



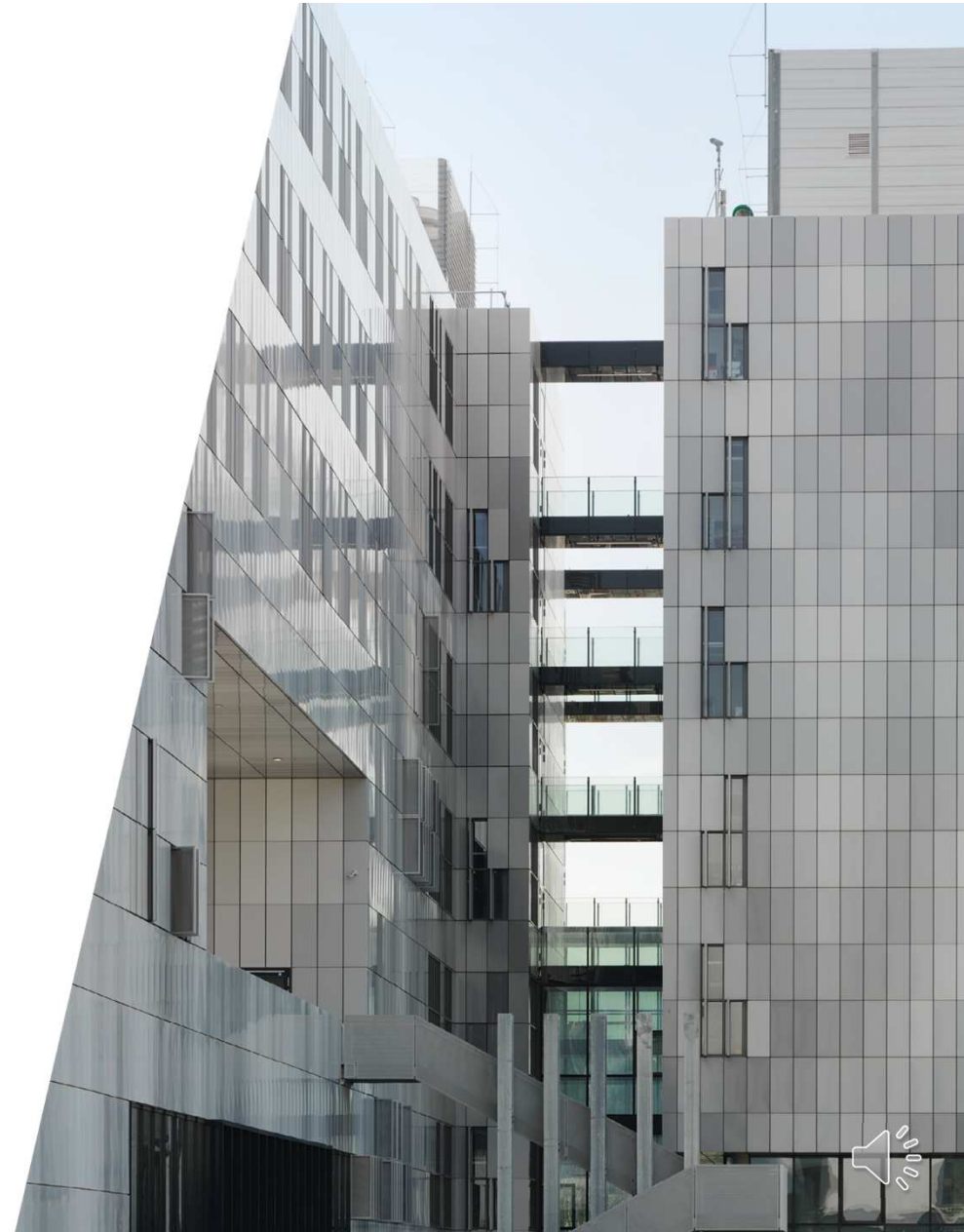
Medical University of Graz

UPPER GI TRACT CASE #3

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Diagnostic & Research Institute of Pathology

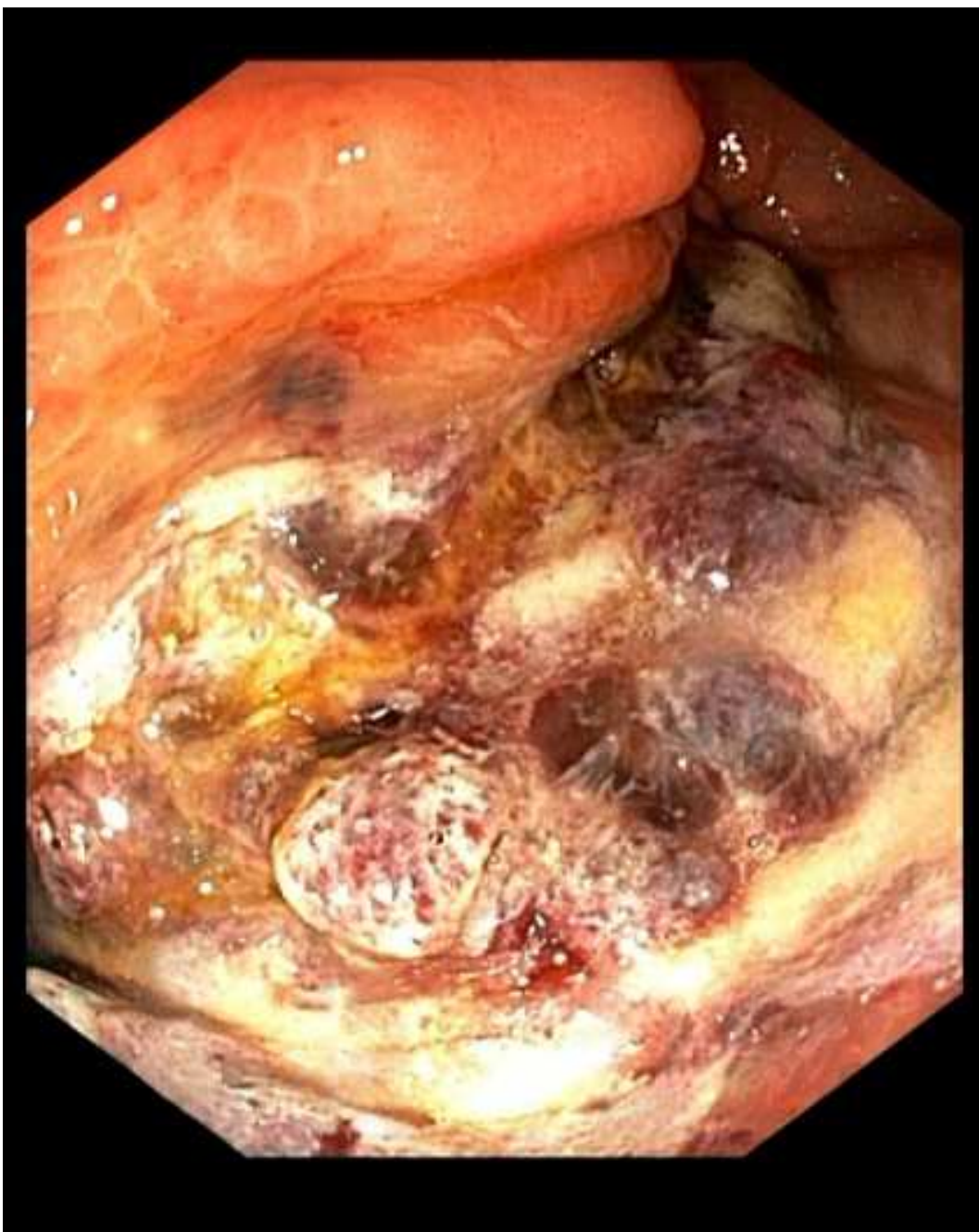
Medical University of Graz / Austria



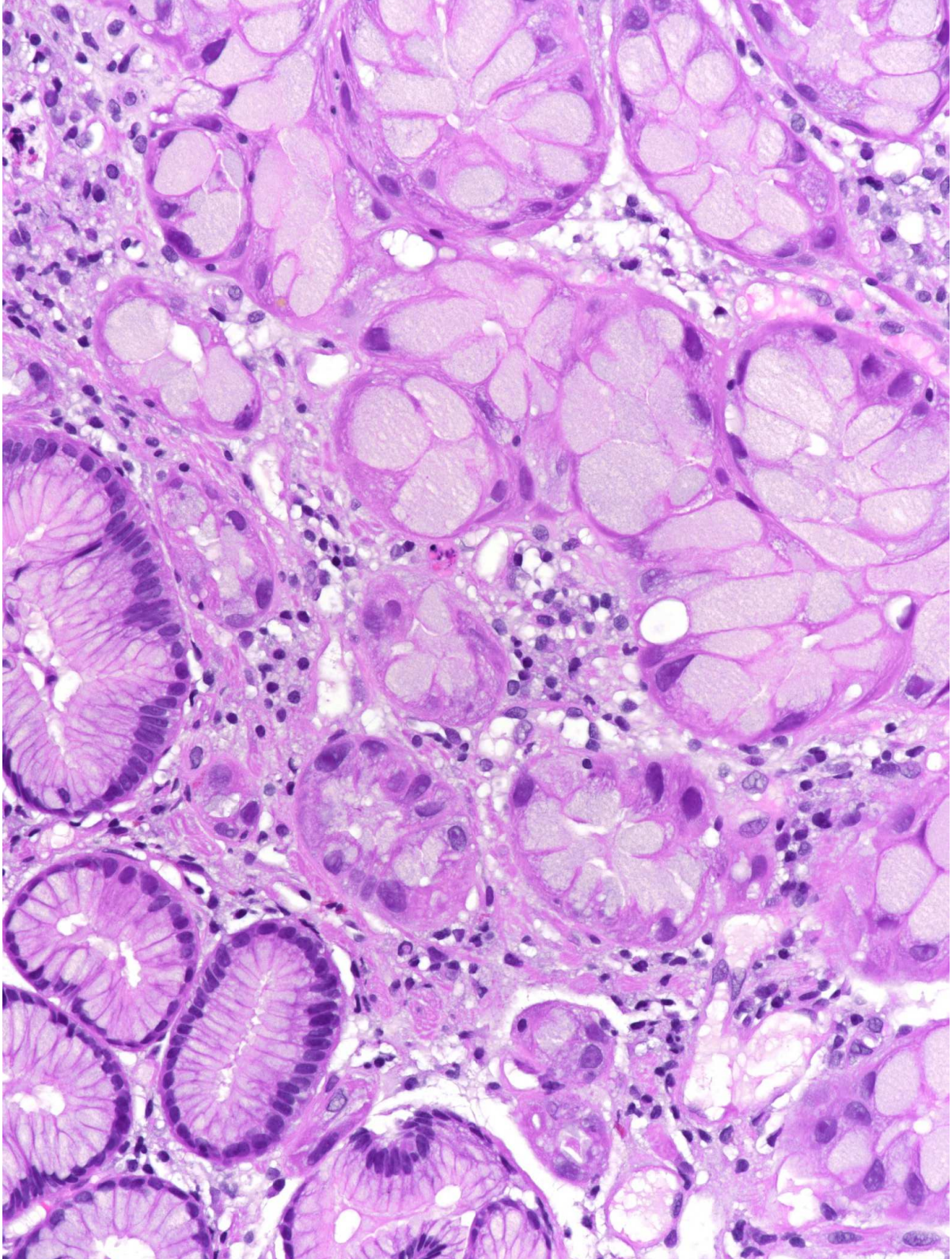
Background story

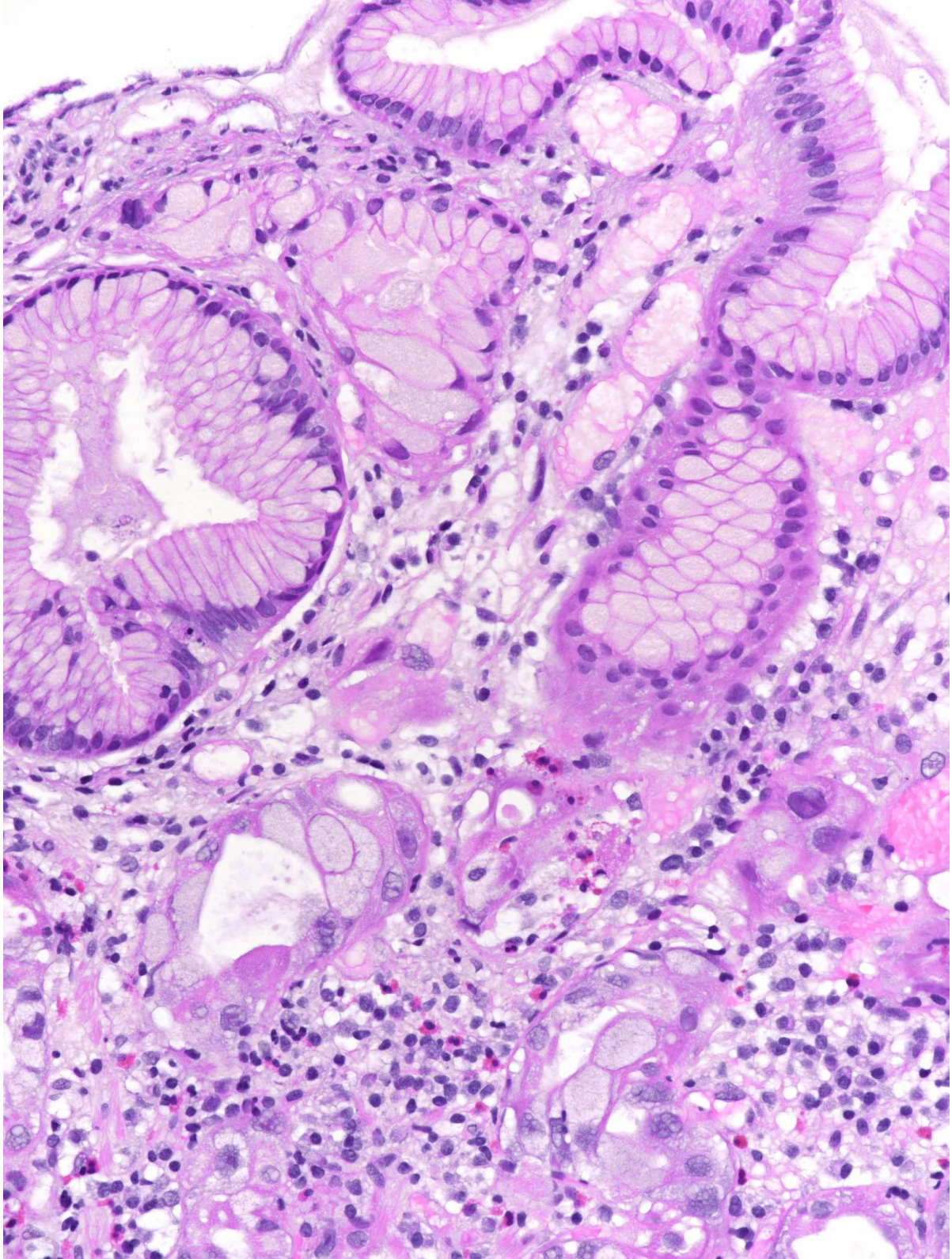
- ▶ 43-year-old female
- ▶ Uveal melanoma with liver metastasis
- ▶ Clinical symptoms: upper abdominal pain
- ▶ Endoscopy: polypoid mass in the stomach (from mid corpus into the pylorus), partly ulcerated, discoloration
- ▶ Pathology request form:
 - ▶ Gastric cancer?
 - ▶ Metastatic melanoma?
- ▶ Biopsies from the ulcerated mass in the stomach

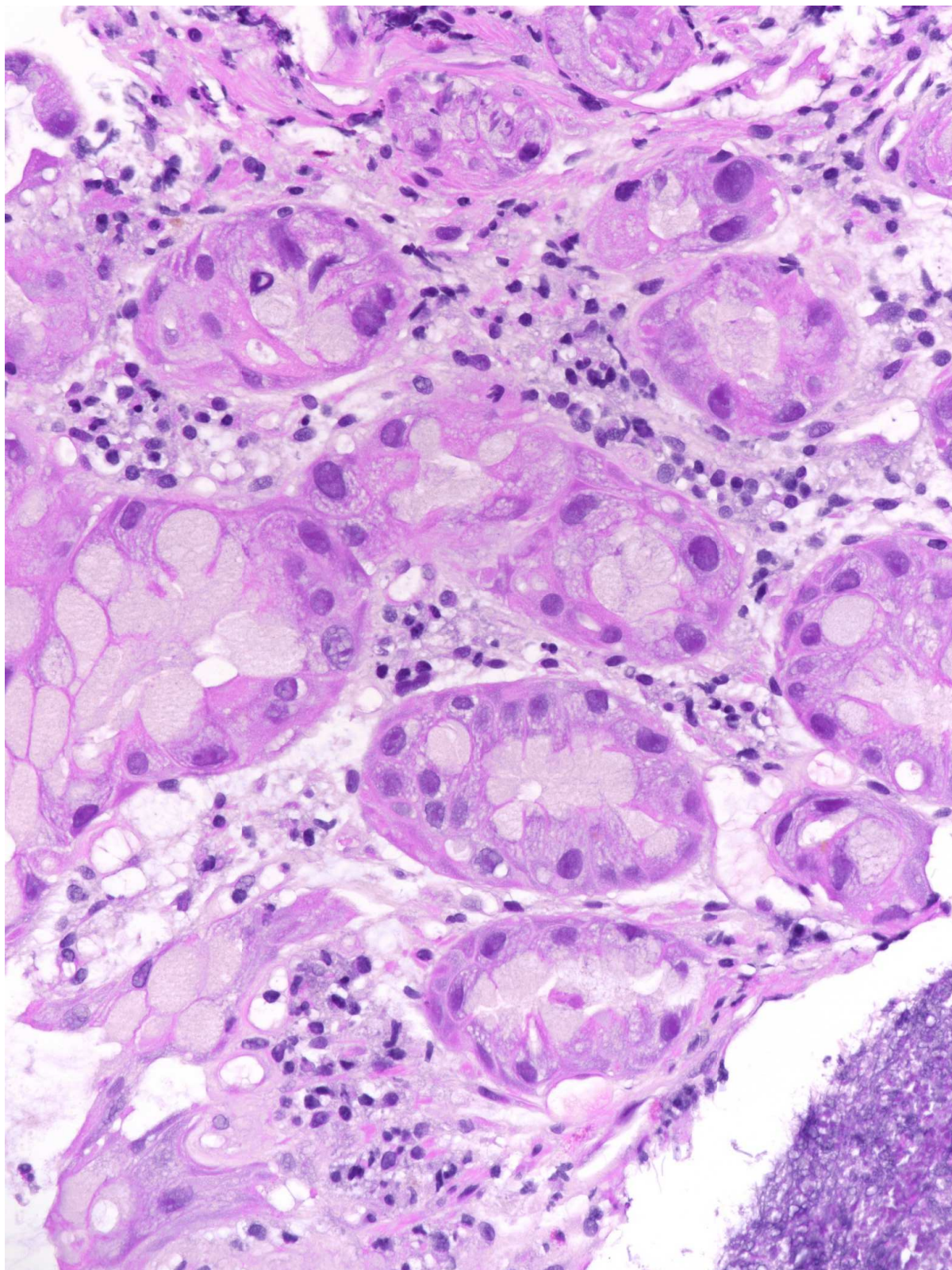


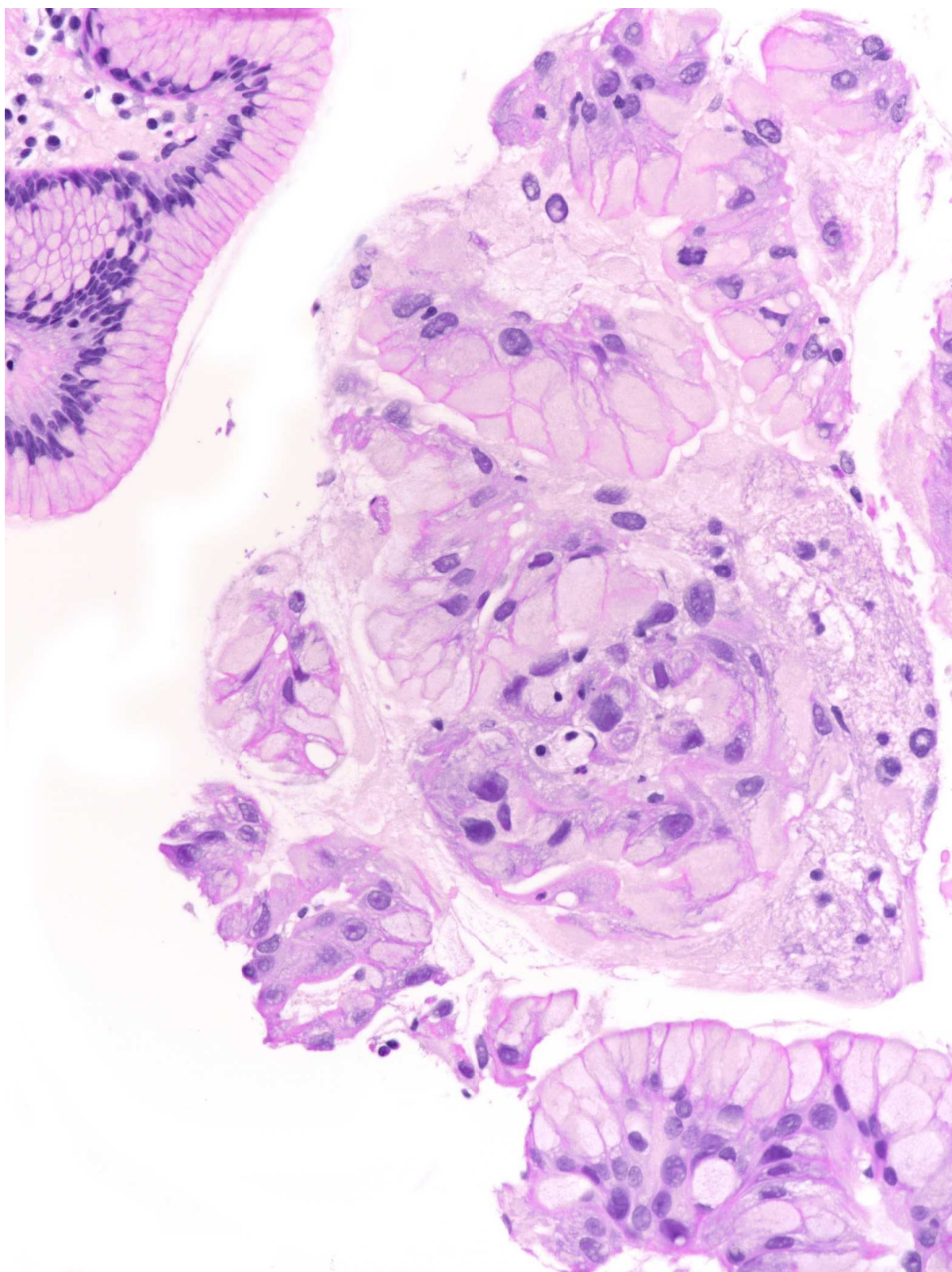


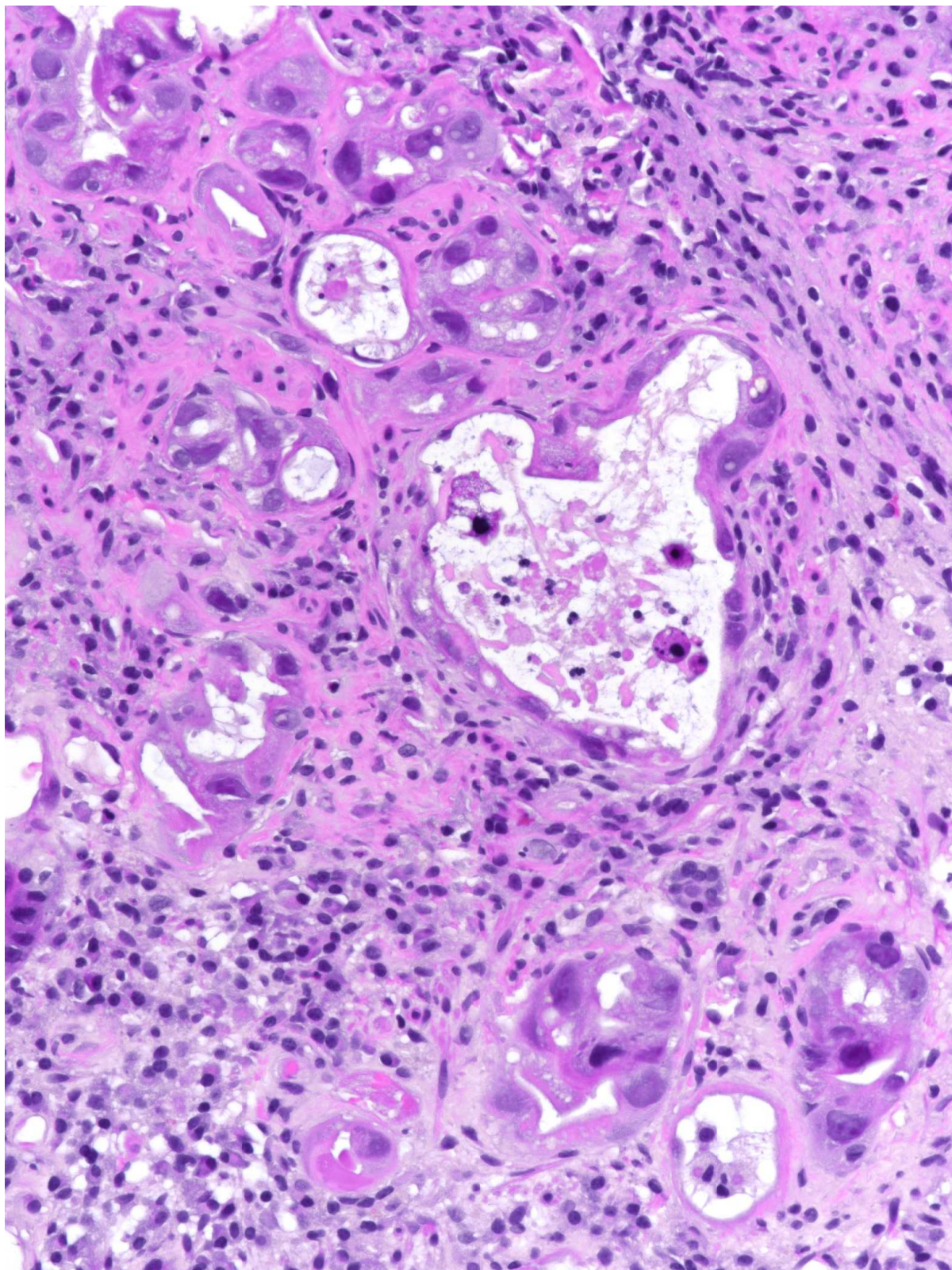


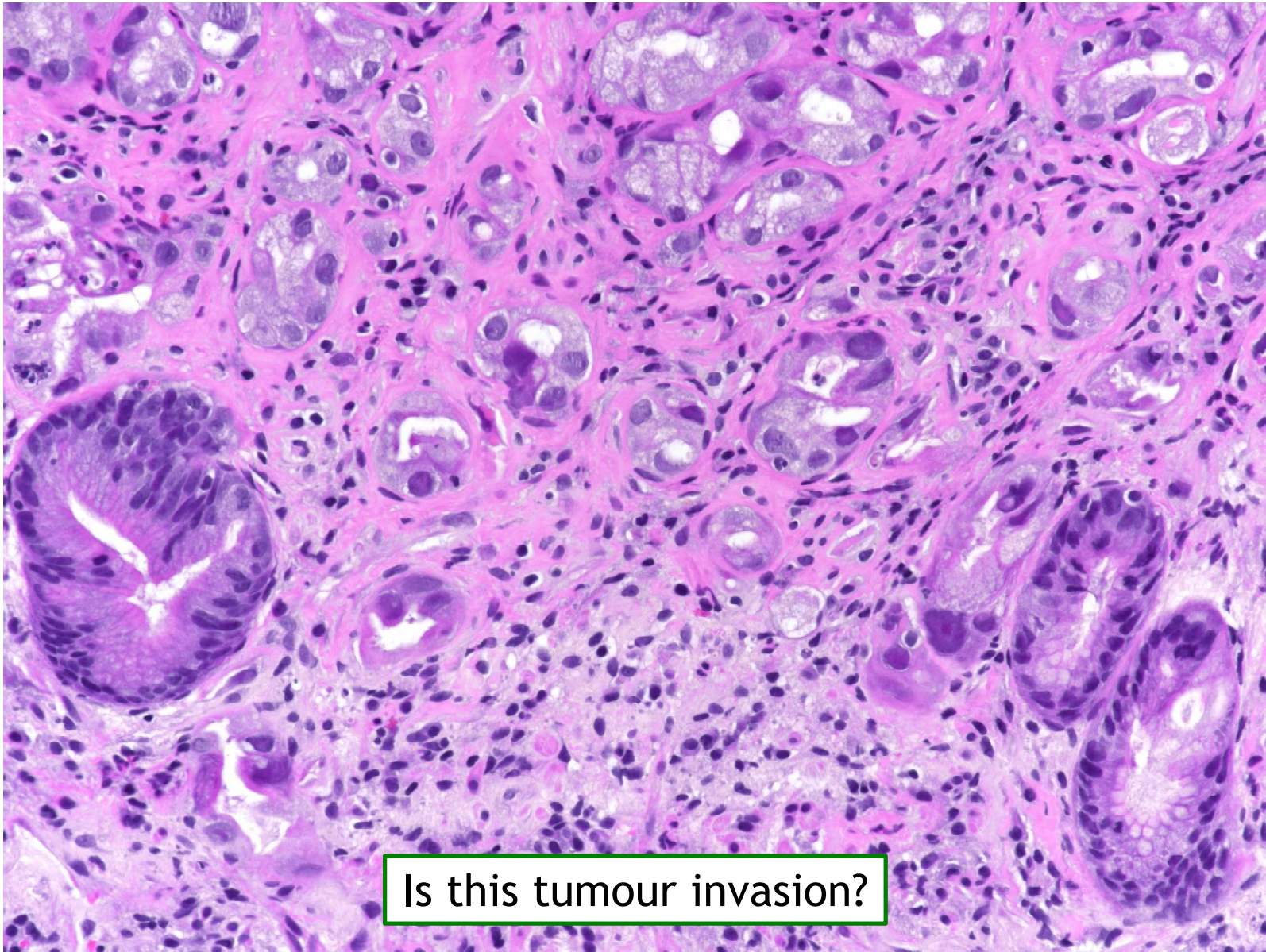












Is this tumour invasion?



What is your diagnosis?

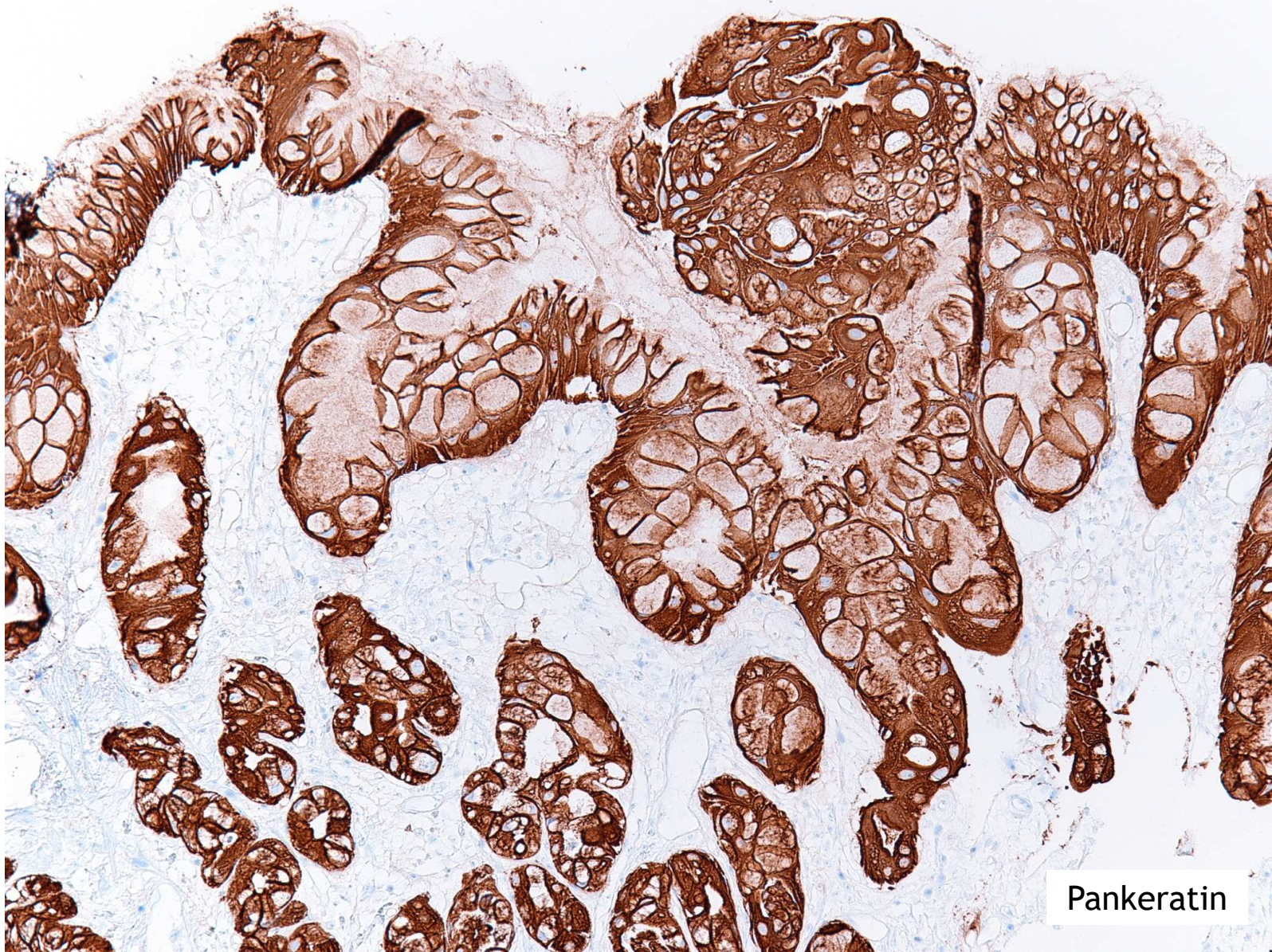
- ▶ Gastric cancer
- ▶ Metastatic melanoma
- ▶ Non-neoplastic ulceration
- ▶ None of the above



Would you like to see extra stains?

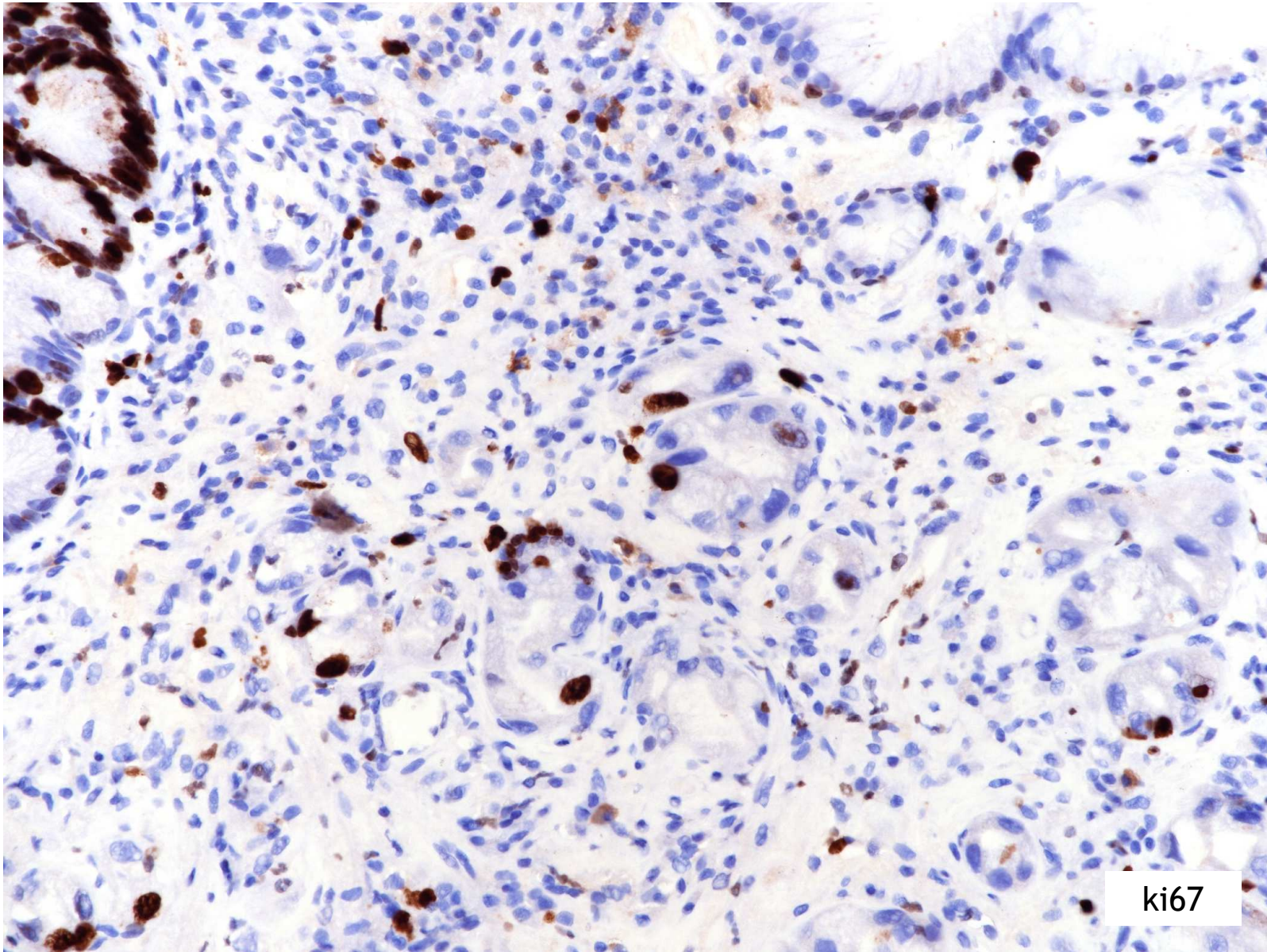
- ▶ Keratin
- ▶ SOX10 (Melan A, others)
- ▶ p53
- ▶ Ki67





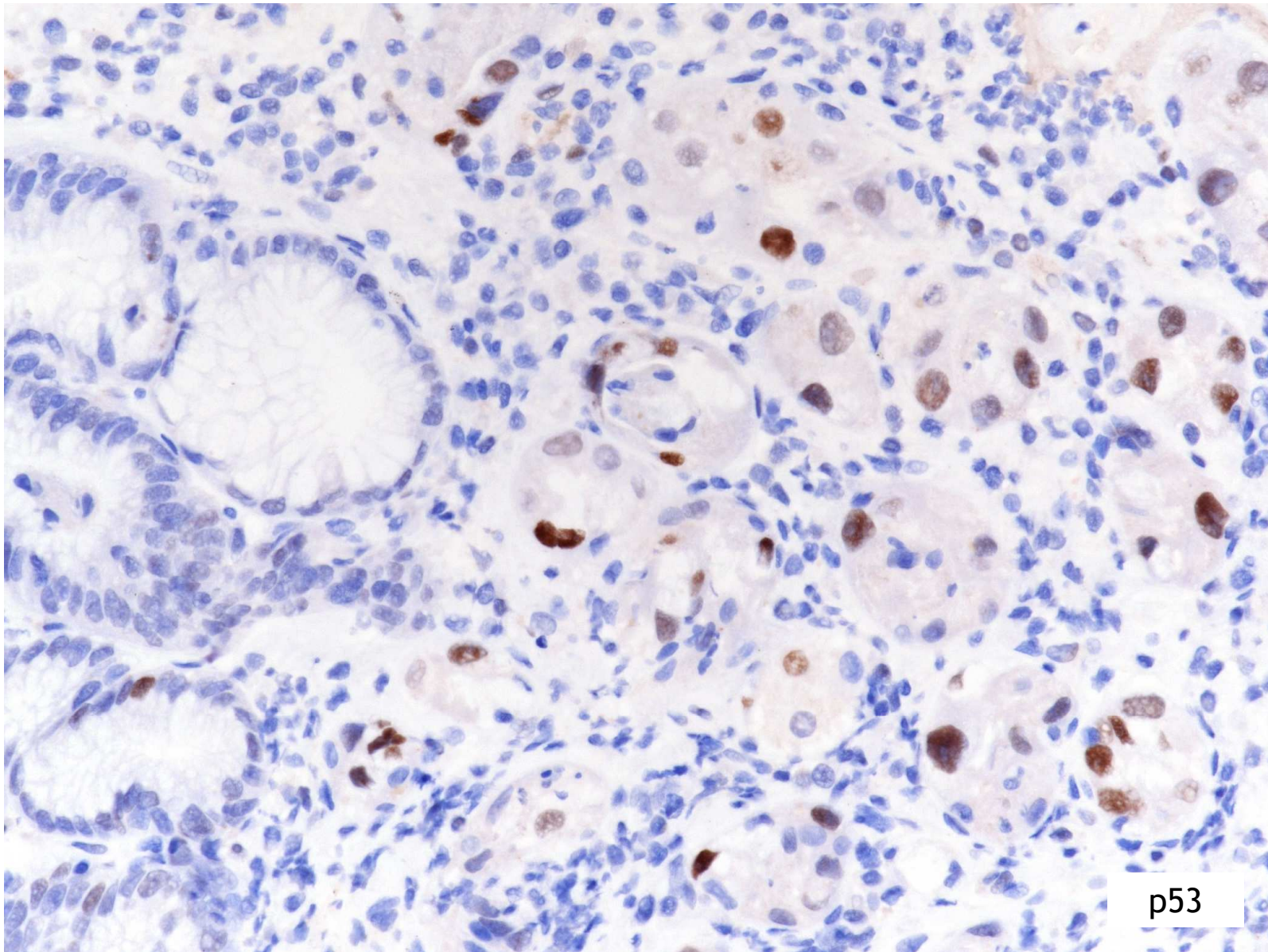
Pankeratin





ki67





... let us expand the background story

- ▶ Uveal melanoma with liver metastasis
- ▶ The patient is under arterial chemoembolization (TACE) with fotemustine
- ▶ During the first course she experienced gangrenous cholecystitis
- ▶ The second and the third course were uneventful
- ▶ The patient developed upper abdominal pain after the fourth course, endoscopy was performed about two weeks later



What is your final diagnosis now knowing the whole story?

- ▶ Gastric cancer
- ▶ Metastatic melanoma
- ▶ Non-neoplastic ulceration
- ▶ None of the above

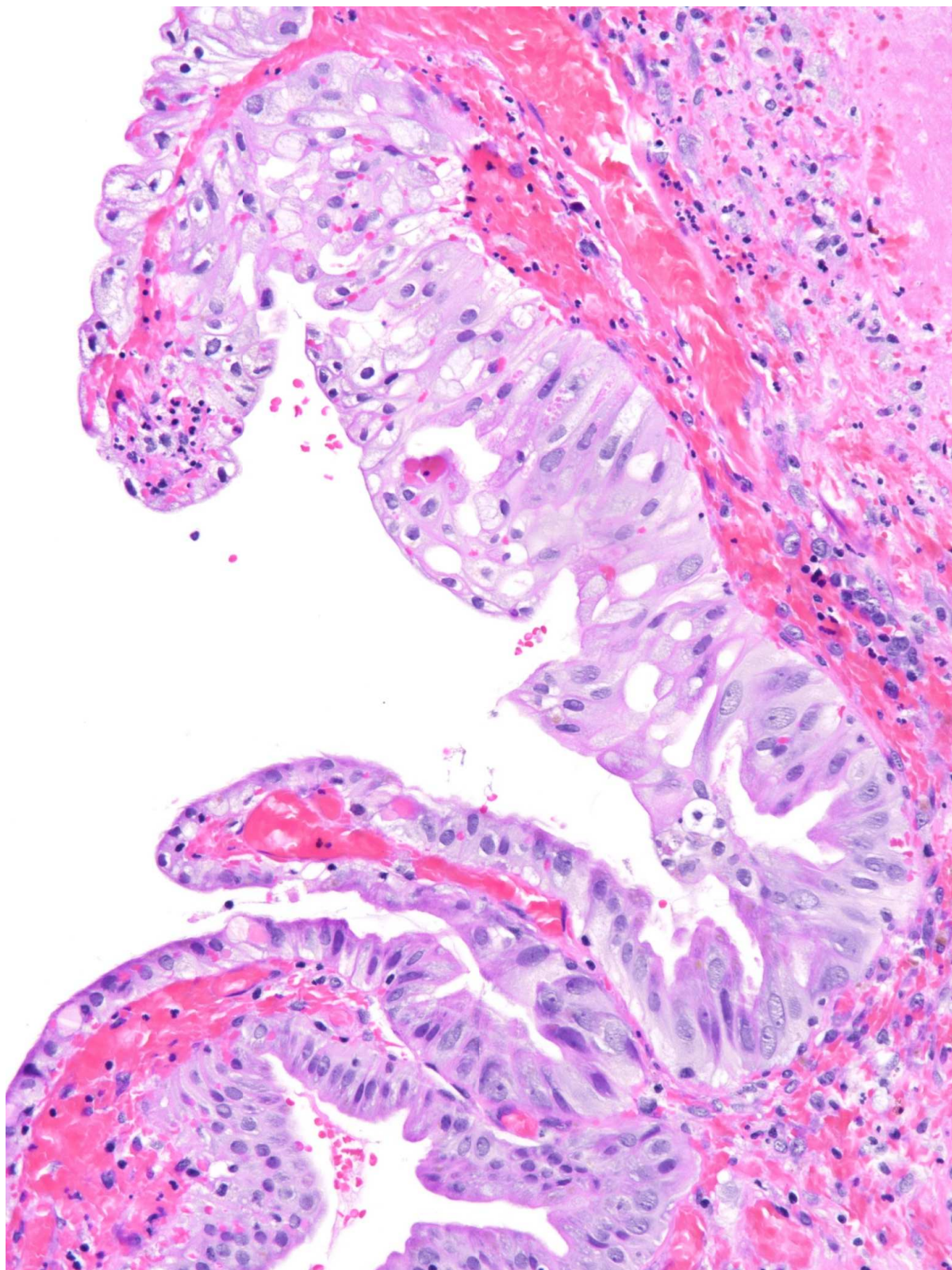


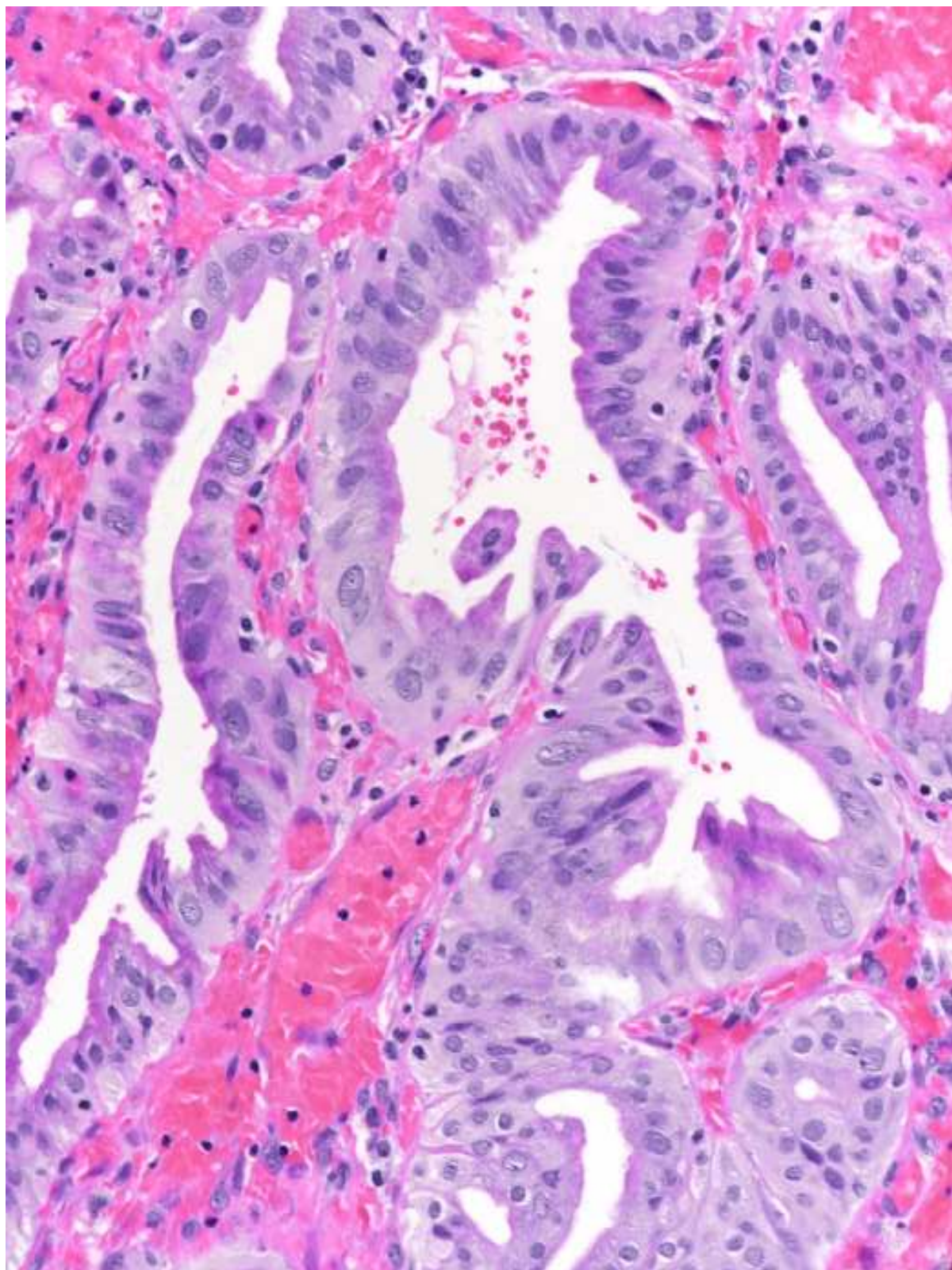
What is the diagnosis I made?

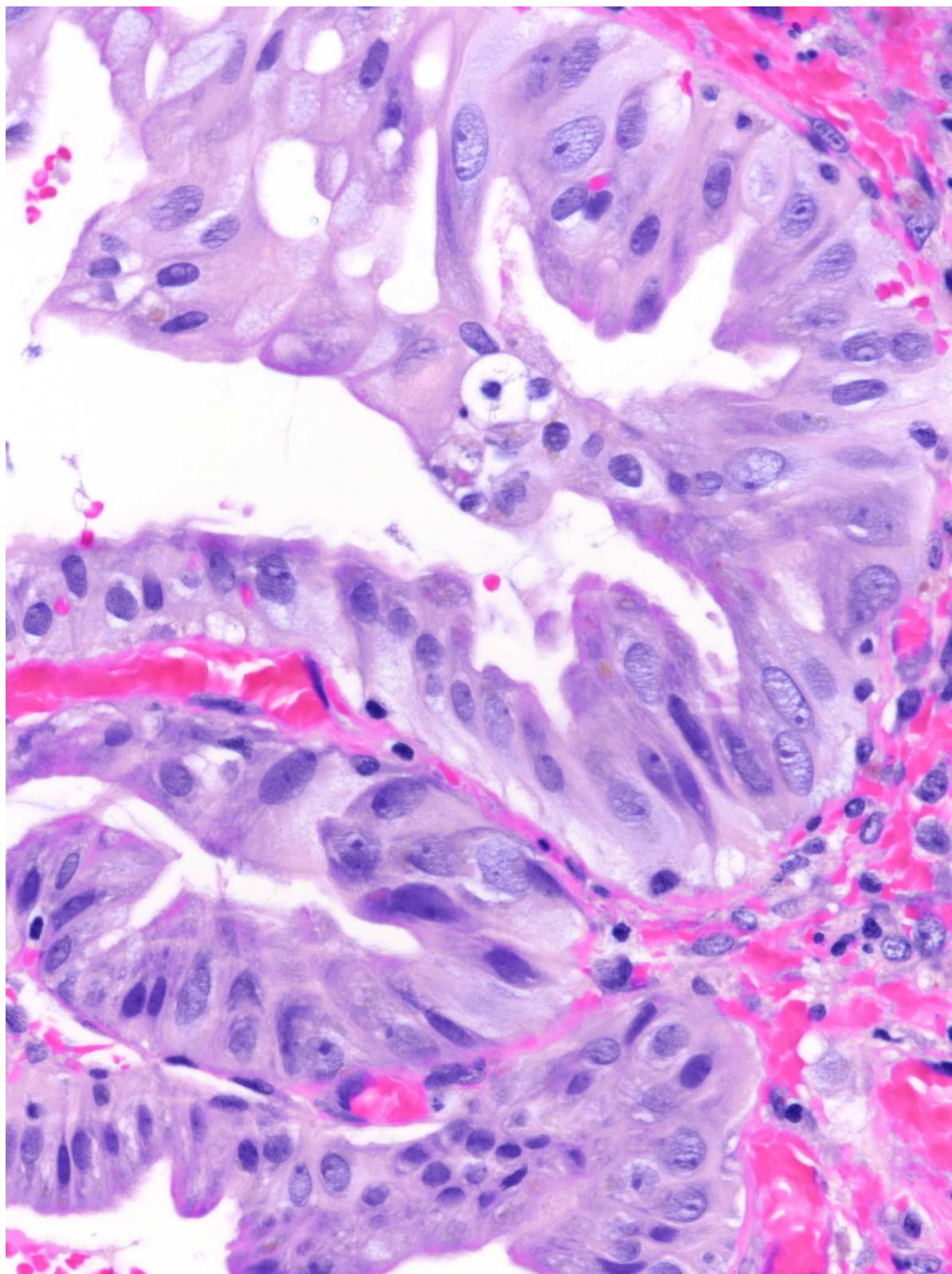
- ▶ Non-neoplastic ulceration
- ▶ Reactive changes due to double-hit injury by arterial chemoembolization (TACE) and fotemustine

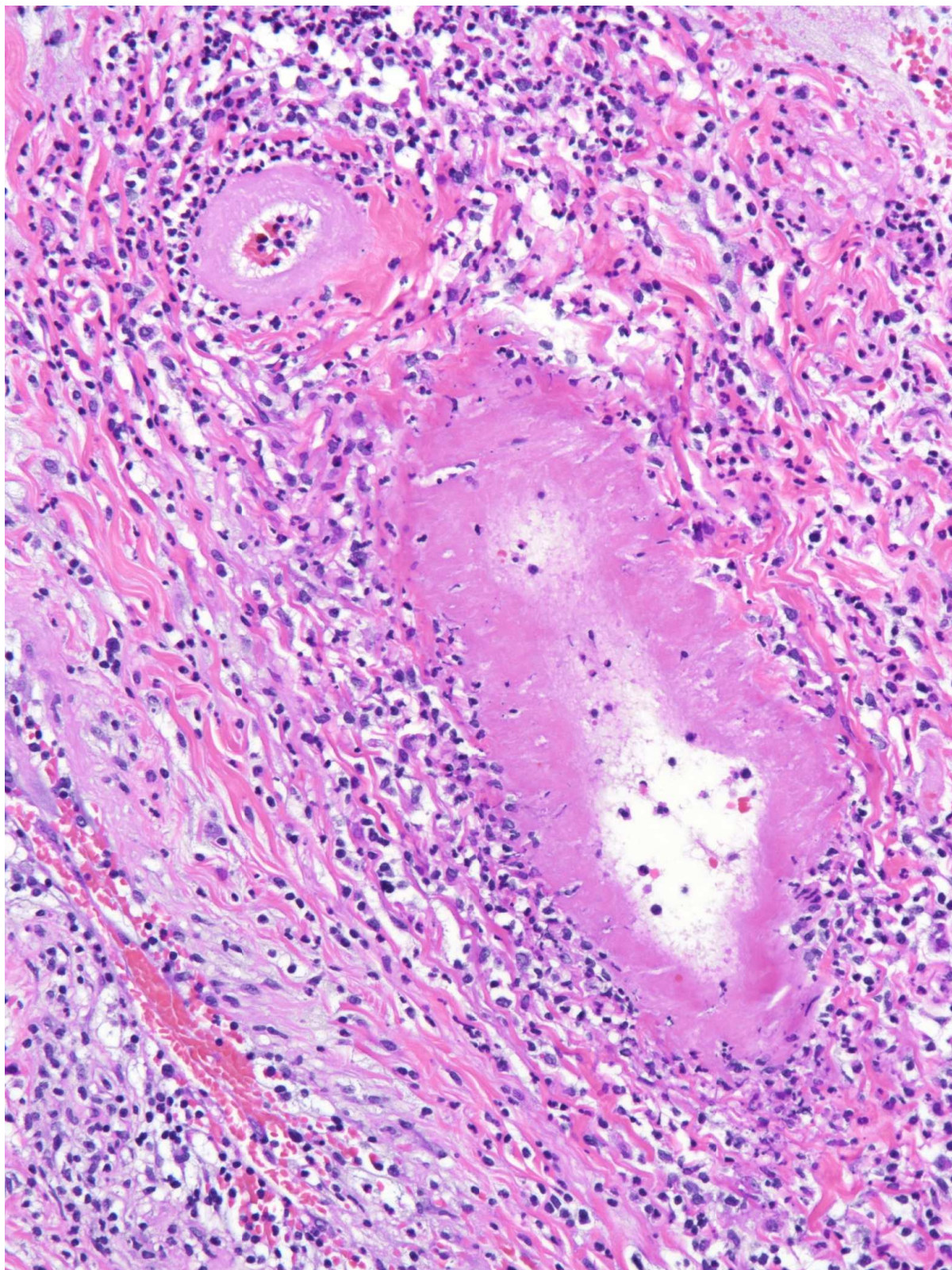
Let us look at the gallbladder...



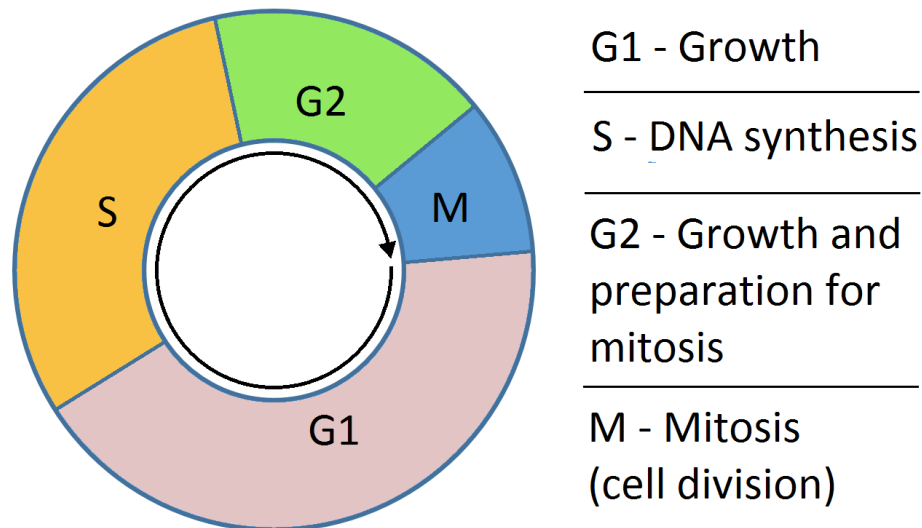








The morphology is the result of a combined ischaemic and toxic (drug-induced) effect...

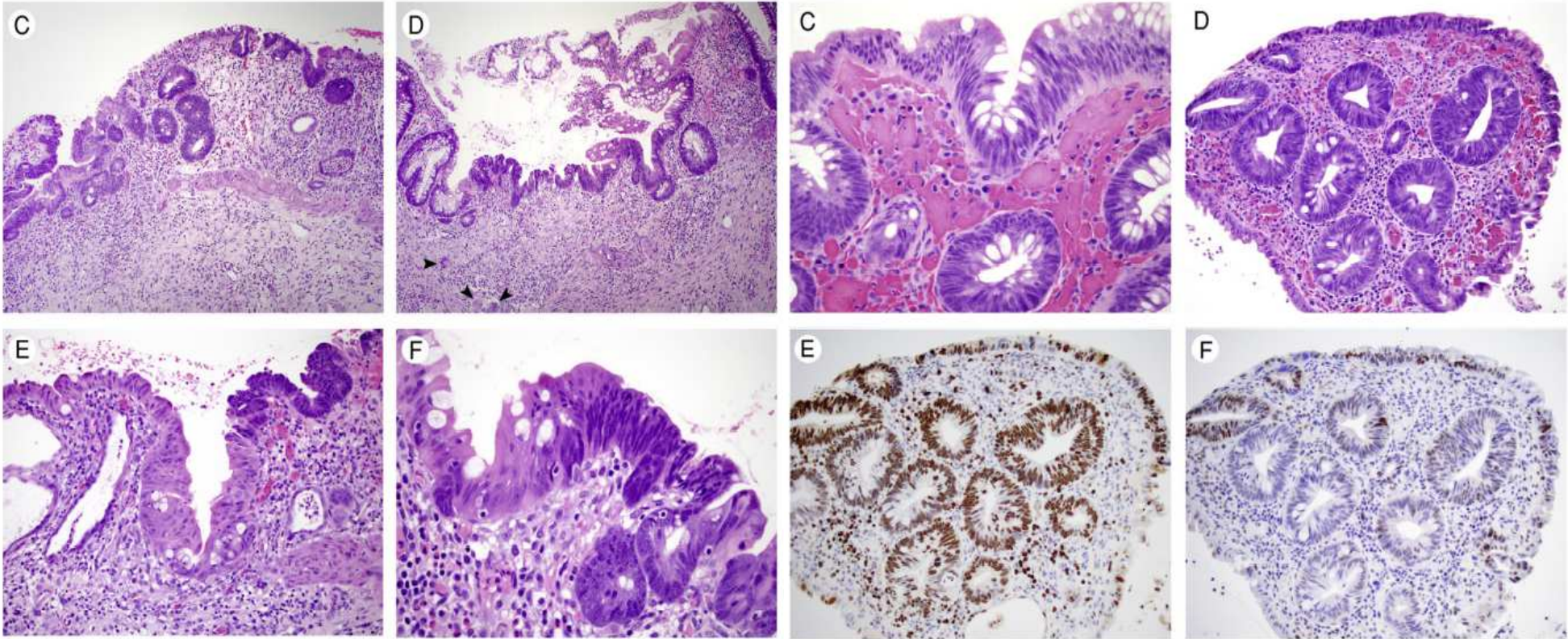


- ▶ Morphology comparable to antimetabolite chemotherapy induced colitis
- ▶ Fotemustine is a nitrosourea alkylating agent: interstrand crosslinking of DNA, which prevents DNA replication, and ultimately leads to apoptosis (in a p53 dependent manner)
- ▶ M phase with highest levels of Ki67 is not reached (p53 > ki67)



Dysplasia-like epithelial atypia in ischemic bowel disease ☆

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Selective Internal Radiation Therapy-induced Extrahepatic Injury

An Emerging Cause of Iatrogenic Organ Damage

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Timothy Sielaff, MD,|| Cynthia A. Sherman, MD,¶ and Kenneth P. Batts, MD*†¶

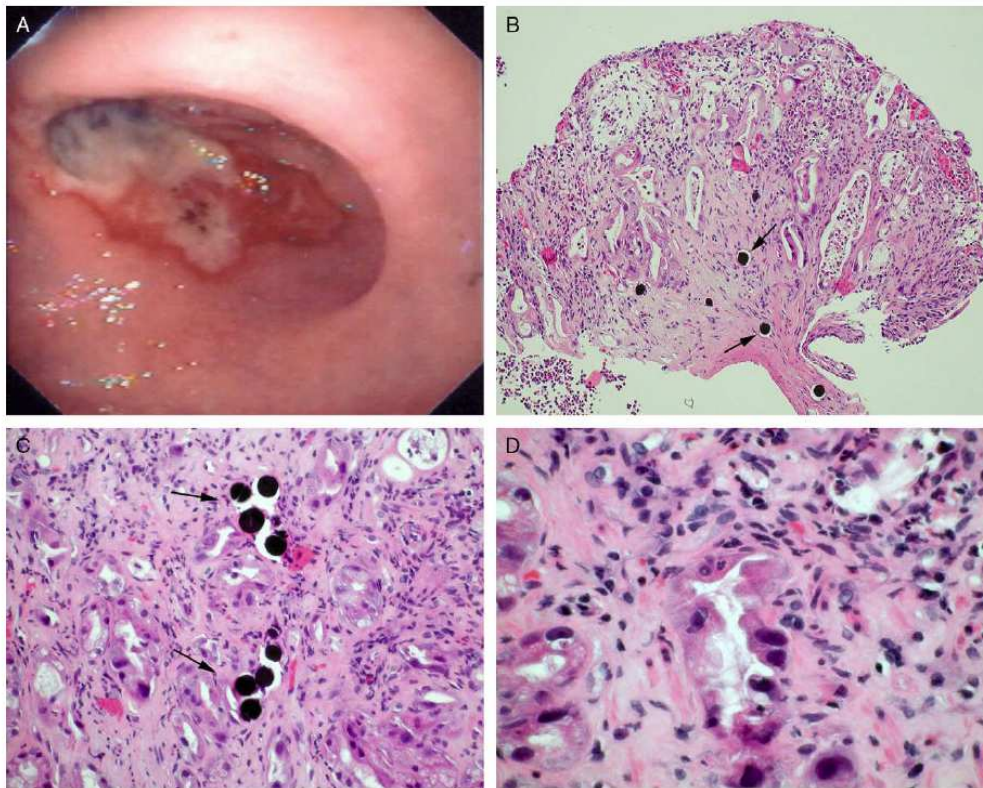



FIGURE 1. SIRT-induced gastric ulcer, patient 1. A, Endoscopic appearance. B and C, SIRT microspheres (arrows) are located in mucosal vessels. D, Radiation-induced epithelial atypia initially interpreted as gastric adenocarcinoma (B–D, H&E stained). H&E indicates hematoxylin and eosin; SIRT, selective internal radiation therapy. 

- ▶ Selective internal radiation therapy (SIRT) using ^{90}Y microspheres can be used for localized treatment of hepatic tumors
- ▶ Extrahepatic particles may lead to radiation-induced atypia mimicking adenocarcinoma (within the upper gastrointestinal tract, e.g. GEJ and stomach) → do not perform Ki67/p53 immunostaining

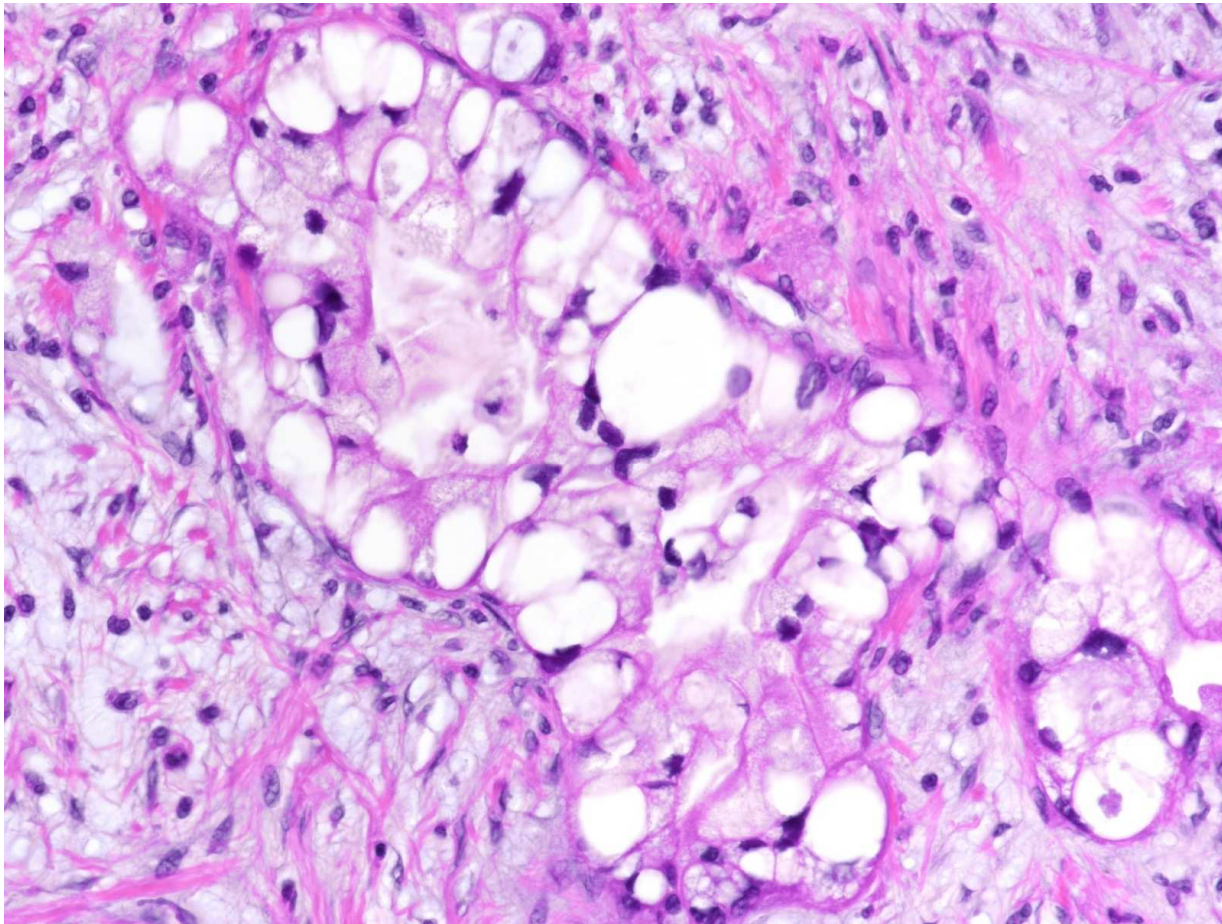


Summary

- ▶ Drug induced injury may lead to cellular / nuclear changes mimicking dysplasia
- ▶ Overall preserved mucosal architecture and distinct cytopathic effects (cytoplasmic eosinophilia and ballooning, nuclear enlargement with bizarre atypia yet preserved nuclear/cytoplasmic ratio) may render important clues to diagnosis
- ▶ Avoid immunohistochemistry (DD p53 overexpression of wild type versus abnormal staining indication p53 mutation)
- ▶ Close collaboration between clinic and pathology is required to avoid overdiagnosis



Ballooning is not a proof of benignity...



... this is an
example of
adenocarcinoma
of pancreato-
biliary type (with
balloon cells)



**Thank you very much for
your kind attention!**

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