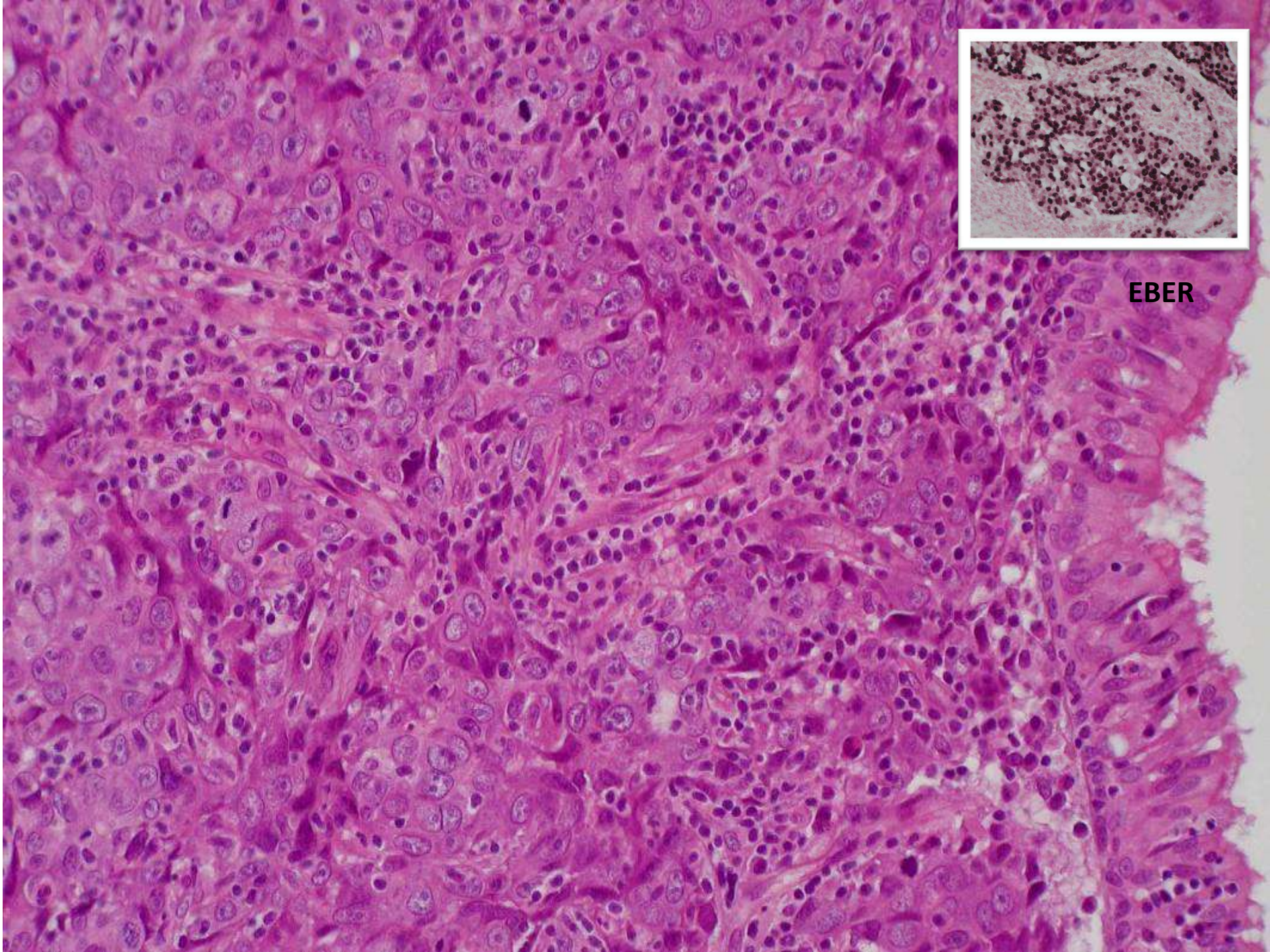




Loss of SMARCB1, SMARCB2 reduced, SMARCB4 and ARID1A intact

Nasopharyngeal carcinoma

- Keratinizing squamous cell carcinoma (Well differentiated)
- Basaloid squamous cell carcinoma
- Non-keratinizing squamous cell carcinoma (eg UCNT)
- Node metastases ++ .
- Epidemiology Tobacco, salted and fermented food (nitrosamine), EBV (EBER +, less diffuse in keratinizers).



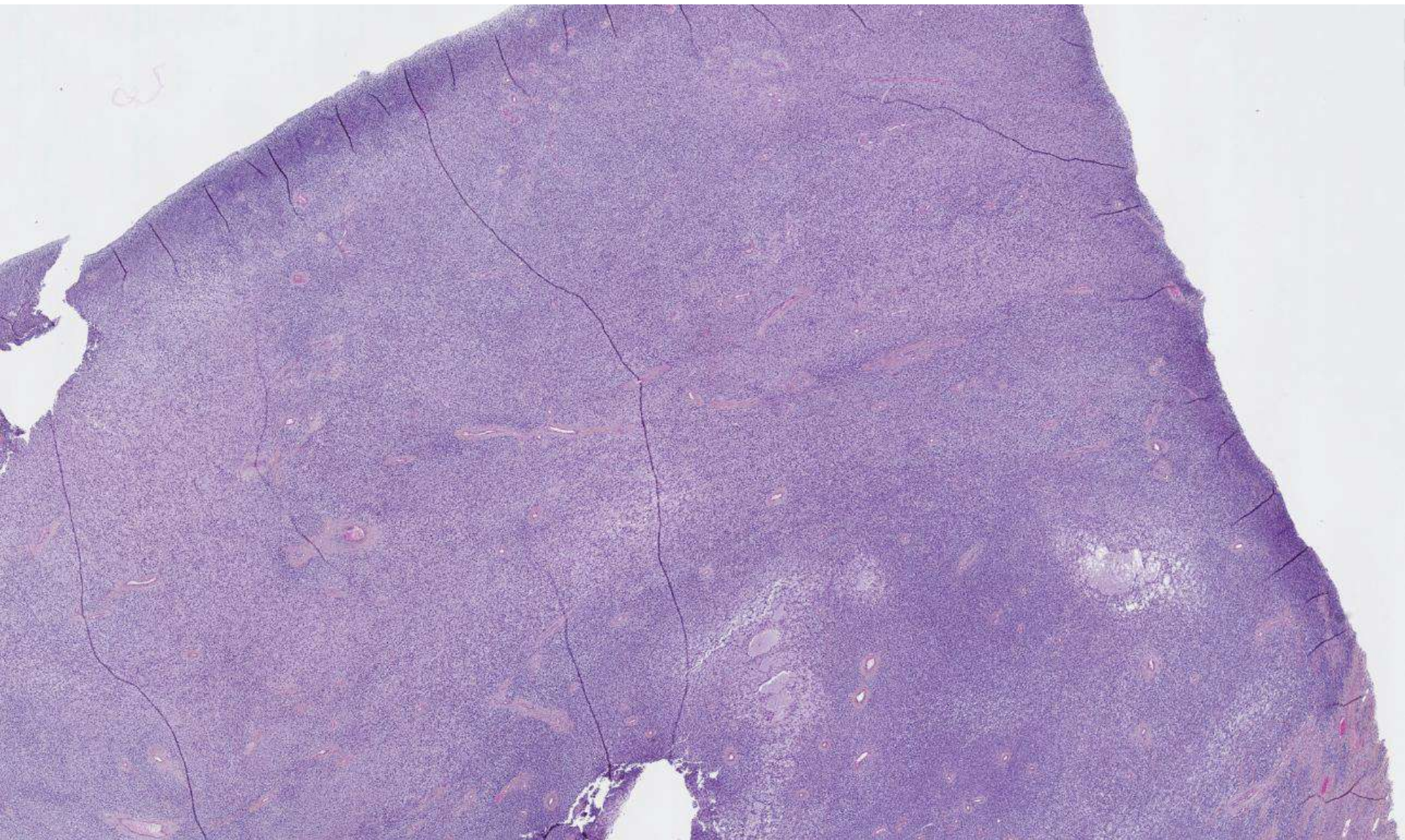
EBER

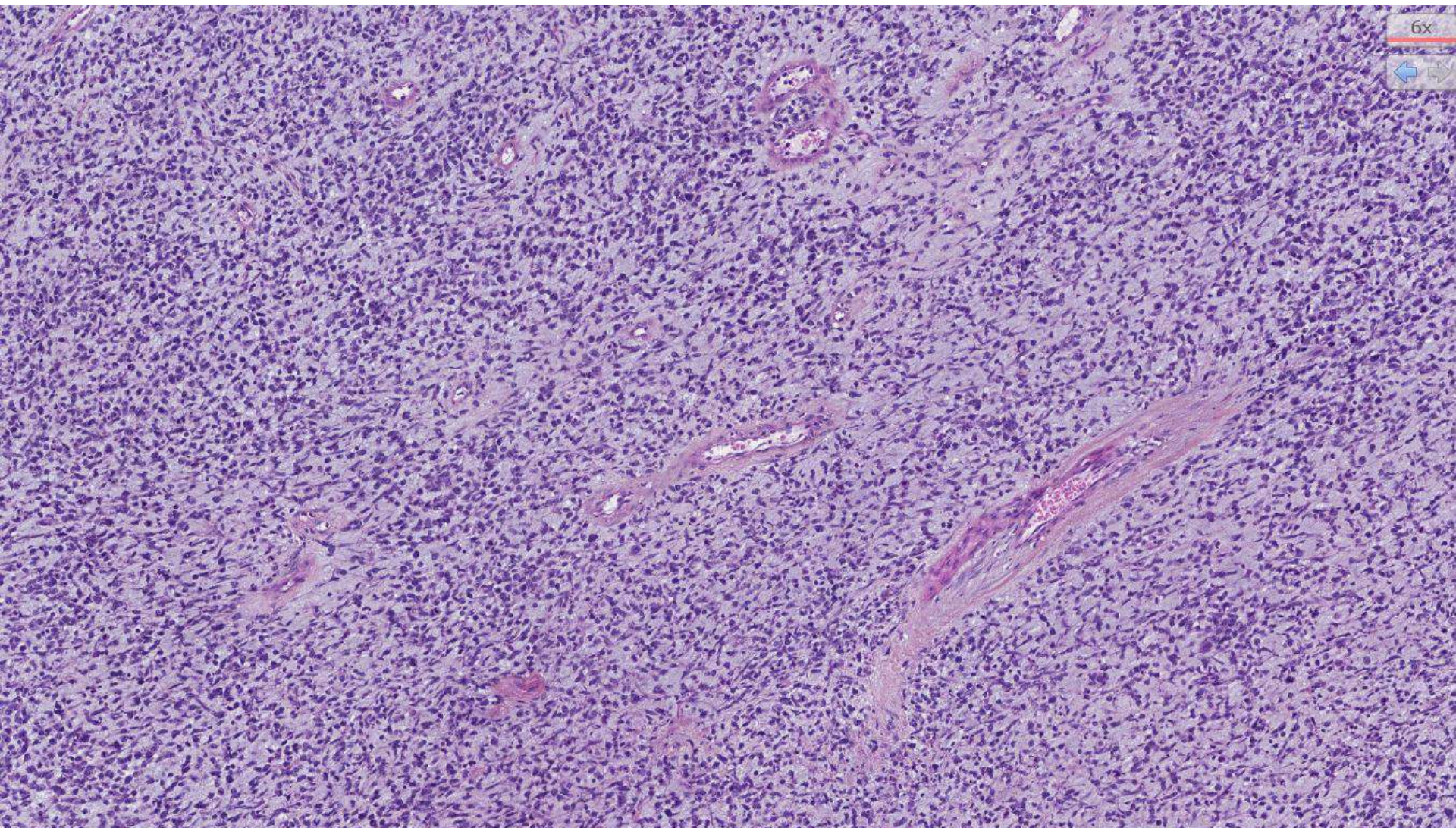
Take home message

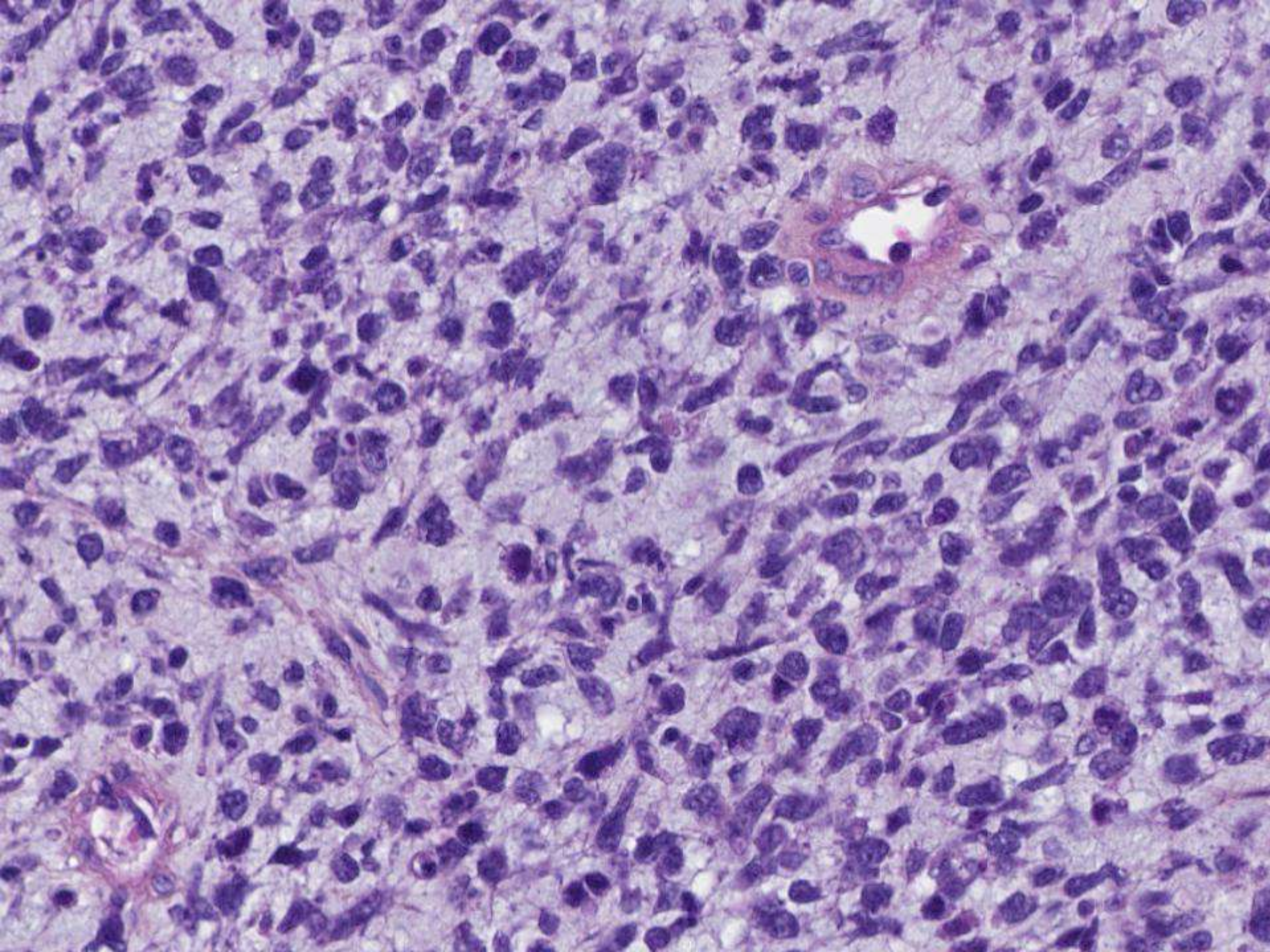
- Histological grade of neuroendocrine carcinomas is quite well correlated with prognosis.
- Neuroendocrine large cell carcinoma of the head and neck should be recognized by the WHO.
- Think about new entities
 - NUT carcinoma
 - INI1 deficient
 - HPV-induced carcinoma with CAK / HPV + C Neuroendocrine

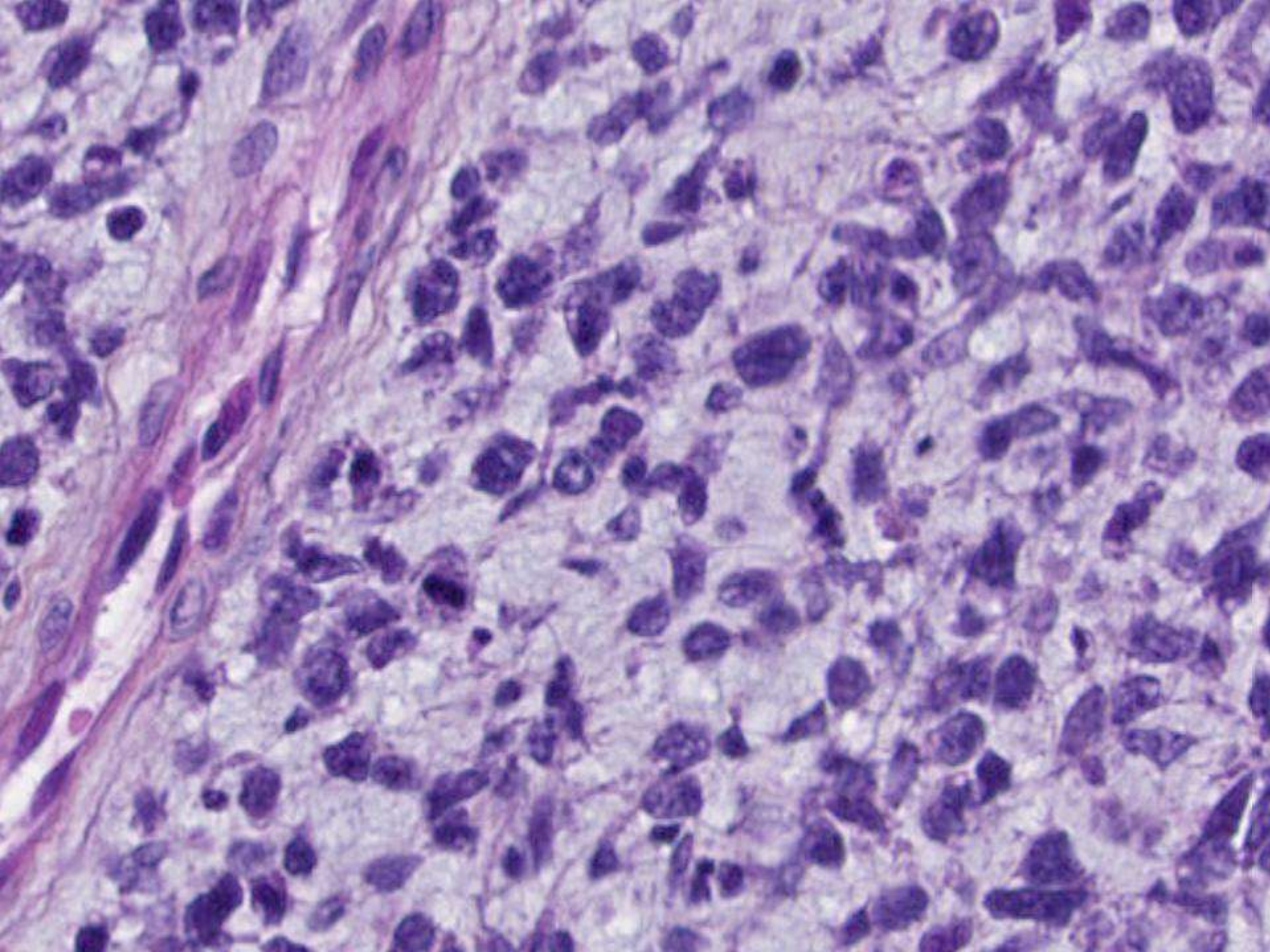
Case 1L

Man 70 yo exophthalmia
nasopharyngeal biopsies









Rhabdomyosarcoma

- Rare malignant mesenchymal tumor with skeletal muscle differentiation
- Embryonal, alveolar, pleomorphic and spindle cell subtypes
- Most common sinonasal sarcoma in both children and adults, pic first decade
- Round to spindle cells, and scant cytoplasm hyperchromatic nuclei
- Alveolar rhabdomyosarcomas harbour a PAX3-FOXO1 fusion and the PAX7-FOXO1 fusion less detected

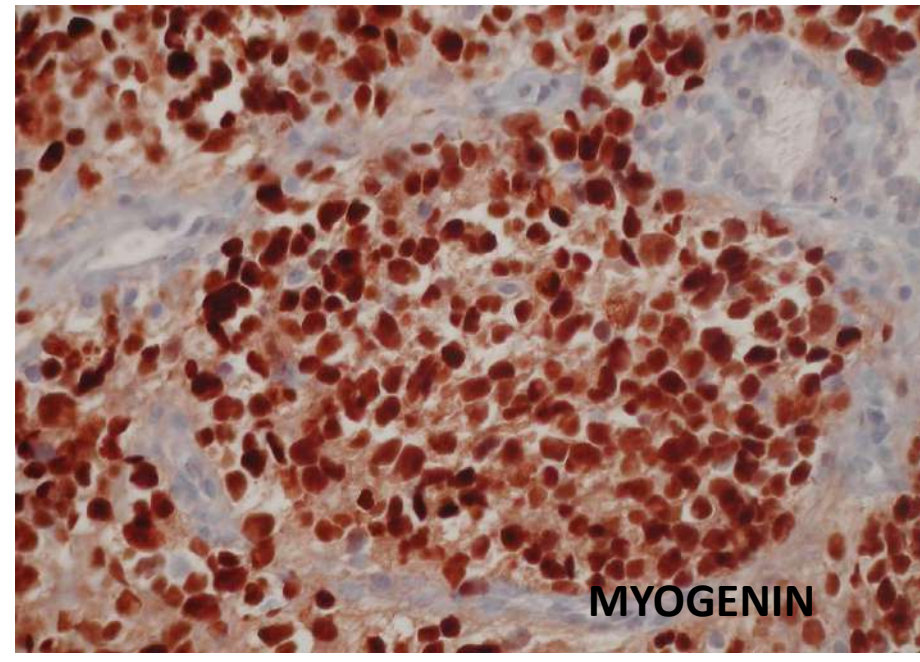
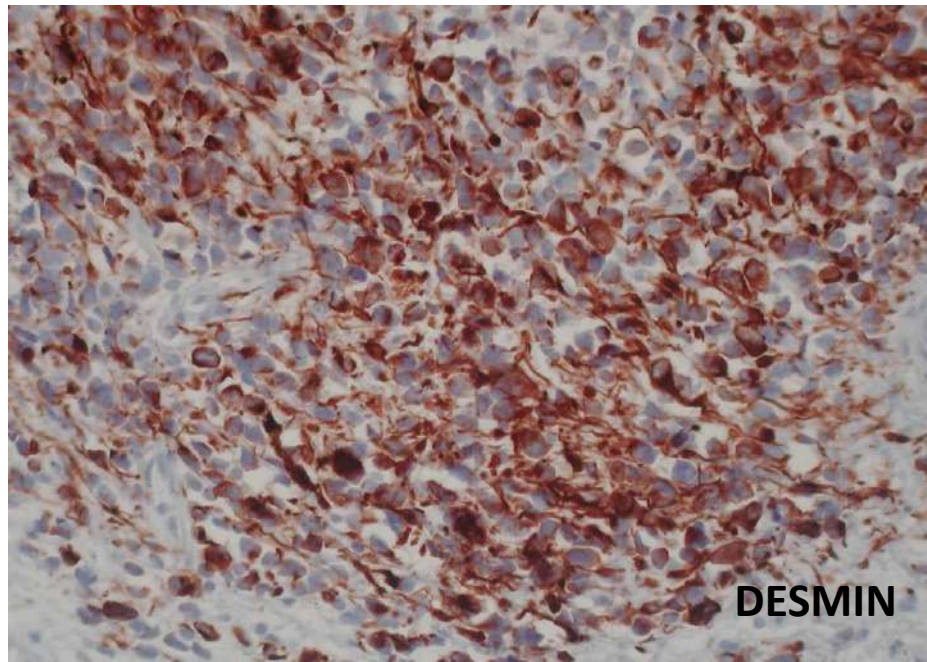
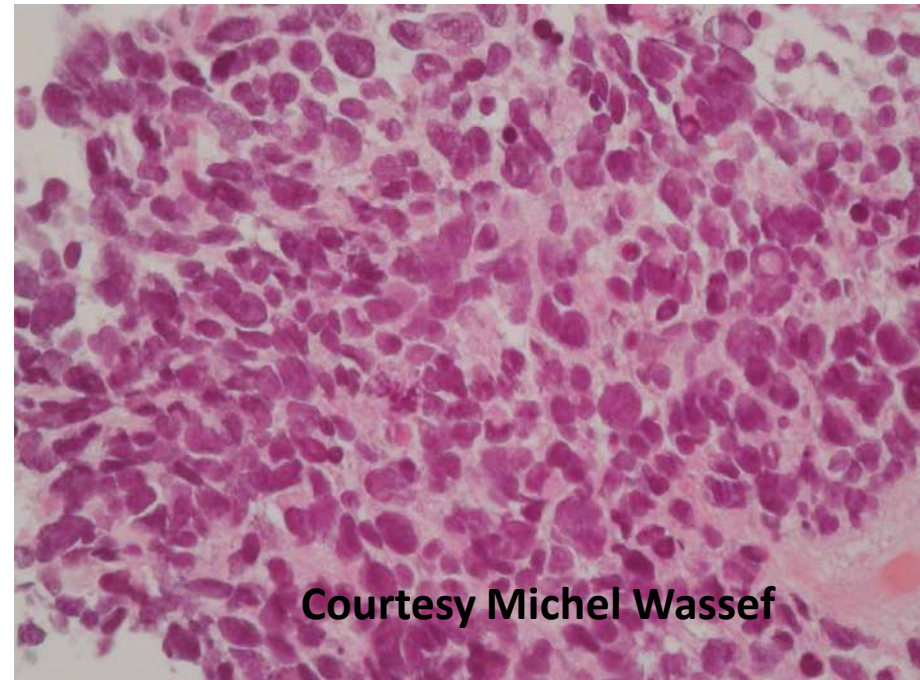


Courtesy Michel Wassef

- Myogenin (MYF4) MYOD1, desmin, fast myosin, myoglobin +

- SMA + 10%

- AE1/AE3, EMA, chromogranin, CD56, synaptophysin, CD20, CD99 can be positive!!



Neuroectodermic et neuroendocrine tumors and their differential diagnosis

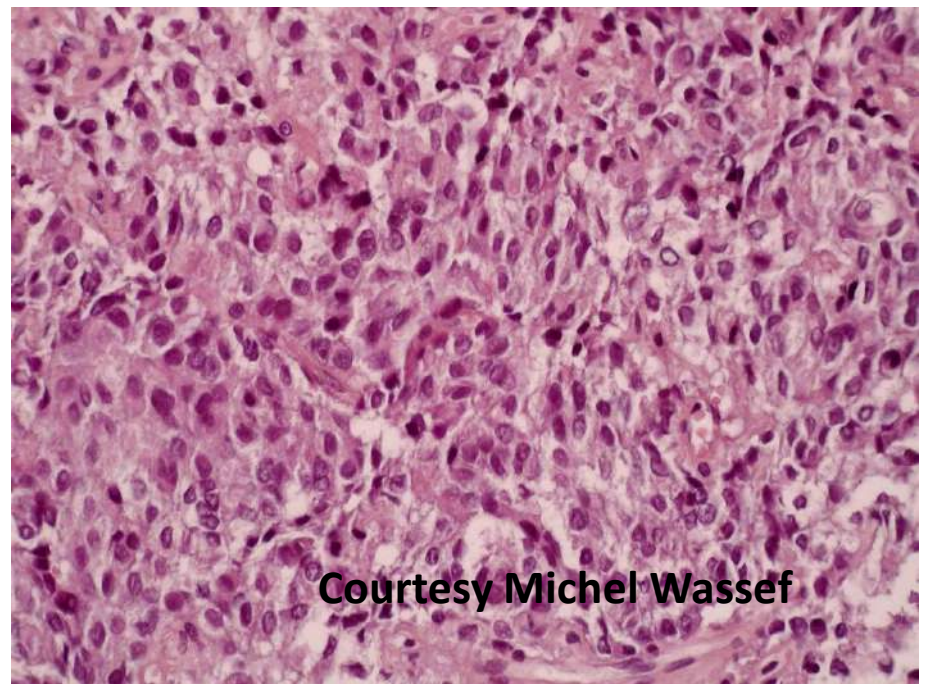
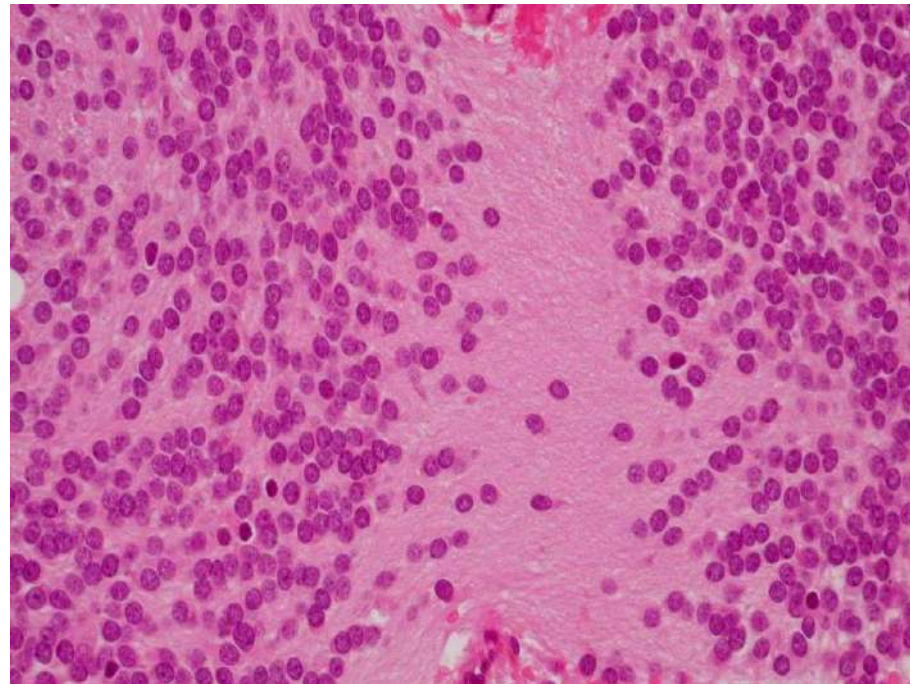
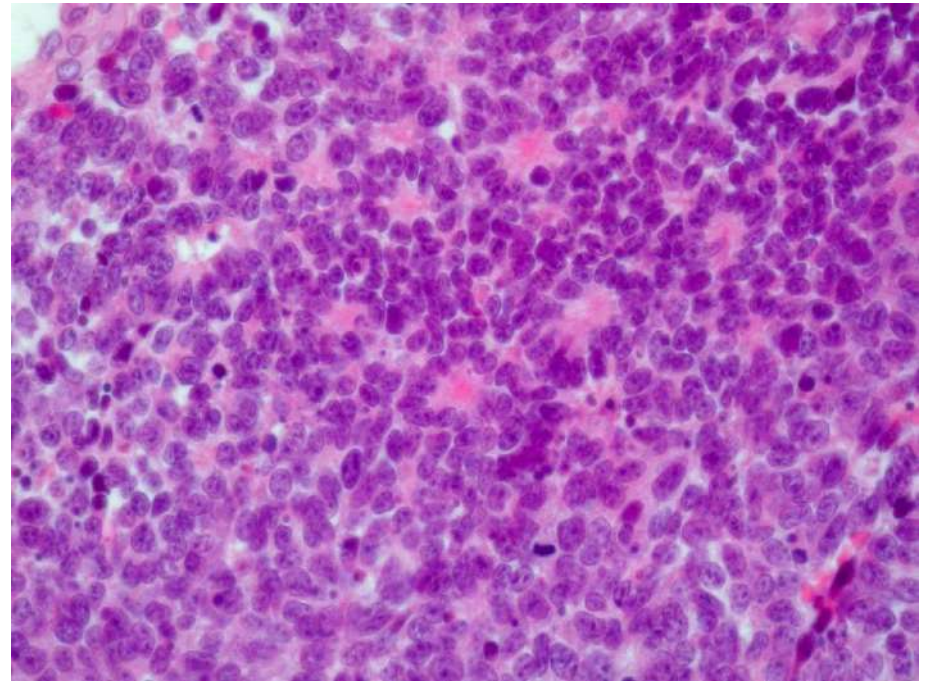
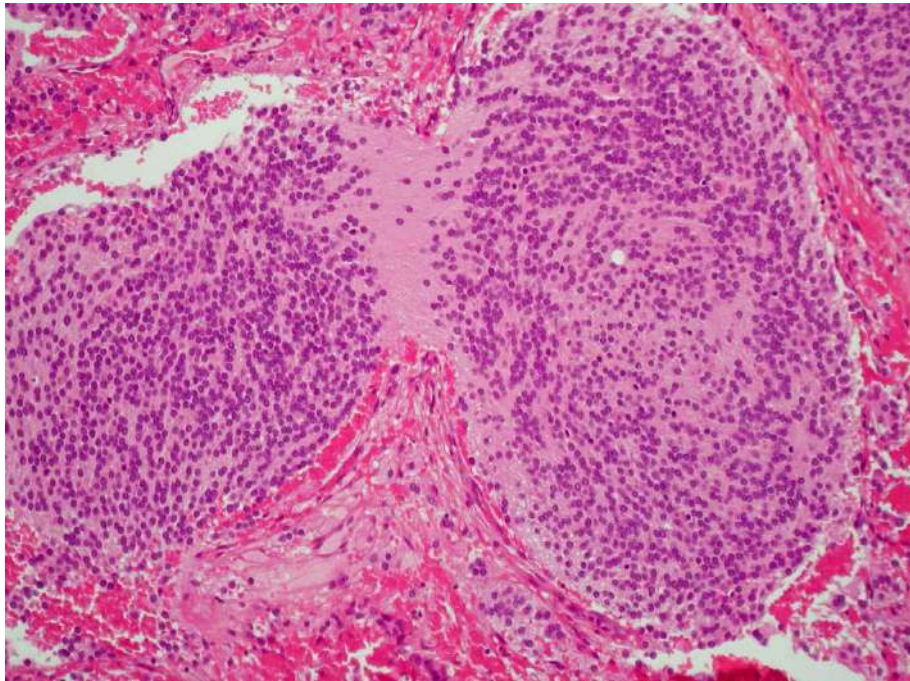
- Olfactory neuroblastoma
- Neuroendocrine carcinoma
- PNET / sarcome d'Ewing
- Melanoma

- Nasosinusal undifferentiated carcinoma

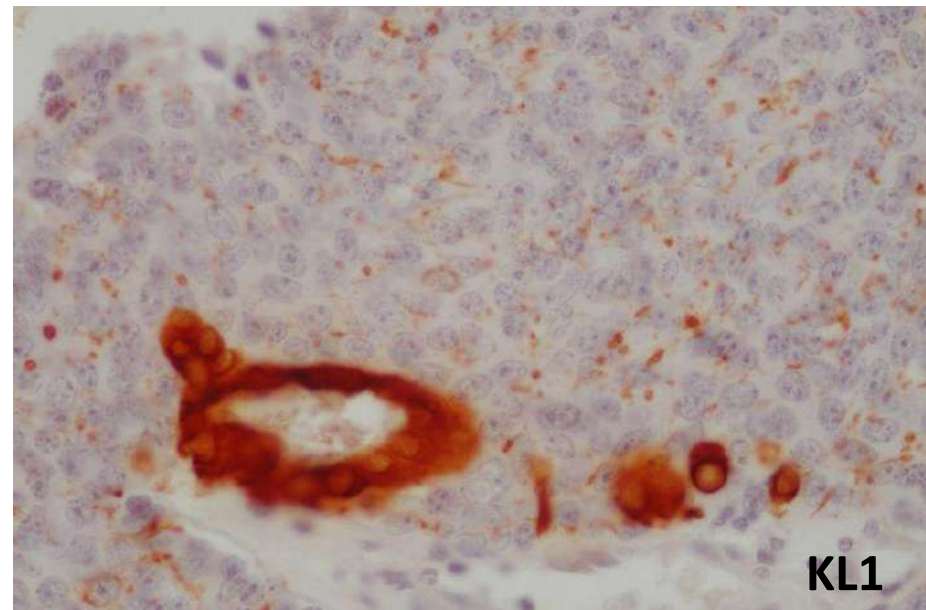
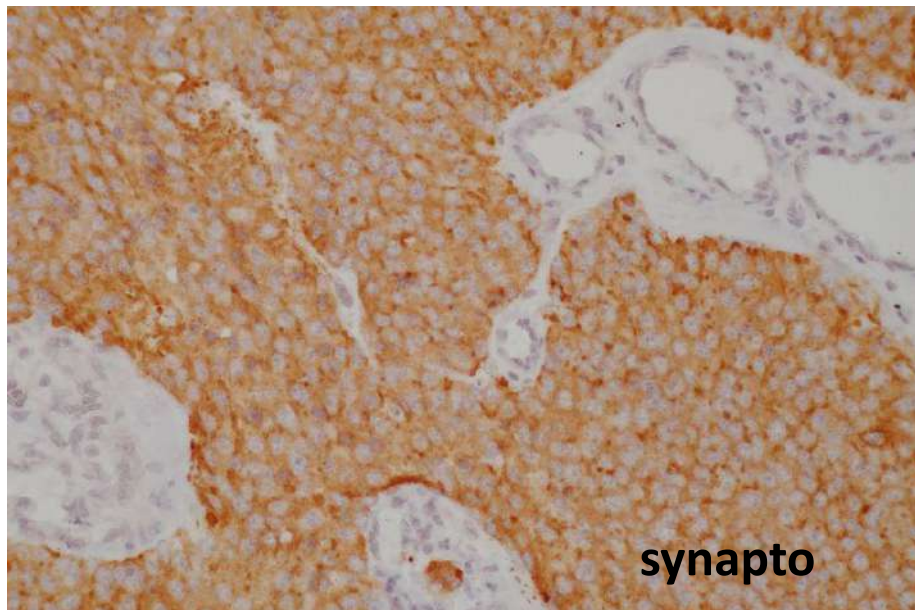
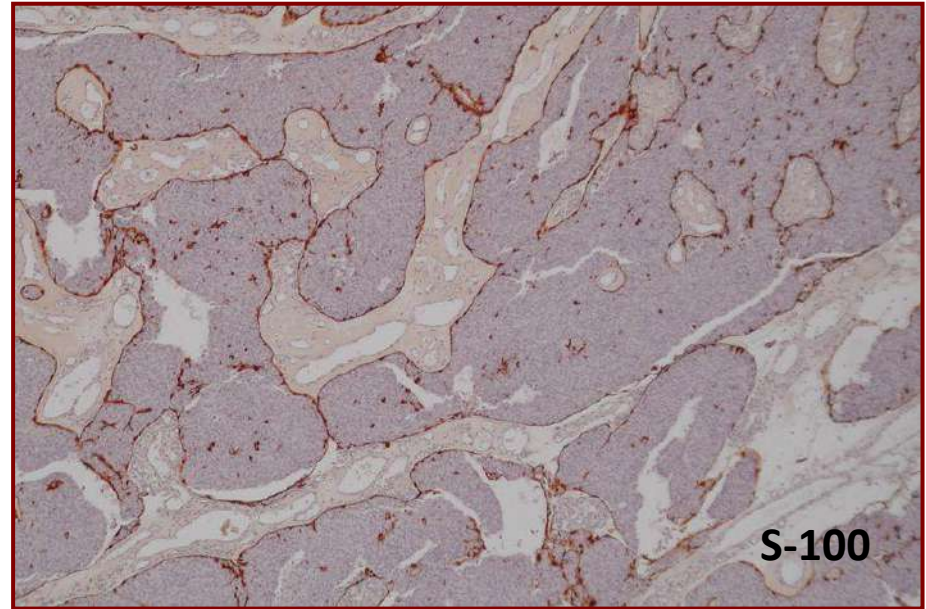
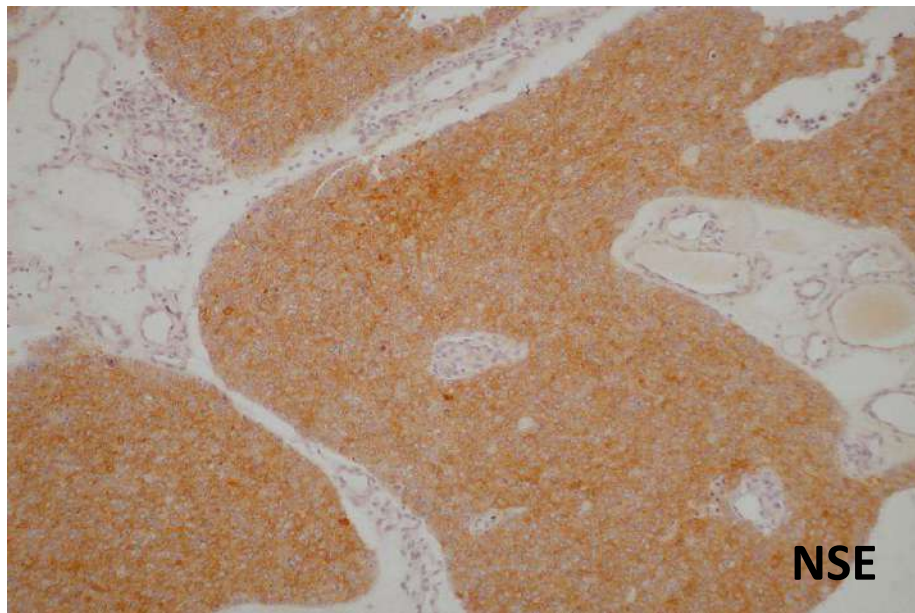
- Plasmocytoma and lymphoma
- Rhabdomyosarcoma
- synovialosarcoma
- Nasal hemangiopericytoma /glomangiopericytoma

Olfactory Neuroblastoma

- Rare, described in 1924 par Berger
- 3% to 5% nasosinal tumors
- Peak 2 to 6 decade
- No known risk factor
- often voluminous at the time of diagnosis
 - top of the nasal cavity
 - others origins (sinus ou endocrâne) discutables
- rare expression hormonale : Cushing, SIADH



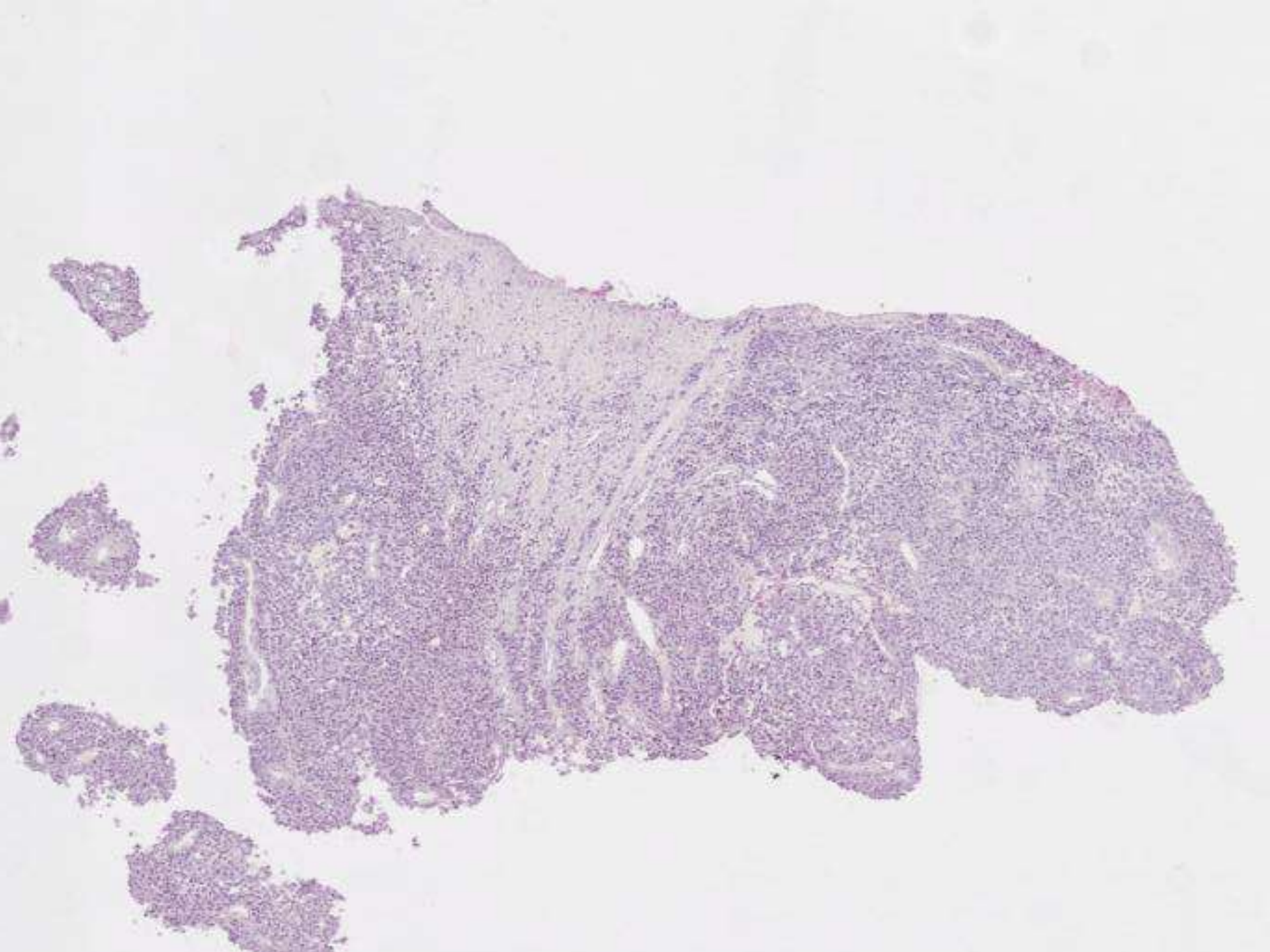
Courtesy Michel Wassef

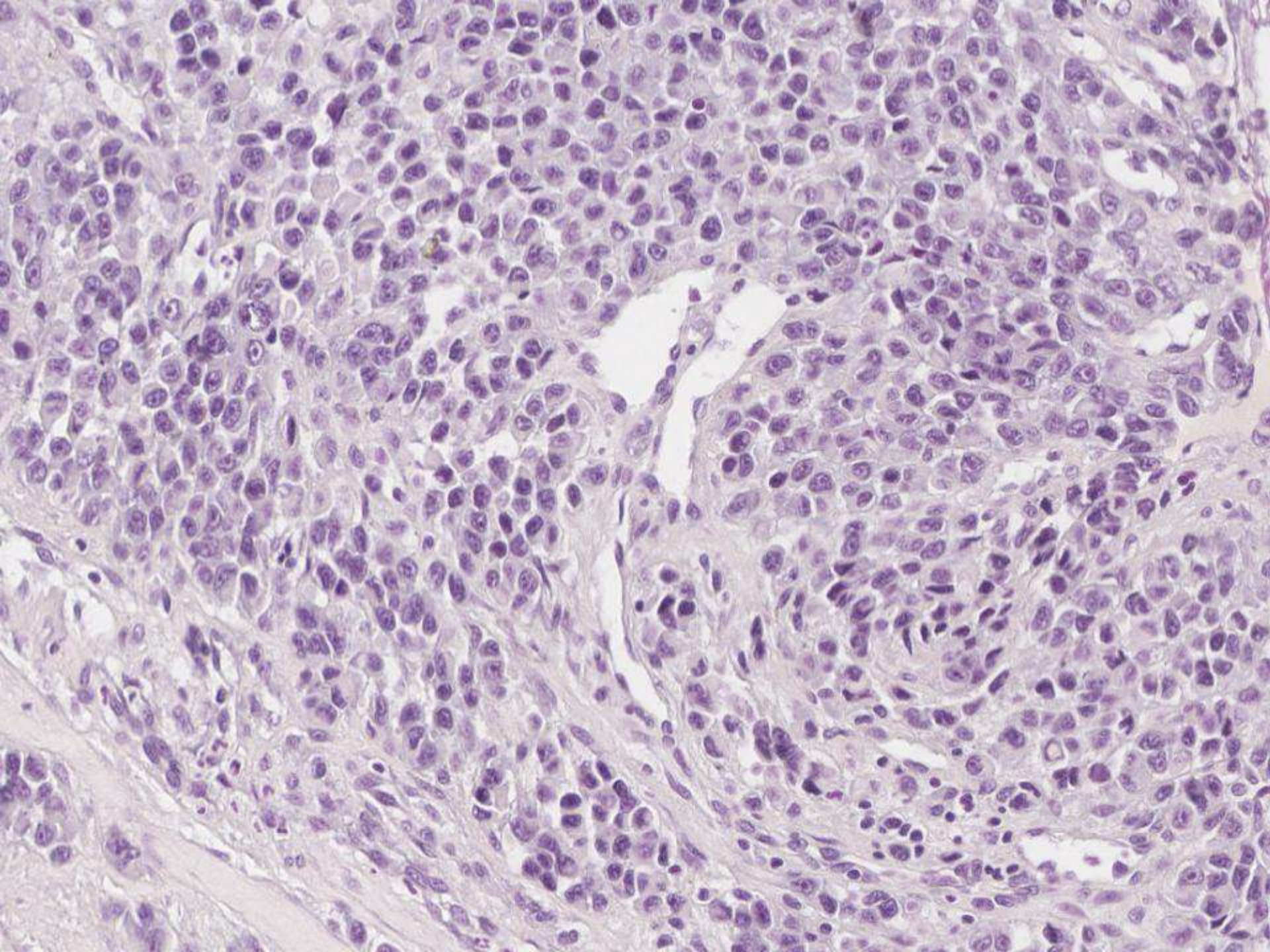


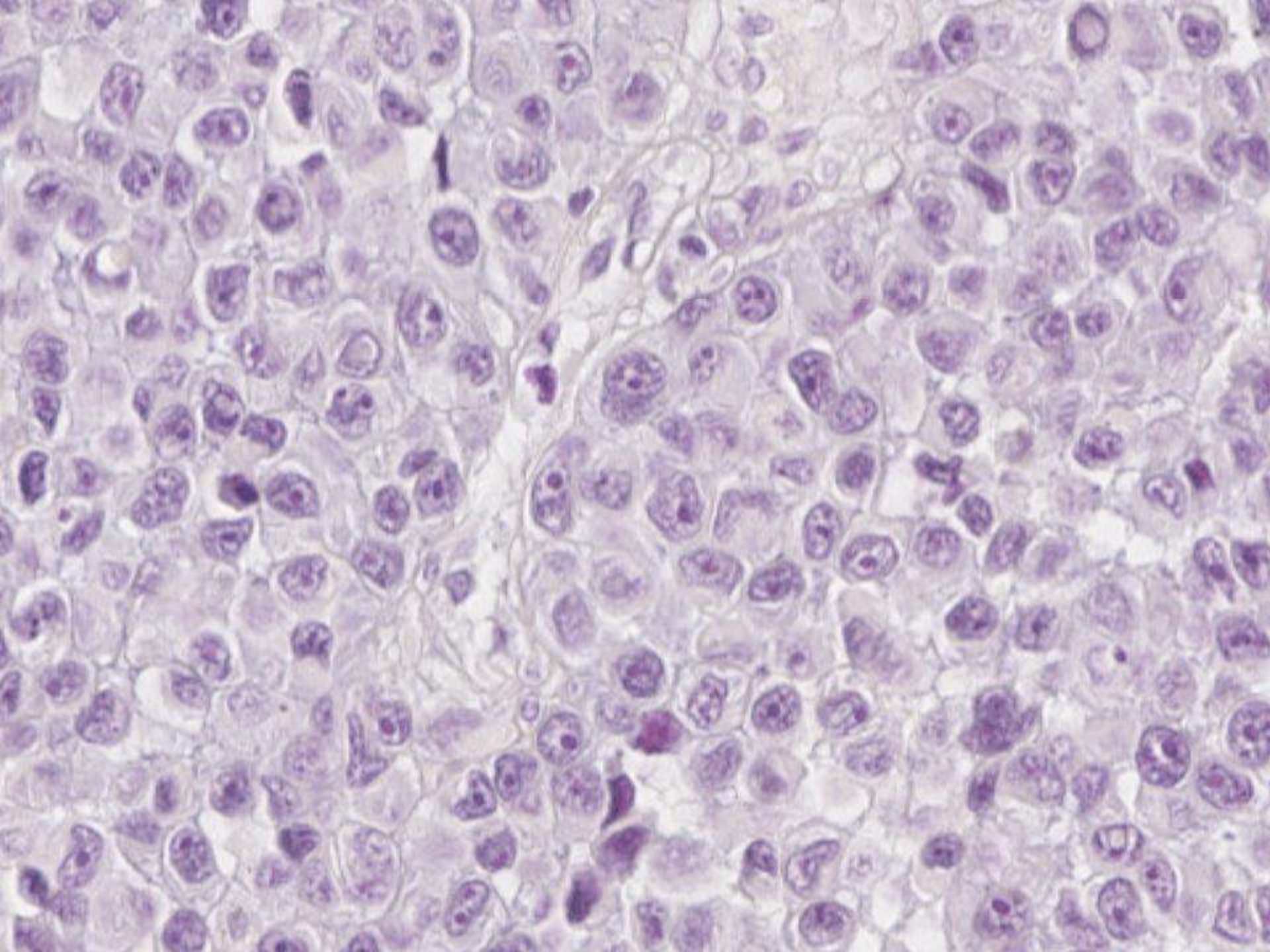
No expression of CD99, no Ewing/PNET translocation

Courtesy Michel Wassef

Case 1H
woman 37 yo
sudden anosmia nasal cavity biopsy

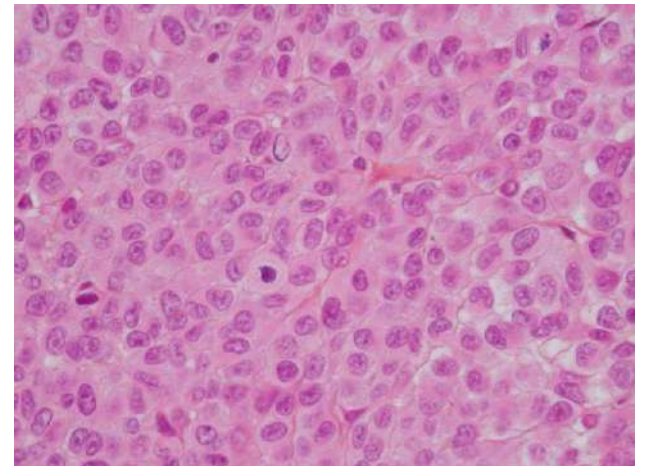
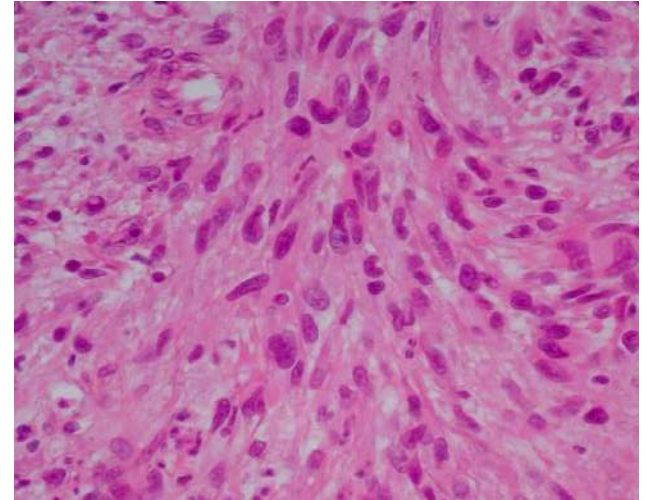






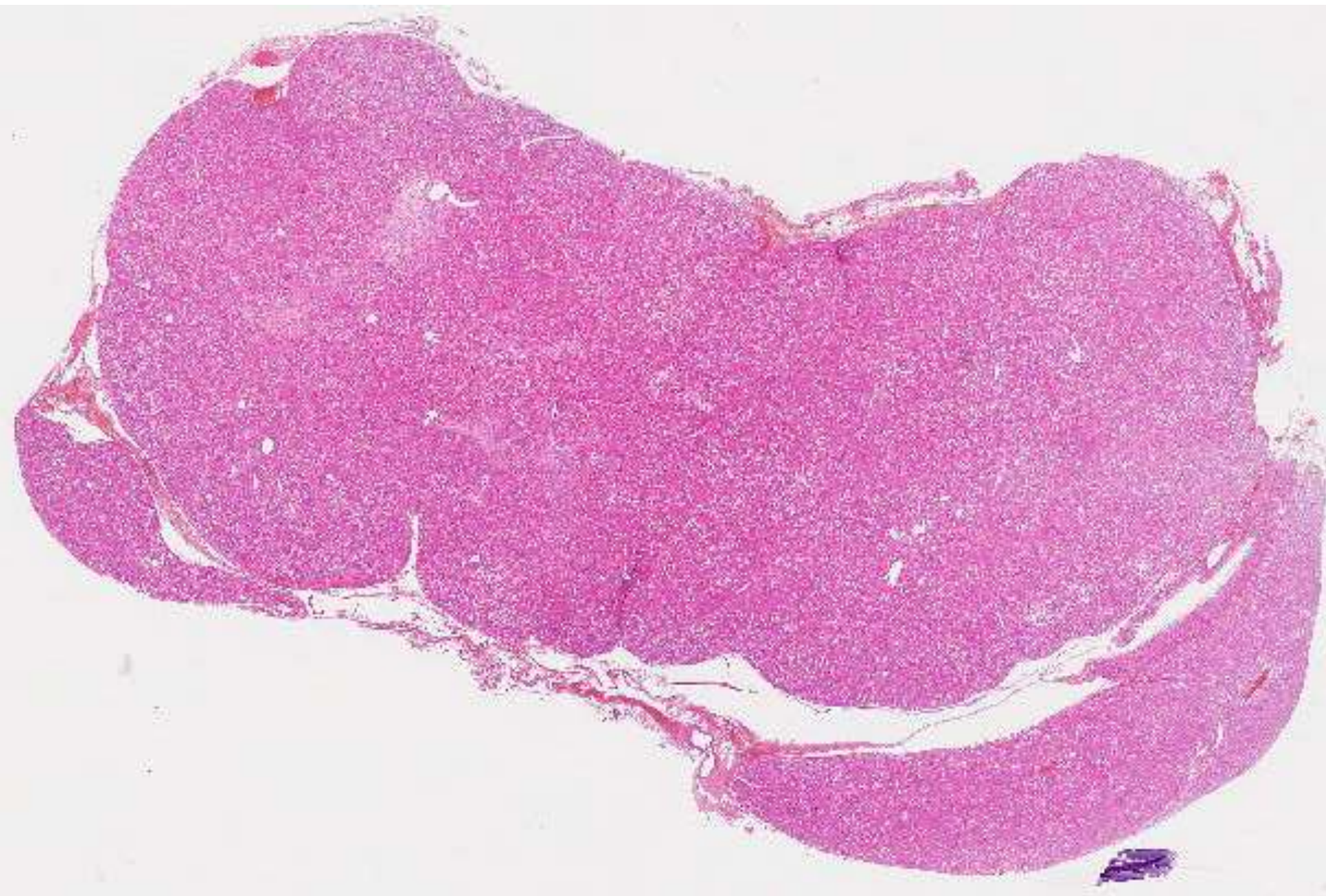
Mucosal melanoma

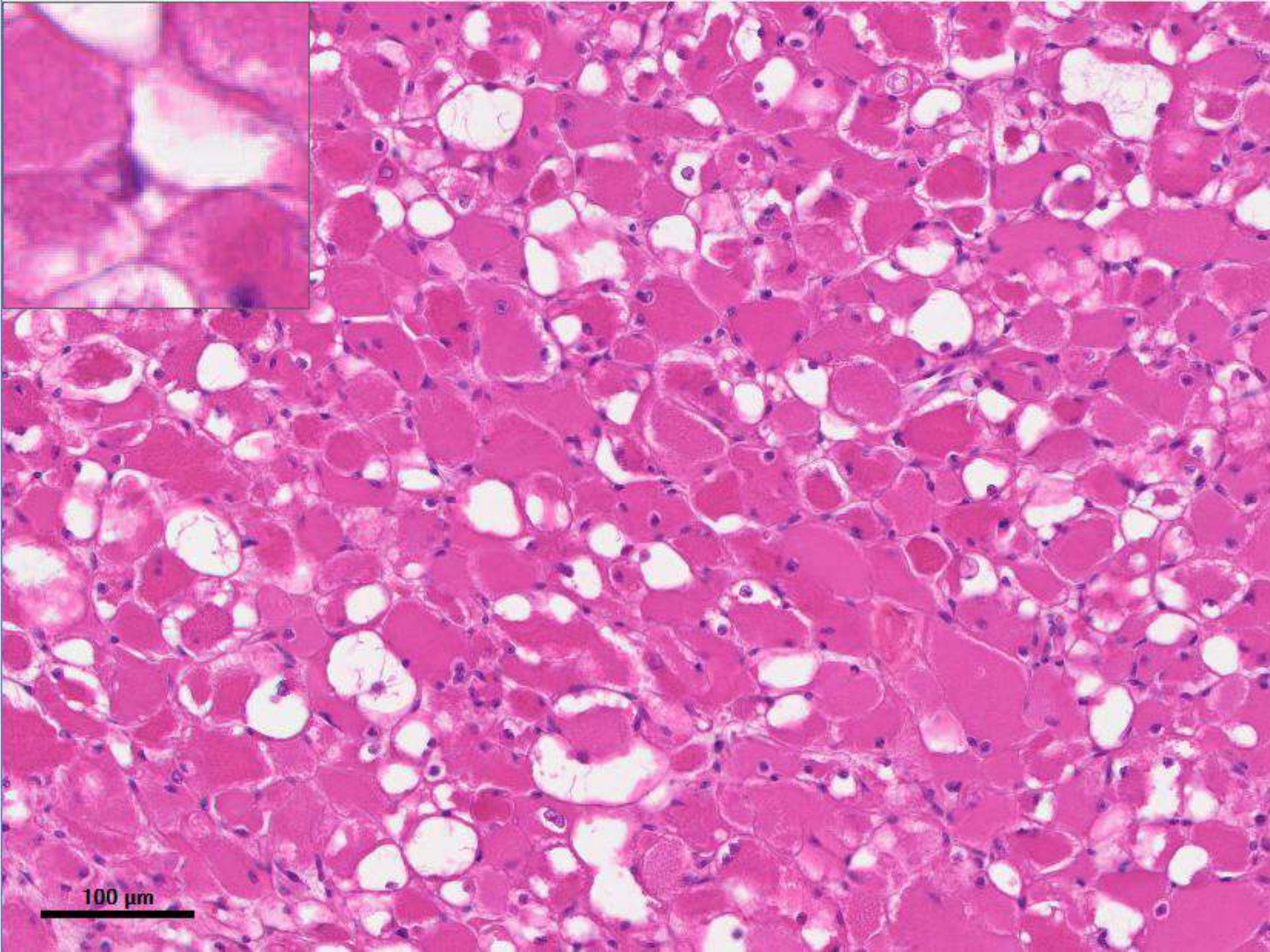
- Tumor rapidly evolutive
- 1% of all melanomas
- Incidence peak 70y
- Often located on nasal septum or vestibule
- Surgery :sinuses wide excision, followed by radiotherapy despite relative radioresistance
- Immunotherapy +++
- metastatic potential 5-year survival of 20 to 30%



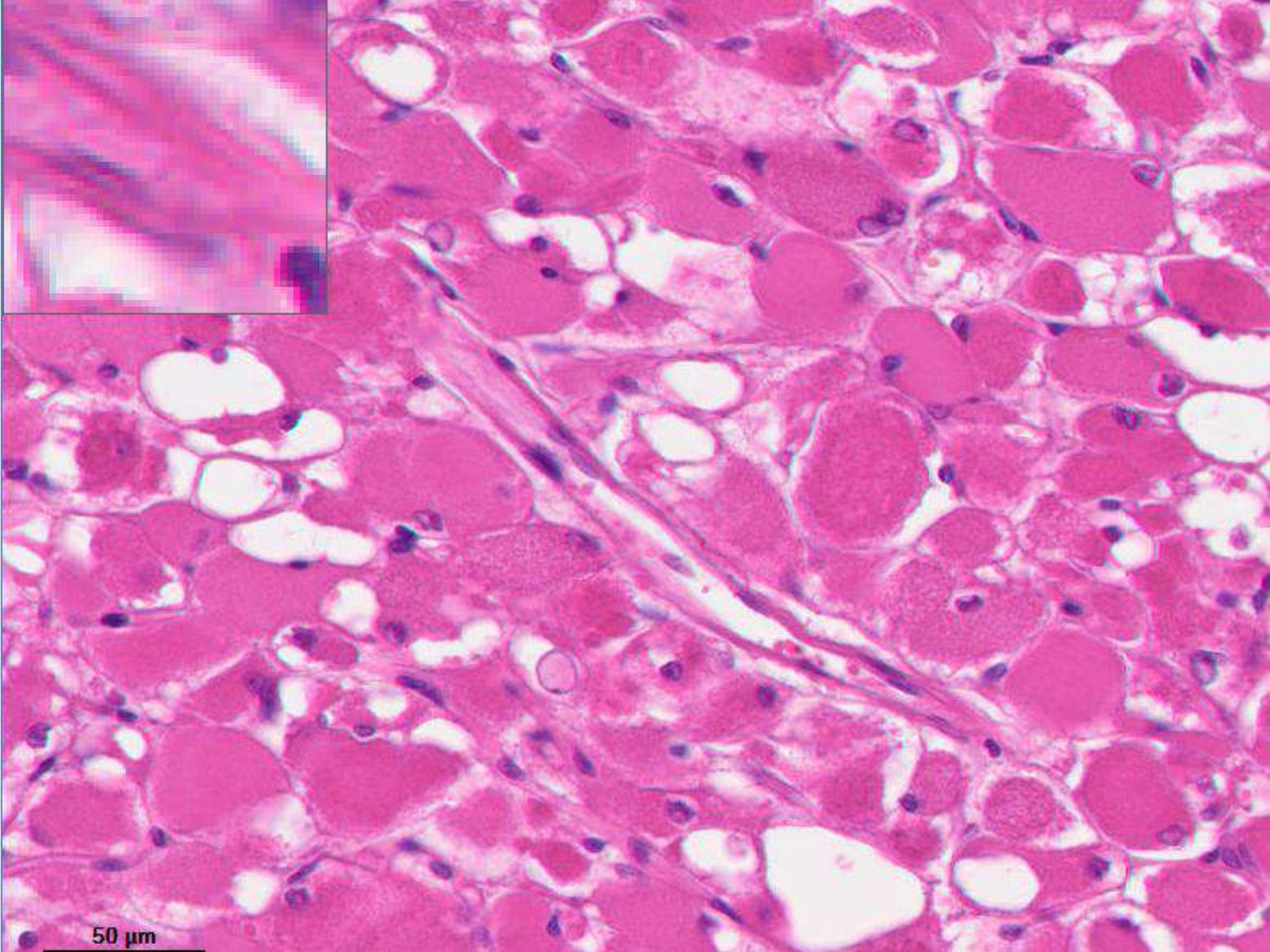
Case 1M

woman 19 yo right parotid lesion
with rapid growth





100 μm



50 μ m