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CONCOMITANT MALIGNANCIES OF THE GALL BLADDER AND PANCREAS: A SYNCHRONOUS ONCOLOGIC CHALLENGE

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INTRODUCTION

- Synchronous gallbladder and pancreatic cancer is extremely rare and fatal with limited case reports worldwide.
- Incidence:- 1.2 cases/100000 population/year
- Here I present a similar case of synchronous malignancy of the gall bladder and pancreas, its diagnosis, complications and successful management.

CASE HISTORY

A 60 year male, presented with chief complaints of:

- Pain in abdomen x 2 weeks
- Yellowish discoloration of eyes and skin x 1 week
- Passage of deep yellow urine x 5 days
- Generalized itching x 3 days.

- No history of fever, loss of appetite or loss of weight
- No passage of clay-colored stools
- No hematuria/ hematemesis/ melena

- He is a known case of Hypertension; on Medication
- He is habituated to Alcohol x 30 years and consumed ~ 180 ml x 3-4 times/week

- No previous surgical history
- No significant family history of Liver diseases, Malignancy, Death due to Malignancy

GENERAL PHYSICAL EXAMINATION

Patient was conscious, cooperative and oriented to time, place and person

- Pulse rate: 88/min
- Blood pressure- 130/80 mm Hg

Pallor +, Icterus +

Scratch marks and yellowish discoloration noted over bilateral upper limb, abdomen and bilateral lower limb

SYSTEMIC EXAMINATION

PER ABDOMEN

- Soft, Non tender
- **2x2 cm lump palpable in the epigastric region**

The lump was firm in consistency, non mobile, did not move with respiration, did not fall forward in knee elbow position

- No organomegaly
- No evidence of free fluid
- Bowel sounds present in all four quadrants

BLOOD INVESTIGATIONS

LFT

- Total Bilirubin- 10.76
- Unconjugated Bilirubin- 2.47
- Conjugated Bilirubin- 8.29
- SGOT/PT- 103/127
- ALP-571
- GGT- 487

Amylase- 85
Lipase-23
CEA- 6.96
CA 19.9- > 1200

Clinical and Laboratory investigations raised a suspicion of Obstructive Jaundice secondary to ?Peri ampullary carcinoma, ?Cholelithiasis with cholecystitis with choledocholithiasis

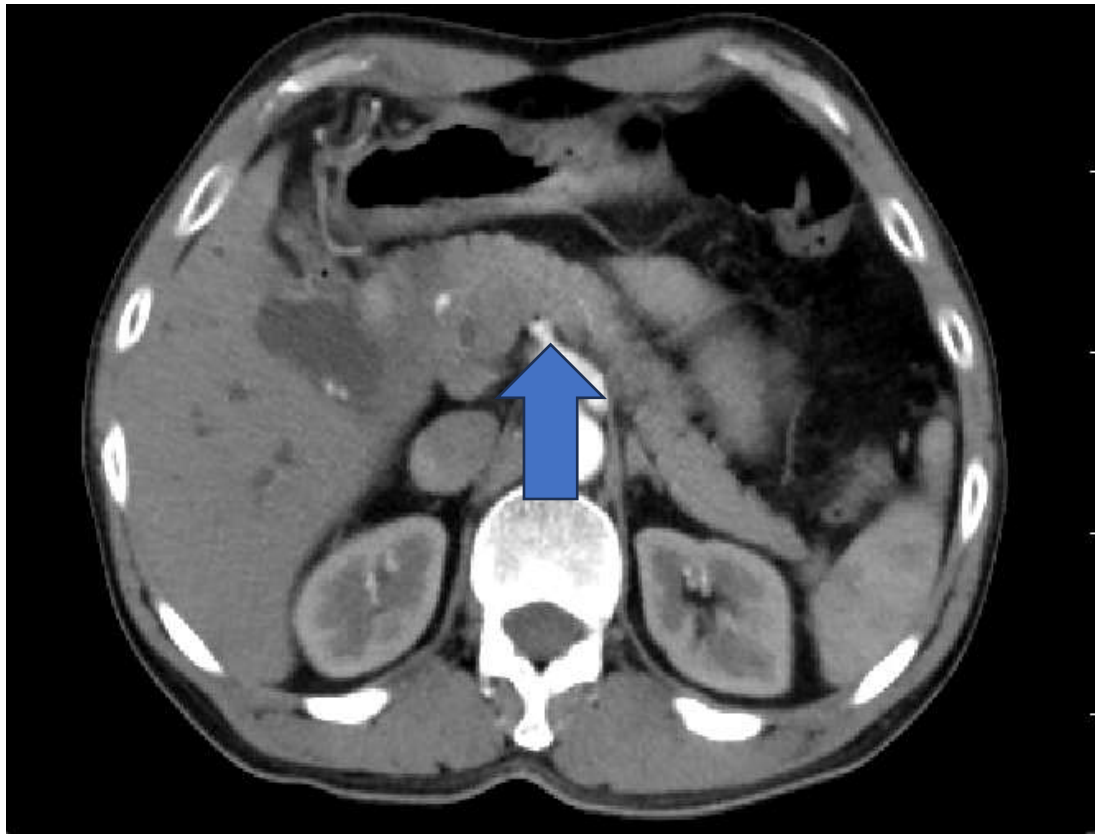
RADIOLOGICAL INVESTIGATIONS

USG Abdomen and Pelvis was suggestive of Cholelithiasis without Cholecystitis with dilated common bile duct with prominent IHBR.

CECT Abdomen and Pelvis was suggestive of

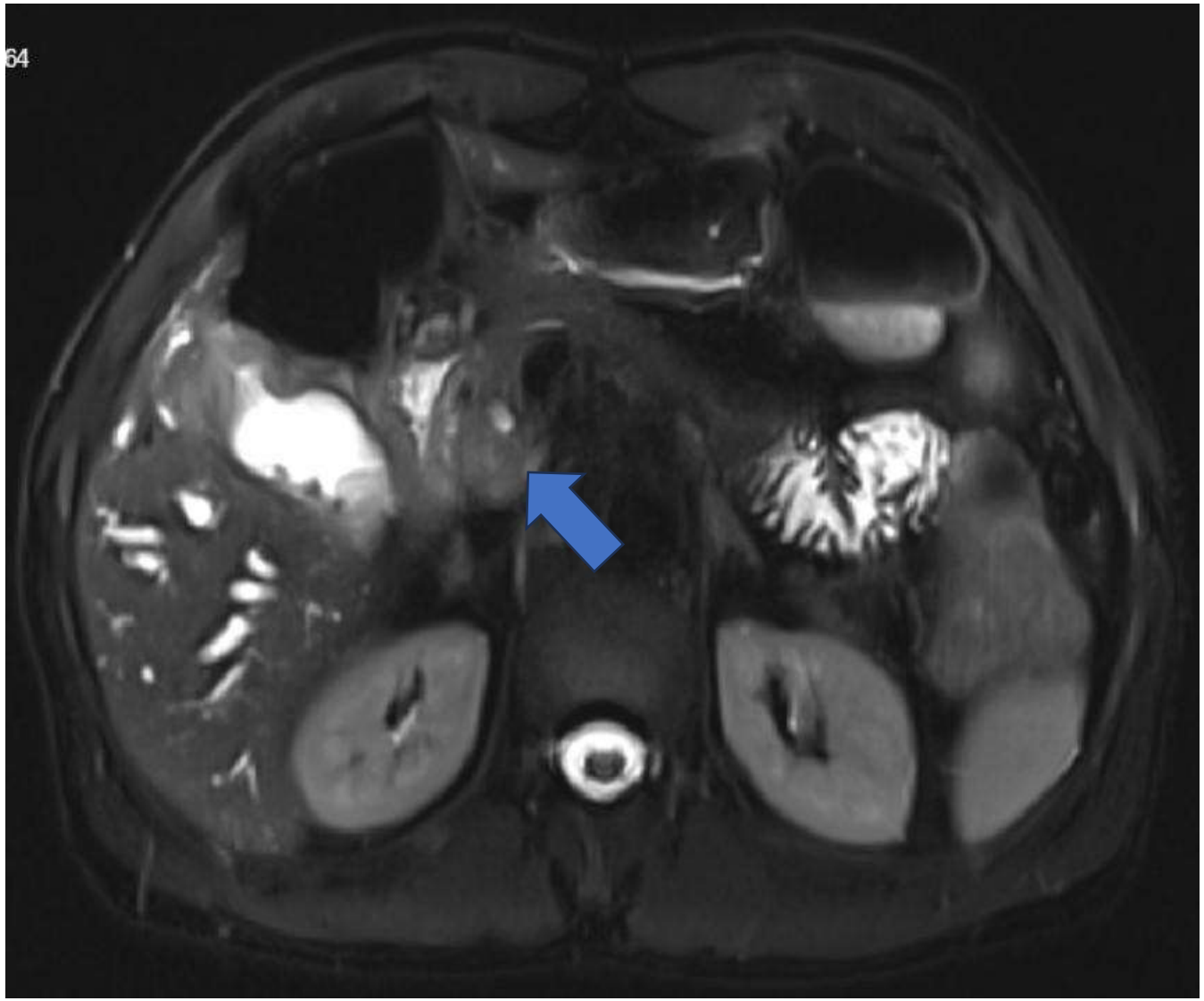
- Multiple hyperdense calculi noted in gall bladder with wall thickening at fundus.
- Dilated cystic duct, intrahepatic biliary radicals and common bile duct.
- A faintly radio-dense calculus is noted in lower CBD just proximal to the ampulla of Vater.

Pancreas is normal in size, attenuation and enhancement. No obvious mass lesion or calcification noted



MRCP was suggestive of An irregular focal lesion involving the head region of pancreas and DWI restriction, involvement and encasement of lower CBD and marked proximal dilated CBD and IHBR-mostly malignant lesion

- ? CA pancreas with few enlarged periportal peripancreatic lymph nodes, precaval nodes.



Based on the clinical history, blood and radiological investigations the patient was planned for Endoscopic Ultrasound (EUS)
To assess the biliary tree/ gall bladder, any suspicious mass/lymph node

EUS was suggestive of a **large hypoechoic mass of size 15 mm x 15 mm in the distal CBD extending to intraductal region** - ?Periampullary carcinoma.
FNAB was sent

HPE: **Adenocarcinoma of distal CBD**

ERCP with STENTING

- No radiolucent shadows
- Intra- hepatic biliary radical dilatation
- Distal CBD stricture
- Sphincterotomy and CBD stenting was performed.

On day 2 s/p ERCP with stenting

- Bilirubin levels continue to increase
- Absence of Pneumobilia

Non functionality of the Stent

ERCP with Endonasal Biliary Drainage
(To relieve Jaundice)

With preoperative diagnosis of Obstructive Jaundice secondary to Periampullary carcinoma, the patient was planned for **Whipple's Procedure (Pancreaticoduodenectomy)** 1 month after optimization of deranged LFTs.

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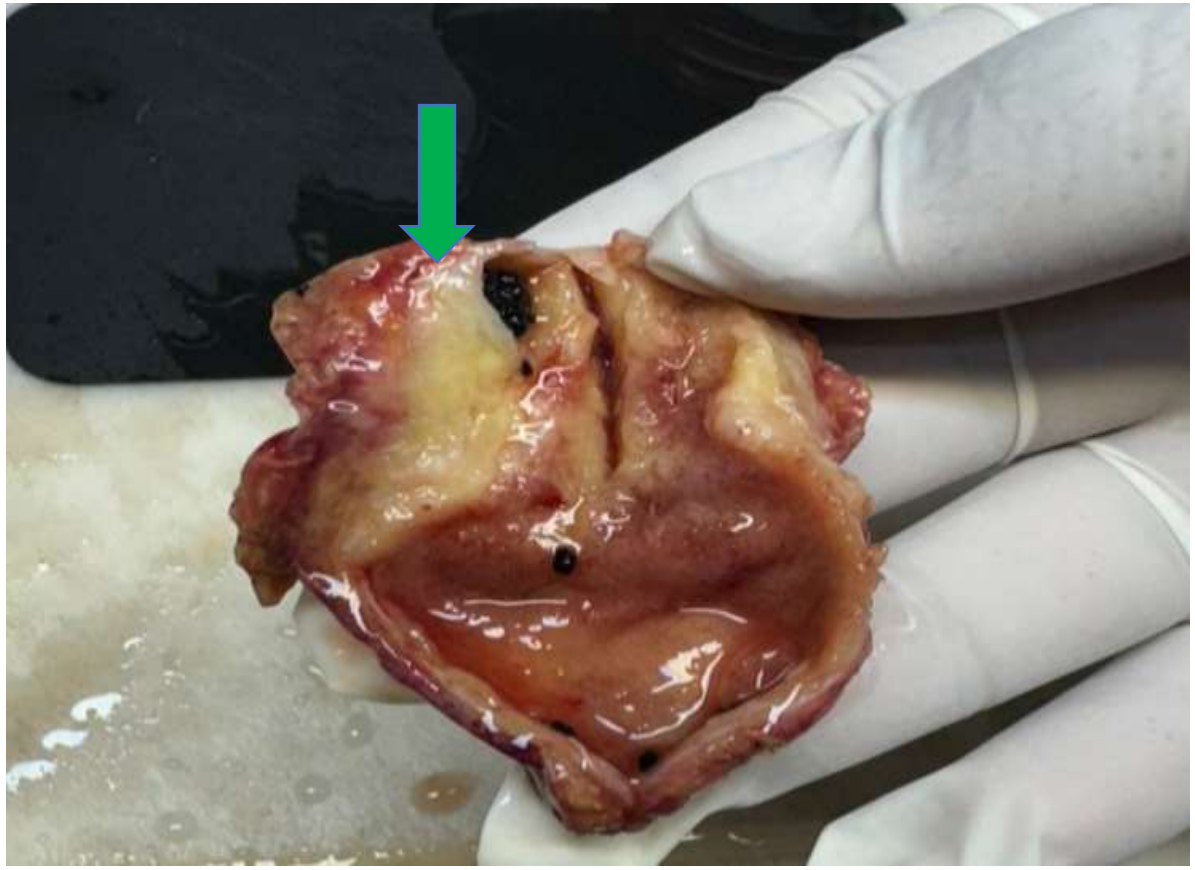
Intraoperatively a **nodule** was felt in the **body of Gall Bladder** for which **Gall bladder specimen** was sent for Frozen section



HPE: Positive for Malignancy

This raised a suspicion of synchronous gall bladder cancer with pancreatic head cancer, which was not visible in any preoperative radiological investigation.

⬇

A decision to perform **Whipple's Procedure with Radical cholecystectomy with Feeding Jejunostomy** was taken. The operation was uneventful.

Post operatively, the patient developed complications:

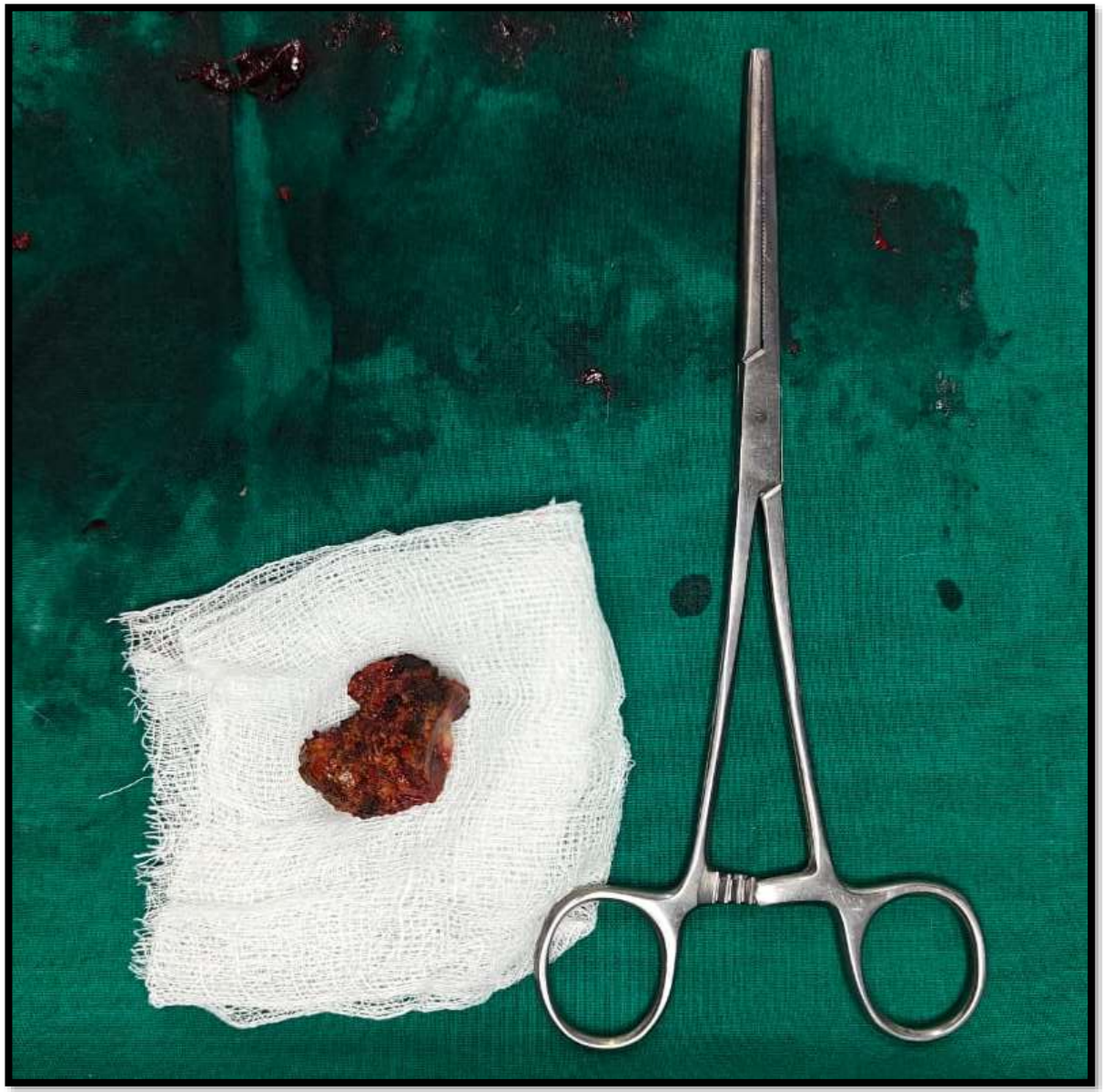
- **Acute hemorrhage** from a ?Branch of splenic artery for which he underwent Exploratory laparotomy on POD-2
- **Intra abdominal abscess with pancreatic fistula** and **Gastric outlet obstruction** on POD-10

which was managed conservatively The patient recovered well and was discharged from the Hospital on POD- 48

Feeding jejunostomy was removed on POD- 74

POST OPERATIVE

WHIPPLE'S PROCEDURE with RADICAL CHOLECYSTECTOMY



HISTOPATHOLOGY

Received 4 specimens:

1. Gall bladder and bile duct cut margin
2. Piece of liver from Gall bladder fossa
3. Whipple’s resection specimen - Pylorus of stomach along with head of pancreas, duodenum and part of proximal jejunum
4. Lymph node from periportal region.

1. Gall bladder measured 6 x 2.8 x 1cm

- Serosal surface of gall bladder fossa appeared rough.
- On opening, the mucosa near fundus and body showed papillary excrescences with thickened wall, measuring 2 x 2 x 1cm.

- Distance of growth from cystic duct cut margin – 3cm.
- Grossly, tumour seen abutting rough area.
- Multiple, small blackish stones identified – Near fundus.

2. Received piece of liver from gall

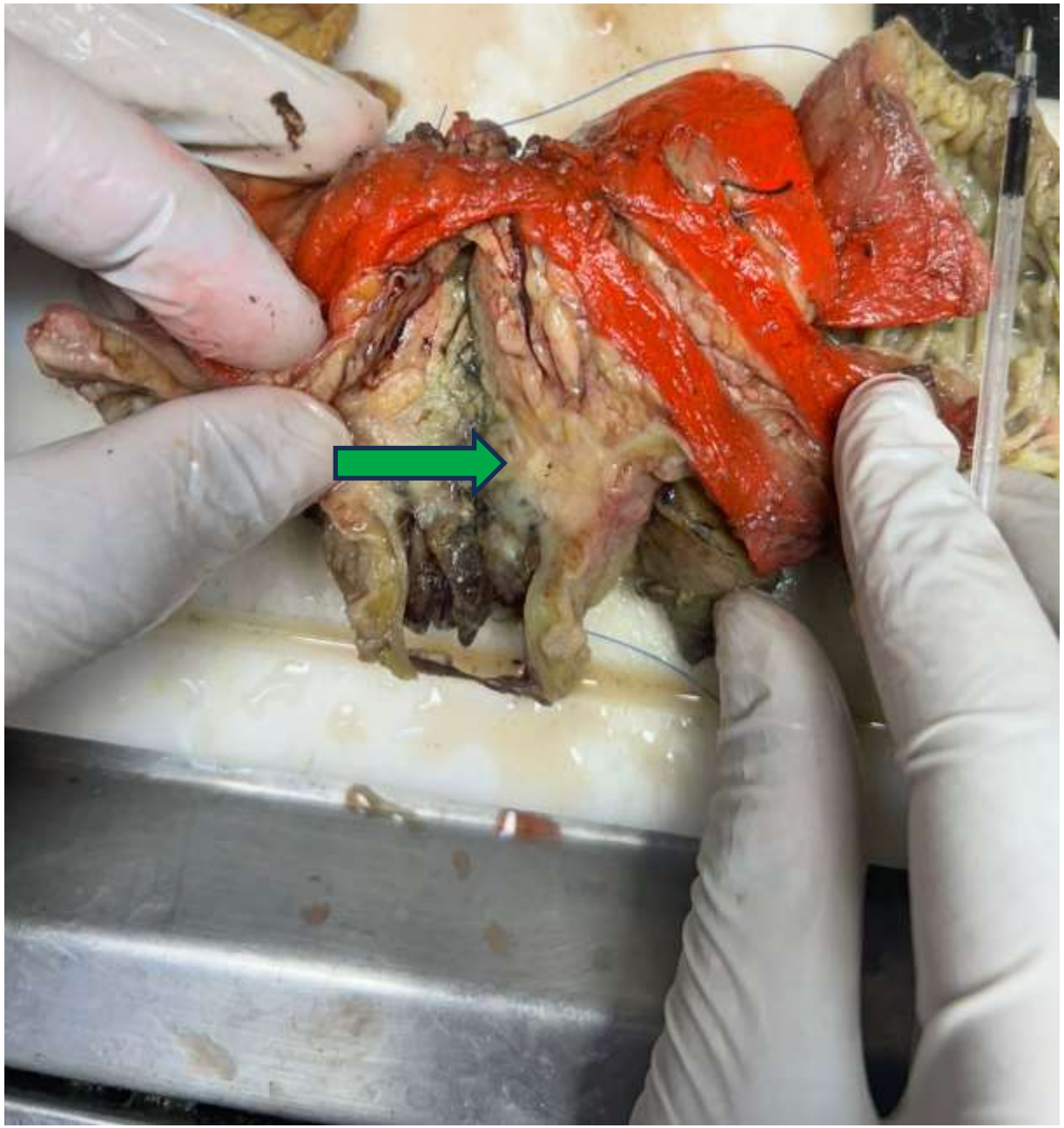
bladder fossa measuring 2.7 x 2 x 1.3cm

- Serial sectioning- Firm, greyish white nodule measuring 1.2 x 1 x 1cm

3. Pylorus of stomach along with head of pancreas, duodenum and part of proximal jejunum altogether measuring 27 cm in length.

- Part of stomach measured 3 cm
- Pancreas measured 7 x 3.5 x 2.5 cm
- Duodenum measured 25 cm
- Jejunum measured 2.5 cm

On serial sectioning of pancreas and adjacent duodenum, greyish white tumour – Distal part of CBD surrounding and blocking the lumen - measuring 1.8 x 1.5 x 1 cm.

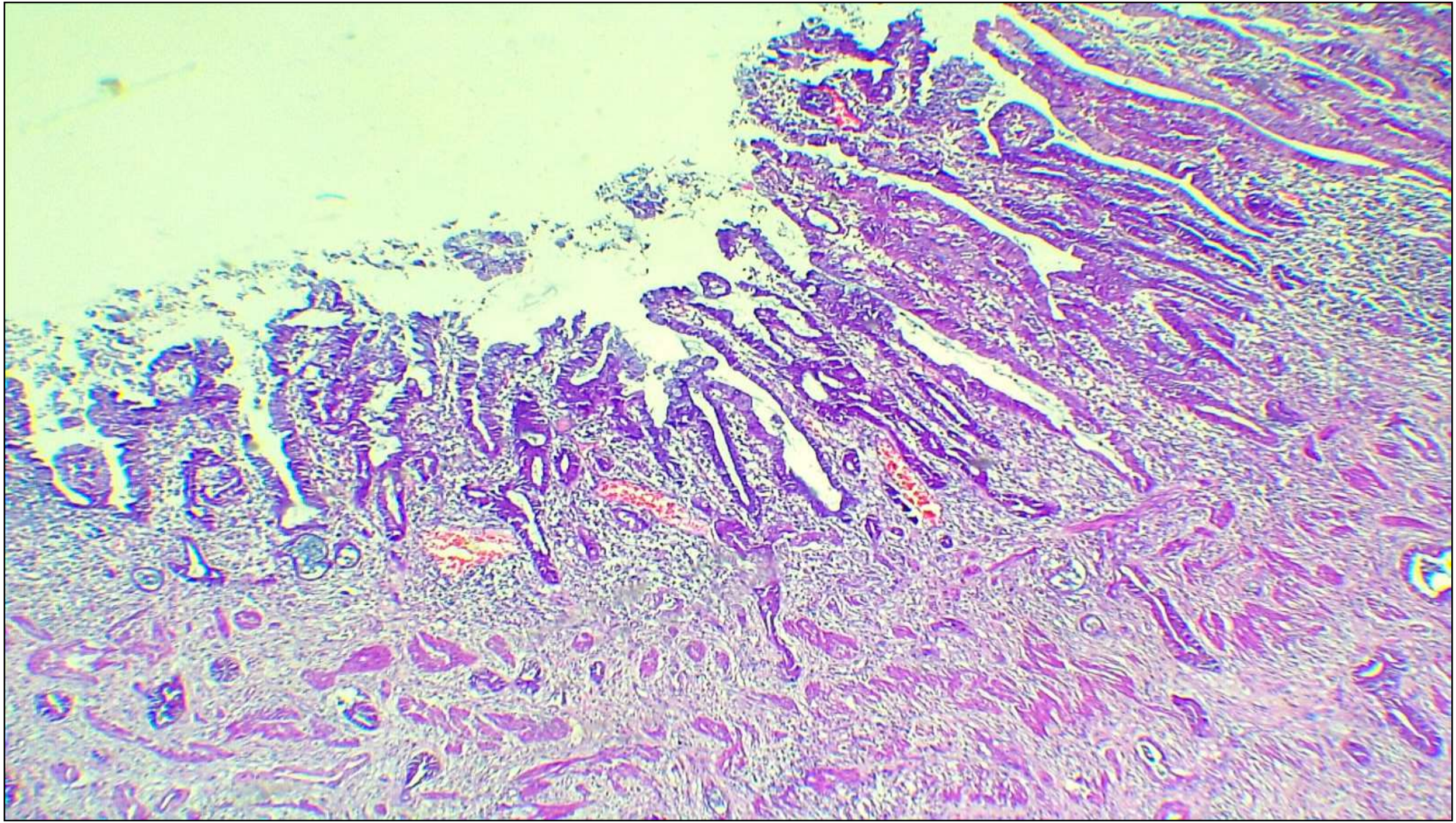


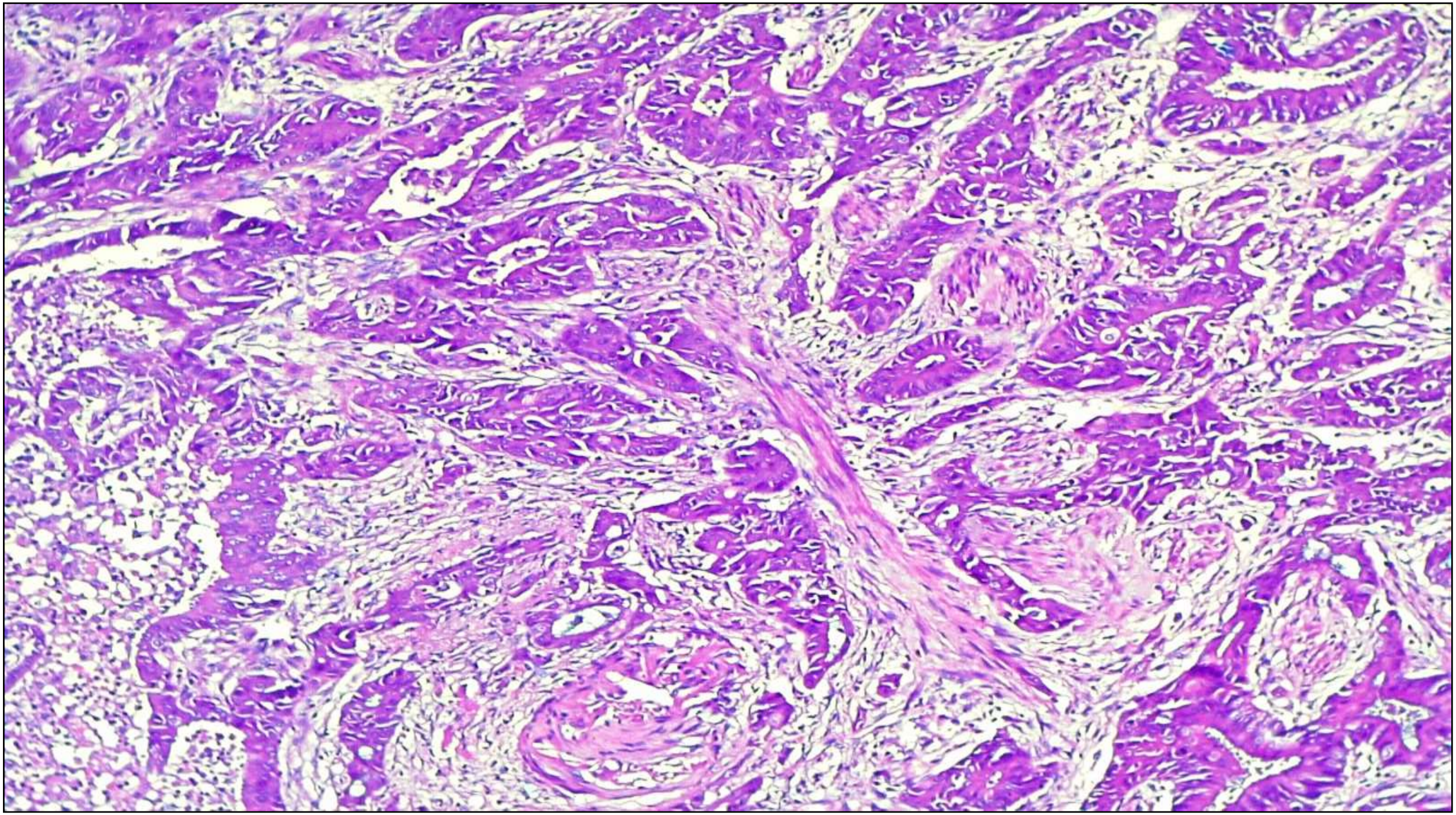
Distance of tumour from various margins:

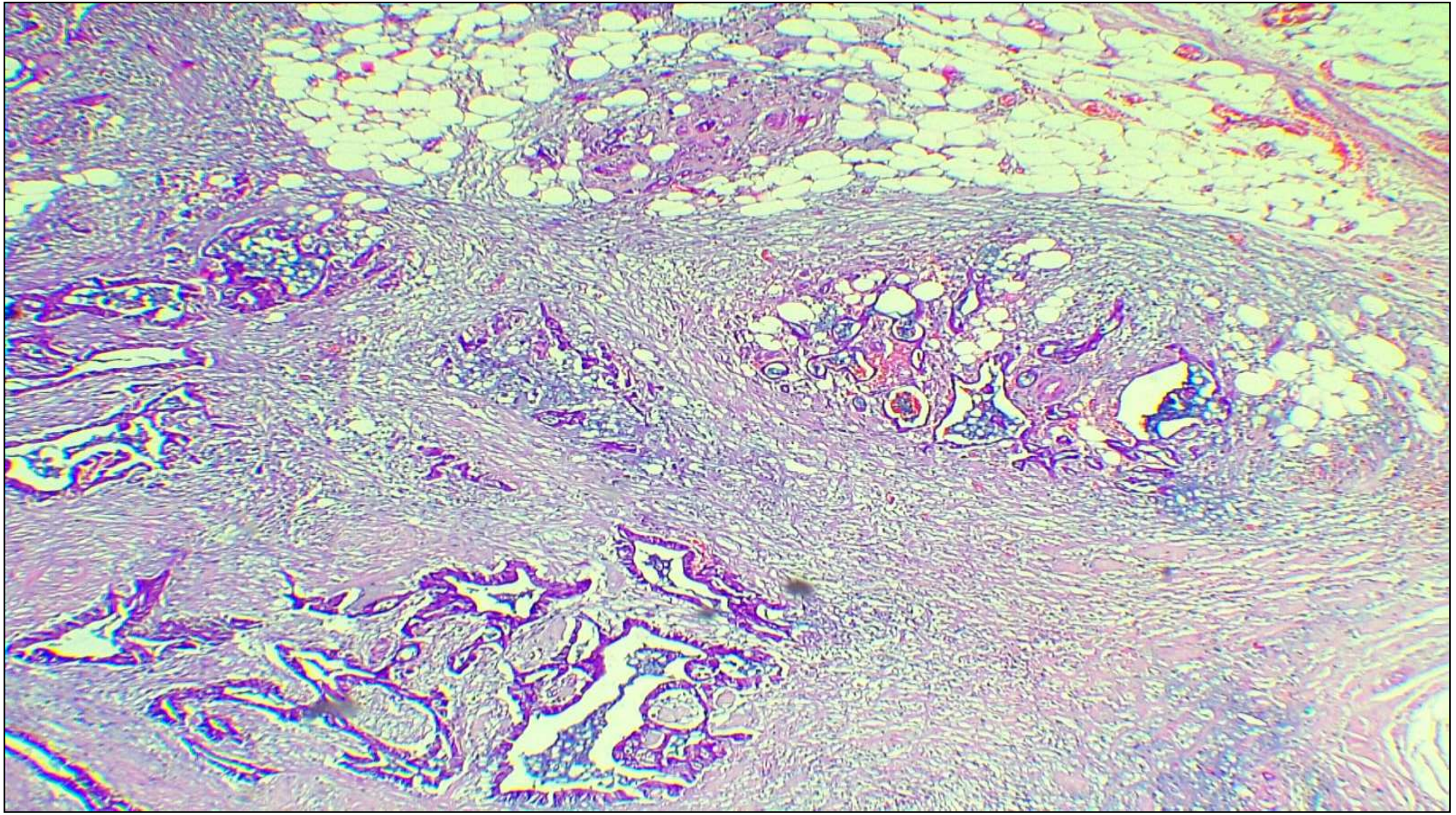
- Proximal margin – 6 cm
- Distal margin – 19 cm
- Anterior pancreatic surface – 2.8 cm
- Tumour – Abuts the posterior surface and SMA groove

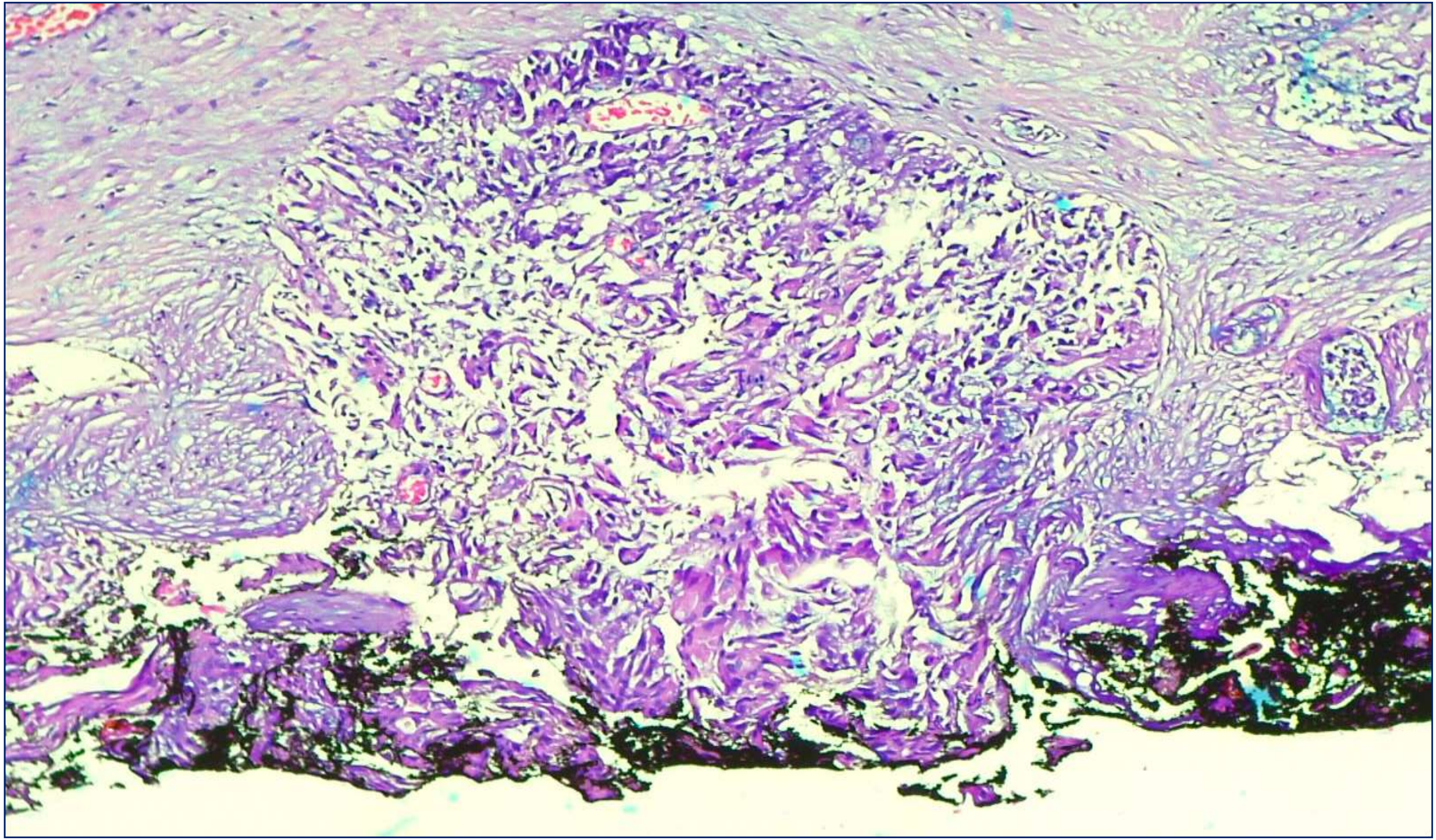
4. Received lymph node from periportal region measuring 3 x 1.3 x 0.8 cm.

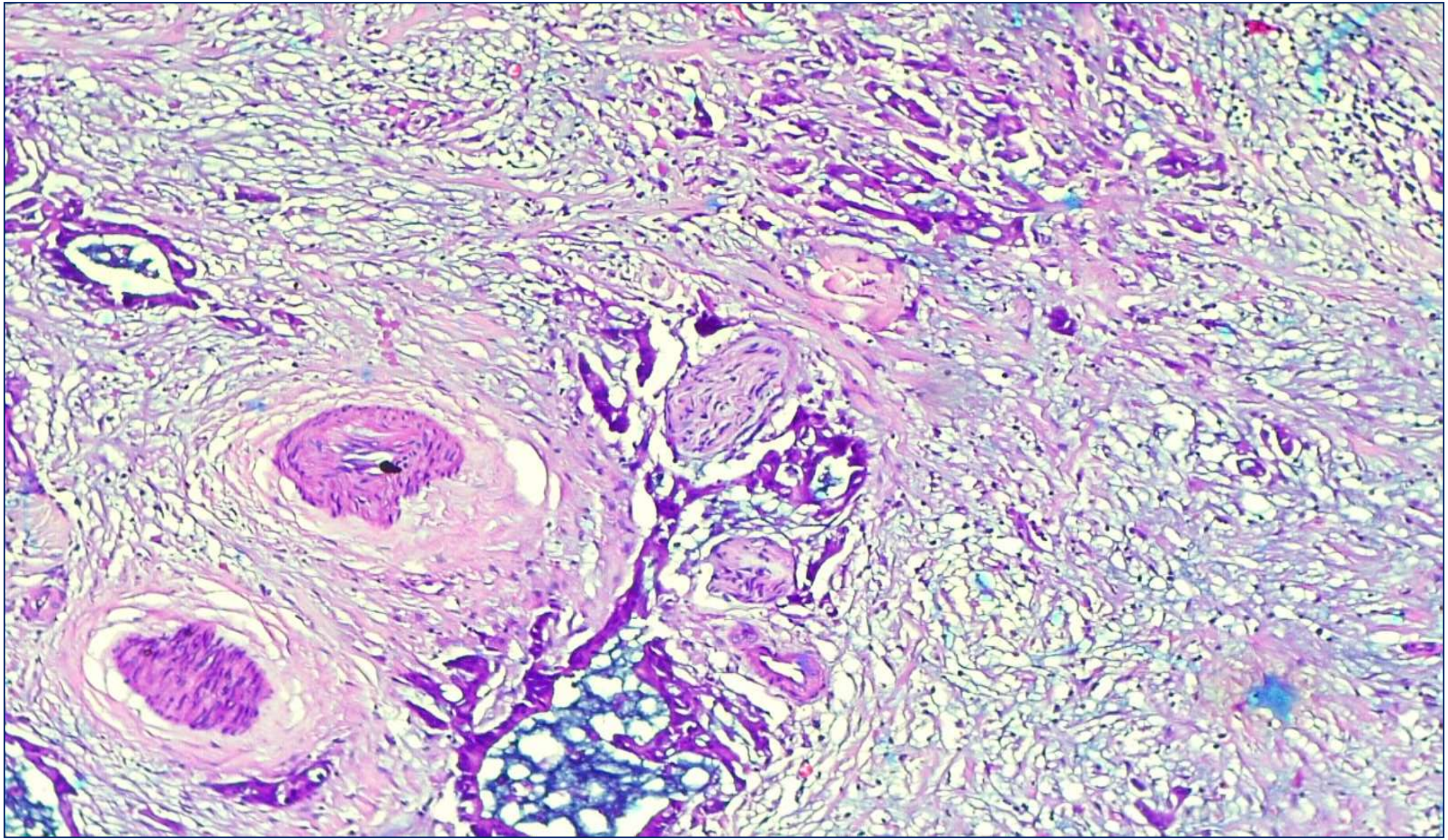
MICROSCOPY

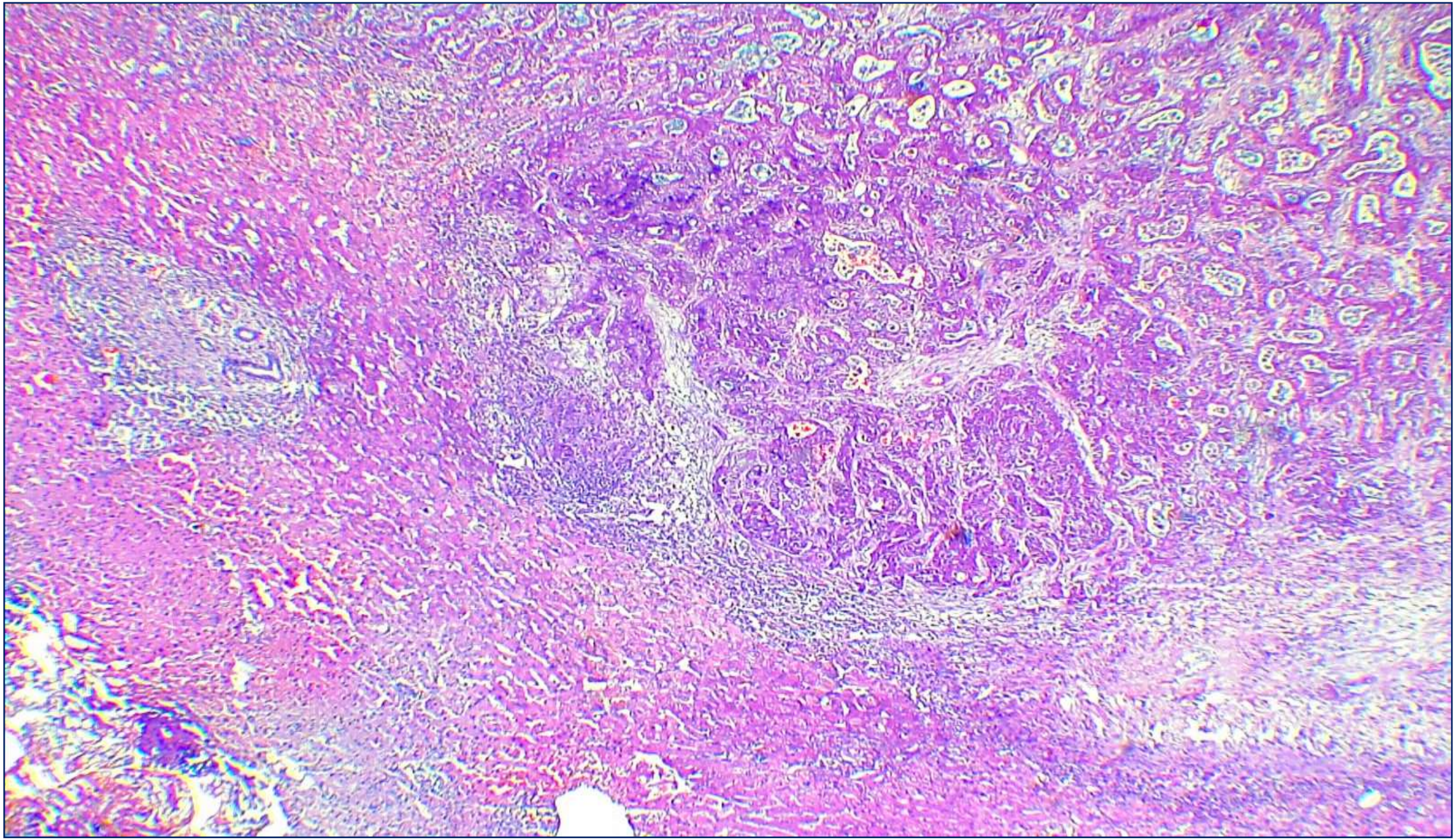


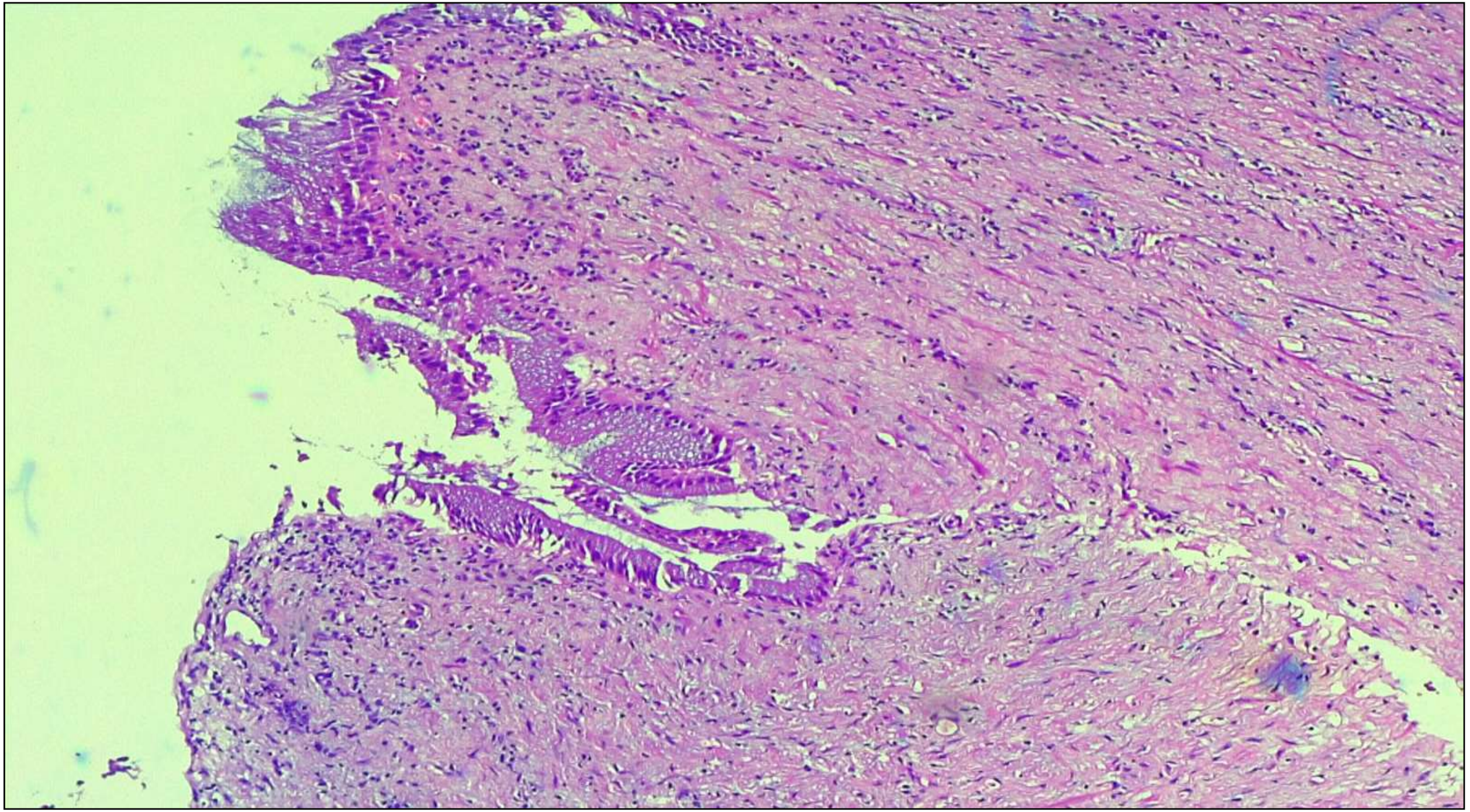


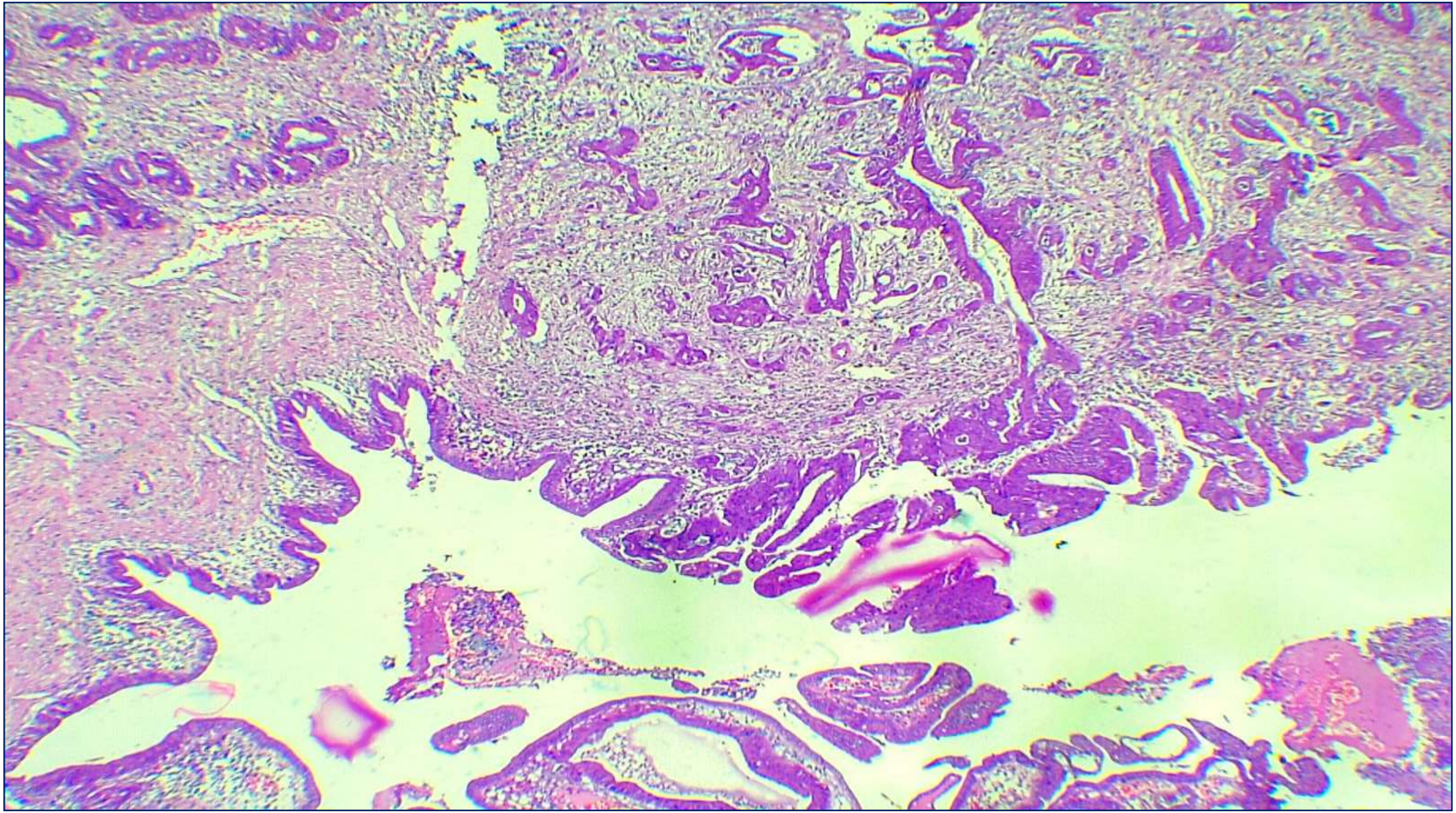


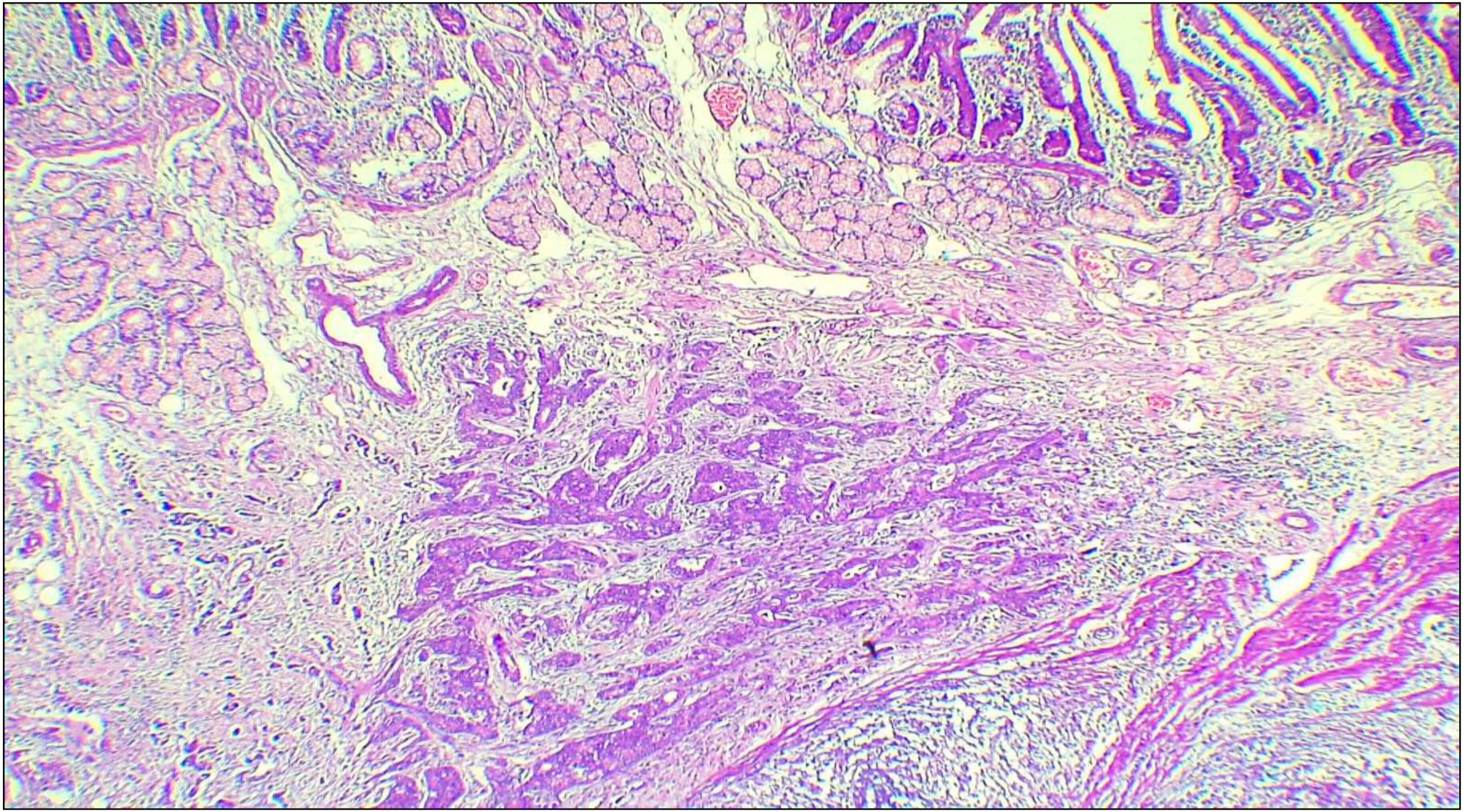


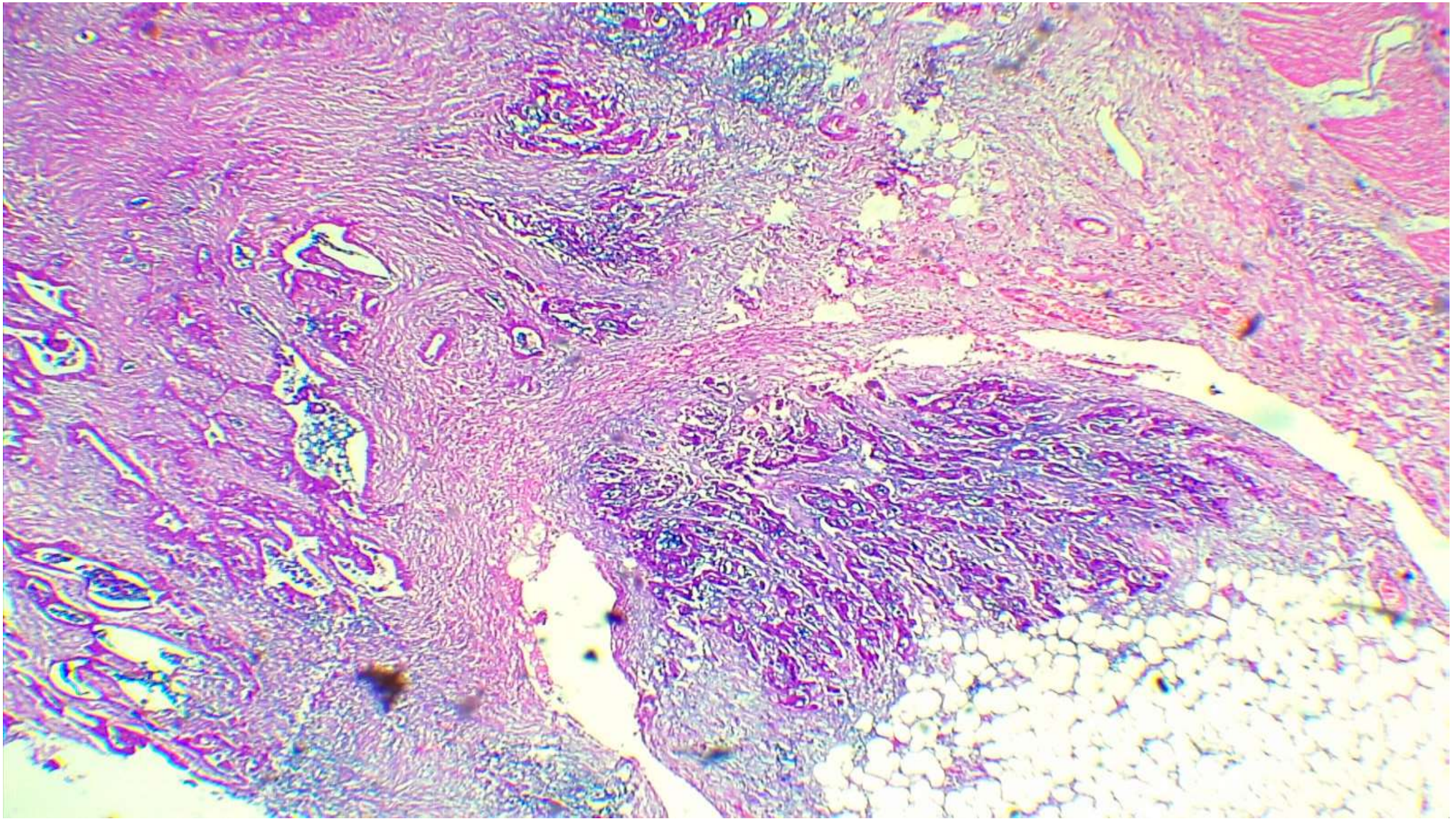


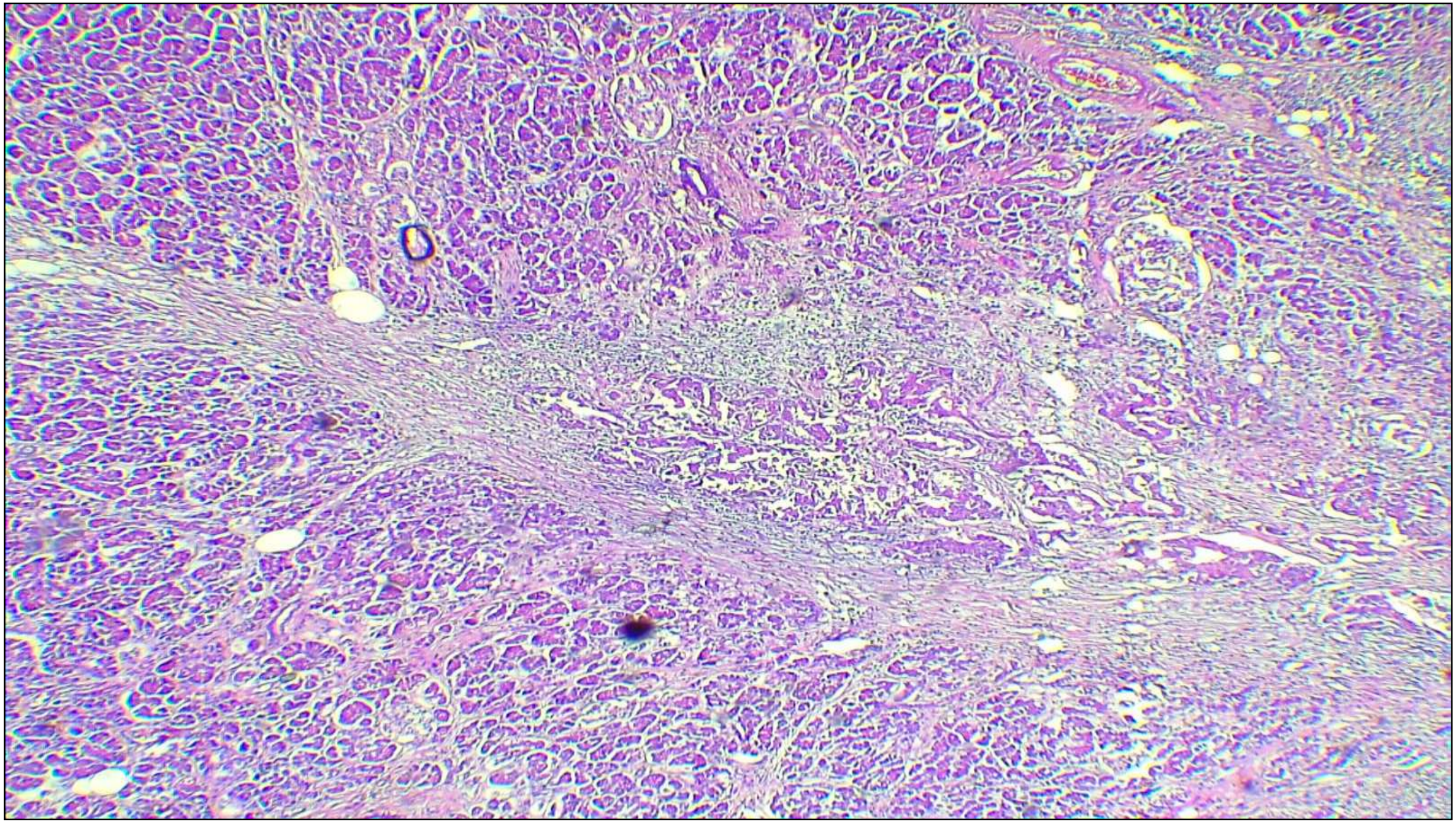


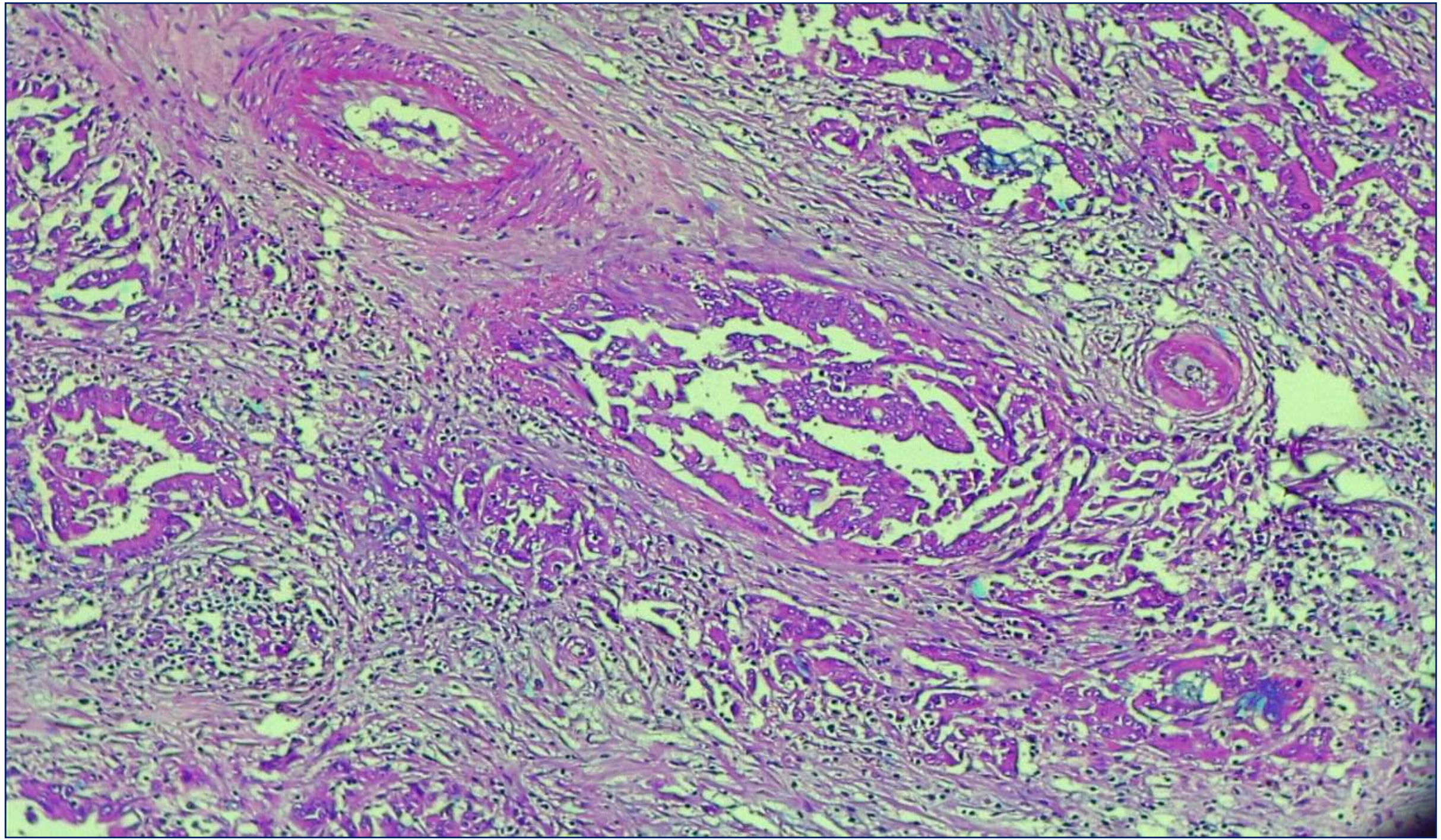


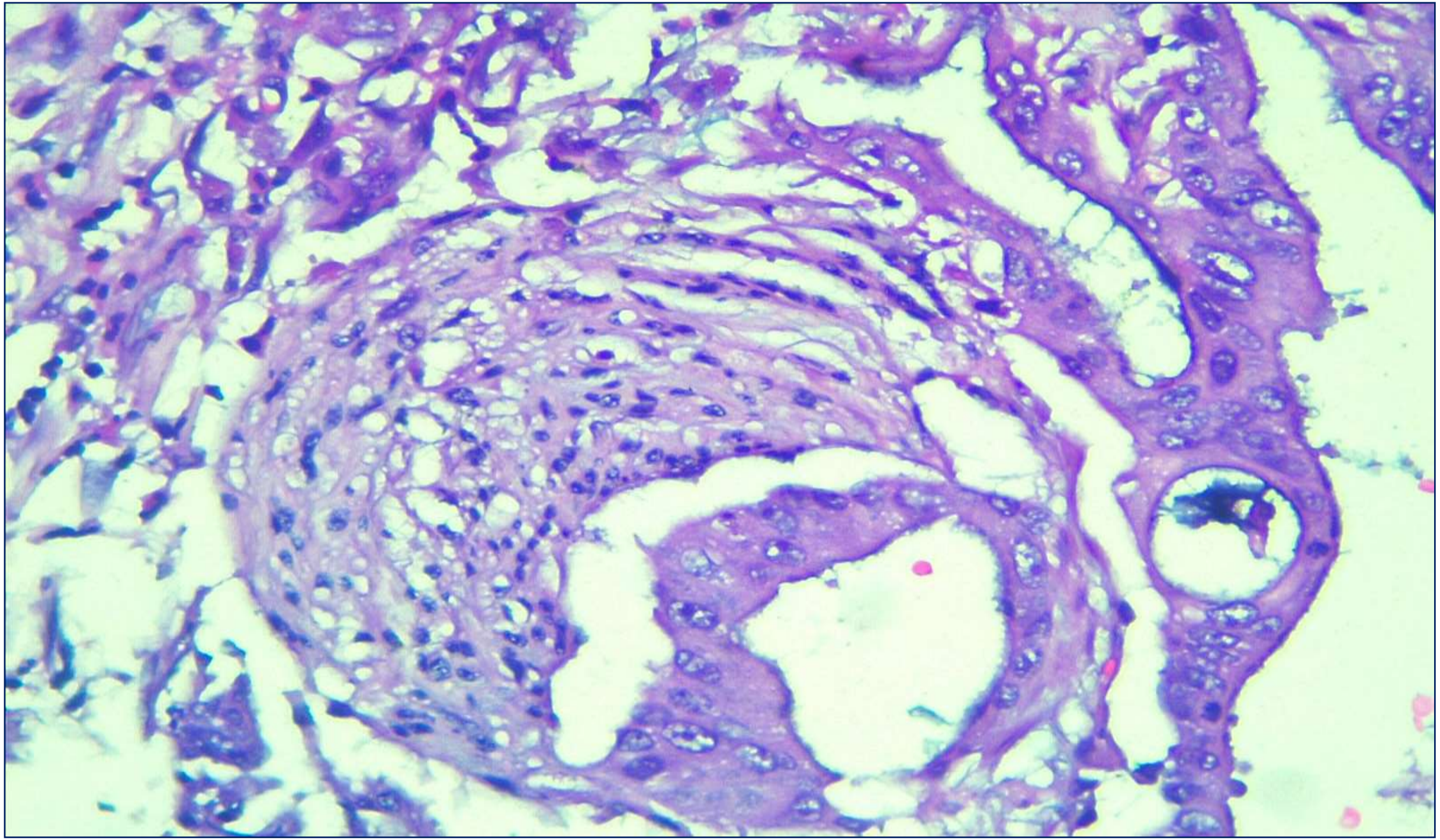


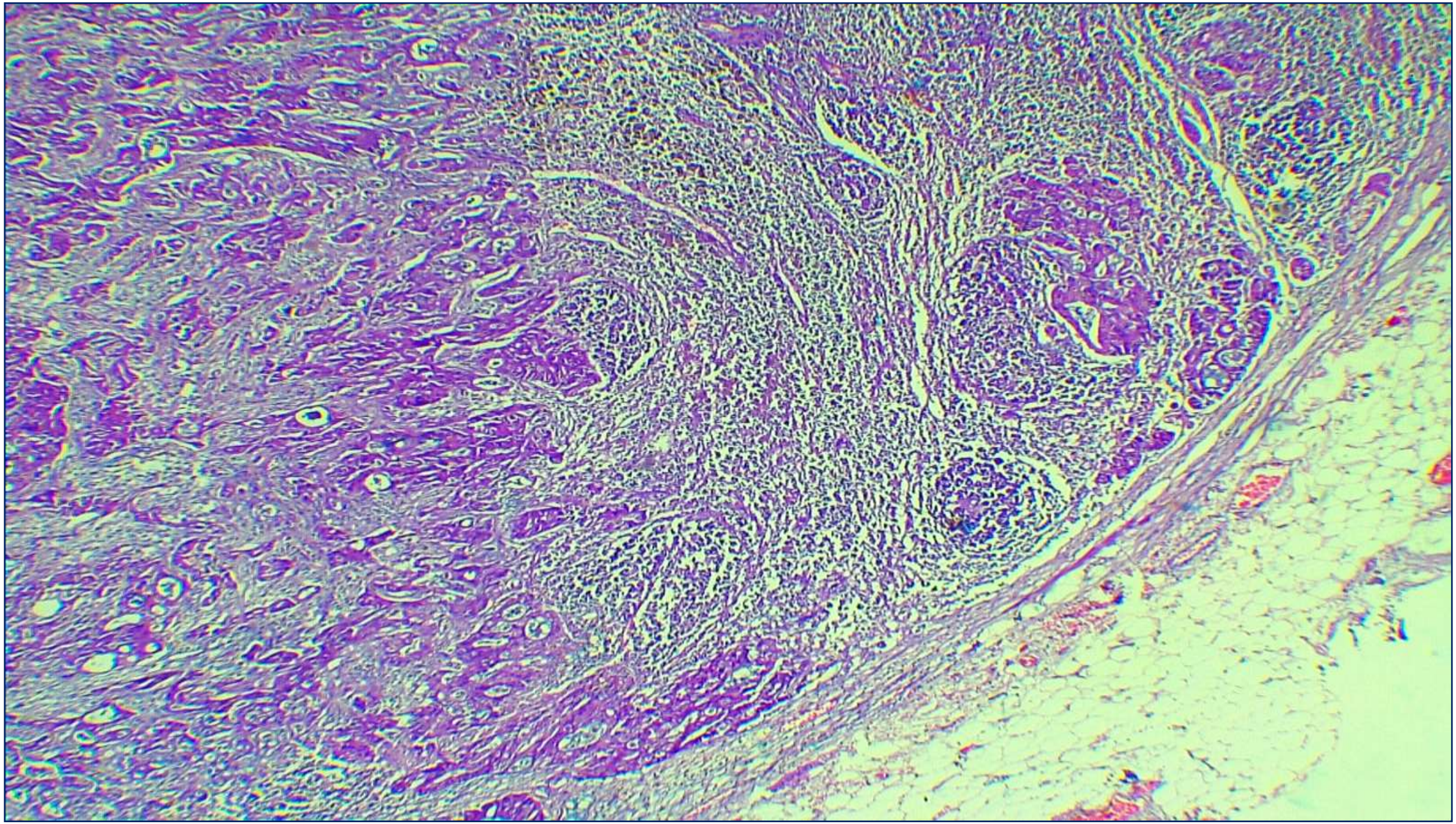












IMPRESSION

- Synchronous pancreaticobiliary type adenocarcinoma, grade-2, of gall bladder and periampullary region
- Pathologic stage of gall bladder – pT3 pN not assigned pM not applicable
- Pathologic stage of periampullary region – pT3b pN2 pM not applicable

ON FOLLOW UP

- 5 months postoperatively, patient developed metabolically active recurrent soft tissue lesion along the suture line, bi lobar liver lesions and periportal, retroperitoneal and omental lymph nodes.
- He is currently receiving palliative chemotherapy with Gemcitabine and Cisplatin.

DISCUSSION

- **Synchronous malignancies** are rare and fatal.
- Definition: A new or second primary cancer that develops within 2-6 months of the first primary cancer, either in the same organ or in a different organ with the same molecular basis [6]
- Most common synchronous cancer sites are colorectal cancer (37.2%), lung cancer (18.6%), esophageal cancer (16.8%), liver cancer (9.7%), kidney cancer (4.4%) and gastric cancer (3.4%) [4]
- Pathogenesis includes genetic factors, hormones, environmental carcinogens, dietary factors, infective agents, previous therapy, alcohol and smoking.

- The differentiating points between synchronous primary malignancies and secondary deposits include:-

- Lack of anatomical continuity between the two tumors
- A growth pattern typical of a primary tumor
- Clear histological differences between the two tumors

- In our patient, all the three criterions were fulfilled as both tumors i.e. Primary adenocarcinomas which had a growth pattern typical of a primary tumor.

PATHOPHYSIOLOGY

- Metastasis of primary tumor and becoming multifocal
- Local extension of primary tumors
- Any anatomical variant
- Pancreaticobiliary maljunction

Synchronous gallbladder and pancreatic carcinomas are associated with an anomalous pancreatic-bile duct junction (APBDJ); however, it is not an absolute necessity.

Pancreaticobiliary Maljunction

A congenital anomaly attributed to an abnormal connection between pancreatic duct and the common bile duct outside the duodenal wall

↓

Intra-pancreatic duct pressure is higher than in the bile duct as a result, due to absence of control of the sphincter of oddi the pancreatic juices reflux into the biliary tract

↓

Chronic biliary inflammation and dysplastic changes in the bile duct mucosa

(Cycles of biliary epithelium breakdown and regeneration)

↓

Abnormal expression and/or mutation of some oncogenes and cancer suppressor genes

Tp53, K RAS and PIK3CA

- To conclude, the clinical challenge in our case was:

✓An incidental gall bladder malignancy on frozen section

✓Intra operative decision to perform Radical cholecystectomy, adding on to the duration and extent of resection during the surgery

✓Histological surprise of a synchronous malignancy

✓Recurrence of tumor

- Hence, it is necessary to develop more accurate diagnostic and management strategies and maintain a high index of suspicion of malignancy while evaluating such lesions.

- Recent technological advances i.e. Next Generation Sequencing (NGS) may be helpful for the determination of whether there is a clonal relationship between different tumor tissues from the same patient.

- The choice of treatment should be made carefully in conjunction with the treatment for the second malignancy, which however, remains a key challenge.

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THANK YOU