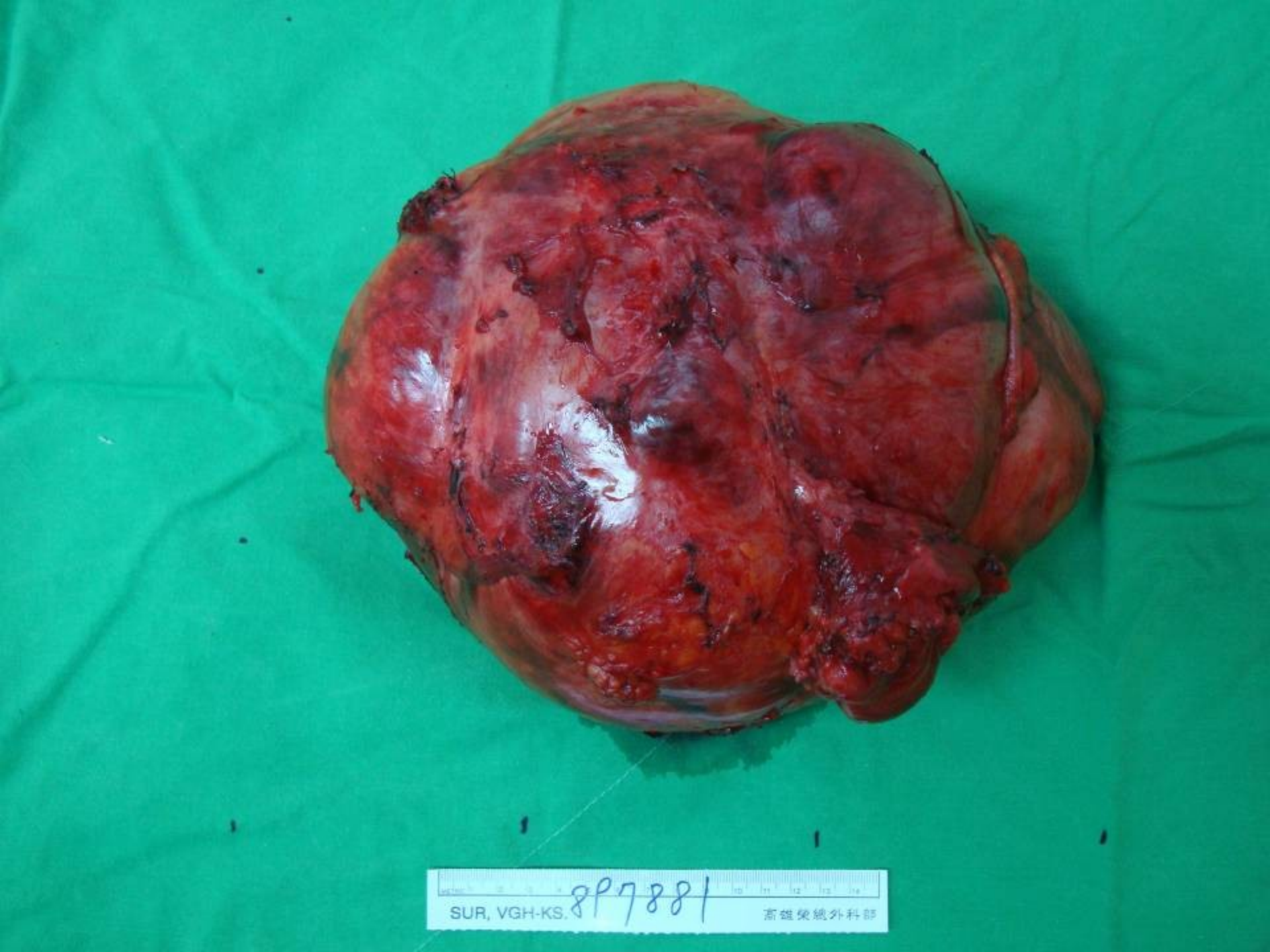
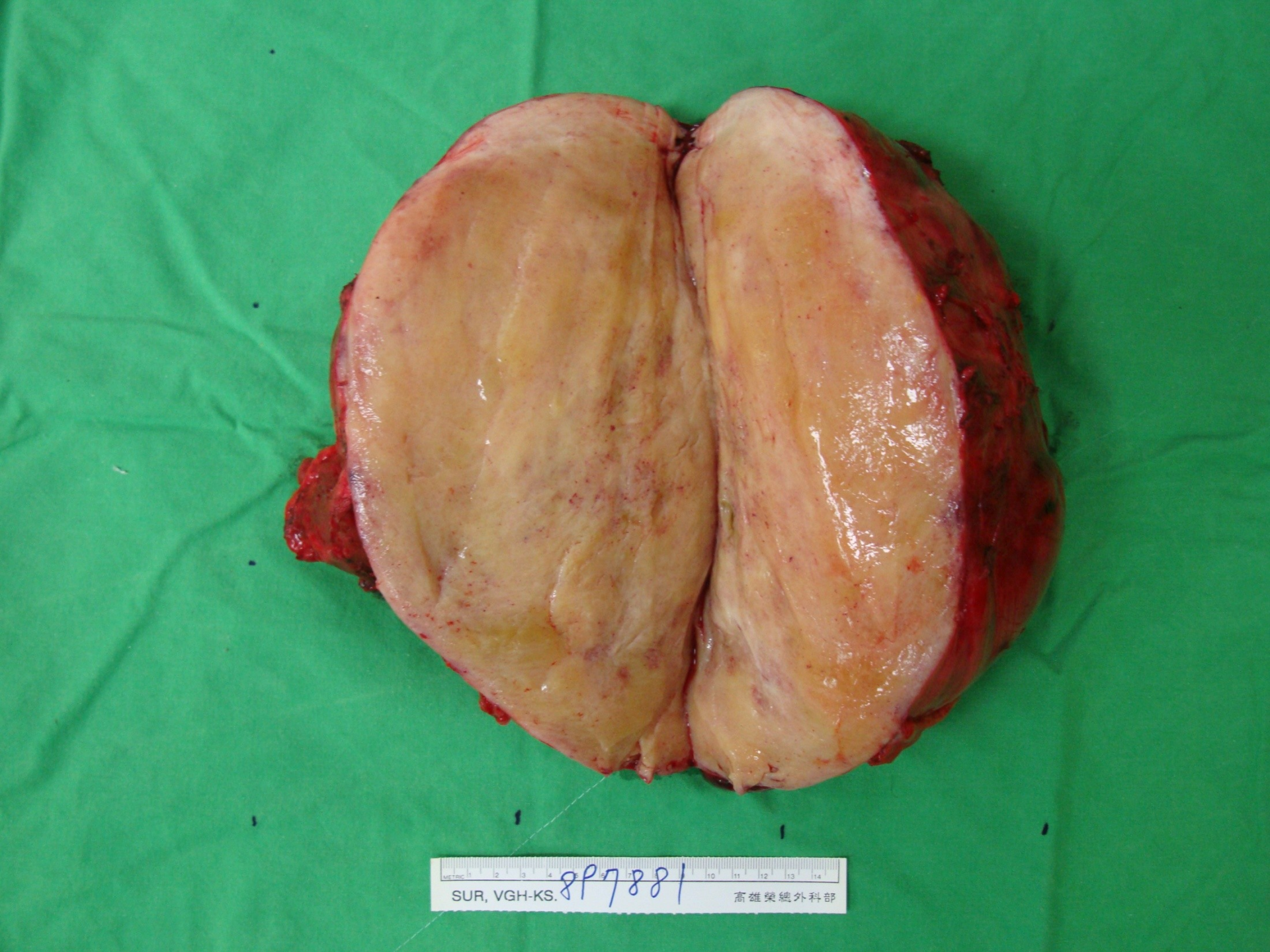
臨床病理討論會

2016-09-22


SUR, VGH-KS. 8P7881
高雄榮總外科部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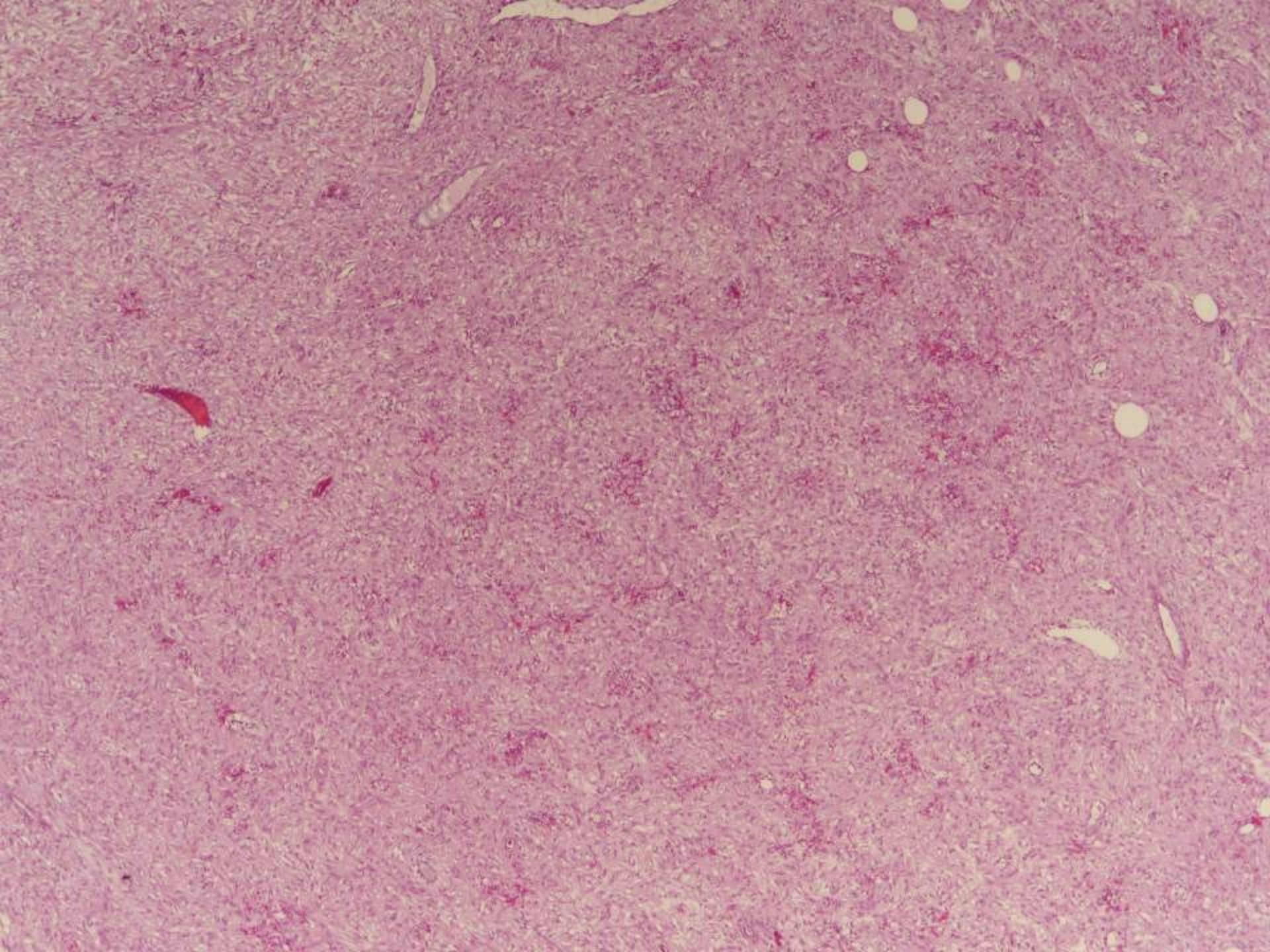
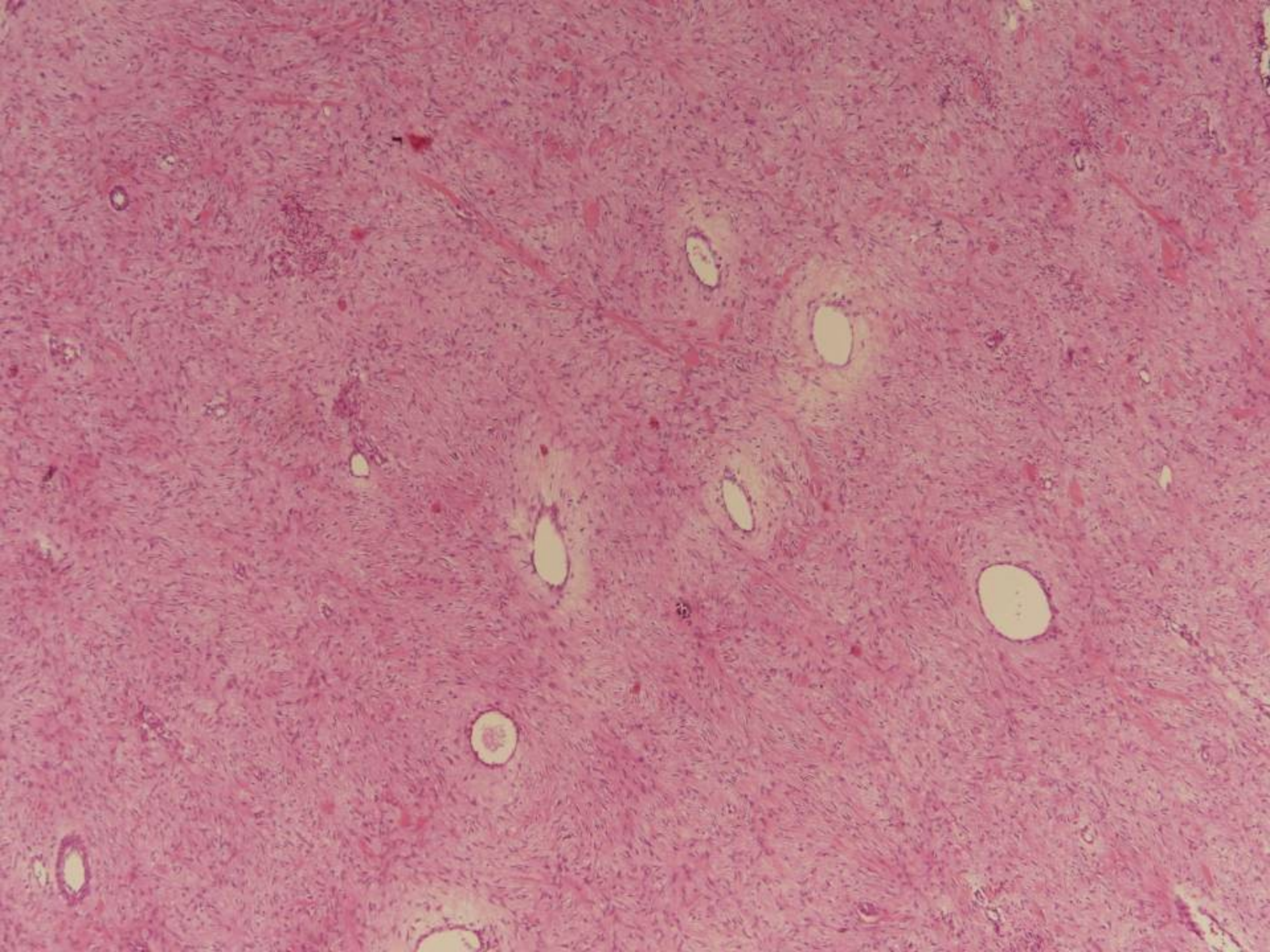
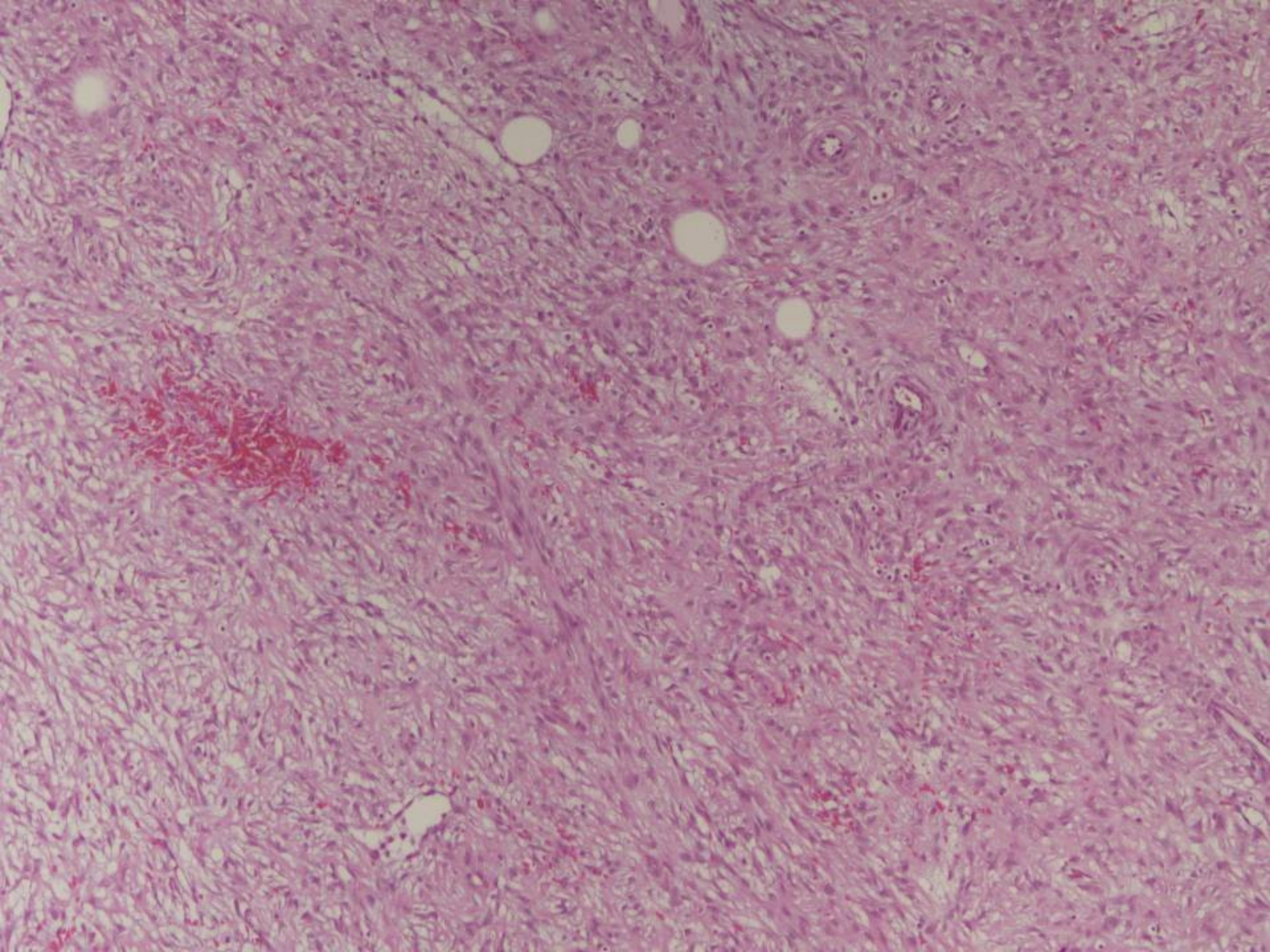
高雄榮總外科部

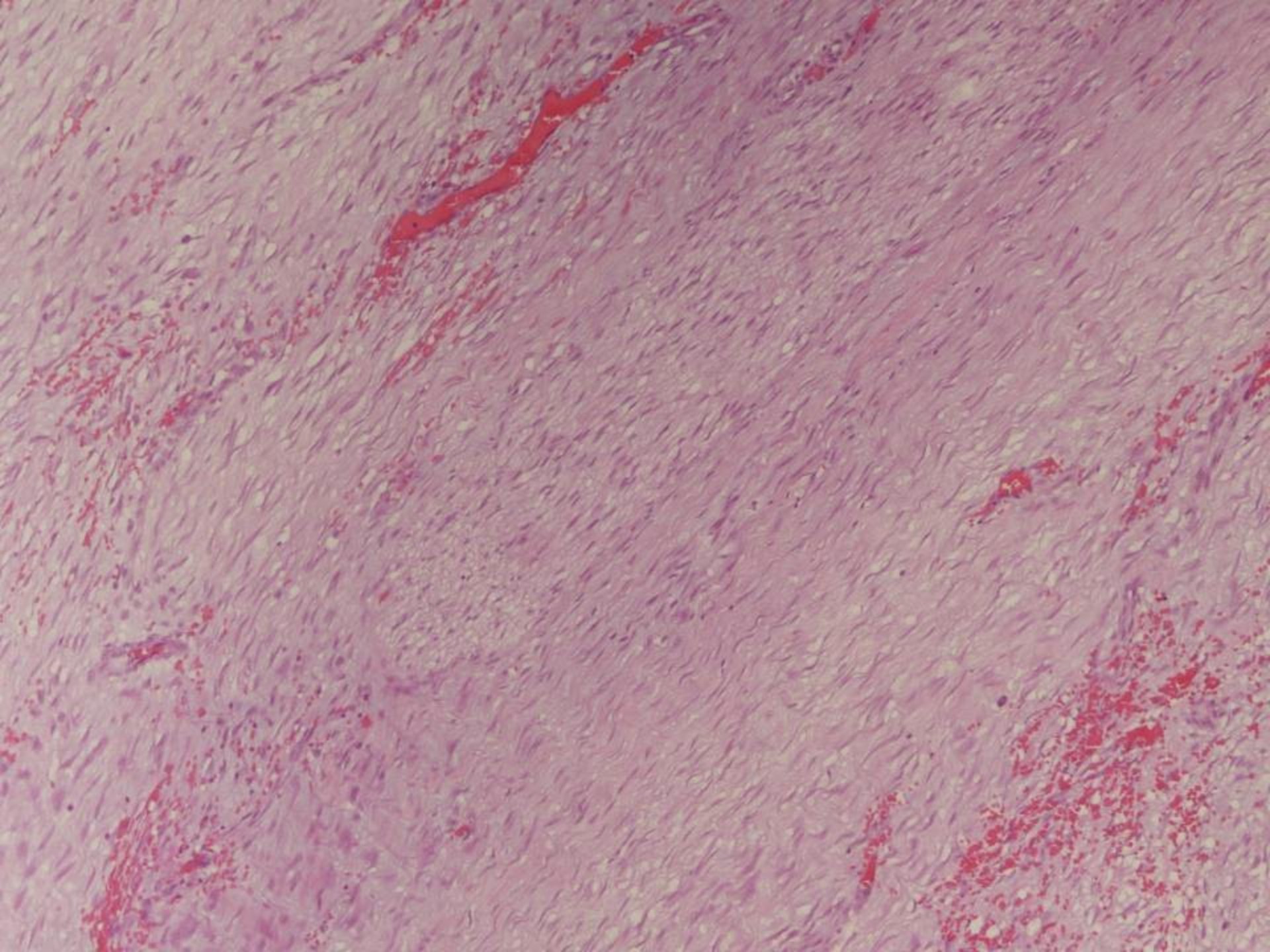
Gross

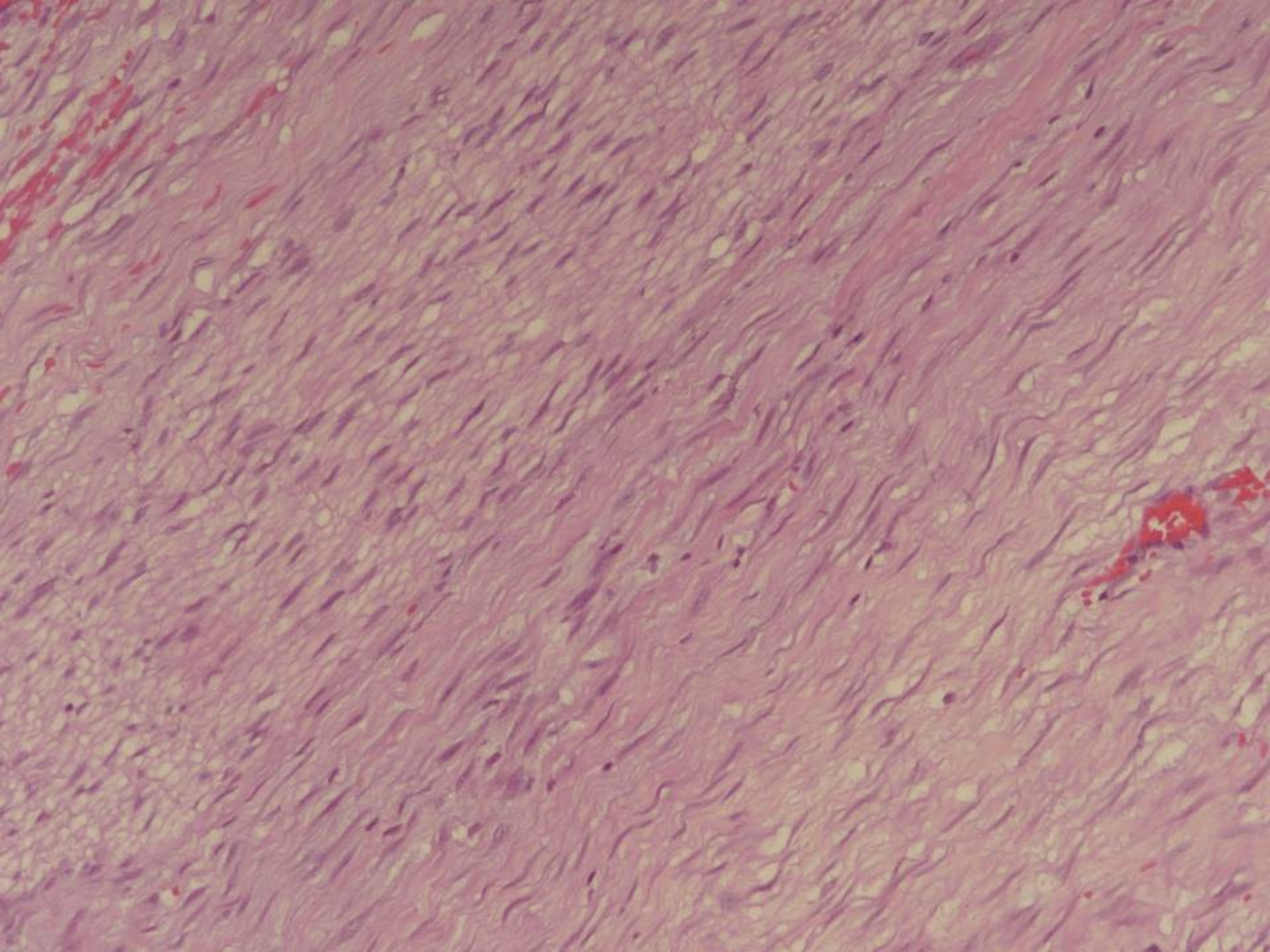
- 23 x 21.8 x 13.4 cm in size
- Attached segmental intestinal tissue and appendix
- One segment of large intestinal tissue, 4.4 cm in length and 3.5 cm in circumference
- Numerous polyps are noted

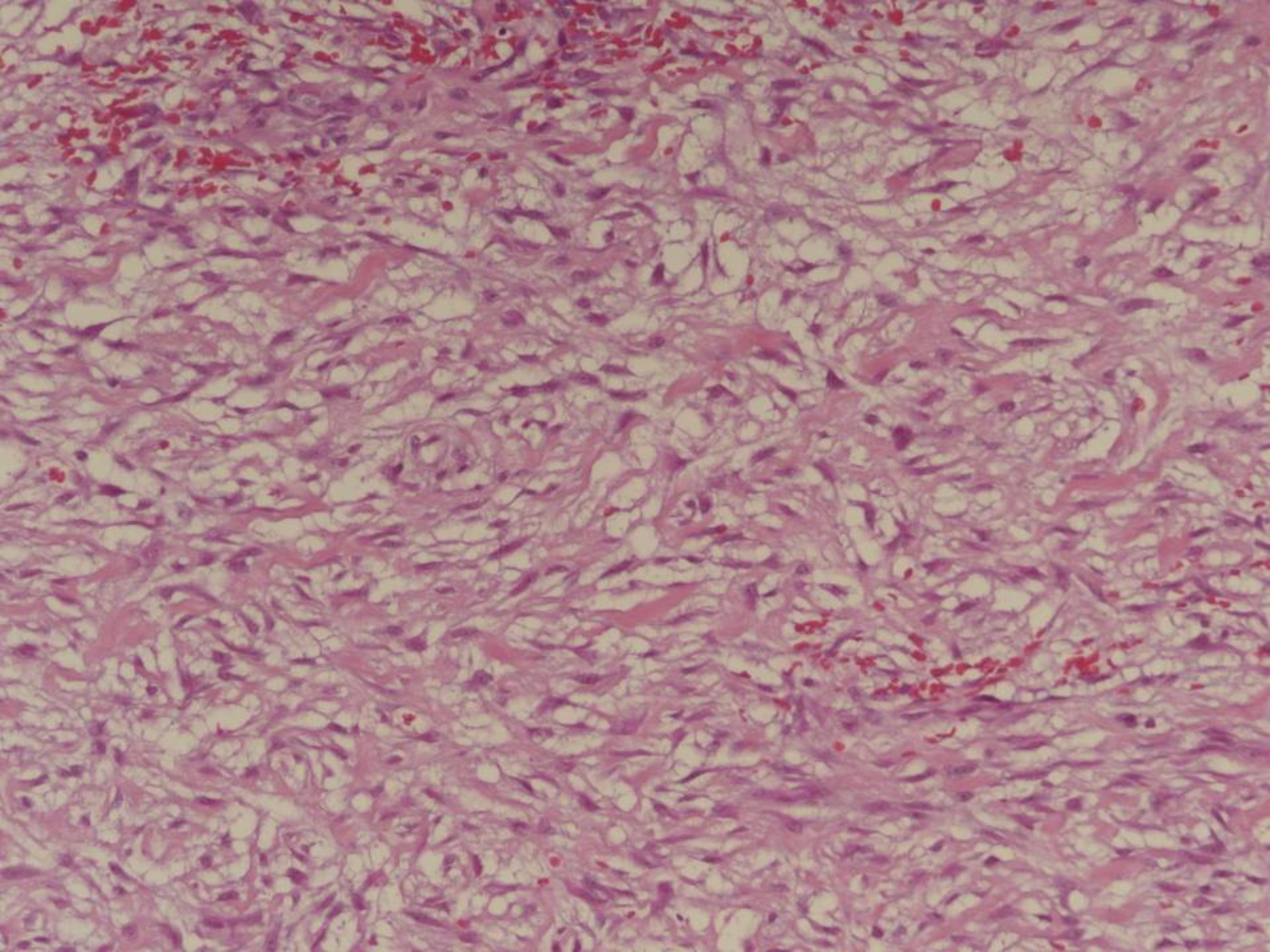


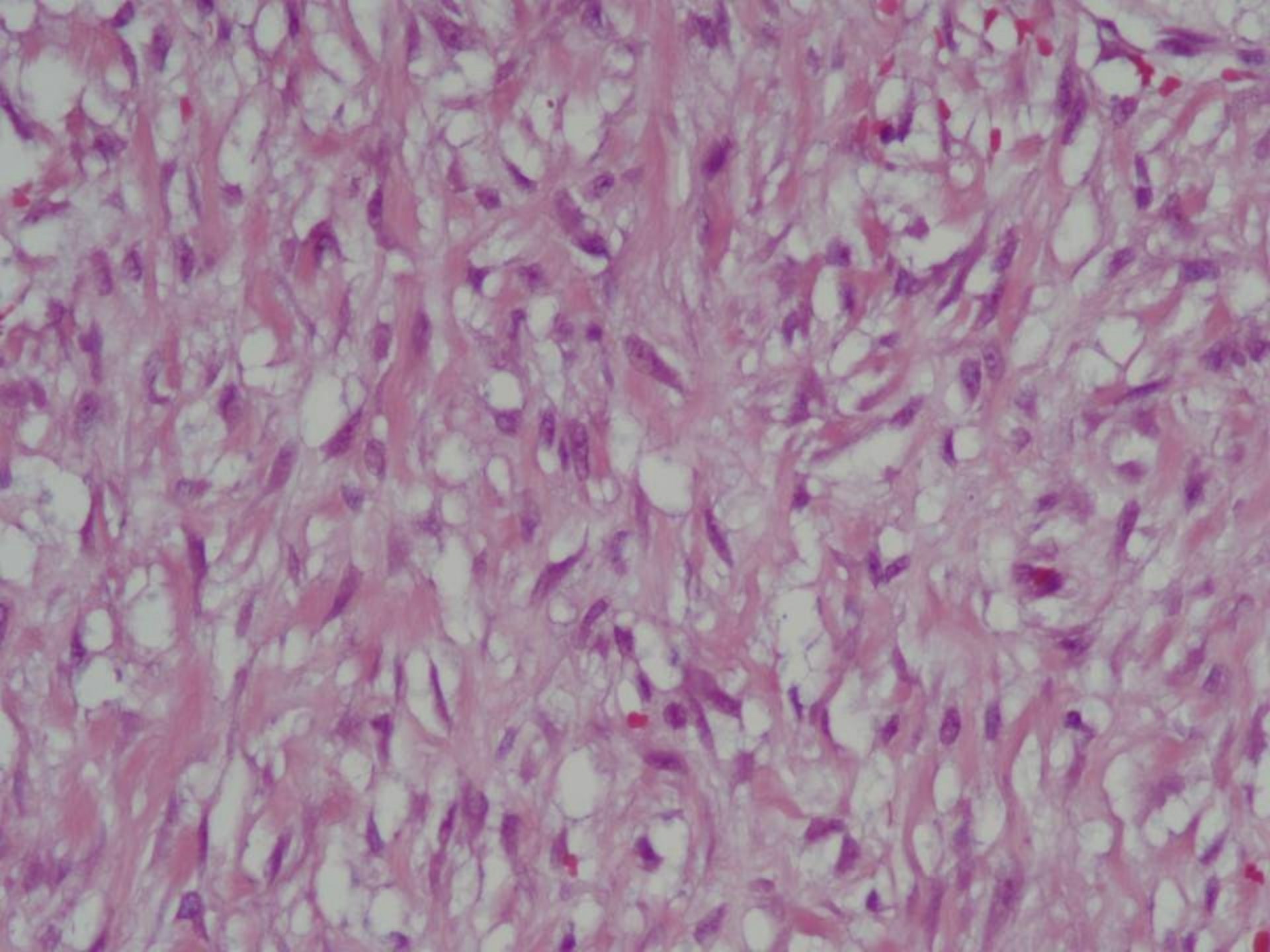


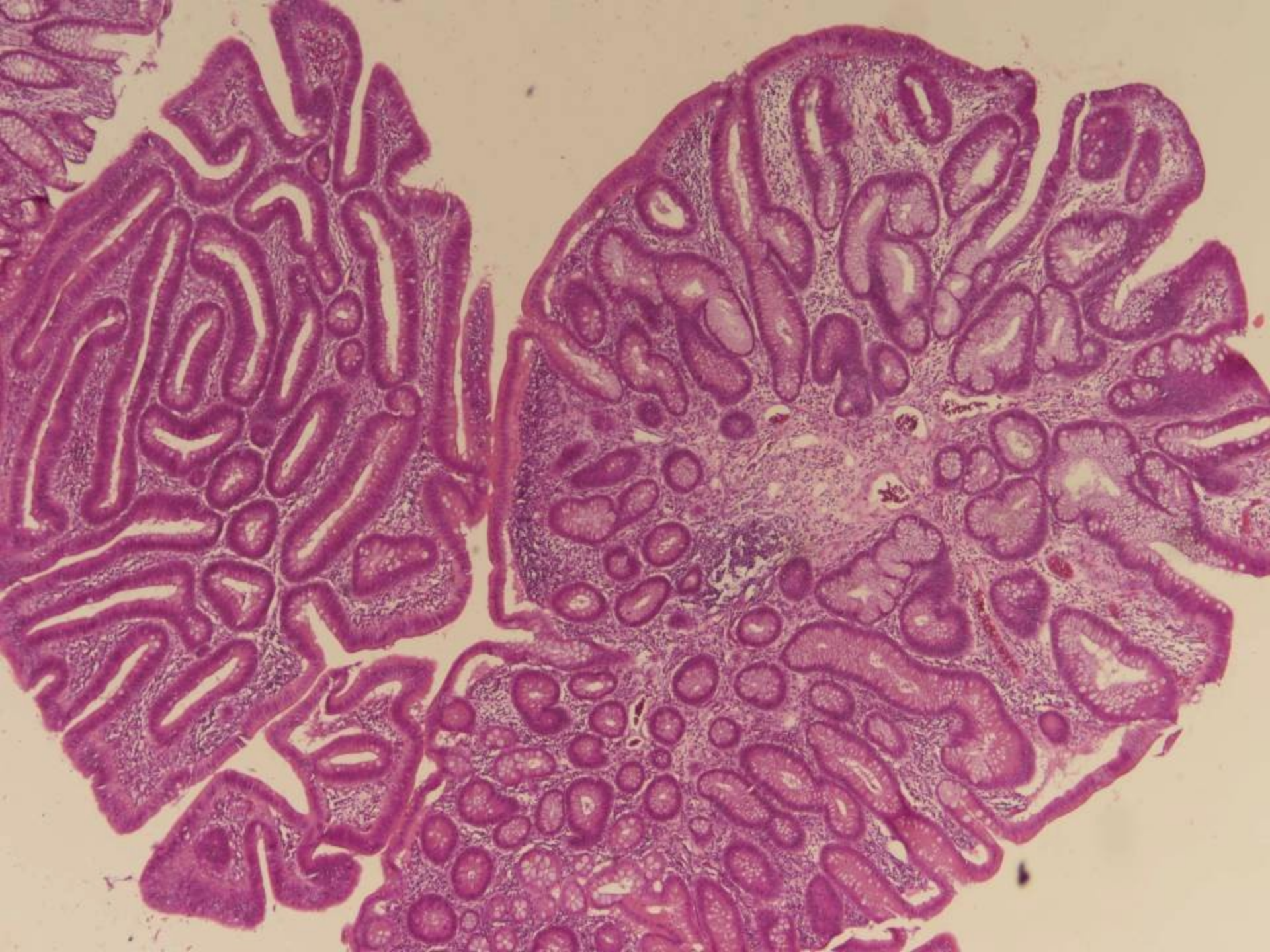


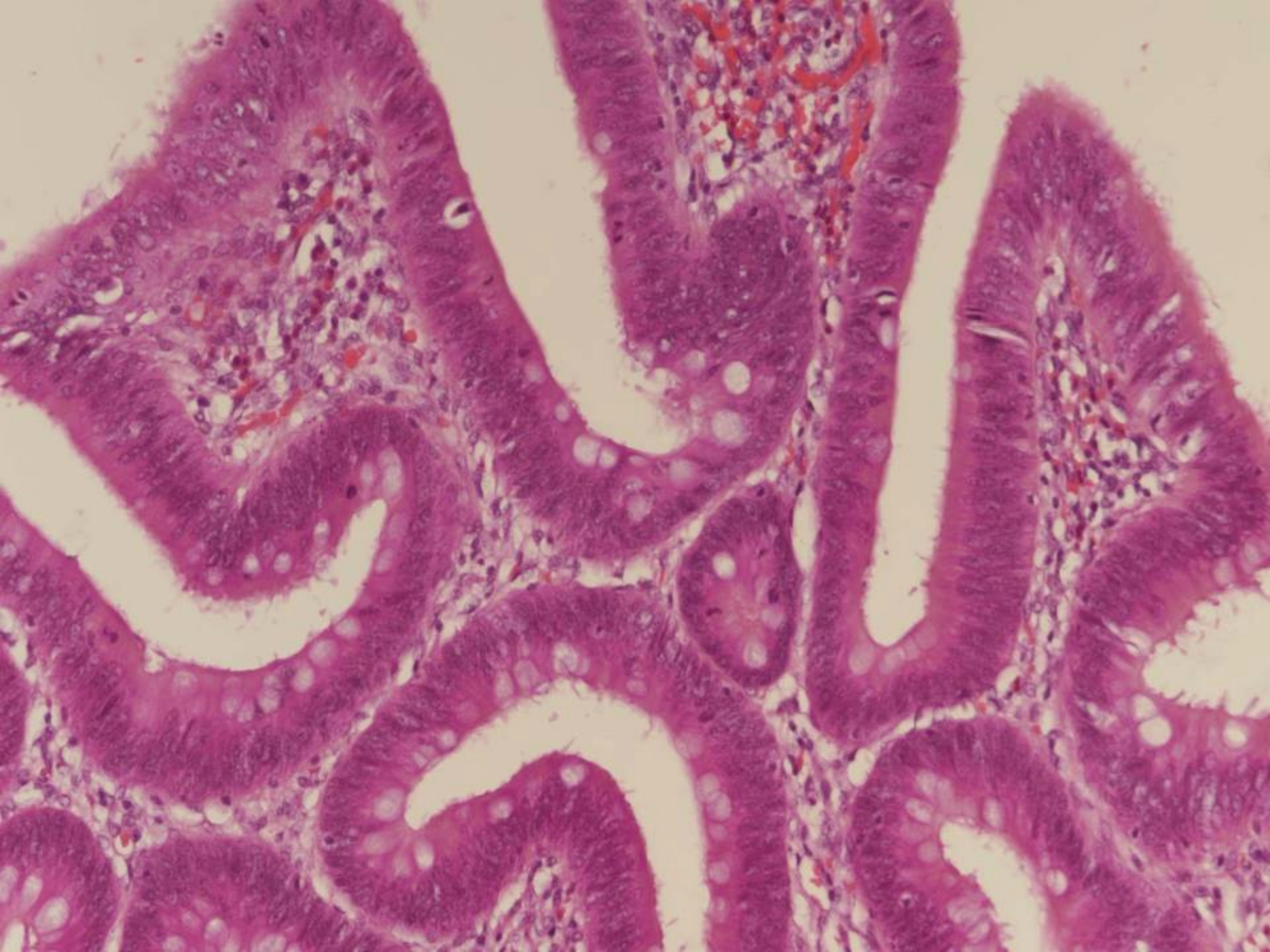












Microscopic findings

- Elongated, bland-looking, stellate and spindle cells
- Arragned into ill-defined fascicles
- Foci of myxoid change and collagen deposition
- Tubular adenoma with low grade dysplasia

Pathological Diagnosis

Fibromatosis (desmoid tumor)

Fibromatosis

- A locally aggressive myofibroblastic neoplasm
- Usually in deep soft tissues
- Infiltrative growth pattern
- Local recurrence
- Lack of metastatic potential

Pathogenesis (Fibromatosis)

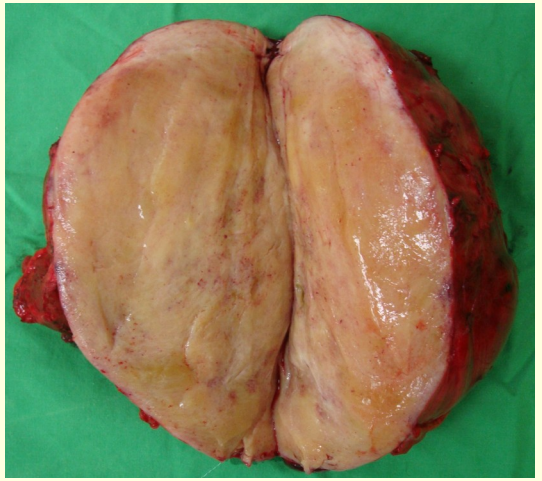
- Multifactorial: genetic and physical factors
- Sporadic
- Familial cases
- Gardner-type familial adenomatous polyposis (FAP)
- Trauma (most often surgery)

Clinical symptom (Fibromatosis)

- Asymptomatic
- Some have mild abdominal pain, gastrointestinal bleeding, or acute abdomen secondary to bowel perforation

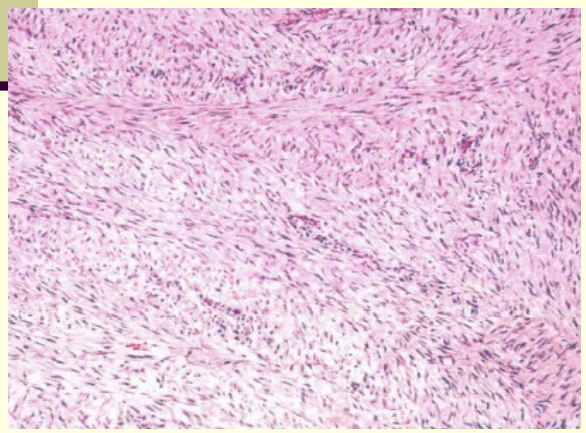
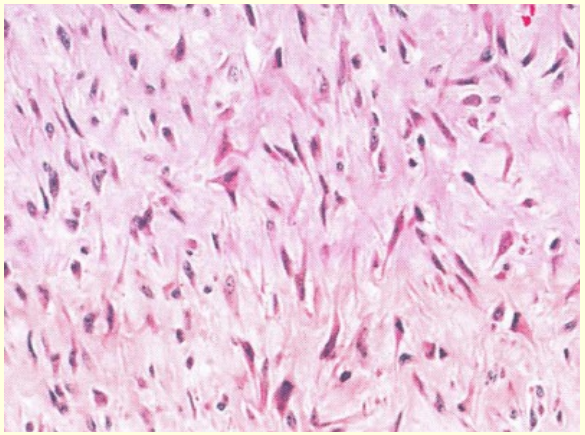
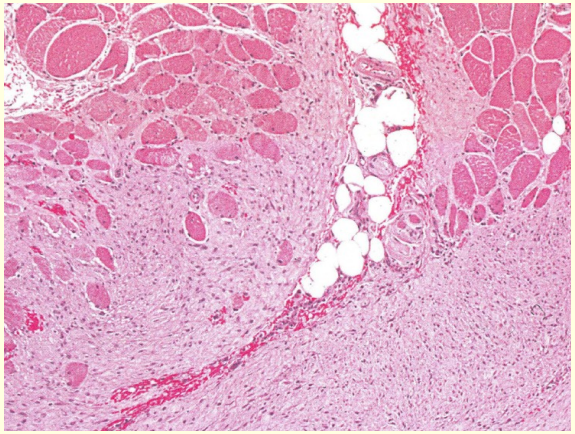
Macroscopy (Fibromatosis)

- Firm and cut with a gritty sensation
- Cut surface: glistening white, coarsely trabeculated surface resembling scar tissue
- Lesions in the abdomen may appear well circumscribed
- Some have myxoid appearance
- Most tumours measure 5-10 cm



Histopathology (Fibromatosis)

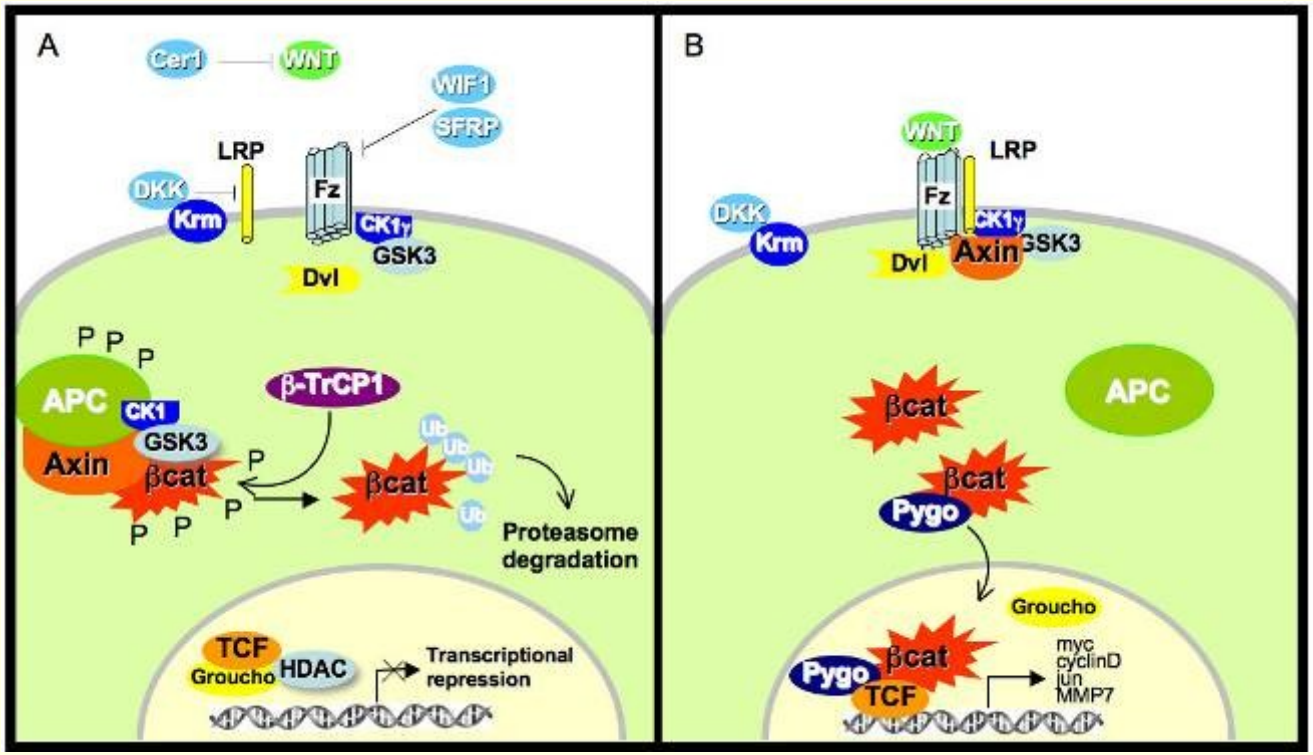
- Poorly circumscribed with infiltration of the surrounding tissue
- Eelongated, slender, spindle-shaped cells
- Arranged in long sweeping bundles
- Collagenous stroma
- Variably prominent blood vessels

Genetics (Fibromatosis)

- In the setting of Gardner-type familial adenomatous polyposis: inactivating mutations of the *APC* gene
- Up to 85% of sporadic lesions: mutations in the gene encoding beta-catenin (*CTNNB 1*)

- Both *CTNNB 1* and *APC* mutations result in the intranuclear accumulation of beta-catenin protein



Prognosis (Fibromatosis)

- Local recurrence is common
- Attempts to achieve tumour-free resection margins may result in significant morbidity
- Lack of metastatic potential

About this patient

- Colorectal adenomatous polyps: many
- Skin: pilomatrixoma
- Mesenteric fibromatosis
- Liver: hepatocellular adenoma
- Deletion of chromosome 5q

Final Diagnosis

Gardner's syndrome

(Familial adenomatous polyposis)

Familial adenomatous polyposis (FAP)

- Autosomal dominant
- Germline mutations in the adenomatous polyposis coli (*APC*) gene
- On the long arm of chromosome 5 (5q)
- Hundreds to thousands of colorectal adenomatous polyps
- Colorectal adenocarcinoma if the colon is not removed
- Fundic gland polyps of the stomach
- Duodenal and small-bowel adenomas

Gardner syndrome

- Variant of FAP
  - Epidermoid cysts
  - Osteomas
  - Dental anomalies
  - Desmoid tumors
  - Gastrointestinal polyps
- Extra-intestinal growths correlate with mutation location in the *APC* gene
- Applied to families in which the extraintestinal manifestations of the disease are particularly obvious and common

Incidence of FAP

- 1 per 7000 to 30,000 newborns
- < 1 % of all new cases of colorectal cancer
- 30% ~ 50% of new FAP patients are de novo cases (new mutations of the *APC*)

Genetics (FAP)

- Autosomal dominant
- Complete penetrance by age 40 years
- Germline mutations in the *APC* gene

Diagnostic criteria (FAP)

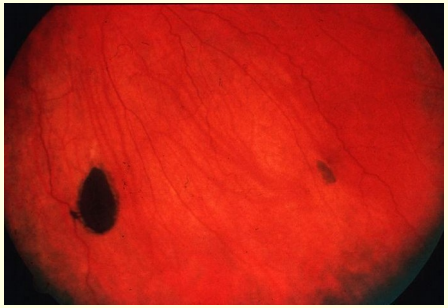
1. Germline mutation in APC gene
   - Identifiable in about 60-80% of cases
2. Or, ≥100 colorectal adenomatous polyps (classical definition)
3. Or, any colorectal adenomas under age 30 in a patient with a family history of FAP
4. Or, intra-abdominal desmoid fibromatosis, osteoma of the mandible, or multiple epidermoid cysts in a patient with a family history of FAP

Clinical manifestation (FAP)

- Colorectal adenomas at an average age of 15.9 years (range, 8-34 years) (Polyps increase in number and size with age)
- The mean age at which cancer develops is about 40 years
- Risk of cancer is 1-6% by the age of 21 years
- By age 50 years, > 90% of untreated patients will have colorectal cancer

Organs involvement in FAP

- Intestinal polyps: adenomatous polyp
- Extraintestinal manifestations
  1. Stomach: fundic gland polyp
  2. Liver and biliary tract: dysplasia
- Extra-gastrointestinal manifestations
  1. Soft tissues: fibromatosis
  2. Bones: exostosis
  3. Teeth: anomalies
  4. Eye: CHRPE
  5. Skin: epidermal cyst
  6. Endocrine system: thyroid papillary carcinoma
  7. Nervous system: glioma



Summary

- Gardner syndrome: variant of familial adenomatous polyposis with extraintestinal manifestation
- Numerous (≥ 100) colorectal adenomatous polyp
- Colorectal cancer if colon not resected
- *APC* mutation (5q21-22)

Thank You For Your Attention.