

XXII. Martinský bioptický seminár

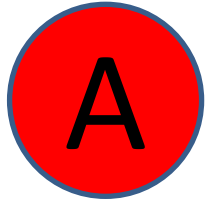
Lúčky 2016

SD-IAP



Prípád č. 619

Ľ. Straka



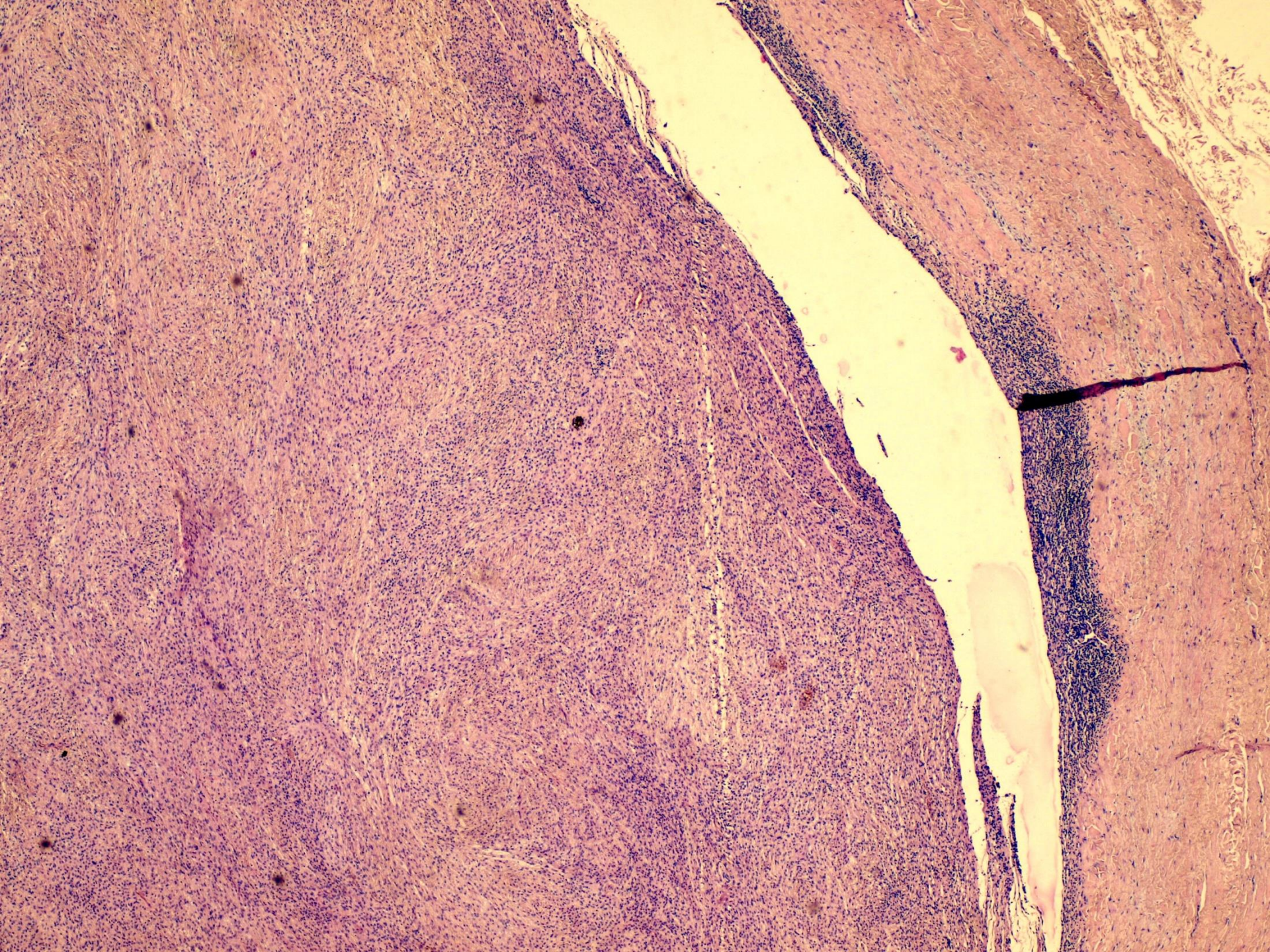
ALPHA MEDICAL

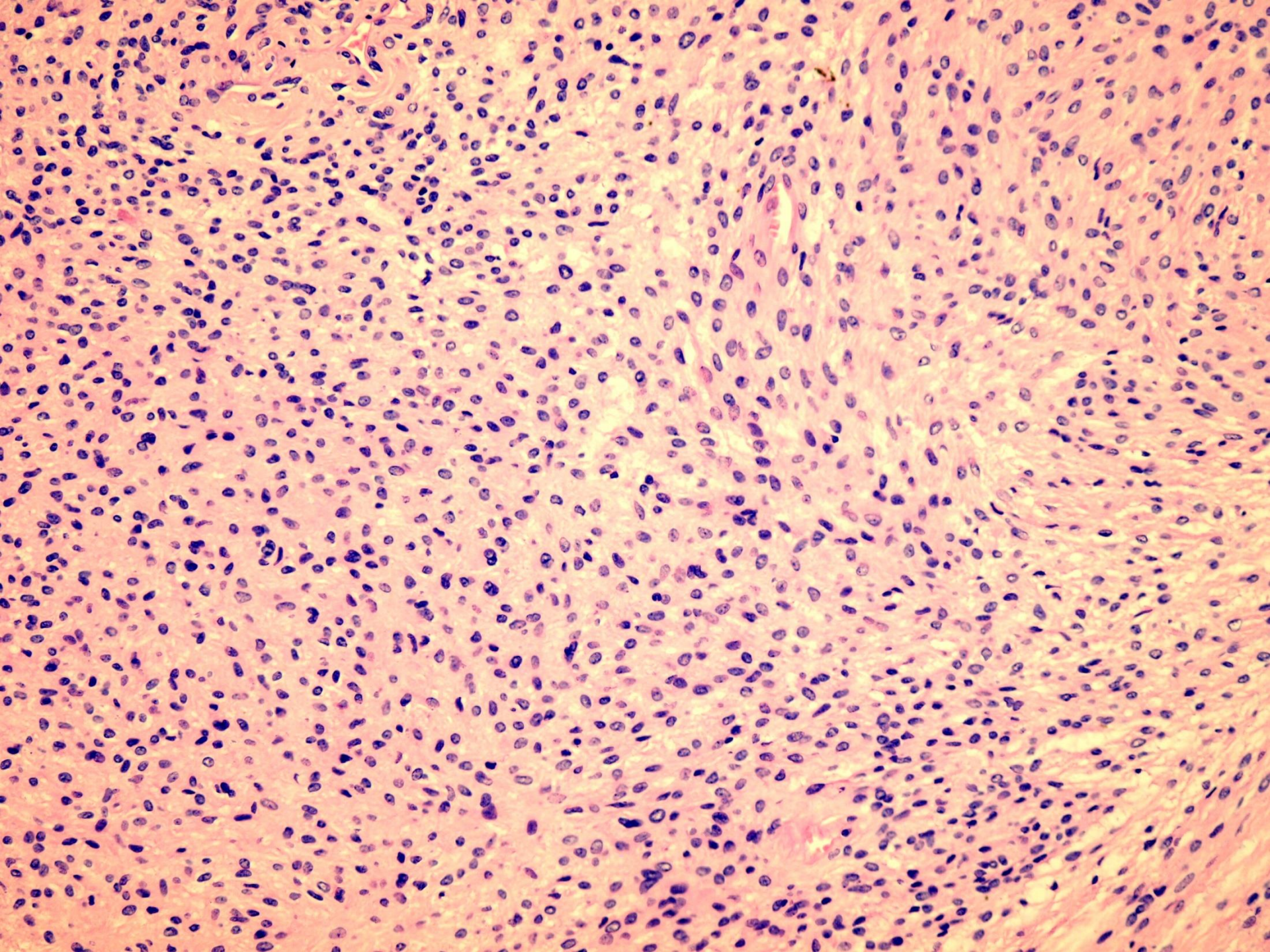


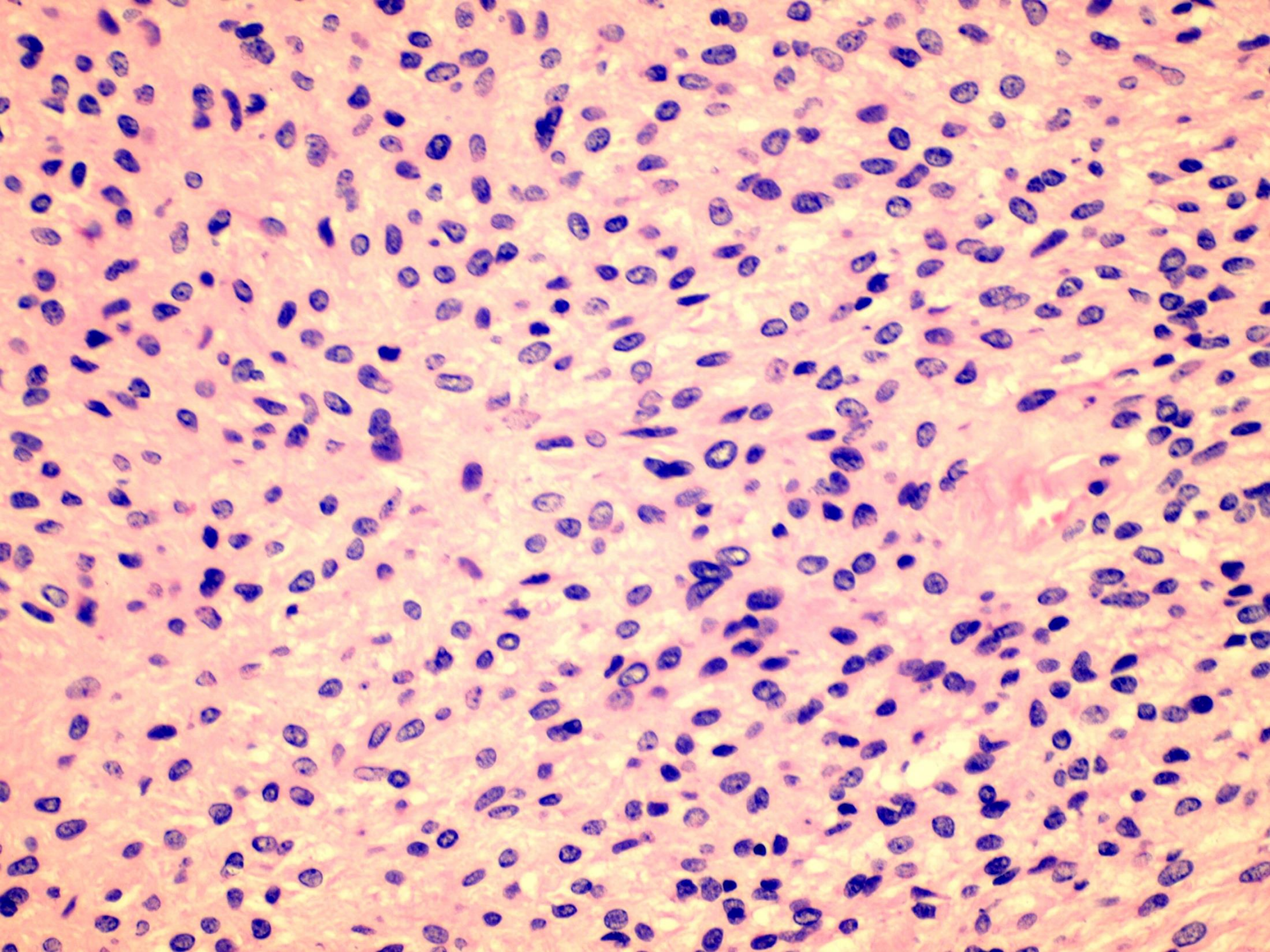
straka.lubomir@alphamedical.sk

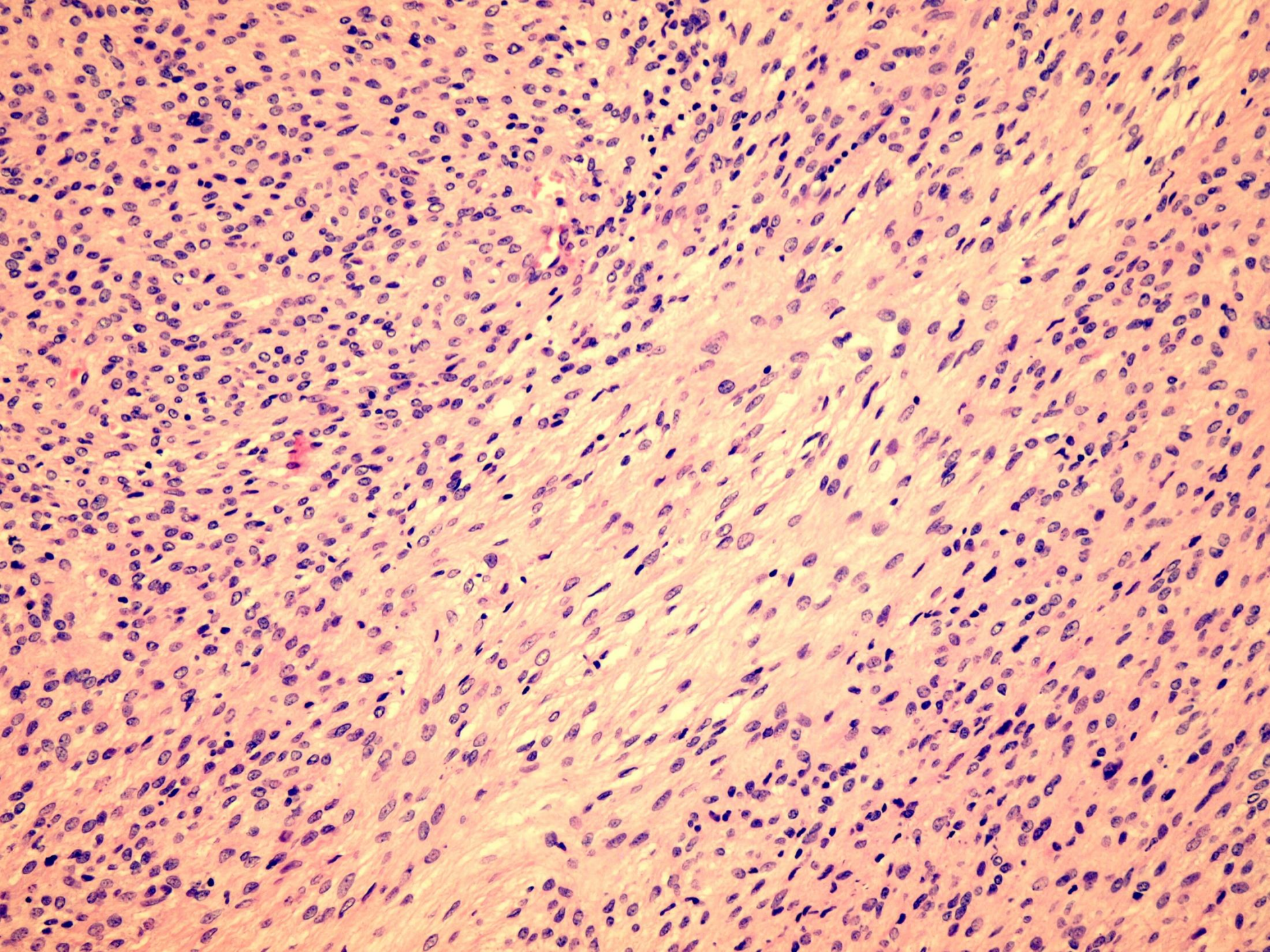
Prípád SD-IAP č. 619

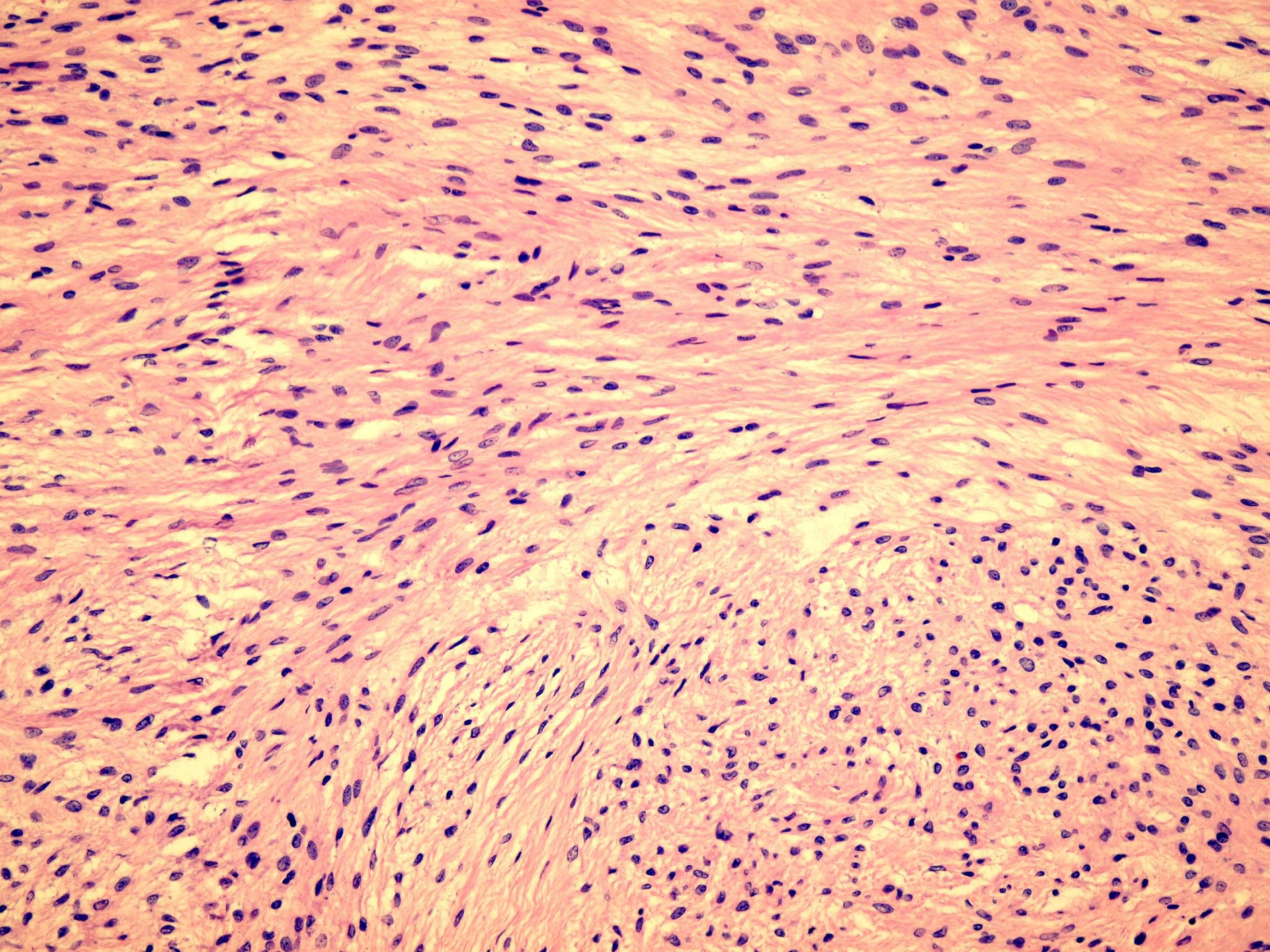
- 32 ročná pacientka
- Lipoma regionis glutealis l. sin.
- 2 excízie šedobelavej farby 3 x 1.5 x 1.3 cm
3,5 x 1,5 x 1 cm

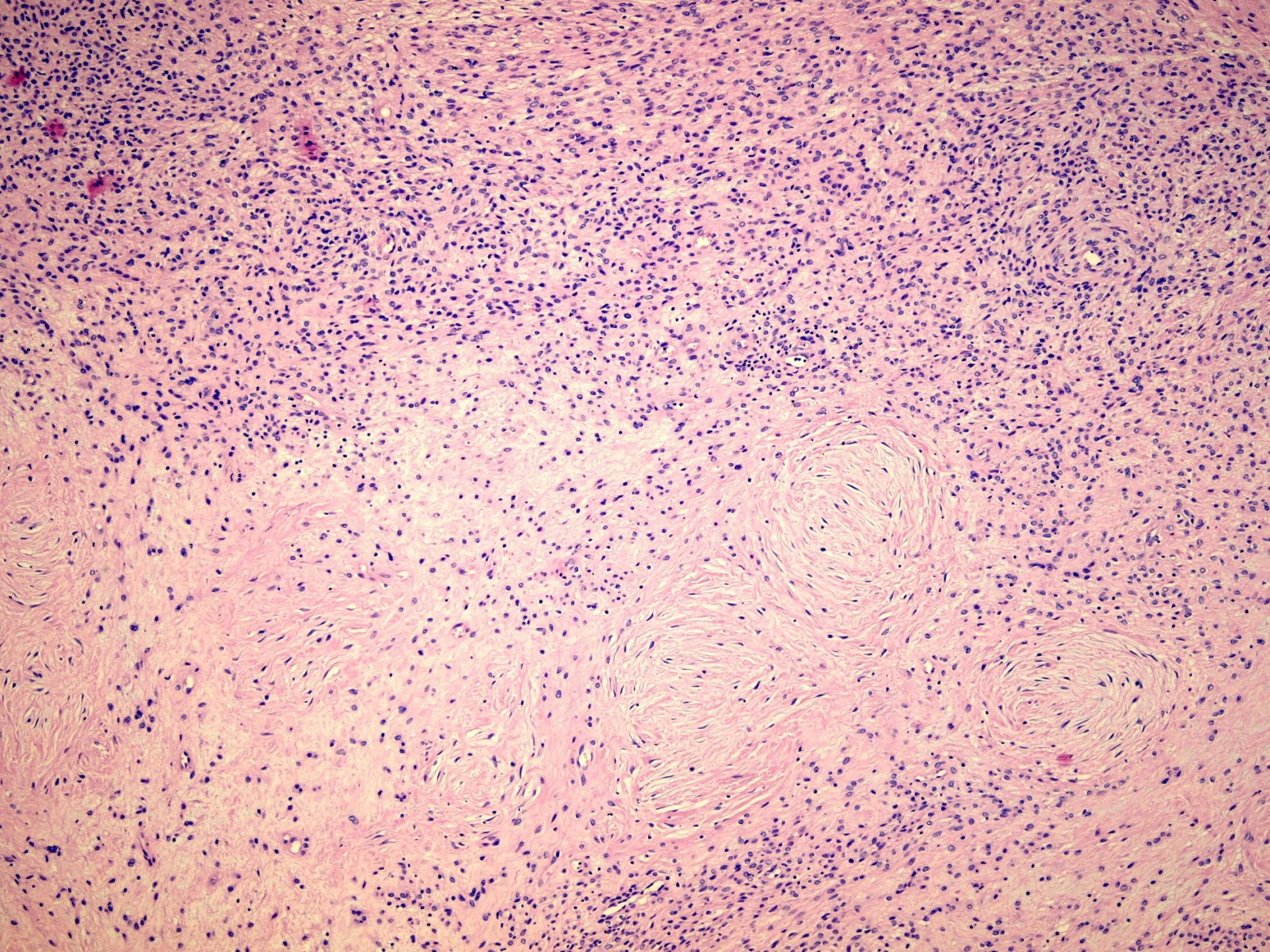


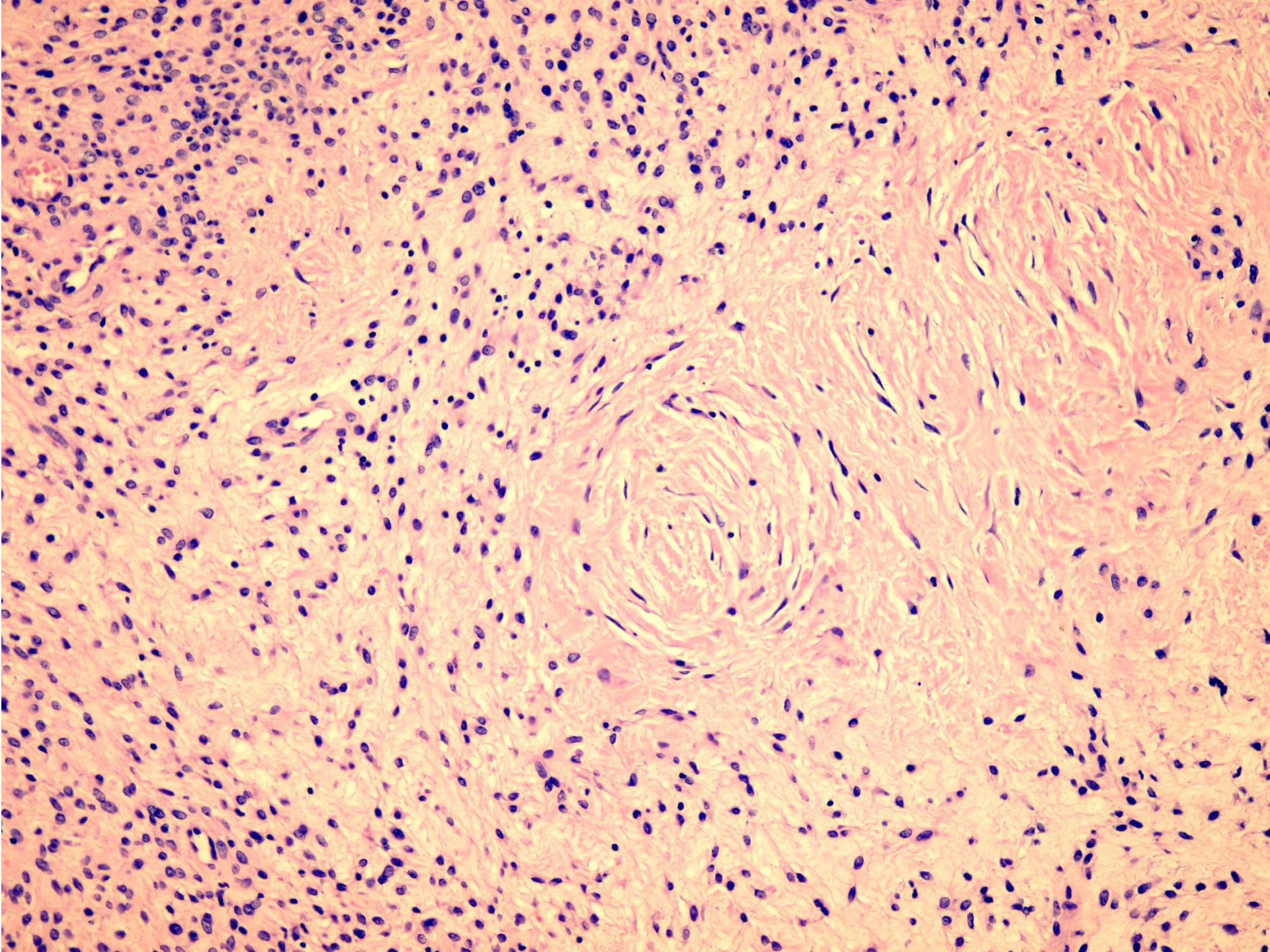


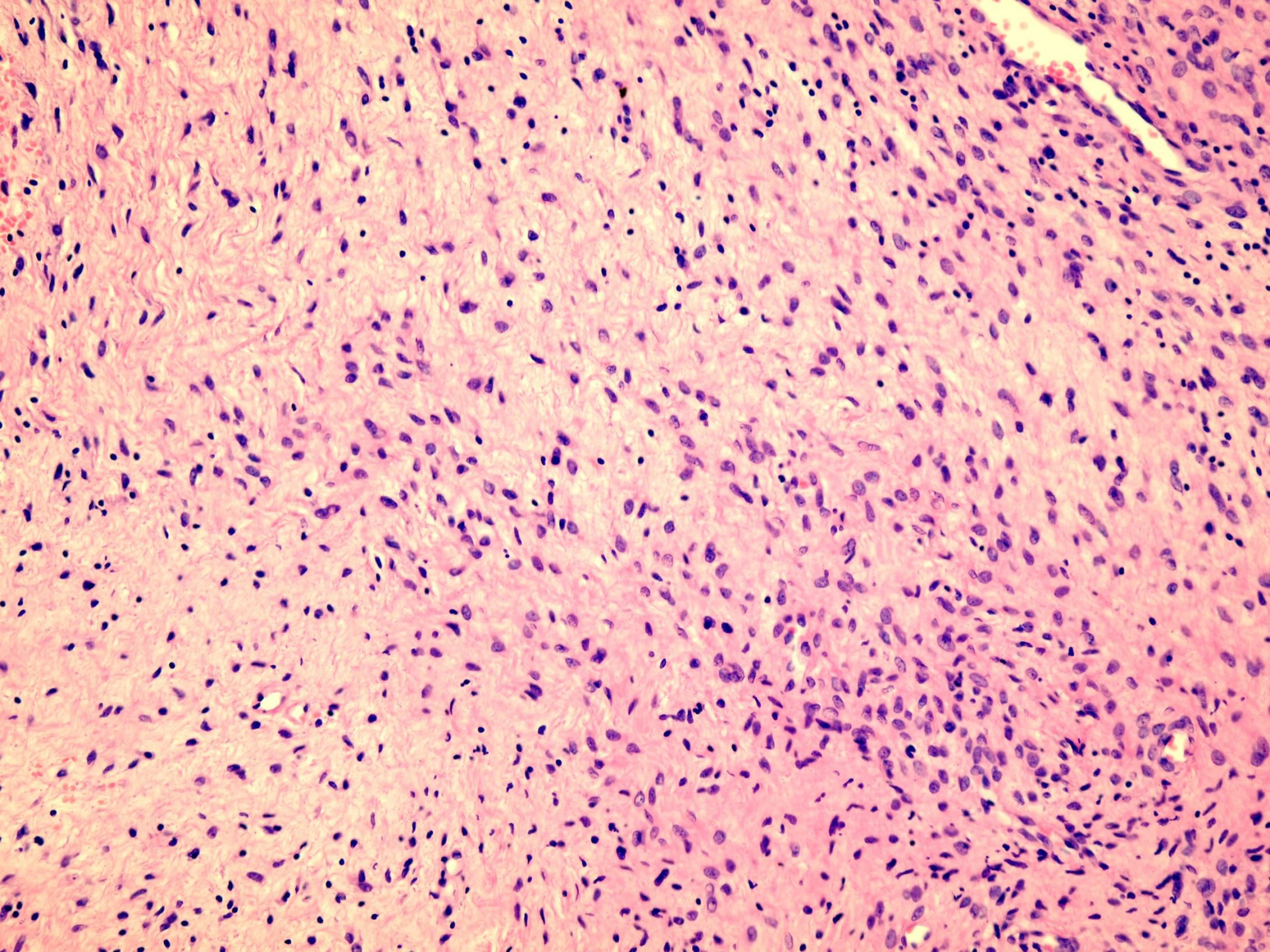


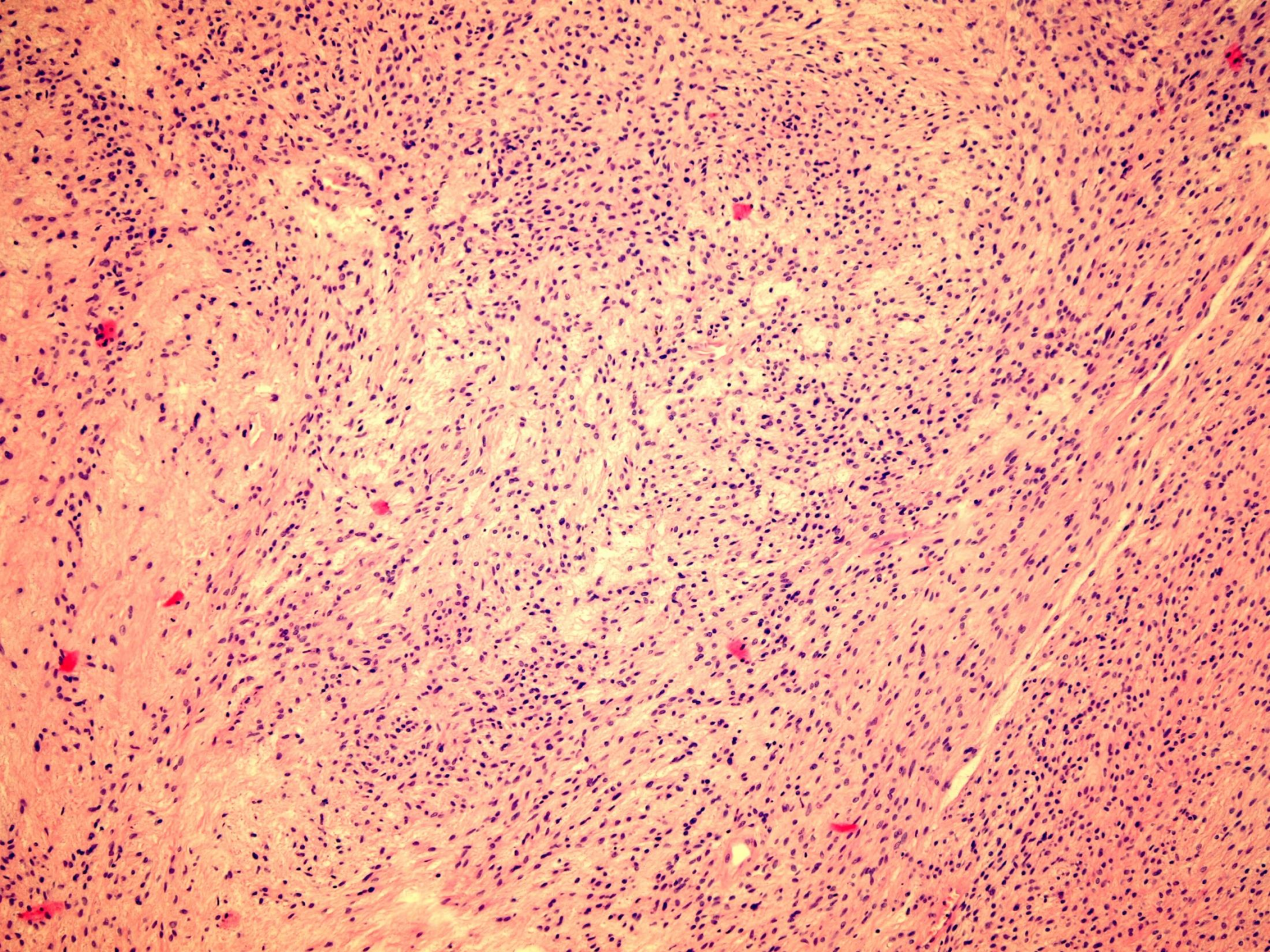


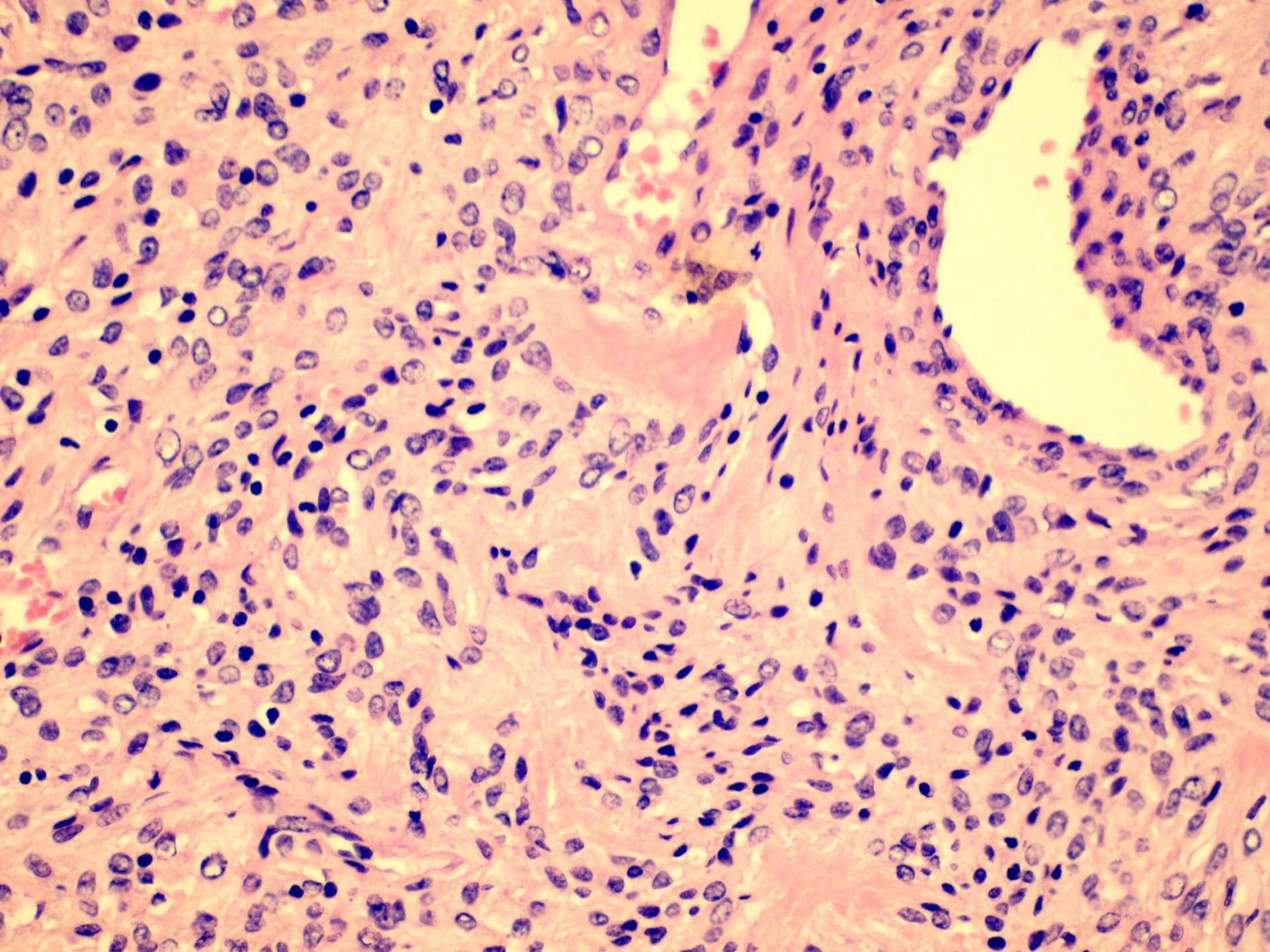


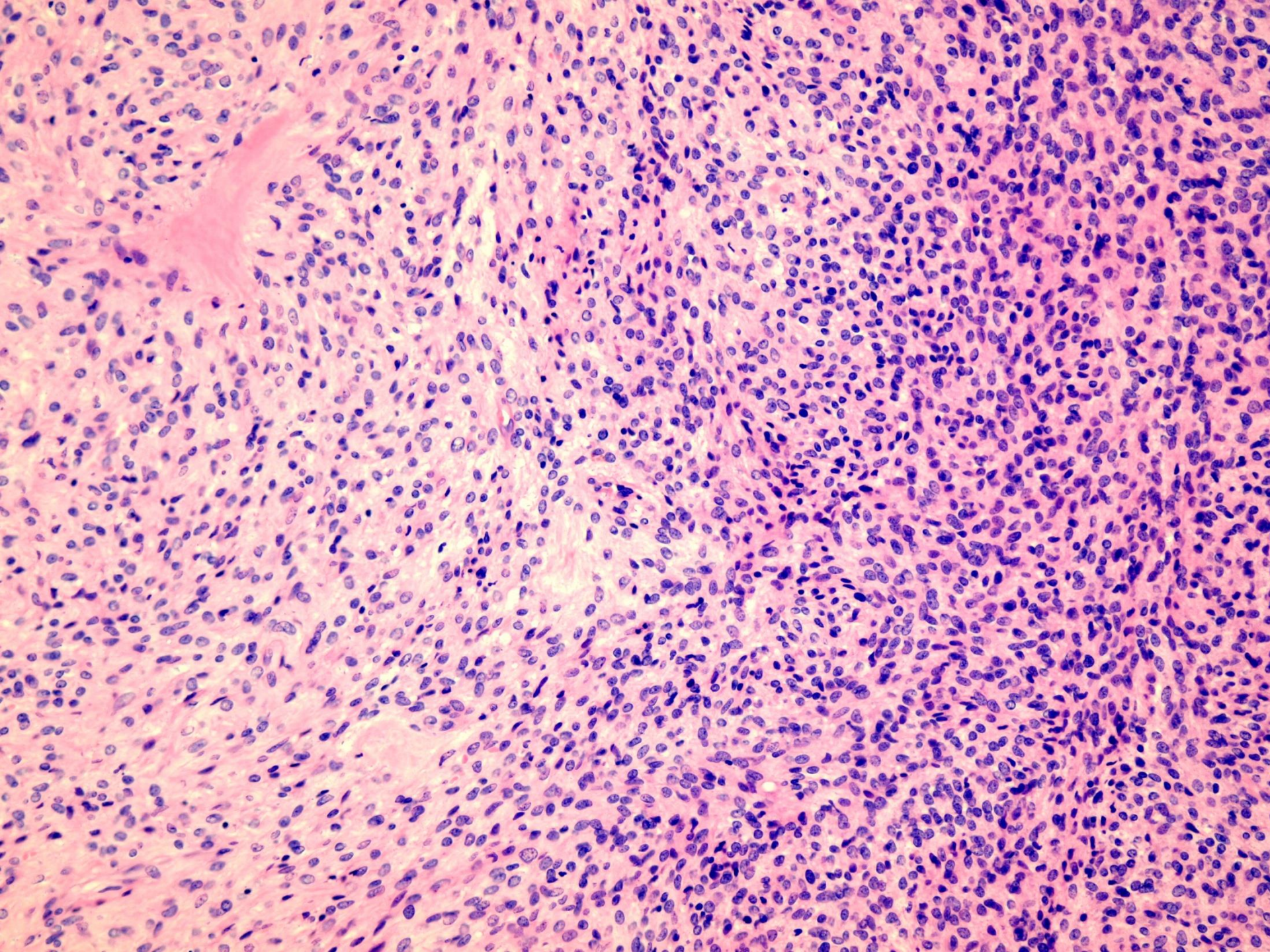


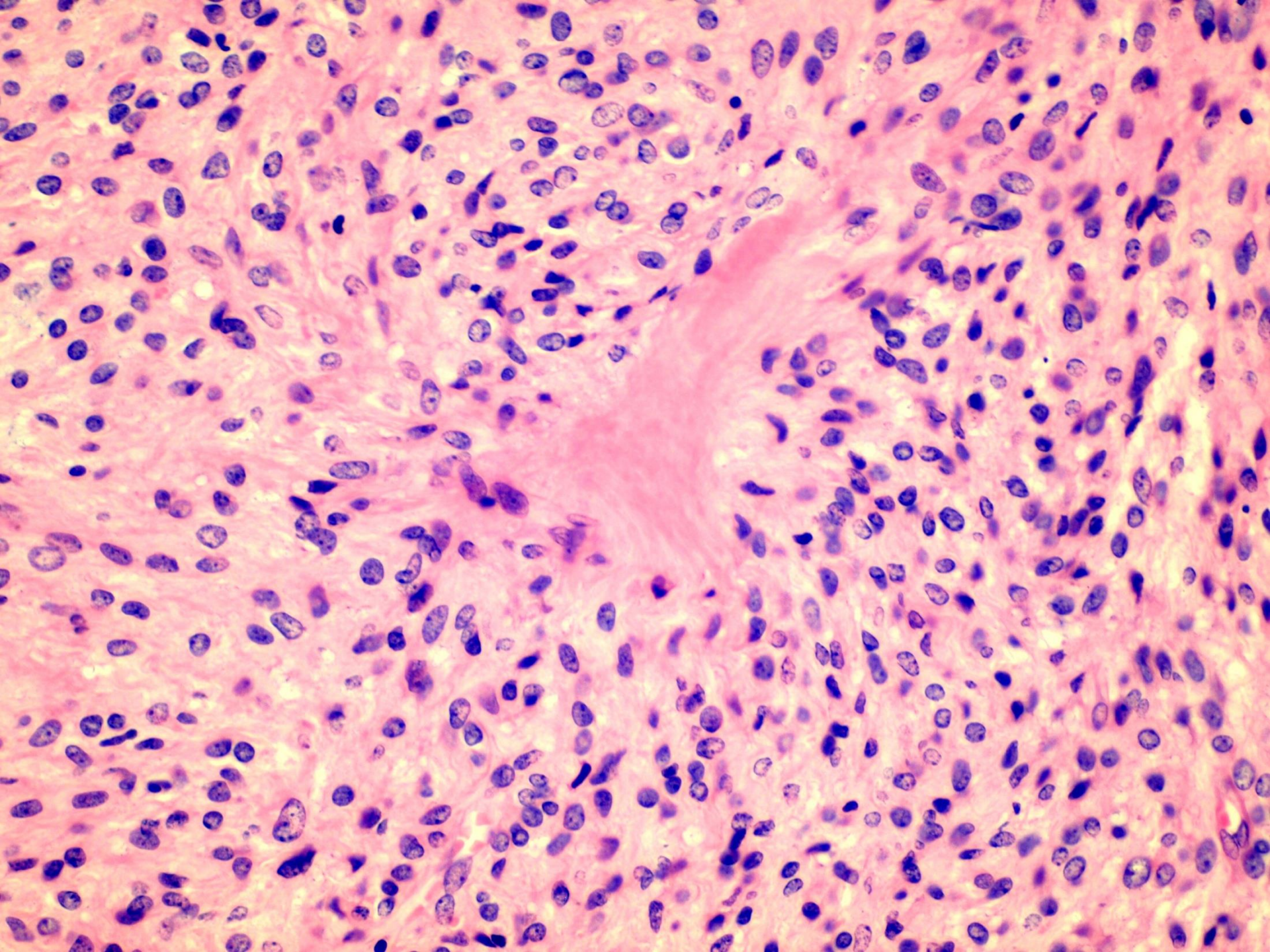


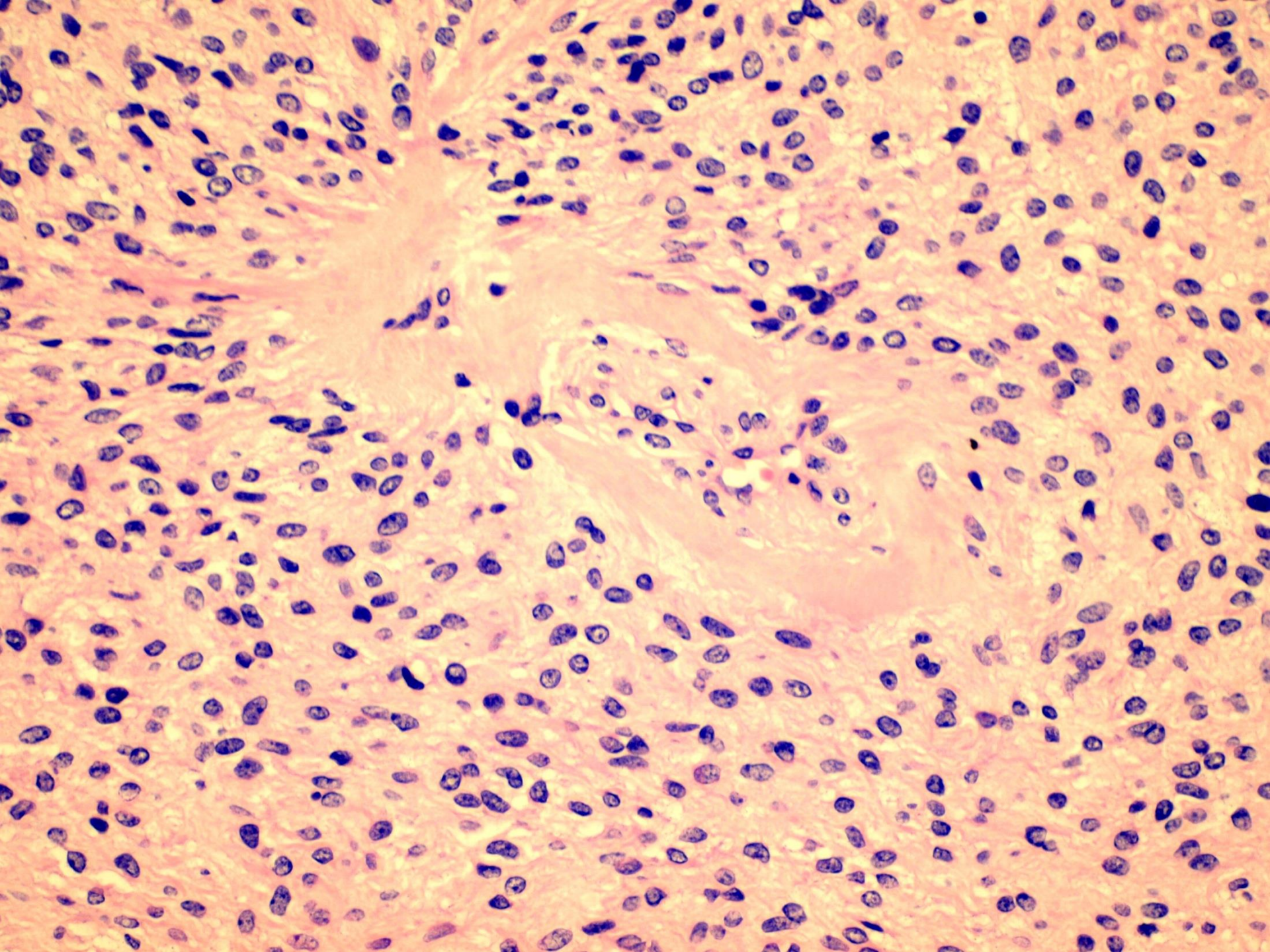


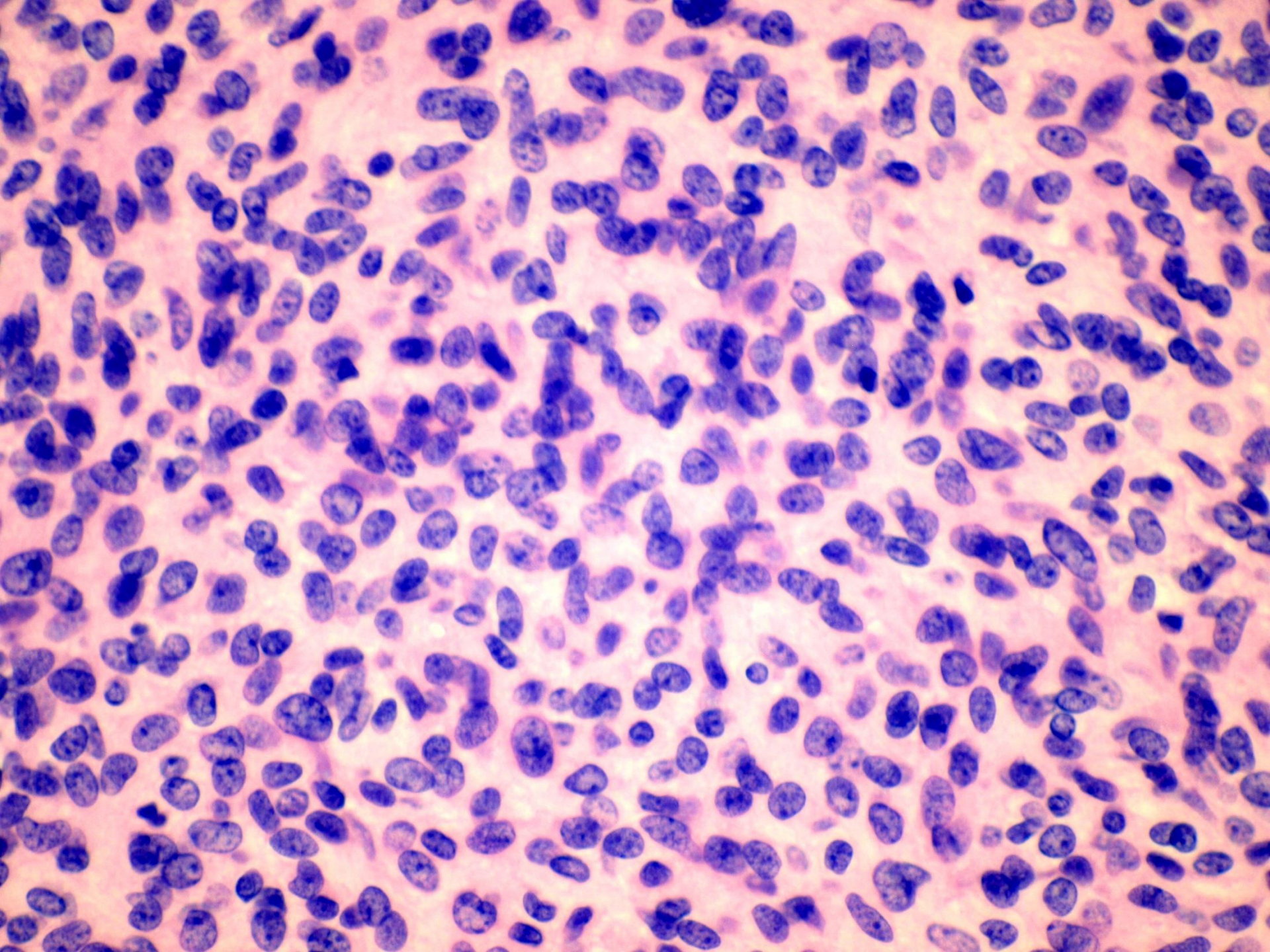


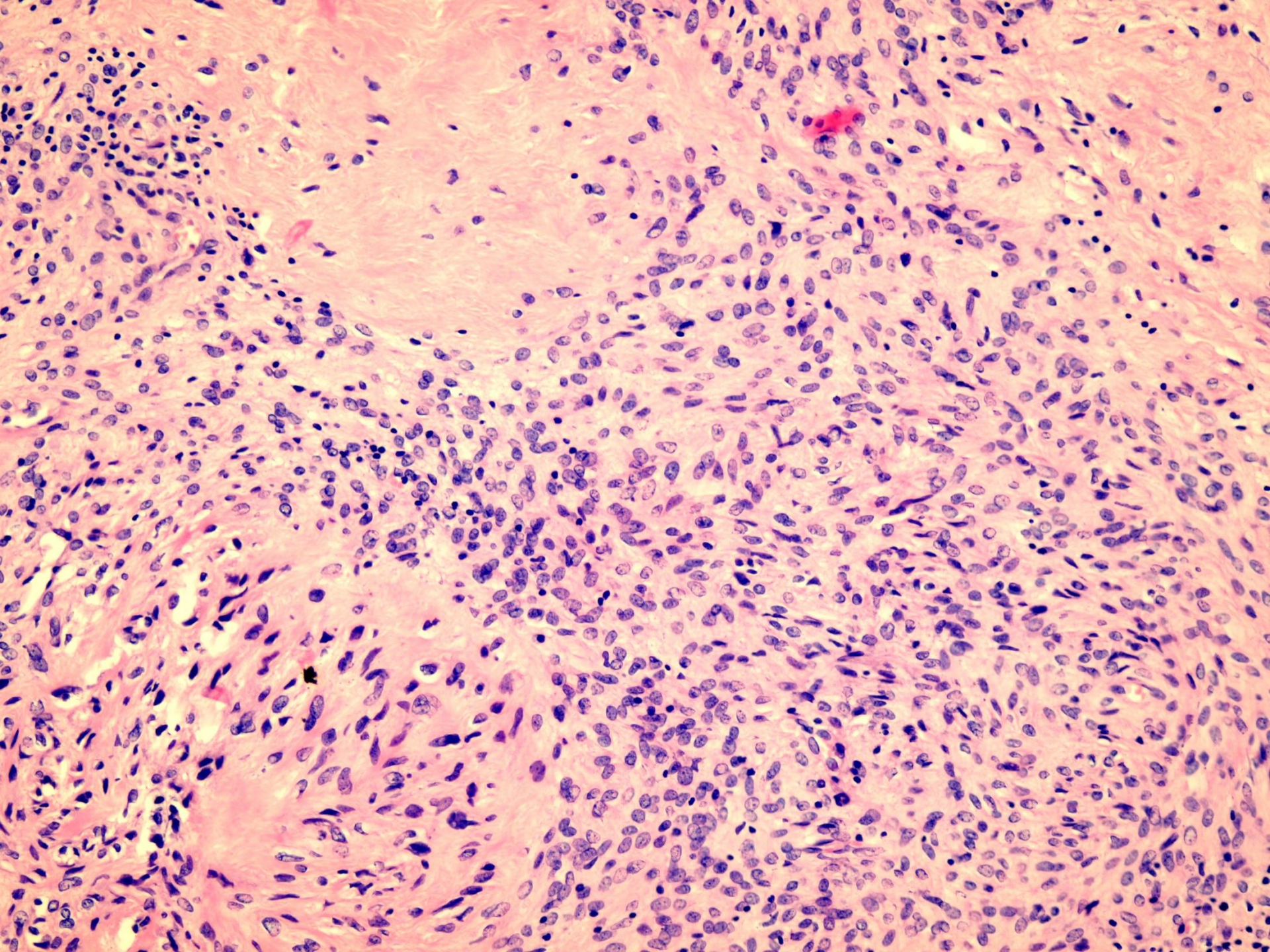


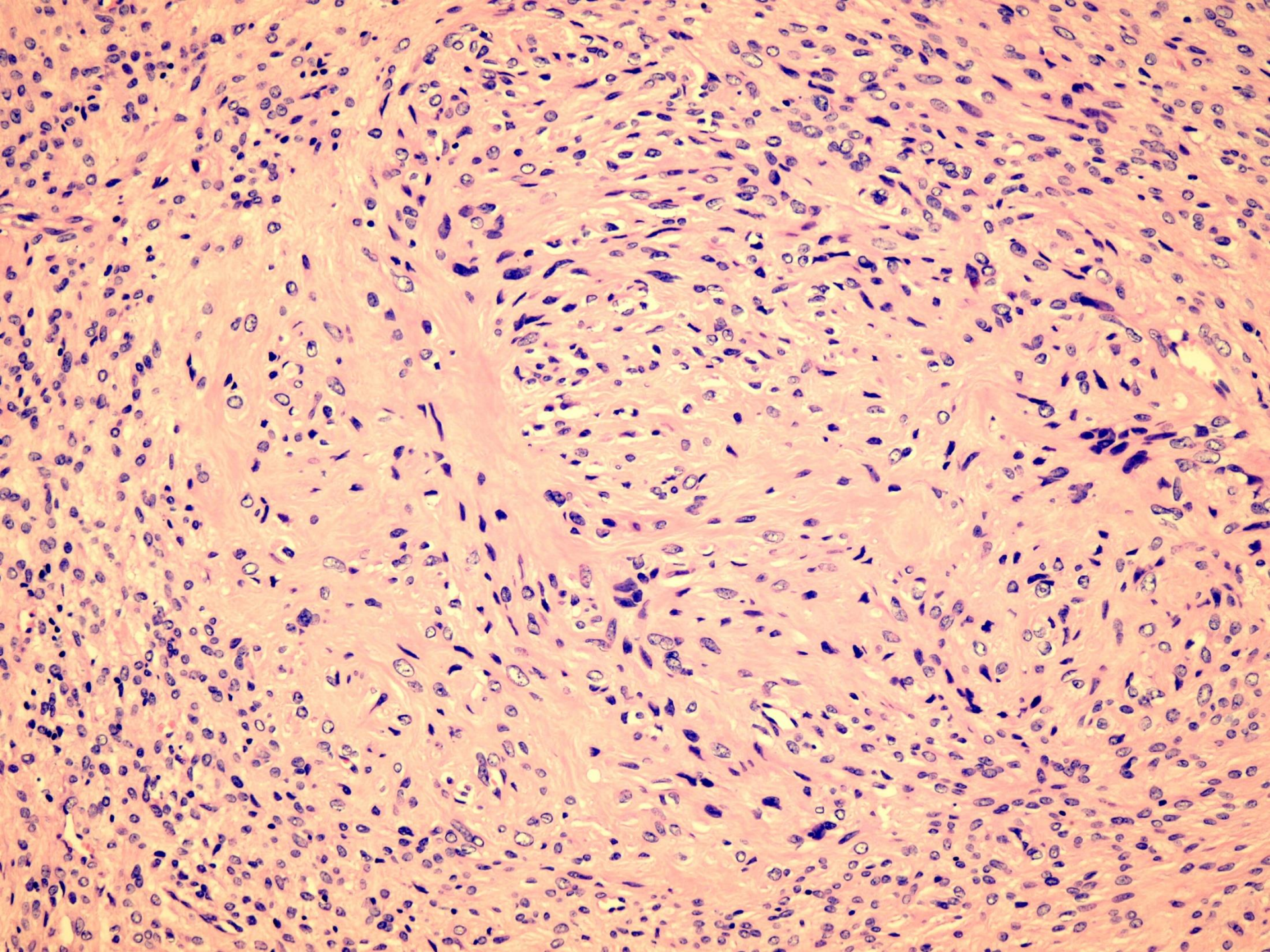


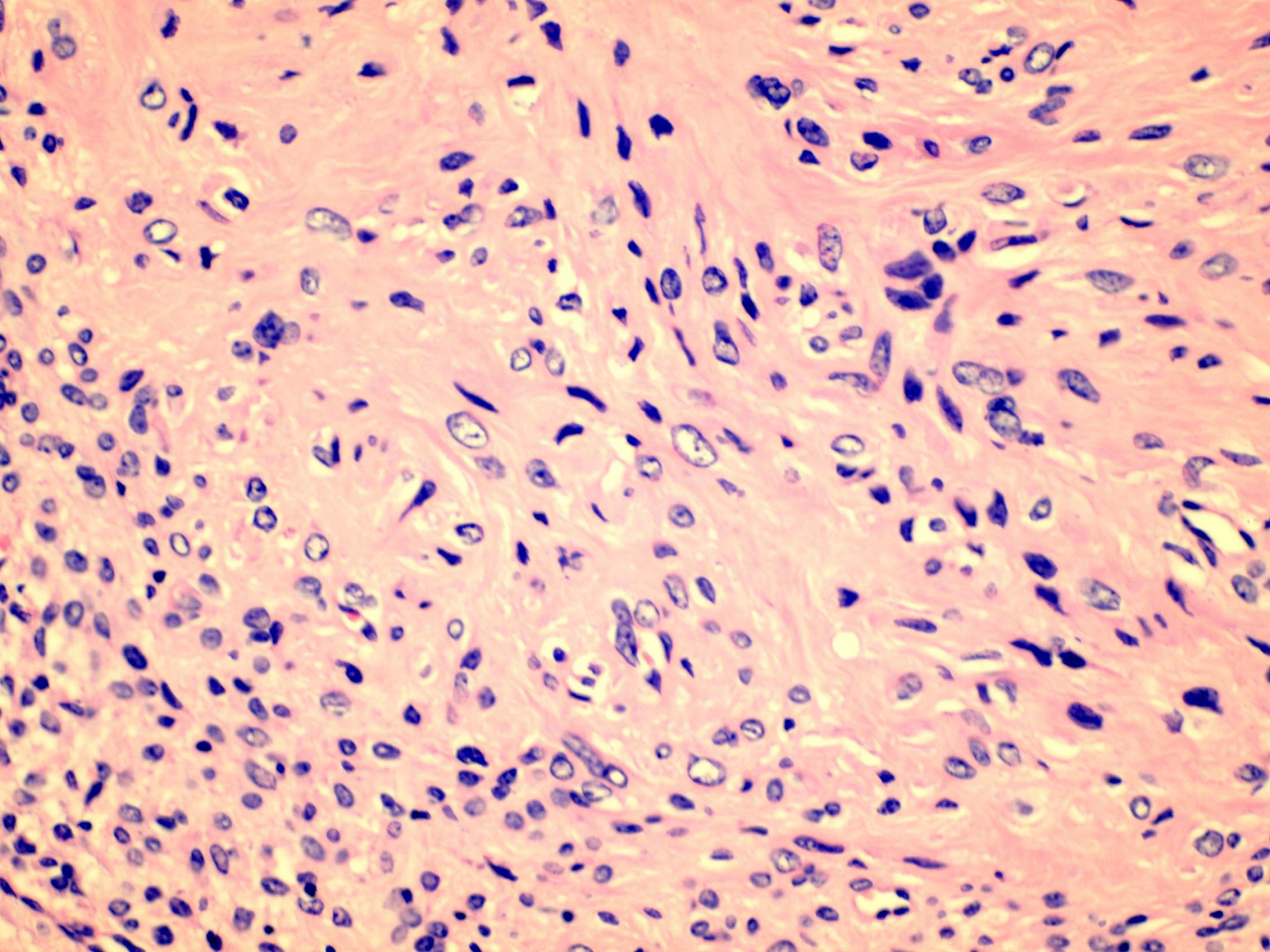


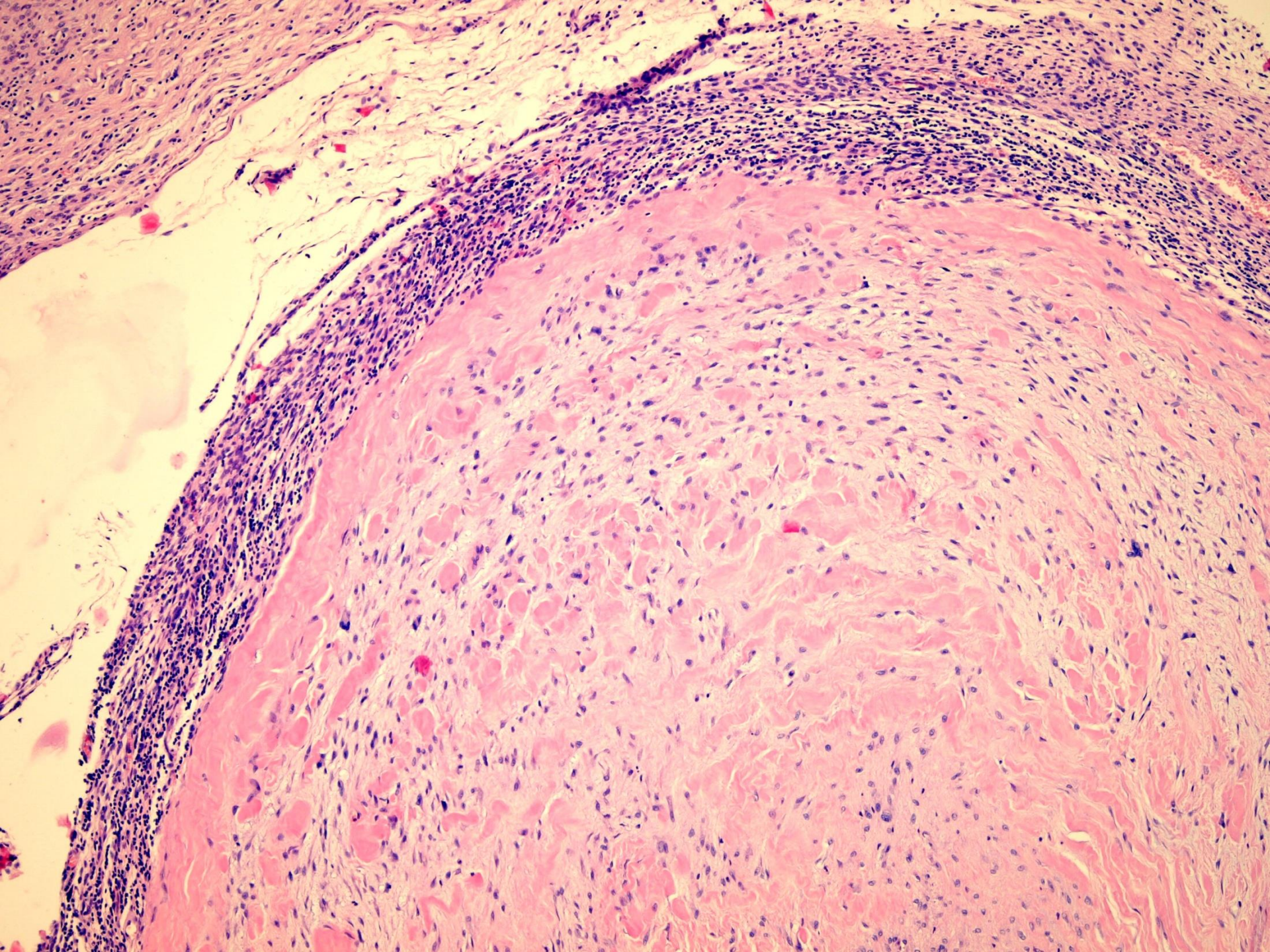


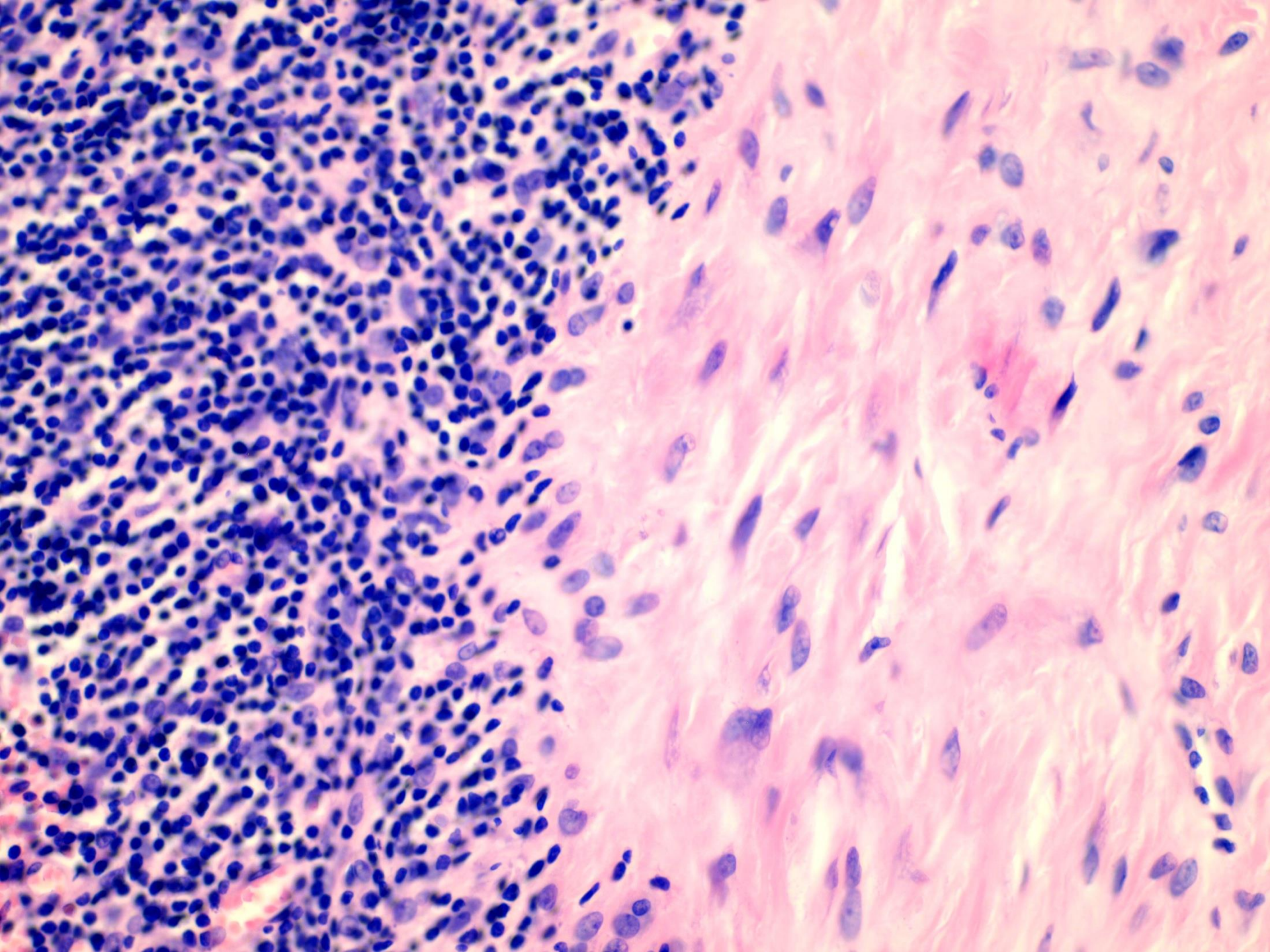




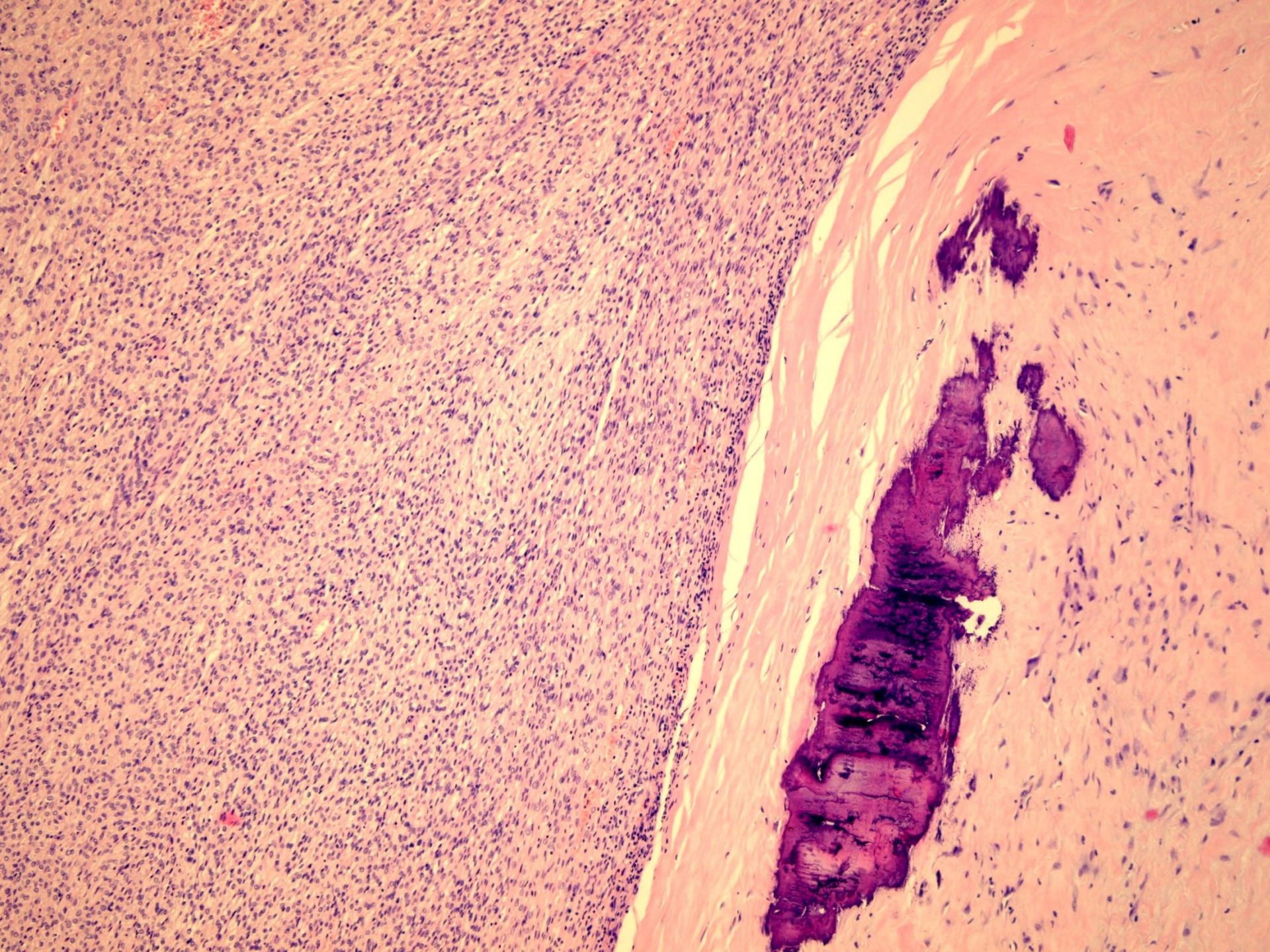


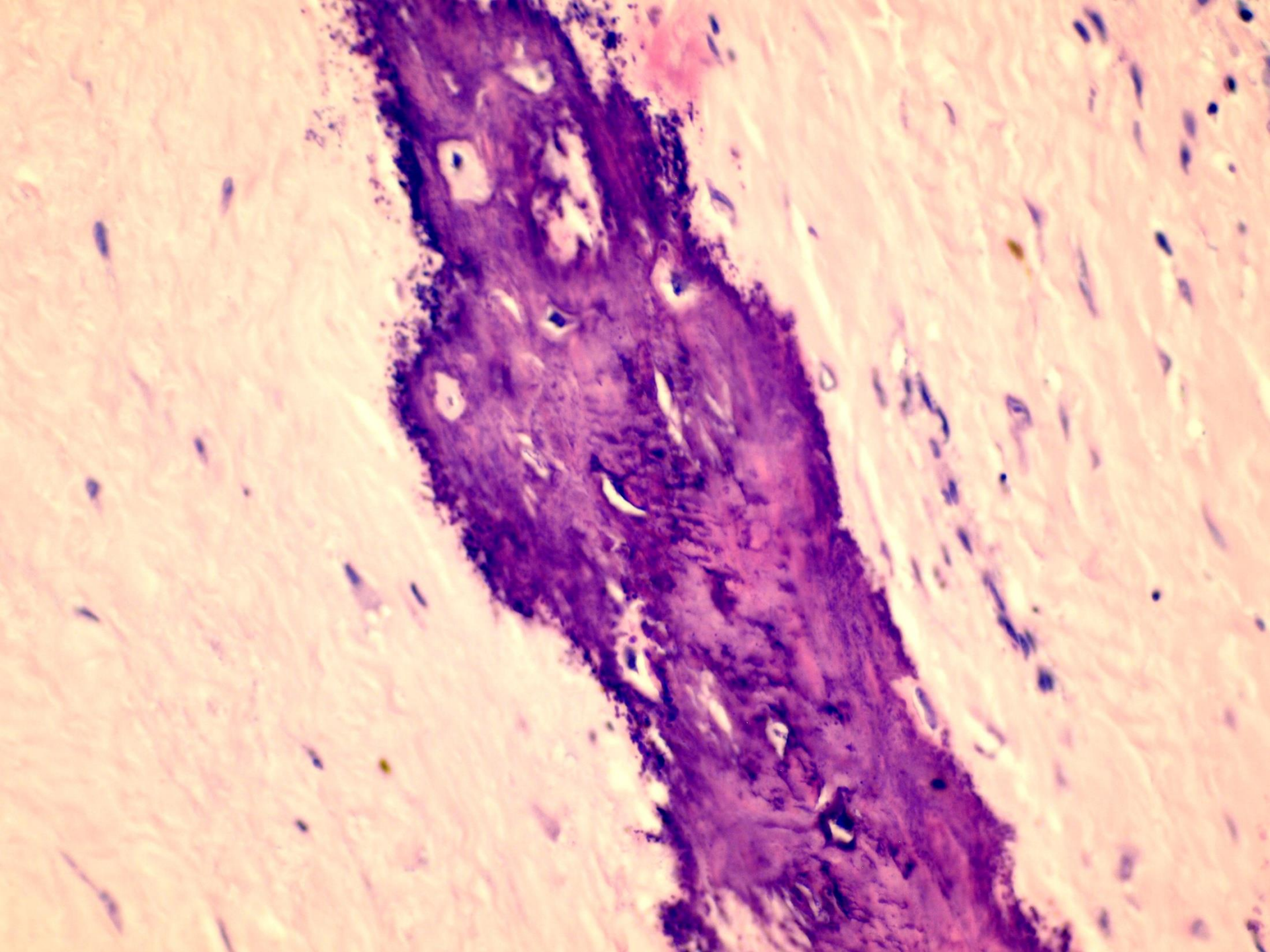


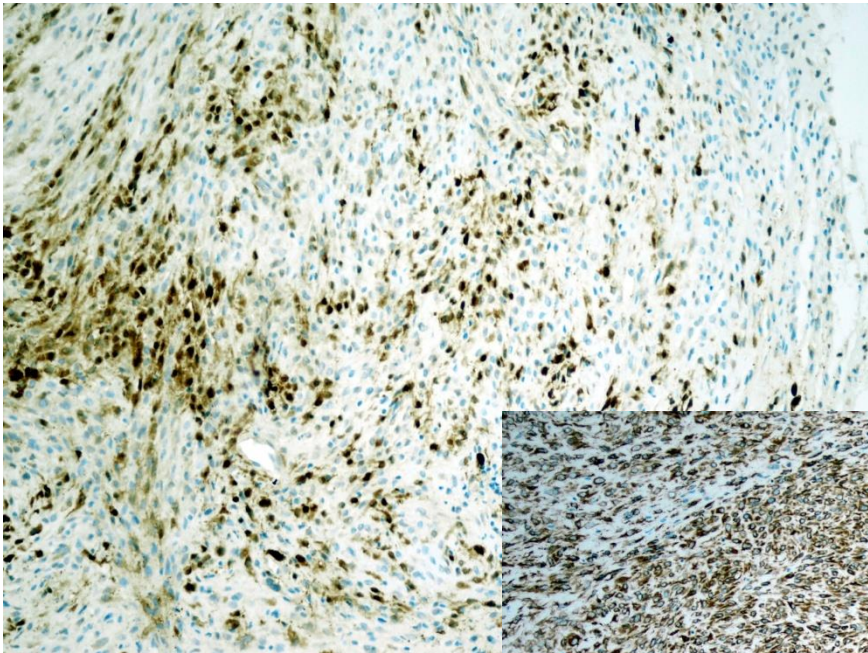




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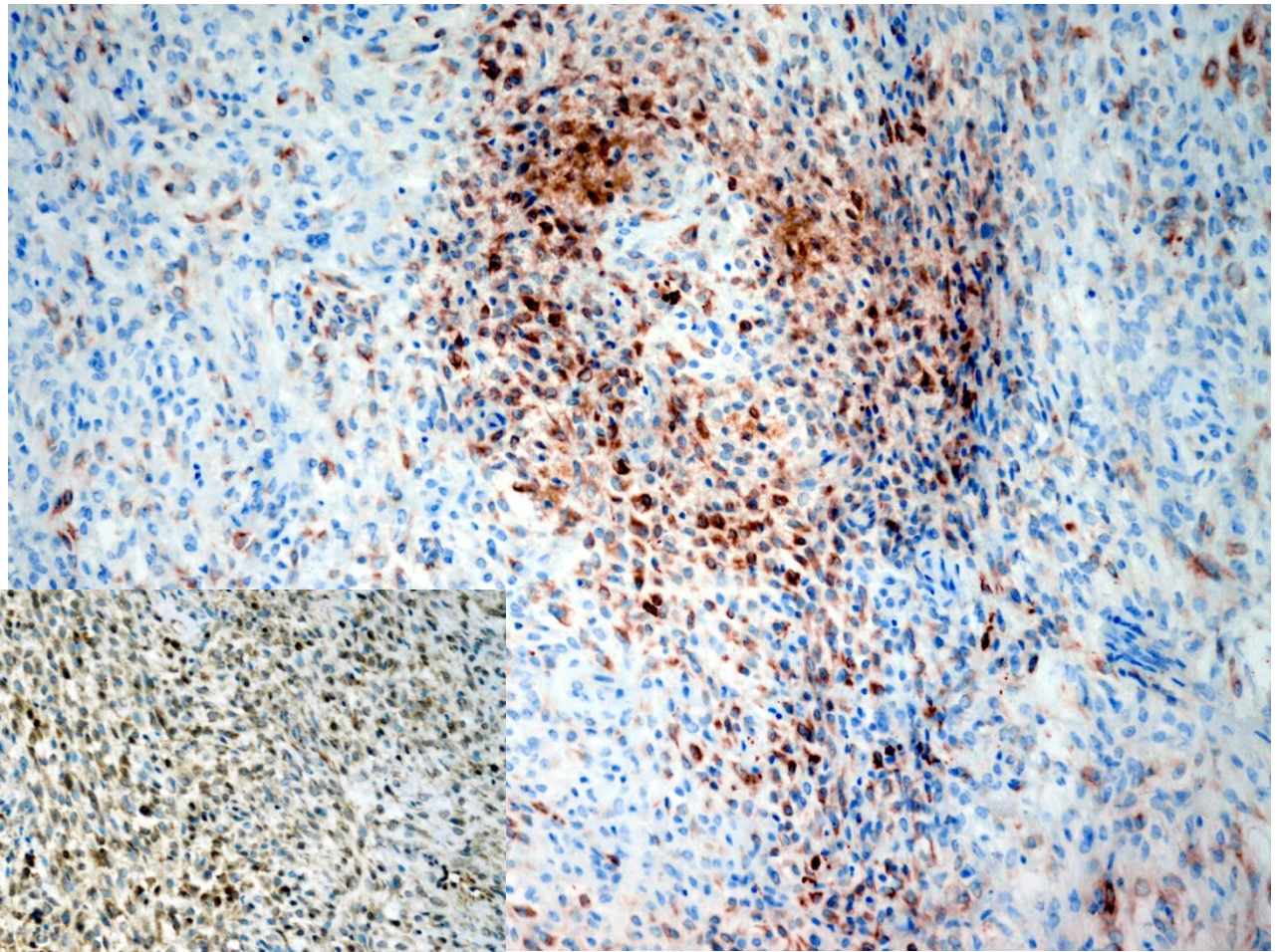


S-100

vimentin

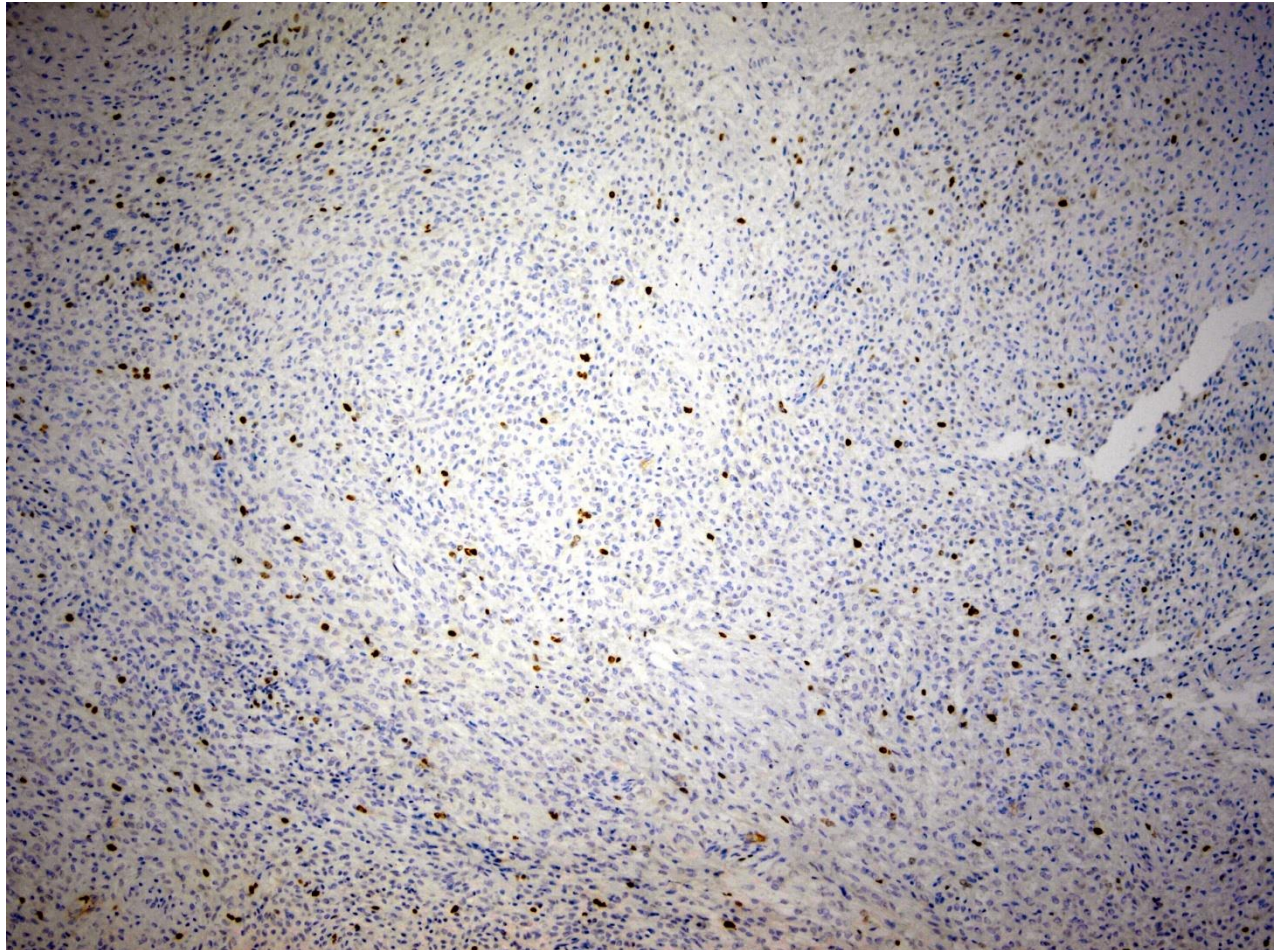


Desmin



NSE

Ki-67



?

OSIFIKUJÚCI FIBROMYXOIDNÝ TUMOR

Osifikujúci fibromyxoidný tumor (OFMT)

- nádor neistej diferenciácie
- intermediárny biologický potenciál
- Enzinger 1989
- dospelí v strednom veku
- pomaly sa zväčšujúca ohraničená masa (4 cm)
- podkožie, sval, končatiny, trup (prsník, paraspinálne)

OFMT

Makroskopicky

- ohraničený, lobulárny
- kompletná alebo nekompletná fibrózna kapsula s areálmi osifikácie (81%)

Mikroskopicky

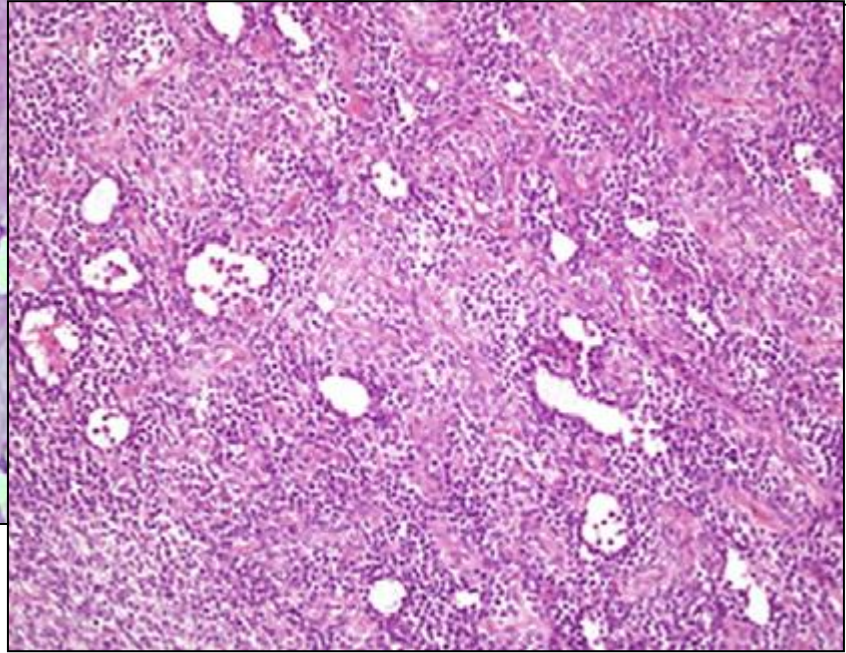
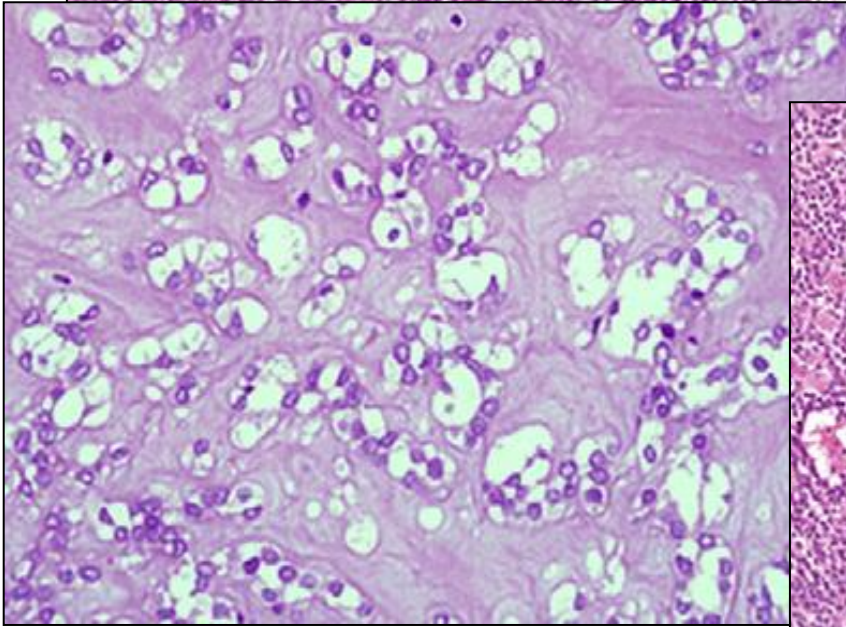
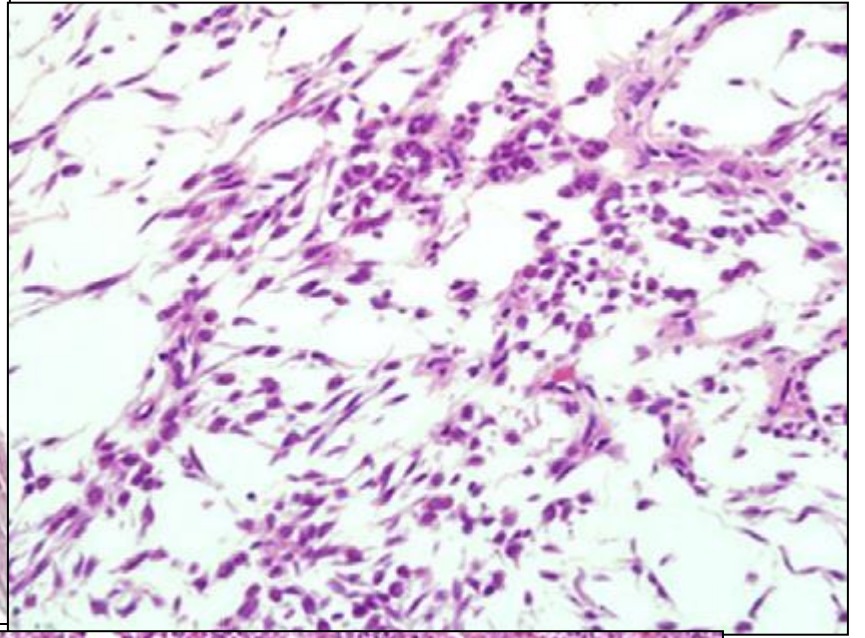
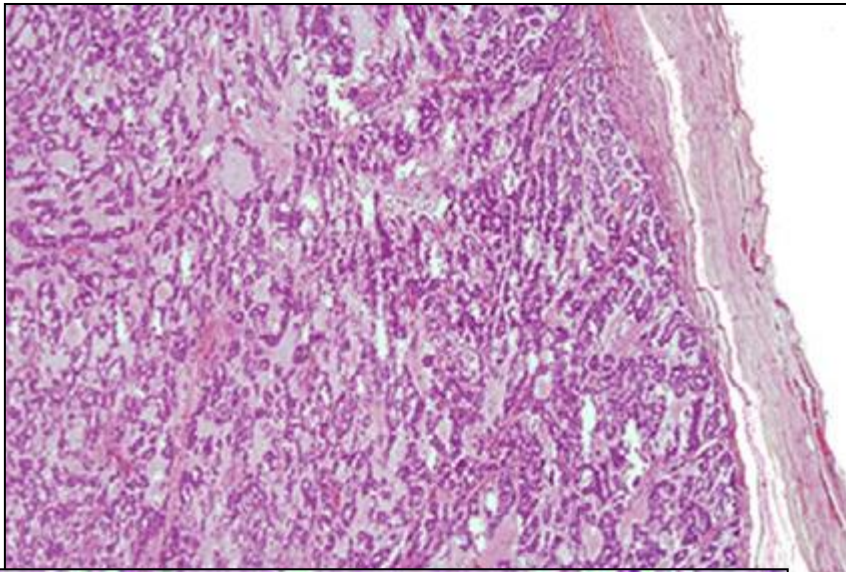
- fibrózne septá s osifikáciami, dystrofické mikrokalcifikácie, kartilaginózne čiapky
- mikroskopické ložiska /mikronoduly aj mimo kapsulu

OFMT

- variabilná celularita
- pruhy, ostrovčeky, plachty, čipkovité vzory, individuálne bunky, fibromyxoidna matrix, hyalinizácia
- MAI: 0-40/50 HPF
- (atypie, nekrózy, angioinvázia, infiltratívny rast)

OFMT

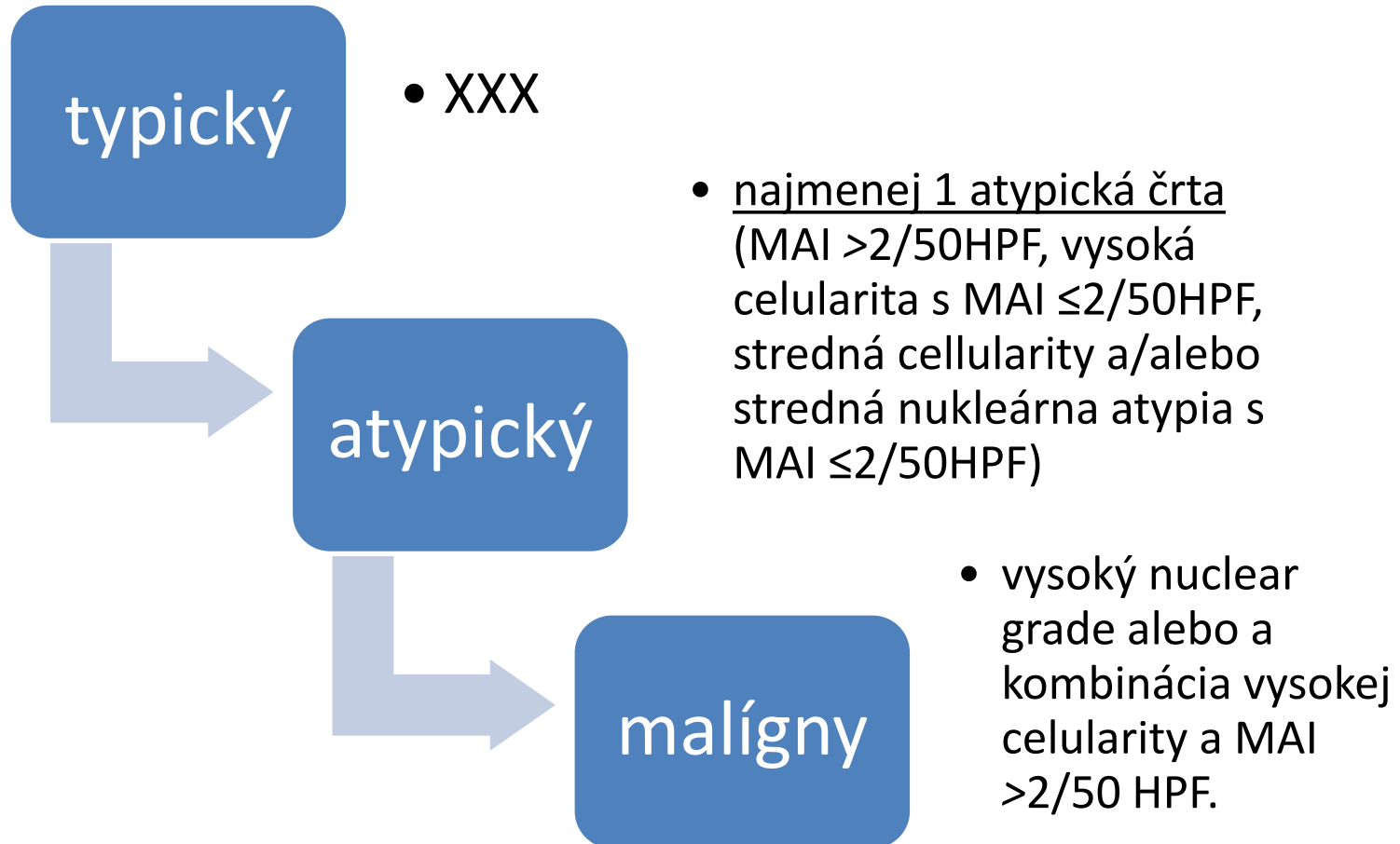
- rhabdoidne bunky
- chondroidná metaplázia
- absencia myxoidných oblastí
- oblasti podobné MFH, MPNST, SEF
- pericytárny rast
- syncytiálne obrovké bunky
- epidermoidné cysty



ICH

- S-100 protein
- Desmin
- MUC4
- Aktin
- CK, EMA fokálne
- CD56, CD57, NSE, CD10, GCDFP15
- mozaikovitá strata INI-1
- Ki-67: 2 - 40

OFMT



OFMT

- väčšinou benígny, zriedkavo mts
- 17-27% recidíva (po kompletnej exstirpácii!)
- lokálna recidíva typického OFMT 17% a 5% riziko vzdialených metastáz (Folpe a Weiss)
- frekvencia recidív a mts v atypických OFMT podobná
- recidívy a mts aj po 10-12 r.

OFMT

- neistá diferenciácia (z nervovej pošvy, myoepiteliálna, kartilaginózna, svalová diferenciácia?)
- nádor spojený s translokáciou (translokačný tumor)
- nerekapituluje normálnu líniu diferenciácie

Genetika

- $t(6;12)(p21;q24.3)$
- preskupenia génu PHF1, 6p21,32
- 85% typických, atypických a malígnych OFMT
- fusion of PHF1 s EP400 na 12q24.3 (44%)
(Antonescu)
- variantné fúzie: ZC3H7B-BCOR $t(X;22)(p11;q13)$,
MEAF6-PHF1, EPC1-PHF1 (aj u ESS)

- [Genes Chromosomes Cancer](#). 2016 Aug 18.
doi: 10.1002/gcc.22400. [Epub ahead of print]

**Expanding the molecular signature
of ossifying fibromyxoid tumors with two
novel gene fusions: **CREBBP-BCORL1** and
KDM2A-WWTR1.**

[Kao YC](#)^{1,2}, [Sung YS](#)², [Zhang L](#)², [Chen CL](#)², [Huang SC](#)^{2,3}, [Antonescu CR](#)²

Abstract

Ossifying fibromyxoid tumor (OFMT) is an uncommon mesenchymal neoplasm of uncertain differentiation and intermediate malignant potential. Recurrent gene fusions involving either PHF1 or BCOR have been found in 85% of OFMT, including typical and malignant examples. As a subset of OFMT still lack known genetic abnormalities, we identified two OFMTs negative for PHF1 and BCOR rearrangements, which were subjected to transcriptome analysis for fusion discovery. The RNA sequencing found a novel CREBBP-BCORL1 fusion candidate in an axillary mass of a 51 year-old male and a KDM2A-WWTR1 in a thigh mass of a 36 year-old male. The gene fusions were validated by RT-PCR and FISH in the index cases and then screened by FISH on 4 additional OFMTs lacking known fusions. An identical CREBBP-BCORL1 fusion was found in an elbow tumor from a 30 year-old male. Both OFMTs with CREBBP-BCORL1 fusions had areas of typical OFMT morphology, exhibiting uniform round to epithelioid cells arranged in cords or nesting pattern in a fibromyxoid stroma. The OFMT with KDM2A-WWTR1 fusion involved dermis and superficial subcutis, being composed of ovoid cells in a fibromyxoid background with hyalinized giant rosettes. The S100 immunoreactivity ranged from very focal to absent. Similar to other known fusion genes in OFMT, BCORL1, CREBBP and KDM2A are also involved in histone modification. In summary, we expand the spectrum of molecular abnormalities in OFMT with 2 novel fusions, CREBBP-BCORL1 and KDM2A-WWTR1, further implicating the epigenetic deregulation as the leading pathogenetic mechanism in OFMT. © 2016 Wiley Periodicals, Inc.

“.....The OFMT with KDM2A-WWTR1 fusion involved dermis and superficial subcutis, being composed of ovoid cells in a fibromyxoid background with hyalinized giant rosettes....”



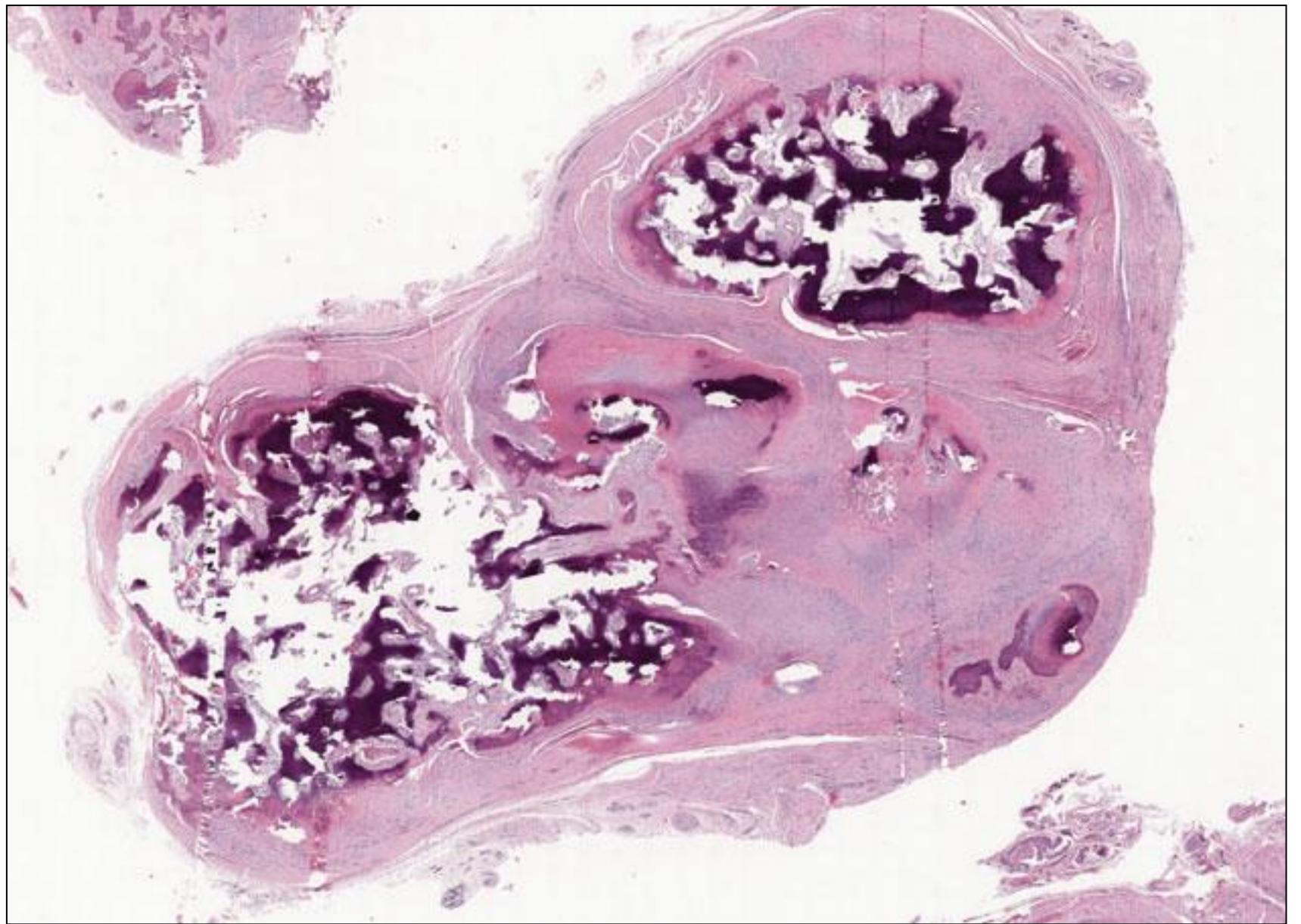
15% OFMT sú bez translokácie

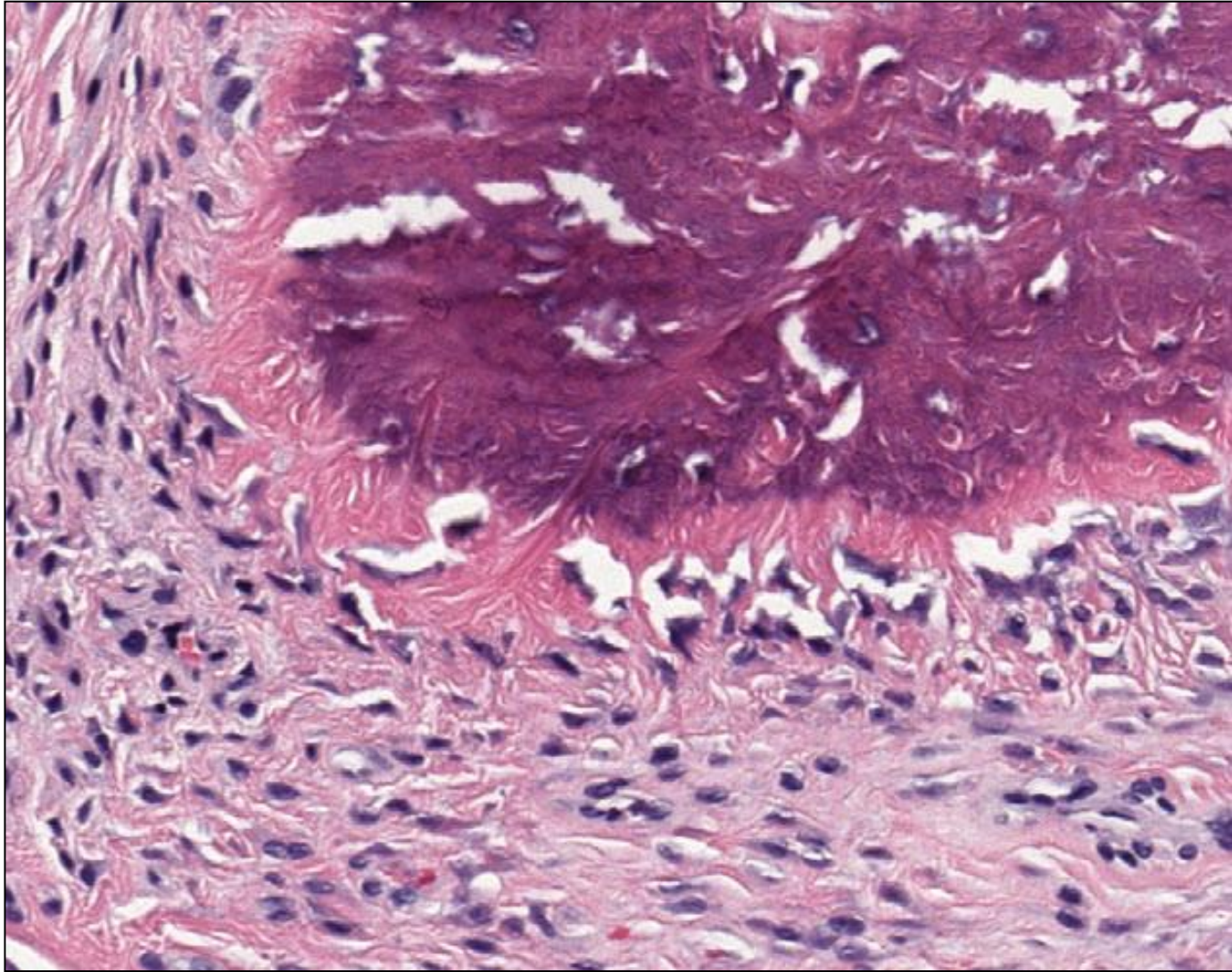
Dif. dg.

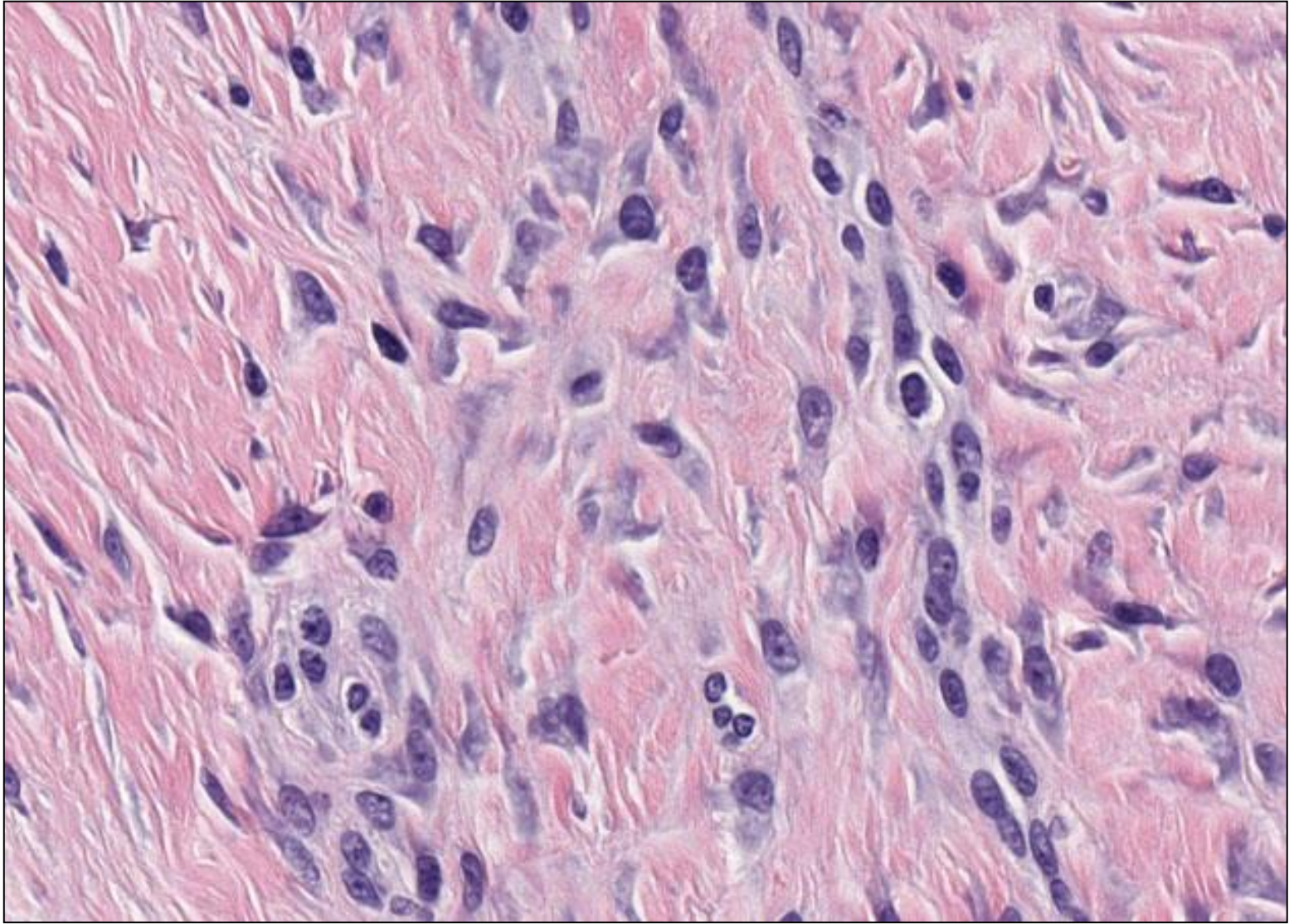
- Epiteloidný schwanóm
- Epiteloidný MNPPN
- Myoepiteliálne nádory (INI-1-, preskupenia EWSR1, FUS, PLAG1) t(1;22)
- EMCHS (S-100-, preskupenia NR4A3 na 9q22) t(9;22)
- LGFMS (MUC-4, osifikácie, FUS-CREB3L2 g.f.) t(7;16)
- SEF (EWSR1-CREB3L1 g.f.)

Dif. dg.

- Glomus tumor
- Melanóm
- Extraskoletálny OSA versus maligny OFMT
- GCT
- Osifikujúca myositída
- **Plexiformný osifikujúci tumor**







ZÁVER

1. OFMT je zriedkavy nádor s intermediárnym biologickým potenciálom - 2 typy: OFMT a malígny OFMT
2. Morfologické „overlap“ s inými nádormi MT, dôležitosť korektnej dg. (riziko recidívy, metastázovania a smrti)

ZÁVER

3. 85% OFMT – rekurentné genetické preskupenia.
4. Je vzťah medzi OFMT a ESS ?
5. Je prítomnosť kolagenových roziet asociovaná s fúziou KDM2A-WWTR1 ?
6. Genetické vyšetrenie – možnosť rizikovej stratifikácie (a terapeutických stratégií)

Literatúra

1. Expanding the molecular signature of ossifying fibromyxoid tumors with two novel gene fusions: CREBBP-BCORL1 and KDM2A-WWTR1. *Genes Chromosomes Cancer*. 2016 Aug 18. doi: 10.1002/gcc.22400. [Epub ahead of print]
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4. Ossifying Fibromyxoid Tumor: An Update. *Arch Pathol Lab Med*. 2016 Apr;140(4):371-5. doi: 10.5858/arpa.2014-0590-RS.
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6. Malignant Ossifying Fibromyxoid Tumors: a report of two rare cases displaying retained INI1/SMARCB1 expression. *Indian J Pathol Microbiol*. 2014 Oct-Dec ;57(4):652-3. doi: 10.4103/0377-4929.142717.

