Lower Female Genital Tract, A Potpourri of Problems

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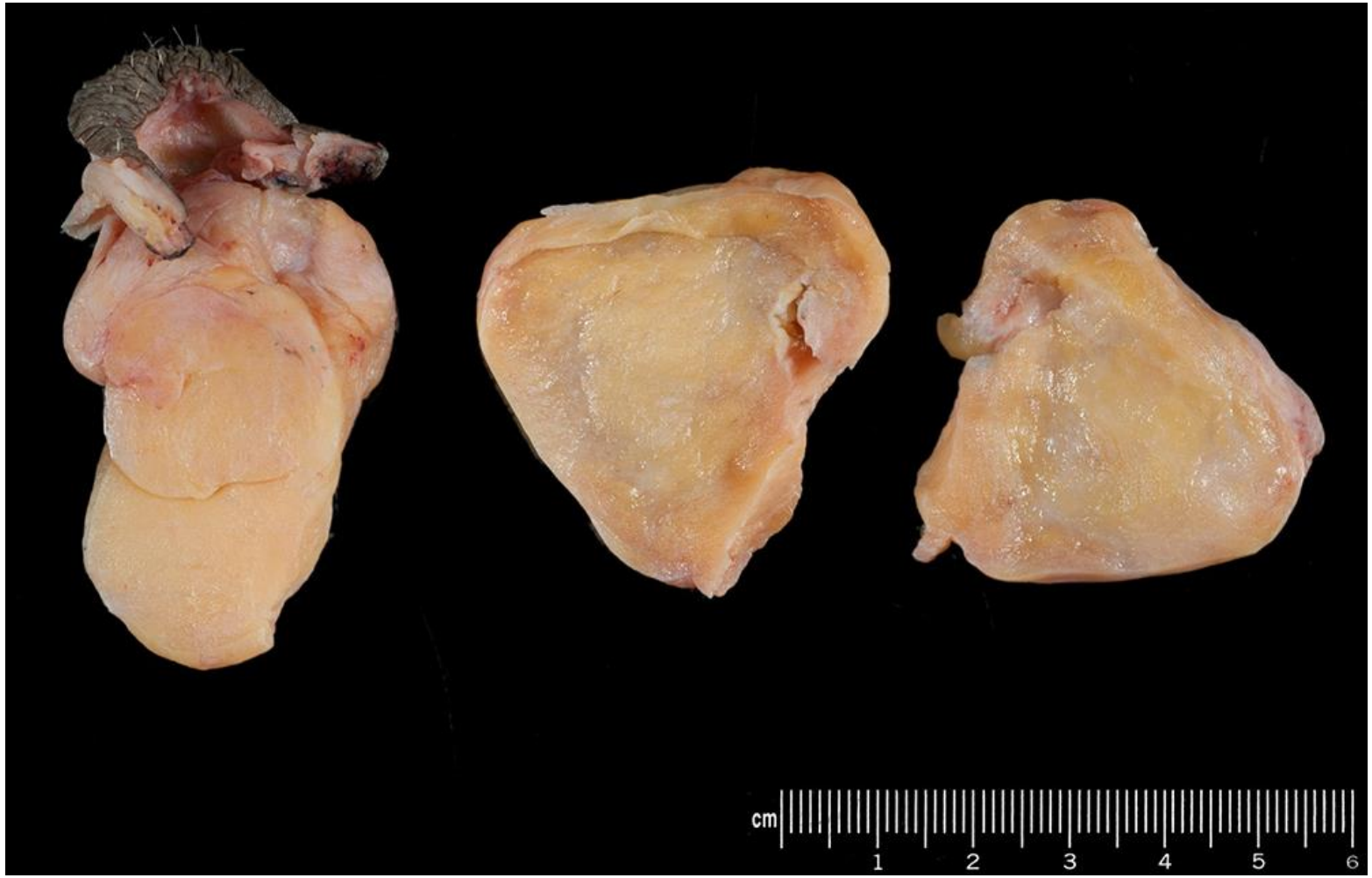
Making Cancer History®

No conflicts of interest

Case 1, Clinical History

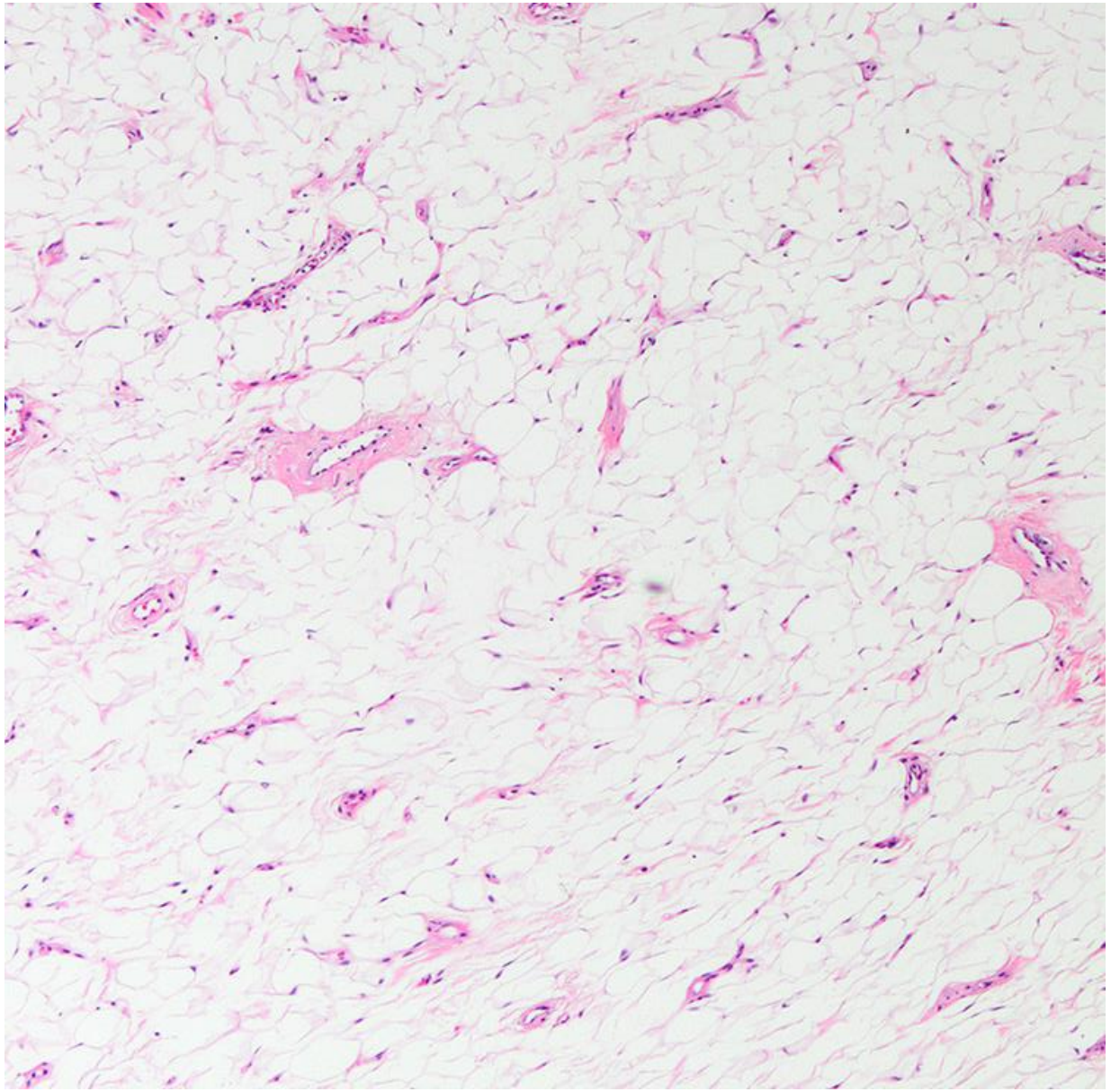
- A 57 y.o. African-American postmenopausal, obese female presented with a left, non-tender, soft vulvar mass that had been enlarging over a 4 year-period
- Wide local excision
- F/u, no evidence of disease at 6 years

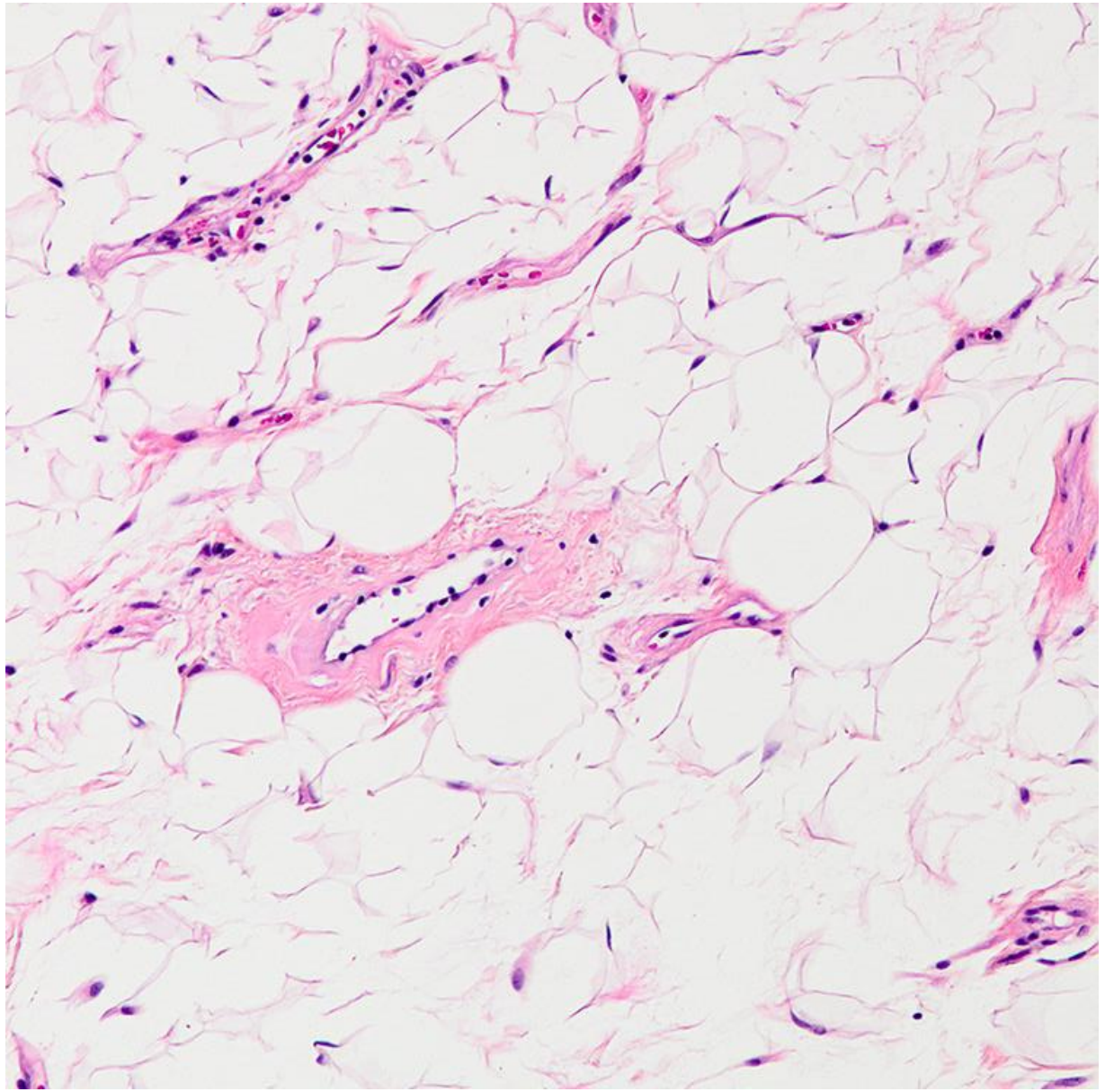
Wide Local Excision of the Vulva
12.0 x 7.5 x 6.5 cm



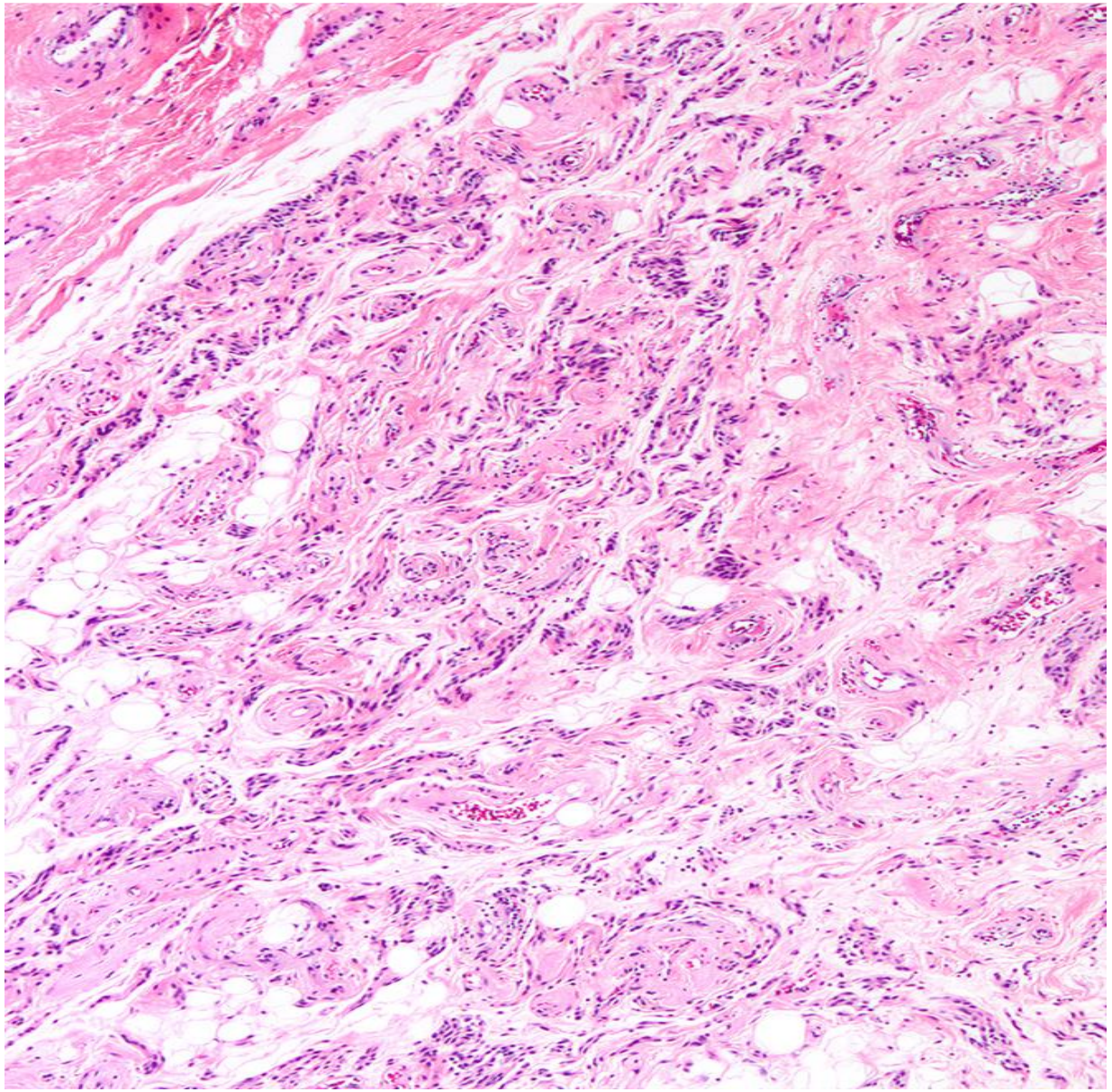
Well-demarcated, fatty, slightly fibrotic, 6.7 x 5.5 x 5.2 cm mass

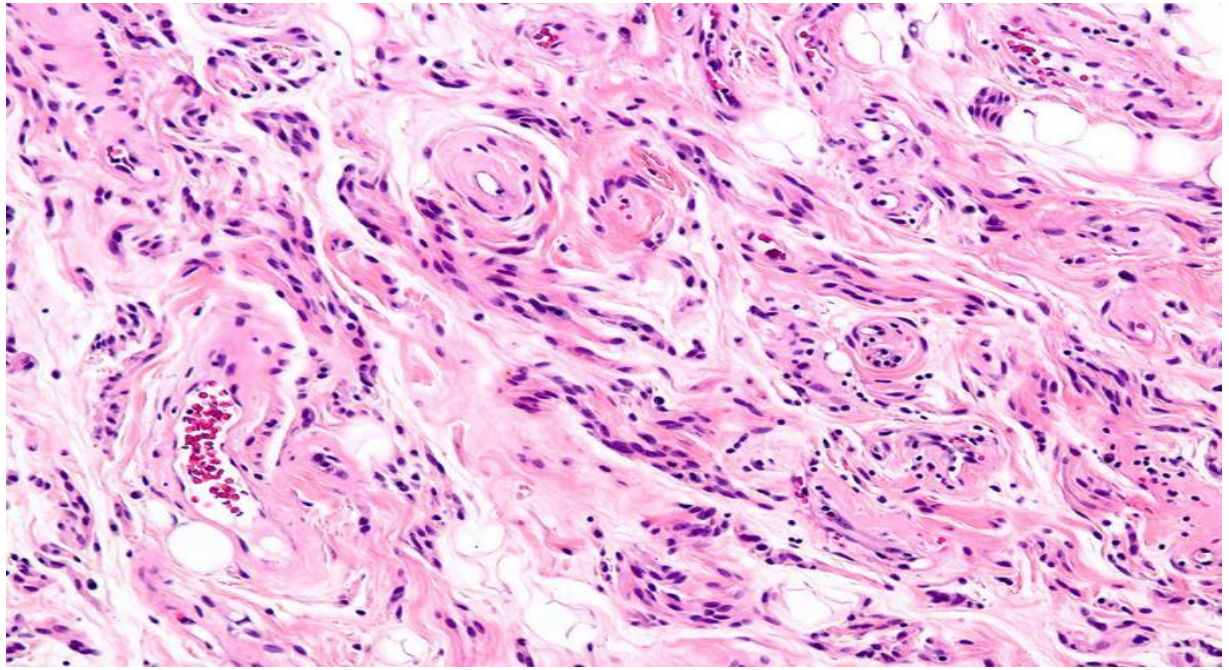
Adipocytes of variable size, delicate small- and medium-sized blood vessels and no lipoblasts

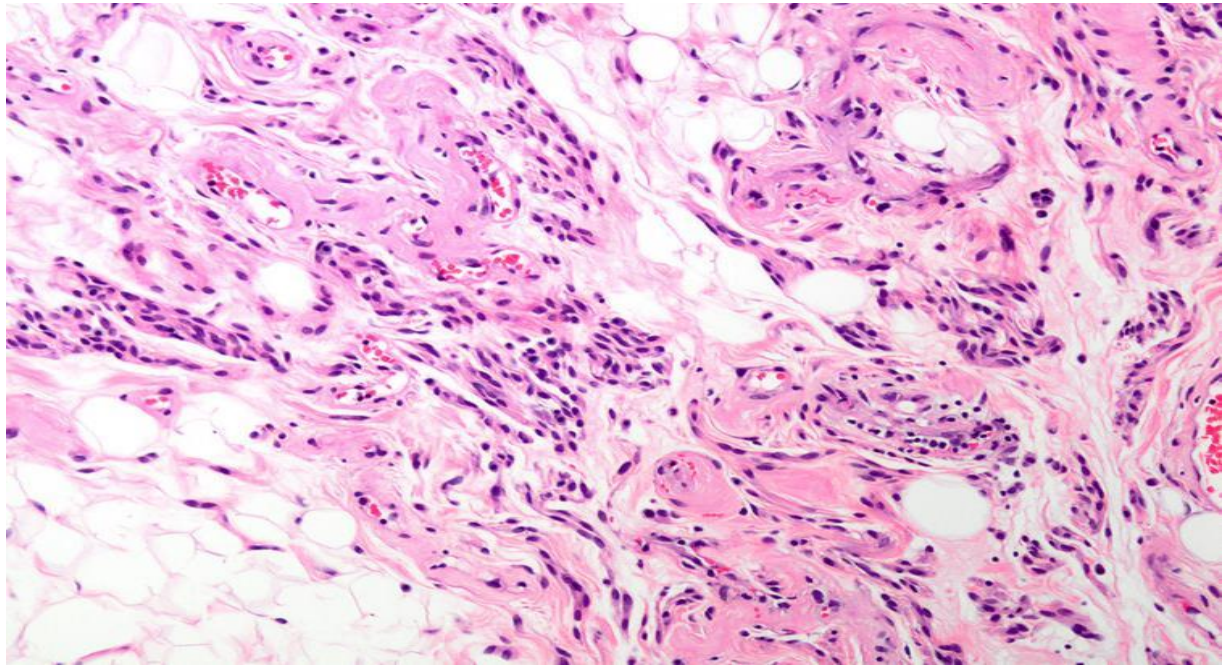


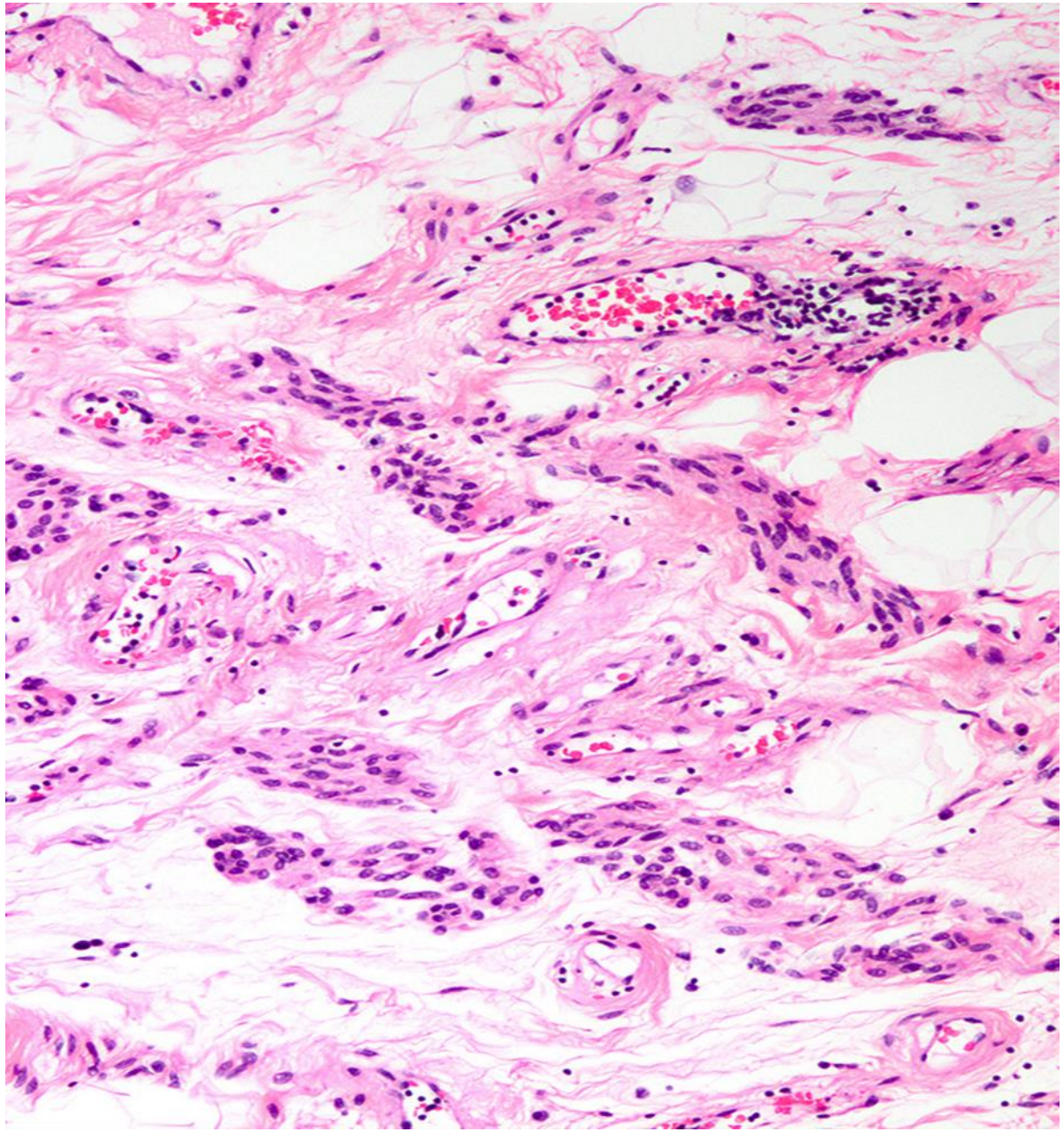


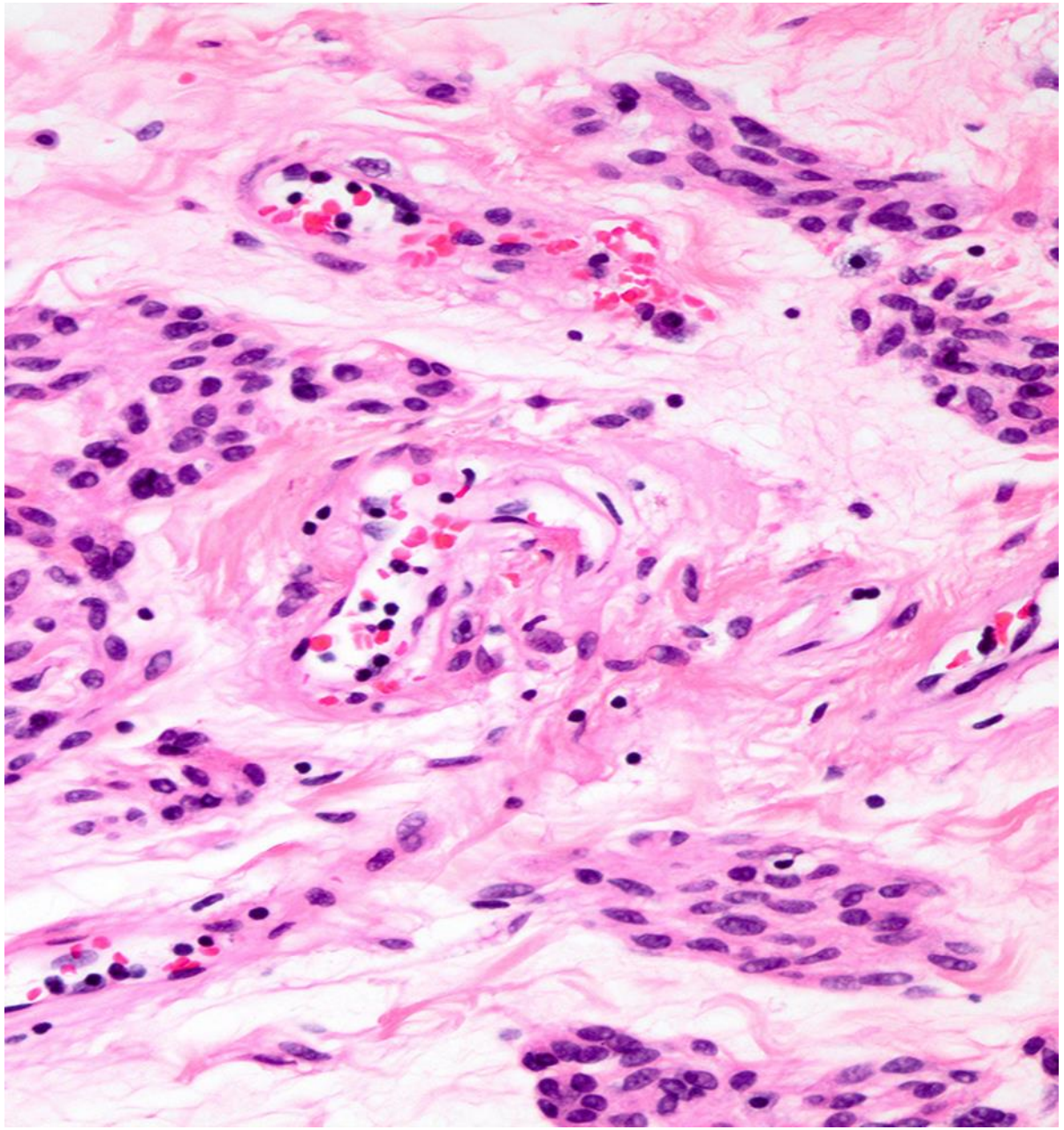
Areas with prominent vascular component with perivascular bland epithelioid and spindle cells and fibrous stroma





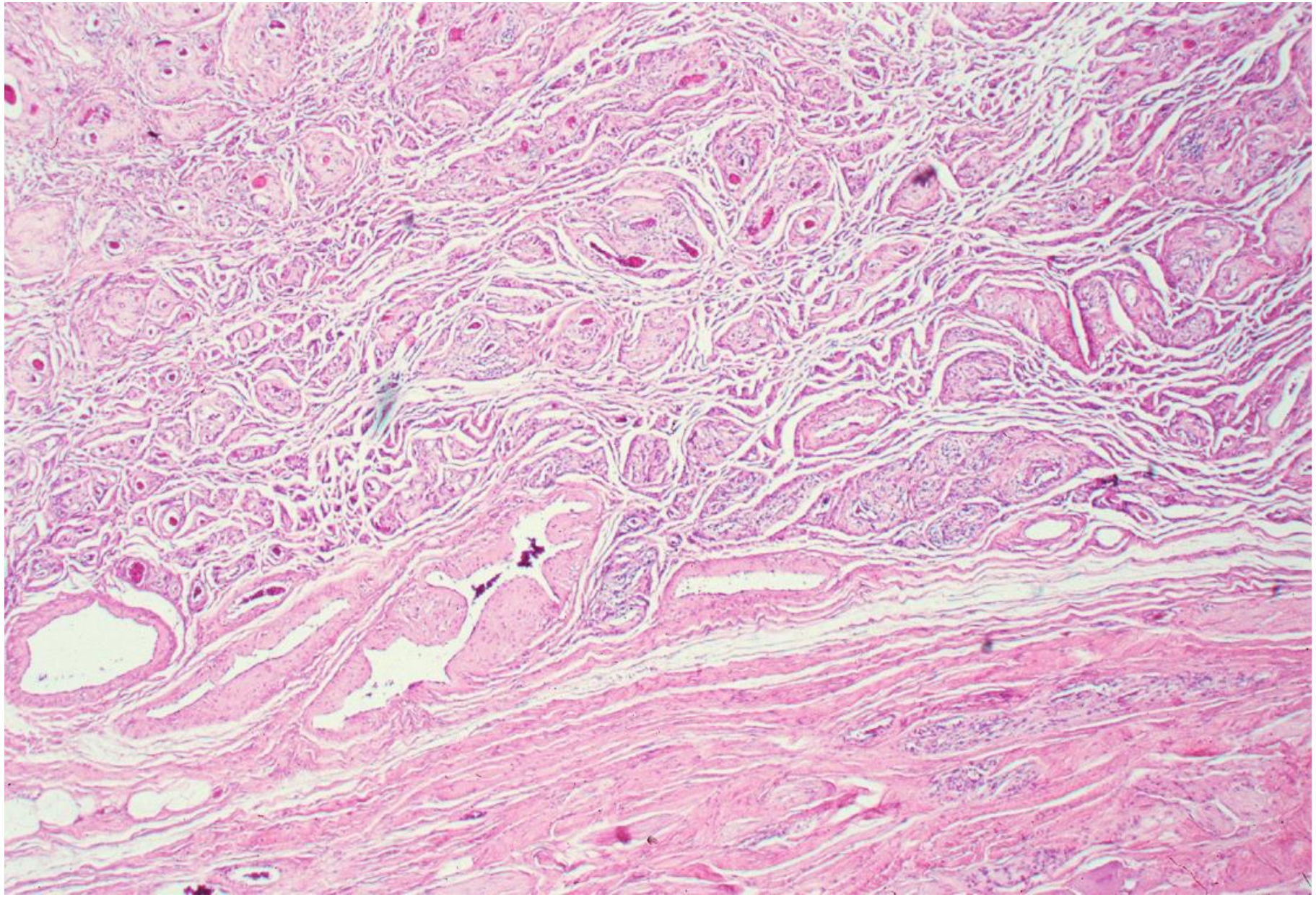






No atypia or mitotic activity

Well-circumscribed



IHC

ER/PR +

Desmin patchy +

CD34 + (F)

Diagnosis

Angiomyofibroblastoma of the vulva, lipomatous variant

The goal is to distinguish

1.- Angiomyofibroblastoma, lipomatous variant, from other tumors with adipocytes

2.- Angiomyofibroblastoma from aggressive angiomyxoma

Angiomyofibroblastoma

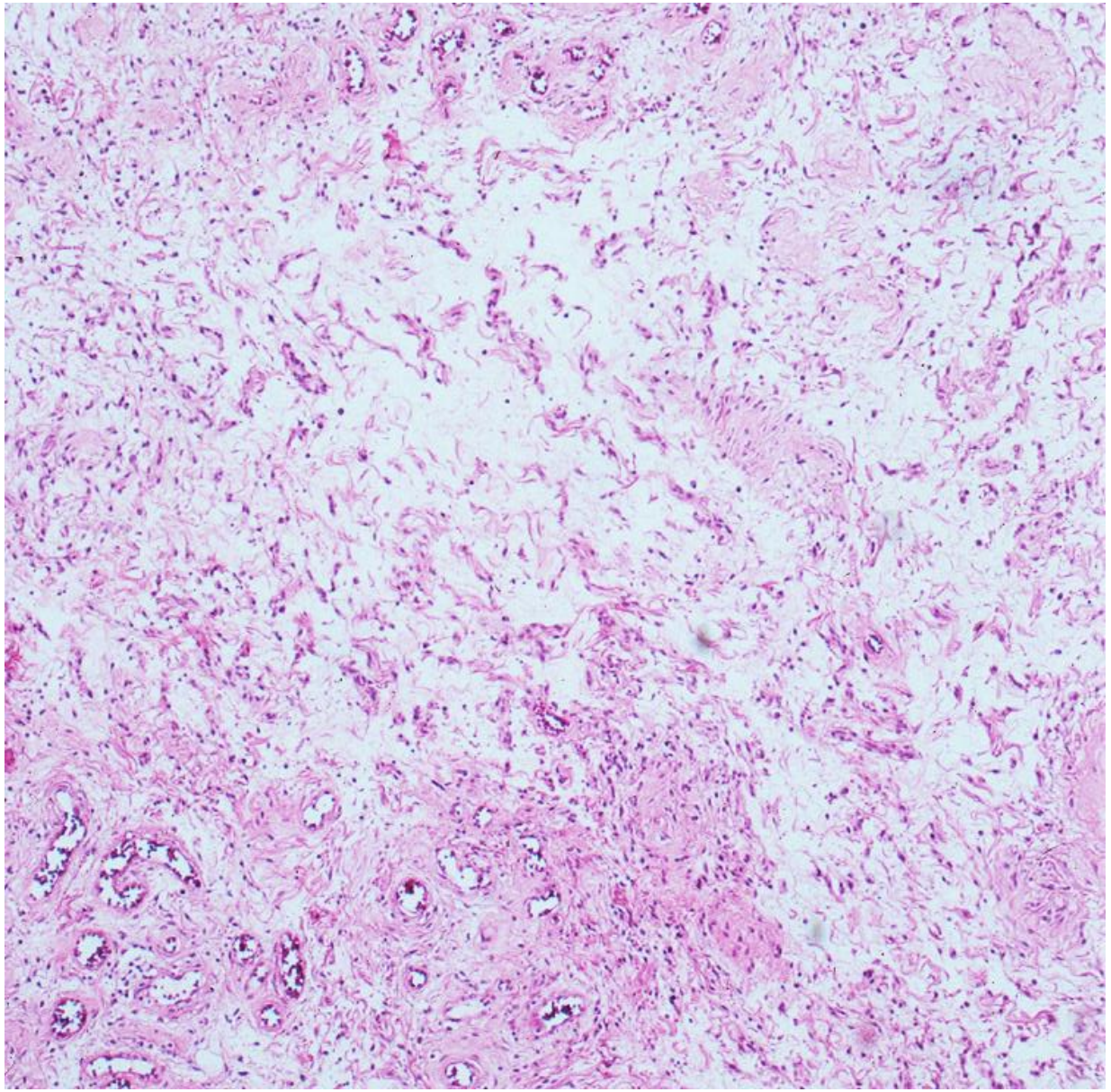
- Uncommon, benign tumor
- Pts have a wide age range
- Usually,
  - women
  - vulvar region

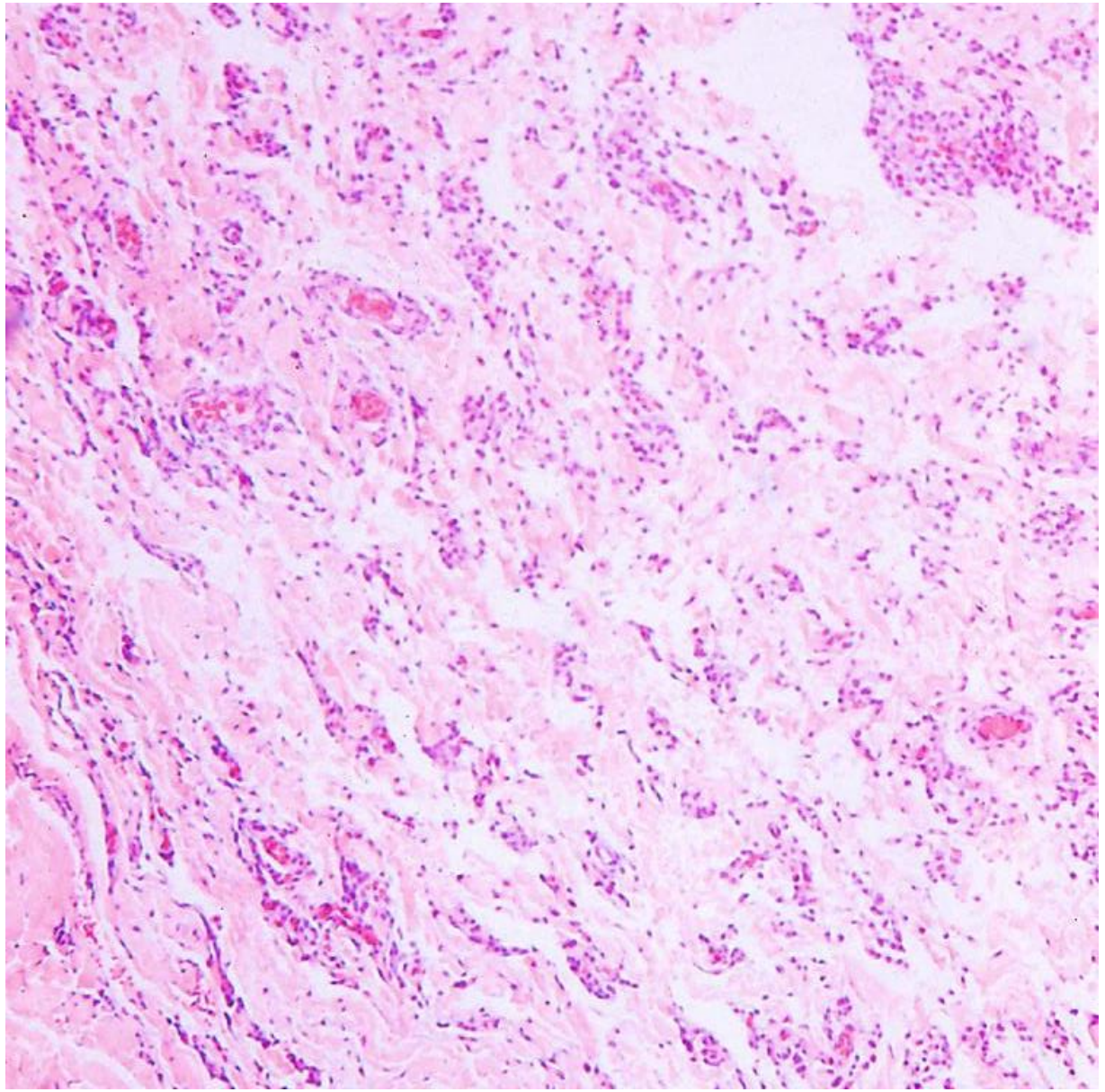
- Also,
  - vagina, fallopian tube or urethra
  - male pts
    - scrotum
    - inguinal region
    - perineum

Angiomyofibroblastoma

- IHC: ER +, PR +, desmin +, CD34 variably +
- Molecularly defined by recurrent *MTG1-CYP2E1* fusions

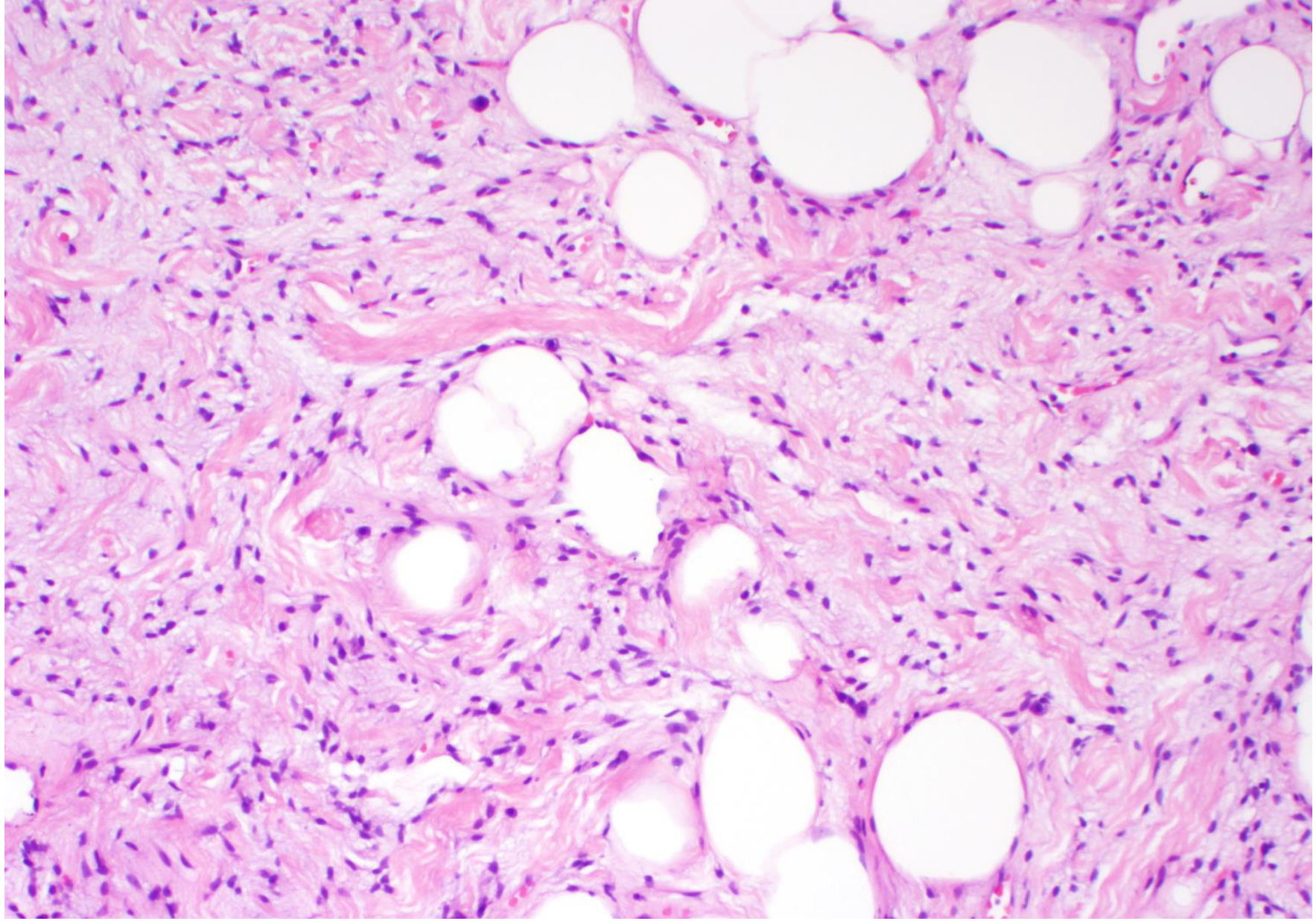
Typical case shows alternating hypercellular and hypocellular areas containing small- or medium-sized vessels surrounded by bland epithelioid, plasmacytoid and/or spindled cells





Angiomyofibroblastoma, Lipomatous Variant

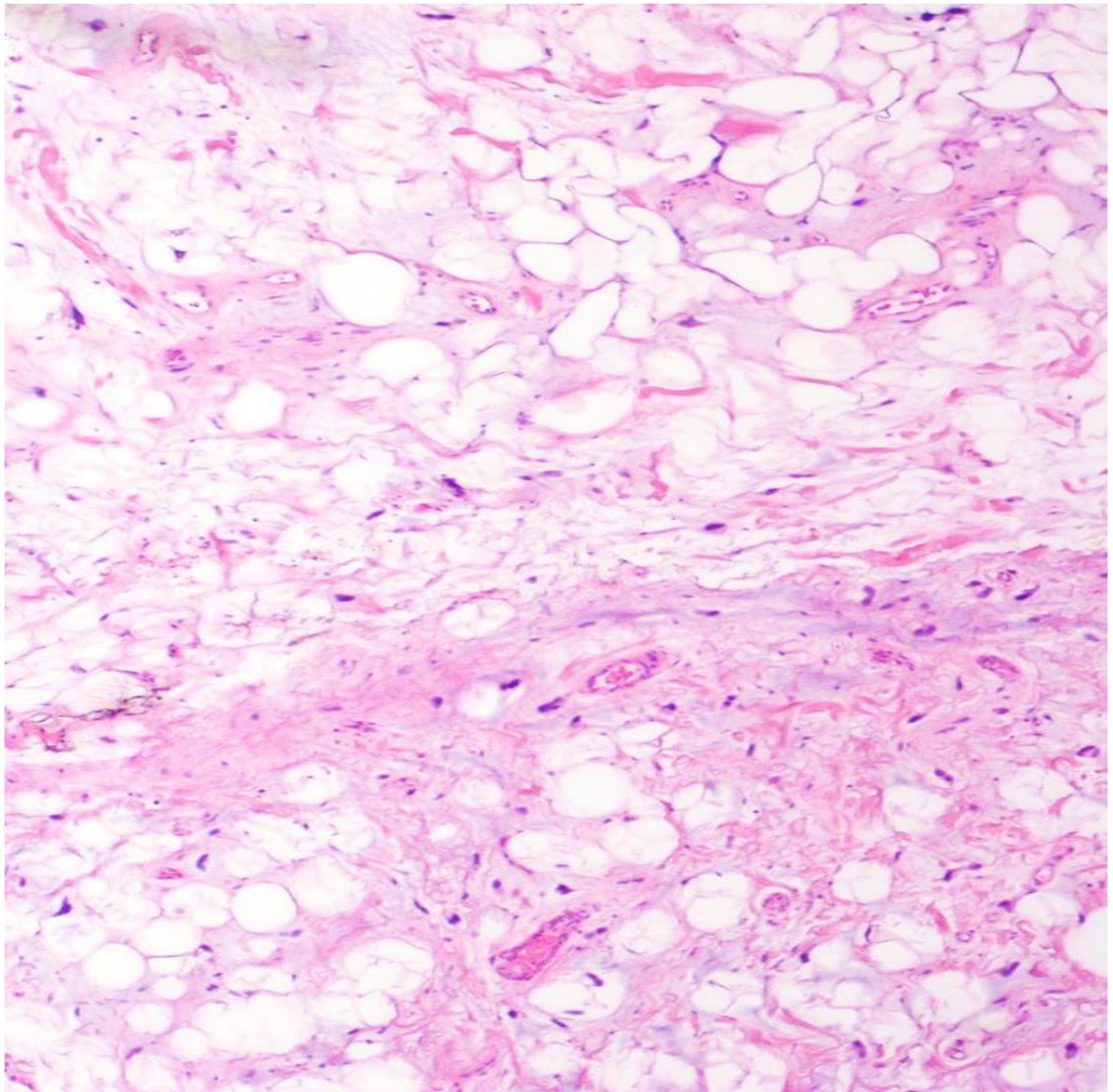
Adipose tissue represents an important component of the tumor, 30% to 90%

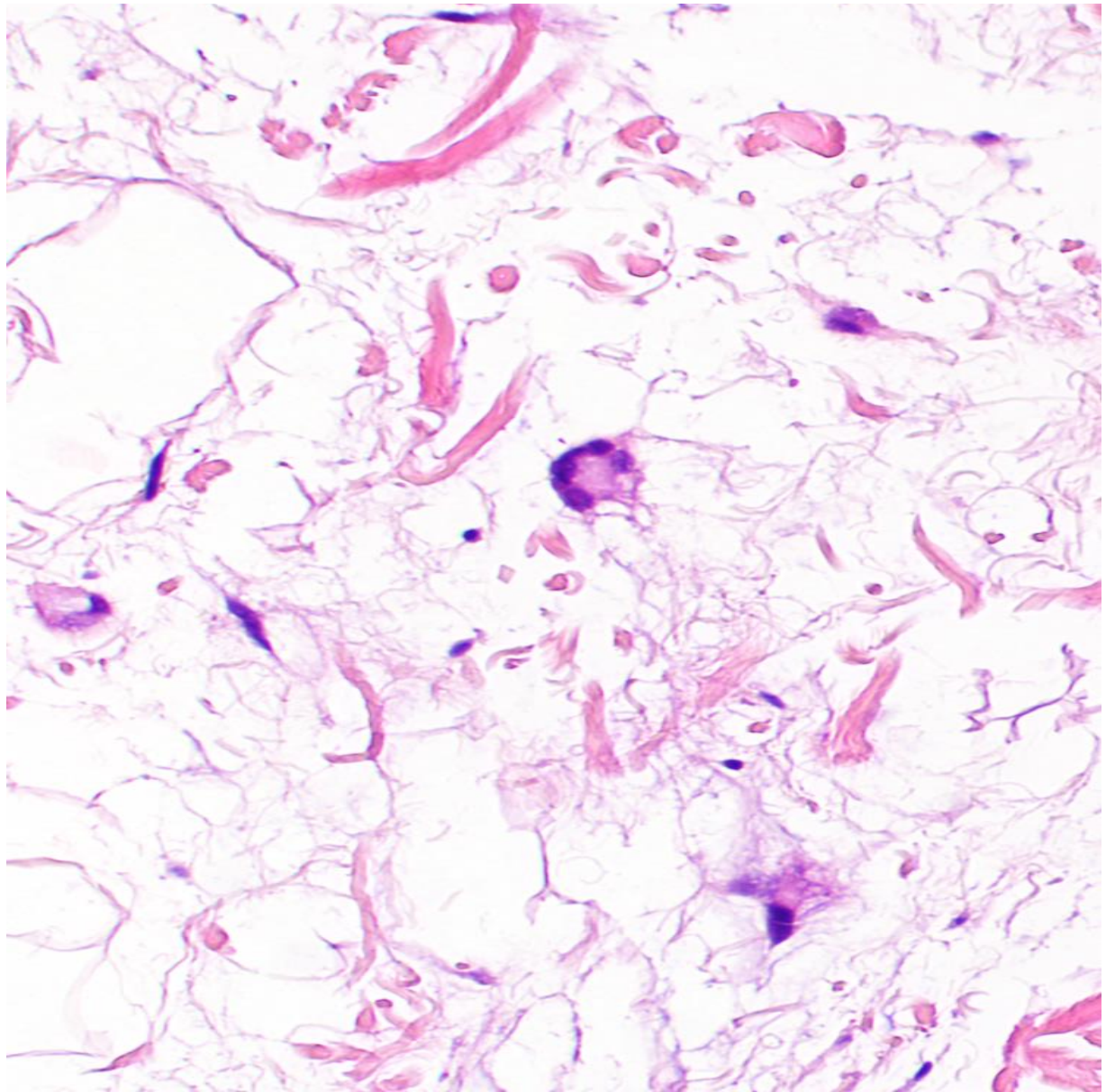


Spindle cell lipoma: myxoid stroma, ropey collagen bundles and bland spindle cells admixed with mature fat. CD34 +, adipocytes S-100 +. RARE IN THE VULVA. Molecular feature: RB1 loss

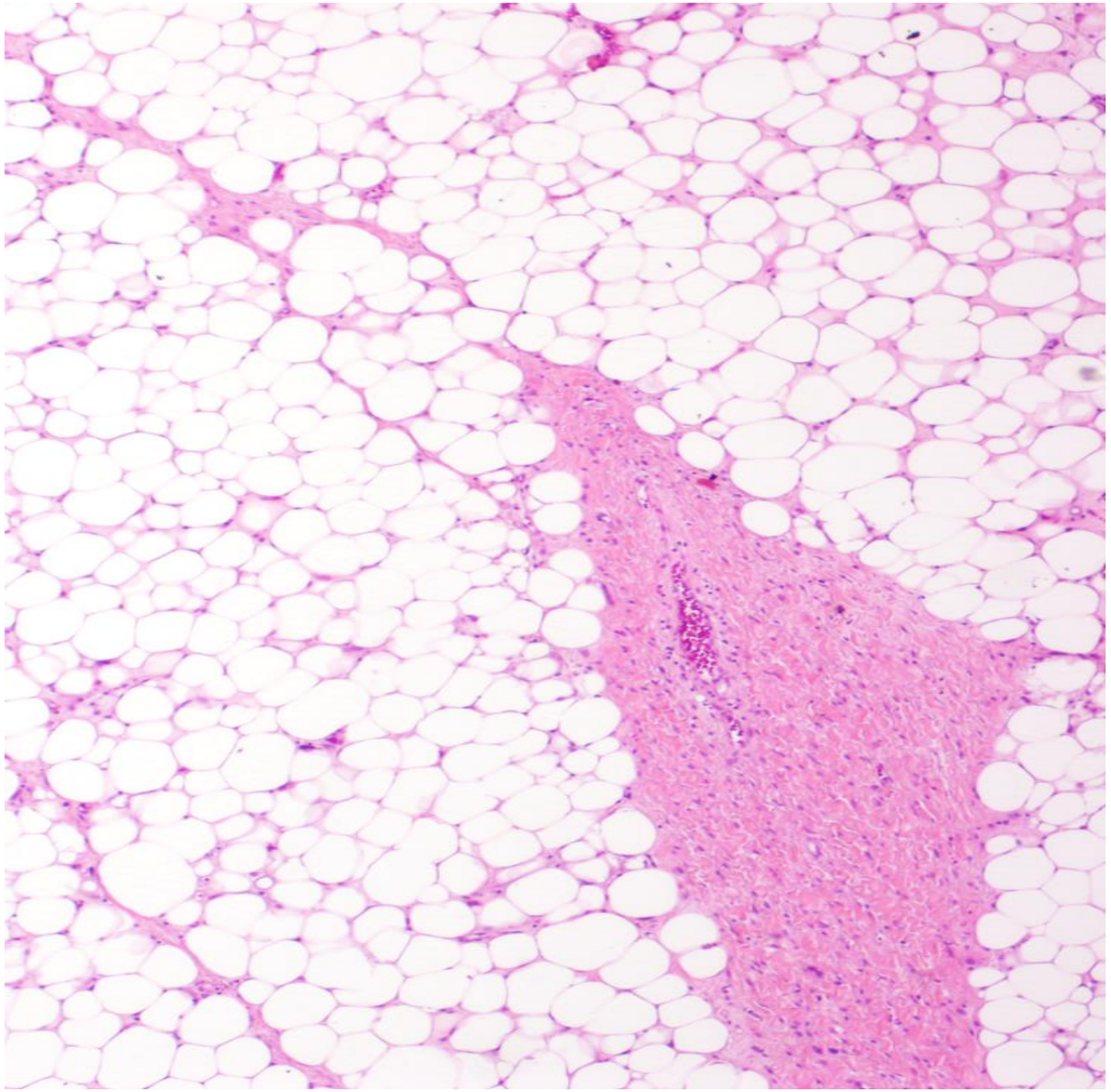
Courtesy of WL Wang

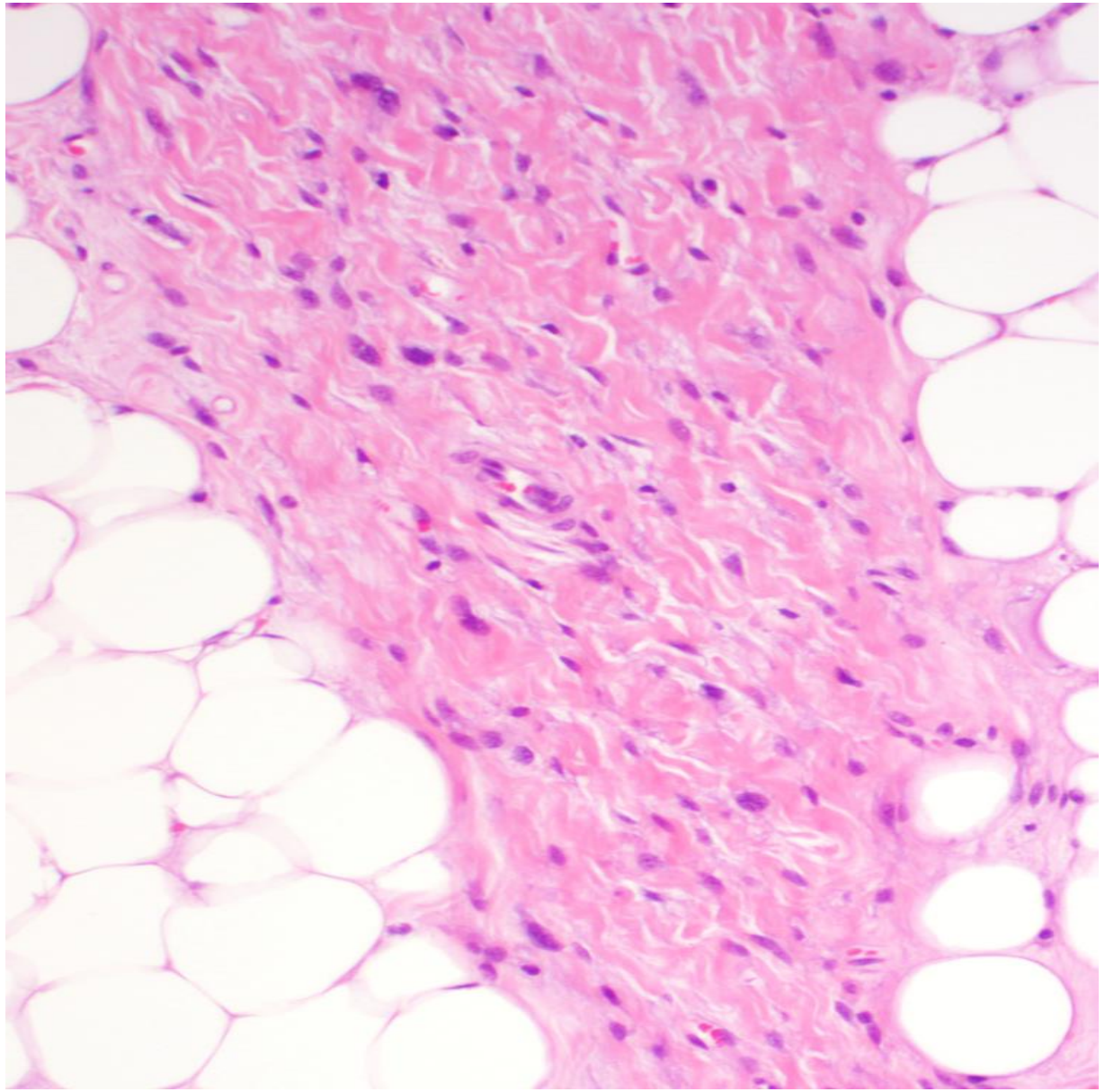
Pleomorphic lipoma: borders poorly demarcated –even infiltrative, mature adipocytes, myxoid stroma, collagen bundles and scattered floret giant cells. CD34 + and adipocytes S-100 +. Molecular feature: RB1 loss. RARE IN THE VULVA

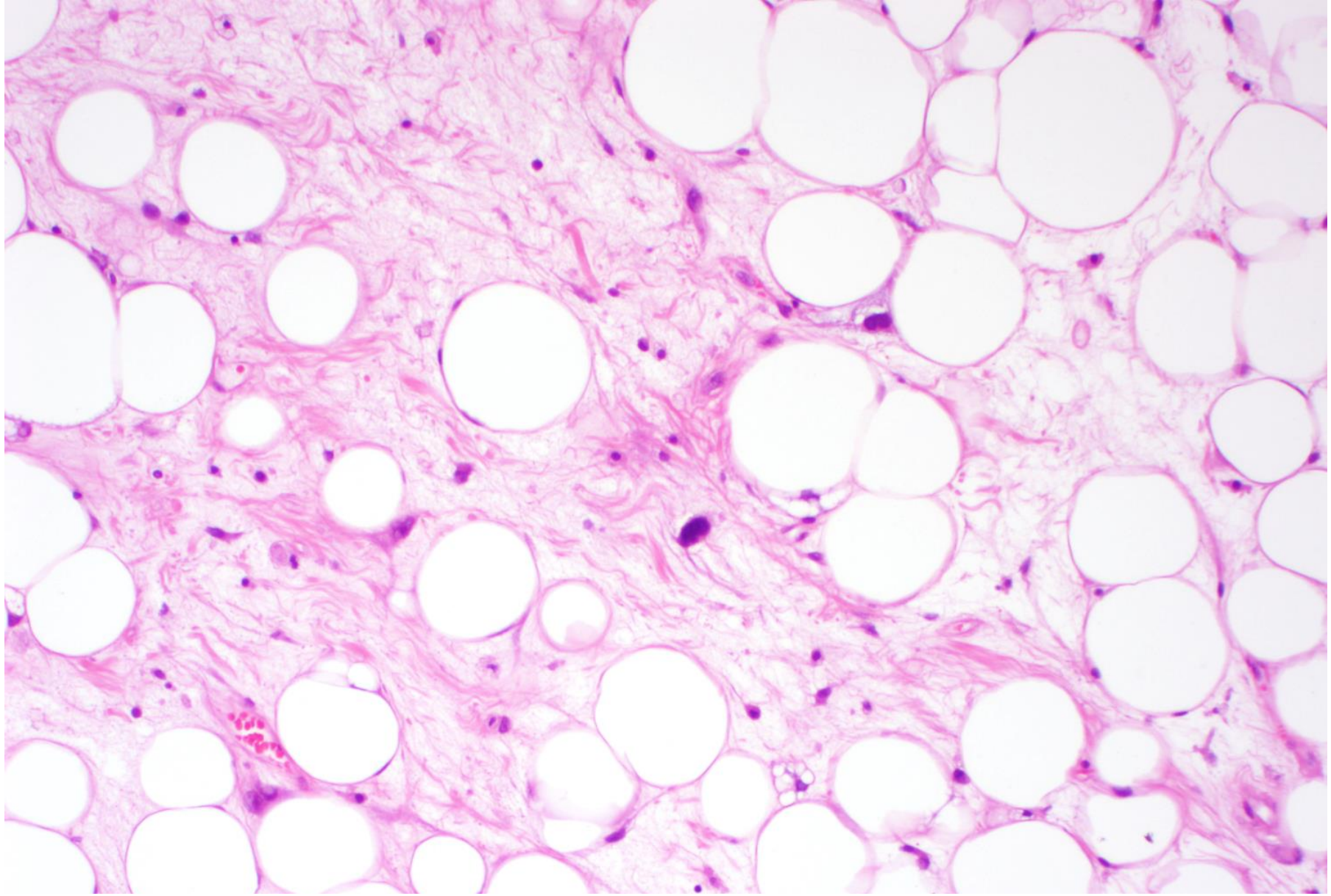




Atypical lipomatous tumor/well-differentiated liposarcoma: variably sized adipocytes with fibrous septae and periadipocytic fibrosis with atypical stromal cells. RARE IN THE VULVA



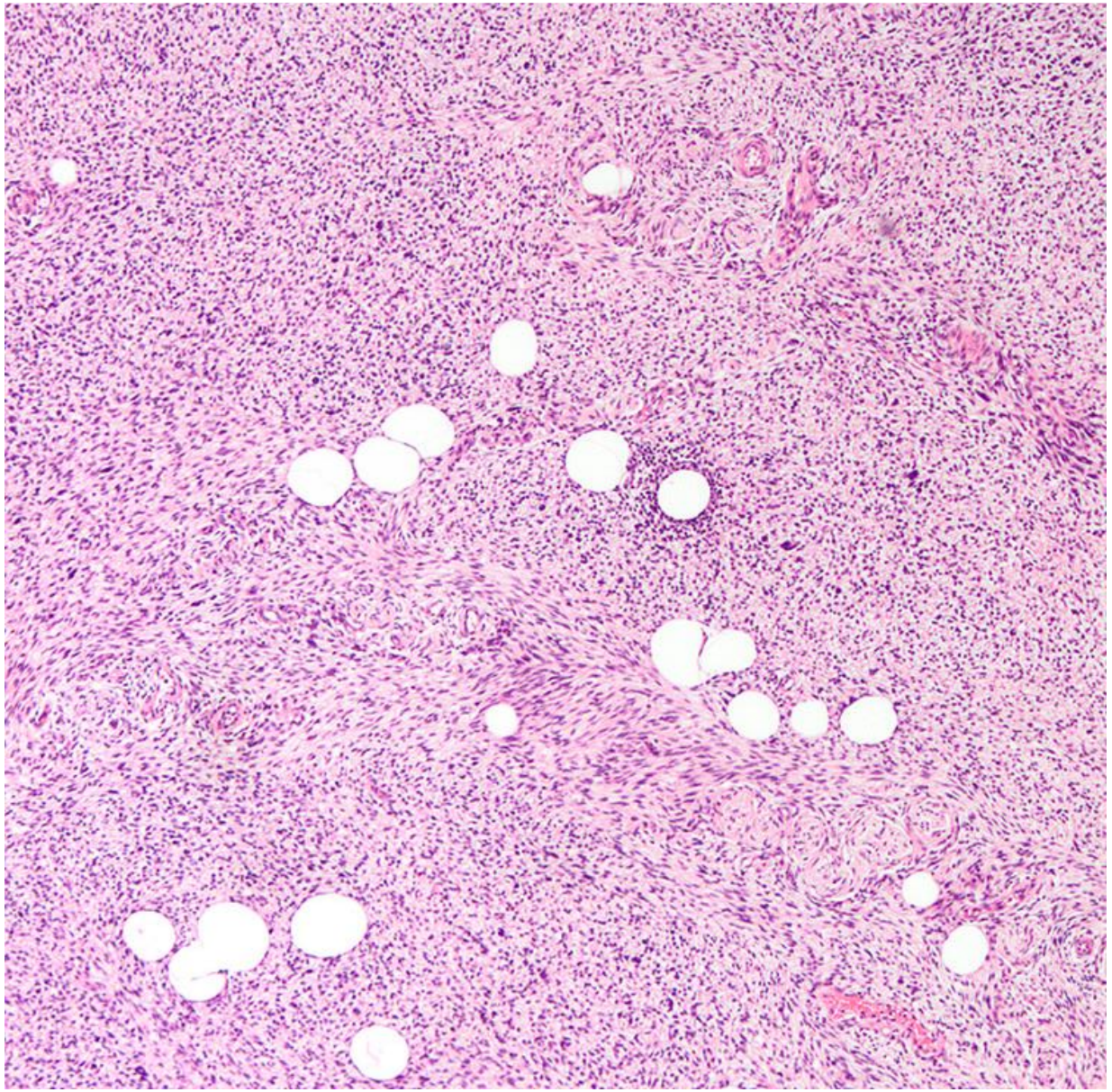


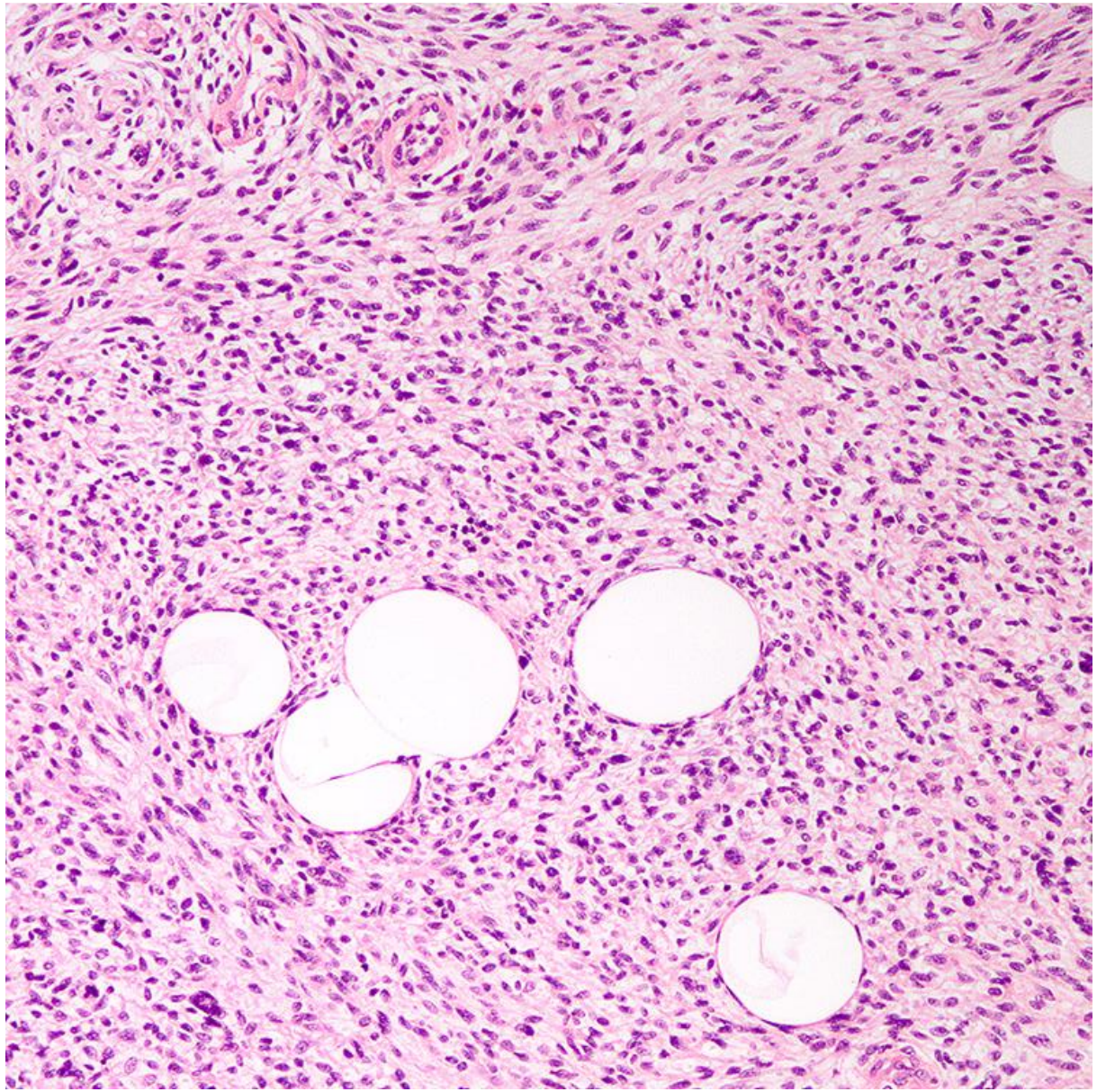


Atypical lipomatous tumor/well-differentiated liposarcoma: periadipocyte fibrosis with atypical stromal cells. Infiltrative margins. *MDM2* and/or *CDK4* gene amplification (IHC, FISH or PCR)

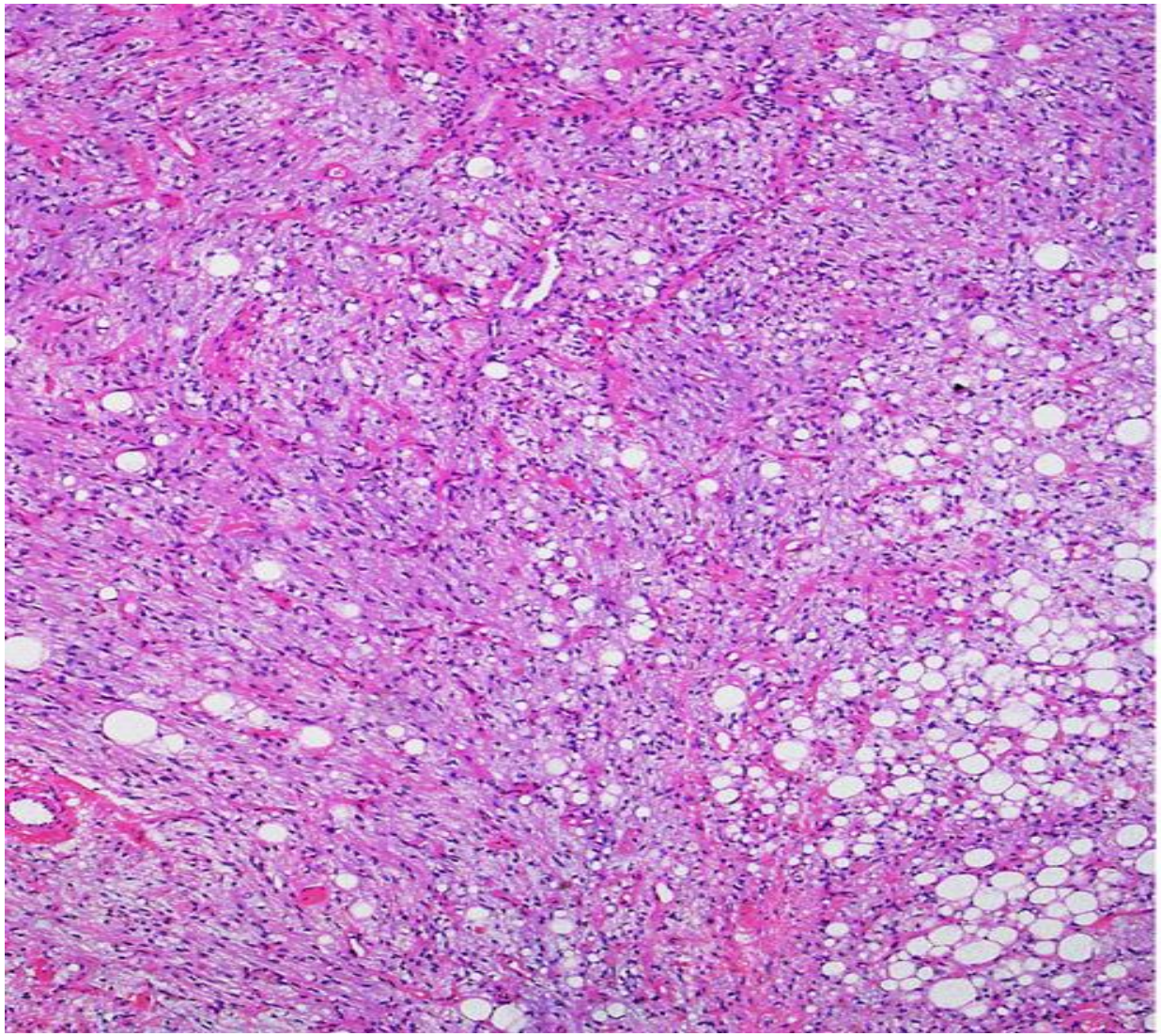
Courtesy of WL Wang

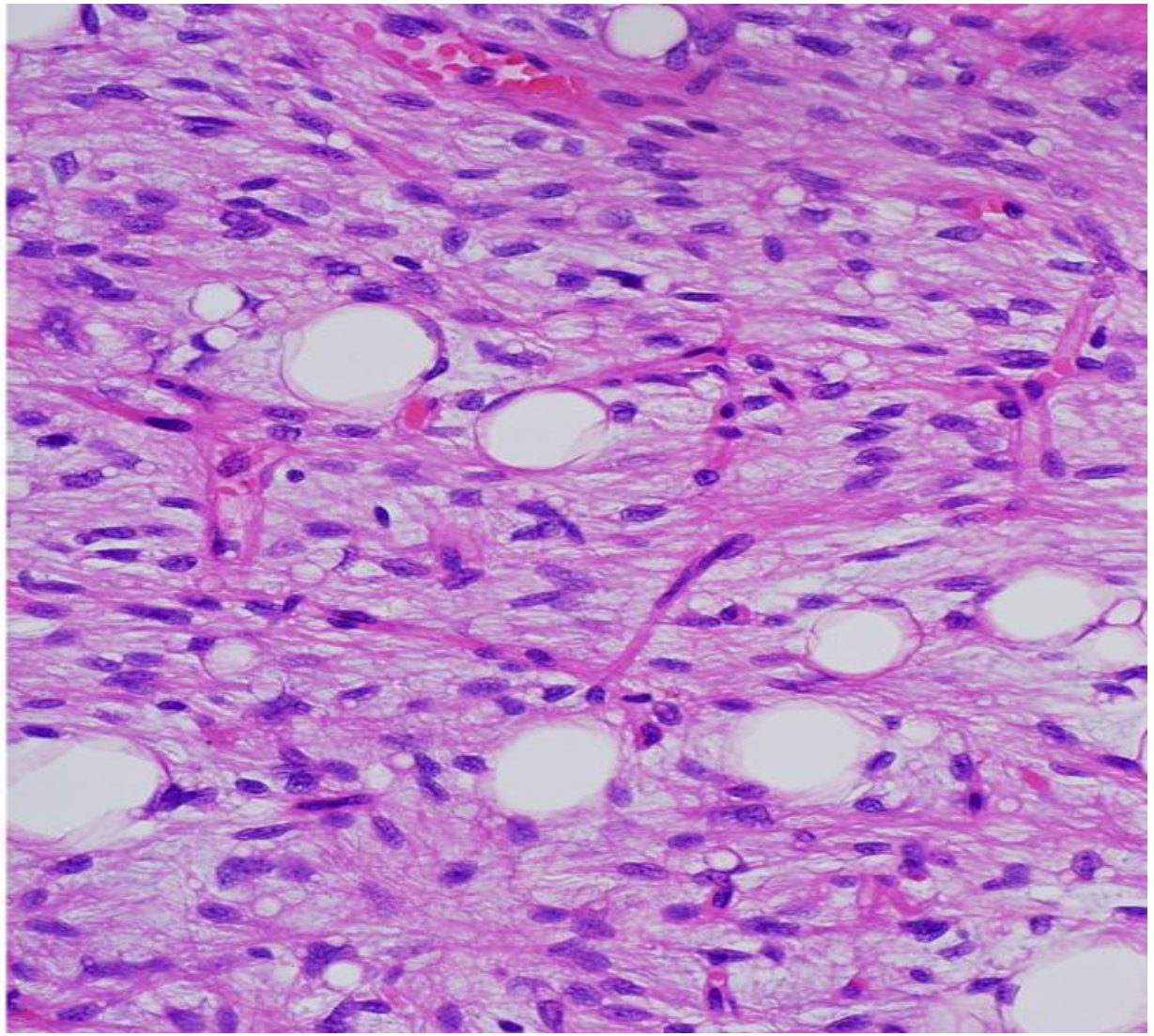
Cellular angiofibroma: intersecting fascicles of spindle cells, “hyalinized vessels“ and entrapped adipocytes. ER/PR +, CD34 + (60% of cases). Desmin typically (-).





Lipoblastoma-like tumor of the vulva, well-circumscribed, lobulated architecture, thin/thick fibrous septa, thin-walled and branching blood vessels, myxoid stroma, nuclear atypia is minimal, mitoses are rare

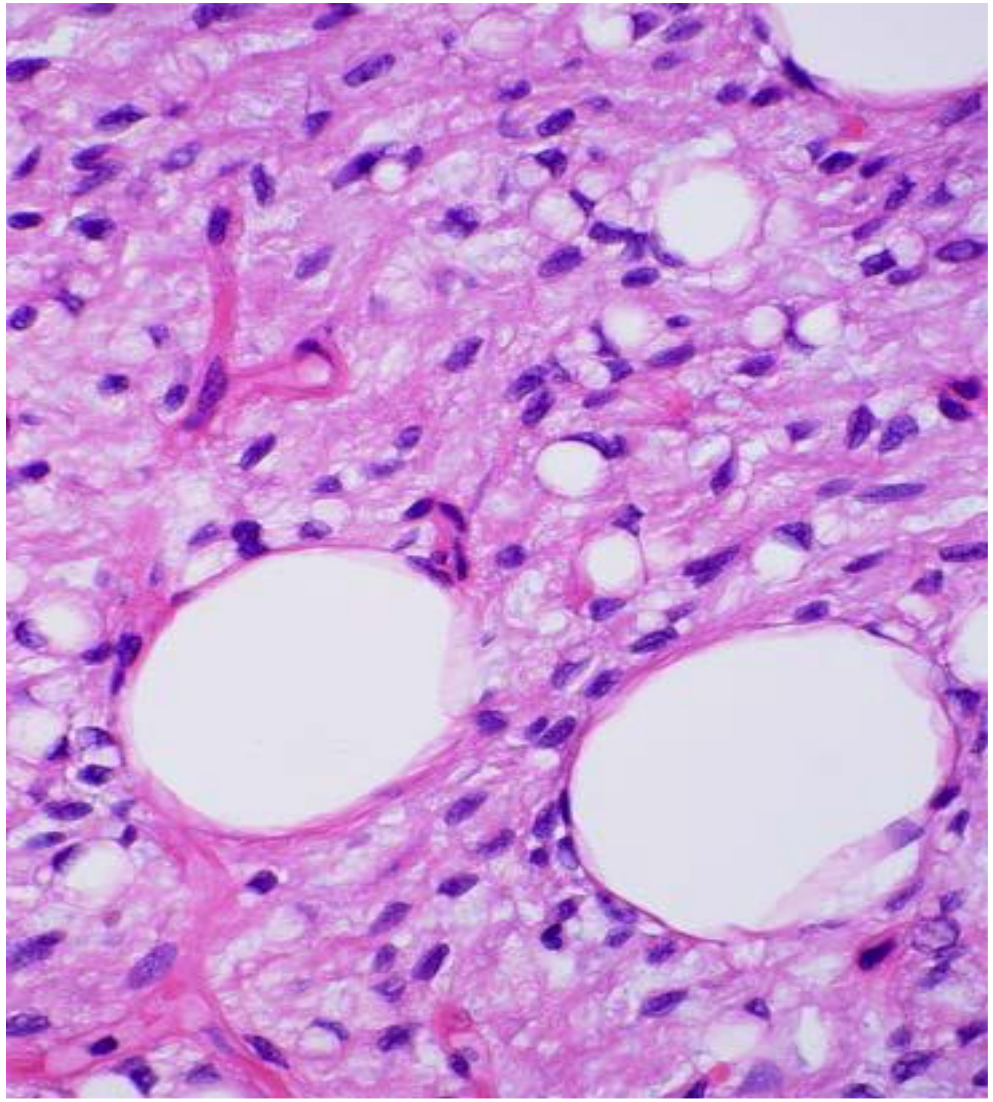




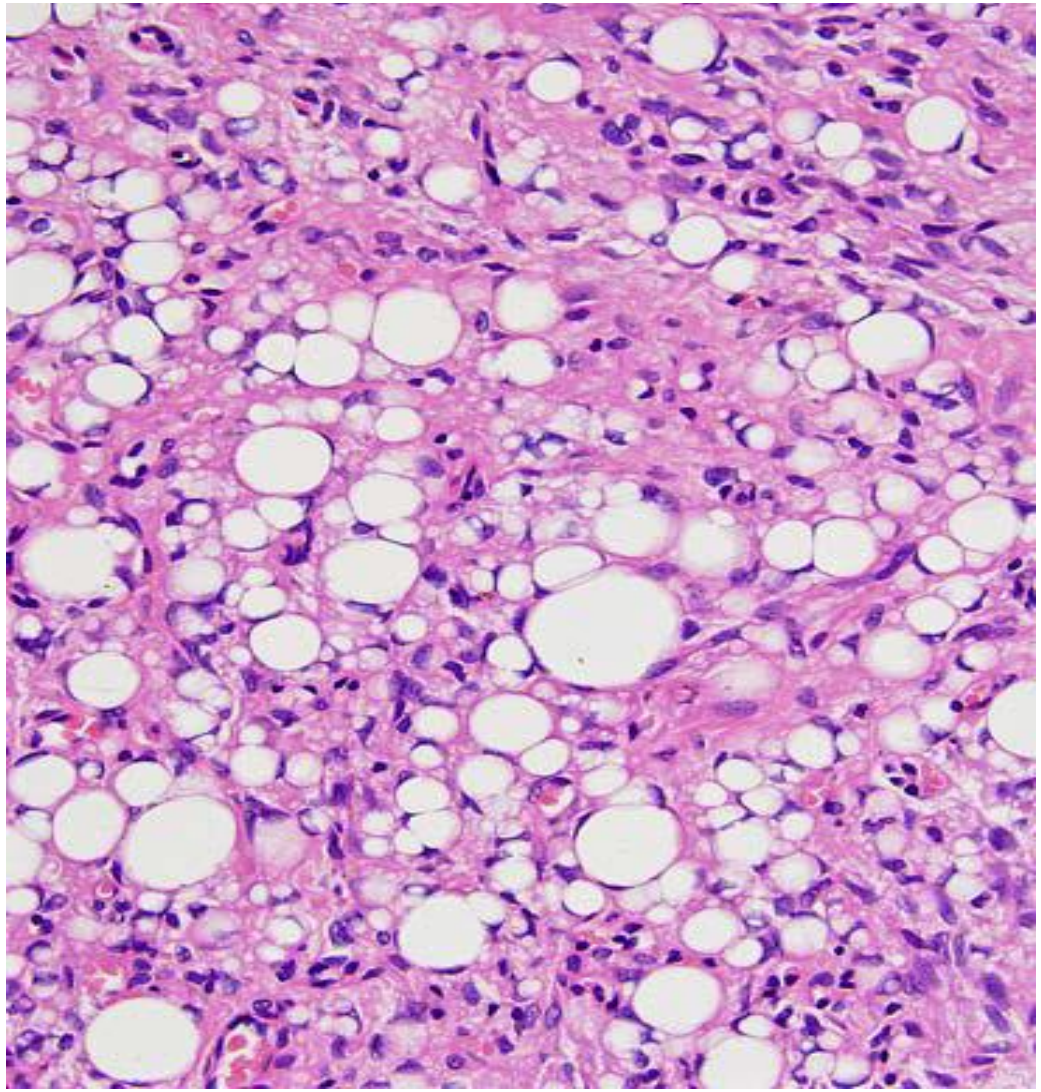
Lacks *MDM2* and/or *CDK4* gene amplification; *PLAG1* or *HMGA2* gene rearrangement

Mirkovic J and Fletcher CD, 2015

Mature adipocytes, bland lipoblasts and bland spindle cells with short, stubby nuclei

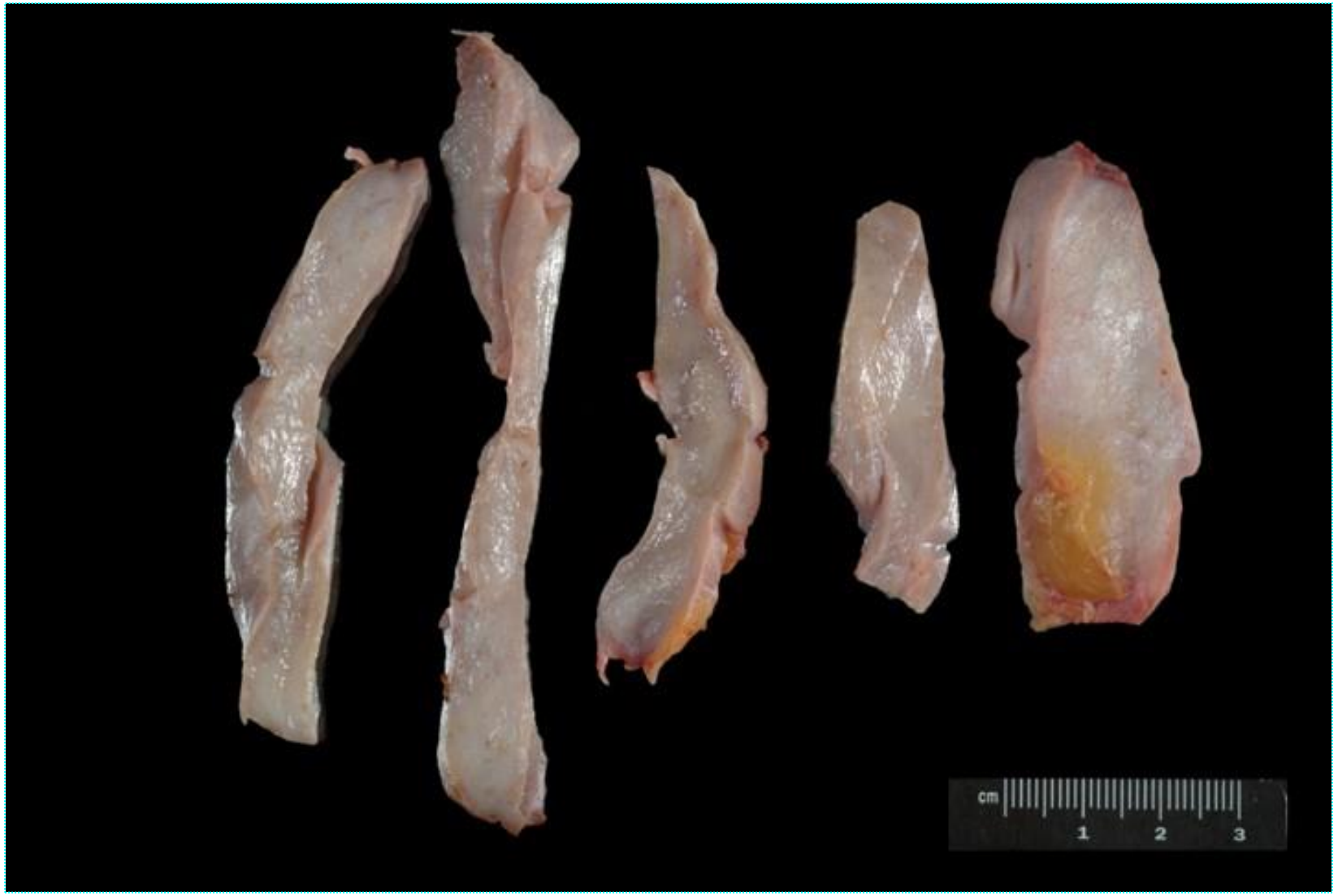


Univacuolated or bivacuolated bland lipoblasts



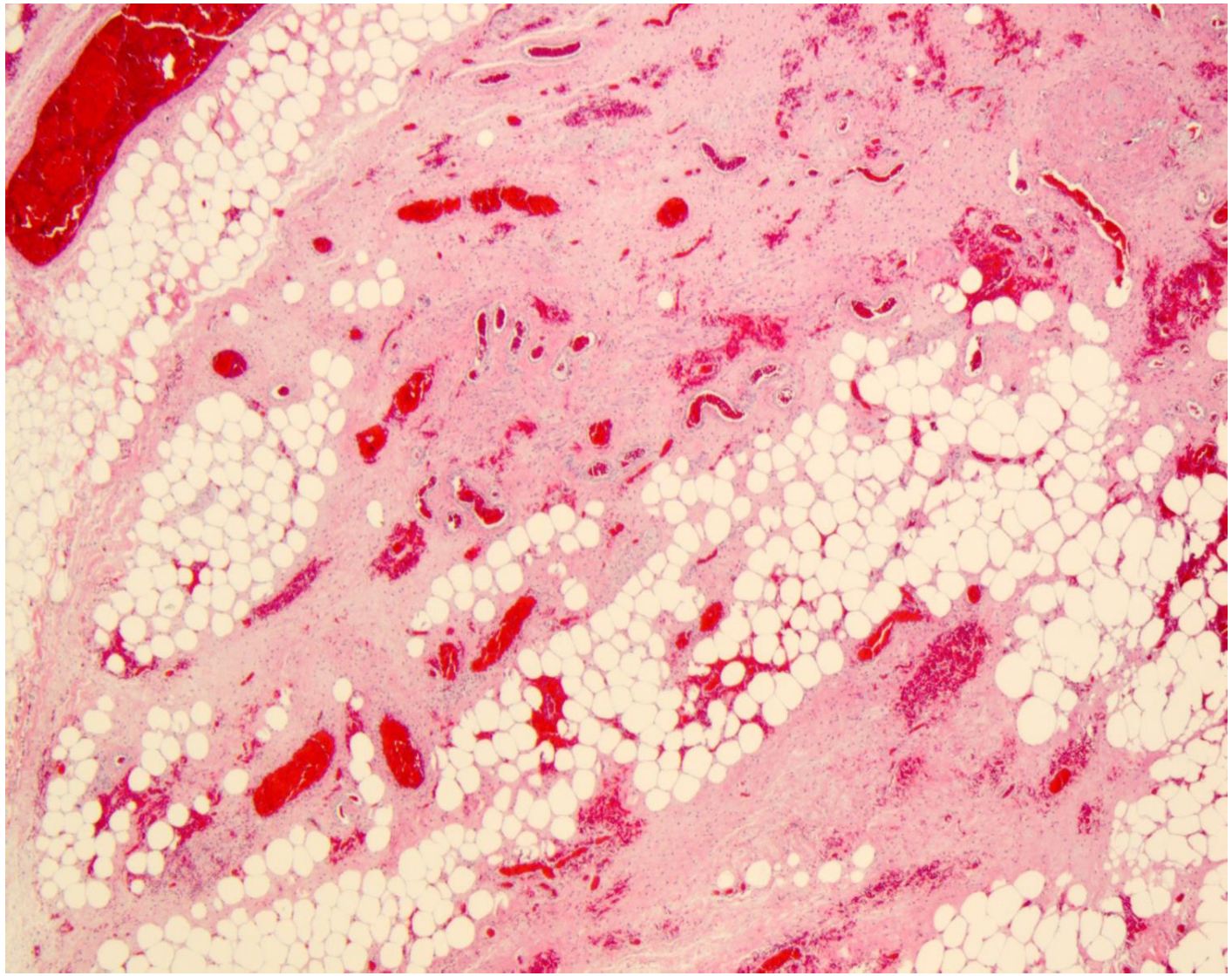
Mirkovic J and Fletcher CD, 2015

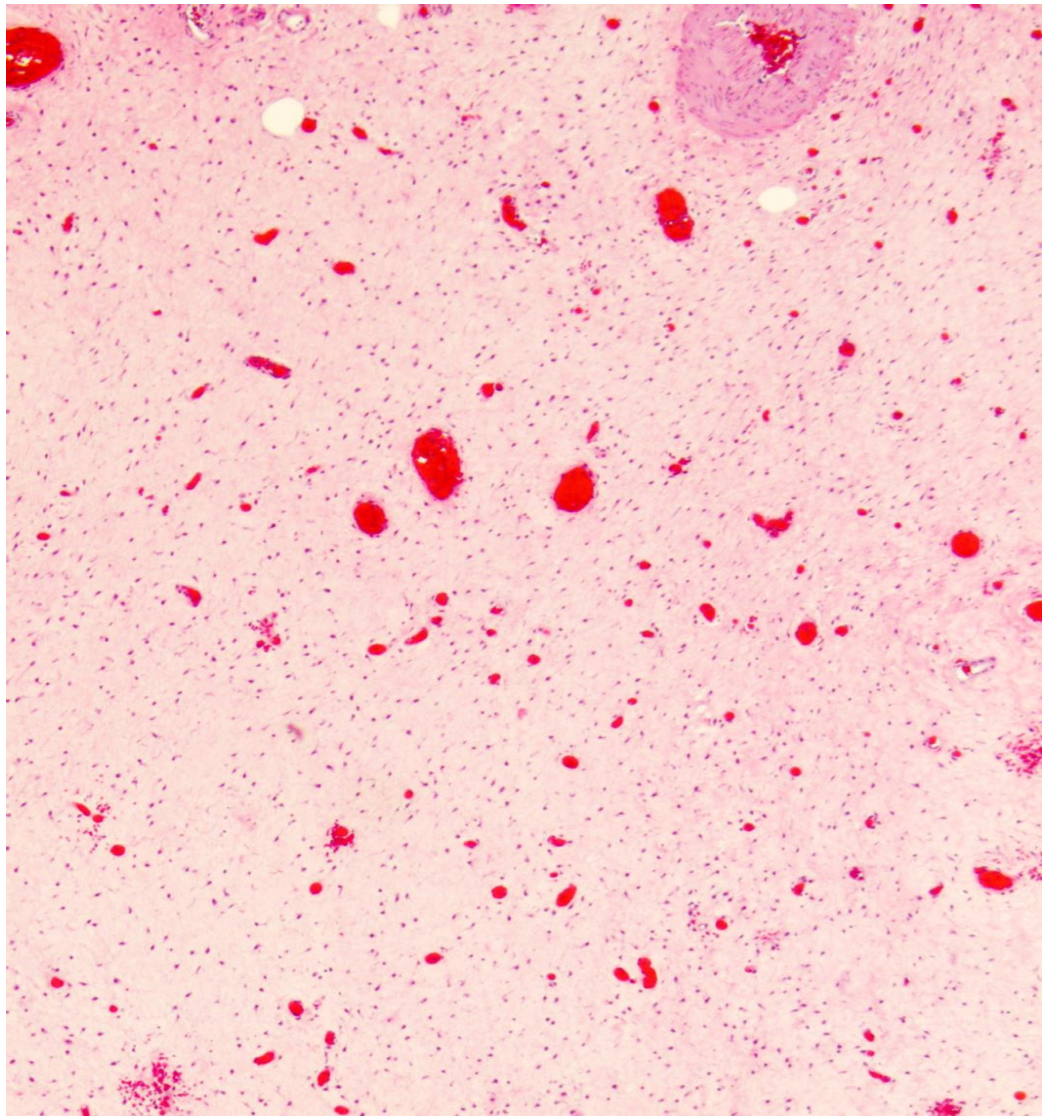
Aggressive Angiomyxoma

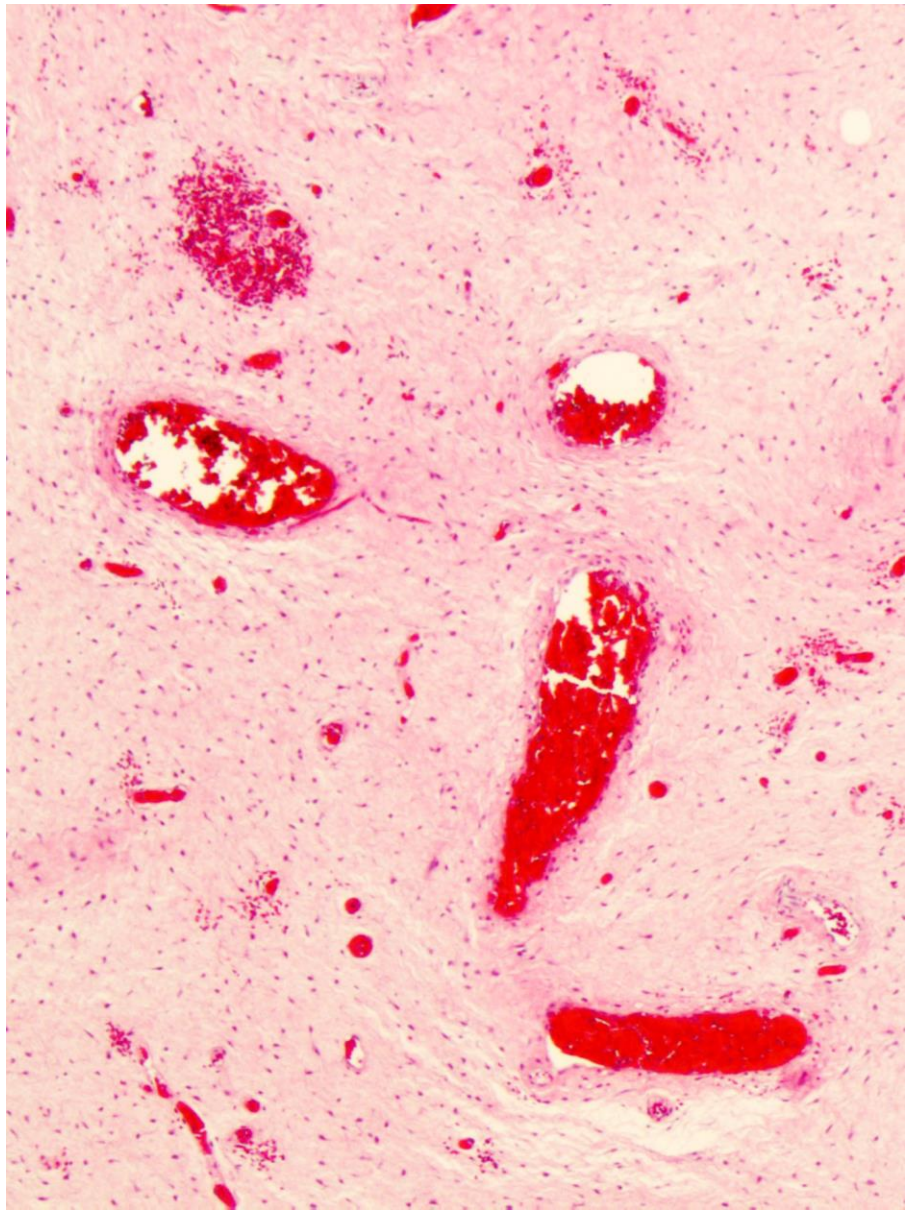


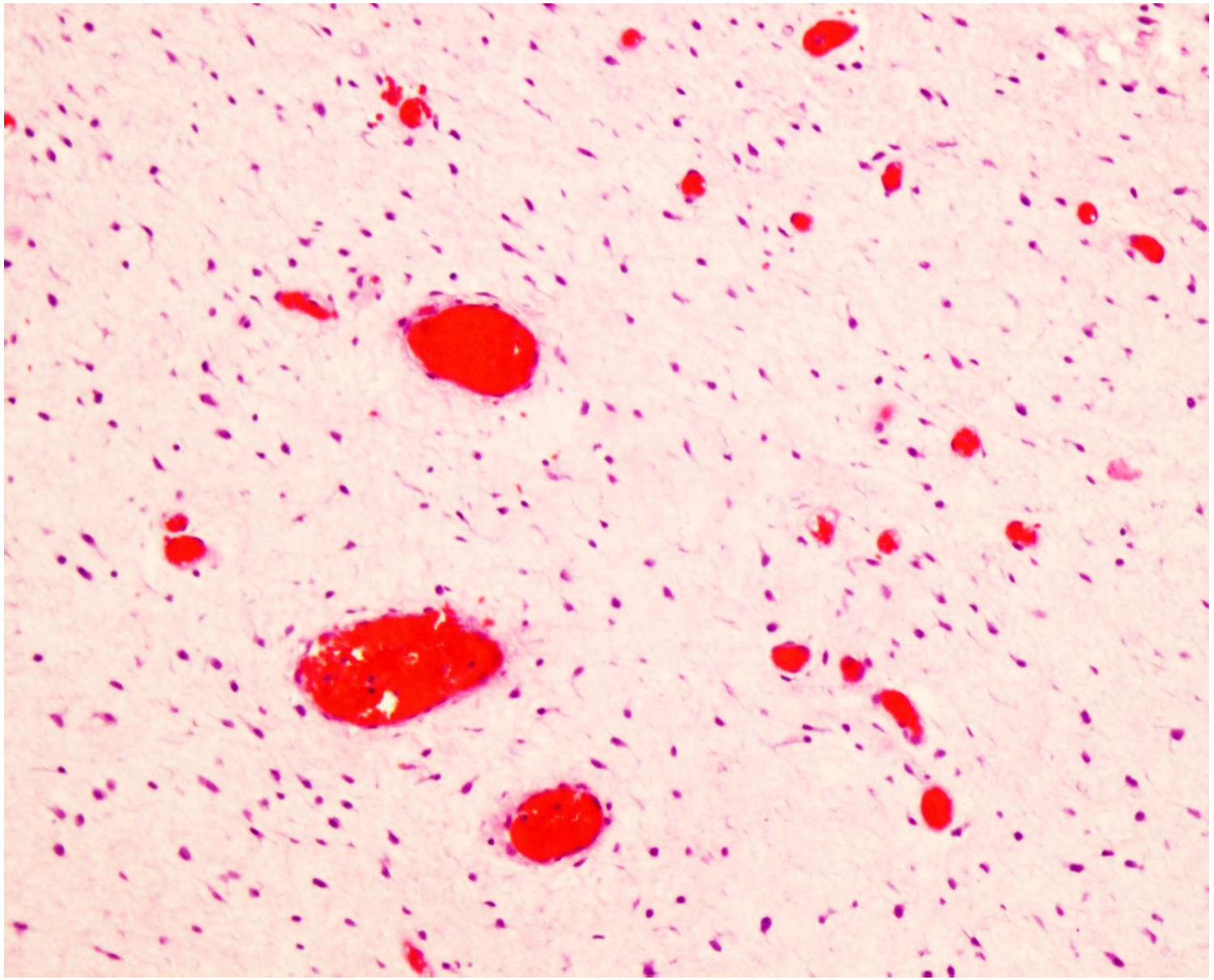
Aggressive Angiomyxoma

- Women < 40 years of age
- Ill-defined swelling
  - it can mimic a Bartholin gland cyst or hernia
- Much larger and extends more deeply than initially appreciated on pelvic examination
- Indolent tumor, with a tendency to recur locally since its complete excision is usually difficult
  - Rare case with lung mt

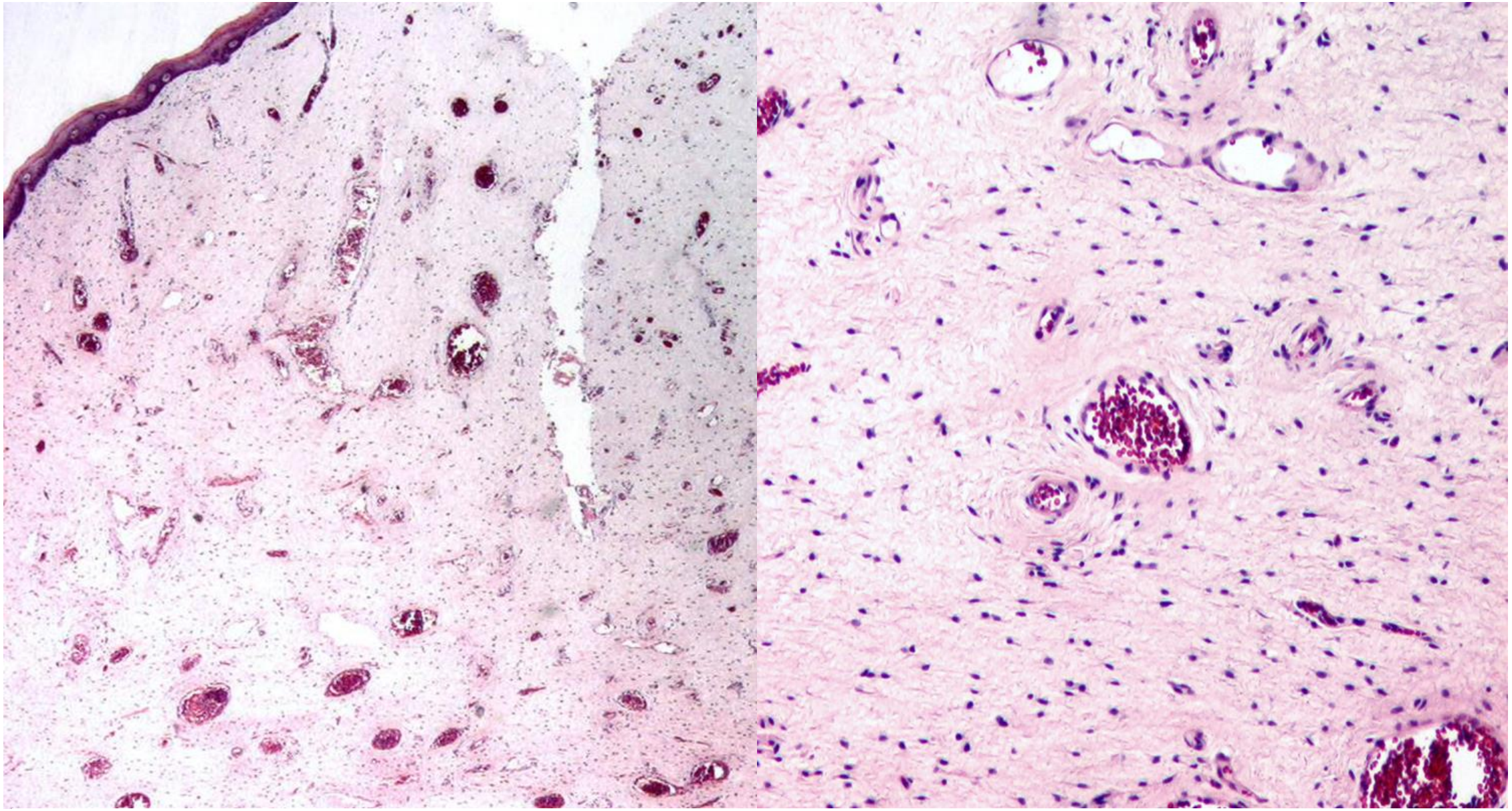








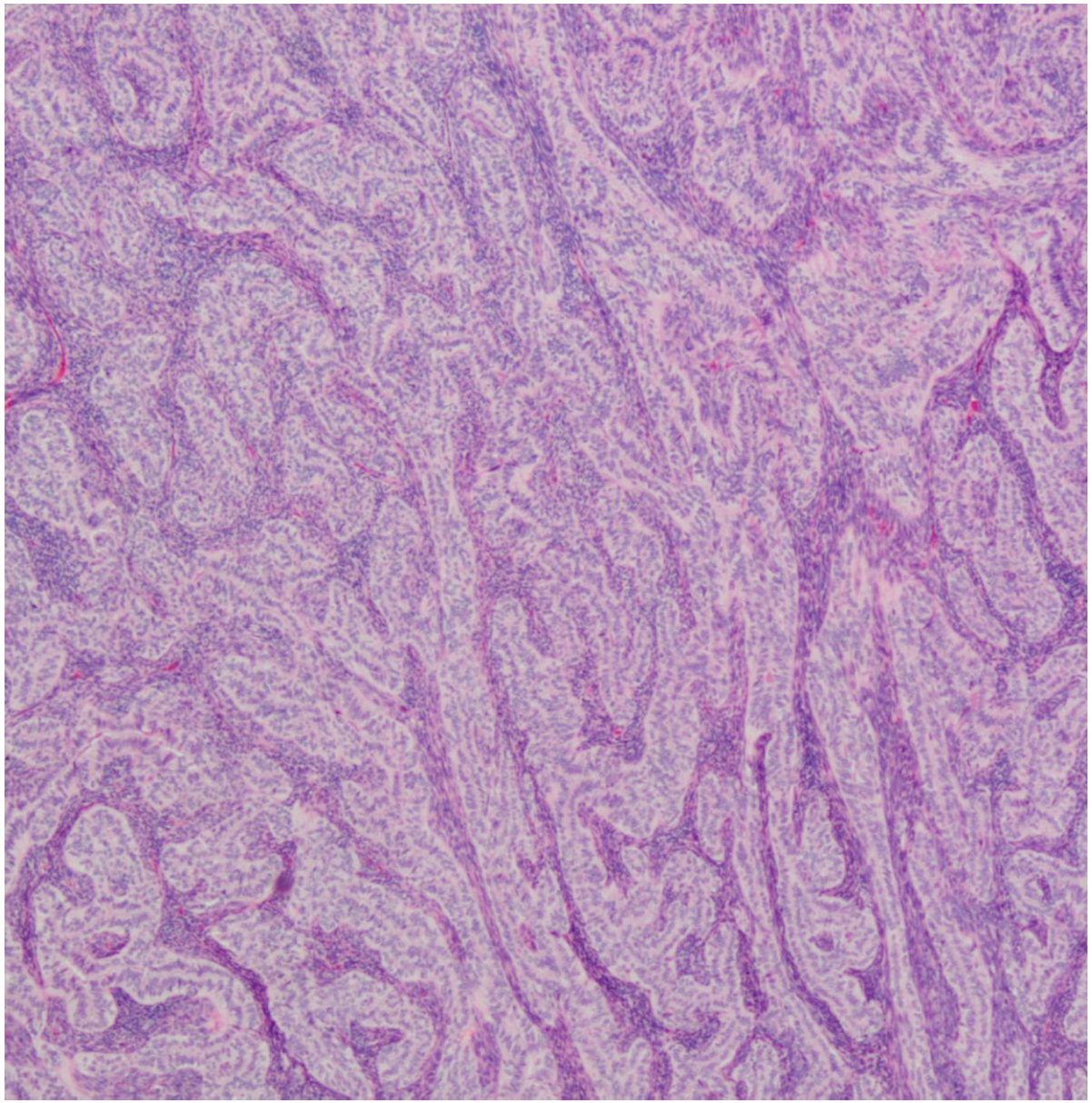
HMGA2 is + in 68% -90% of cases, but not entirely sensitive or specific

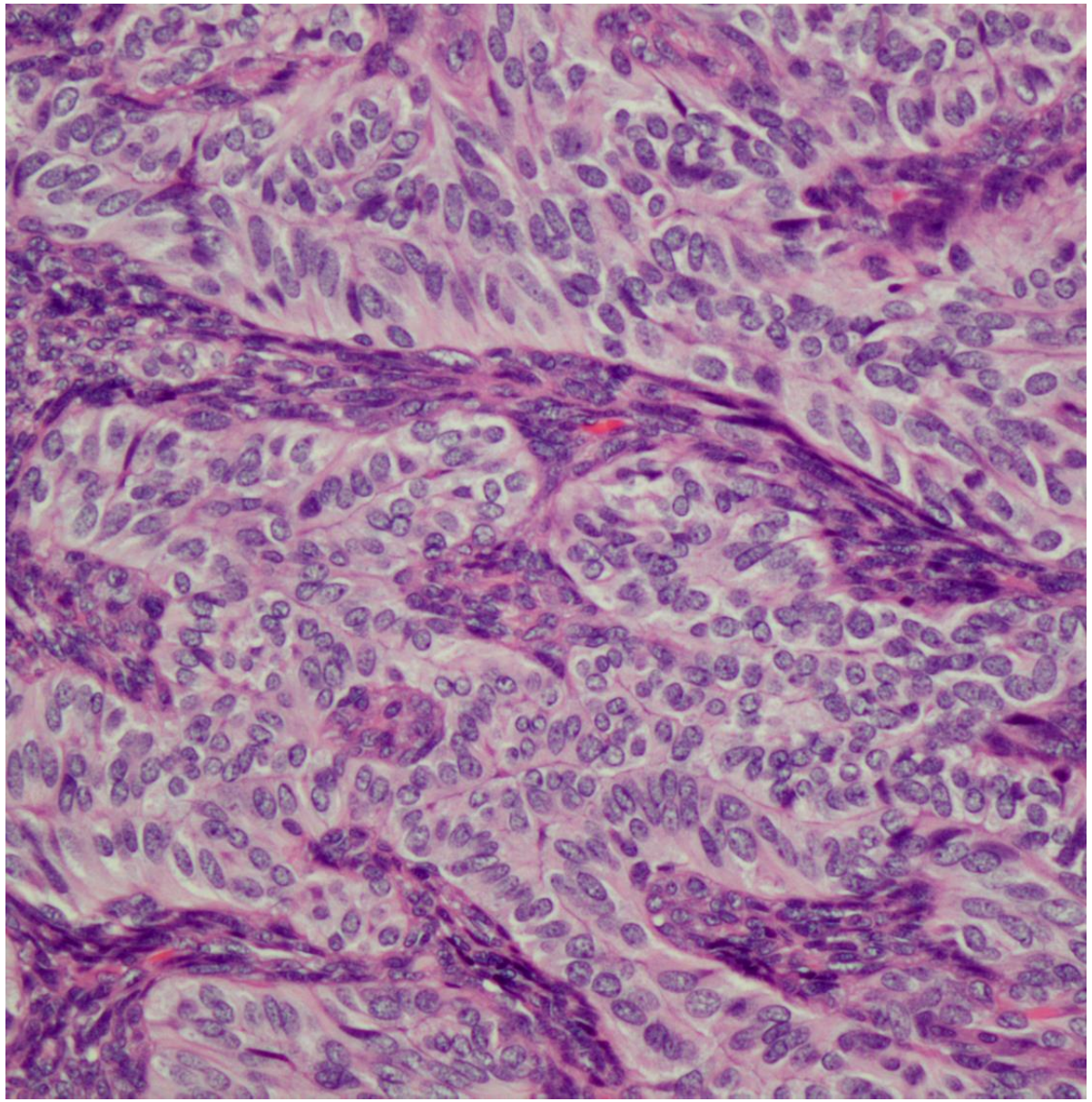


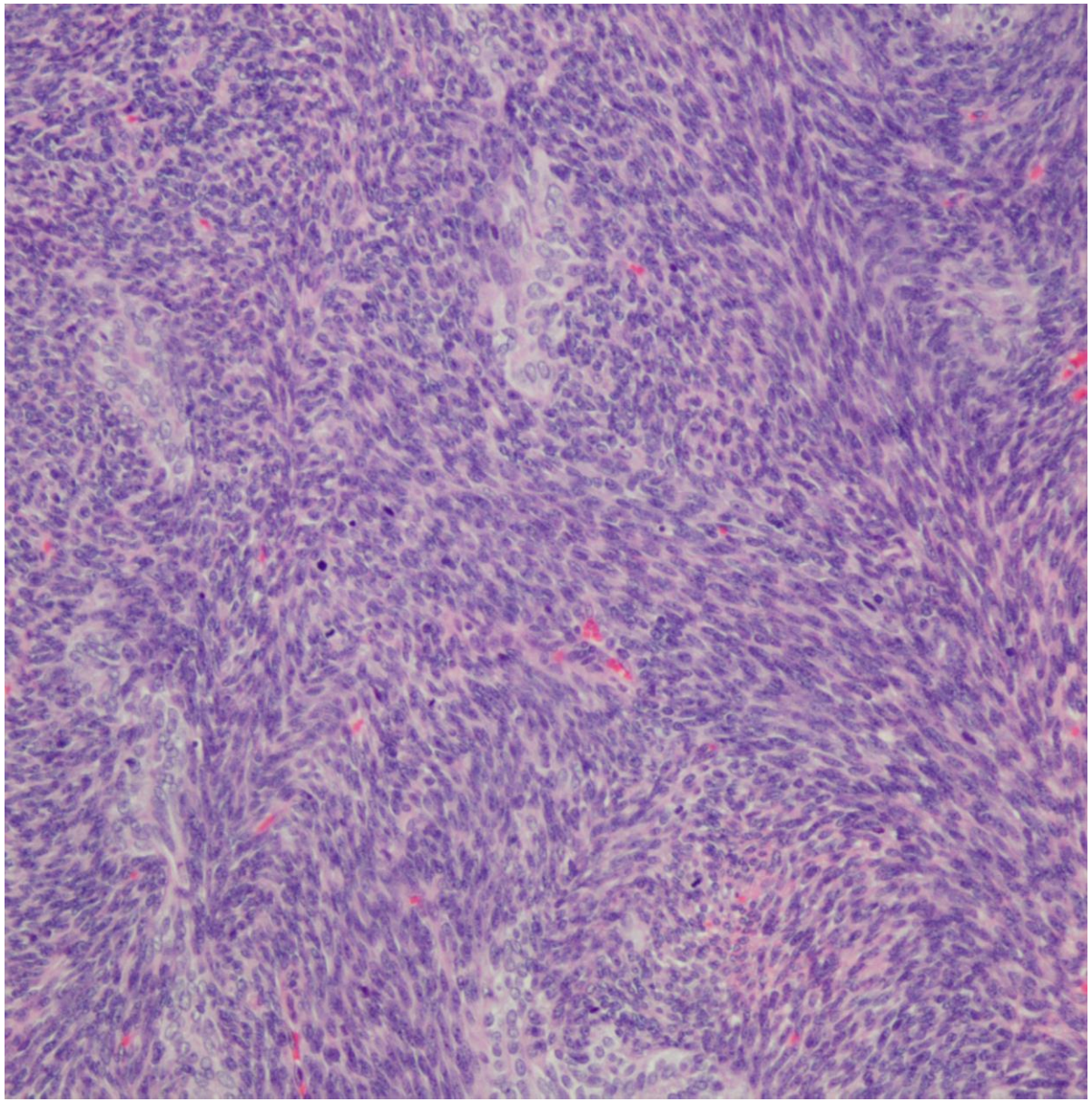
Loose stroma and delicate vessels mimicking the histology of aggressive angiomyxoma can be seen in a normal cervix or vagina

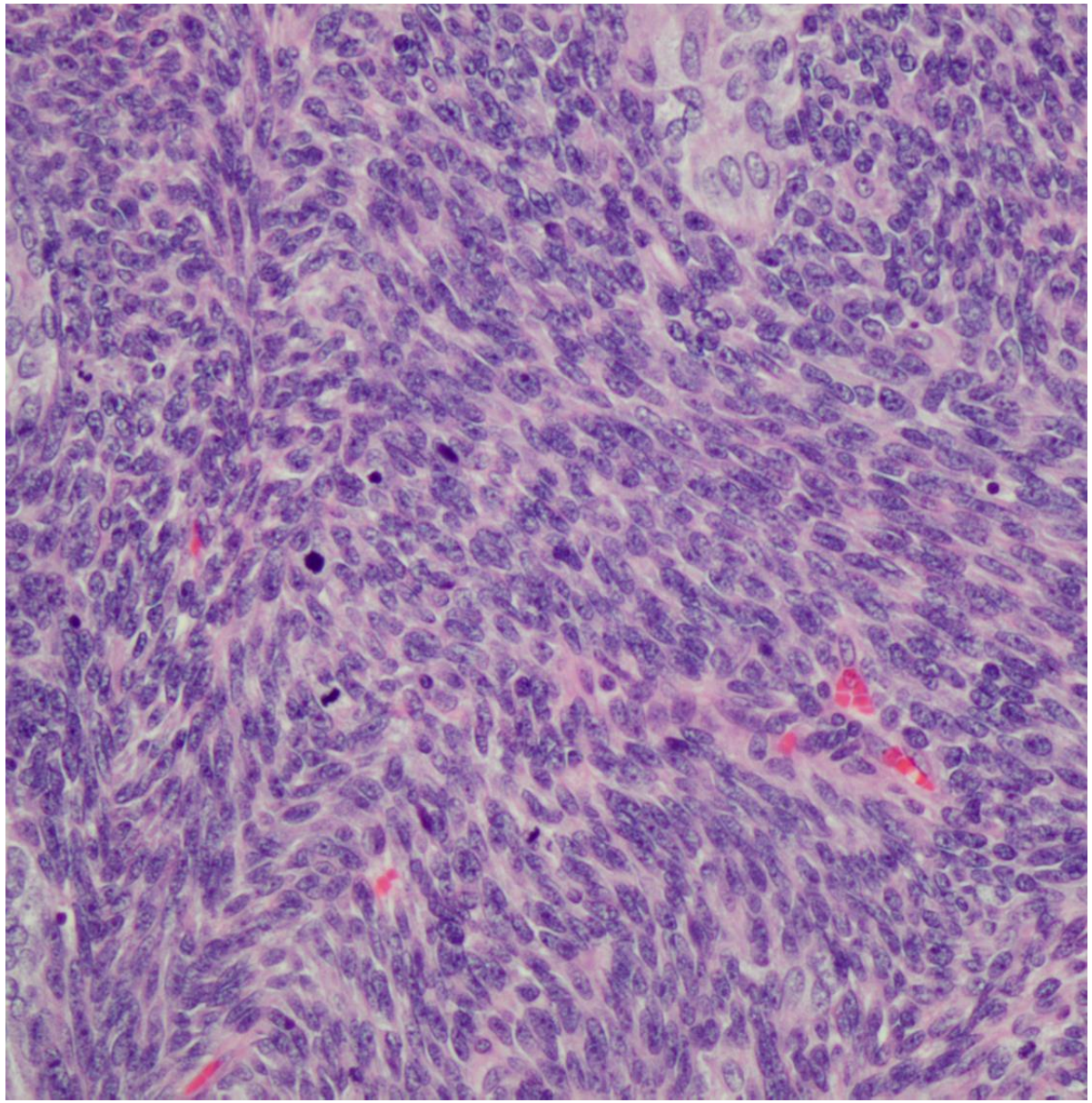
Case 2, Clinical History

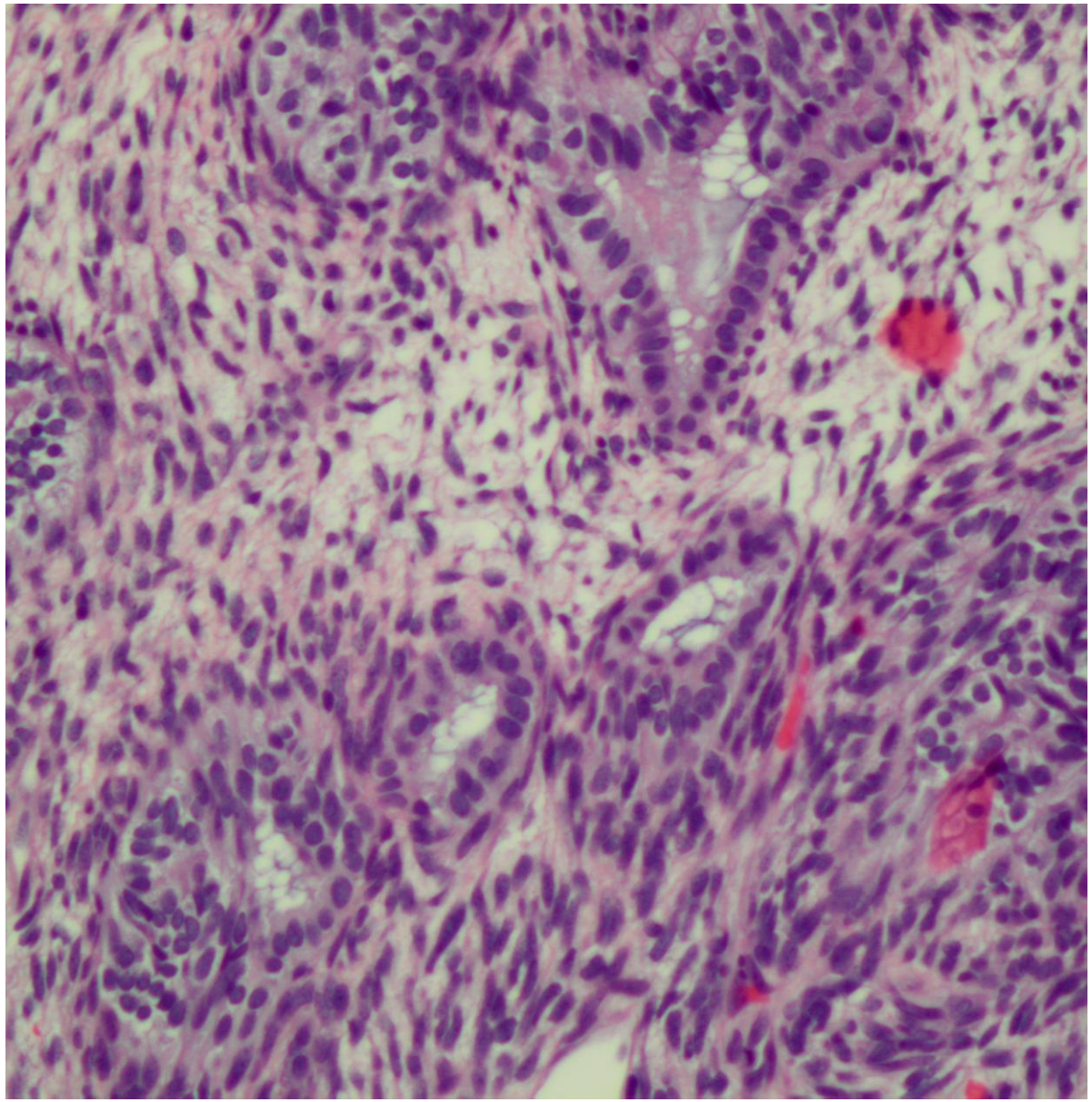
- A 29 y.o. African-American female presented with a right, non-tender, soft vulvar mass
  - Family Hx:
    - Mother, breast and ovarian carcinomas
- Wide local excision
  - 8 cm mass extending to the margins
- Chemotherapy
- Radiotherapy
- Radical resection
  - 2 mm residual tumor
    - 3 mitoses per 10 HPFs
    - No vascular/lymphatic invasion
    - Margins free
- F/u, no evidence of disease at 8 years

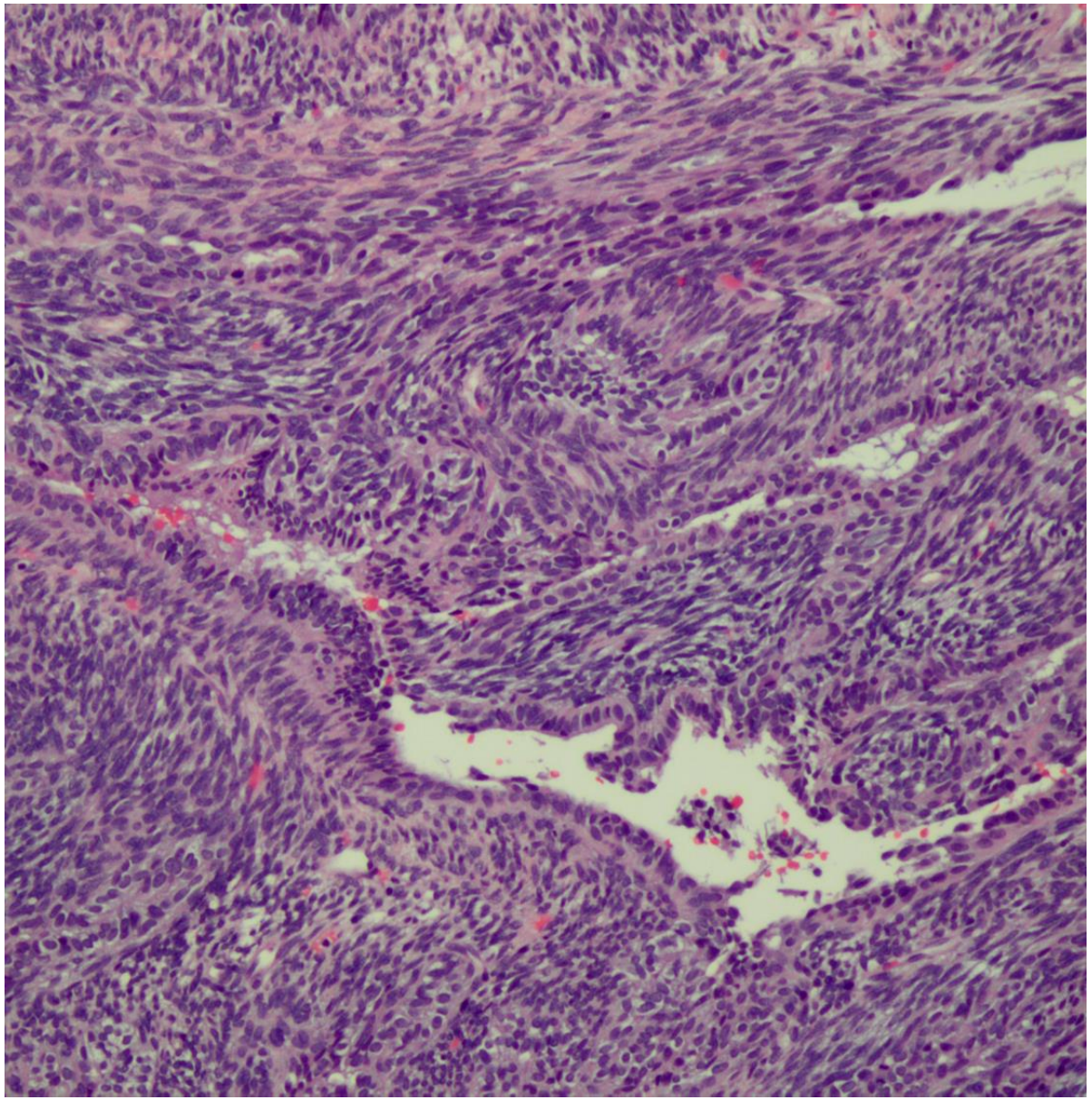


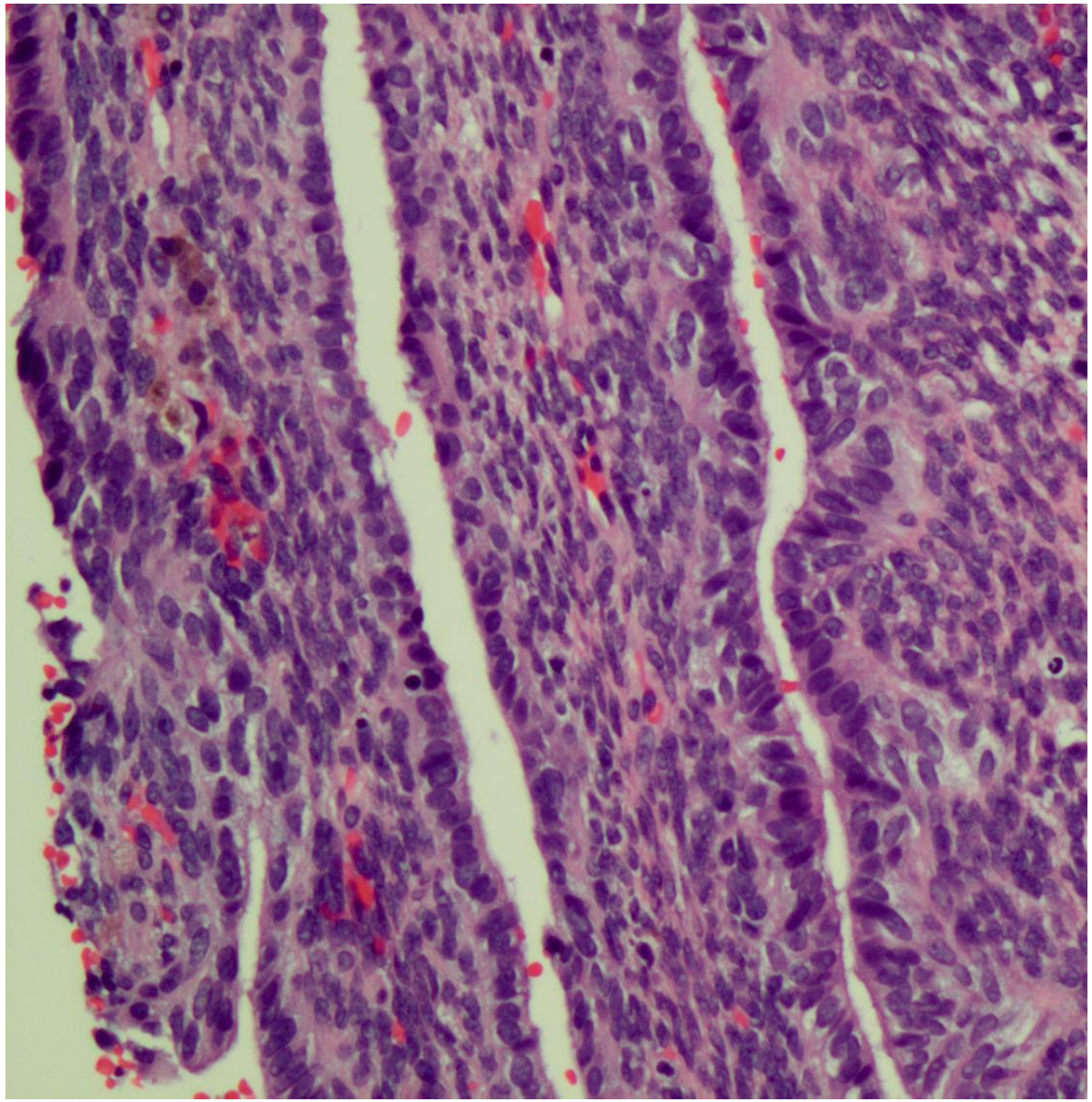


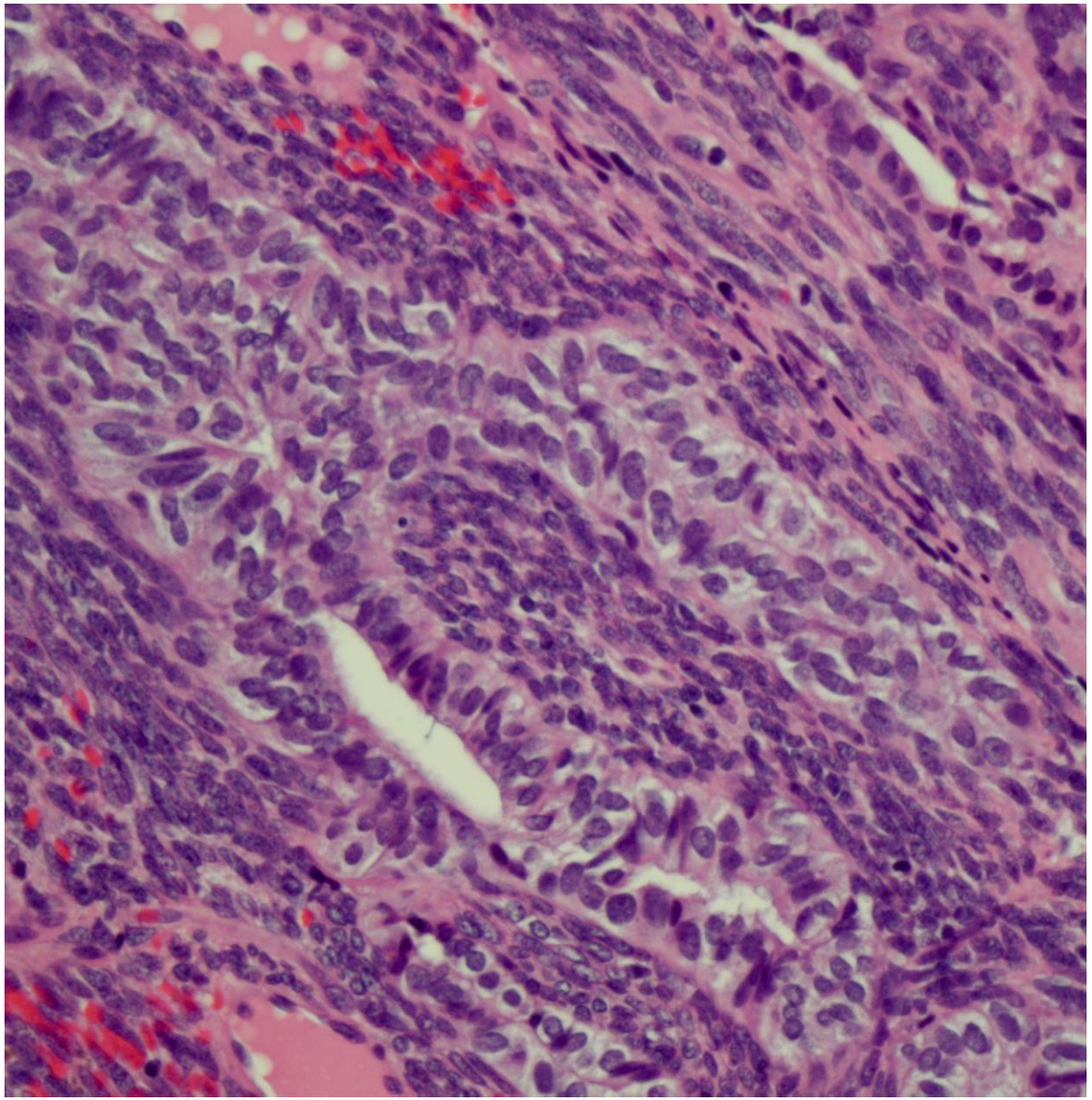


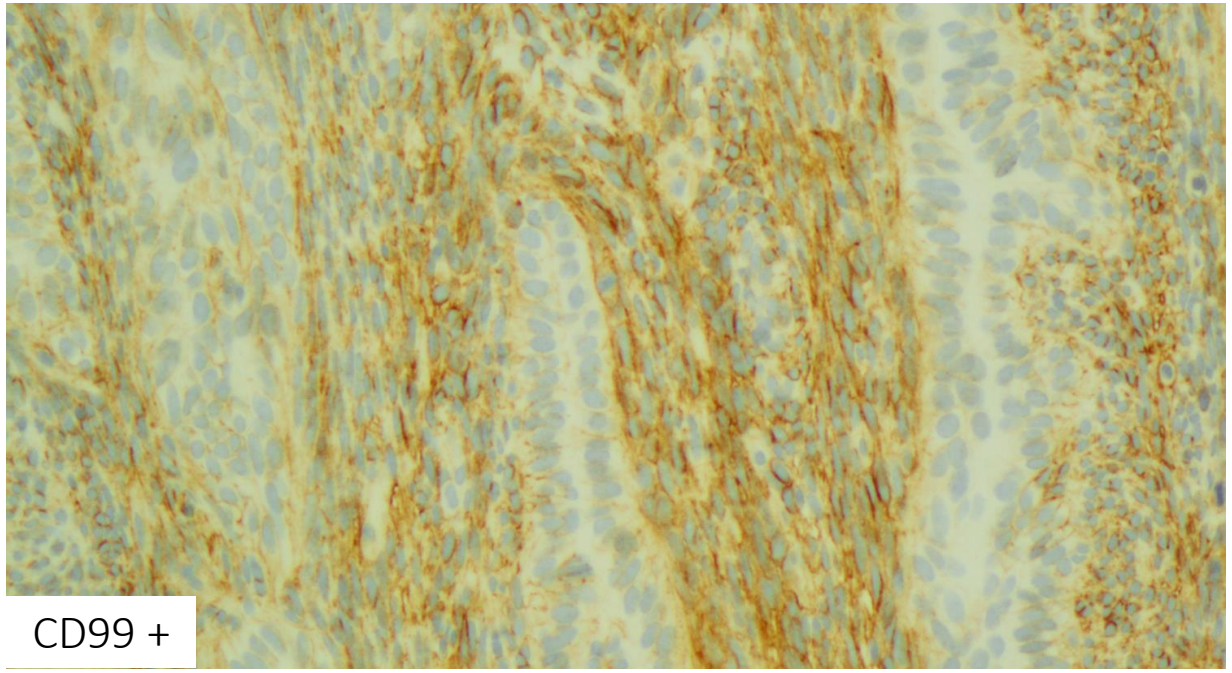




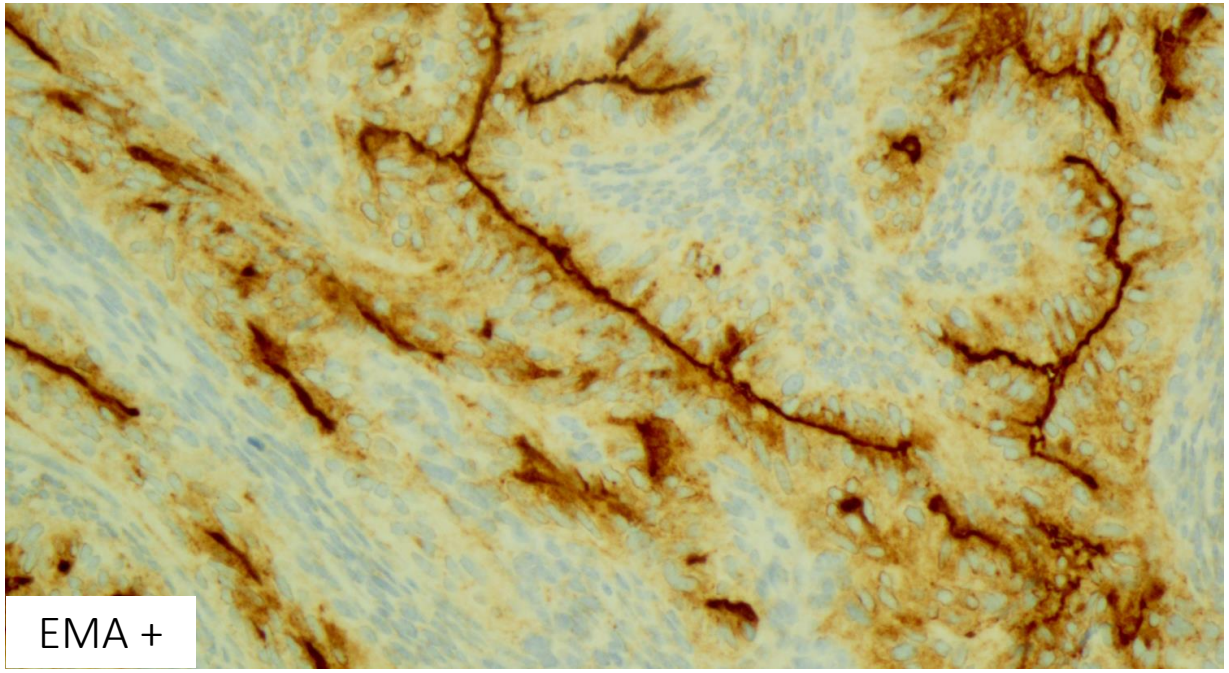




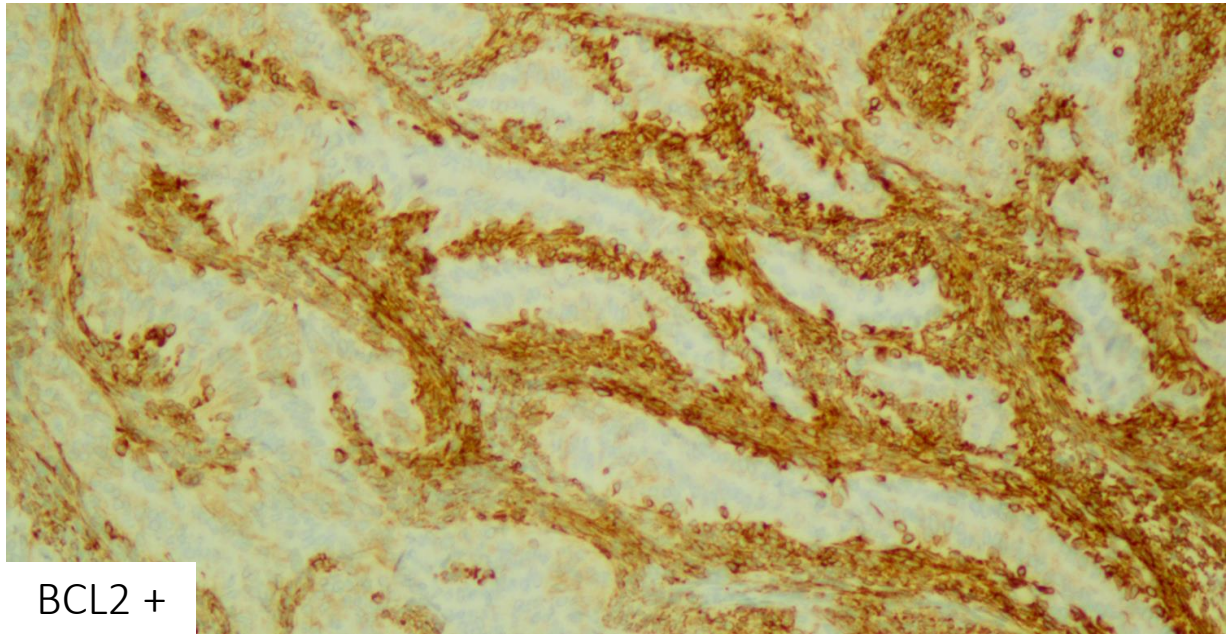




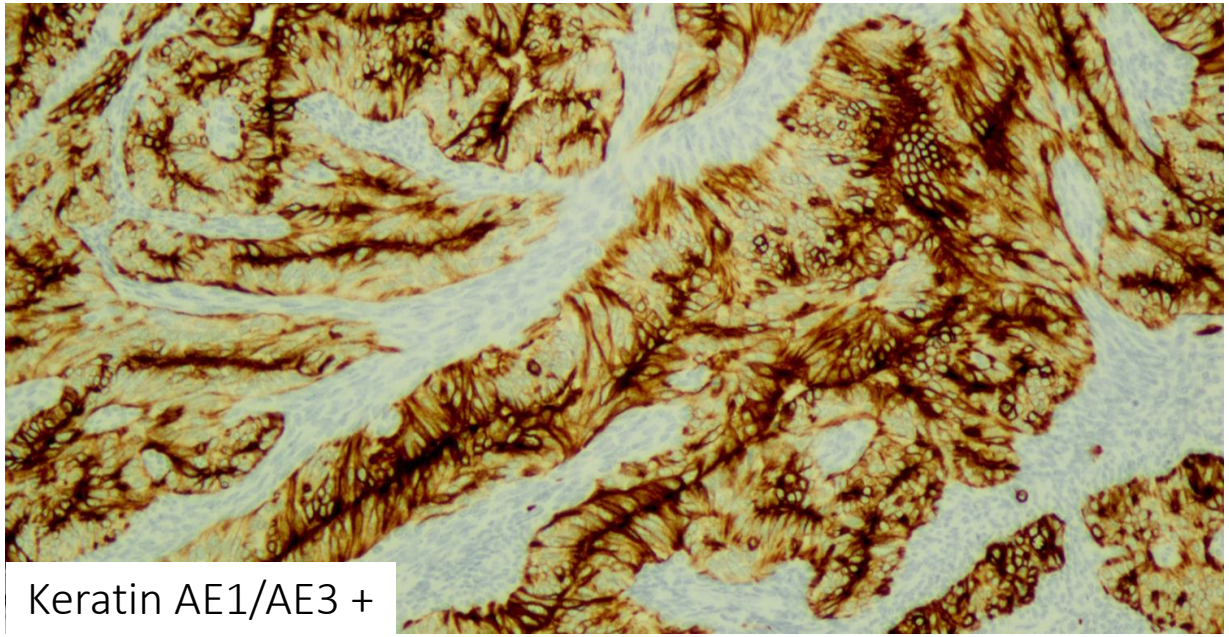
CD99 +



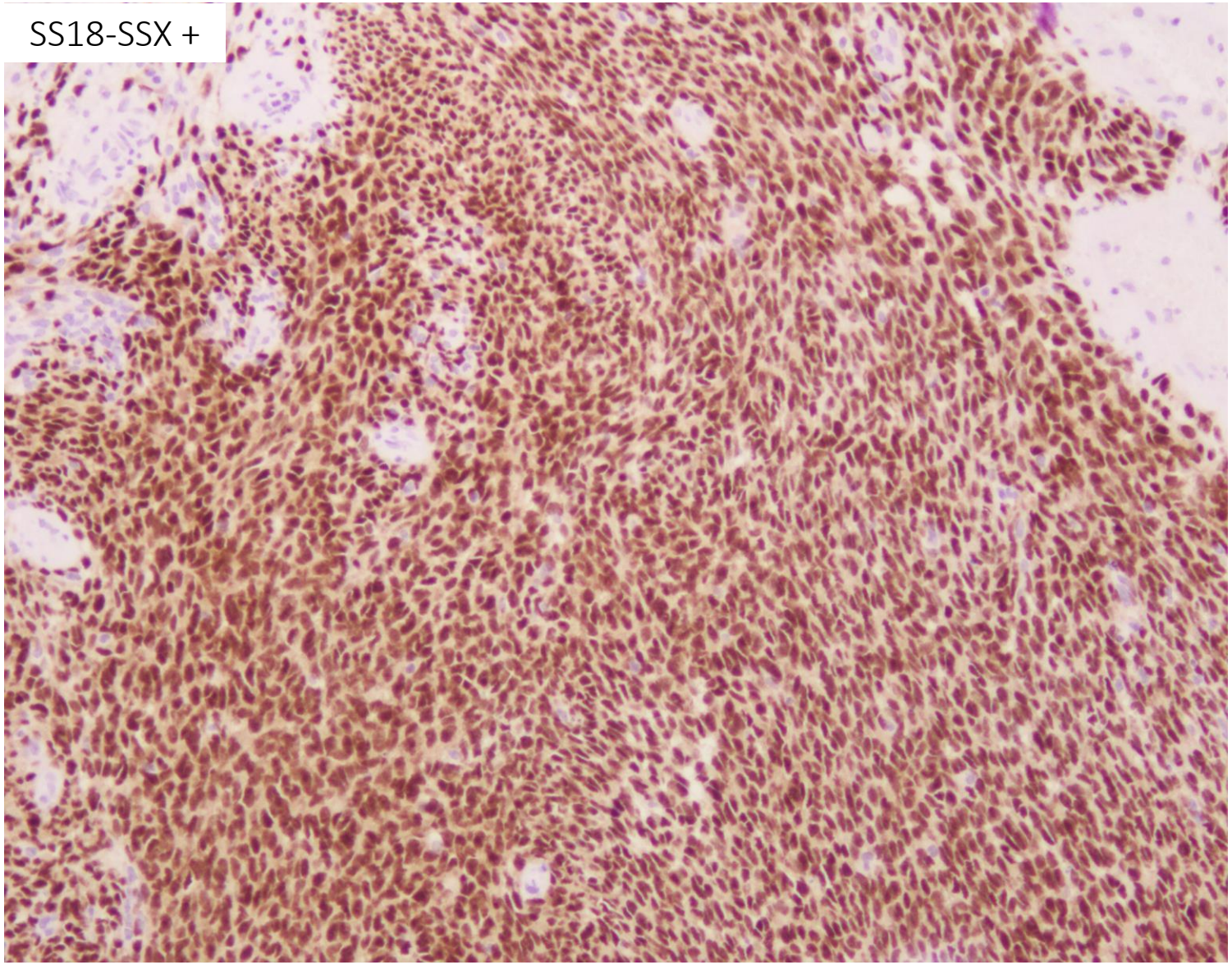
EMA +



BCL2 +



Keratin AE1/AE3 +



FISH: *SS18* rearrangement

Diagnosis

Synovial sarcoma of the vulva

Synovial sarcoma of the vulva

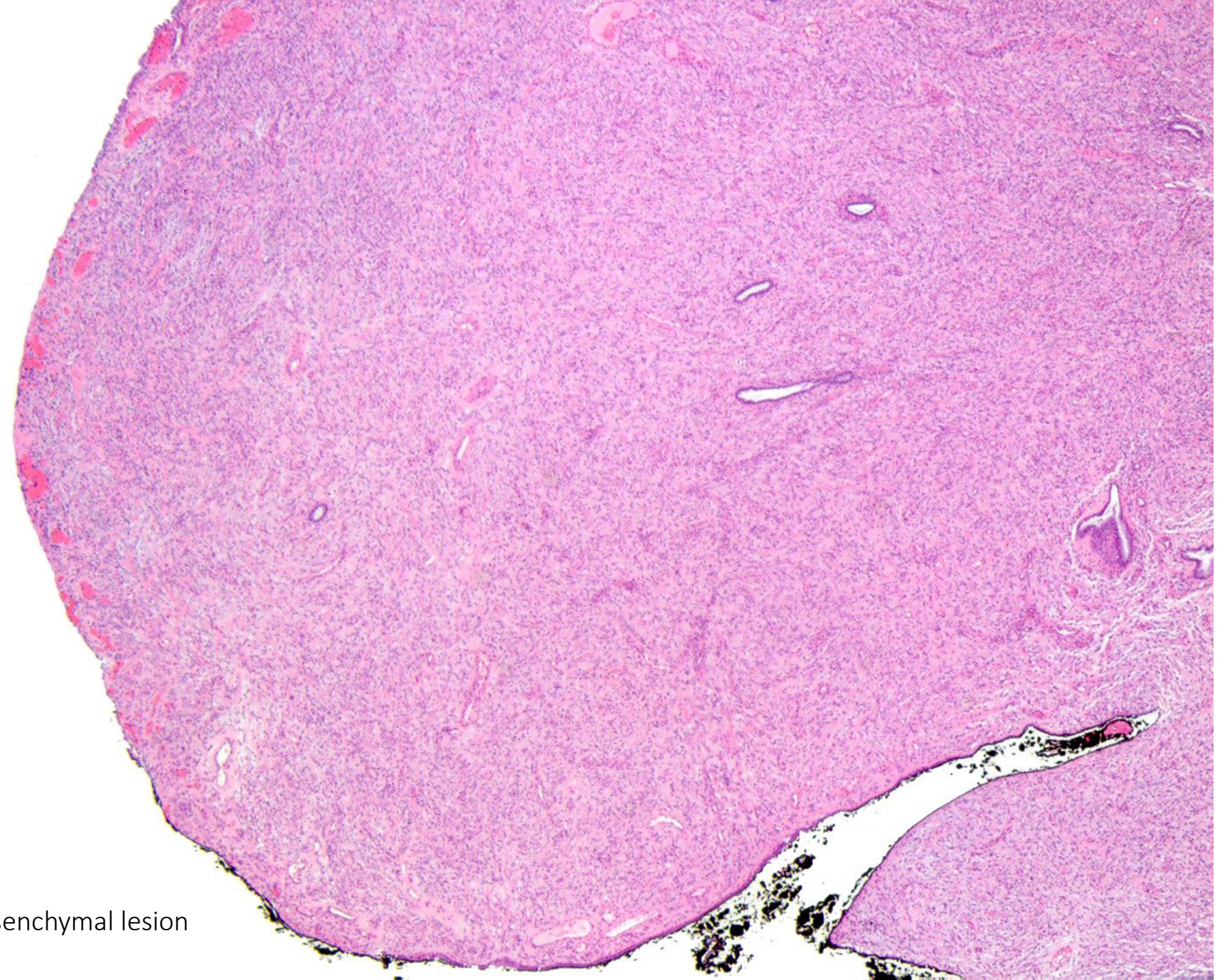
- Extremely rare
- Painless and deep-seated tumor
- Pts' age, 21-62 years
- Tumor size, 0.8-9 cm
- Monophasic (spindle cell) or biphasic (spindle and epithelial cells)
- T (X;18) (p11;q11) translocation resulting in a *SS18-SSX* fusion

Synovial Sarcoma of the Vulva

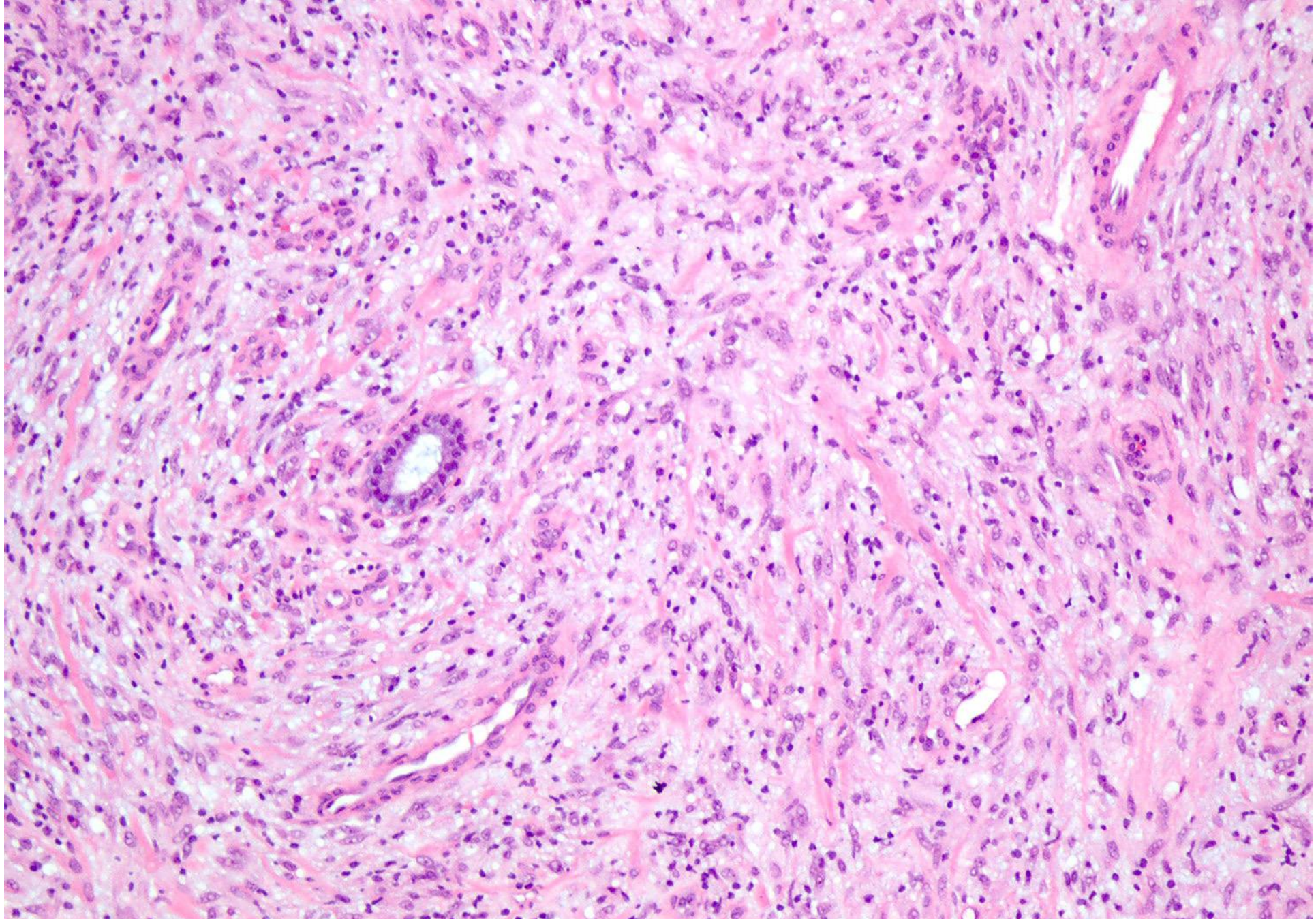
- Risk of local recurrence and mt
  - Long term follow-up is required
- Multimodality therapy

Case 3, Clinical History

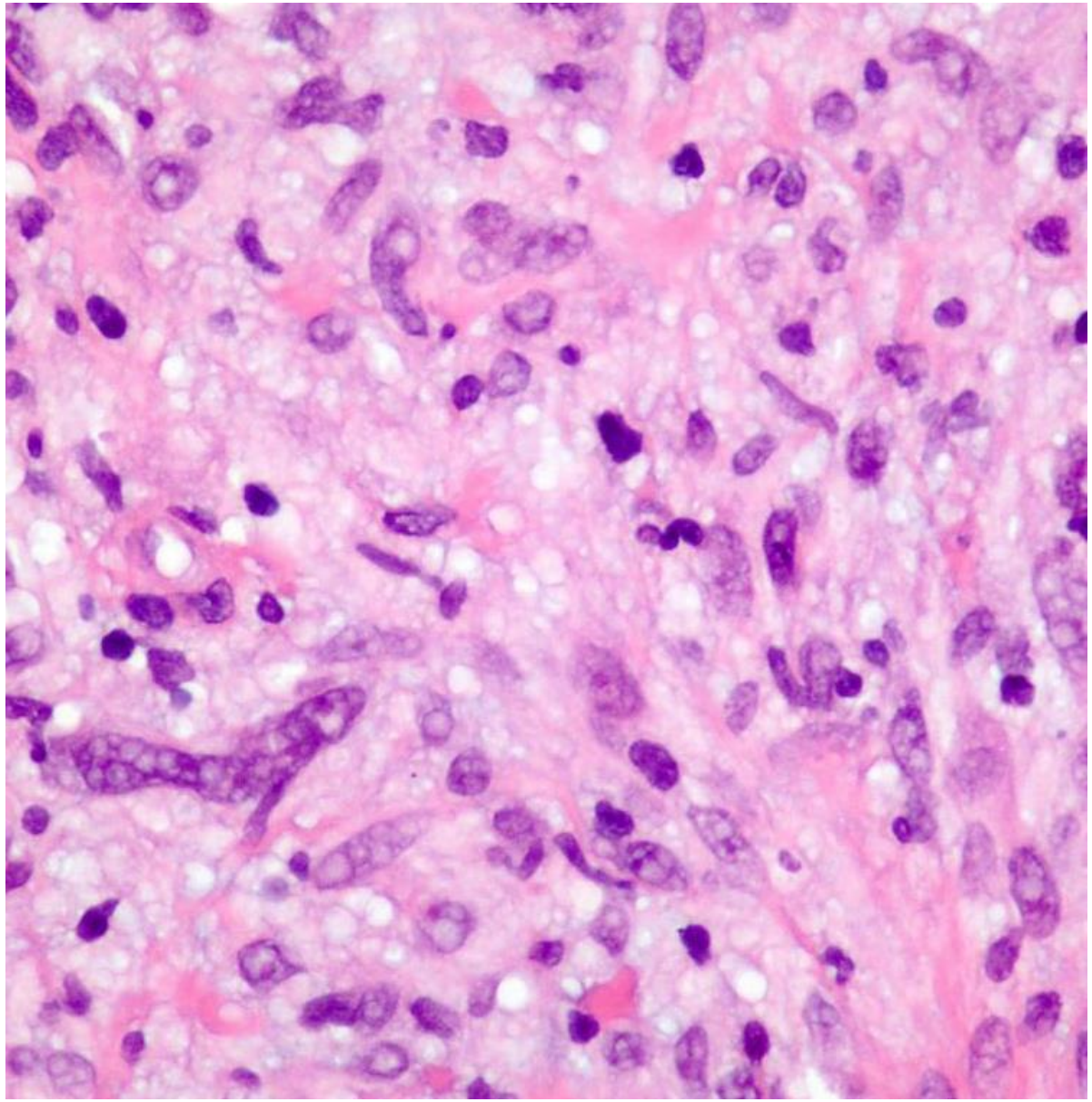
- A 30 year-old woman presented for a routine check-up
- Pap smear:
  - LSIL, cannot rule out HSIL
- HRHPV, +
- LEEP

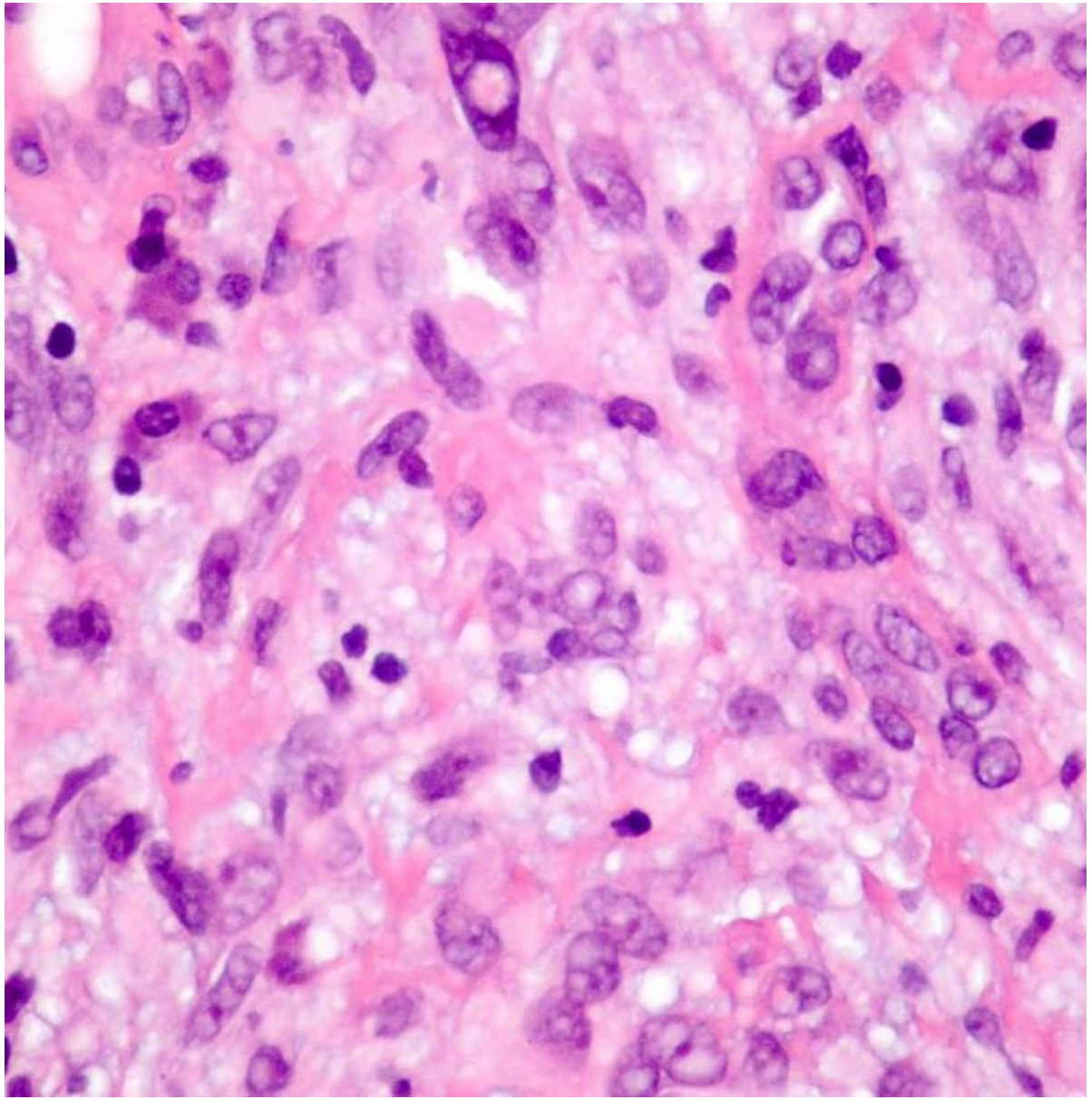


Polypoid mesenchymal lesion

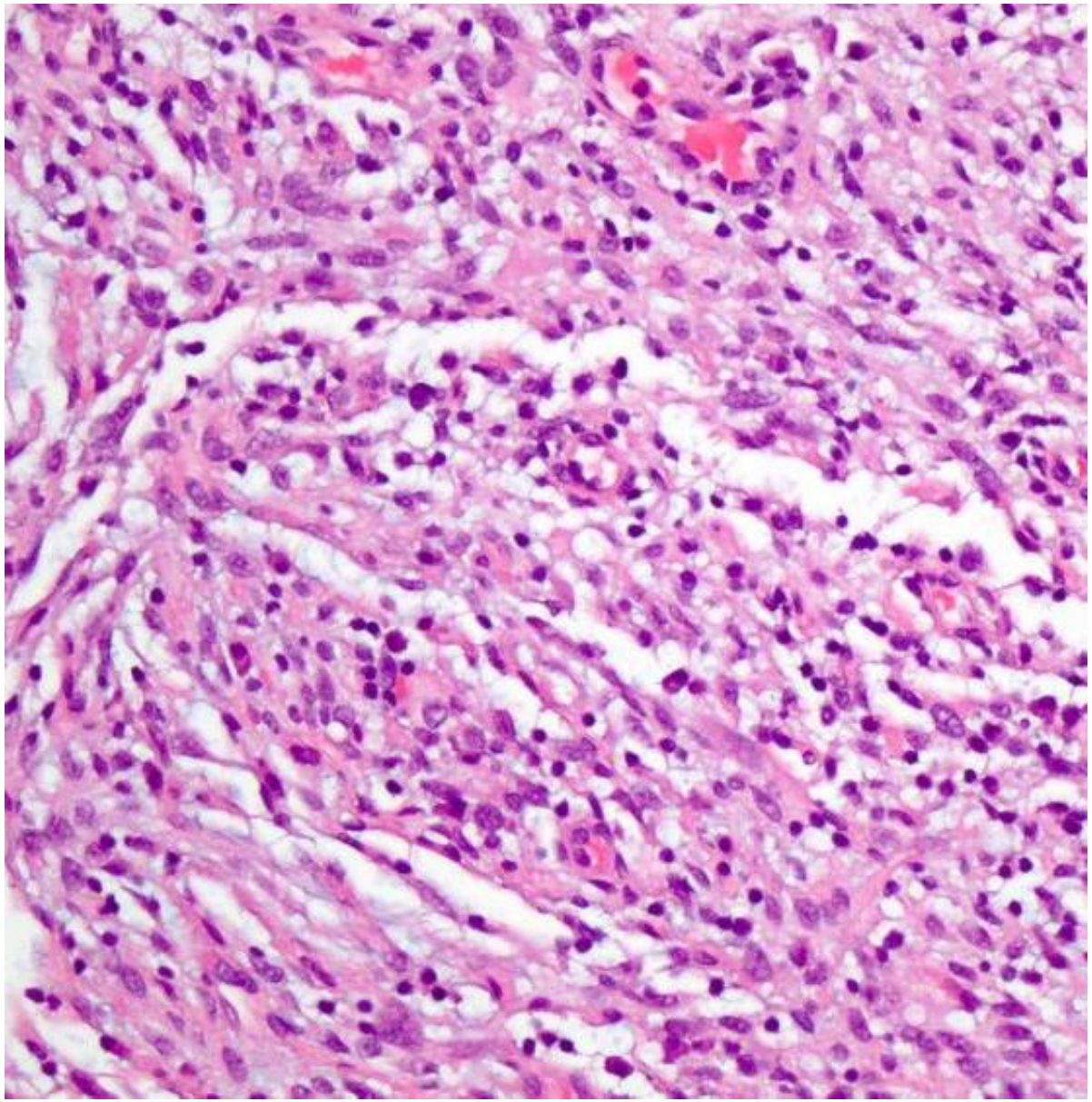


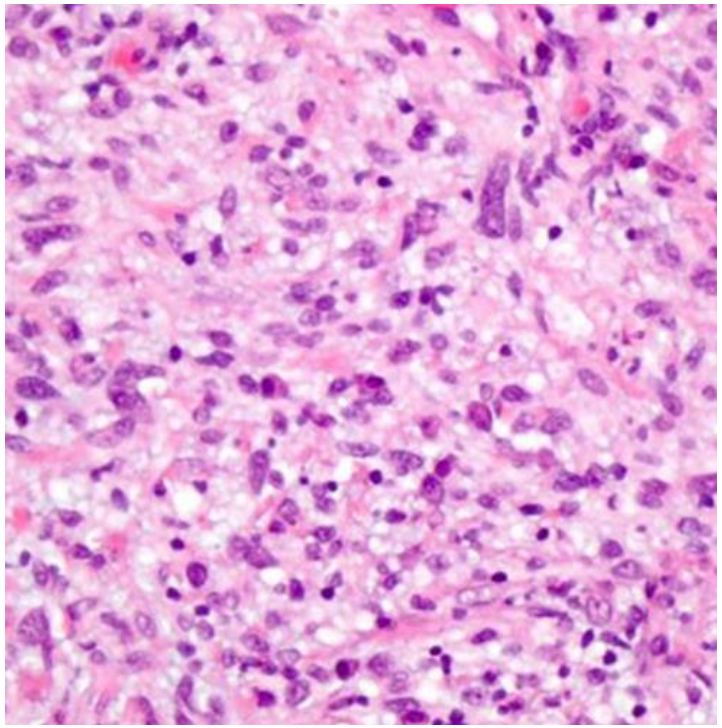
Proliferation of mesenchymal cells intermixed with inflammatory cells



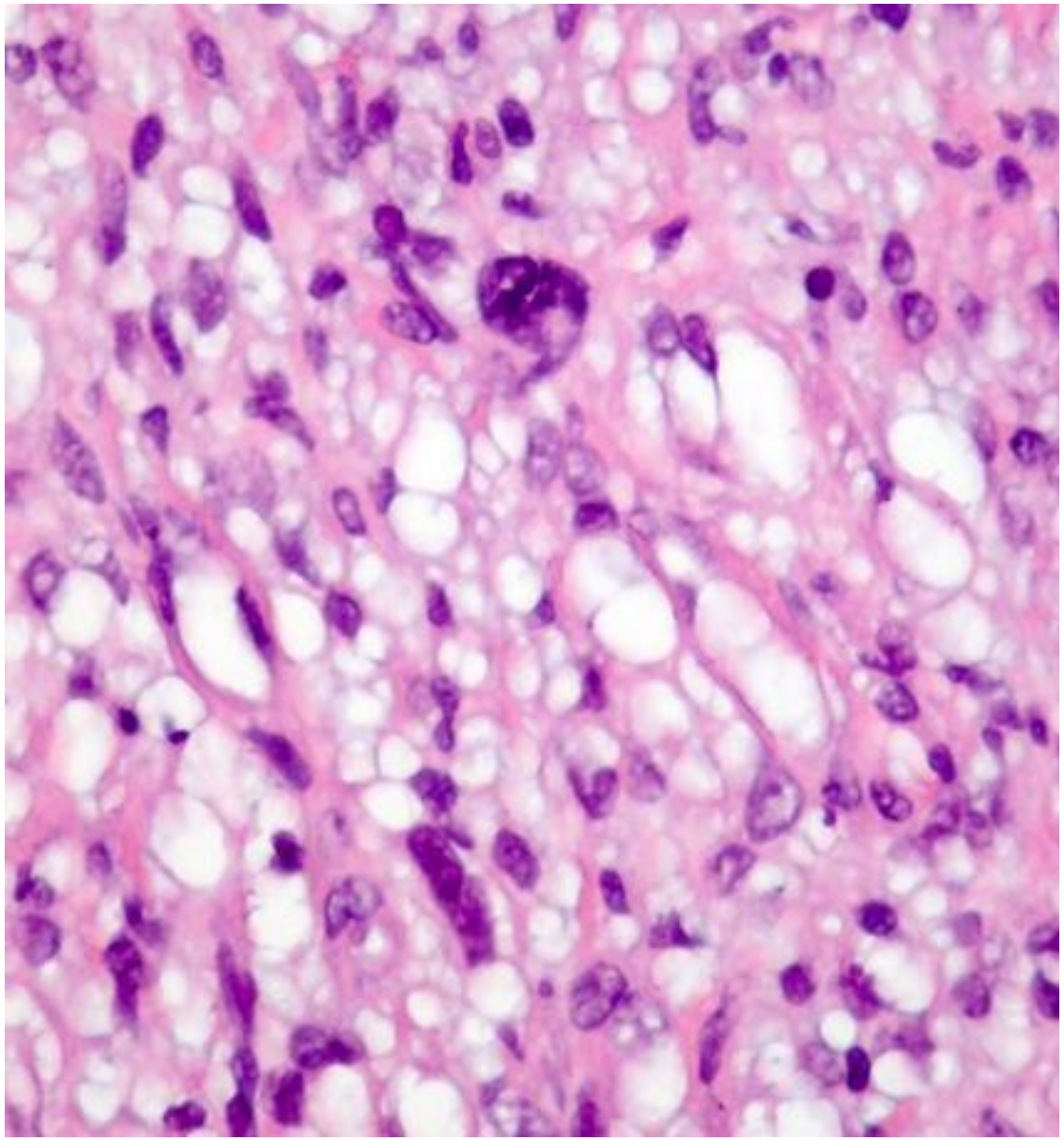


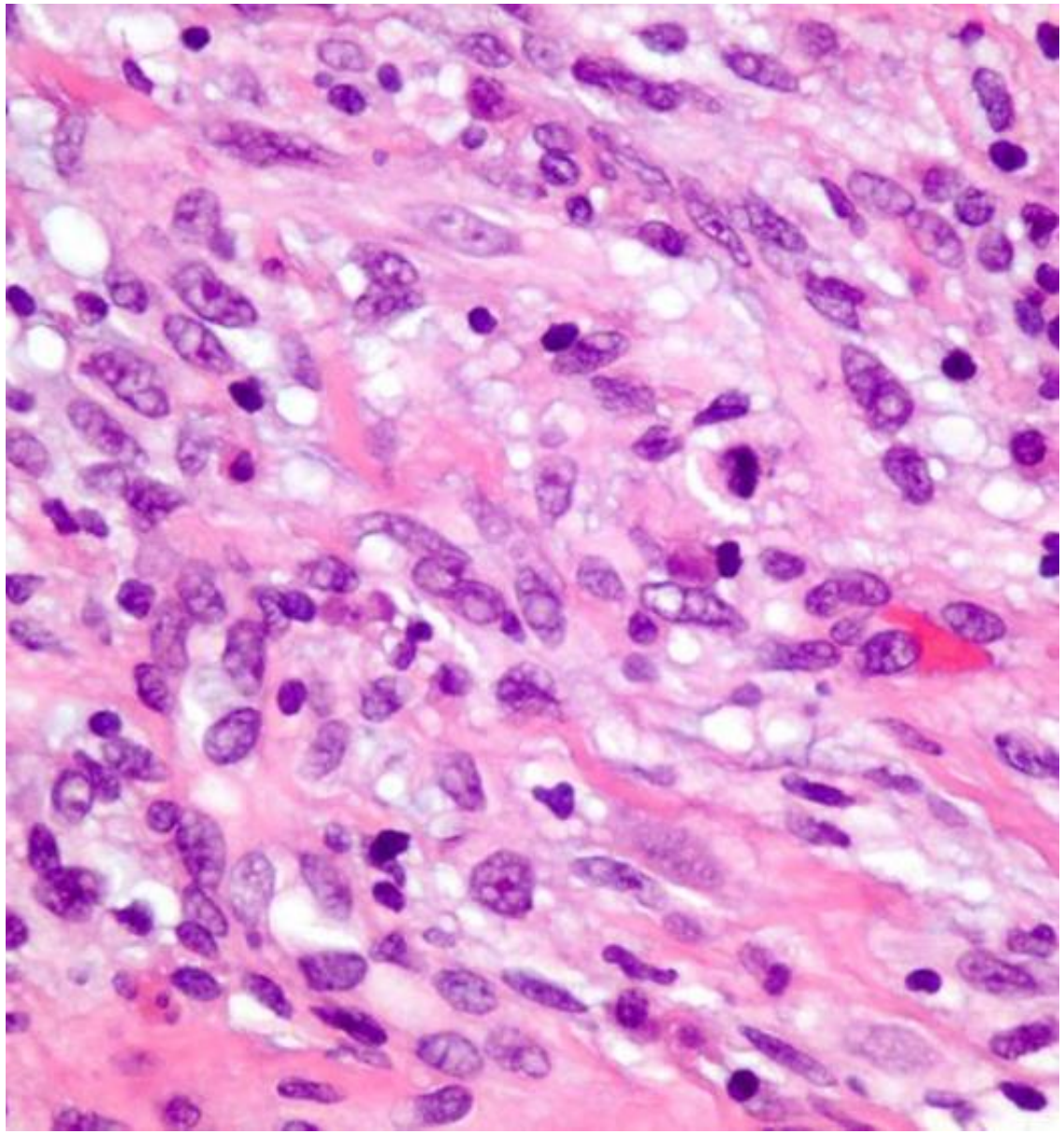
Marked nuclear pleomorphism



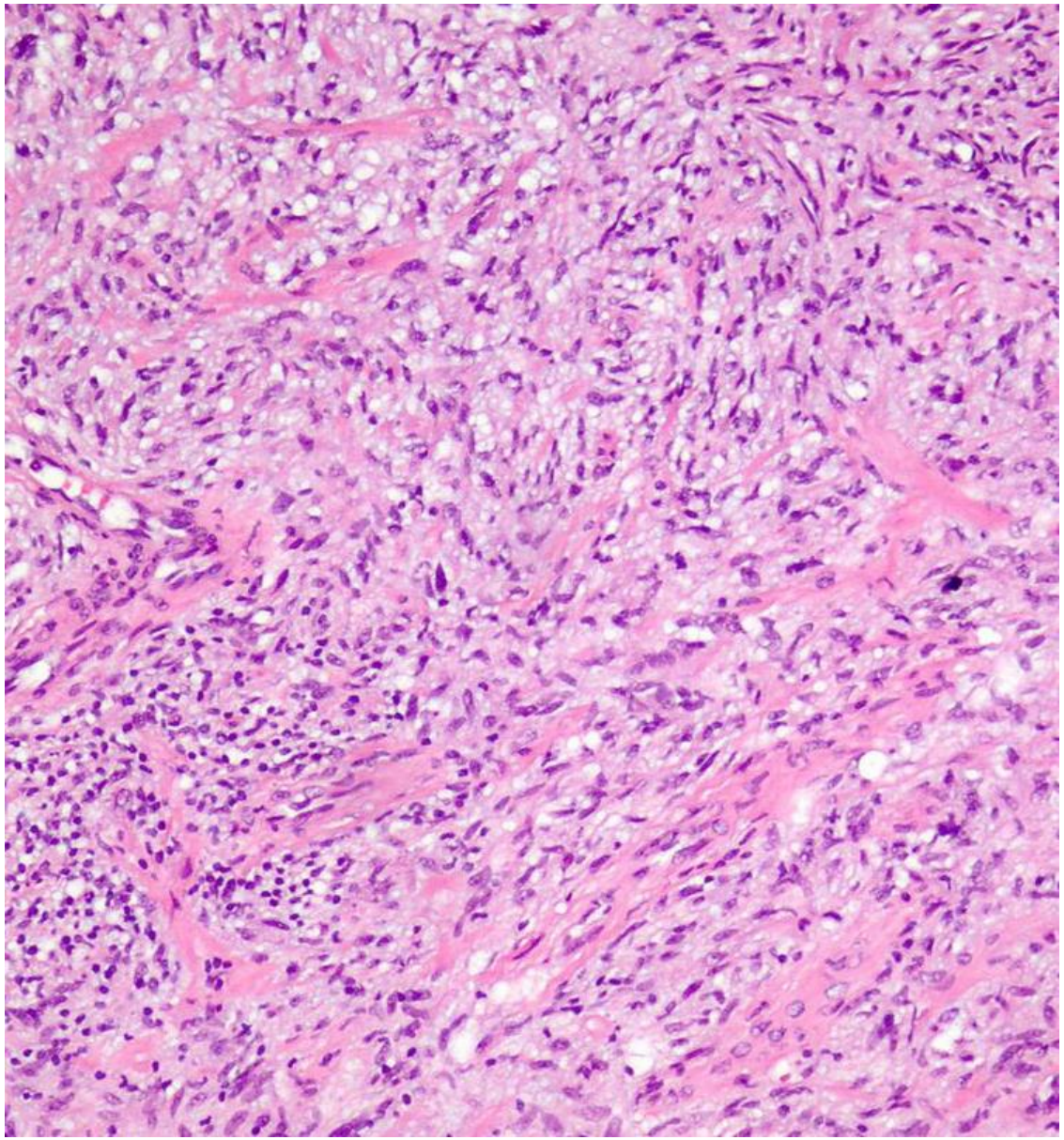


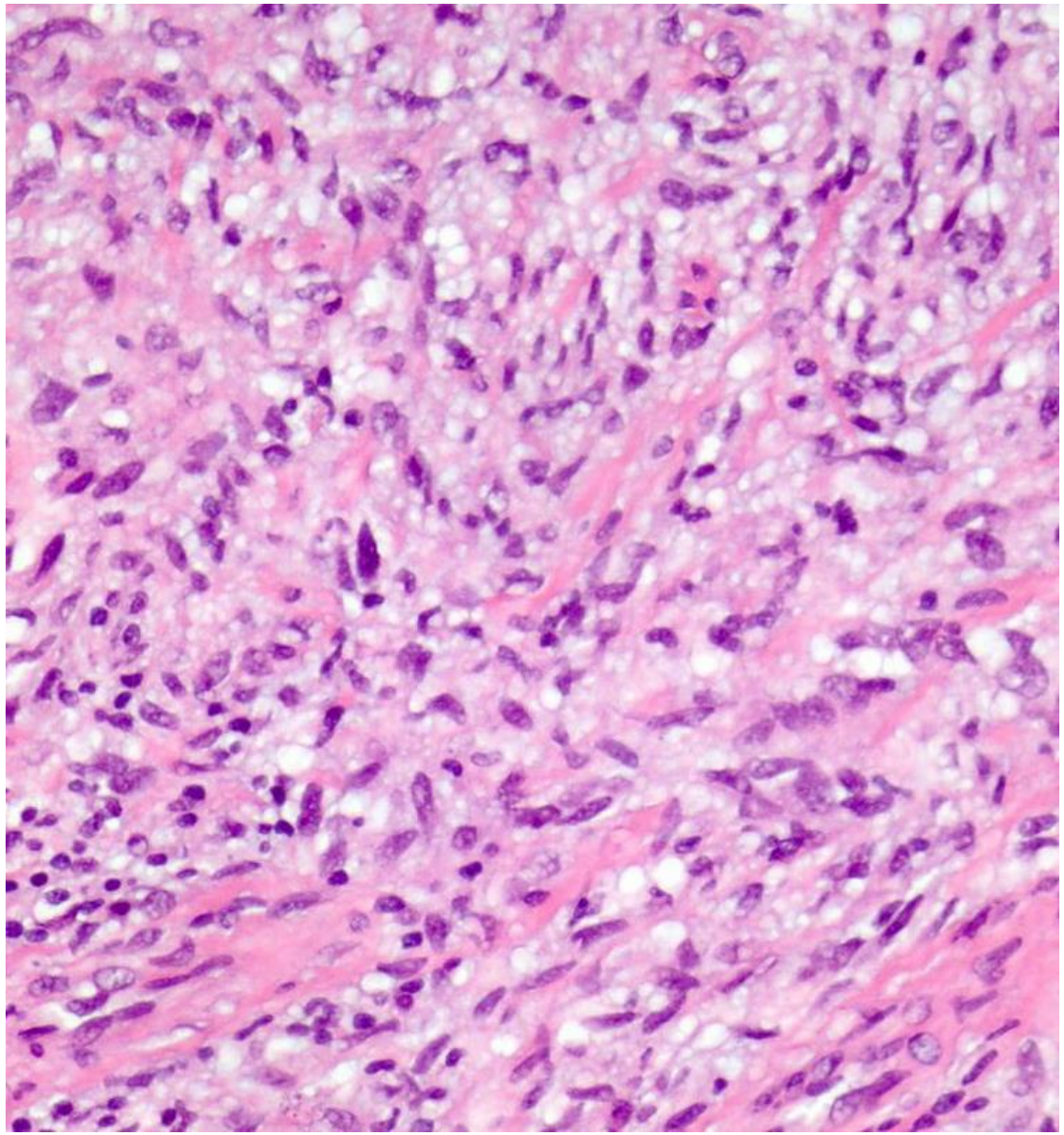
Pockets of inflammatory cells





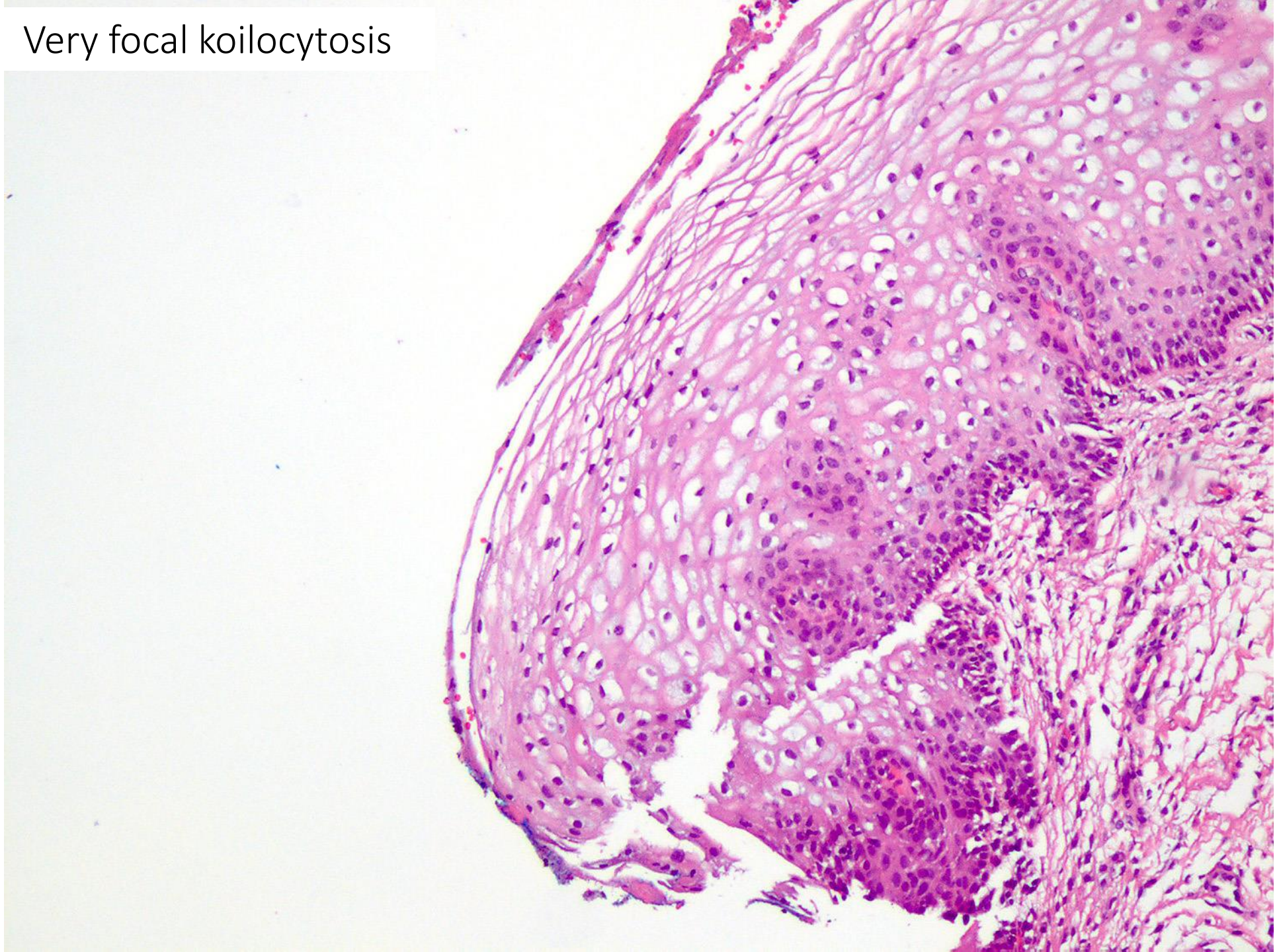
Mitotic Index: 2 mitoses per 10 HPFs

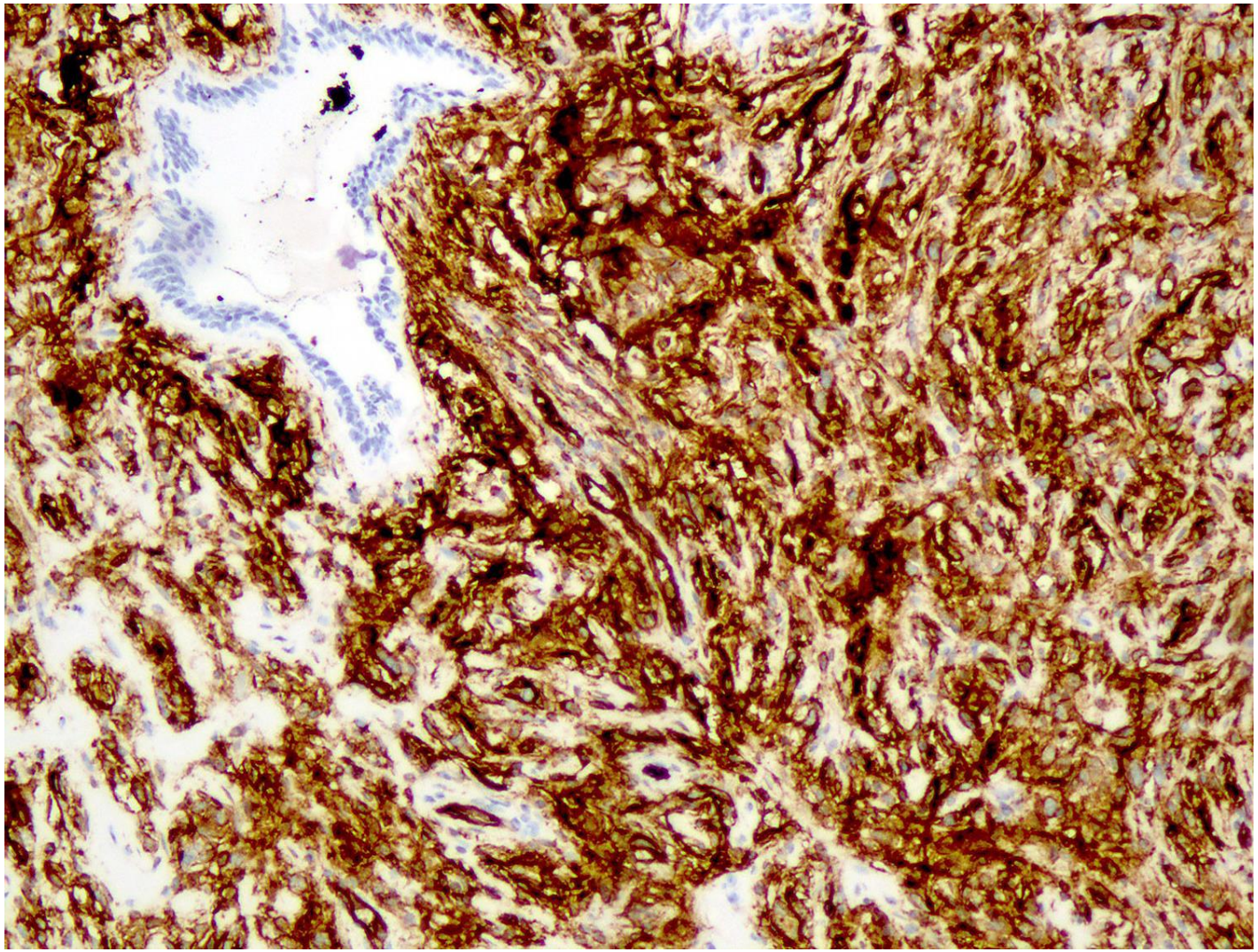




Skinny spindle cells and plump cells with pleomorphism

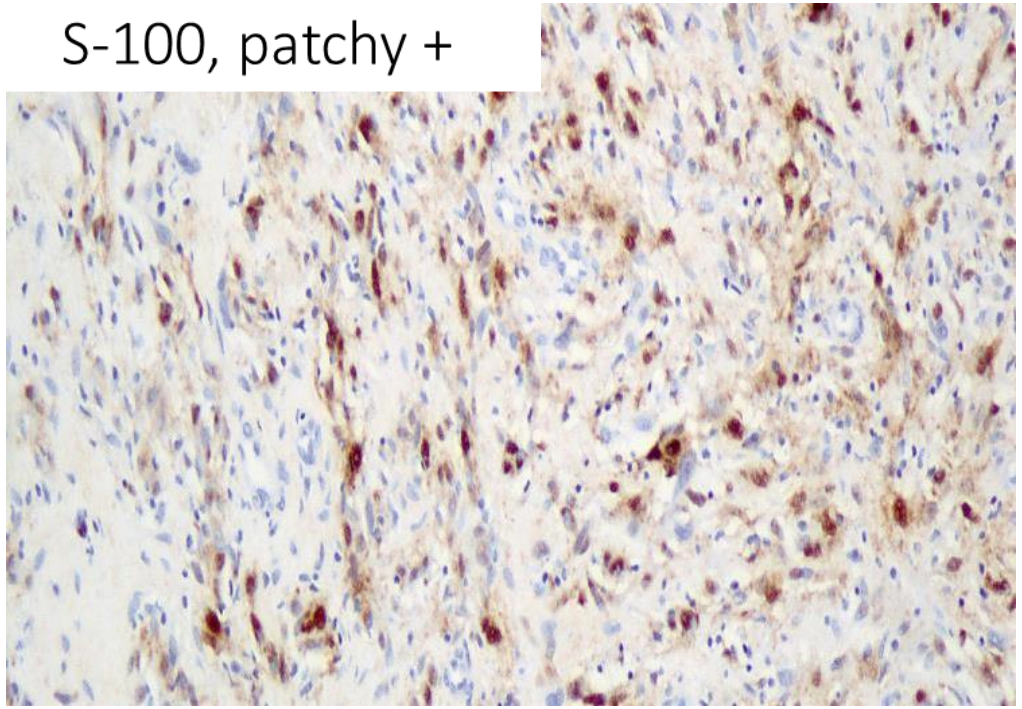
Very focal koilocytosis



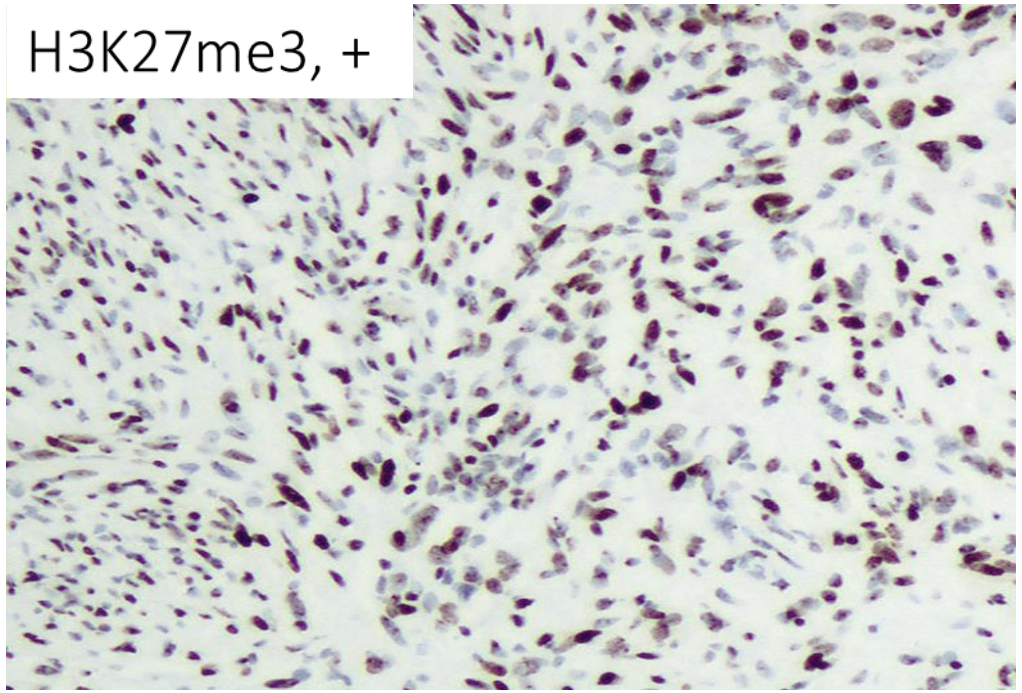


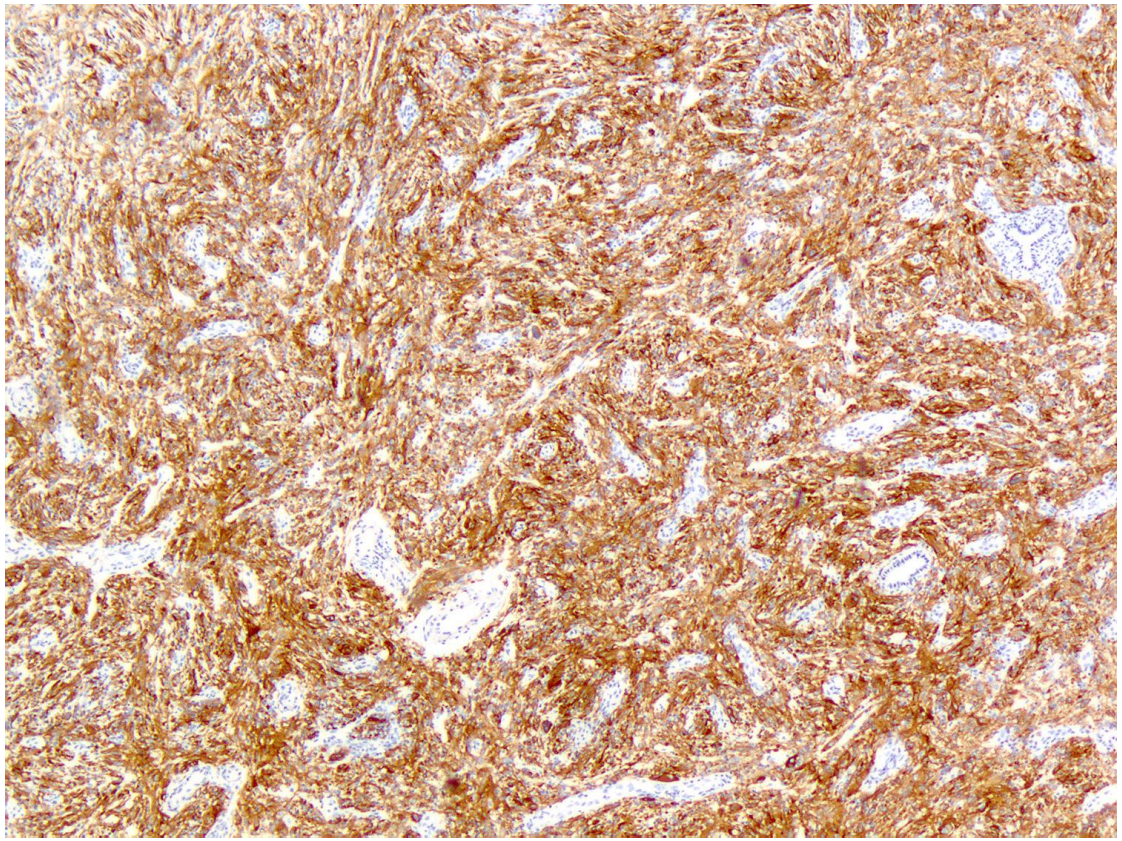
CD34,+

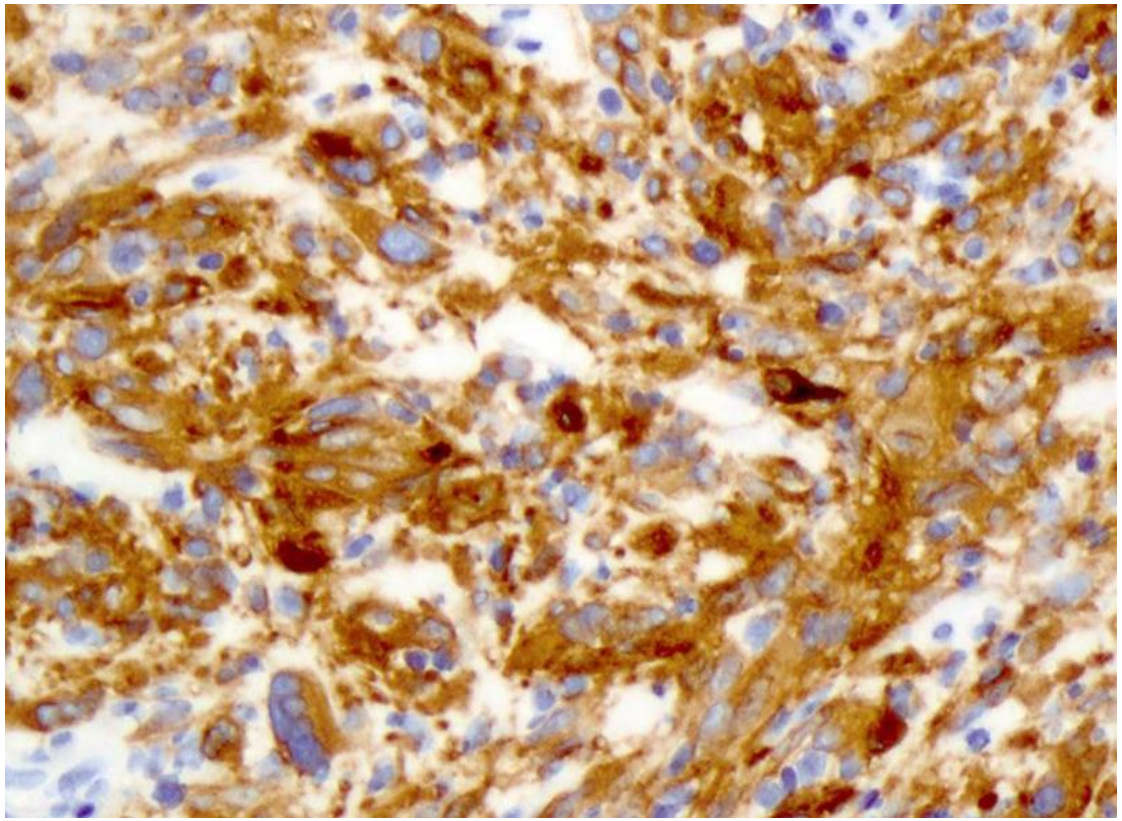
S-100, patchy +



H3K27me3, +







PANTRK, +

Additional Testing

Targeted next-generation RNA sequencing
→*TPM3/NTRK1* fusion

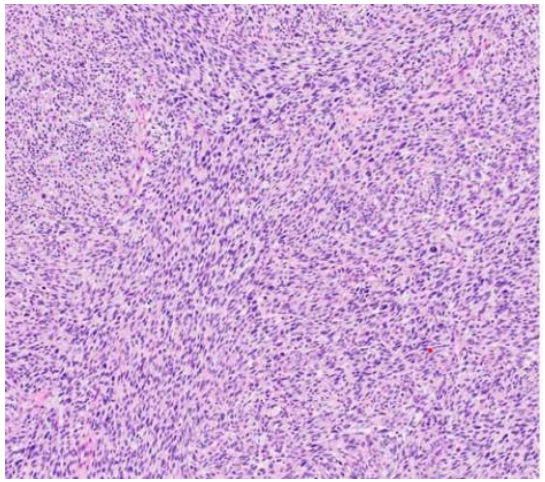
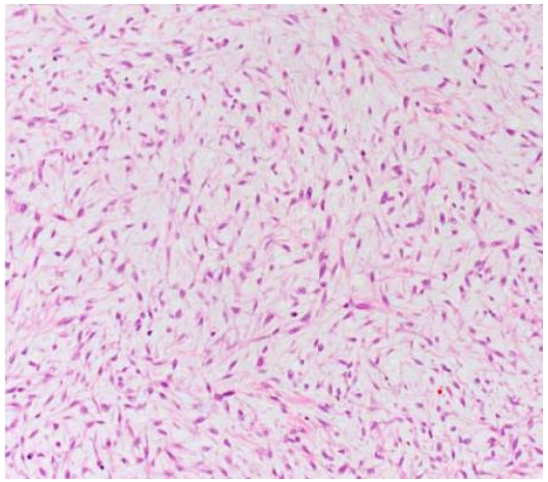
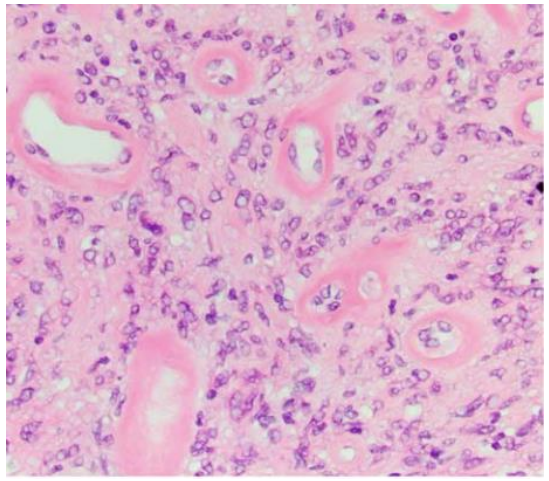
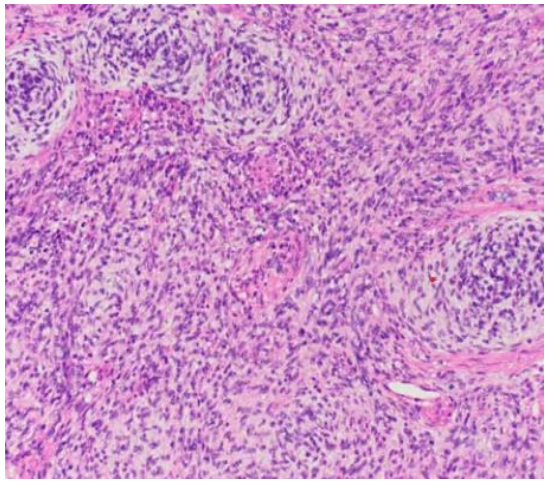
Targeted RT-PCR and Sanger sequencing
→fusion transcripts confirmed

Diagnosis

NTRK-Rearranged Uterine Sarcoma

NTRK-Rearranged Uterine Sarcoma

- Rare tumor
- Pts' age range: 13-69 yrs (average, 37.7 yrs)
- Tumor size: 1.3 to 23 cm (average, 6.9 cm)
- Cx>>>>corpus
- Atypia, variable
- MI: 0-43 mitoses per 10 HPFs

Costigan DC, et al. *NTRK*-Rearranged Uterine Sarcomas: Clinicopathologic Features of 15 Cases, Literature Review, and Risk Stratification. Am J Surg Pathol 2022; 46:1415-1429

NTRK-Rearranged Uterine Sarcoma

- *NTRK1* fusions> *NTRK3* fusions >>>*NTRK2* fusion
- Outcome, 35 pts:
  - NED, 66%
  - AWD, 20%
  - DOD, 14%
- High risk tumors, if 1 of the following is present :
  - L/V invasion
  - Necrosis
  - MI ≥ 8 mitoses per 10 HPFs
  - *NTRK3* fusions

Costigan DC, et al. *NTRK*-Rearranged Uterine Sarcomas: Clinicopathologic Features of 15 Cases, Literature Review, and Risk Stratification. Am J Surg Pathol 2022; 46:1415-1429


YOU'LL
BE
FINE.


PURE JOY
MARFA