Prípad č.13

SD IAP 536

Peter SZÉPE

ÚPA JLF UK a UN, Martin

XX. Martinský bioptický seminár SD IAP, Lúčky , 14.-15.11. 2014

Klinické údaje

- 67 ročná žena s recidivujúcim tumorom (primárne v malej panve) nasadajúcim na stenu rekta
- prvýkrát vyšetrená v r. 1988 s dg. nízkomalígneho sarkómu, radikálne extirpovaného s následnou CHT
- v r. 1998 recidíva tumoru v omente
- v r. 2009 druhá recidíva, typizovaná ako high grade stromálny sarkóm a nami vyslovené podozrenie na endometriálny stromálny sarkóm uteru
- absolvovala adjuvantnú CHT
- v r. 2014 3.recidíva v ľavom subfréniu a pri bifurkácii aorty
- v preparáte 536/A je recentná biopsia zo 3. recidívy, v 536/B je biopsia z 2.recidívy v r. 2009

- Klinická dg.: Sarcoma pelvis minoris recidivans, GIST ?

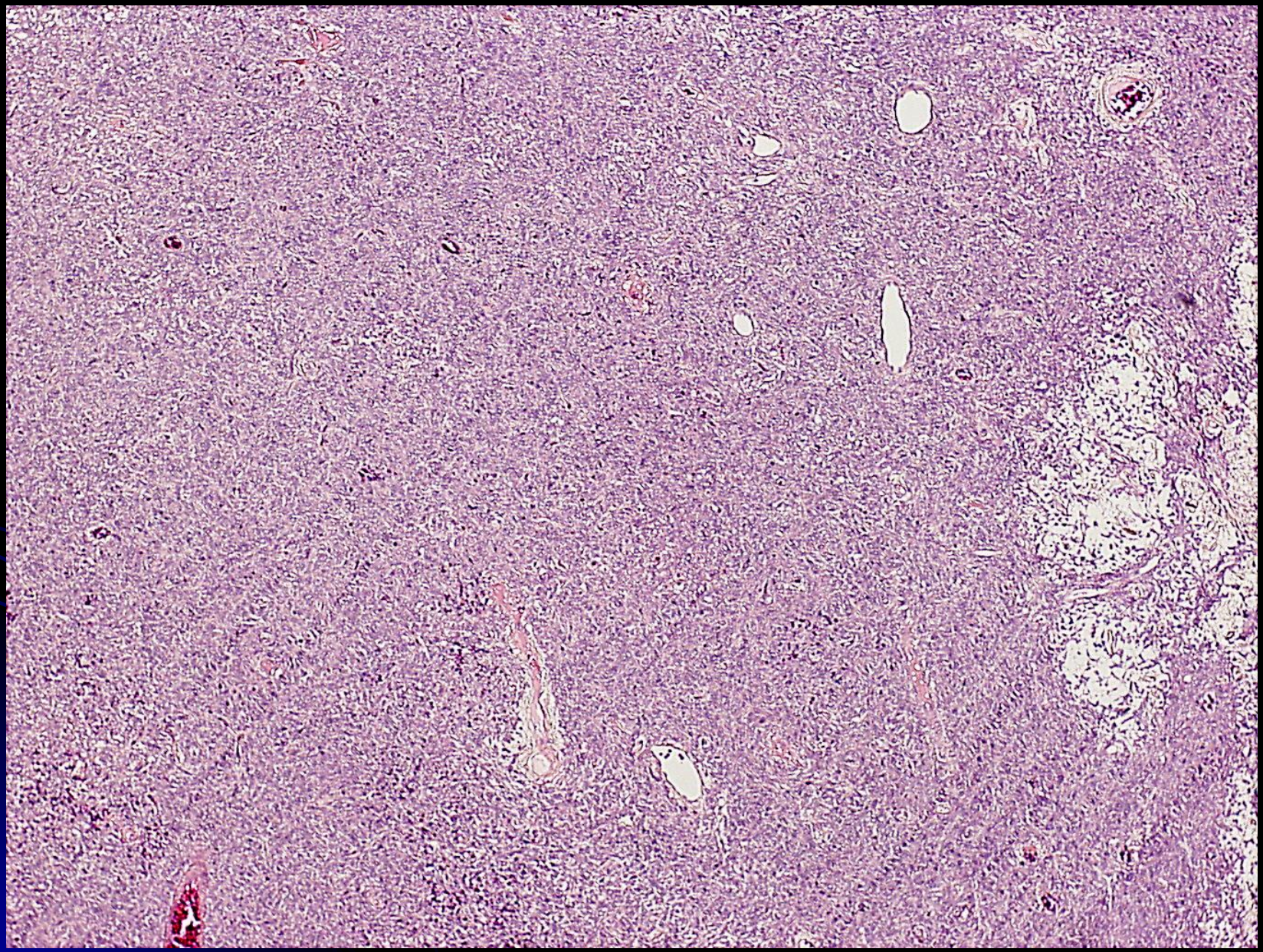
1988 – 2014
Spolupracovali:

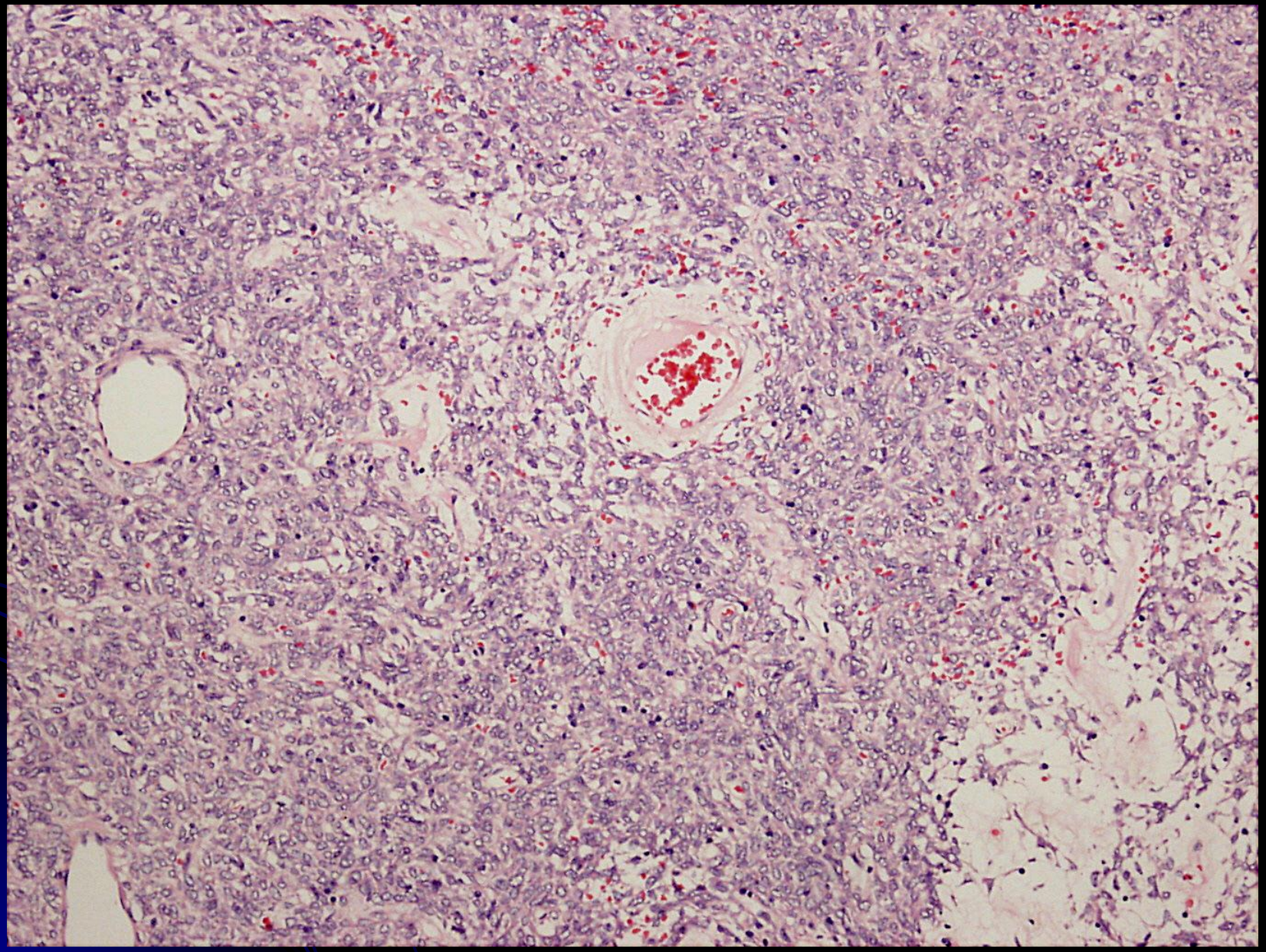
- PAO Ružinov (1988) – ?
- PAO Galanta a NOÚ (1998) – ? + P. Hlavčák
- PAO NOÚ (2009) – M. Majerčík
- ÚPA MFN (2009) – K. Kajo + P. Szépe
- PAO NOÚ (2014) – J. Macúch
- INT. ODD A NOÚ (2014) – J.Šufliarsky

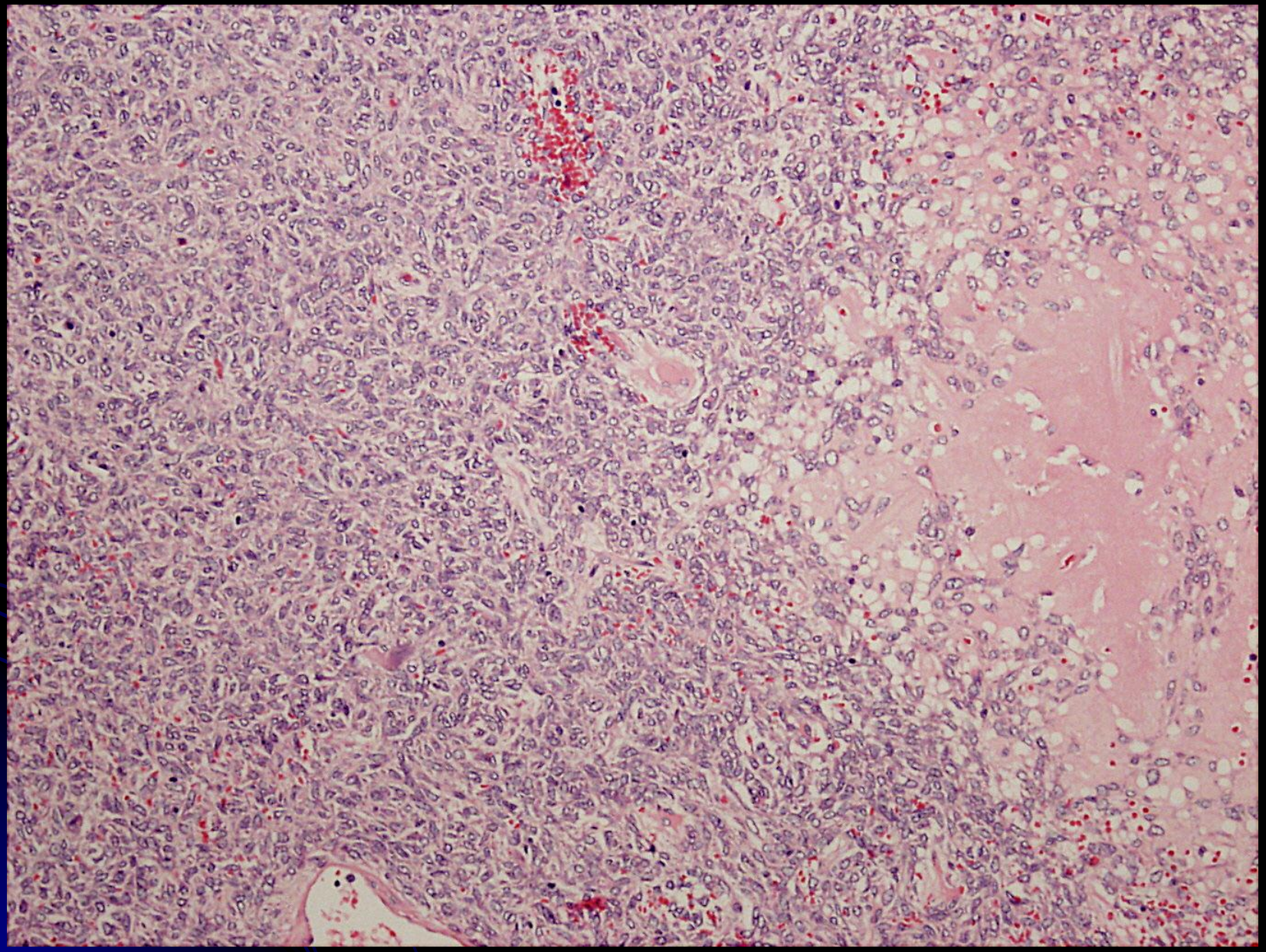
Š. Líšková

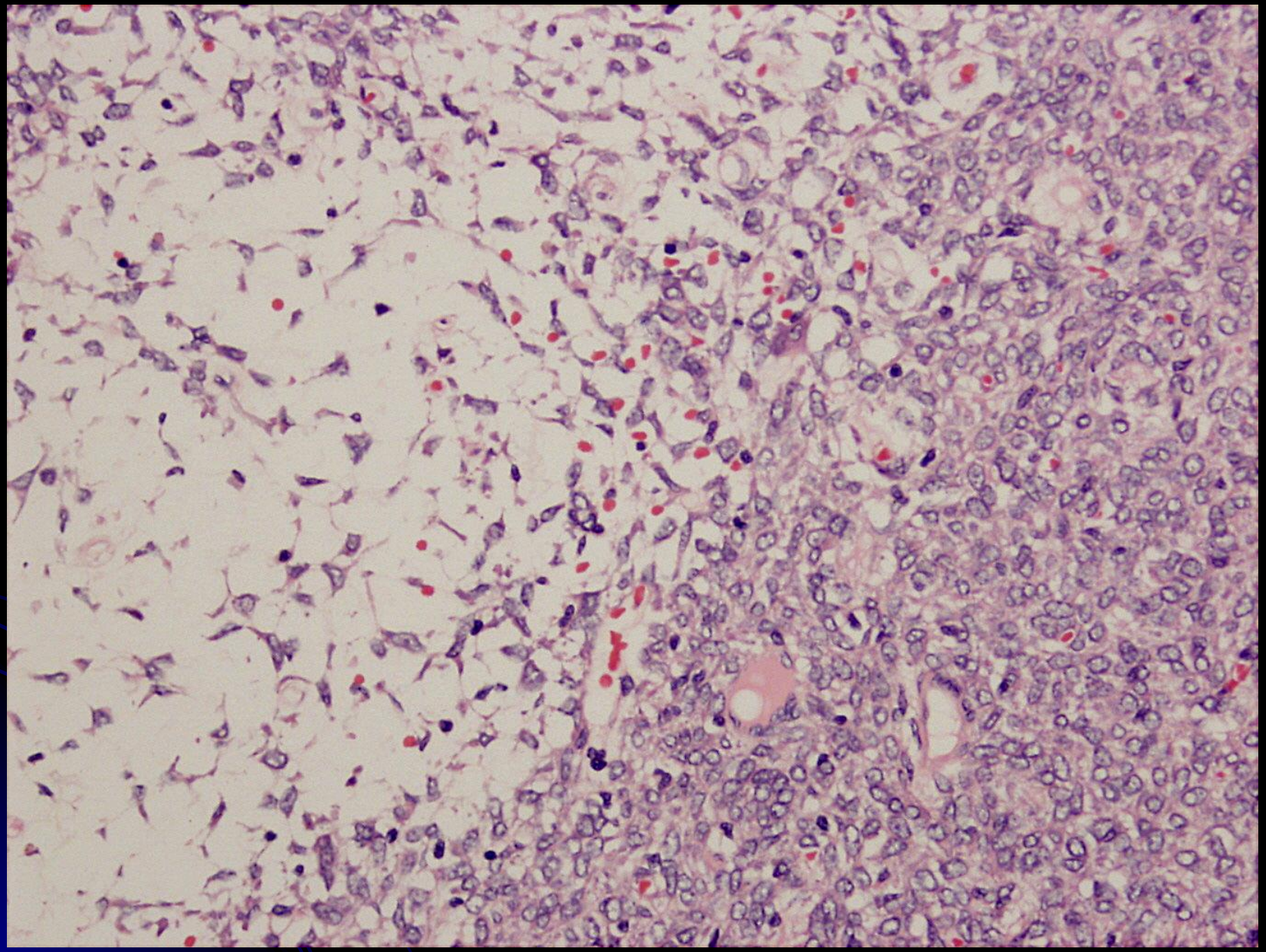
Otázka na úvod:

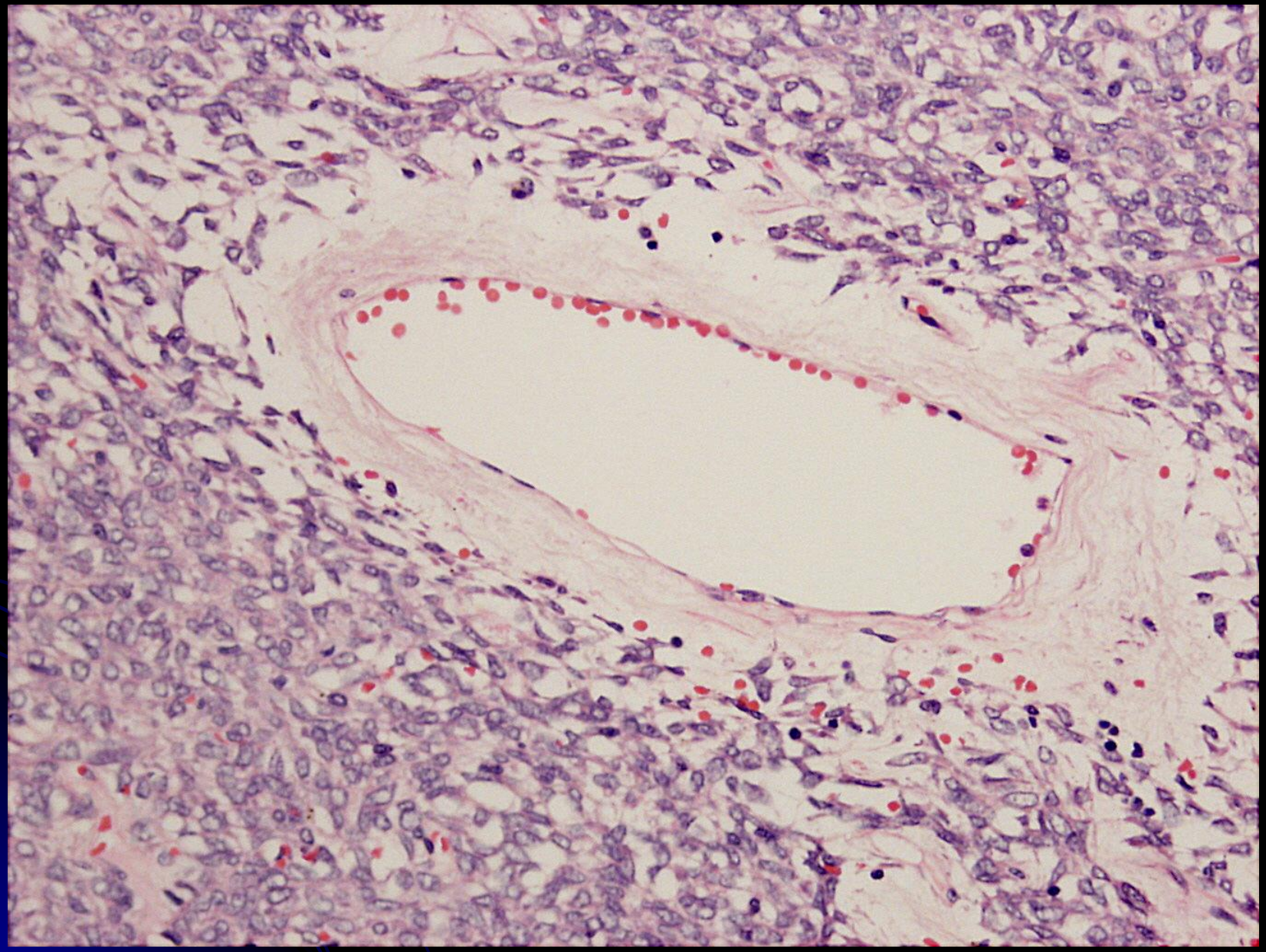
536 A – 4. biopsia 2014

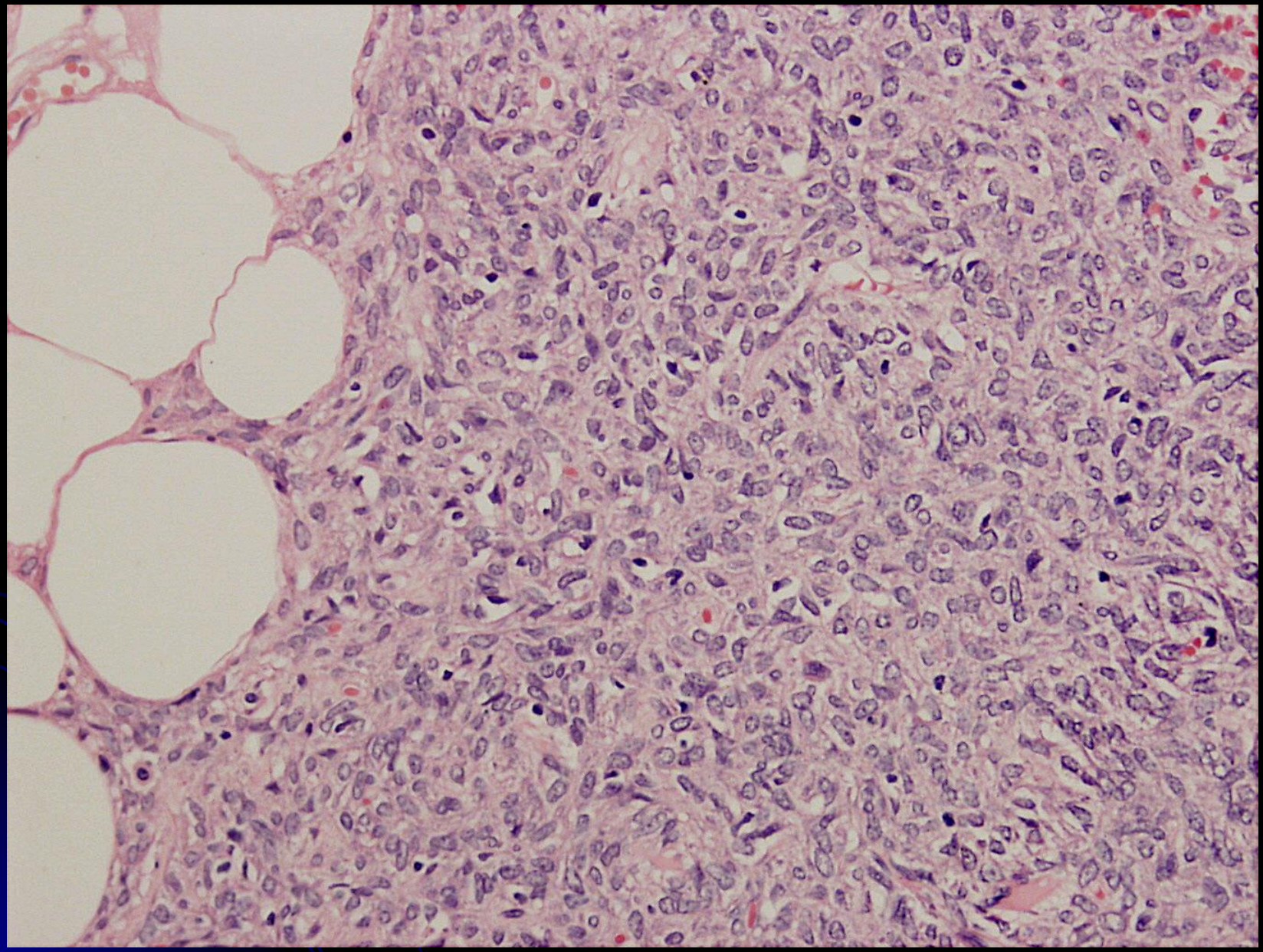


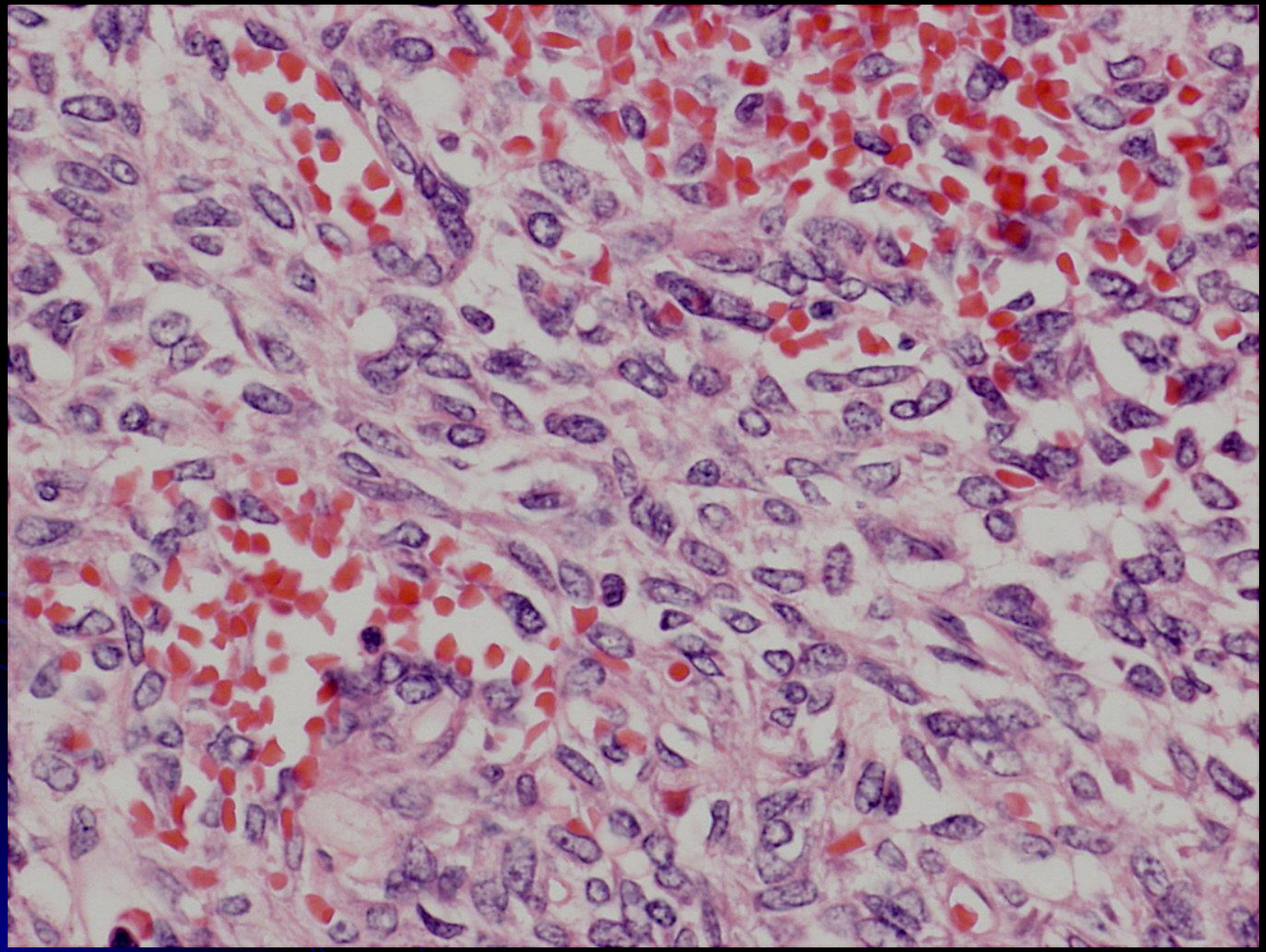


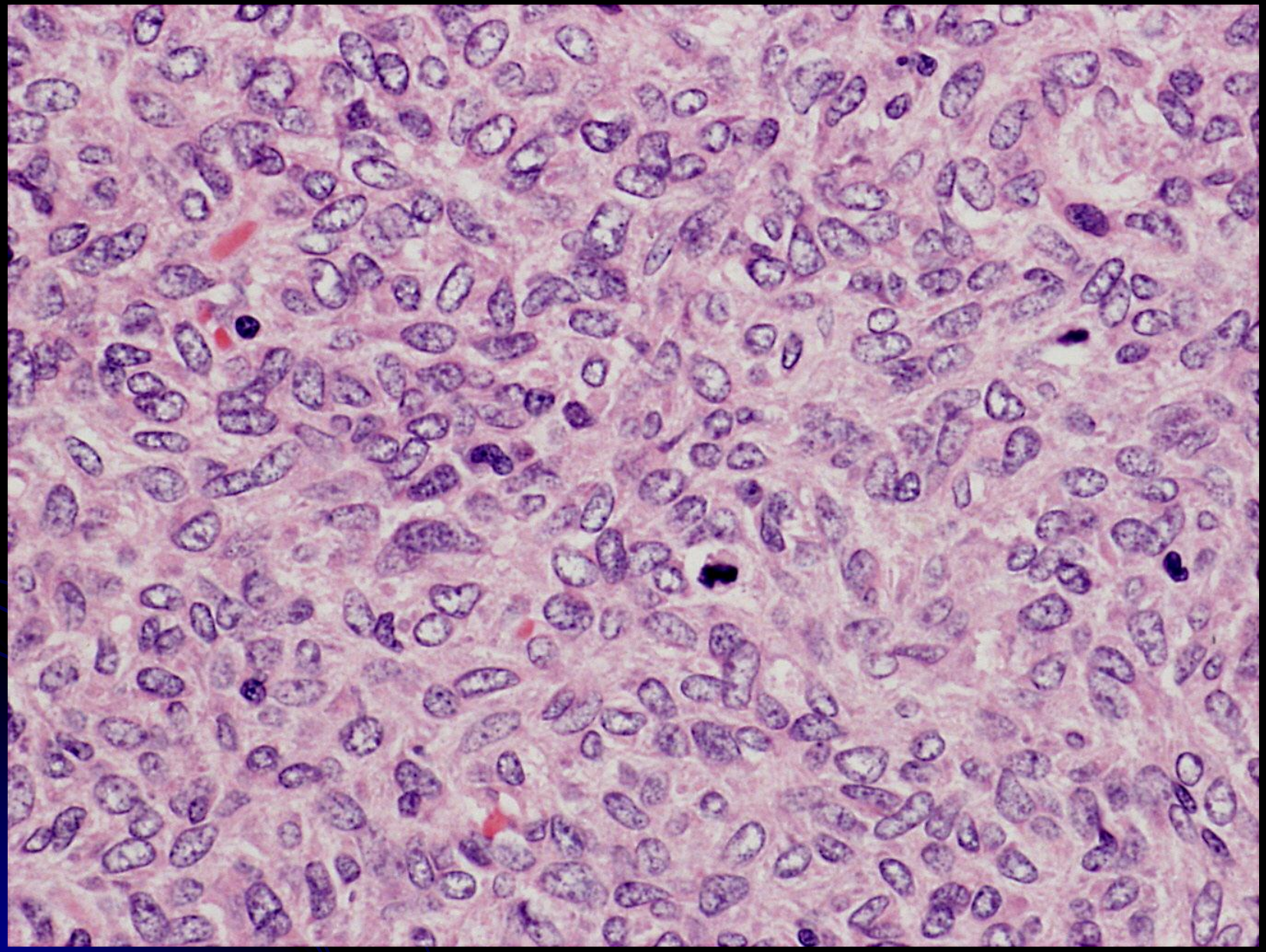


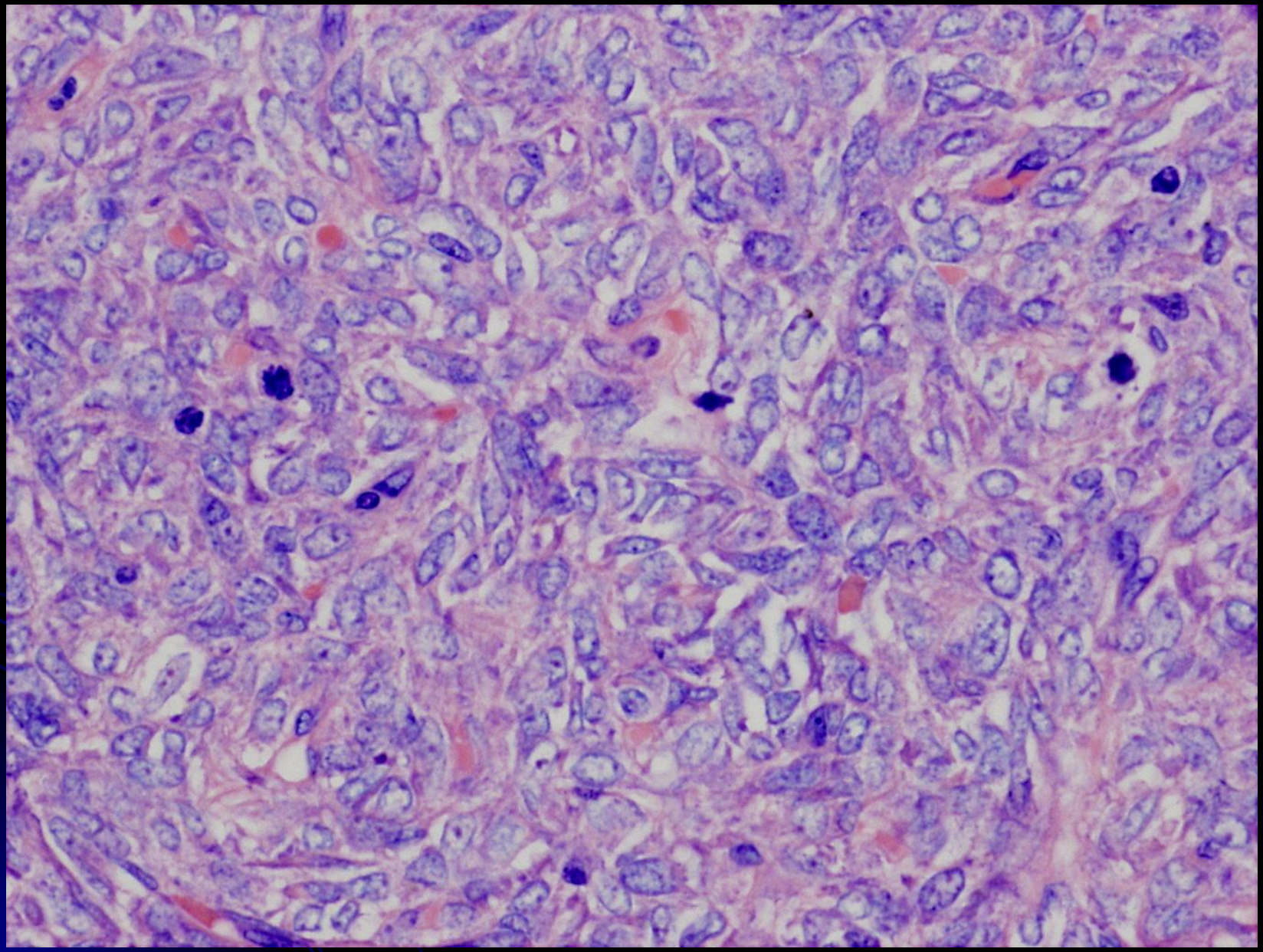


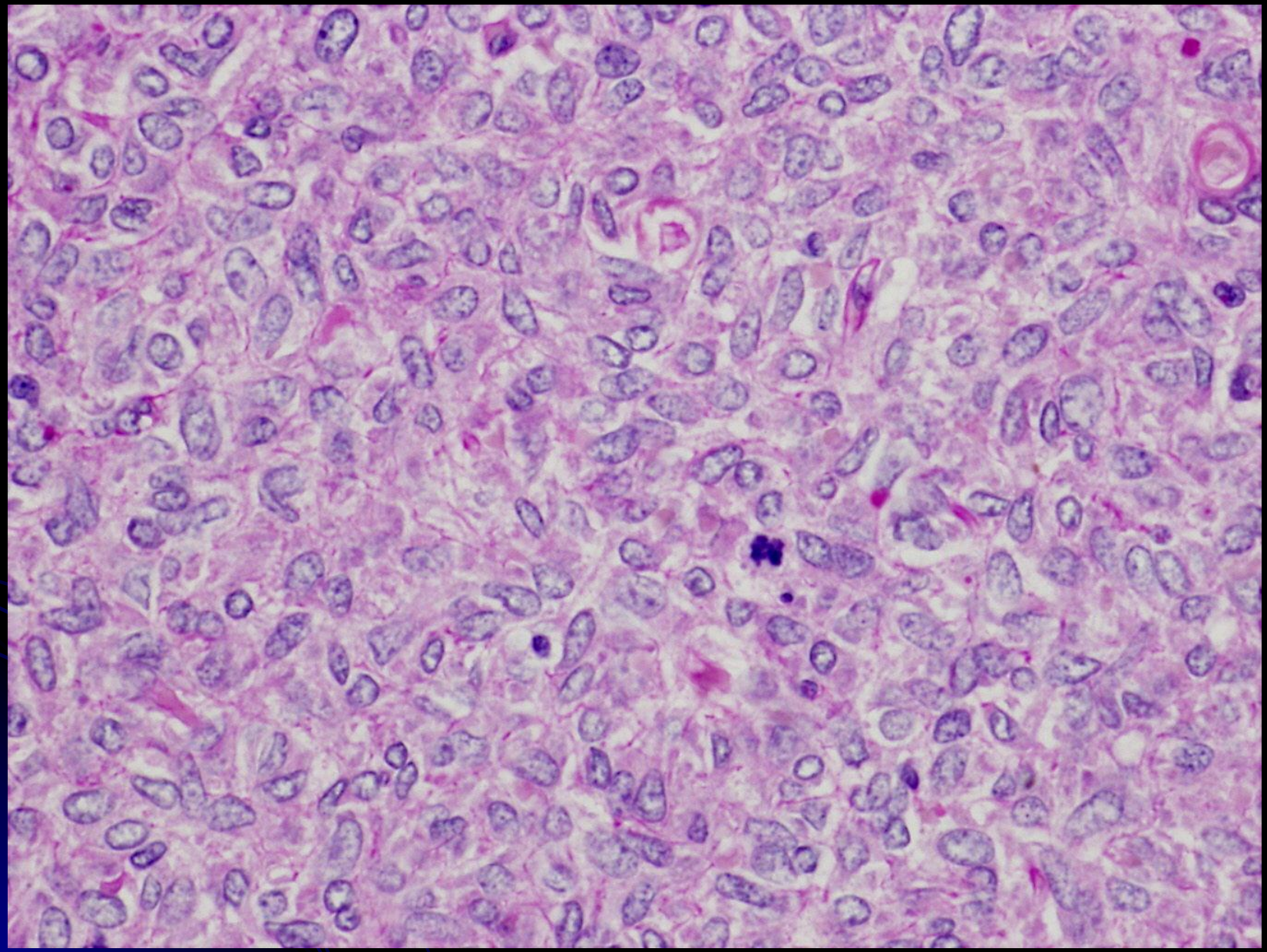












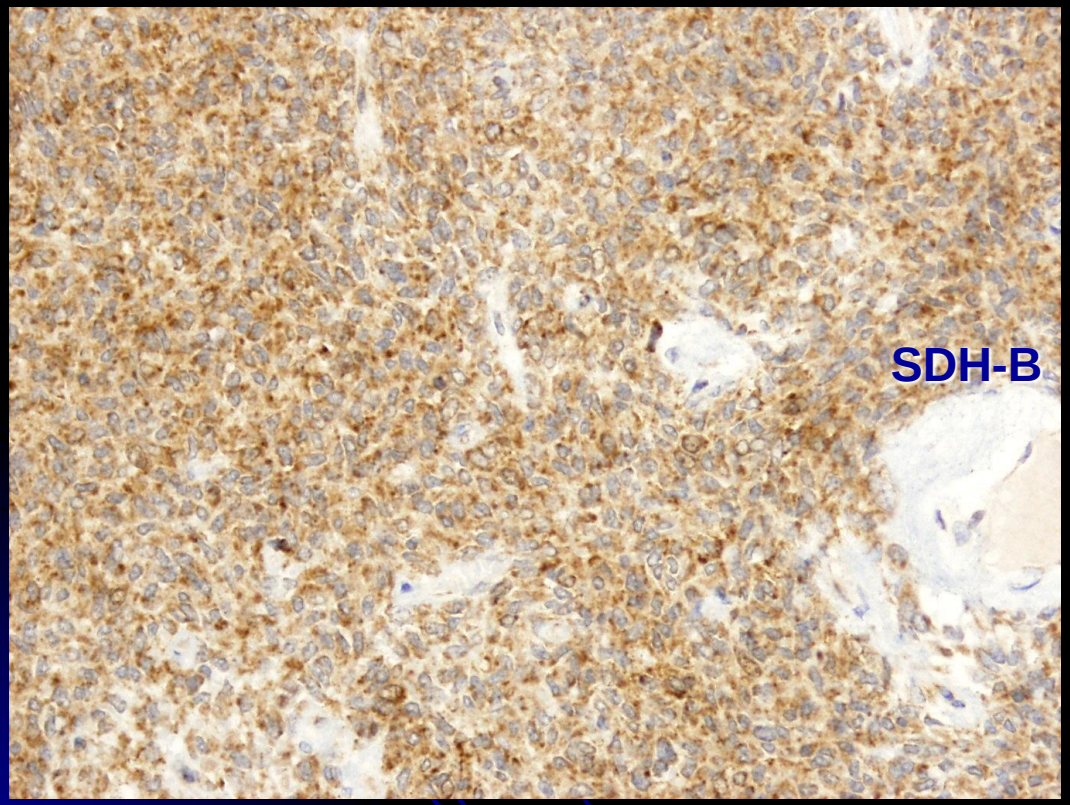
Sumarizácia morfológie

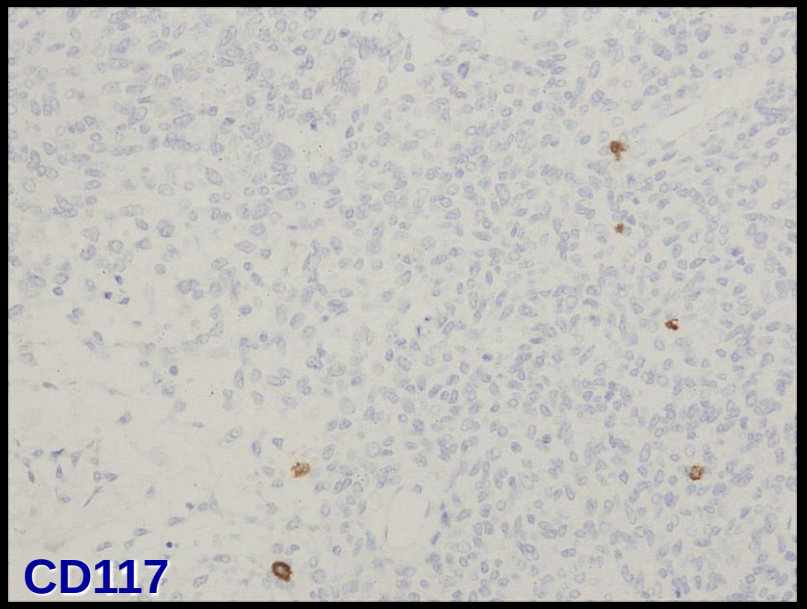
- mitoticky aktívny (MAI cca 10mf/10HPF) vretenobunkový nádor s nepravidelnými jadrami
- časť povrchu nádoru je krytá jemným puzdrom, pod ktorým sú drobné okrsky tukového spojiva
- bohatá vaskularizácia
- drobné okrsky myxoidného rozvoľnenia a hyalinizácie, ktorá je prítomná aj v stenách väčších ciev
- bez nekróz

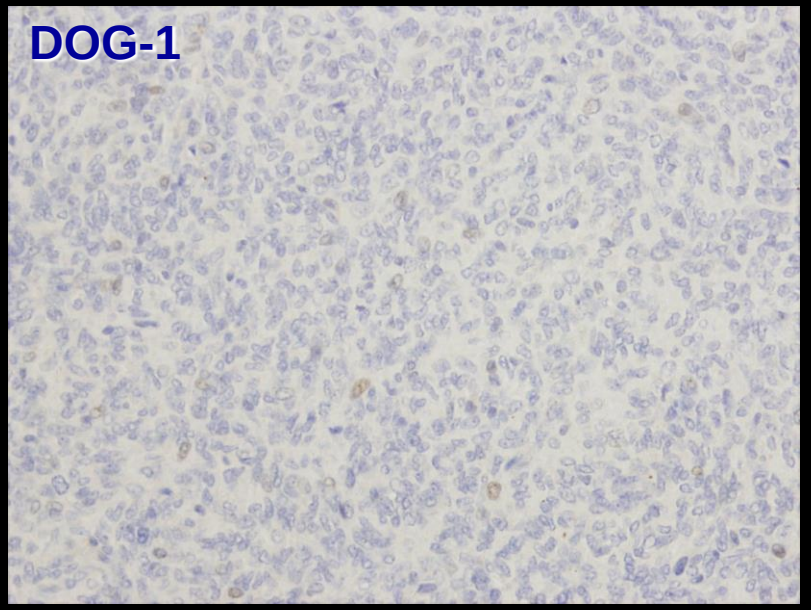
Diagnóza

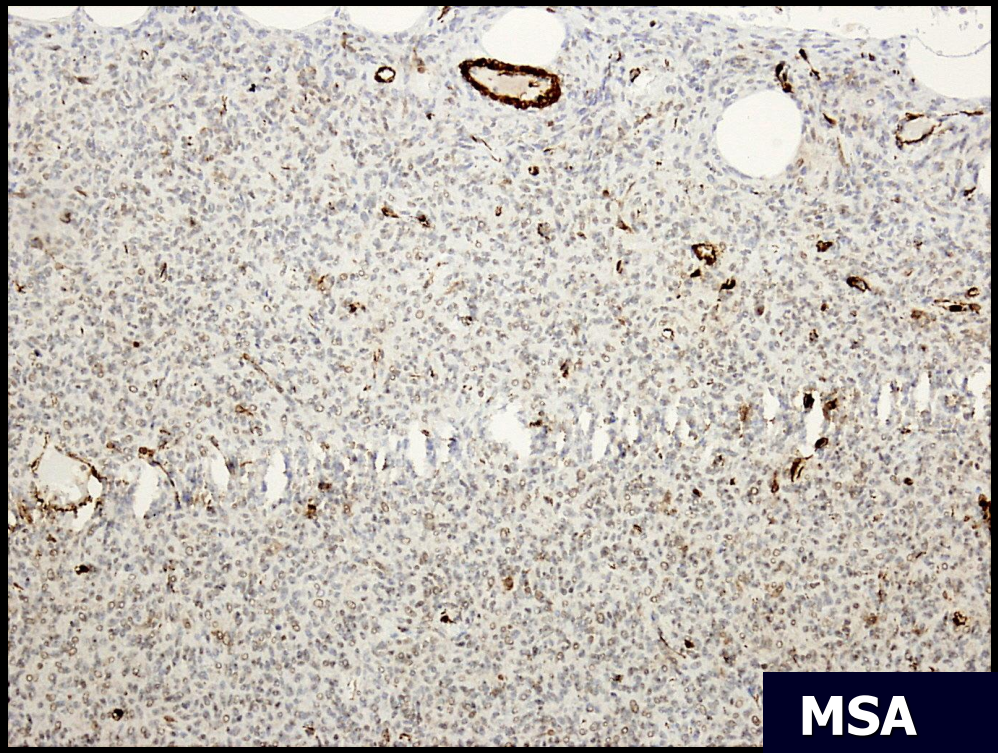

Imuno ...

GIST ?



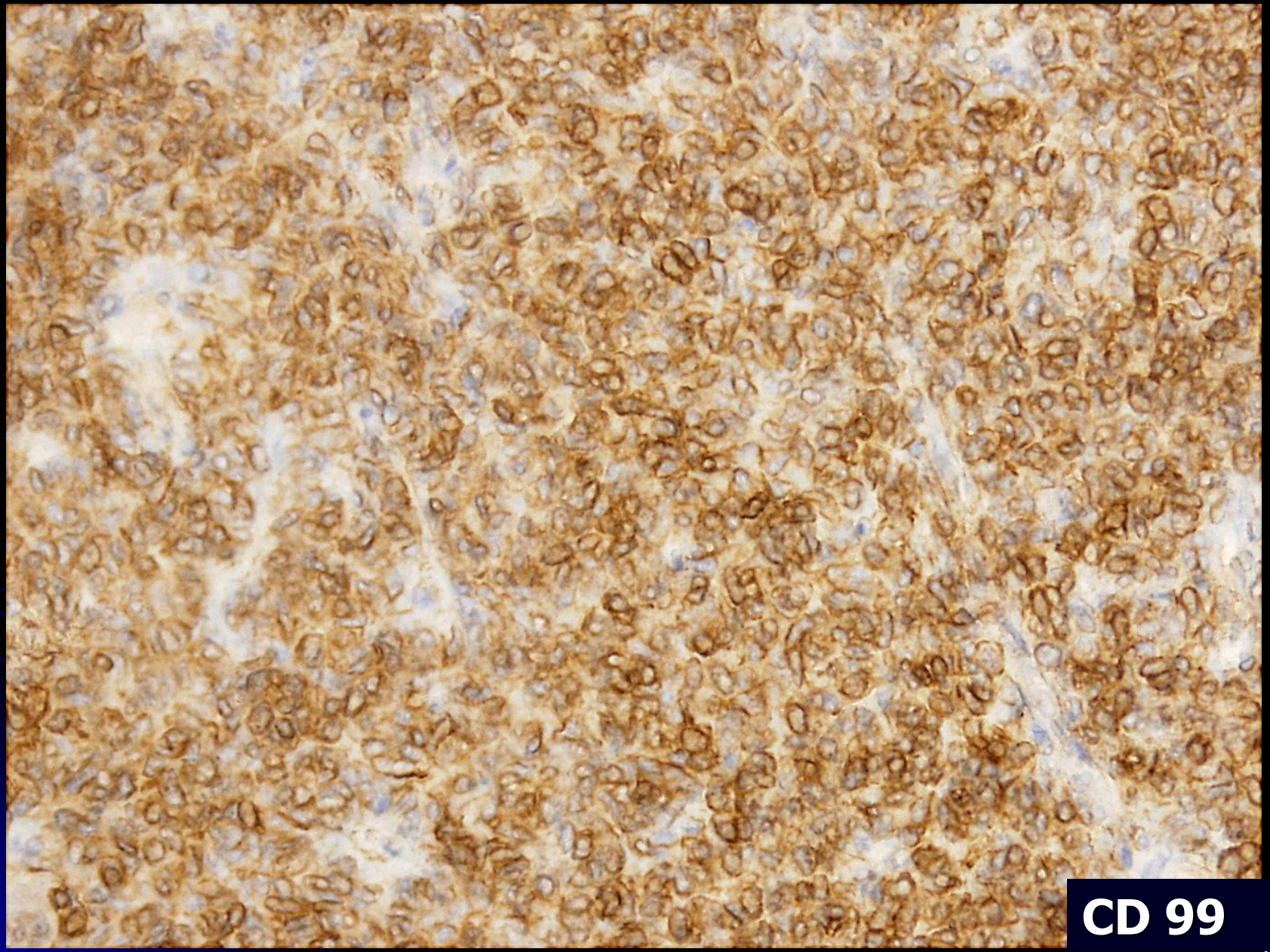




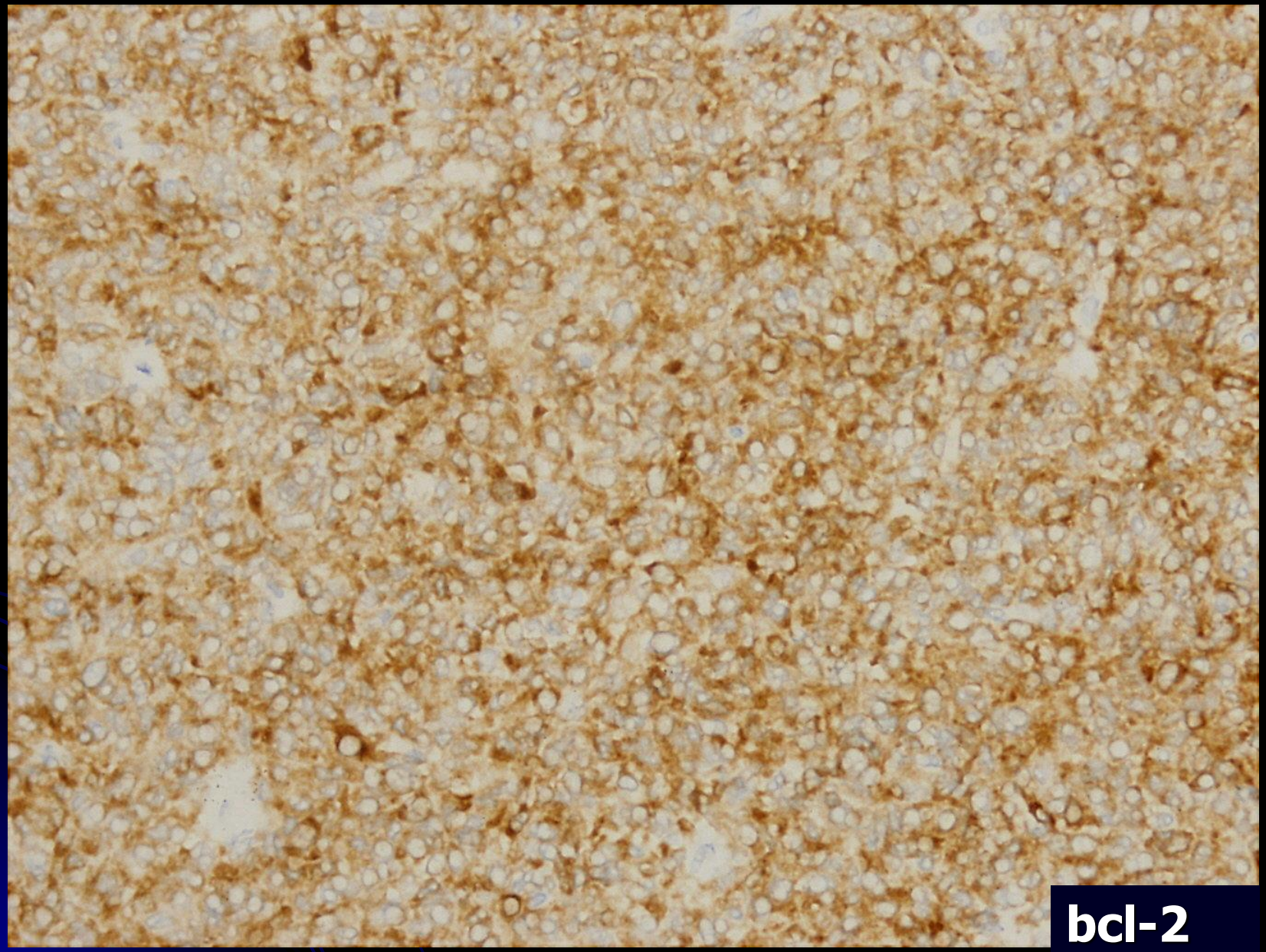


MSA EMA

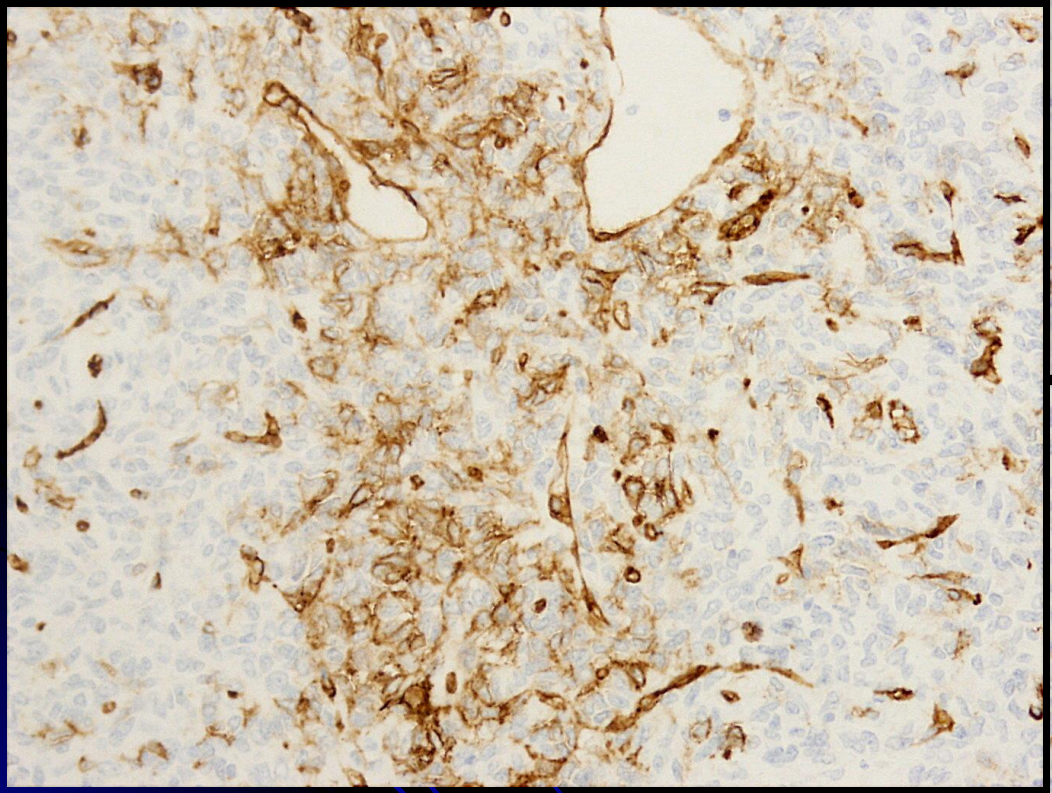
CK8/18, S-100, Inhibín,

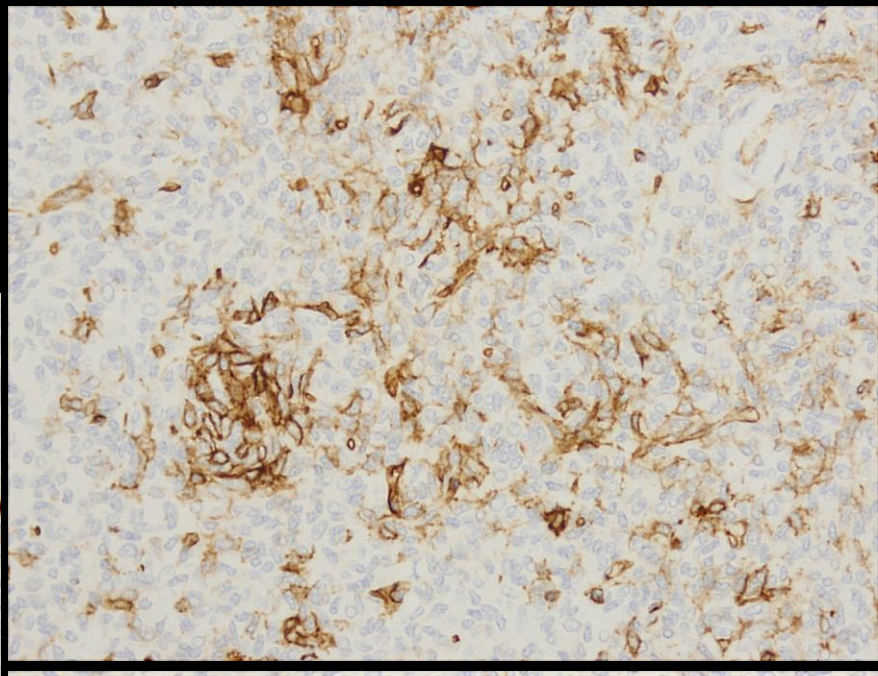


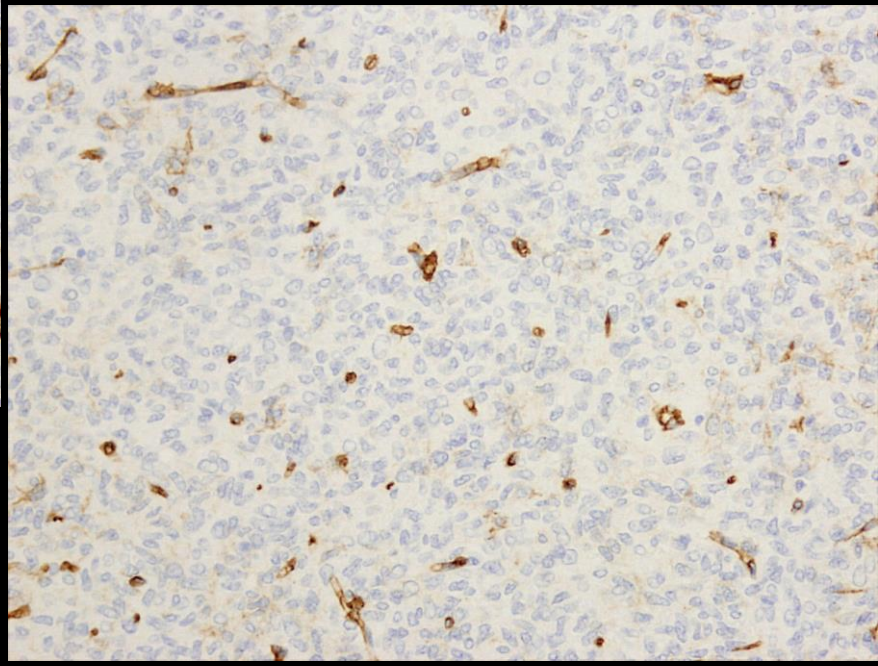
CD 99

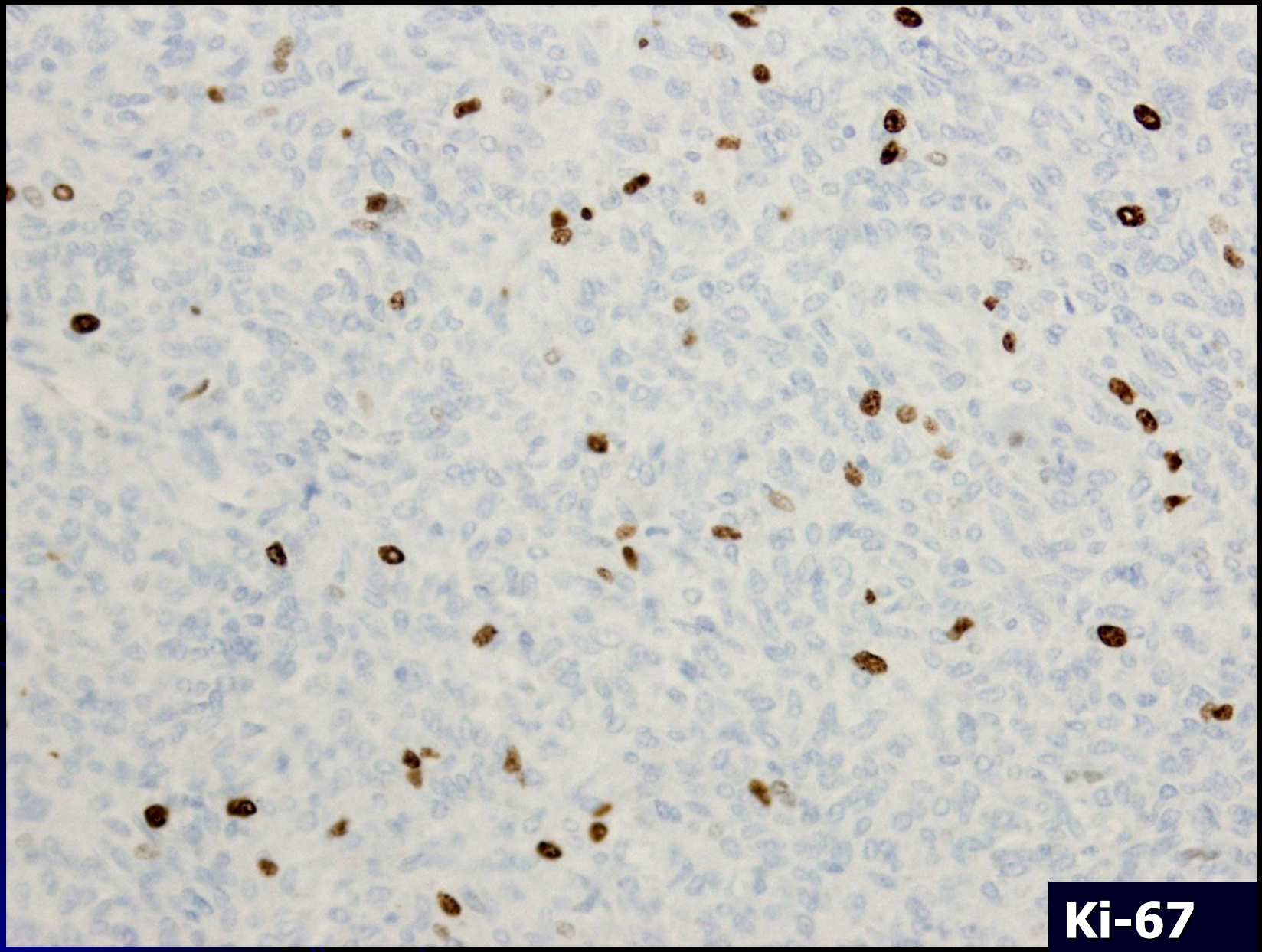

bcl-2

CD34







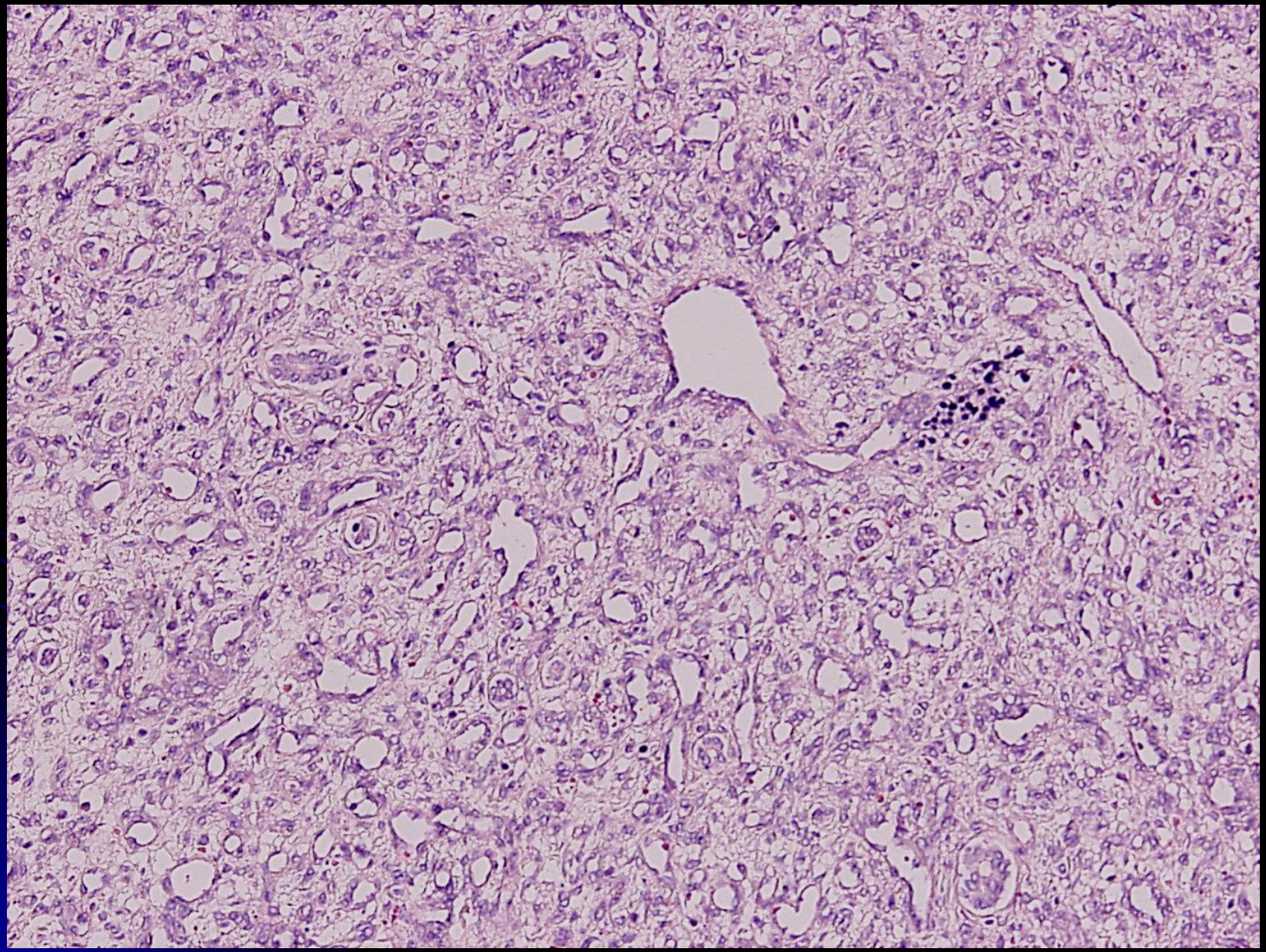

Ki-67

Sumarizácia imunoprofilu

- **Pozitivita: CD99, SDH-B, bcl-2, CD34 fokal.**
- Negativita: CD117, DOG-1, CK8/18, SMA, S-100 proteín, alfa-inhibín

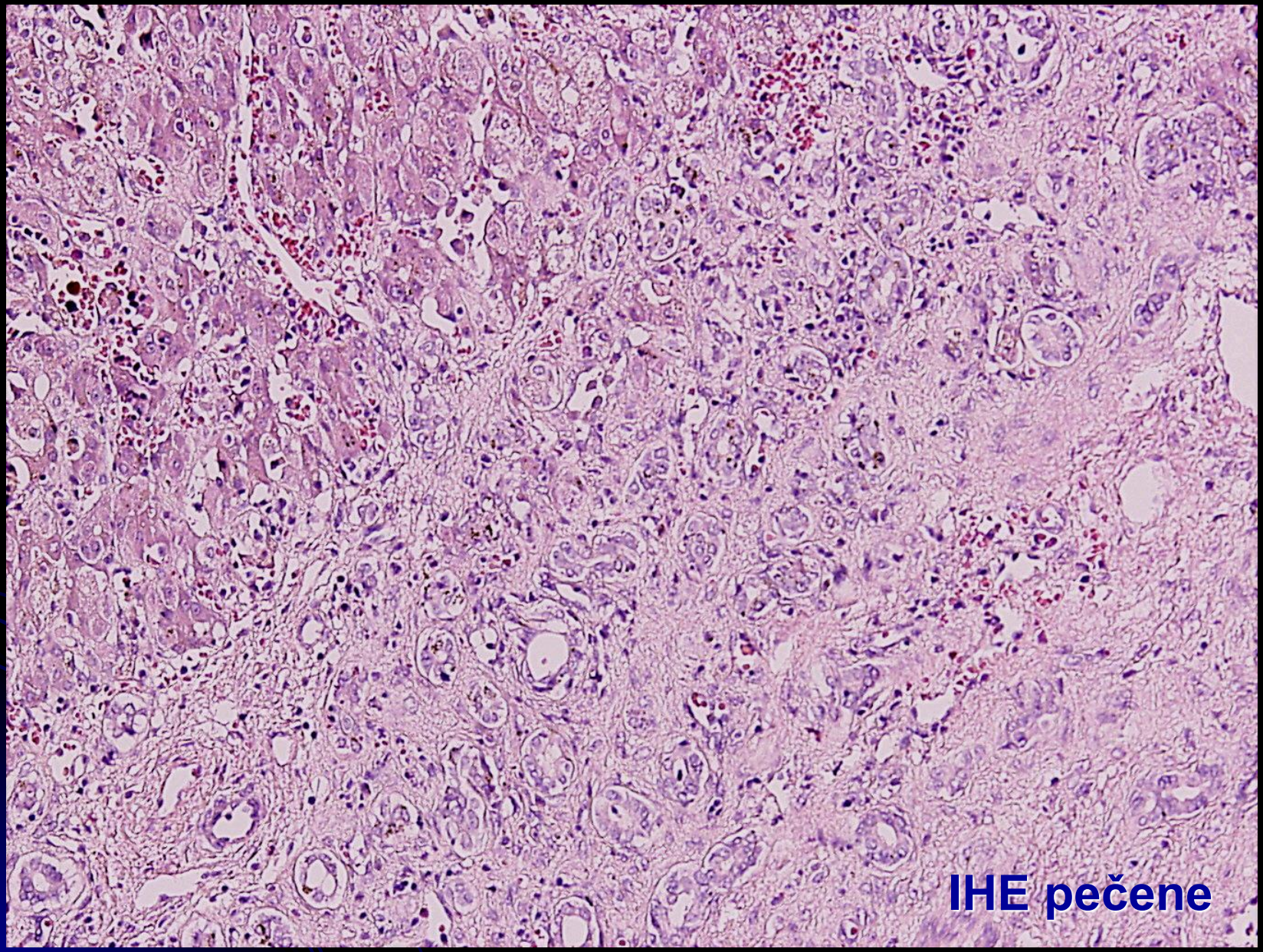
Diagnóza

536 B – 3. biopsia 2009

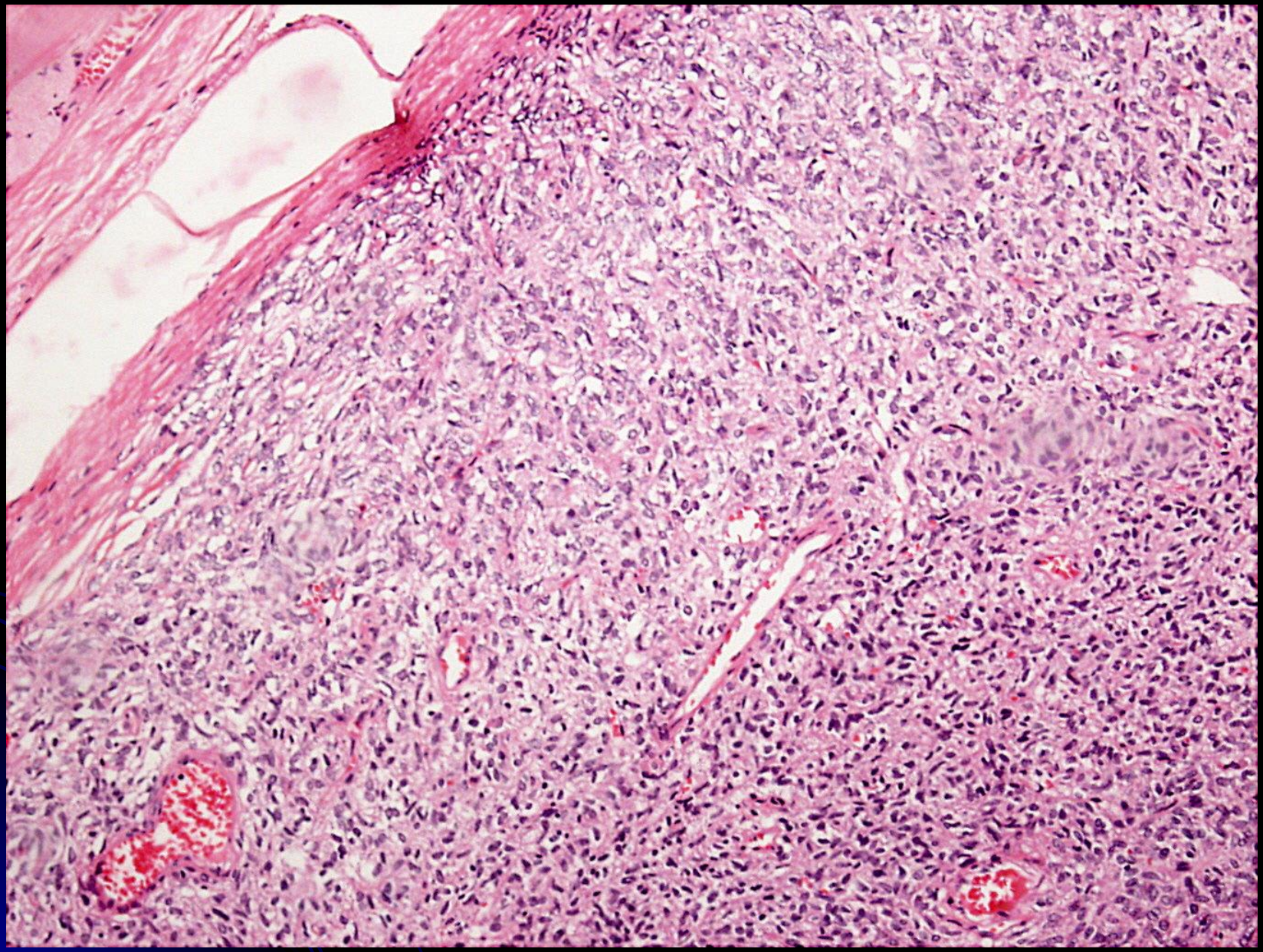


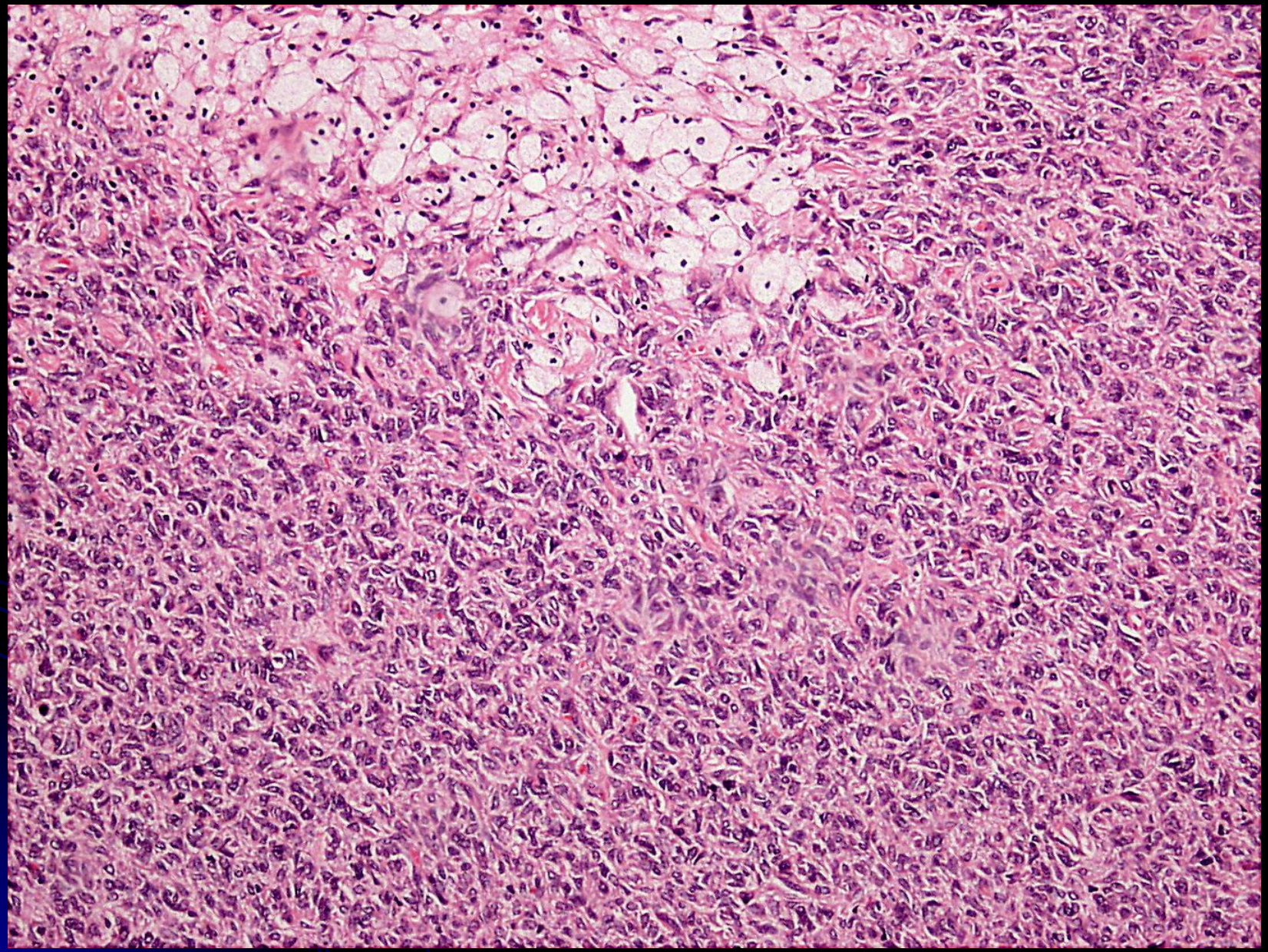
OSPRAVEDLNENIE

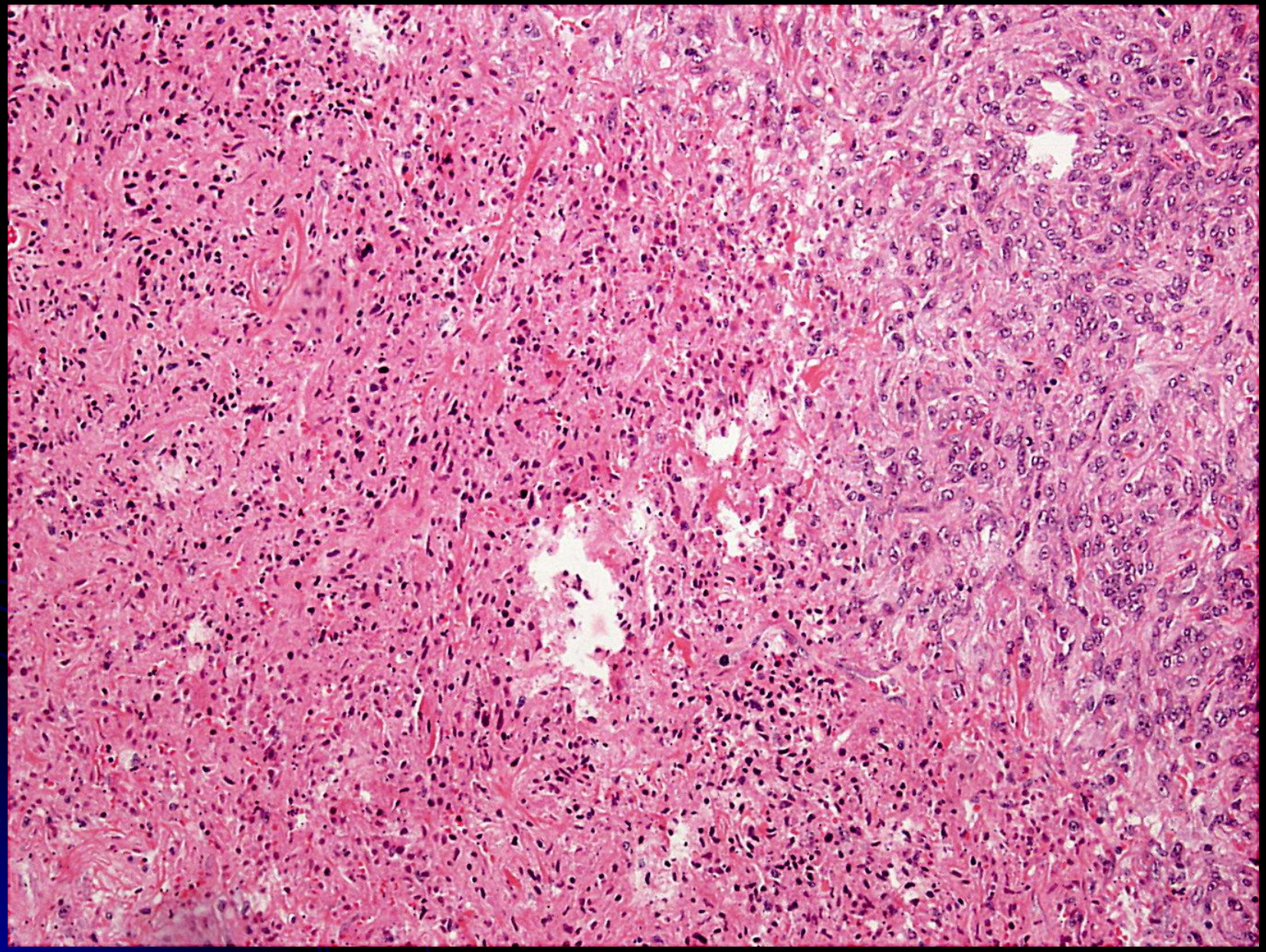
- zámena archívnych blokov
- recentná biopsia z r. 2014 je správna
- preparát 536 B je od inej pacientky
- všetko je raz prvý raz ...

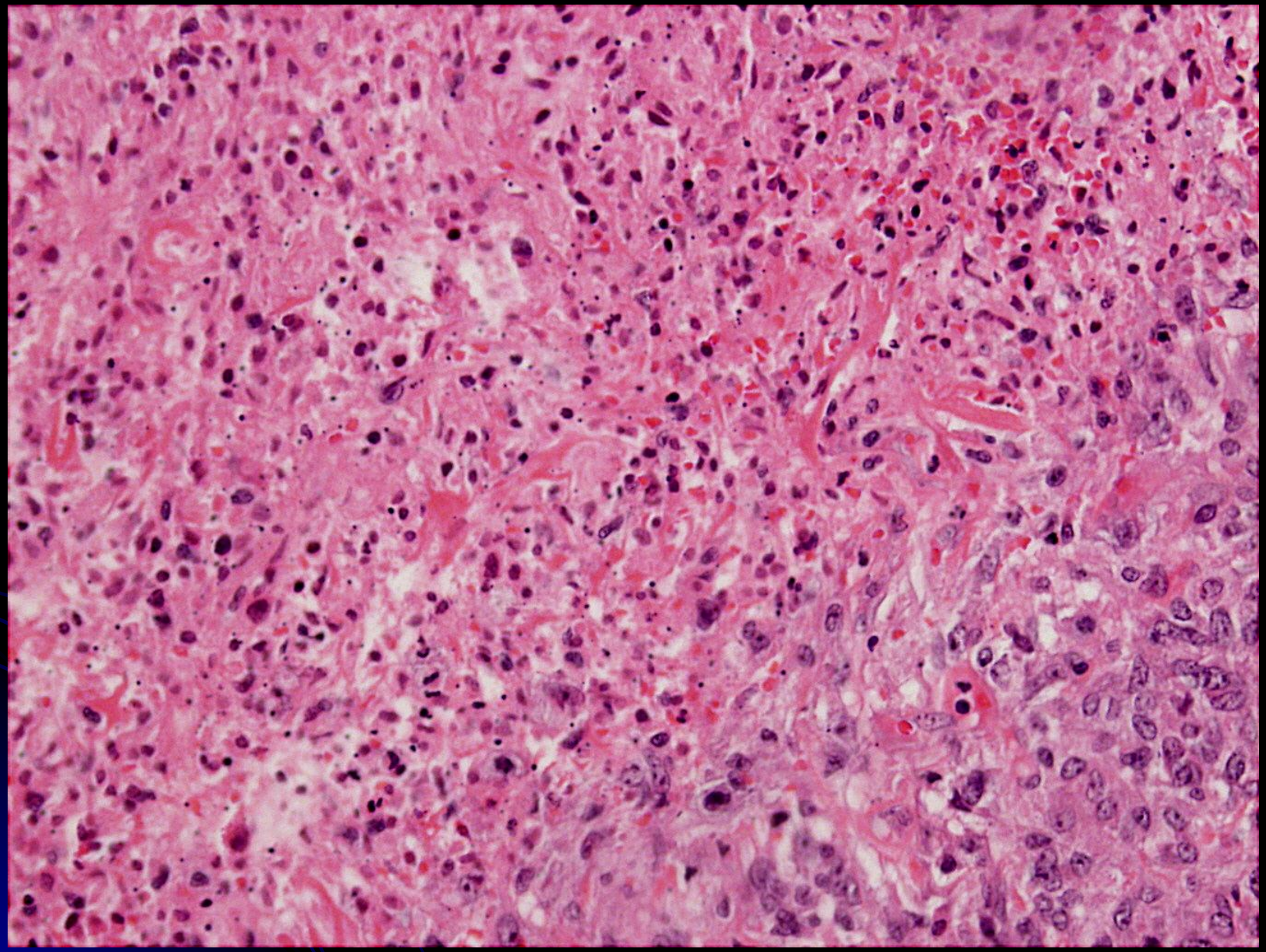


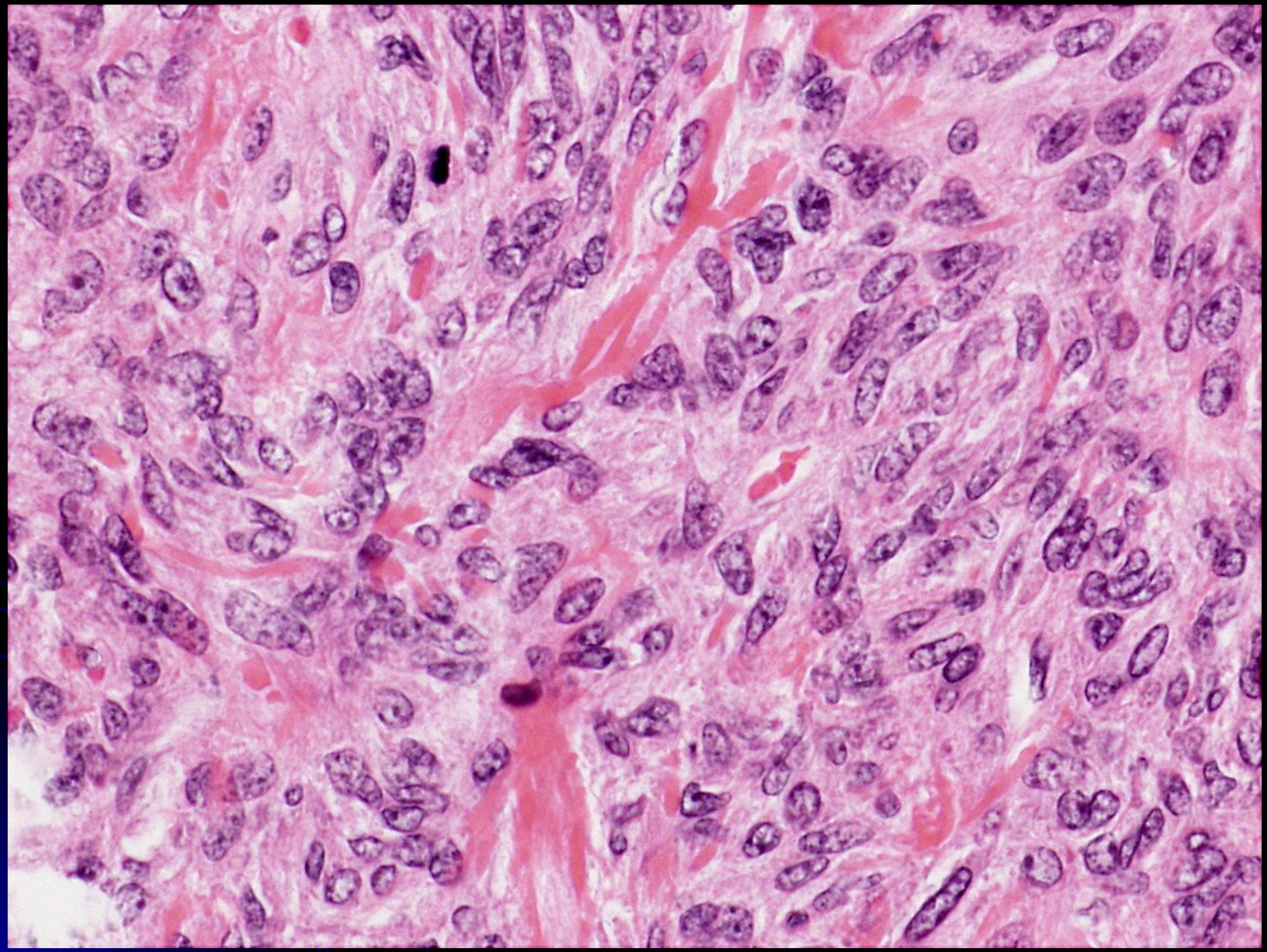
IHE pečene

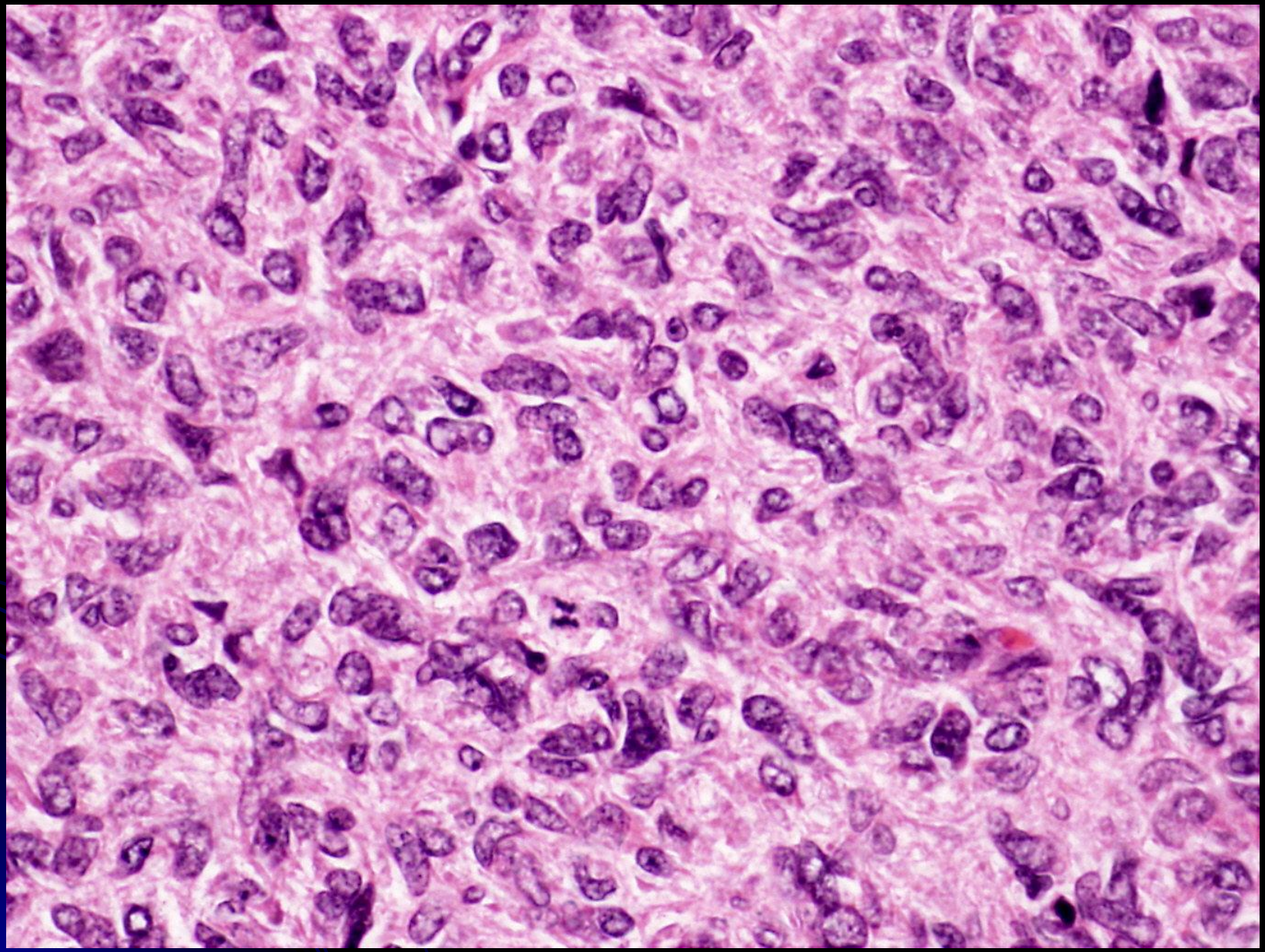


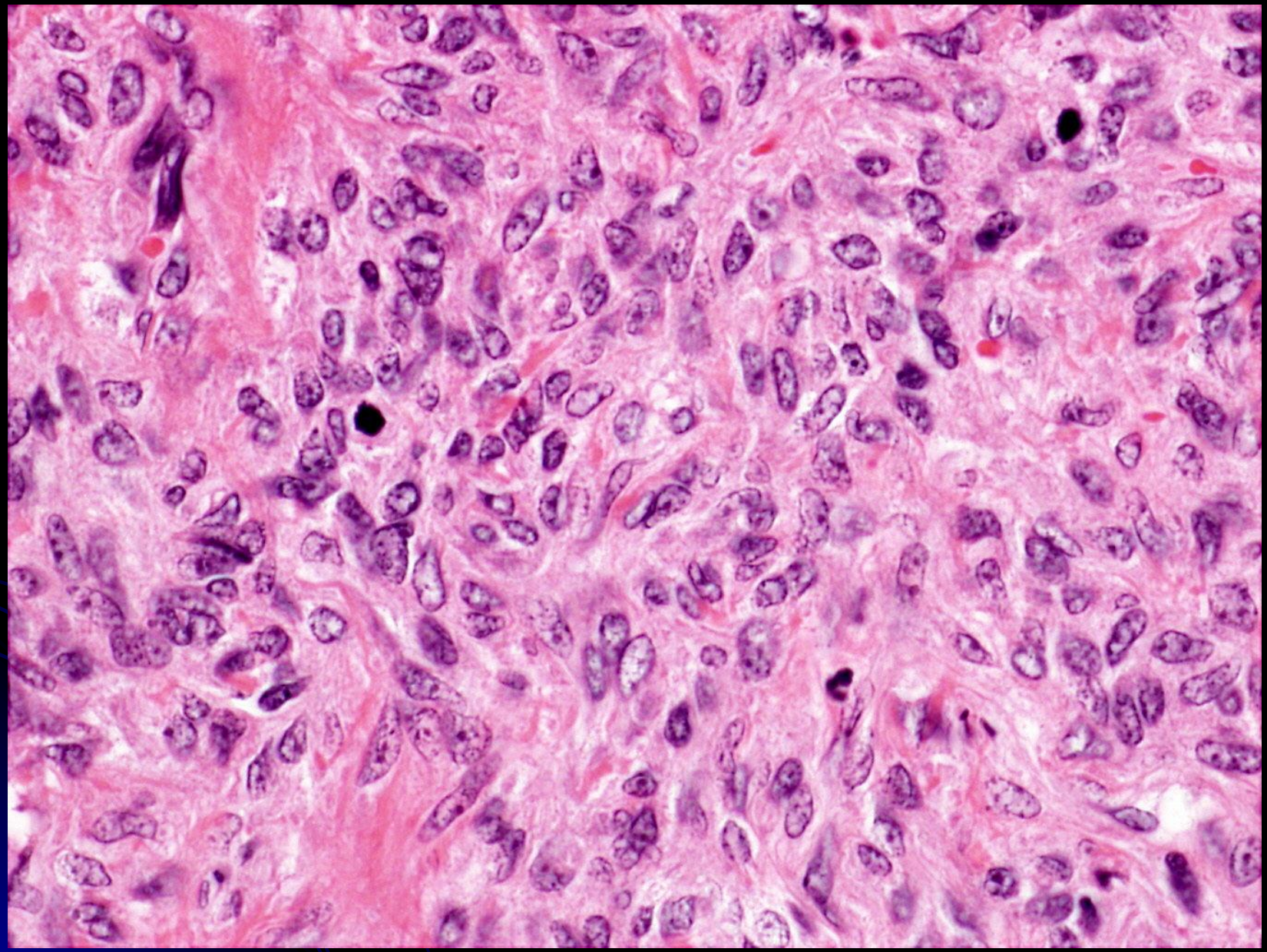


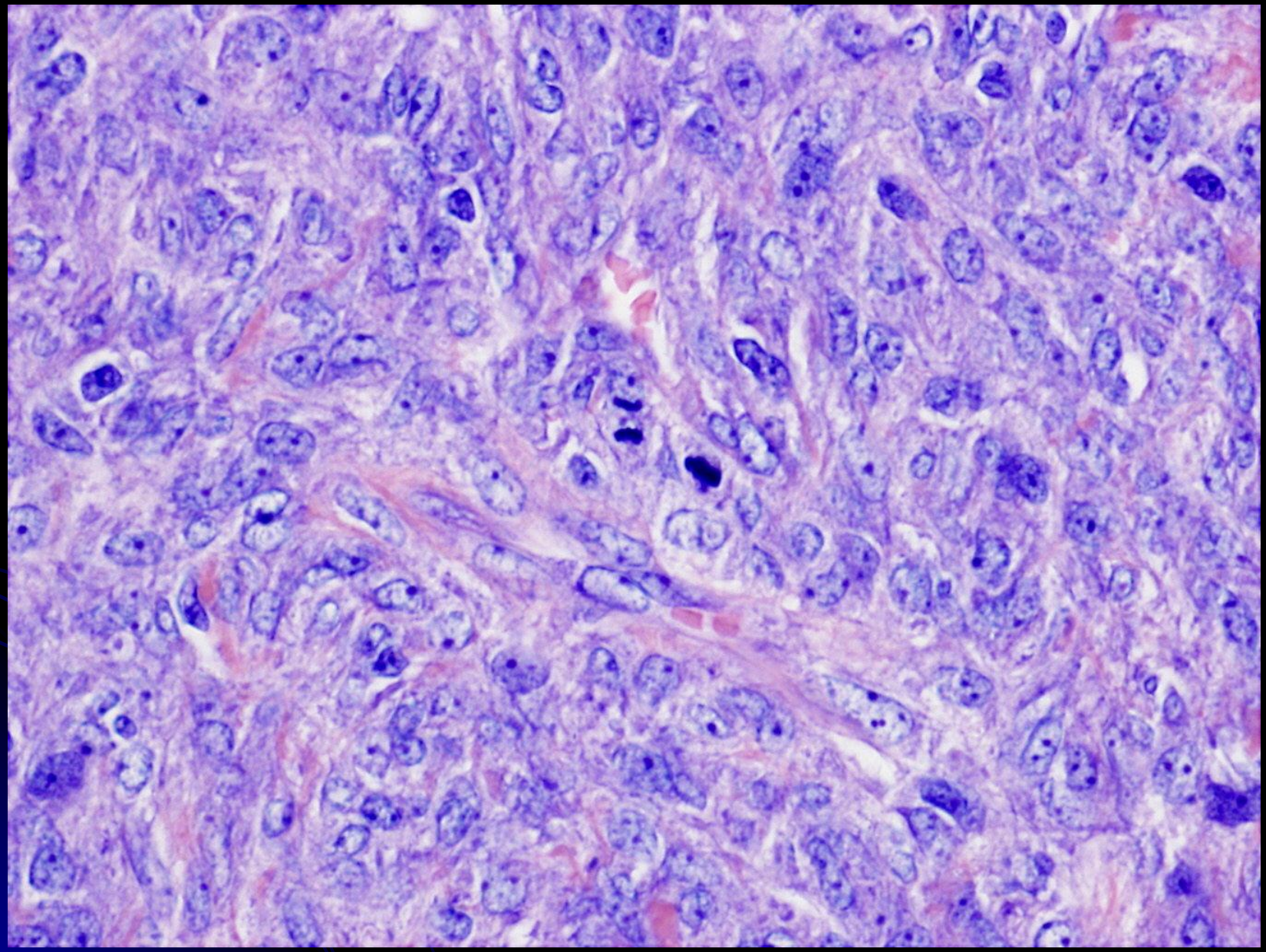






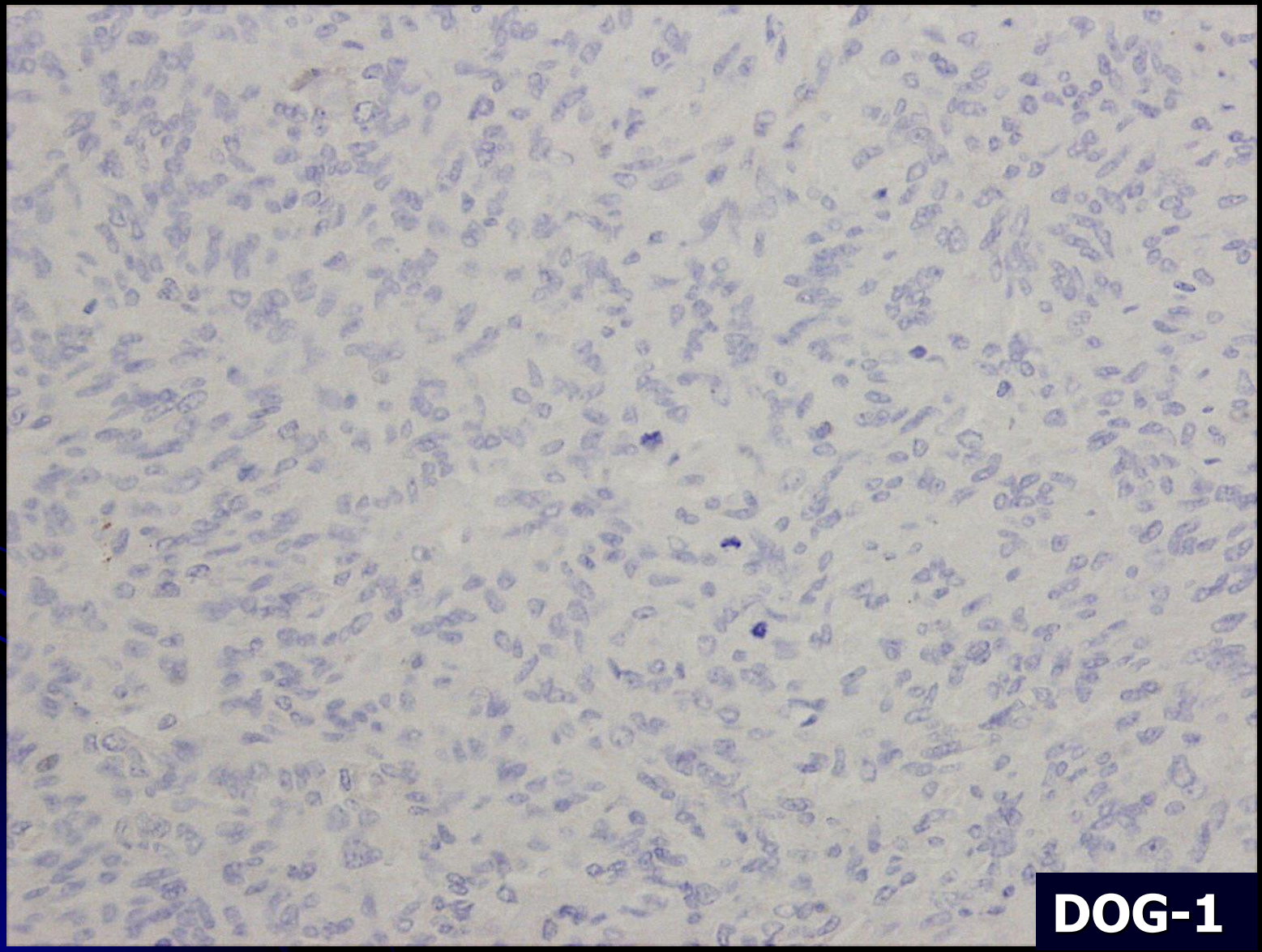






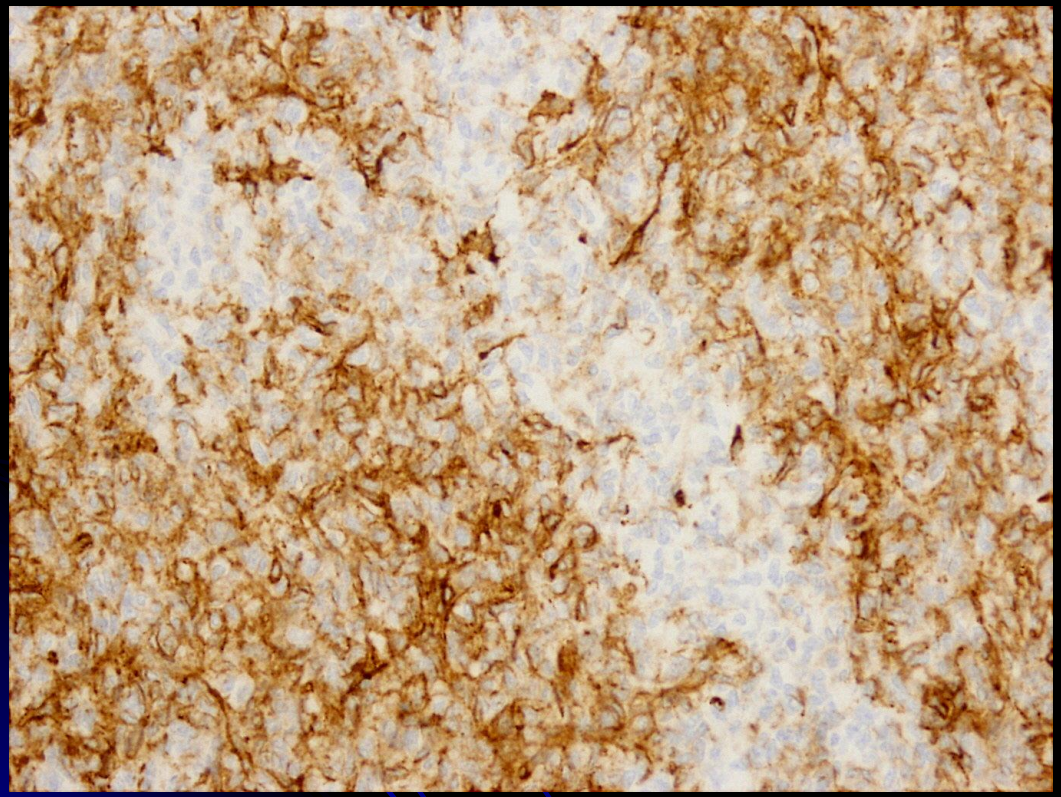

Imuno ...

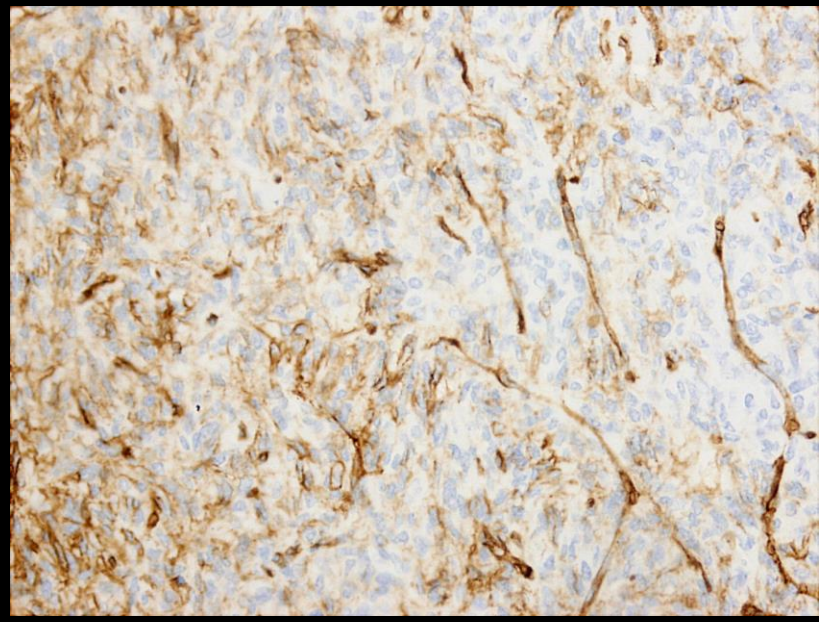
GIST ?

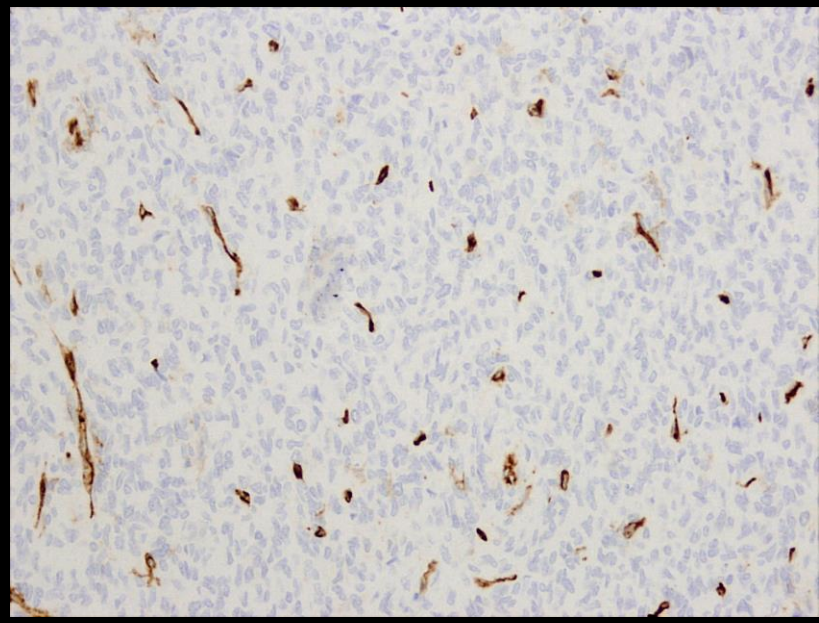


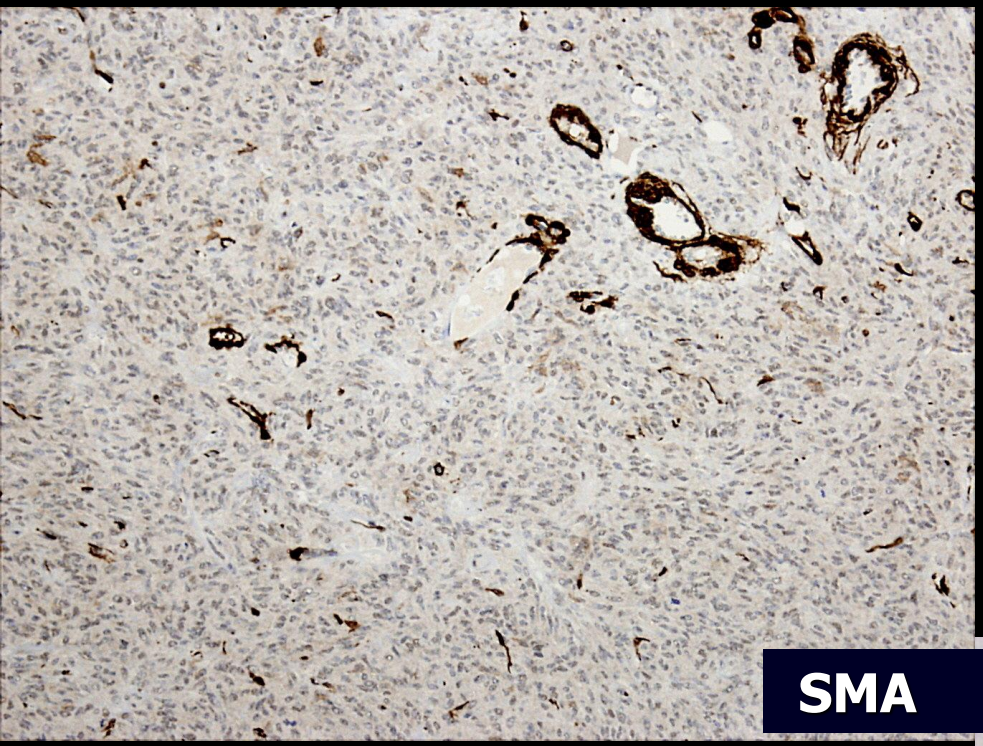
DOG-1

CD34

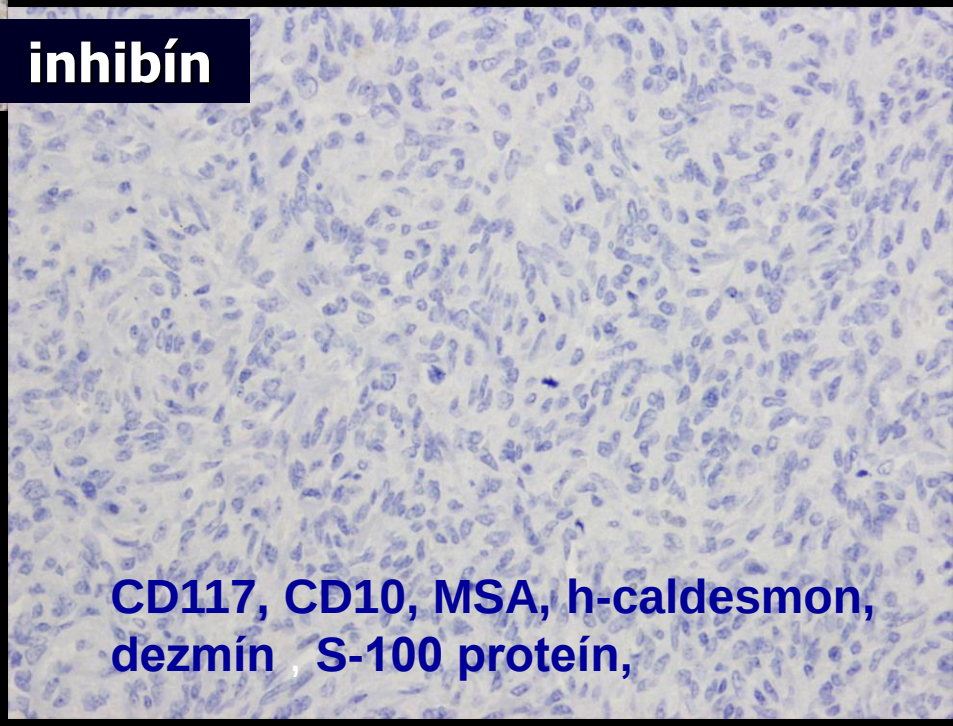




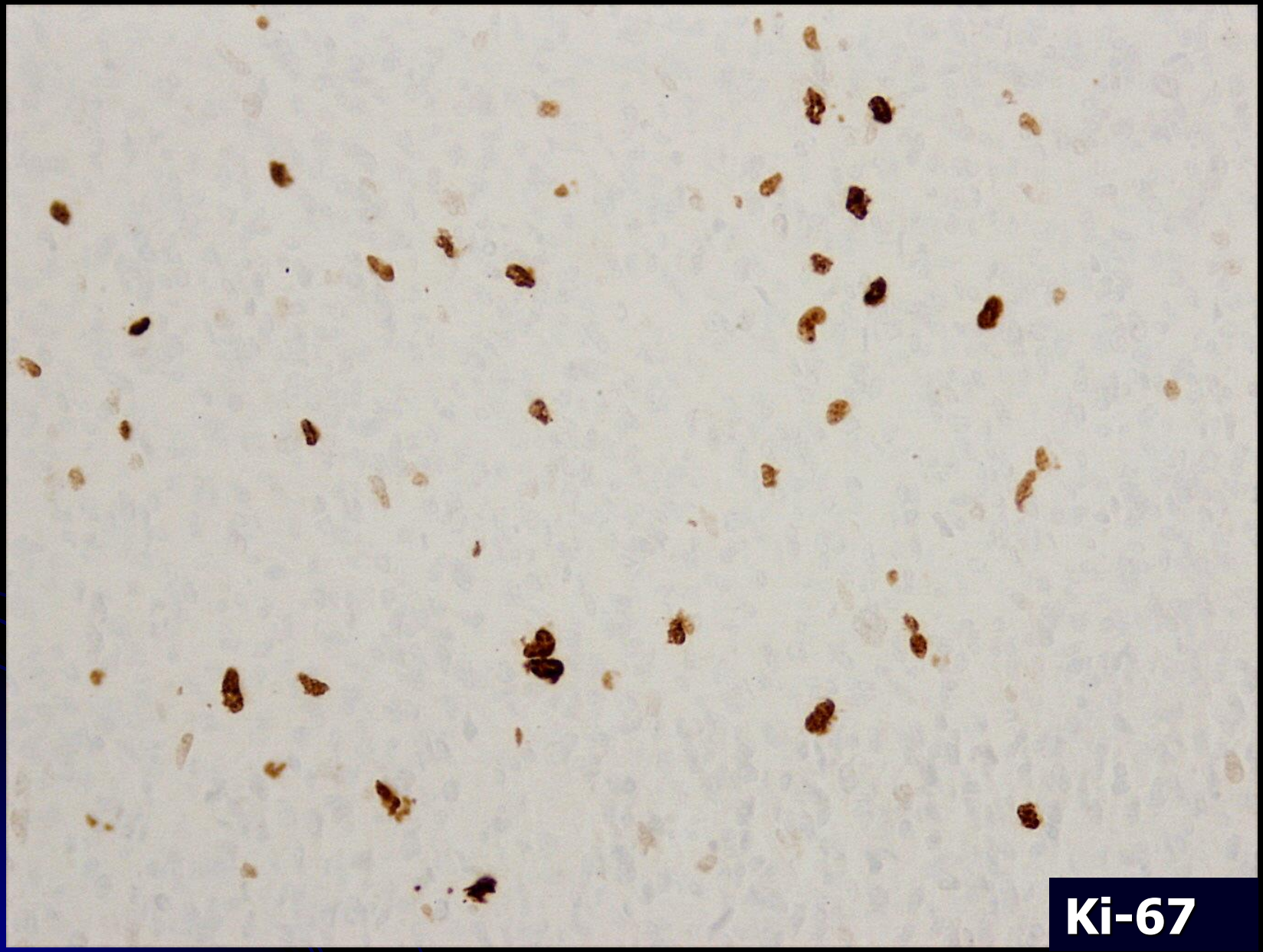




SMA inhibín



CD117, CD10, MSA, h-caldesmon,
dezmín , S-100 proteín,



Ki-67

Sumarizácia morfológie

- vretenobunkový pleomorfný nádor
- mitoticky aktívny (MAI cca 10mf/10HPF)
- ložiská nekróz

Sumarizácia imunoprofilu

- **Pozitivita: vimentín, CD34 fokal.**
- Negativita: CD117, MSA, SMA, dezmín h-caldesmon

Klinické údaje 2009

- 62 ročná žena s recidivujúcim tumorom v dutine brušnej
- v.s. generalizácia ochorenia

- **Klinická dg.:**
  Stp. extirp. leiomyoSa cum recid.

ZÁVER 2009 MFN

Morfologický obraz favorizuje (aj napriek negativite dôkazu CD10) dg. endometriálneho stromálneho sarkómu, pričom časť nádorových buniek exprimuje pozitivitu CD34, ktorá nie je v tomto nádore obvyklá.

Vzhľadom k tomu, že ide o generalizovaný malígny proces v stave po terapii odporúčame tento nález korelovať s biopsiou primárneho tumoru, ktorého lokalizácia z priloženého sprievodného listu nie je zrejmá. Negativita svalových markerov nepodporuje uvedenú dg. leiomyosarkómu, dif. dg. zvažovaná možnosť GIST-u je nepravdepodobná.

KLINICKÁ POMOC jún 2014

- „... nie, že by som neveril Vašej diagnóze, ale nevidel som ešte pacientku s ESS, ktorá by nevyžadovala hysterektómiu ...
- pacientka sa má celkom dobre, oboch nás prežije, ale chcel by som vedieť čo to je, máte rebiopsiu, pozrieš sa na to ?“

prim. J. Šufliarsky

Follow up 1988 - 2014

- 1988 - vretenobunkový sarkóm G1 malej panvy
  - Stav po laparotómii , 5 kúr CHT a RAT, observácia
- 1998 - 1. recidíva v omente - resekcia
- 2009 - 2. recidíva brušná stena, retroperitoneum a oblička
  - resekcia, nefrektómia, 6x CHT
- 2014 - 3.recidíva
  - resekcia, 1 kúra CHT

Pridružené dg: Hypertenzia, Stav po hypertenznej kríze
ICHS, bolestivá forma
Stav po STEMI (2006), 2x by-pass
Stav po plastike MCH (2006)
Permanentá fibrilácia predsiení
Plastika karotídy pre stenózu
DM 2.typu
Hypofunkcia štítnej žľazy

Histologický nález tumorov 1988-98 „nízkomalígny sarkóm malej panvy“

- malígny mezenchýmový nádor tvorený vretenovitými bunkami s málo zreteľnou cytoplazmou bez nápadnejšej pleomorfie
- mitotická aktivita 5-6 mitóz/10HPF
- fascikulárne usporiadanie, sčasti storiformné, sčasti hemangiopericytomatózne
- vaskularizovaná stróma, fokálne hyalinizovaná, úseky myxoidného presiaknutia
- disperzná prímes buniek osteoklastoidného typu
- Imuno: CK, EMA, CEA, dezmín, vimentín, SMA, MSA, CD31, CD34, fVIII., Chrg. A – všetko negatívne

  CD68 pozitívne v obrovských bunkách, minimlána proliferačná aktivita (Ki-67 prakticky areaktívne)

Recidíva (MTS) z omenta -1998

- konzultácia z Galanty:
- celularita zvýšená, ale monotónny vzhľad
- storiformita menej výrazná, skôr úseky fibrosarkomatózneho charakteru a fascikulárne formácie s náznakom palisádovania
- bunky osteoklastoidného typu chýbajú
- Imuno nerobené (neposkytnuté bloky)

ZÁVER 1998

Ide o malígny mezenchýmový nádor, vretenobunkový sarkóm s nízkym stupňom malignity v malej panve s MTS do omenta.

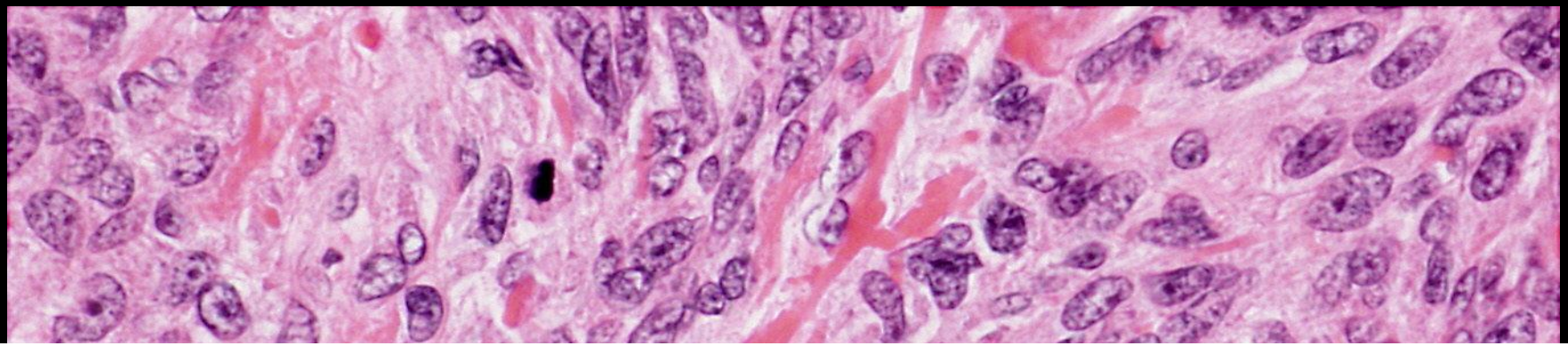
Dif. dg. prichádza do úvahy MPNST (ak nádor vychádza z extragastrointestinálnych mäkkých tkanív), ďalej GIST (ak nádor vyrastá zo steny čreva) alebo diferencovaný MFH. Pravdeopodobnejšie sú prvé dve možnosti, menej pravdepodobný je SS a iné malignity.

ZÁVER 2009 a 2014 NOÚ

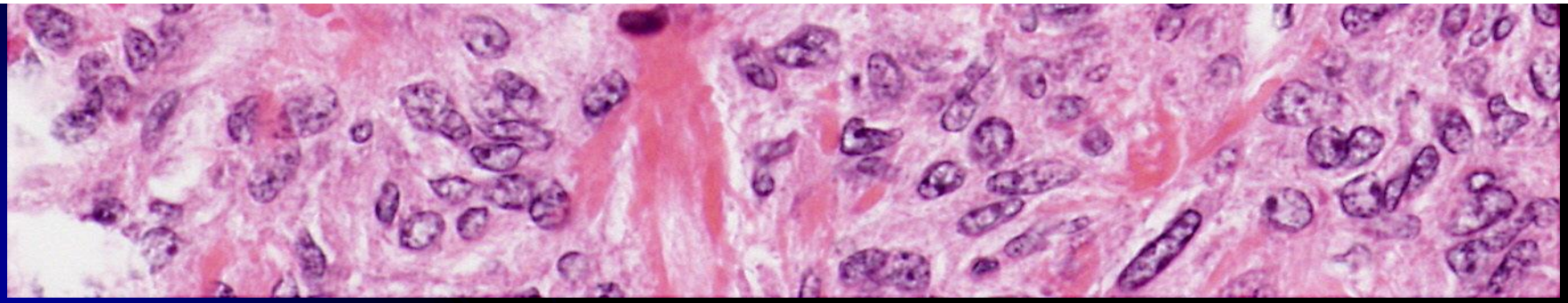
Stromálny sarkóm už high grade typu

Imuno: AE1/AE3-, vimentín+/fokálne+,S-100-, SMA-, dezmín-, CD34+, CD31-, HMB-45-, Ki-67 cca 15%, CD10 fokálne monocelulárne náznak+

DIAGNÓZA



EXTRAPLEURÁLNY MALÍGNY SOLITÁRNY FIBRÓZNY TUMOR (ESFT)



DIFERENCIÁLNA DIAGNÓZA

- Hemangiopericytóm
- Leiomyóm / Leiomyosarkóm
- GIST
- Schwannóm / MPNST
- Fibrózny histiocytóm / USCSa (MFH)

SFT

WIKIPEDIA
The Free Encyclopedia

Main page

Solitary fibrous tumor

From Wikipedia, the free encyclopedia

References [edit]

1. ^ [a] [b] [c] Travis WD, Brambilla E, Muller-Hermelink HK, Harris CC (Eds.): World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart. IARC Press: Lyon 2004.
2. ^ http://www.sciencedirect.com/science/article/pii/S0899707112001660
3. ^ [a] [b] [c] [d] [e] Robinson LA. Solitary fibrous tumor of the pleura. Cancer Control 2006;13:264-9.
4. ^ Wagner E. Das tuberkelahnliche lymphadenom (der cytogene oder reticulirte tuberkel). Arch Heilk (Leipig). 1870;11:497.>
5. ^ de Perrot M, Fischer S, Brundler MA, et al. Solitary fibrous tumors of the pleura. Ann Thorac Surg. 2002;74:285-293.
6. ^ [a] [b] Briselli M, Mark EJ, Dickersin GR. Solitary fibrous tumors of the pleura: eight new cases and review of 360 cases in the literature. Cancer 1981;47:2678-89.
7. ^ Pinedo-Onofre JA, Robles-Pérez E, Peña-Mirabal ES, Hernández-Carrillo JA, Téllez-Becerra JL. [Giant solitary fibrous tumor of the pleura.] Cir Cir 2010;78:31-43. [Article in Spanish].

ESFT sec. WHO 2013
M 8815/1 a M 8815/3

- ubikvitárny mezenchymálny tumor fibroblastického typu, vykazujúci prominentnú „hemangiopericytomatóznu“ vaskularizáciu (hemangiopericytóm)
- vek obvykle 20-70rokov, M:Ž cca 1:1
- je zriedkavý, ale može sa vyskytovať prakticky kdekoľvek: podkožie (40%), ostatné – končatiny, orbita, hrudná stena, mediastínum, perikard, retroperitoneum, brušná dutina, ale aj meningy, miecha, slinné žľazy, pľúca, pečeň, štítna žľaza, GIT, nadobličky, urogenitálny trakt a kosti.

SFT

Solitary Fibrous Tumor

Definition

- **Tumor composed of small cells individually separated by thin bands of collagen fibers**

Alternate / Historical Names

- Hemangiopericytoma
- Localized fibrous tumor
- Fibrous mesothelioma

Diagnostic Criteria

- May be grossly circumscribed but frequently infiltrates microscopically
- **Unifying pattern is small cells individually separated by collagen**
  - Cells typically small
    - Nuclei dense or vesicular
    - Scant cytoplasm
  - Thin bands of collagen surround and separate individual cells
- Usually has alternating hypercellular and hypocellular areas
- **Variable architectural patterns**
  - Haphazard, patternless
  - Sheets
  - Fascicles
  - Herringbone
  - Perivascular aggregation
  - Storiform

http://surgpathcriteria.stanford.edu/

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- **Vessels often ectatic, with staghorn appearance**
- Stroma may be myxoid or hyalinized in areas
  - Amianthoid fibers reported in one case
- Most tumors cytologically bland
  - Metastasis does occur in such tumors but is rare
  - Minimal pleomorphism is not clinically significant
- **CD34 is most sensitive and specific marker**
  - Diagnosis can be made in its absence, but should be made cautiously and with consultation
- Following features predict increased incidence of recurrence and metastasis
  - Significant pleomorphism and atypia
  - High cellularity
  - Mitotic figures >4/10 hpf
  - Atypical mitotic figures
  - Tumor cell necrosis
  - Even one or two of these features may be associated with aggressive behavior
- SFT with dedifferentiation has been described (Mosquera)
  - Discrete anaplastic component
    - Epithelioid, round cell, spindled, hypercellular patterns
    - Necrosis, cystic degeneration, frequent mitotic figures
    - CD34 positive in half
  - Prognosis reported much worse if over 8 cm diameter
- **Solitary fibrous tumor is considered by many to form a spectrum with hemangiopericytoma**
- Stromal fat may be present, especially in malignant SFT
  - Ranges from mature fat to lipoblasts to areas resembling atypical lipomatous tumors (Lee 2011)

Sumarizácia diagnóz 1988-98 „nízkomalígny sarkóm malej panvy“

- malígny mezenchýmový nádor tvorený vretenovitými bunkami s málo zreteľnou cytoplazmou bez nápadnejšej pleomorfie
- mitotická aktivita 5-6 mitóz/10HPF
- fascikulárne usporiadanie, sčasti storiformné, sčasti hemangiopericytomatózne
- vaskularizovaná stróma, fokálne hyalinizovaná, úseky myxoidného presiaknutia
- disperzná prímes buniek osteoklastoidného typu
- Imuno: CK, EMA, CEA, dezmín, vimentín, SMA, MSA, CD31, CD34, fVIII., Chrg. A – všetko negatívne !

  CD68 pozitívne v obrovských bunkách, minimlána proliferačná aktivita (Ki-67 prakticky areaktívne)

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Supplemental studies

Immunohistology

CD34	>90%
bcl2	>90%
CD99	70-90%
Factor XIIIa	80%
Beta catenin	20%
S100	<10%
Smooth muscle actin	<10%
Keratin	<5%*
Desmin	negative
CD117	negative
Calretinin	13%

*One report of 11% focal pos (Barak 2012)

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Histopathology. 1991 Dec;19(6):515-22.

Solitary fibrous tumour arising at unusual sites: analysis of a series.

Goodlad JR[1], Fletcher CD.

Author information

Abstract

Solitary fibrous tumours ('pleural fibromas') are well-recognized in the pleura, but their rare occurrence at other sites has only become appreciated in recent years, as a consequence of which extrapleural examples often go unrecognized or misdiagnosed. Eight cases (three peritoneal, two retroperitoneal, two intrapulmonary and one mediastinal) are presented herein. All but one presented in adulthood, and three were asymptomatic chance findings. Size ranged from 0.8 to 26 cm in maximum diameter. To date, none has behaved in an aggressive fashion. Histologically, these lesions are entirely comparable to their pleural counterparts, and accurate diagnosis is largely dependent on appreciation of their potential extrapleural location. Immunohistochemistry in seven cases favoured myofibroblastic/fibroblastic differentiation, in keeping with the putative submesothelial origin of these lesions.

ESFT

ONCOLOGY LETTERS 7: 1067-1072, 2014

Clinicopathological findings in a case series of abdominopelvic solitary fibrous tumors

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Abstract. Solitary fibrous tumors (SFTs) represent a rare type of soft tissue tumor. Extrathoracic SFTs (ESFTs) in the soft tissues of the abdominopelvic cavity are extremely rare. Between January 2002 and January 2013, 10 patients were identified with abdominopelvic SFTs at the Northern Jiangsu People's Hospital. The clinicopathological data, treatment and follow-up results were retrospectively analyzed in this study. Patients included four females and six males, whose age ranged between 21 and 75 years (mean, 53.3 years). The maximum diameter of the tumors was 2.5-28 cm (mean, 12.7 cm). Two cases were diagnosed as malignant variants of ESFTs. R_0 resection was performed in eight patients, while one patient underwent R_1 resection, and one patient received palliative chemotherapy for an inoperable mass. Follow-up time ranged between 6 and 126 months (mean, 50 months).

Although the majority of reported tumors arise in the thoracic cavity, SFTs from a wide range of anatomic sites have been reported (3-6). Extrathoracic SFTs (ESFTs), particularly those in the abdominal and pelvic cavities, are rare among soft tissue tumors. In a more recent retrospective study, abdominopelvic SFTs accounted for 34% of all SFTs, illustrating that the abdominopelvic cavity has become the major primary site of SFTs (7). Patients with abdominopelvic SFTs may present with abdominal distention/pain, a palpable mass and neurological or vascular symptoms. Hypoglycemia may also be observed in certain cases. However the association between clinical behavior and histopathological characteristics of abdominopelvic SFTs requires further clarification. Usually, the tumor follows an indolent clinical course with no recurrence and metastasis, yet its elusive clinical behavior makes it impossible

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Editorial

Solitary fibrous tumor: A pathological enigma and clinical dilemma

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Solitary fibrous tumors are ubiquitous rare spindle cell neoplasms, most commonly arising from the pleura. Whilst now considered to be derived from mesenchymal cells, the histiogenesis has been the subject of debate. In 1931 Klemperer and Rabin first documented the occurrence of a distinctive localized pleural based tumour and proposed a submesothelial cell origin (1). Later, based on tissue culture experiments, Stout and Murray claimed derivation from mesothelial cells (2). This controversy is reflected in the variety of synonyms used for solitary fibrous tumors in the past including localized fibrous tumor, localized fibrous mesothelioma, solitary fibrous mesothelioma, fibrous mesothelioma, subserosal fibroma and submesothelial fibroma. With the advent of immunohistochemistry a fibroblastic origin, occasionally with myofibroblastic differentiation, is firmly established. This is further reinforced by the description of solitary fibrous tumors in extrathoracic sites devoid of mesothelial cells.

SFT

Spindle cell mesenchymal neoplasms represent a diverse group of benign and malignant tumors, the diagnosis of which relies on histomorphological features supported by ancillary investigations which include immunohistochemistry and, increasingly, molecular analysis. Microscopically solitary fibrous tumors are characterised by hypocellular collagen rich areas alternating with a proliferation of uniform elongated spindled cells in a haphazard distribution. Imunohistochemistry is extremely useful in establishing the diagnosis, no more so than CD34. CD34 is a myeloid progenitor cell antigen which is also positive in endothelial cells and some mesenchymal cells, including subsets of fibroblasts (3). It is no coincidence that since the description of CD34 expression in solitary fibrous tumors there has been a flurry of case reports in a wide range of sites. Cytogenetic and fluorescence in situ hybridization has shown no specific chromosomal abnormality (4) and, unlike a growing number of sarcomas, molecular tests are not utilised in confirming the diagnosis.

The pathological enigma surrounding solitary fibrous tumor is twofold. The first is identifying those tumors which have malignant potential and the second is the histological diagnosis of dedifferentiated solitary fibrous tumors. Most solitary fibrous tumors behave in a benign fashion. When arising from the pleura, 13-23% are classified as malignant in contrast to most extrapleural tumors which, with the exception of those of mediastinal origin, have a benign outcome (5). England et al used high cellularity, mitotic activity (more than four mitotic figures per 10 high-power fields), pleomorphism, hemorrhage and necrosis as criteria for distinguishing tumors with a favourable course from those that have the propensity for recurrence, local invasion and metastatic spread (6). Unfortunately biological behaviour does not always correlate with atypical histological features. De Perrot et al stratified the risk of recurrence based on histologic and morphologic

SFT

As sarcomas progress they may acquire additional molecular alterations which aids tumor progression. This is accompanied by transformation of the typical histological appearance to an anaplastic component, a process referred to as dedifferentiation, with frequent loss of CD34 expression (9). Frankly sarcomatous solitary fibrous tumors can only be recognized as such if they are associated with typical solitary fibrous tumors or recur at the site of a previous documented benign-looking solitary fibrous tumor (5). The largely favourable outcome of extrathoracic solitary fibrous tumors may be that only the typical ones are recognized and those showing cytomorphological atypia are diagnosed as something else.

The clinical management of malignant solitary fibrous tumors remains a dilemma, especially in cases were surgical excision is not feasible. Oncologist marvel in the success of gastrointestinal stromal tumors, a neoplasm, which like solitary fibrous tumor, is a spindle cell lesion which may behave in a benign or malignant fashion. However that is where the similarities stop. There are well defined morphological and histological parameters for defining risk of progression in gastrointestinal stromal tumors and specific molecular events have been identified which are exploited for therapy and prognosis. Indeed imatinib, a tyrosine kinase inhibitor, has revolutionised the management of patients with gastrointestinal stromal tumors. In an attempt to mirror this success, investigators have used imatinib in malignant solitary fibrous tumors overexpressing platelet-derived growth factor, both in vitro (12) and in vivo (13), with promising results.

Follow up júl 2014

- pacientka zomrela v júli 2014 náhle, bez zjavného kauzálneho vzťahu k základnému ochoreniu
- pitvaná nebola

TAKE HOME MESSAGE

- 

nie sme zlí ...
- cesta k diagnóze je niekedy ťažká a dlhá
- stále sa máme čo učiť ...
- ... dôležité je poučiť sa
- biologické správanie je ťažko predpovedať
- *kardiotoxicita ? – efekt terapie ?*

Ďakujem za pozornosť