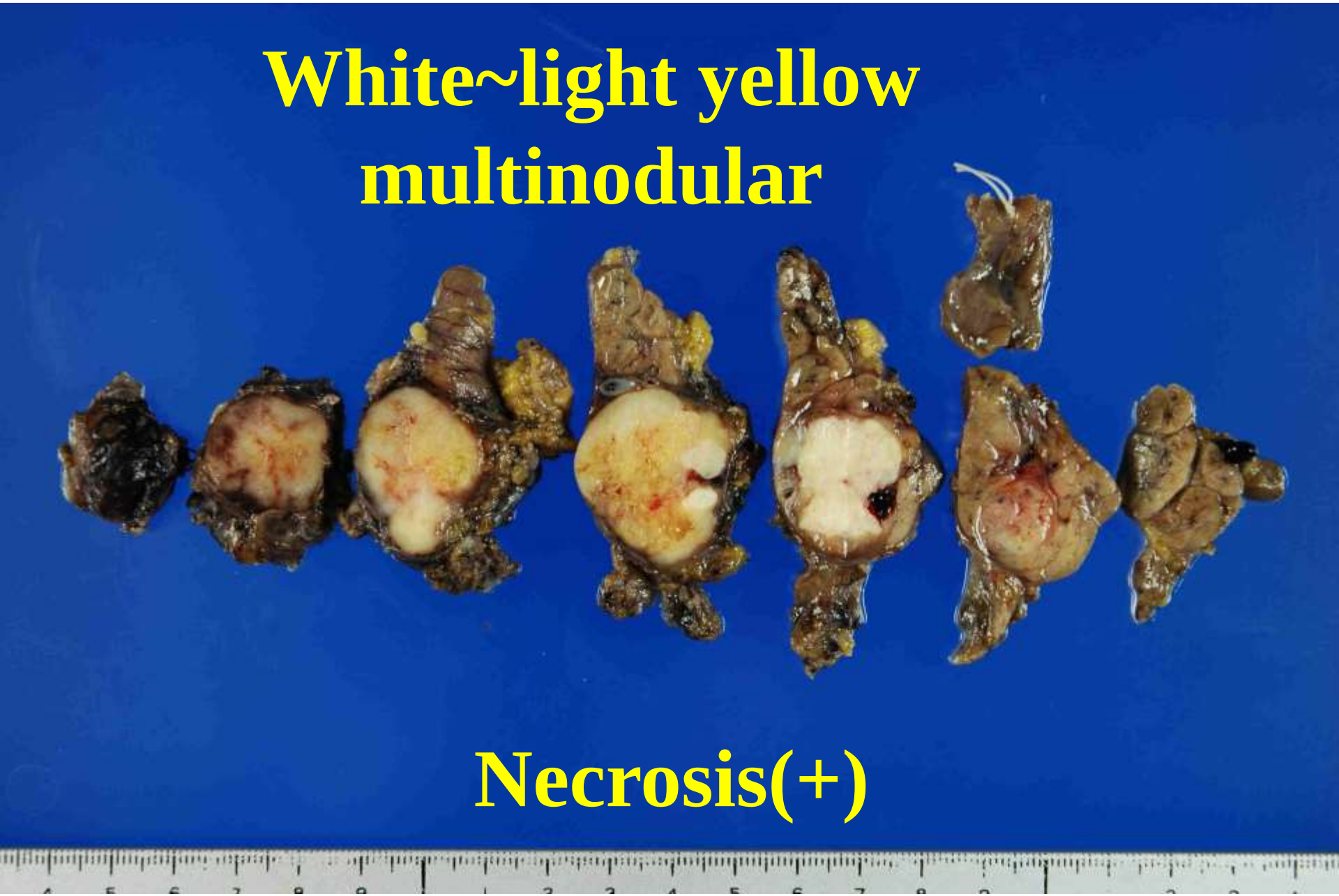
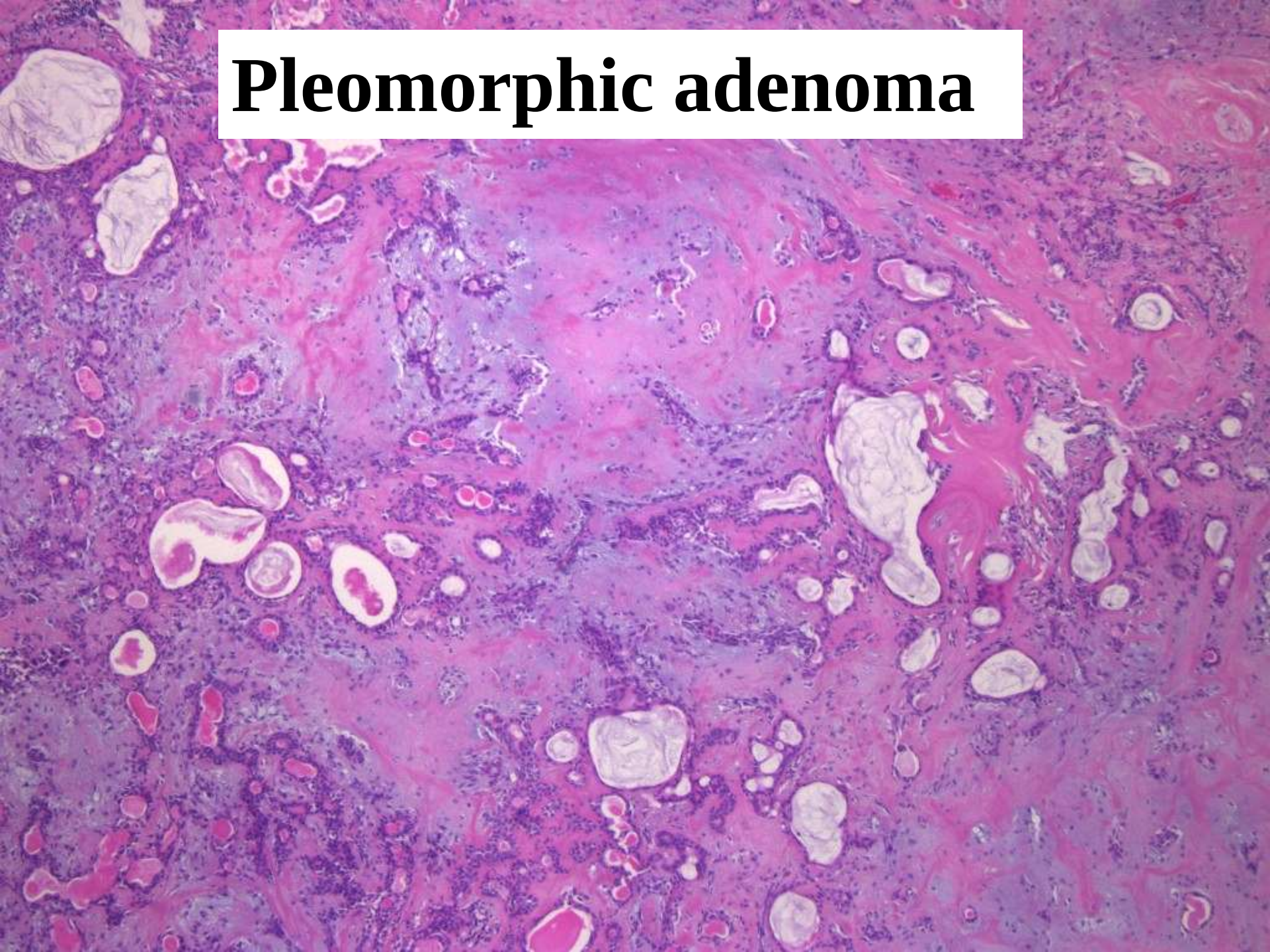
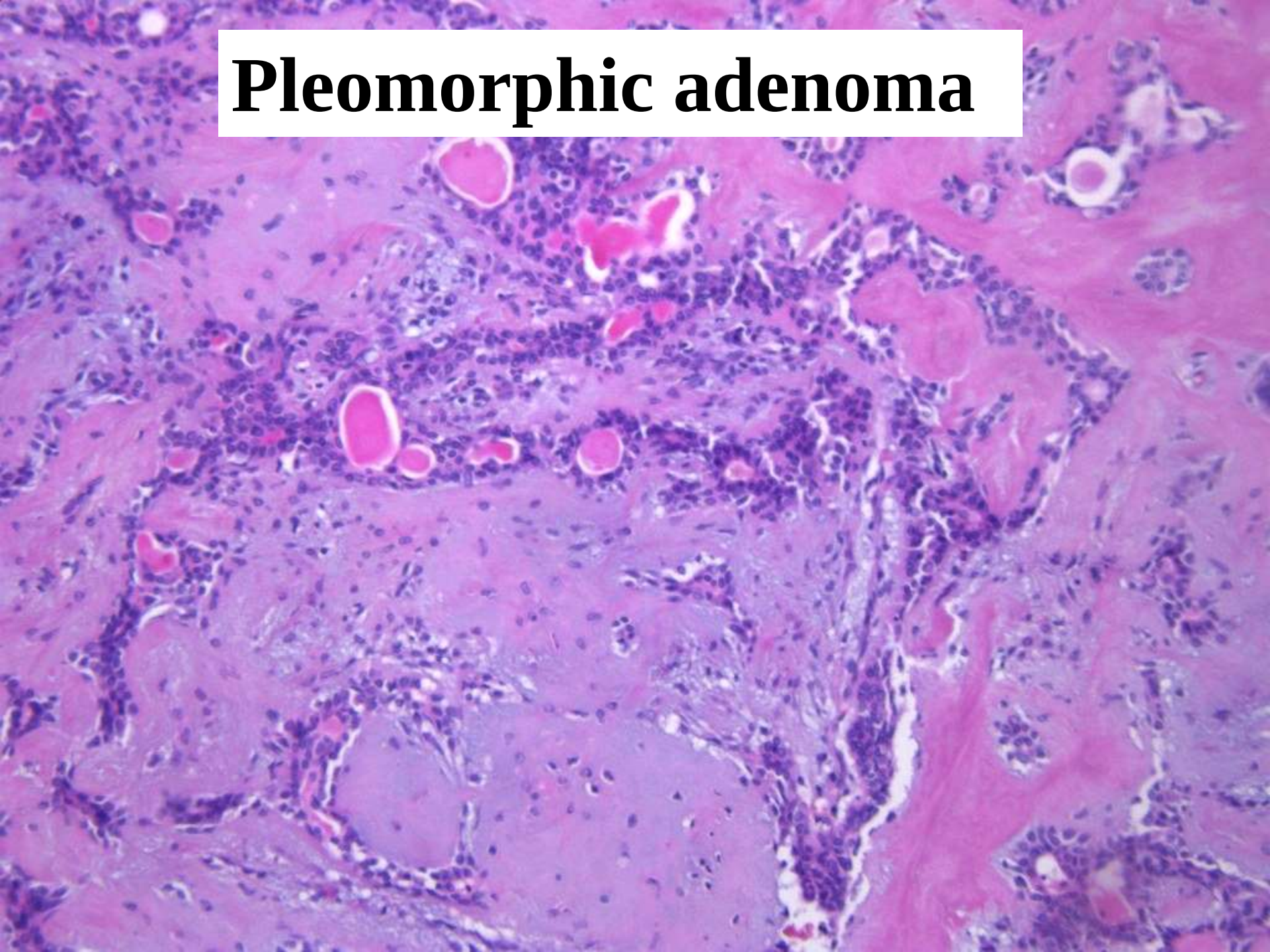

Tumor 32x27x24mm

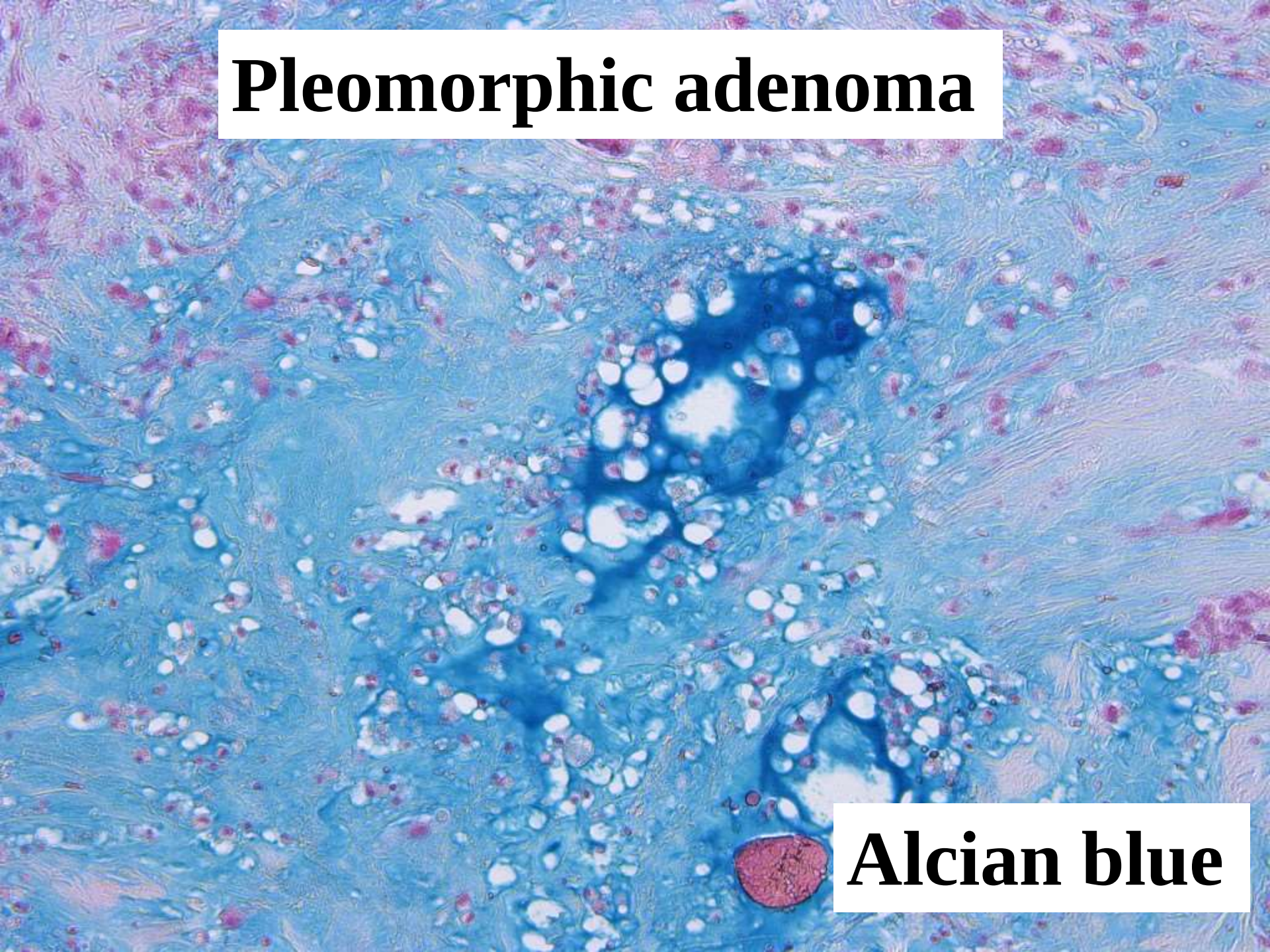

White~light yellow multinodular
Necrosis(+)

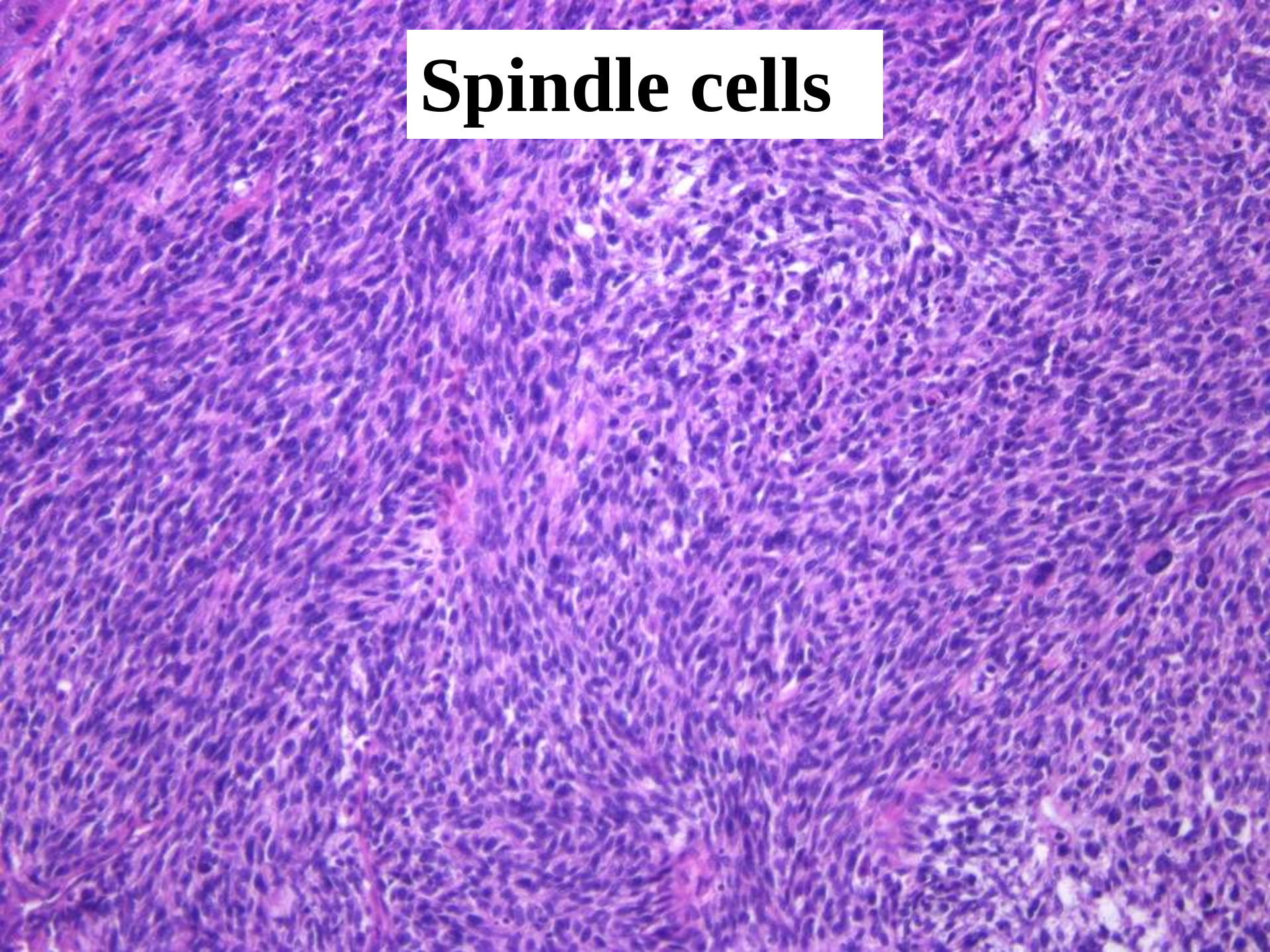
Pleomorphic adenoma

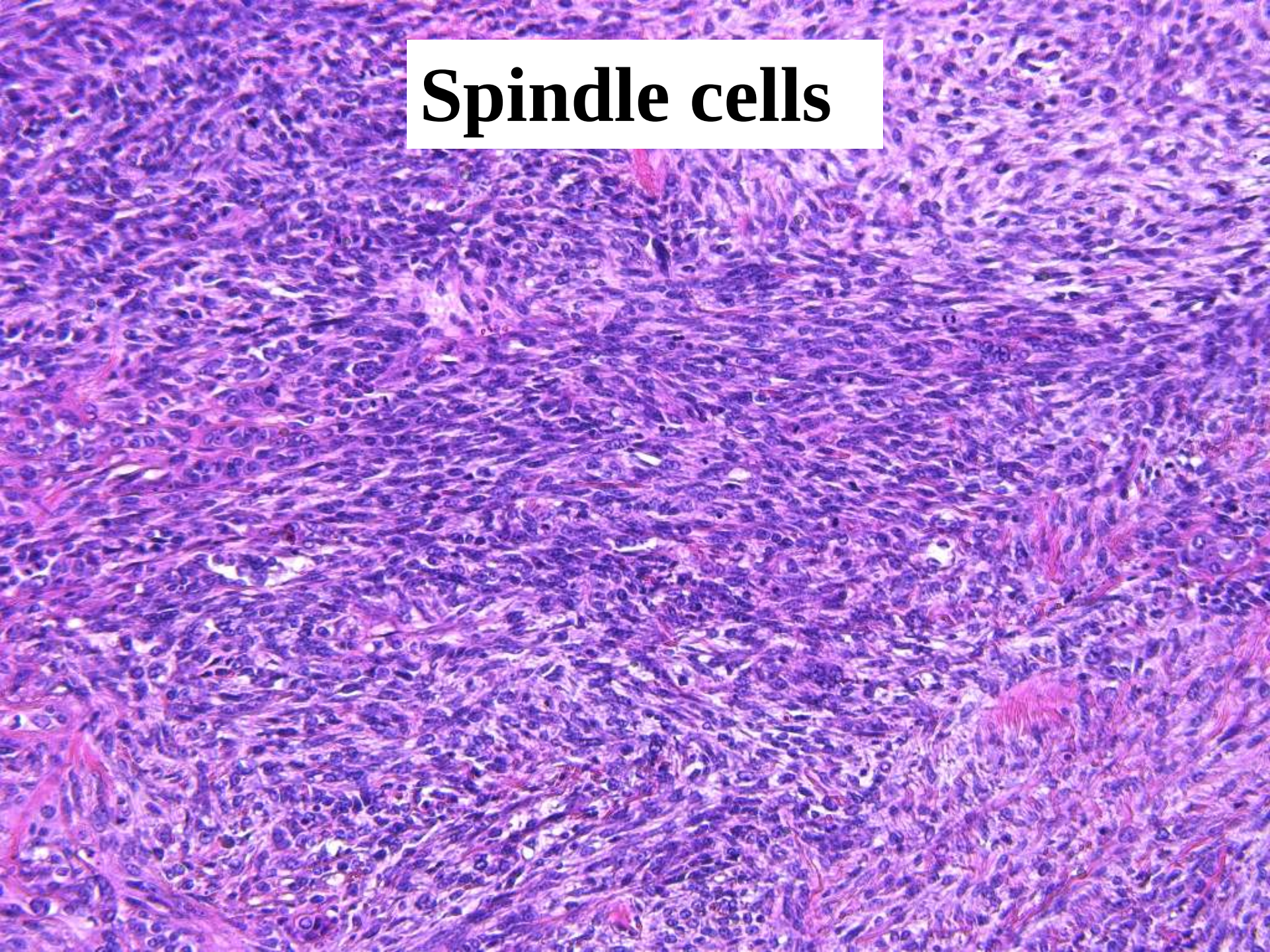


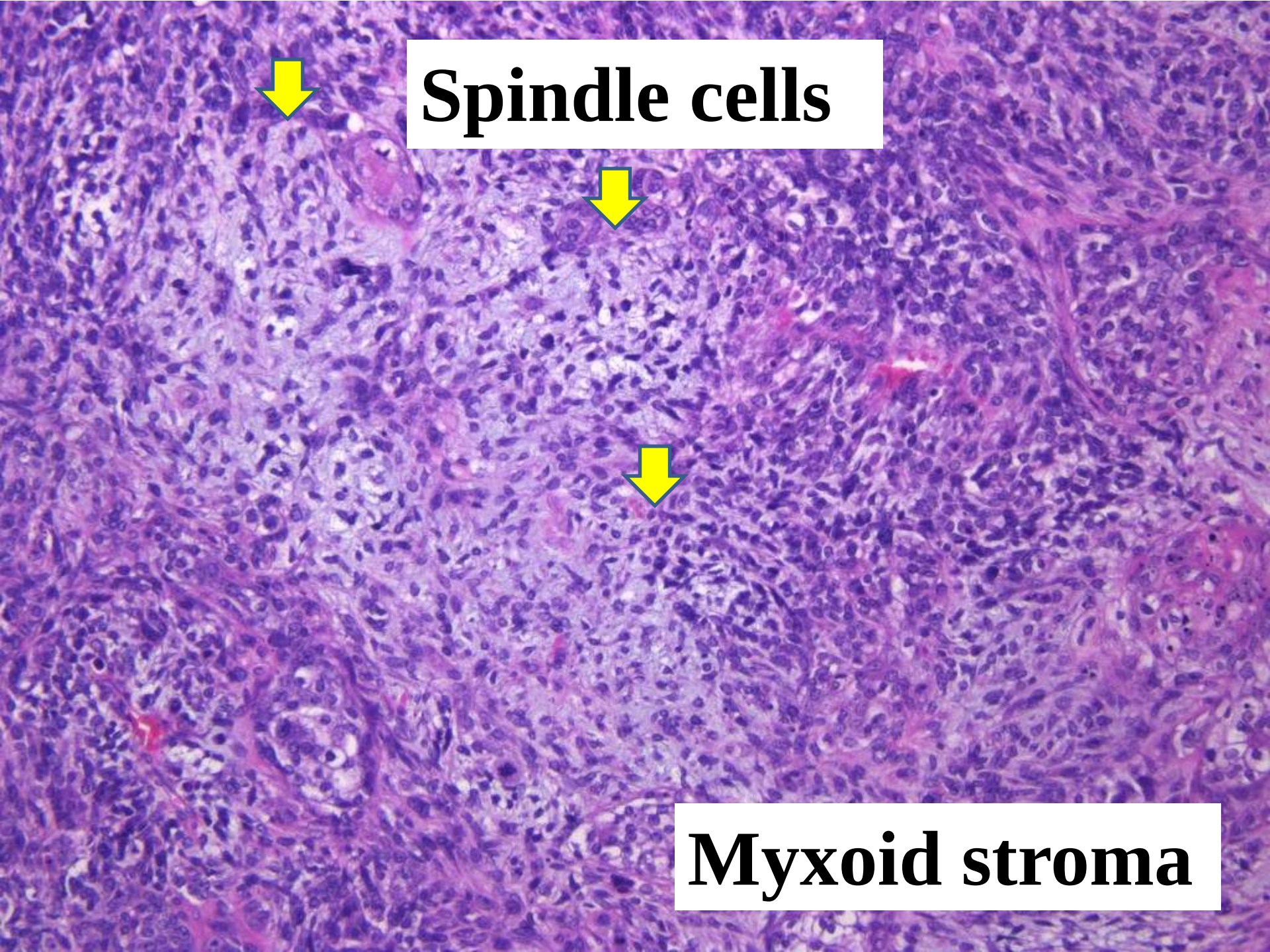
Pleomorphic adenoma

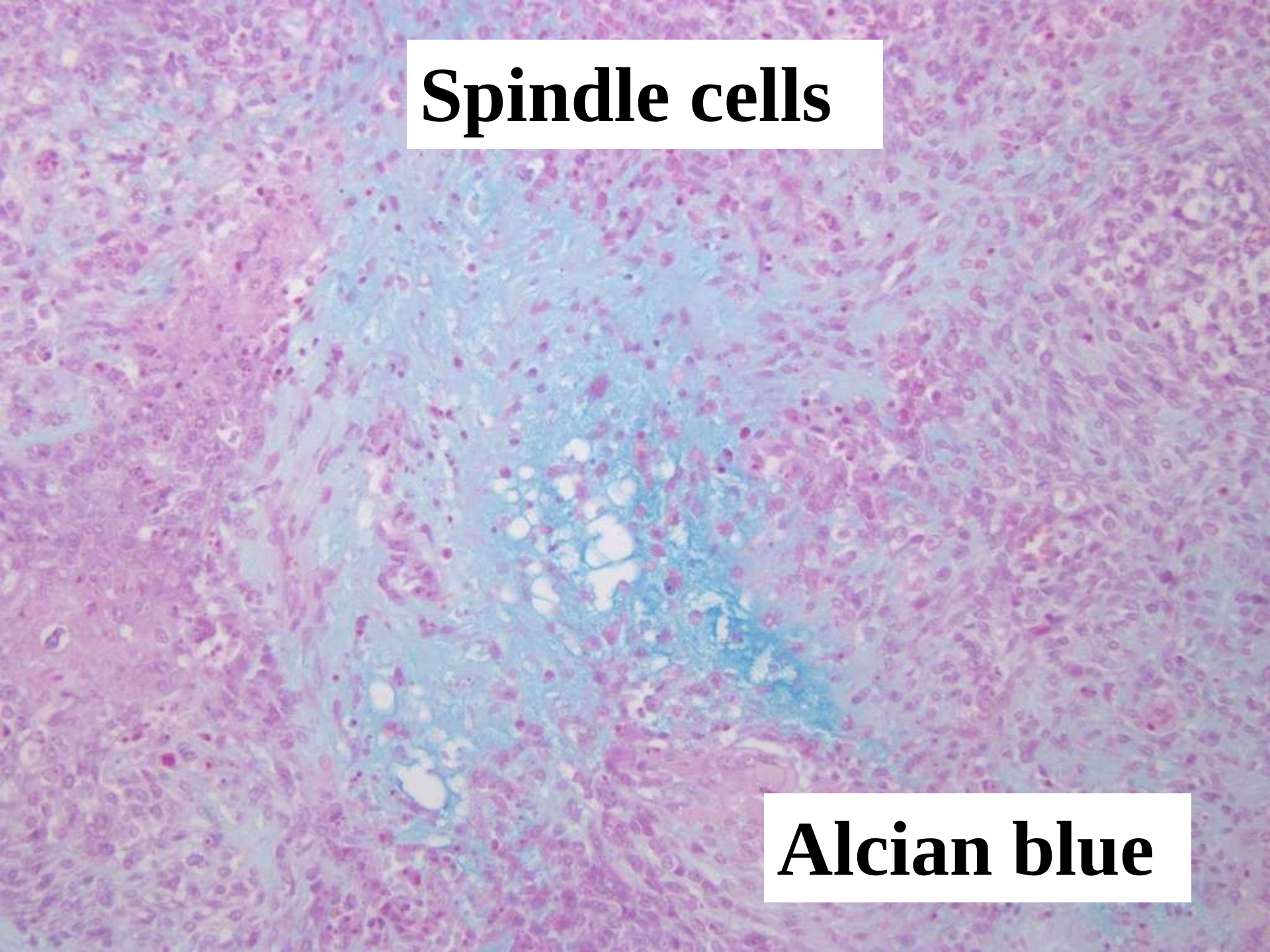


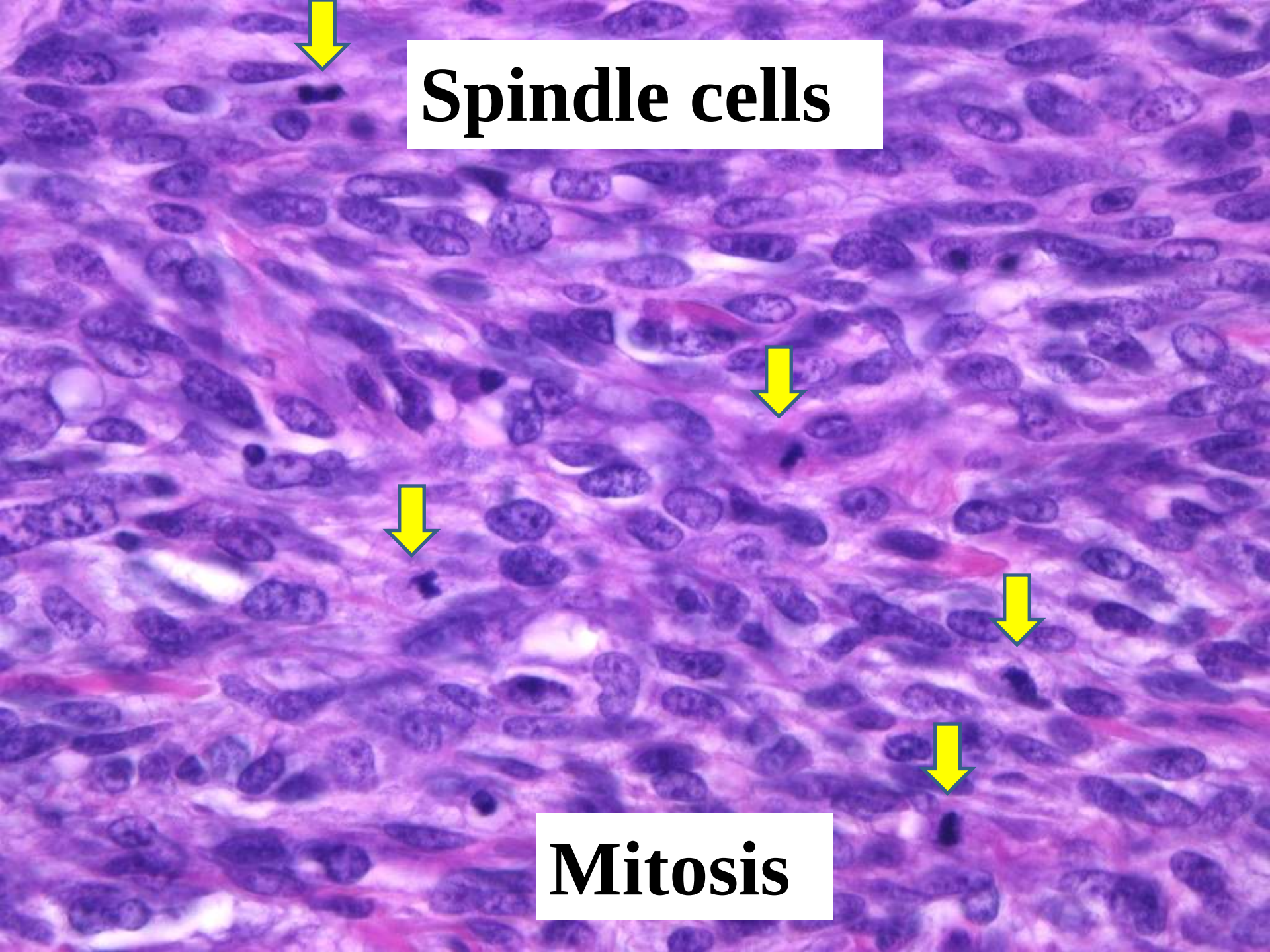

Pleomorphic adenoma
Alcian blue

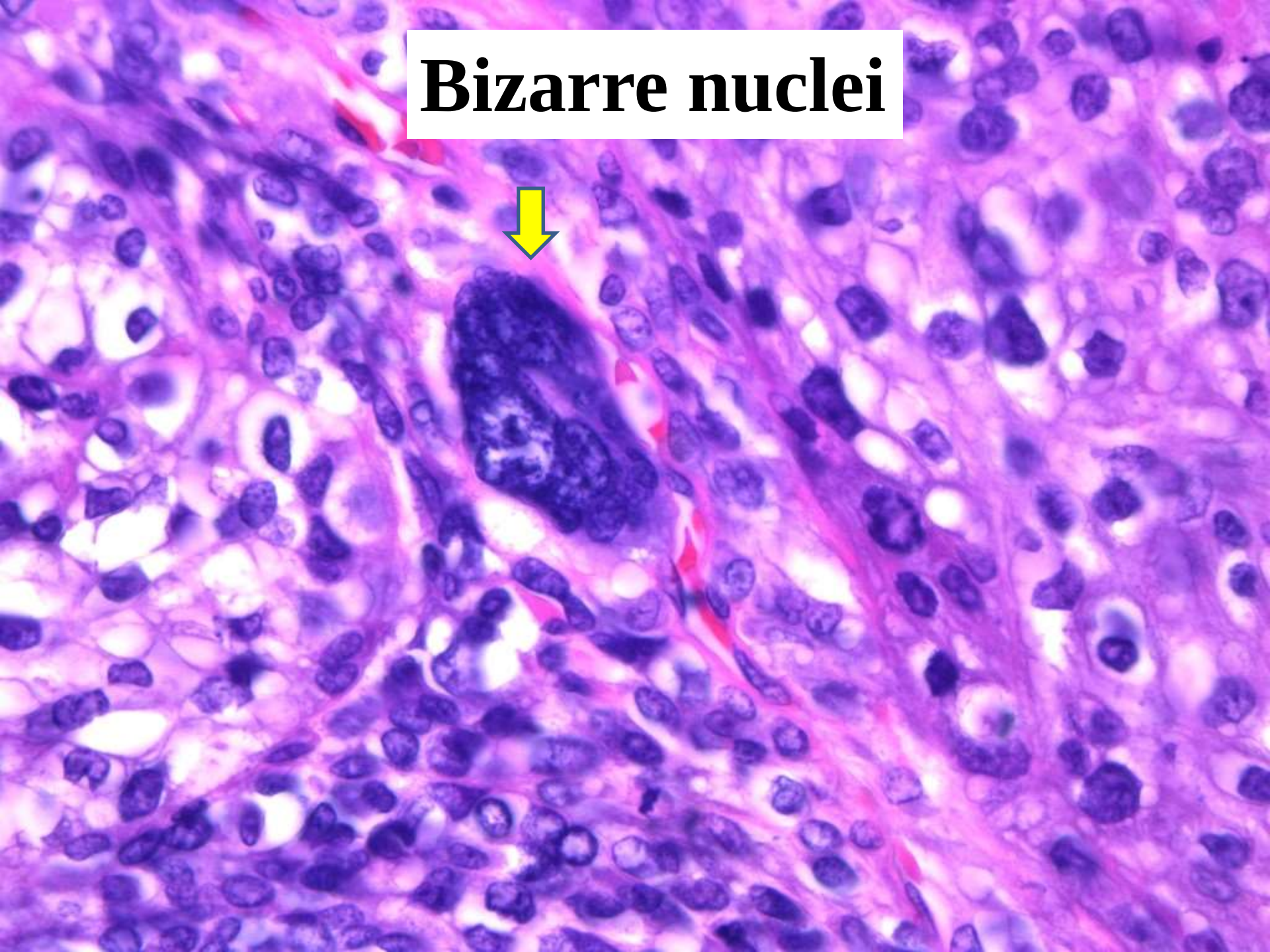

Spindle cells

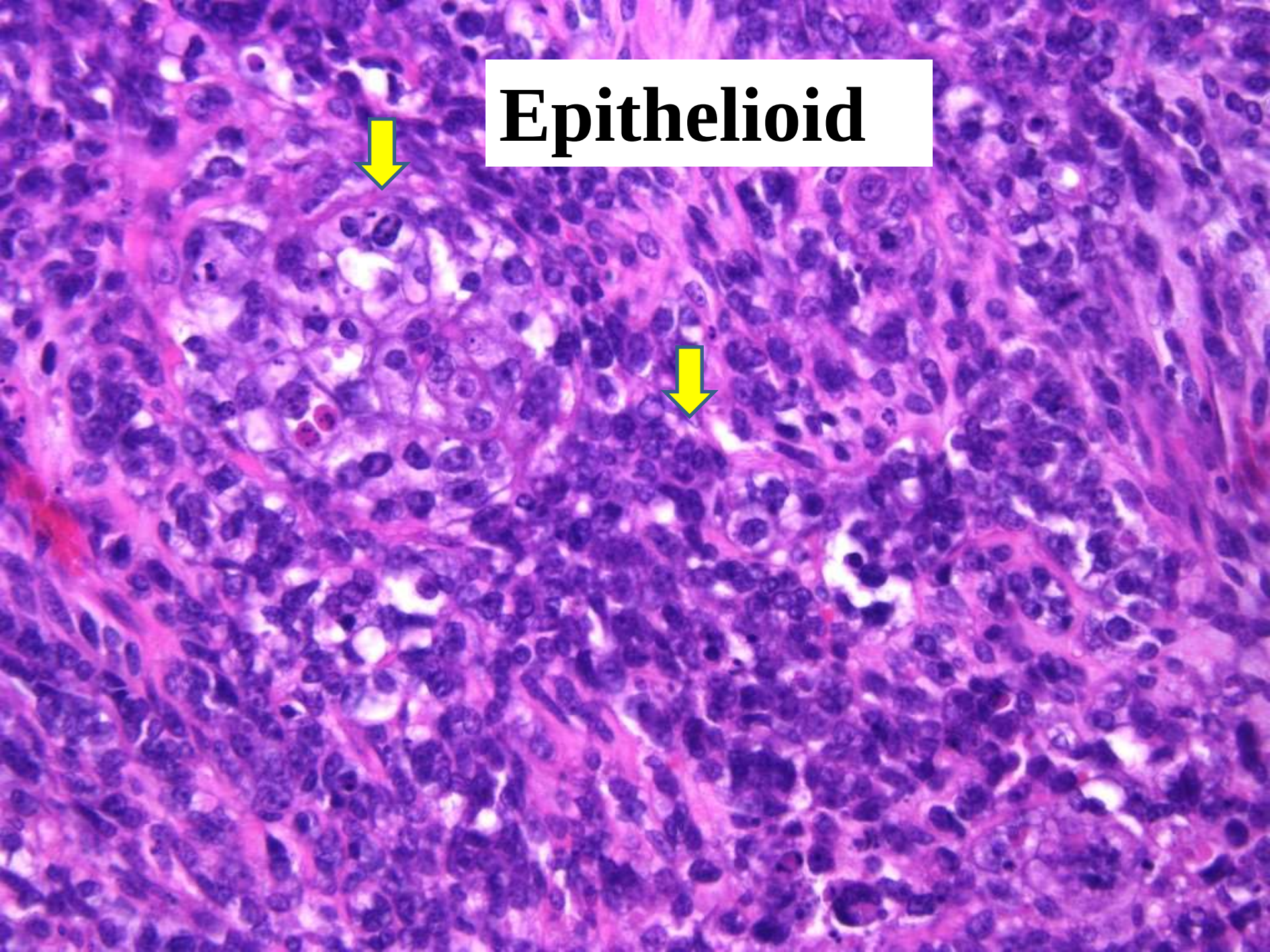

Spindle cells

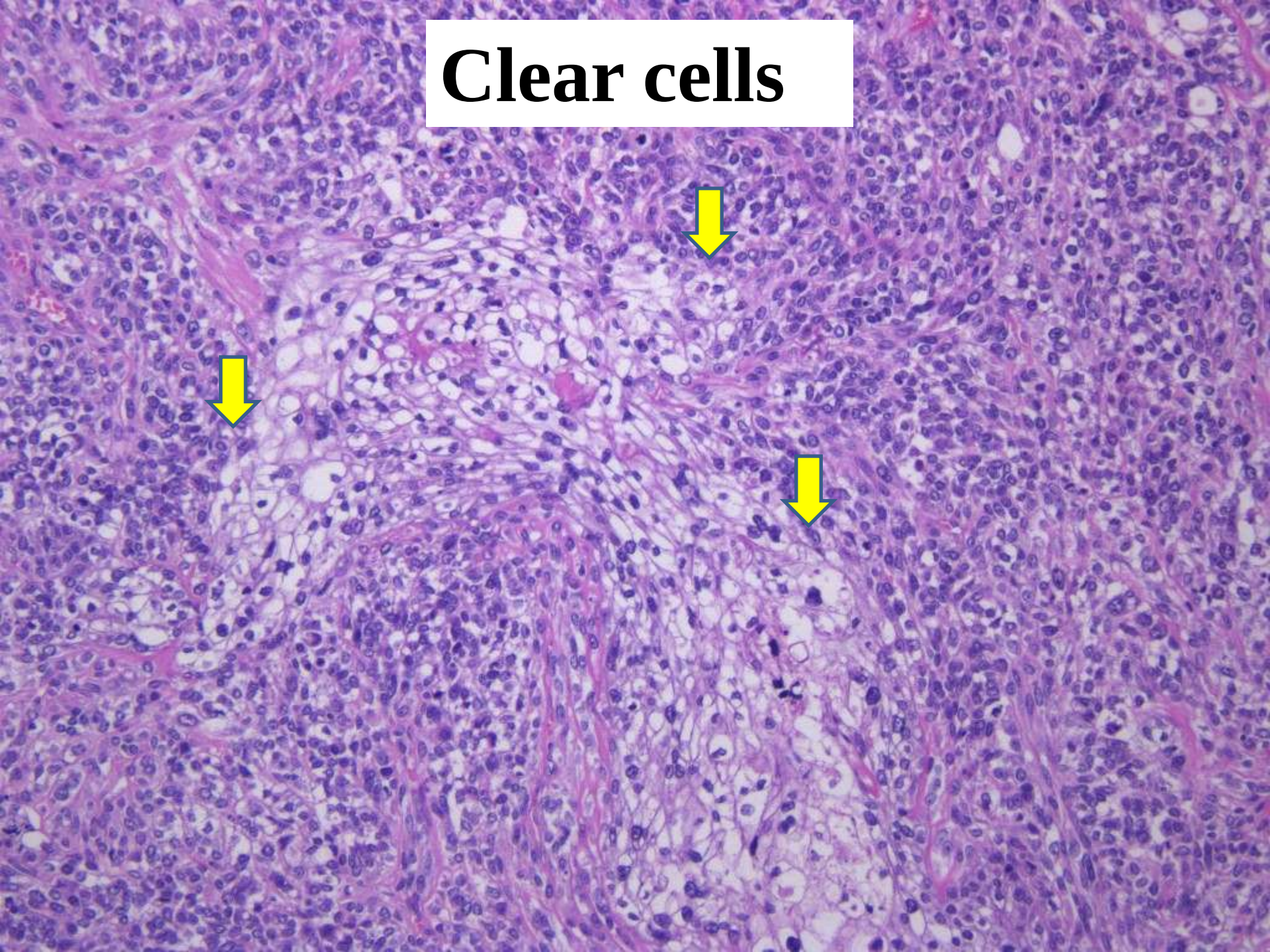

Spindle cells
Myxoid stroma

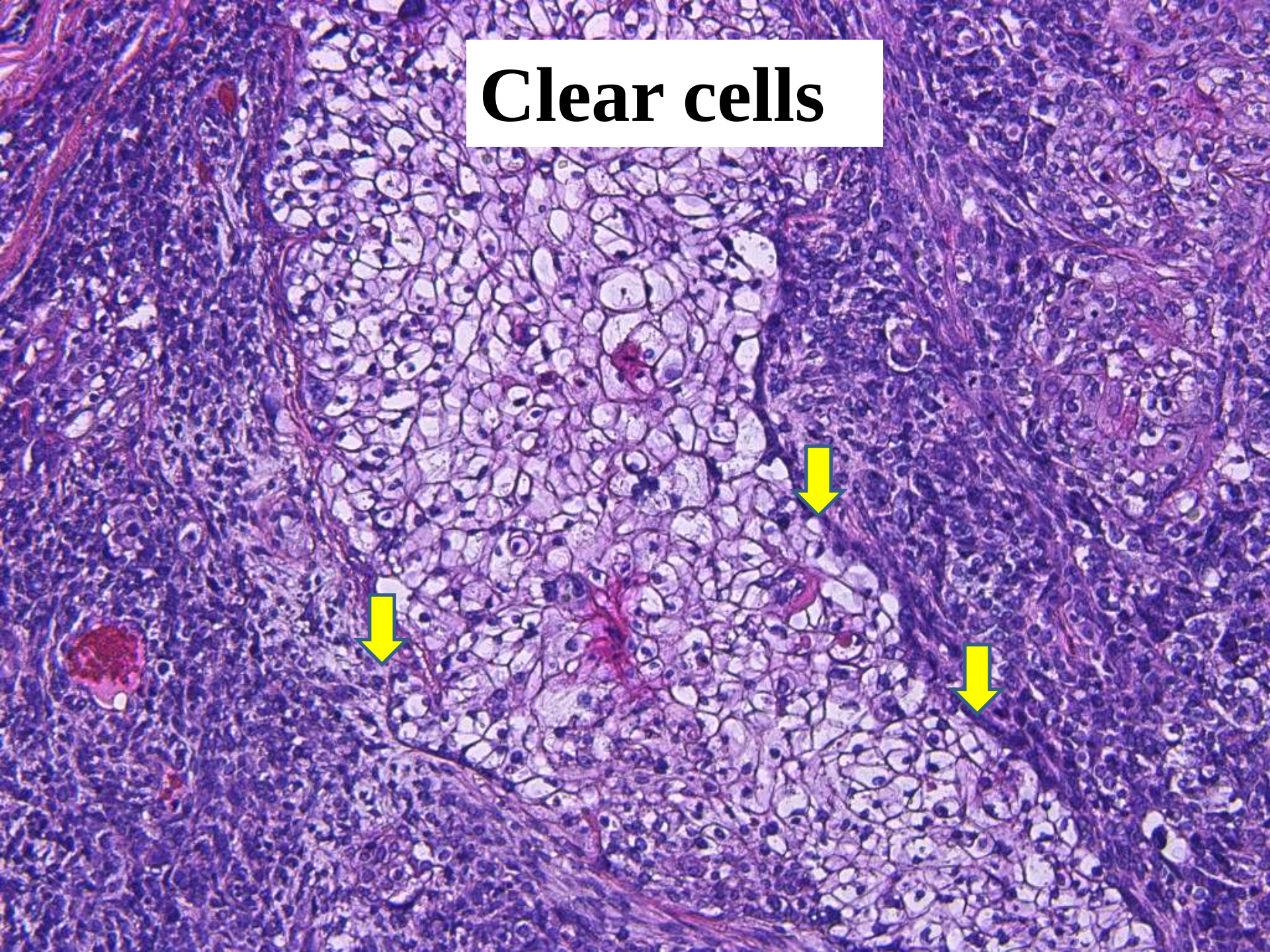

Spindle cells
Alcian blue

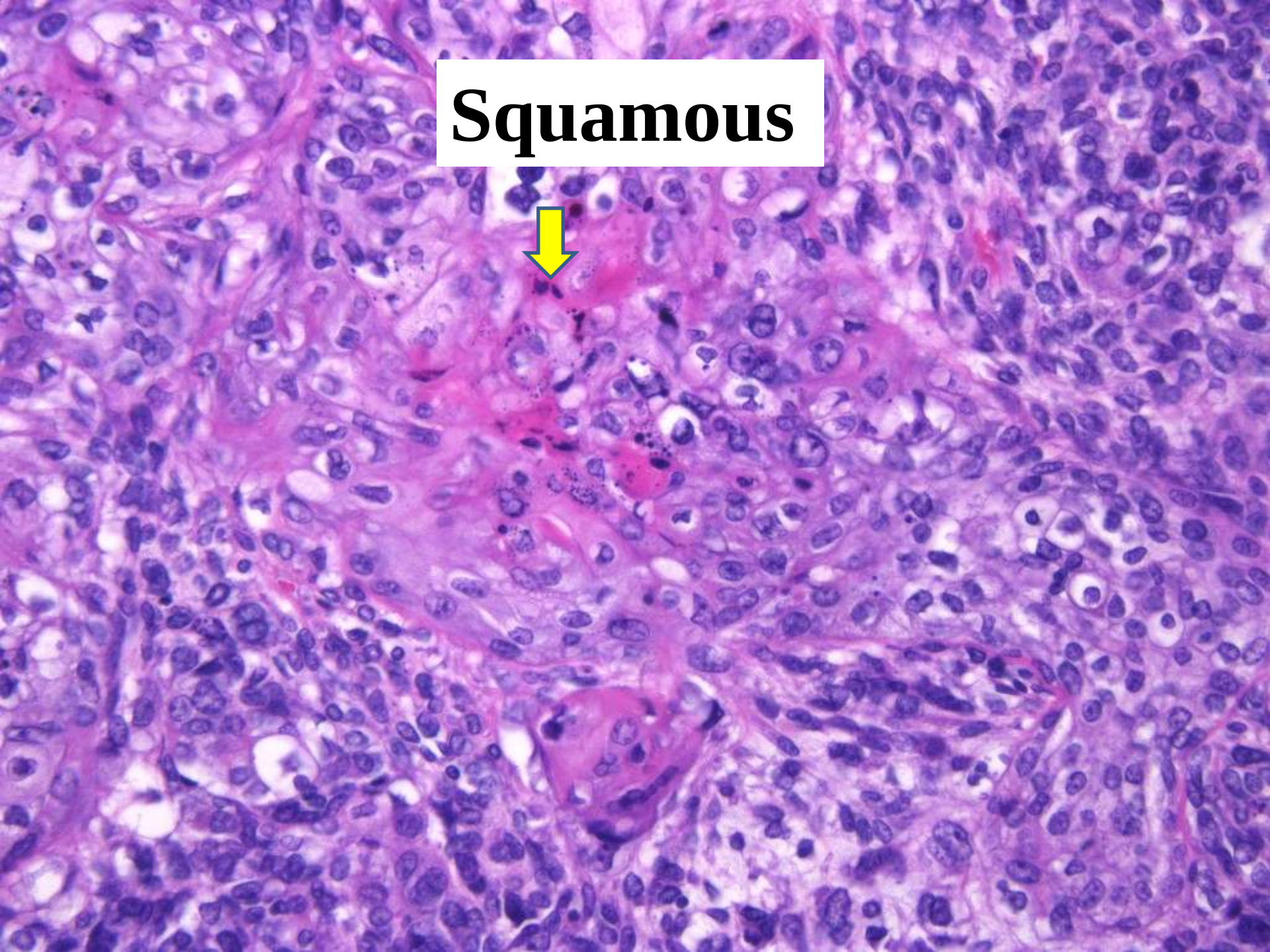

Spindle cells
Mitosis

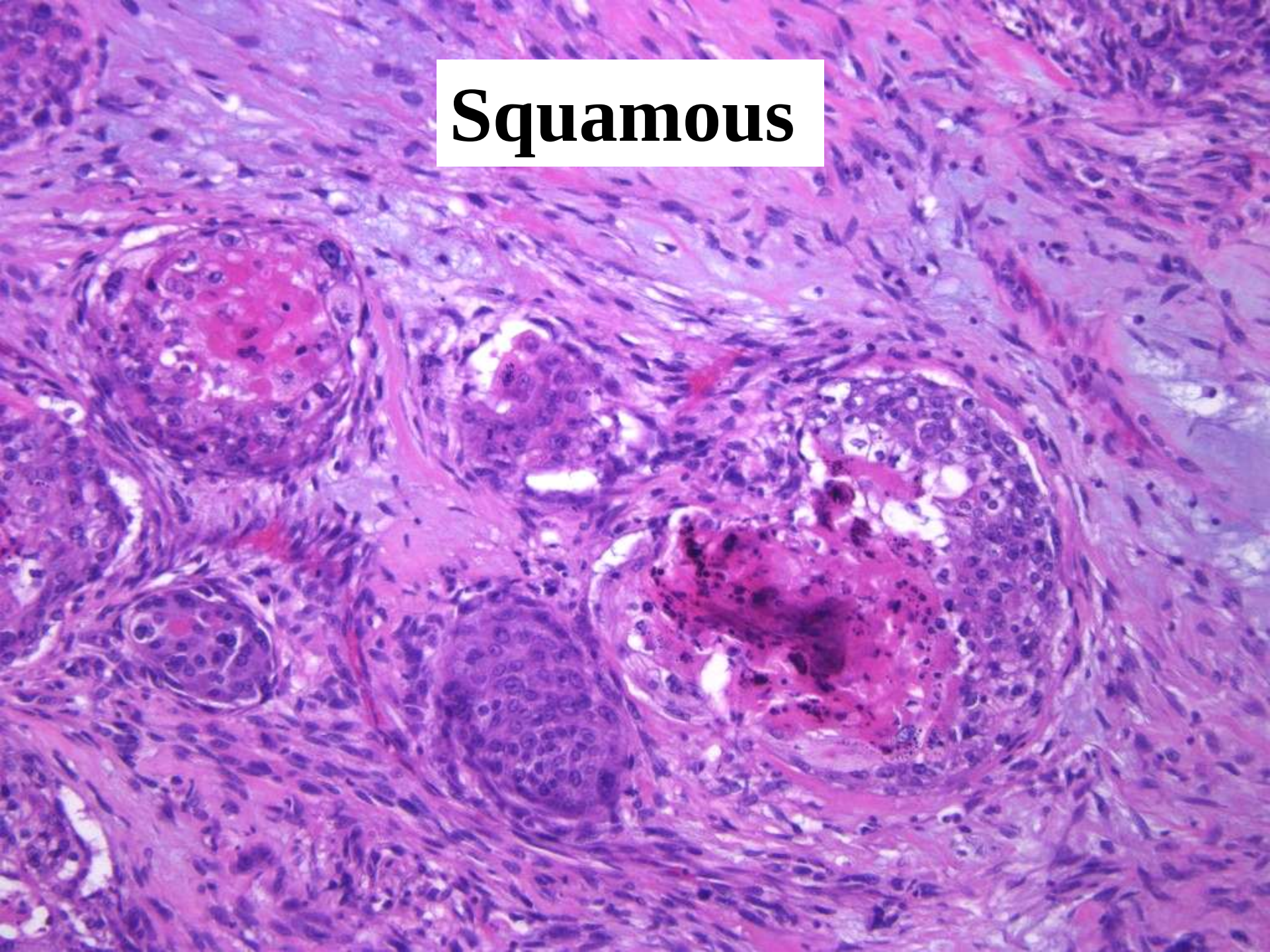

Bizarre nuclei

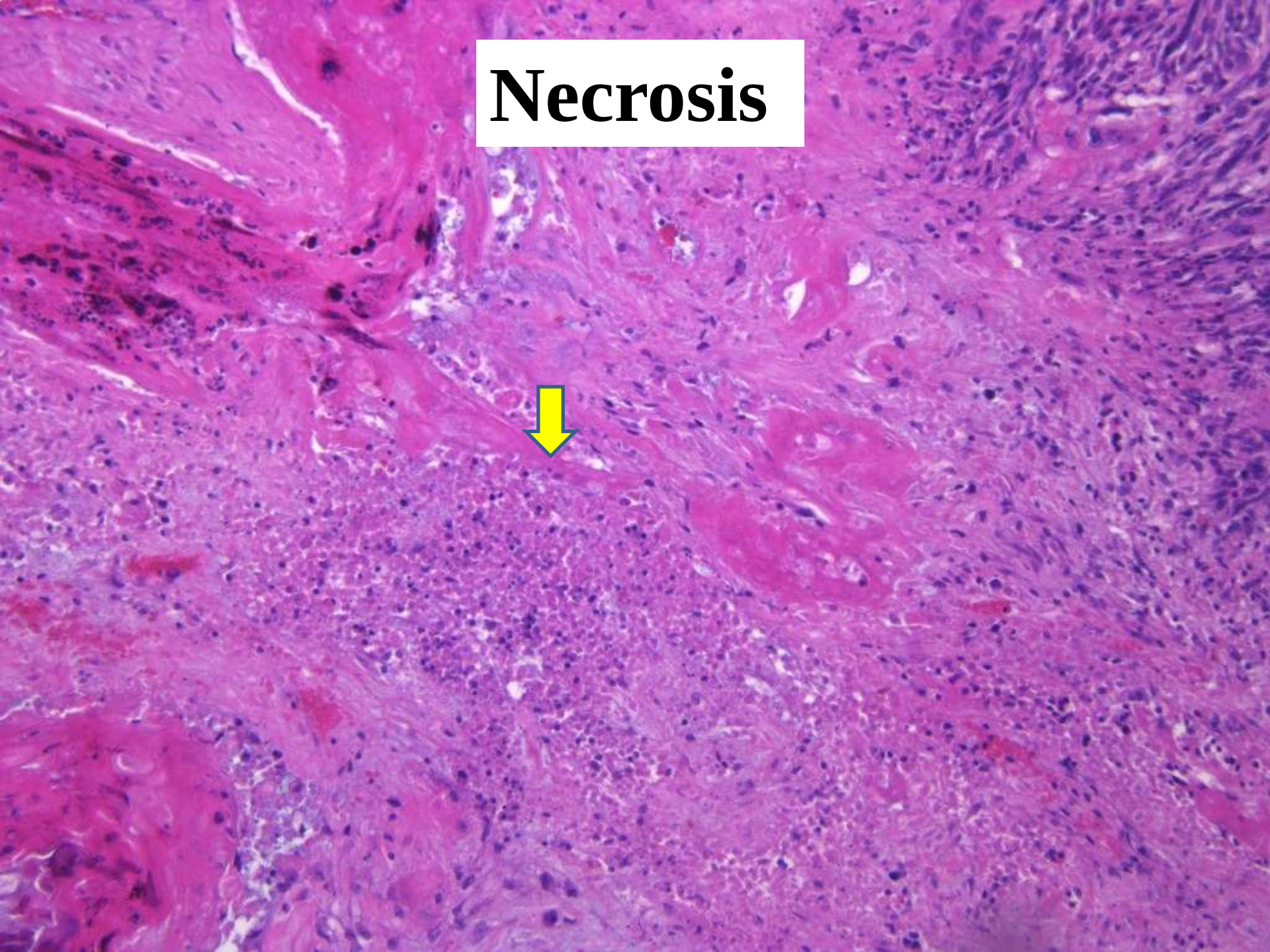

Epithelioid

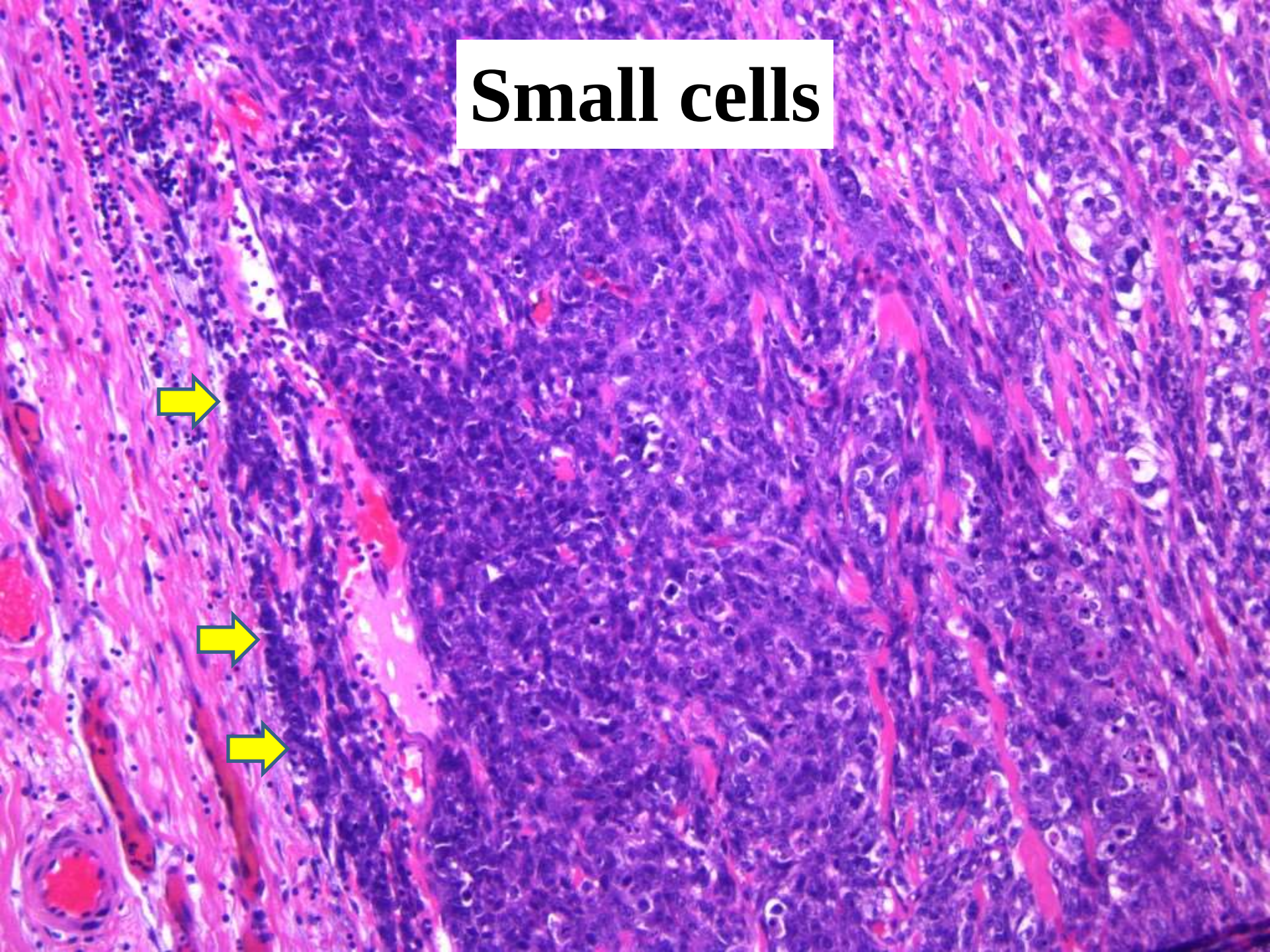

Clear cells

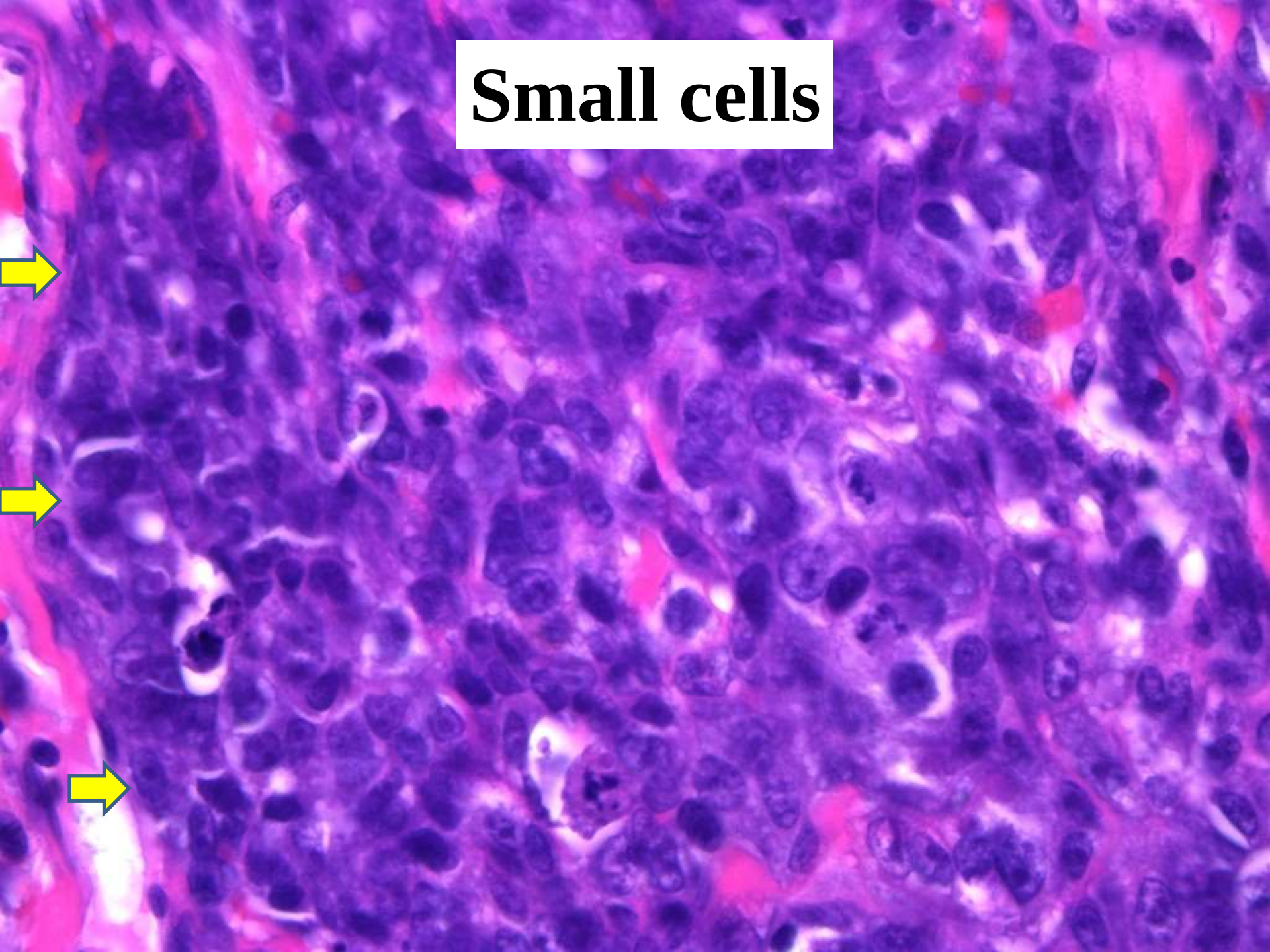

Clear cells


Squamous


Squamous


Necrosis


Small cells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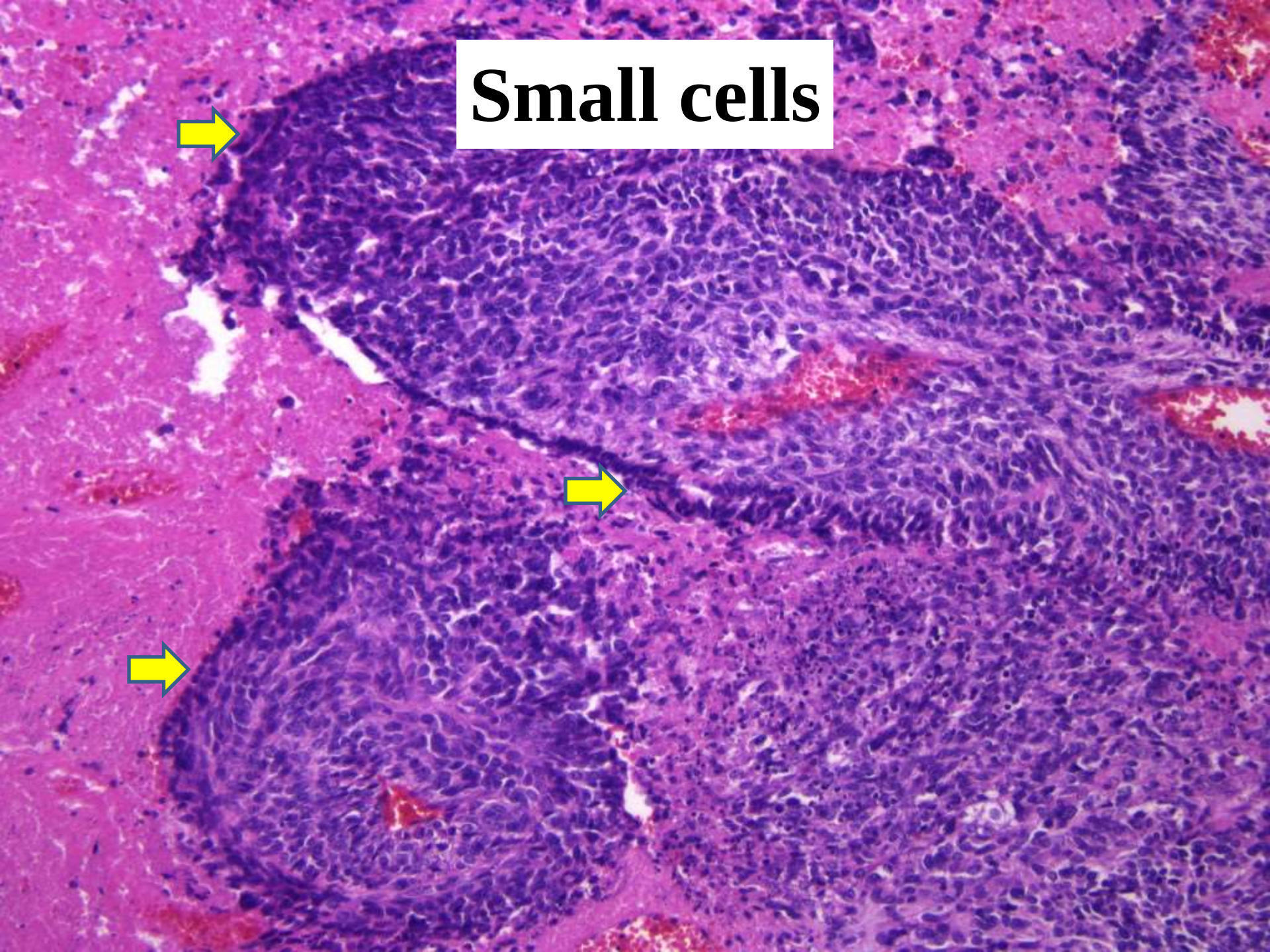
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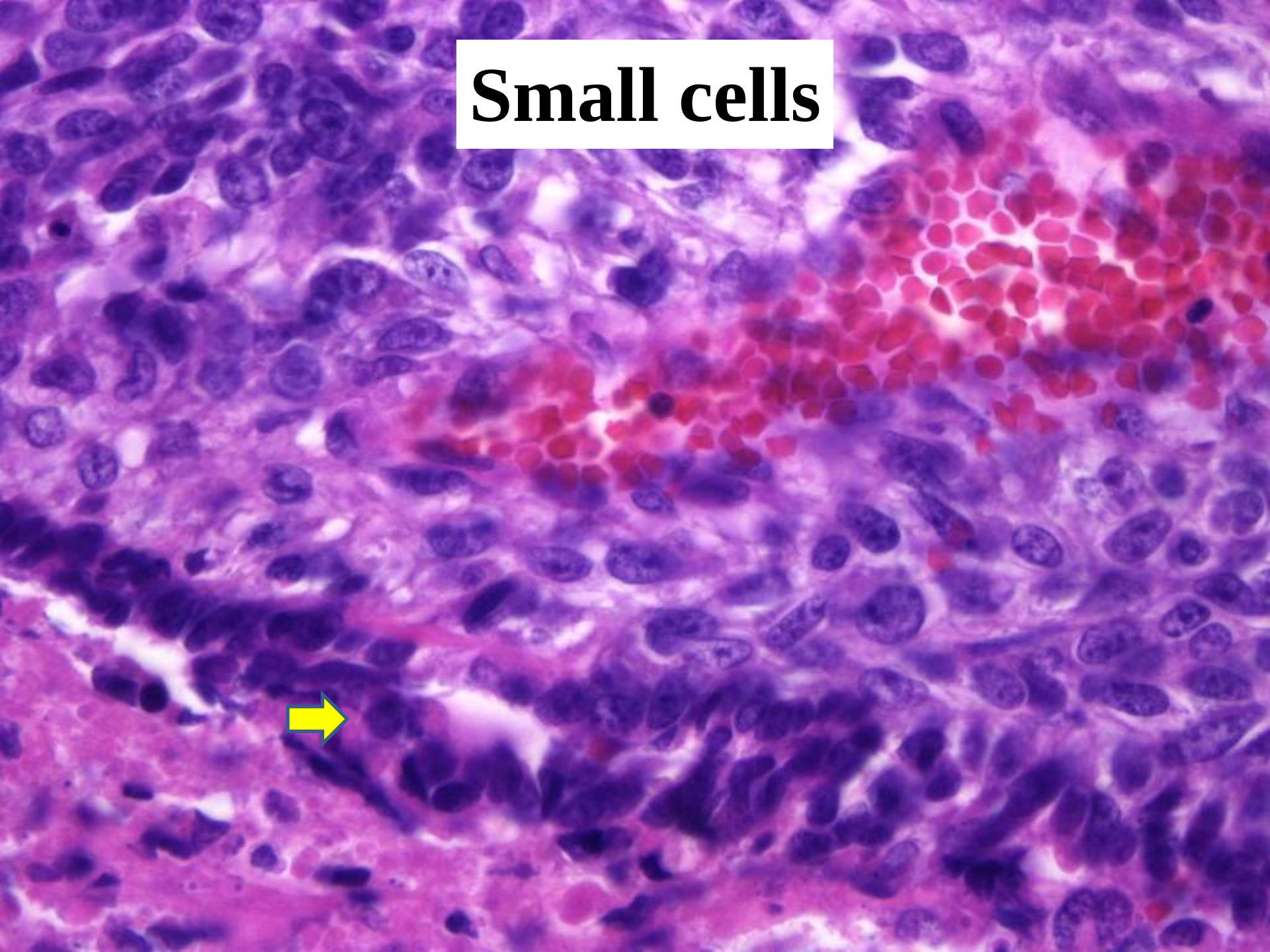
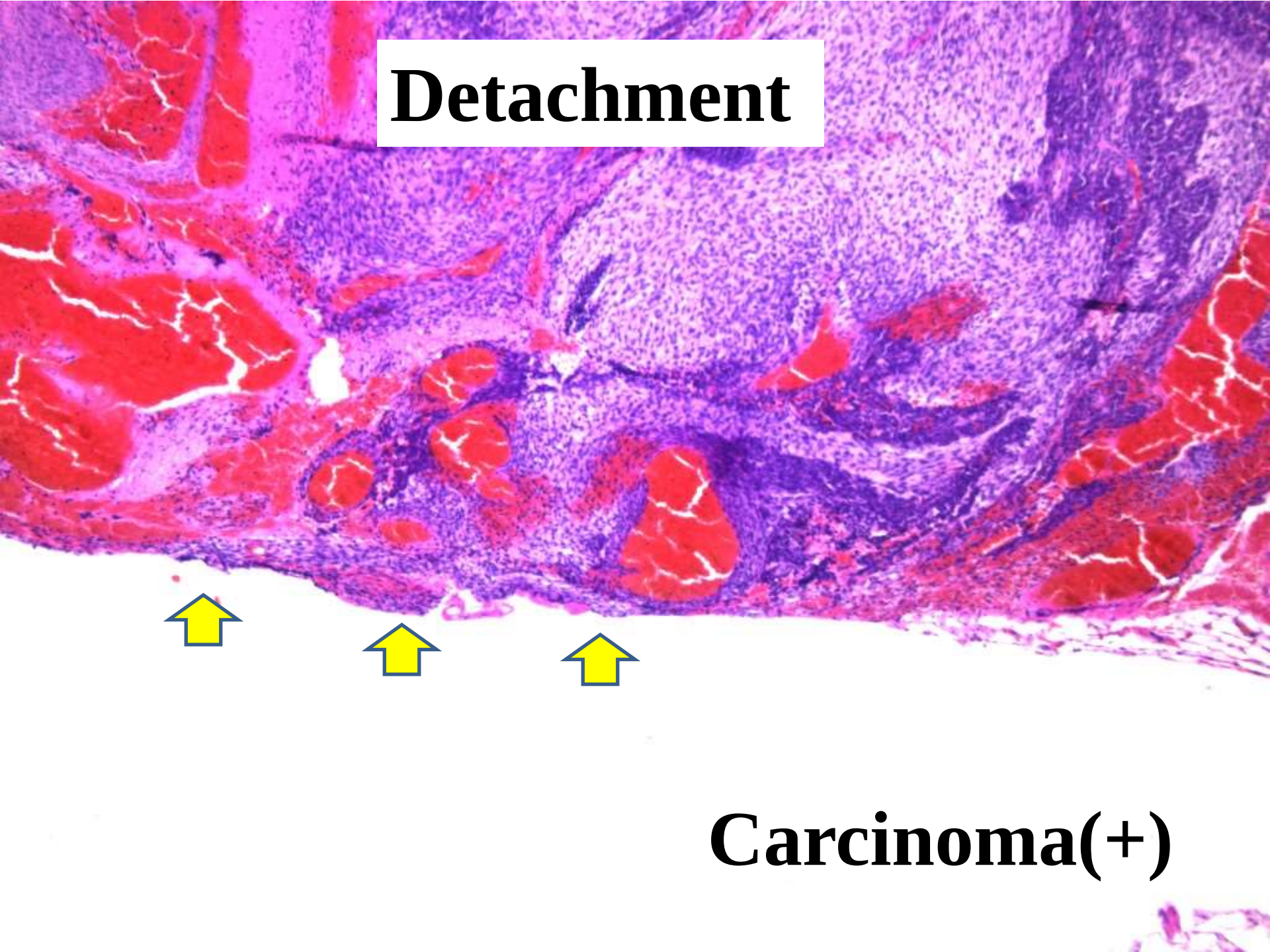

Small cells

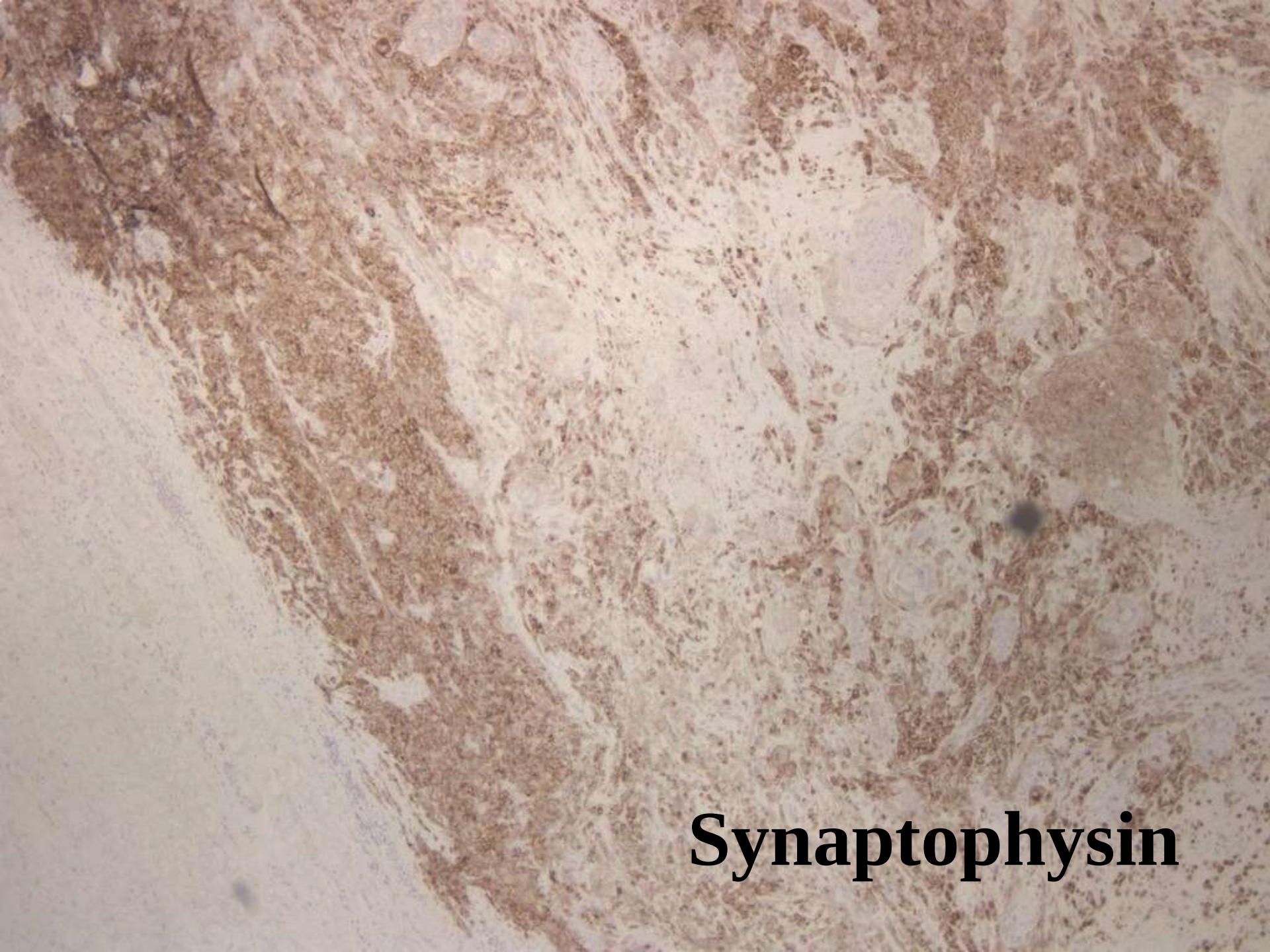

Detachment
Carcinoma(+)

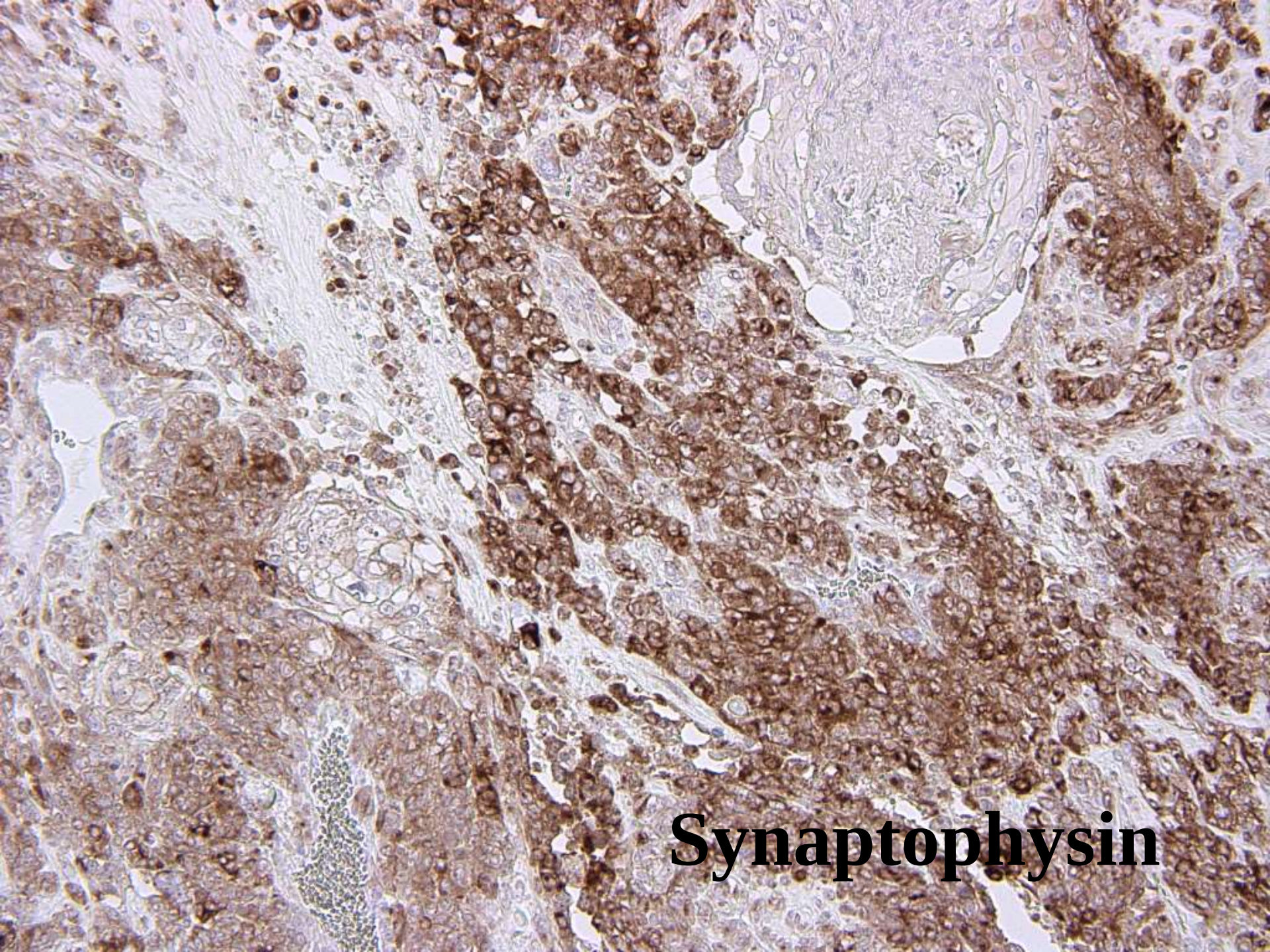
Differential Diagnosis

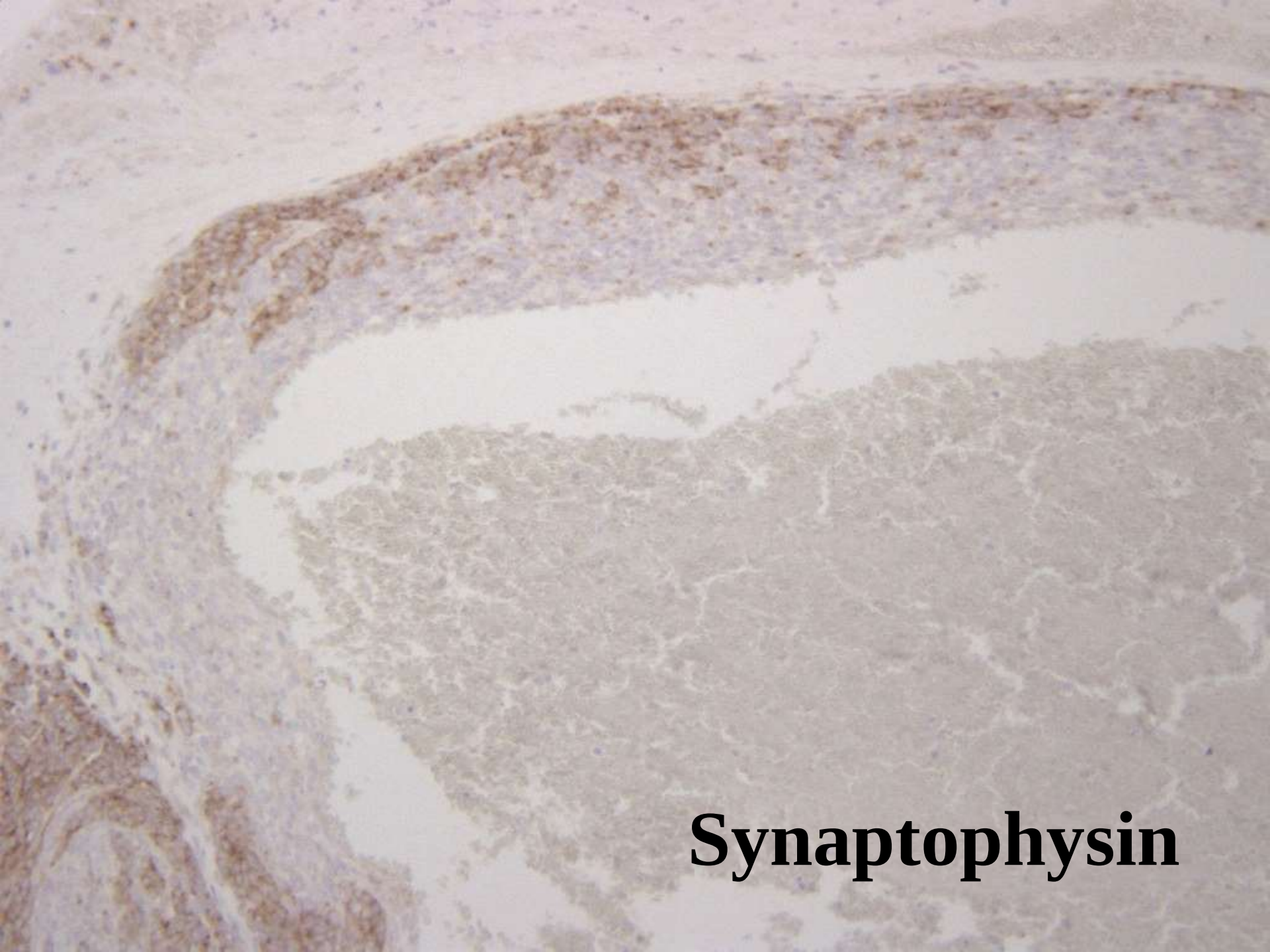
1) Carcinoma ex pleomorphic adenoma
2) Epithelial-myoepithelial carcinoma
3) Carcinosarcoma
4) Others

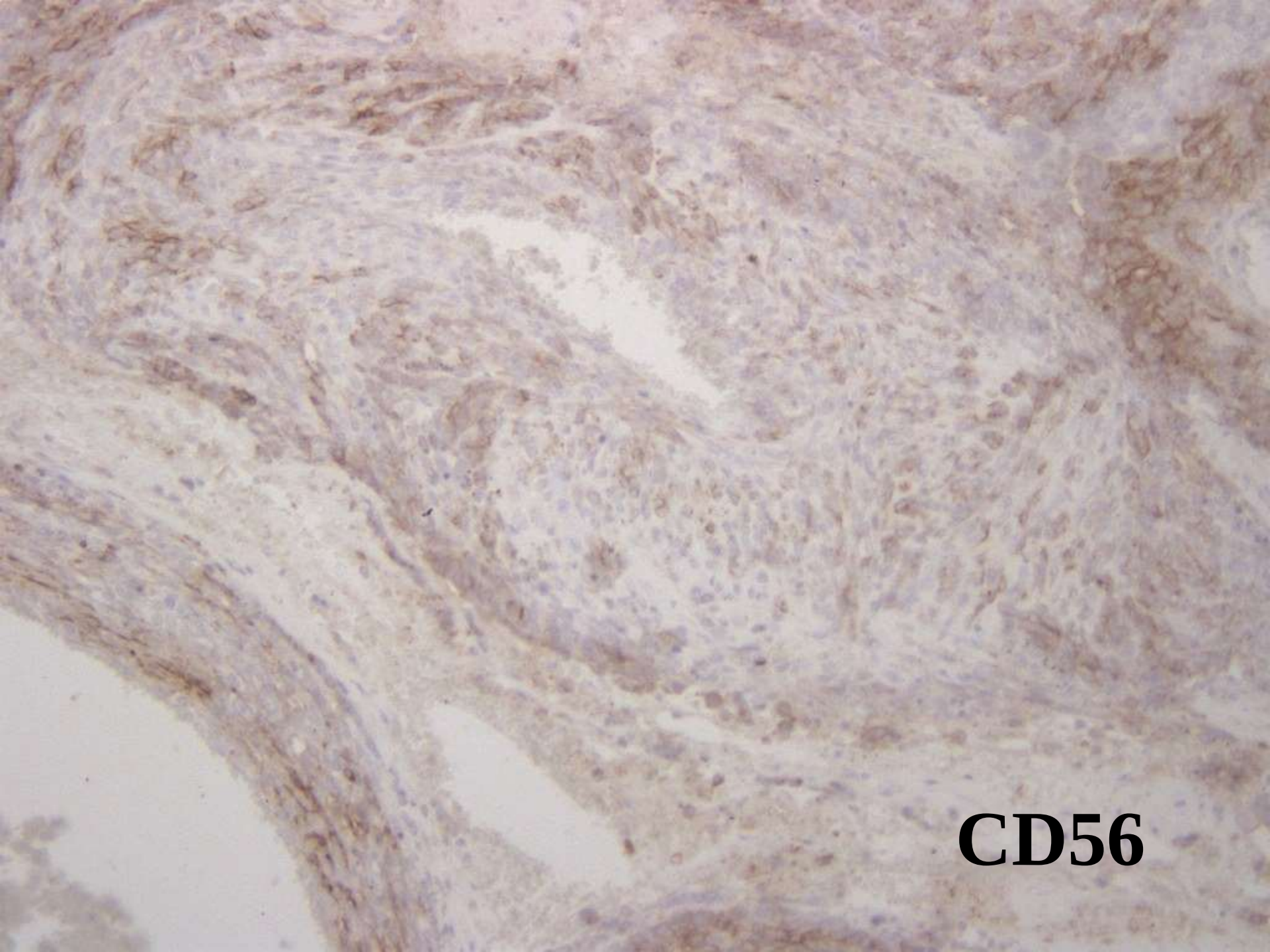
Carcinoma成分は何？

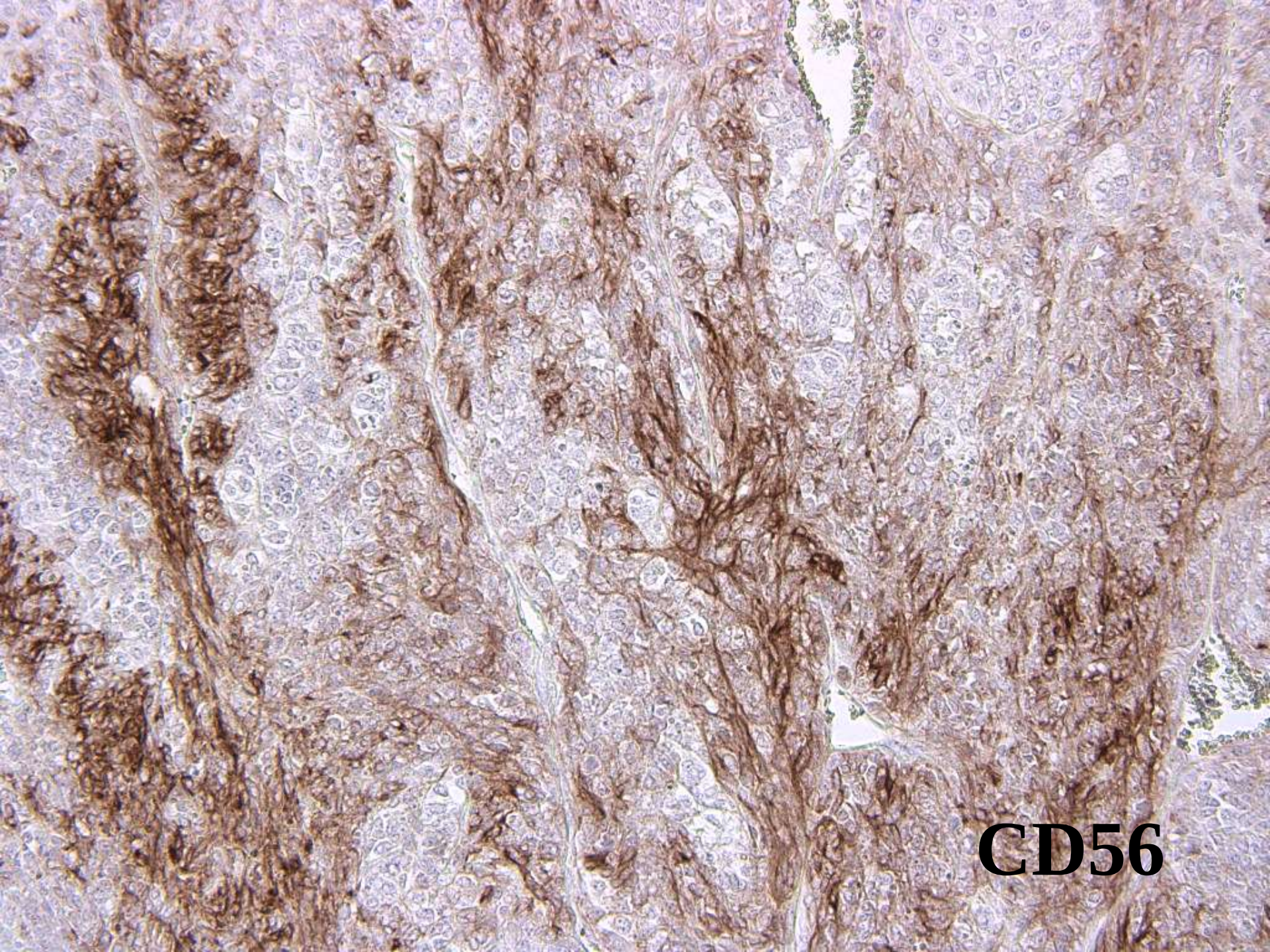
1) Myoepithelial carcinoma
2) Epithelial-myoepithelial carcinoma
3) Carcinosarcoma
4) Others

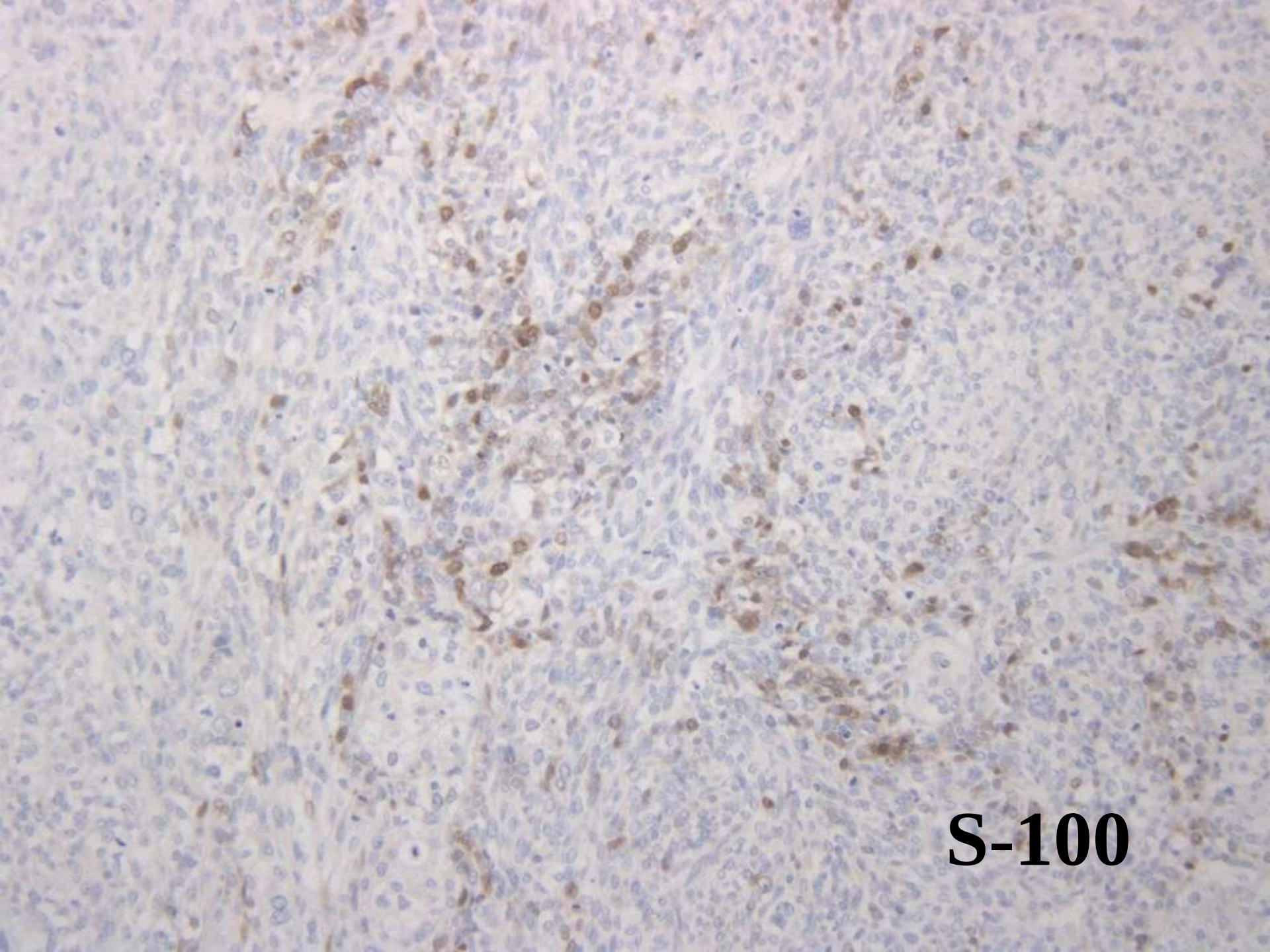

Synaptophysin

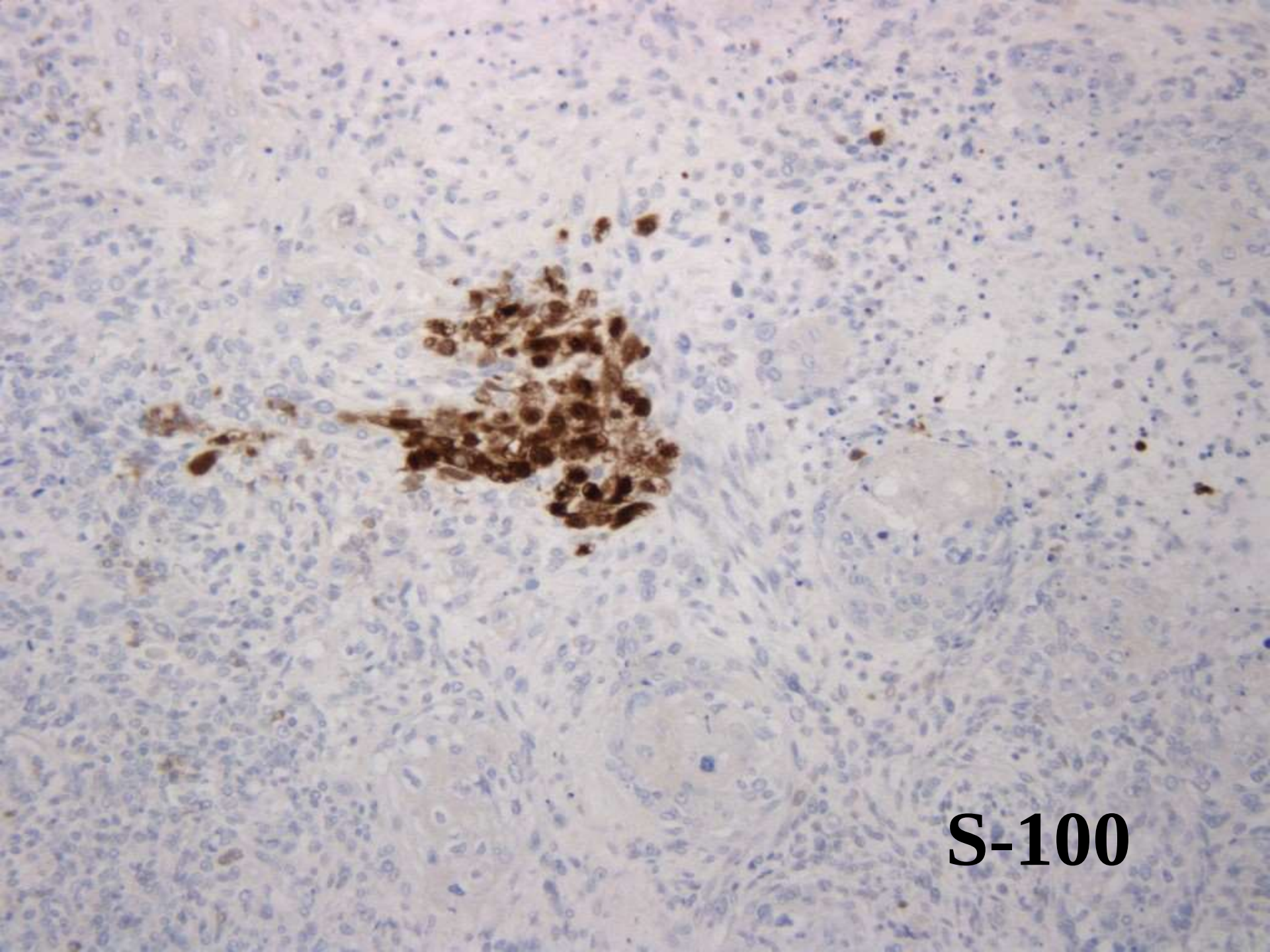

Synaptophysin

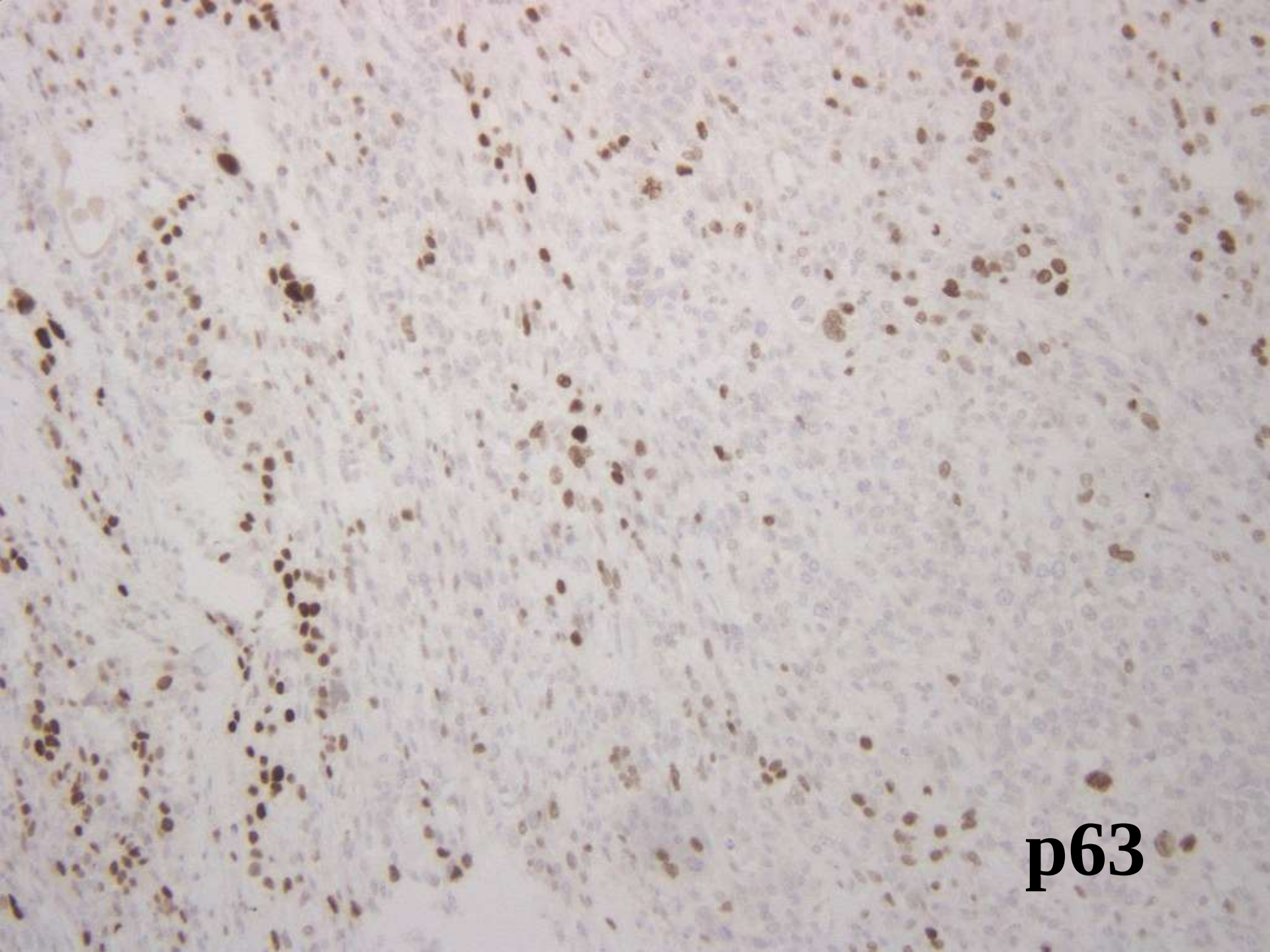

Synaptophysin

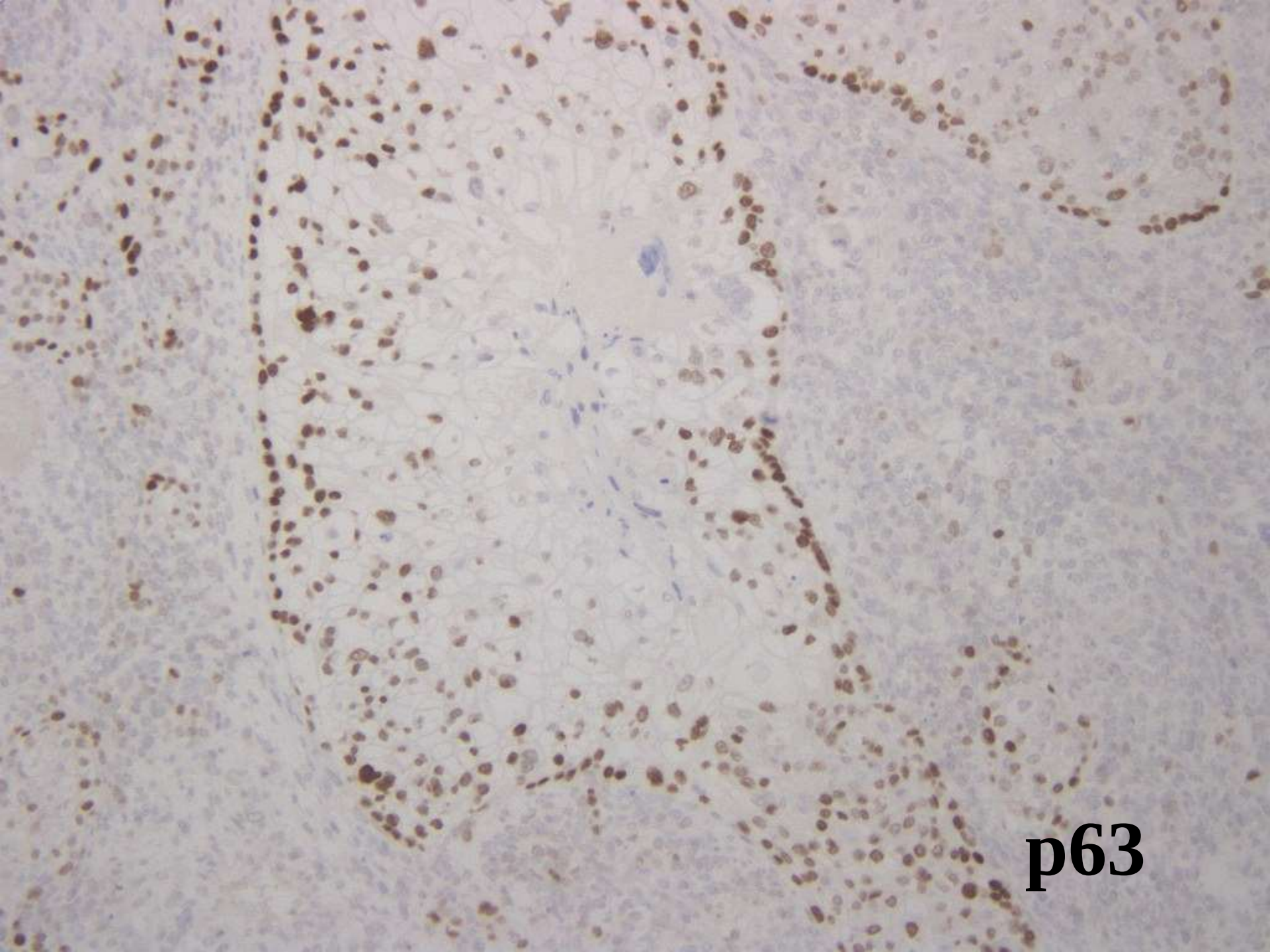

CD56

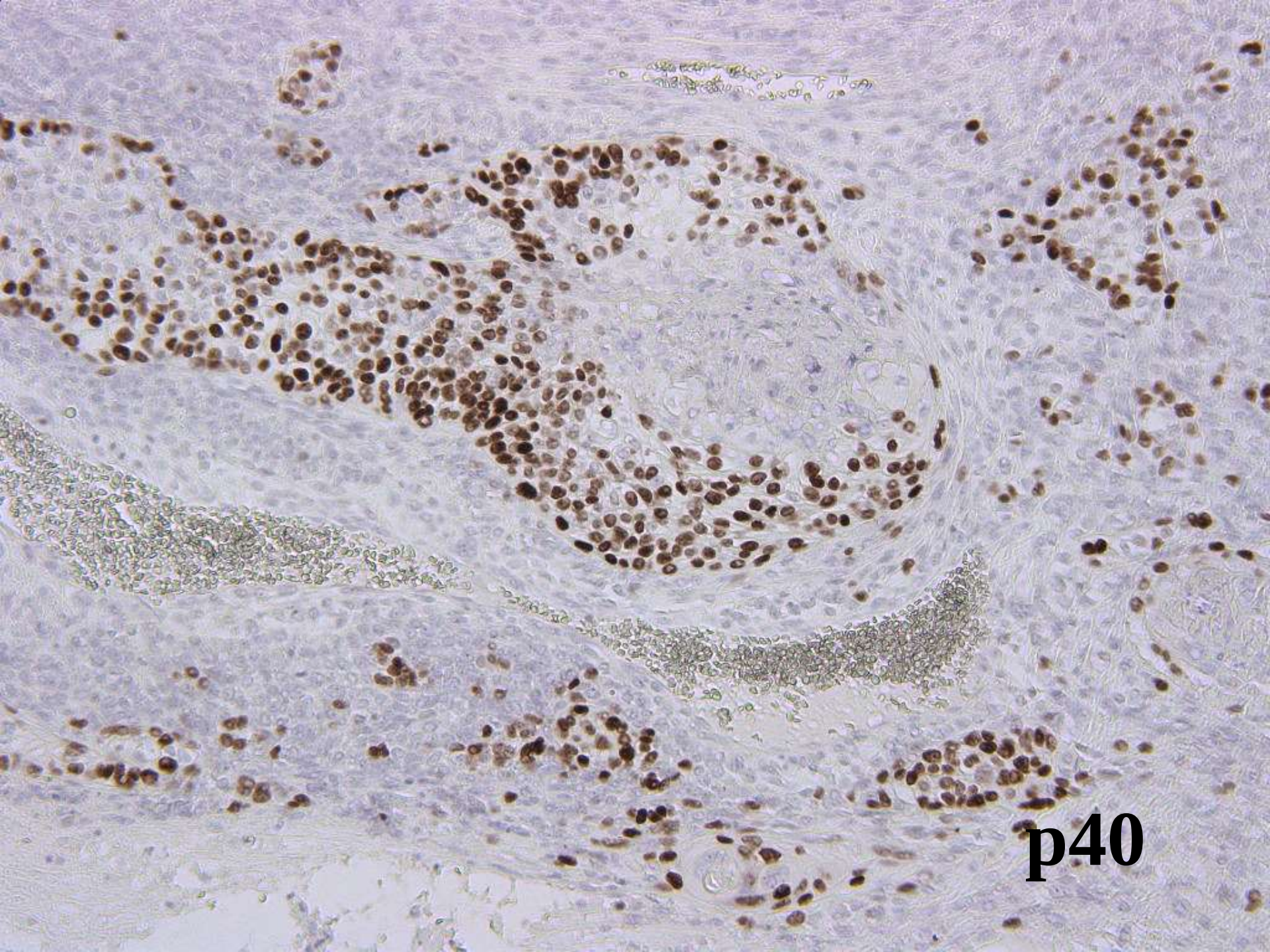

CD56

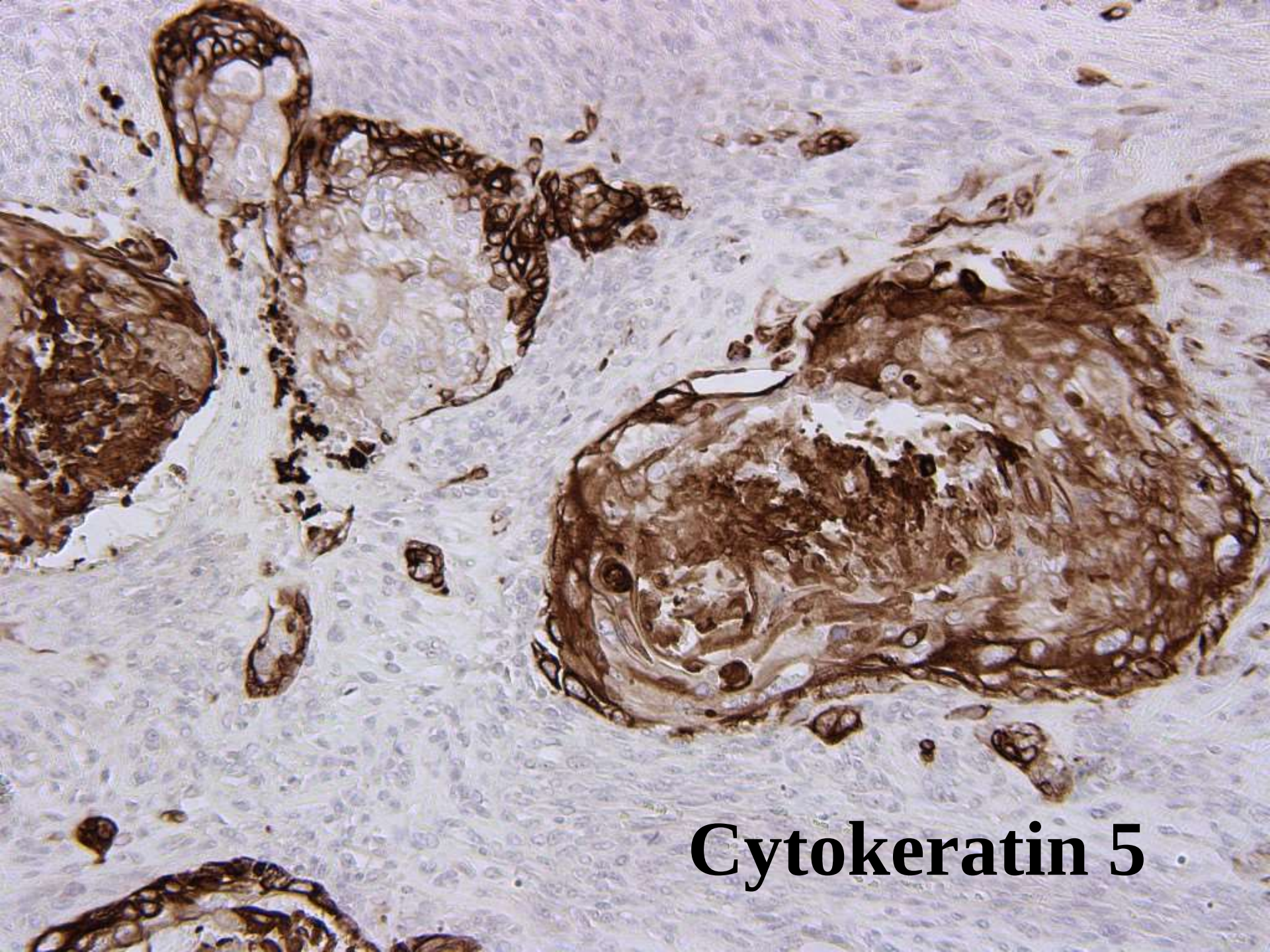

S-100

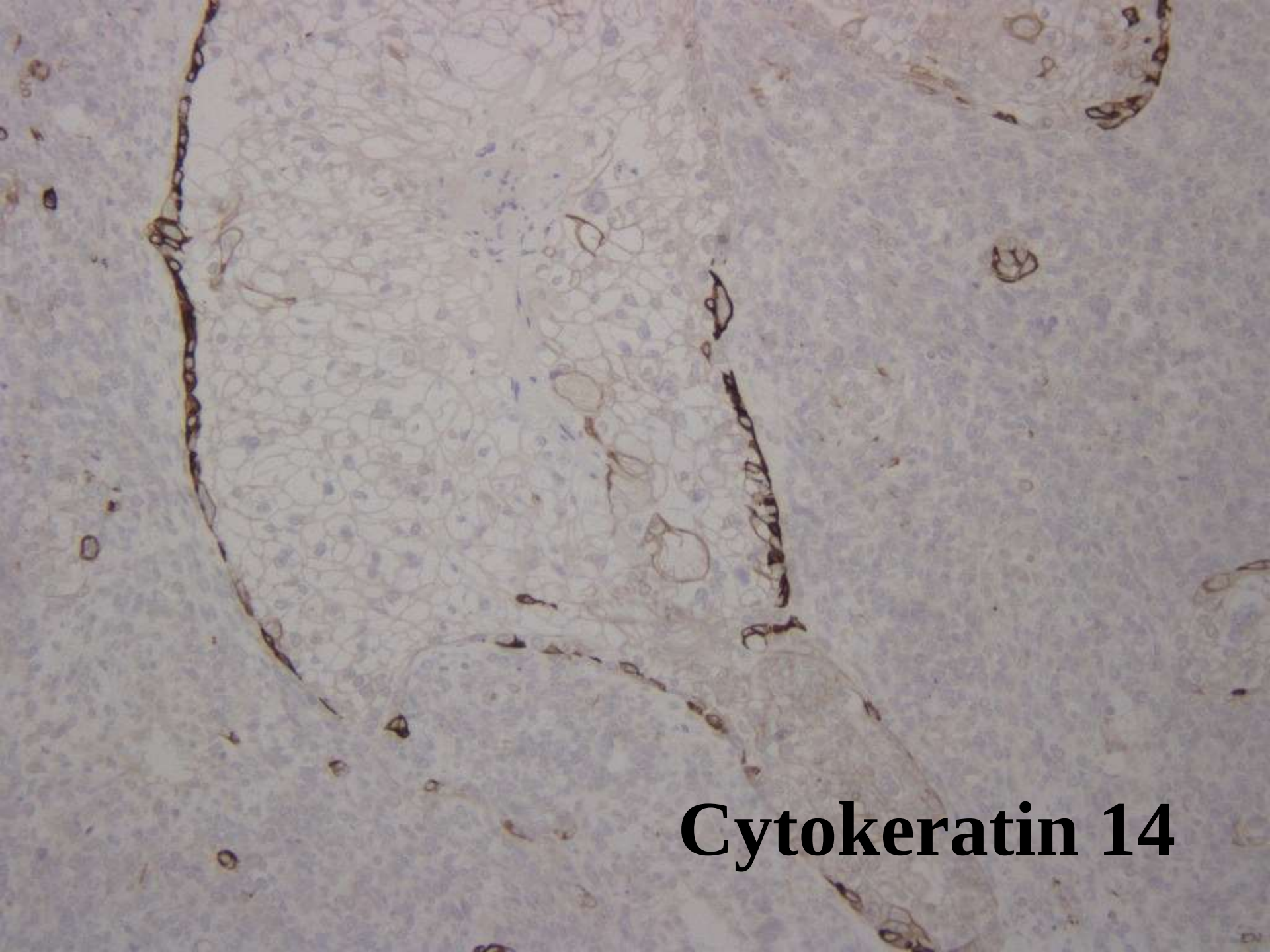

S-100

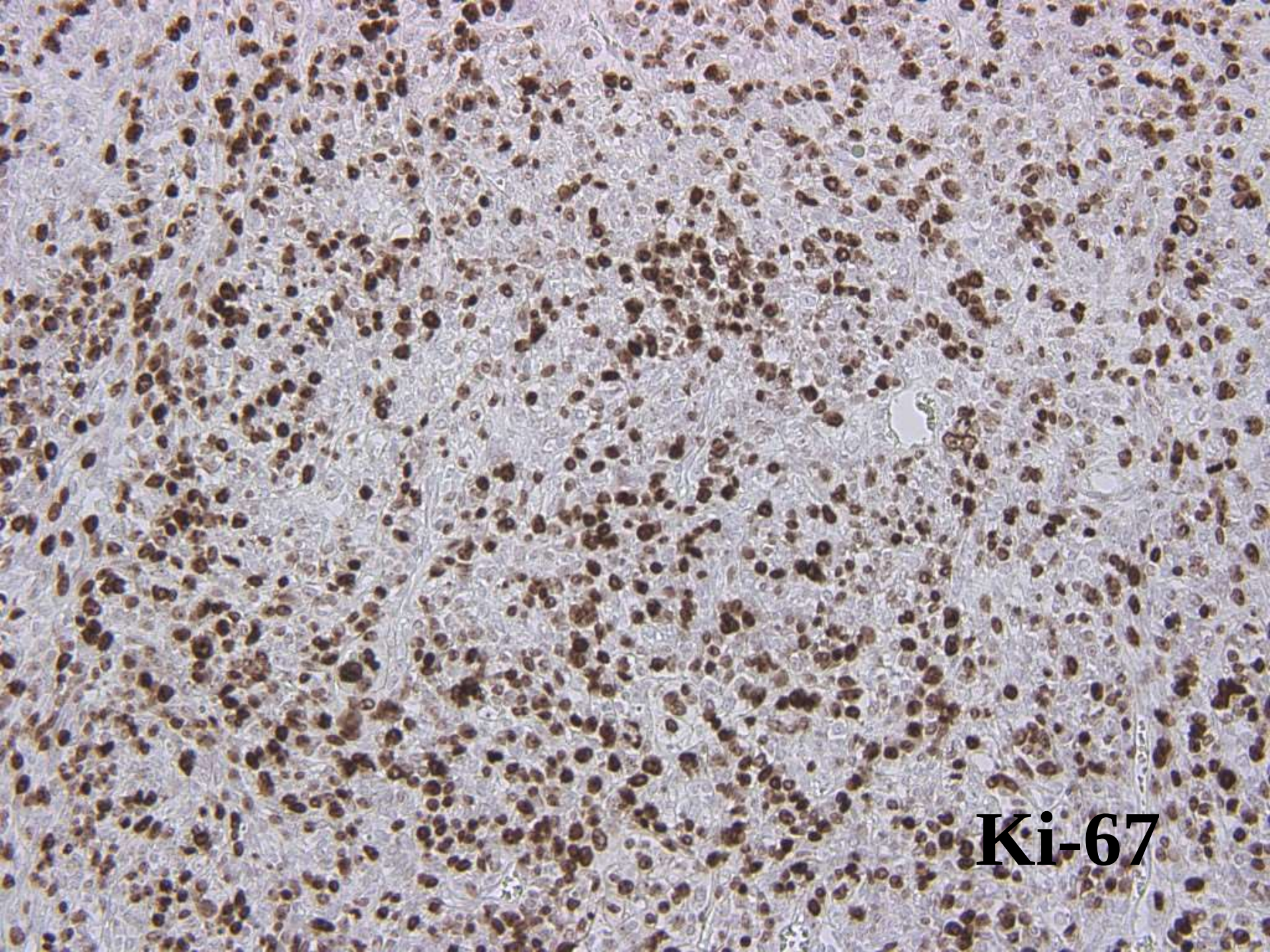

p63


p63


p40


Cytokeratin 5


Cytokeratin 14


Ki-67

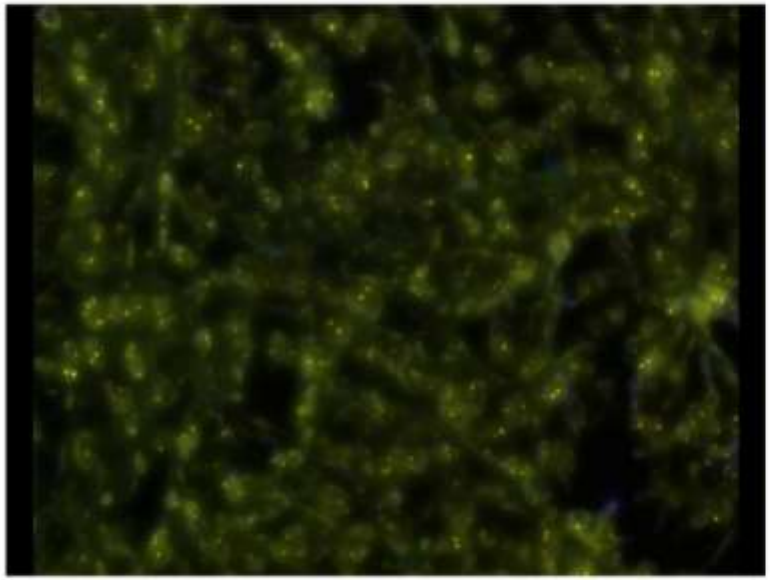
Immunohistochemical results

	Spindle	Epithelioid	Squamous	Small
AE1/AE3	F+	F+	F+	F+
CK CAM5.2	-	F+	-	-
CK5	-	D+	D+	-
CK14	F+	F+	F+	F+
CK20	-	-	-	-
p40	F+	F+	D+	F+
p63	F+	F+	D+	F+
GFAP	-	-	-	-
S-100	F+	F+	-	-
ASMA	F+	F+	F+	F+
CD10	F+	F+	F+	-
H-caldesmon	-	-	-	-
Chromogranin A	-	-	-	-
Synaptophysin	F+	F+	F+	D+
CD56	F+	F+	-	D+
TTF-1	-	-	-	-
Ki-67	>50%	>50%	>50%	>50%
p53	<1%	<1%	<1%	<1%

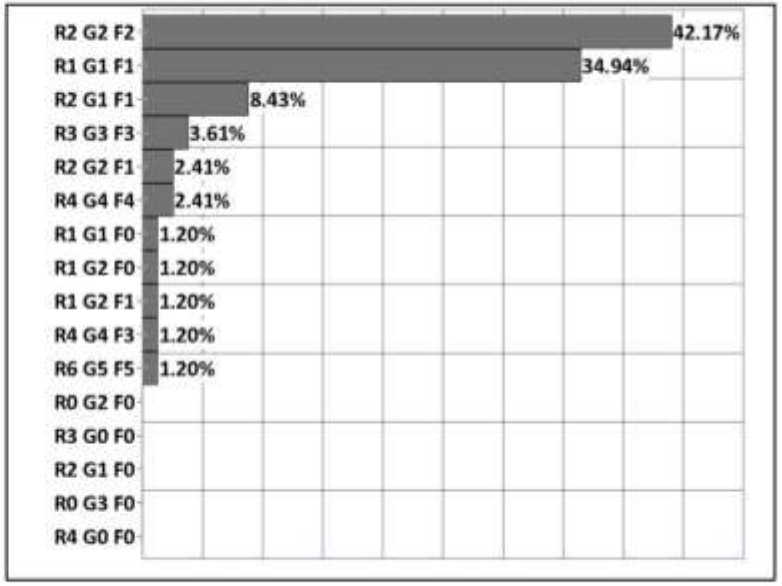
Carcinoma ex pleomorphic adenomaの carcinomaの成分は myoepithelial carcinomaが主体で、neuroendocrine differentiationも存在する？

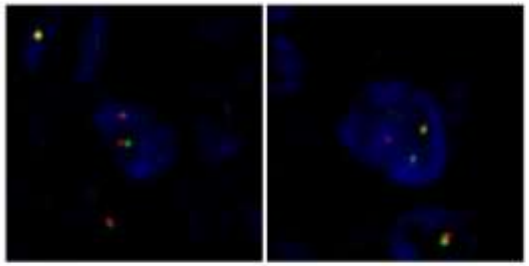
EWSR1 gene break apart FISH

EWSR1遺伝子 (FISH) [×400]



シグナル比の分布 (カウント数： 83)





Equivocal?

所見
81細胞をカウントし、陽性シグナルは 15.64%にみられました。

【診断意見】
Submandibular gland, right, glandectomy:
- Carcinoma (myoepithelial carcinoma with focal neuroendocrine differentiation, suspected) ex pleomorphic adenoma, widely invasive type.

【所見】
ご報告が遅れて申し訳ございません。
確かに癌腫成分の組織型に悩む症例です。形態学的に癌腫成分は、一部で粘液腫様になっており、扁平上皮分化成分を含めて筋上皮癌として矛盾しないと考えます。免疫組織化学的にも、癌腫成分はpan-CK(AE1/AE3), a-SMA, calponin, p63(一部), p40(一部), S-100(一部)で筋上皮細胞への分化がみられます。SynaptophysinとCD56陽性所見は、chromogranin Aには陰性であるものの、pan-CK(AE1/AE3)のドット状陽性像と併せて、神経内分泌分化ありとしてよろしいかと思います。神経内分泌分化は癌腫全体に不規則に分布しており、またこれらのマーカーと平滑筋系マーカーが共発現している癌細胞もあります。以上の所見から、極めて稀で未報告だと思われますが、癌腫成分は神経内分泌分化を伴った筋上皮癌が第一に疑われます。なお、扁平上皮分化は筋上皮癌でしばしばみられる所見です。
貴重な症例をコンサルトして頂きまして誠にありがとうございました。

【参考文献】

報告書作成日　　:2017/01/04
コンサルタント氏名:長尾　俊孝 先生

Final Diagnosis

Carcinoma (myoepithelial carcinoma with focal neuroendocrine differentiation) ex pleomorphic adenoma

Genes Chromosomes Cancer. 2016 October ; 55(10): 767–776. doi:10.1002/gcc.22376.

Secondary *EWSR1* Gene Abnormalities in *SMARCB1*-Deficient Tumors with 22q11-12 Regional Deletions: Potential Pitfalls in Interpreting *EWSR1* FISH Results

Shih-Chiang Huang[1,2], **Lei Zhang**[1], **Yun-Shao Sung**[1], **Chun-Liang Chen**[1], **Yu-Chien Kao**[1,3], **Narasimhan P. Agaram**[1], and **Cristina R. Antonescu**[1,*]

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[3]Department of Pathology, Shuang Ho Hospital, Taipei Medical University, NewTaipei City, Taiwan

Abstract

SMARCB1 inactivation occurs in a variety of tumors, being caused by various genetic mechanisms. Since *SMARCB1* and *EWSR1* genes are located close to each other on chromosome 22, larger *SMARCB1* deletions may encompass the *EWSR1* locus. Herein, we report four cases with *SMARCB1*-deletions showing concurrent *EWSR1* gene abnormalities by FISH, which lead initially to misinterpretations as *EWSR1*-rearranged tumors. Our study group included various morphologies: a poorly differentiated chordoma, an extrarenal rhabdoid tumor, a myoepithelial carcinoma, and a proximal-type epithelioid sarcoma. All cases showed loss of SMARCB1 (INI1) by immunohistochemistry (IHC) and displayed characteristic histologic features for the diagnoses. The *SMARCB1* FISH revealed homozygous or heterozygous deletions in three and one case, respectively. The co-hybridized *EWSR1* probes demonstrated either unbalanced split signals or heterozygous deletion in two cases each. The former suggested *bona fide* rearrangement, while the latter resembled an unbalanced translocation. However, all the FISH patterns were quite complex and distinct from the simple and uniform split signals seen in typical *EWSR1* rearrangements. We conclude that in the context of 22q11-12 regional alterations present in *SMARCB1*-deleted tumors, simultaneous *EWSR1* involvement may be misinterpreted as equivalent to *EWSR1* rearrangement. A detailed clinicopathologic correlation and supplementing the *EWSR1* FISH assay with complementary methodology is mandatory for correct diagnosis.

Clear Cell Myoepithelial Carcinoma of Salivary Glands Showing *EWSR1* Rearrangement

Molecular Analysis of 94 Salivary Gland Carcinomas With Prominent Clear Cell Component

Alena Skálová, MD, PhD, Ilan Weinreb, MD,† Martin Hyrcza, MD, PhD,‡ Roderick H.W. Simpson, MD,§ Jan Laco, MD, PhD,‖ Abbas Agaimy, MD,¶ Marina Vazmitel, MD, PhD,# Hanna Majewska, MD, PhD,** Tomas Vanecek, RNDr, PhD,†† Peter Talarčik, MD,‡‡ Spomenka Manajlovic, MD, PhD,§§ Simona N. Losito, MD,‖‖ Petr Šteiner, MSc,†† Adela Klimkova, MSc,†† and Michal Michal, MD**

Abstract: This study examines the presence of the *EWSR1* rearrangement in a variety of clear cell salivary gland carcinomas with myoepithelial differentiation. A total of 94 salivary gland carcinomas with a prominent clear cell component included 51 cases of clear cell myoepithelial carcinomas de novo (CCMC), 21 cases of CCMCs ex pleomorphic adenoma (CCMCexPA), 11 cases of epithelial-myoepithelial carcinoma (EMC), 6 cases of EMC with solid clear cell overgrowth, and 5 cases of hyalinizing clear cell carcinoma of minor salivary glands. In addition, 10 cases of myoepithelial carcinomas devoid of clear cell change and 12 cases of benign myoepithelioma were included as well. All the tumors in this spectrum were reviewed, reclassified, and tested by fluorescence in situ hybridization (FISH) for the *EWSR1* rearrangement using the Probe Vysis *EWSR1* Break Apart FISH Probe Kit. The *EWSR1* rearrangement was detected in 20 of 51 (39%) cases of CCMC, in 5 of 21 (24%) cases of CCMCexPA, in 1 of 11 (9%) cases of EMC, and in 4 of 5 (80%) cases of hyalinizing clear cell carcinoma. The 25 *EWSR1*-rearranged CCMCs and CCMCexPAs shared similar histomorphology. They were arranged in nodules composed of compact nests of large polyhedral cells with abundant clear cytoplasm. Necrosis, areas of squamous metaplasia, and hyalinization were frequent features. Immunohistochemically, the tumors expressed p63 (96%), cytokeratin CK14 (96%), and S100 protein (88%). MIB1 index varied from 10% to 100%, with most cases in the 20% to 40% range. Clinical follow-up information was available in 21 cases (84%) and ranged from 3 months to 15 years (mean 5.2 y); 4 patients were lost to follow-up. Ten patients are alive with no evidence of recurrent or metastatic disease in the follow-up period from 3 months to 15 years (mean 5 y), 3 patients are alive with recurrent and metastatic disease, and 8 died of disseminated cancer 9 months to 16 years after diagnosis (mean 6 y). Lymph node metastasis appeared in 5 patients within 5 months to 4 years after diagnosis (mean 22 mo), distant metastases were noted in 7 patients with invasion of orbit (2 cases), and in 1 case each metastasis to the neck soft tissues, liver, lungs, mediastinum, and thoracic vertebra was noted. We describe for the first time *EWSR1* gene rearrangement in a subset of myoepithelial carcinomas arising in minor and major salivary glands. The *EWSR1*-rearranged CCMC represents a distinctive aggressive variant composed predominantly of clear cells with frequent necrosis. Most *EWSR1*-rearranged CCMCs of salivary glands are characterized by poor clinical outcomes.

Key Words: salivary gland, clear cell myoepithelial carcinoma, *EWSR1* rearrangement

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From the *Department of Pathology, Faculty of Medicine in Plzen, Charles University; ††Bioptic Laboratory Ltd, Molecular Pathology Laboratory, Plzen; ‖The Fingerland Department of Pathology, Faculty of Medicine and University Hospital, Charles University in Prague, Hradec Kralove, Czech Republic; †Department of Pathology, University Health Network, Toronto, ON; ‡Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC; §Department of Anatomical Pathology, University of Calgary, Foothills Medical Centre, Calgary, AB, Canada; ¶Institute of Pathology, University Hospital, Erlangen, Germany; #Department of Pathology, N.N. Alexandrov's Research Center of Oncology and Medical Radiology, Minsk, Republic of Belarus; **Department of Pathology, Medical University of Gdansk, Poland; ‡‡Department of Pathology, Cytopathos, Slovakia; §§Department of Pathology, University of Zagreb, Croatia; and ‖‖Department of Pathology, National Cancer Institute, Fondazione "G.Pascale", Naples, Italy.

Preliminary study was presented at the United States and Canadian Academy of Pathology, 103rd Annual Meeting, 2014, San Diego, CA.

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The Ewing sarcoma breakpoint region 1 (*EWSR1*) is translocated in many sarcomas. As is apparent from the name, rearrangements involving the *EWSR1* region

Carcinoma ex pleomorphic adenomaで、neuroendocrine carcinomaを含む論文は検索して2つあった。

Head and Neck Pathol (2013) 7:163–170
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CASE REPORT

Carcinosarcoma ex Non-Recurrent Pleomorphic Adenoma Composed of TTF-1 Positive Large Cell Neuroendocrine Carcinoma and Myofibrosarcoma: Apropos a Rare Case

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Abstract We present a carcinosarcoma ex non-recurrent pleomorphic adenoma composed of a large cell neuroendocrine carcinomatous component and a spindle cell sarcoma with myofibroblastic differentiation. The tumor contained a hyalinized transition zone where the classical PA appeared to acquire two different histopathological patterns of malignant transformation of the epithelial component. The carcinomatous component was strongly and diffusely positive for low-molecular weight cytokeratins (AE1-3), synaptophysin, thyroid transcription factor-1 and focally positive for chromogranin A. All these markers were negative in the sarcomatous component. The sarcomatous component displayed immunoreactivity for smooth muscle actin with a predominantly linear, subplasmalemmal pattern. No expression of CD31, S100 protein, h-caldesmon, desmin, CD34, p63, myogenin, Myo D1 and c-kit was detected. Strong immunohistochemical expression of p53 was documented in both the carcinomatous and sarcomatous components as well as in the atypical epithelial component in the transition zone associated with the hyalinized pleomorphic adenoma.

Introduction

Carcinosarcoma (CS) arising in salivary glands is a very rare tumor accounting for less than 0.5 % of all malignant salivary gland tumors [1]. CS may or may not be associated with a concurrent or recurrent pleomorphic adenoma (PA). Although rare, CS frequently displays a multitude of histological patterns corresponding to varying lines of histological differentiation in both the carcinomatous and sarcomatous components. Reportedly, the most common epithelial malignancy is adenocarcinoma NOS and the most common sarcomatous component is chondrosarcoma [2]. Salivary gland CS with large cell neuroendocrine carcinoma has, to the best of our knowledge, only been reported in one previous case [3]. This case was not associated with a previous or concurrent PA and was associated with a sarcomatous component which featured rhabdomyosarcomatous differentiation. Herein we present a unique case of a parotid gland CS ex (non-recurrent) PA which was composed of a large cell neuroendocrine carcinoma and spindle cell sarcoma showing myofibroblastic differentiation.

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CASE REPORT

Small Cell Carcinoma ex-Pleomorphic Adenoma of the Parotid Gland

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Abstract Small cell carcinoma (SCC) is a high-grade malignancy usually encountered in the lungs but also seen in almost any site including the salivary glands. SCC is important to recognize because it often metastasizes widely and is treated with systemic chemotherapy. Carcinoma ex pleomorphic adenoma is a malignant epithelial neoplasm arising in a pre-existing benign mixed tumor (i.e., pleomorphic adenoma, PA). While virtually any salivary carcinoma can arise from a PA, to our knowledge SCC ex-PA has not been described. We report a case of a woman presenting with fullness of the right neck and a parotid gland mass. The tumor was resected and evaluated grossly, by light microscopy, and by immunohistochemistry. Grossly, a 1.6 cm well-circumscribed nodule was identified within the parotid. Microscopic examination revealed foci of SCC associated with high-grade adenocarcinoma, in the background of a PA. The SCC was immunoreactive for cytokeratin in a dot-like pattern and neuroendocrine markers synaptophysin and CD56. Despite the focal nature of the SCC in the parotid, a pure SCC metastasis was present in one neck level II lymph node. The patient was free of disease with 8 months of follow-up. Our case illustrates that: (1) although rare, in the salivary glands SCC may arise from lower grade neoplasms including PAs; (2) SCC ex PA may metastasize as pure SCC even if the primary SCC component was focal; (3) adequate sampling of PAs is crucial to prevent missing a rare SCC that must be treated with chemotherapy.

Keywords Carcinoma ex pleomorphic adenoma · Carcinoma ex mixed tumor · Malignant mixed tumor · Small cell carcinoma · Parotid gland · Salivary glands

Introduction

Carcinoma ex pleomorphic adenoma (CXPA) is a malignant epithelial neoplasm arising from a pleomorphic ade-

Neuroendocrine tumorとmyoepithelial carcinomaとの関係を示す論文は？

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Case Report

Small cell undifferentiated carcinoma of the submandibular gland: Immunohistochemical evidence of myoepithelial, basal and luminal cell features

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A primary small cell undifferentiated carcinoma of the submandibular gland is reported. Histological studies revealed that the major part of this tumor was composed of cells slightly larger (10–14 μm) than lymphocytes. These tumor cells showed myoepithelial-cell differentiation, which was confirmed by the immunohistochemical and ultrastructural findings. Furthermore, some of them showed luminal-cell and basal-cell differentiation immunohistochemically. However, there was no evidence of neuroendocrine differentiation. These findings demonstrated that the tumor had the features of all the salivary ductal components (myoepithelial , basal, and luminal cells) and supported that the tumor might arise from the salivary duct. Furthermore, it supports the hypothesis of multipotential stem cells as the origin for small cell undifferentiated carcinomas in salivary glands.

structural absence or presence of neuroendocrine granules.[9,11] Furthermore, one small cell undifferentiated carcinoma with both neuroendocrine and ductal features[10] and two incidences of small cell undifferentiated carcinoma showing squamous differentiation[12,13] have been reported. For these reasons, there is some postulation that small cell undifferentiated carcinoma arises from a presumed ductal stem cell, which may undergo a multidirectional differentiation.

In the present study, we demonstrated that a small cell undifferentiated carcinoma had the features of all the salivary ductal components (myoepithelial, basal, and luminal cells), and we also present a review of the literature on histological findings.

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Case Report

Primary cutaneous neuroendocrine tumor (atypical carcinoid) expressing KIT and PDGFRA with myoepithelial differentiation: a case report with immunohistochemical and molecular genetic studies

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Abstract: Primary cutaneous neuroendocrine tumors (NET) except for Merkel cell carcinoma have rarely been reported. Herein reported is a very unique case of primary cutaneous NET with immunohistochemical markers of myoepitheliomas. A 47-year-old woman presented a tumor measuring 0.8x0.9x0.6 cm of the face. The tumor was excised completely with wide margins. Morphologically, the tumor was located in the dermis, and the tumor was composed of epithelioid cells arranged in trabecular, sinusoidal, rosette, ribbon-like, and cord-like patterns. Focal areas show tubular formations. The tumor cells were homogenous, and their nuclei showed hyperchromasia but no apparent histological features of malignancy were seen. The stroma was very scant. No invasive features were seen. Immunohistochemically, the tumor cells were strongly positive for cytokeratin (CK) 34BE12, CD5/6, CK14, NCAM (CD56), p63, and KIT (CD117), and moderately positive for CK AE1/3, p53, chromogranin, synaptophysin, neuron-specific enolase (NSE), PDGFRA, CA19-9, and Ki-67 antigen (labeling index=23%). The tumor cells were negative for CK CAM5.2, CK7, CK8, CK18,CK19,CK20, EMA, vimentin, CEA, HMB45, S100 protein, α-smooth muscle antigen, desmin, CD34, GFAP, neurofilaments, CD99 (MIC2), CD45, CD57, ErbB2, TTF-1, MUC1, MUC2, MUC5AC, and MUC6. Mucins examined by d-PAS and Alcian blue techniques were negative. A genetic analysis using PCR-direct sequencing method in paraffin sections identified no mutations of *KIT* (exons 9, 11, 13 and 17) and *PDGFRA* (exons 12 and 18) genes. Imaging modalities including CT and MRI identified no tumor in the body. The clinicians thought that the tumor was cured. She was a sailor and immediately visited other countries; therefore the follow-up could not be done.