RAJIV GANDHI CANCER INSTITUTE
& RESEARCH CENTRE

Case of the month
September 2020

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ATTENDING CONSULTANT

DEPARTMENT OF PATHOLOGY

RGCIRC

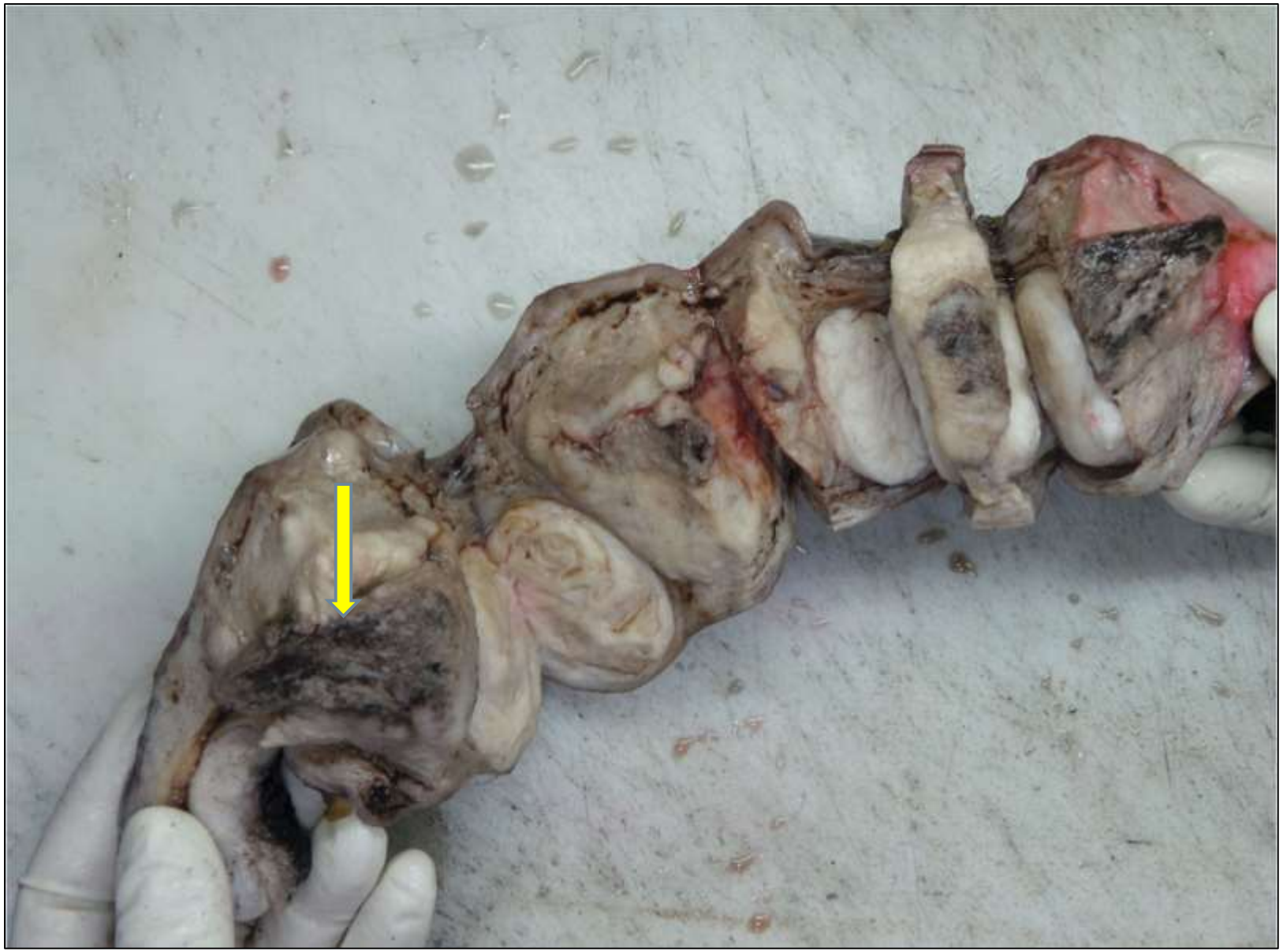
CASE

- 56 year old lady
- Presented with irregular menstrual cycles for past 2-3 years
- On Magnetic resonance imaging (outside)
  - Uterus was bulky with multiple subserosal fibroids
  - Thickened heterogeneous endometrium with
  - Endometrial polyp

- Diagnostic biopsy (outside)
  - Moderately differentiated adenocarcinoma
- Patient underwent
  - Total hysterectomy with bilateral salpingo-oophorectomy
  - Bilateral pelvic nodal dissection
- Gross Examination
  - Uterus was enlarged and measures 12×6.5×6 cm in dimensions and 325 gm in weight.
  - The outer surface was smooth and glistening
  - There was a polypoid tan friable mass measuring 6.0 x 3.5 x 2.0 cm occupying the entire endometrial cavity

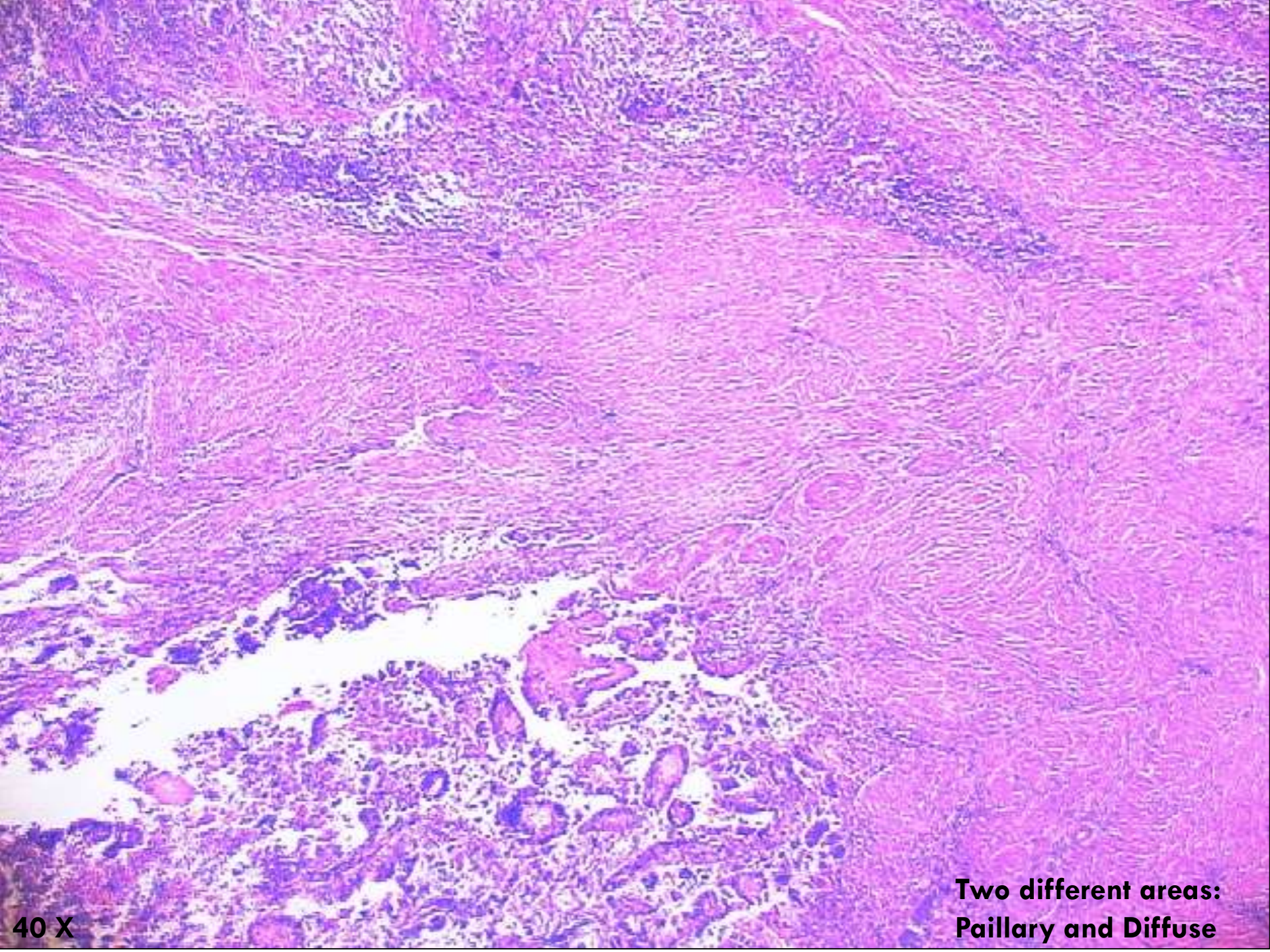
Gross examination

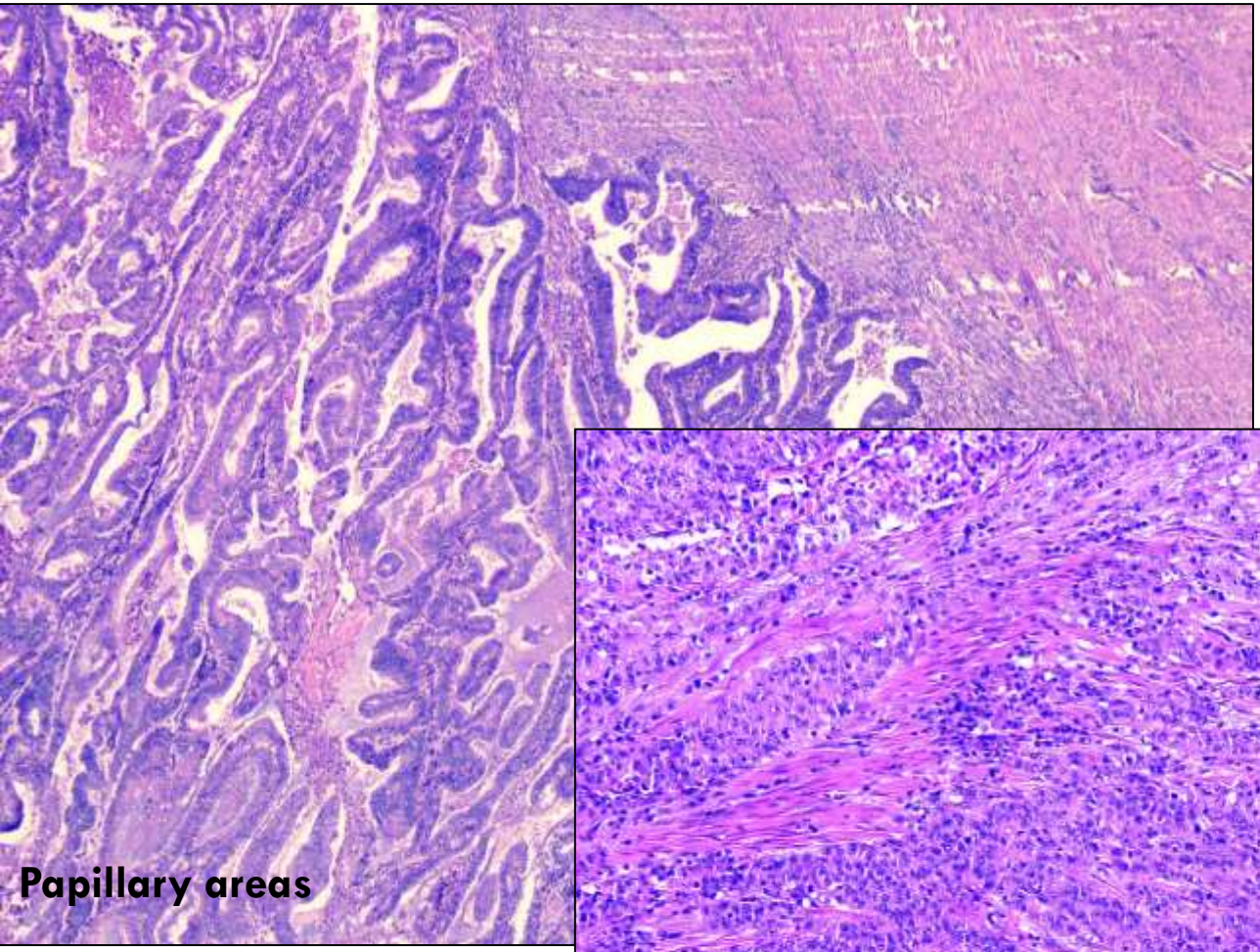
Large Friable polypoidal mass filling entire endometrial cavity

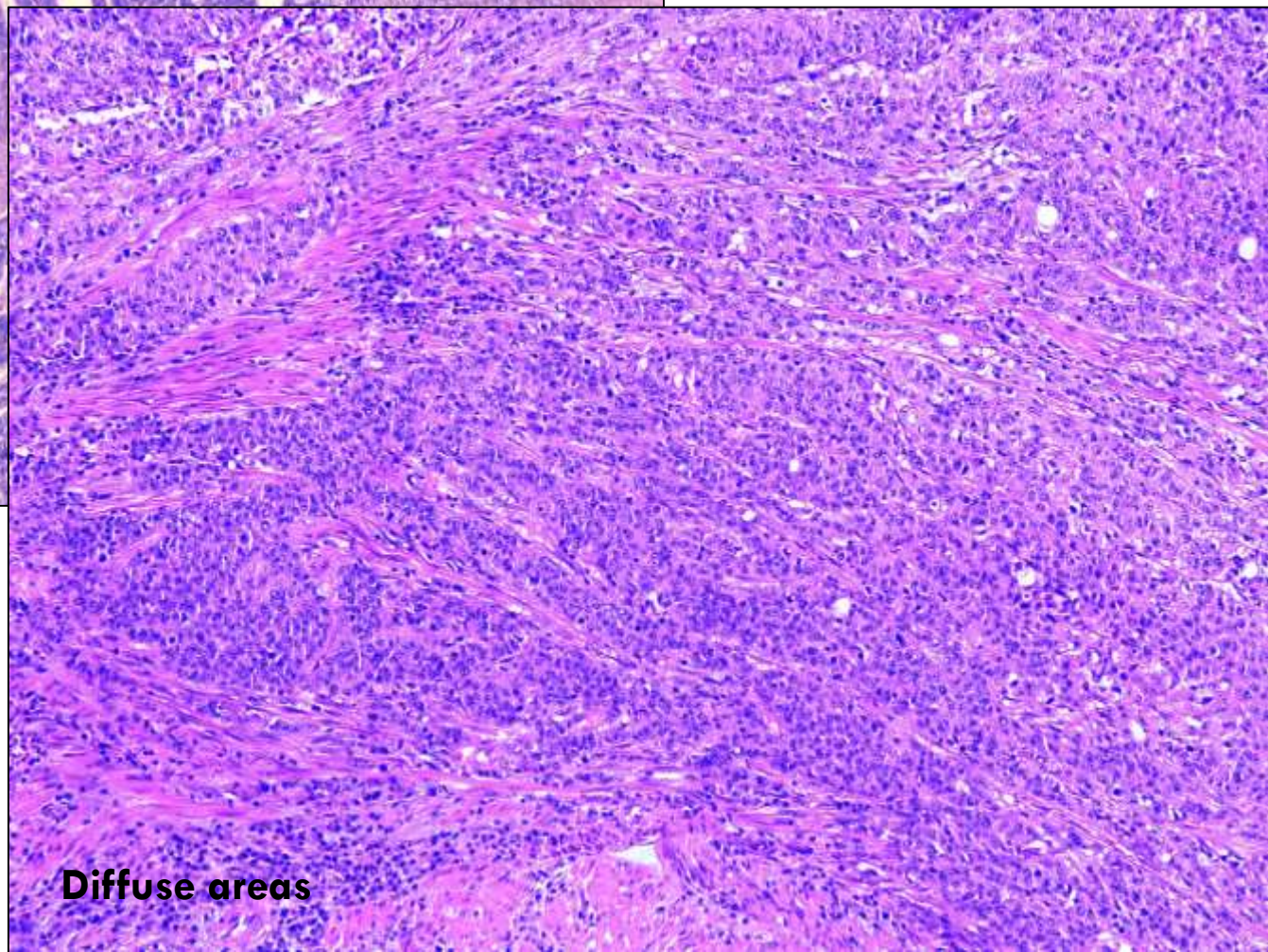


Histopathological examination

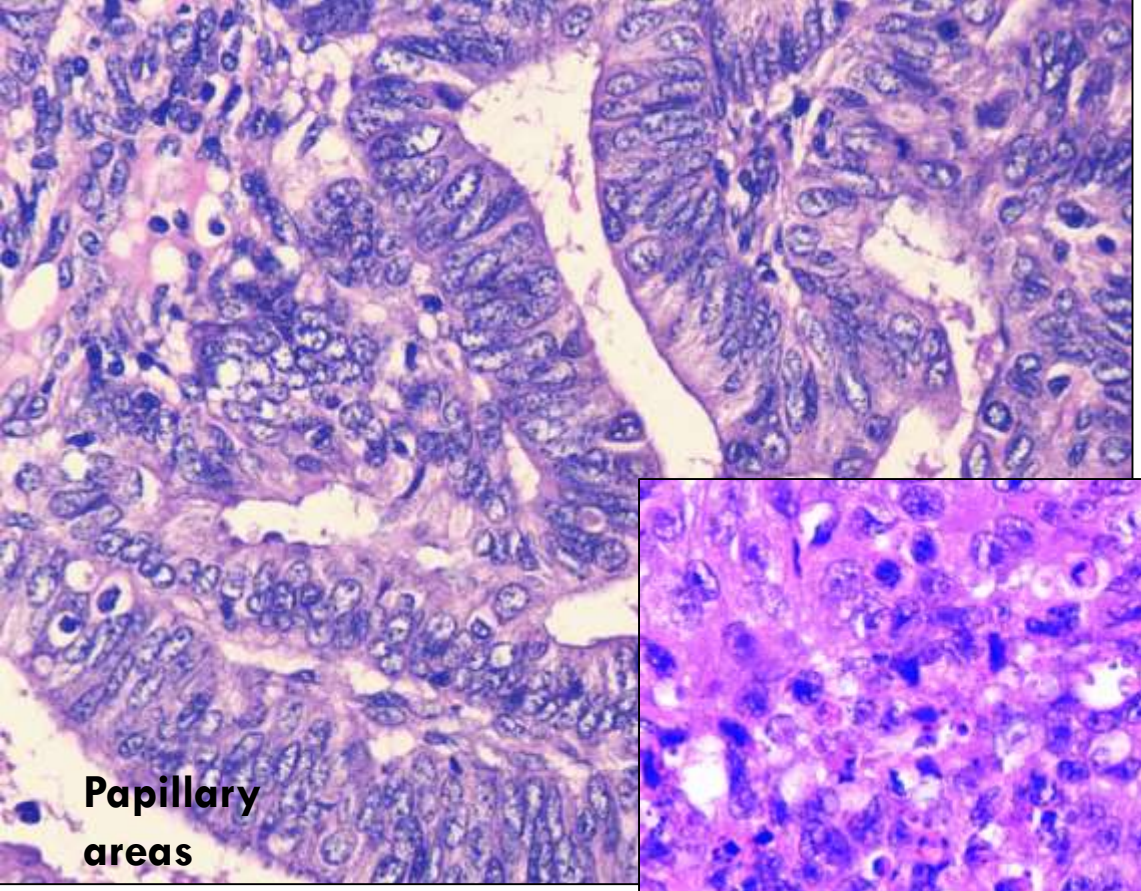
- Two morphologically distinct tumors with minimal intermingling were evident
- One of the component was
  - Diffuse composed of Sheets of round to oval cells with hyperchromatic nuclei and prominent nucleoli
  - Accompanied with areas of necrosis and frequent mitosis
  - Extensive lymphovascular emboli identified
- The other component was
  - Predominantly papillary tumor lined by tall columnar cells and low grade vesicular nuclei

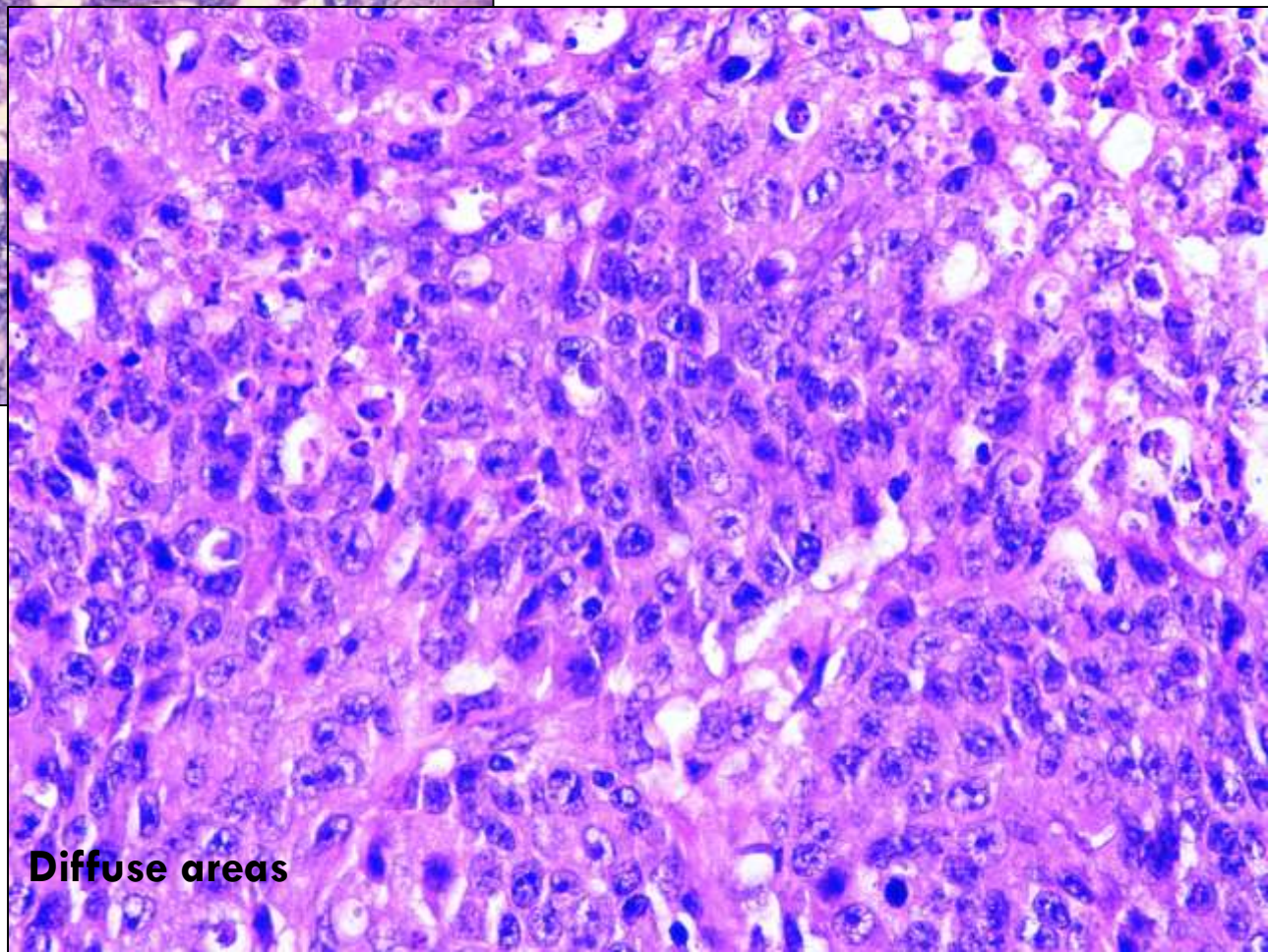

40 X
Two different areas:
Paillary and Diffuse



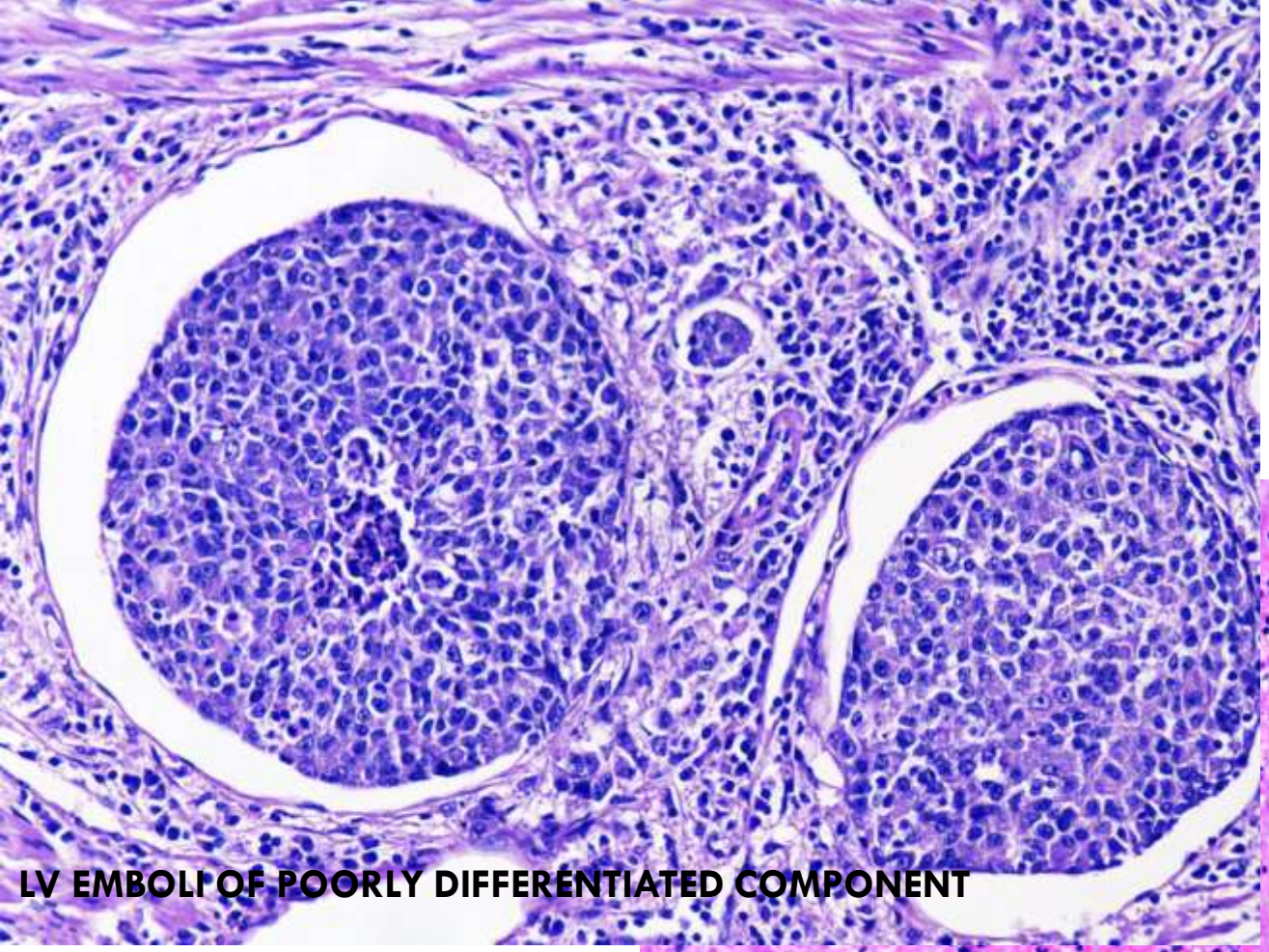


40 X

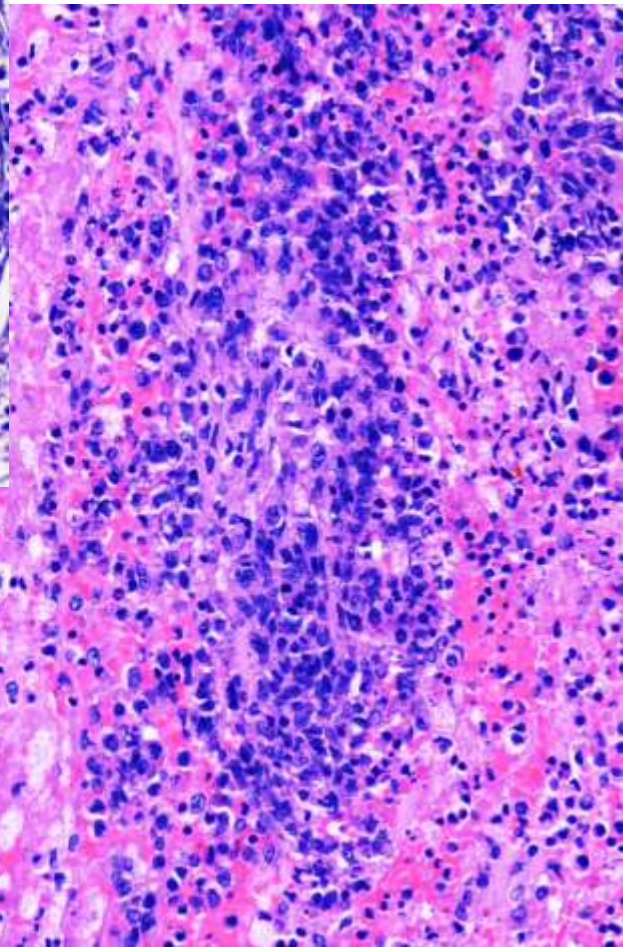


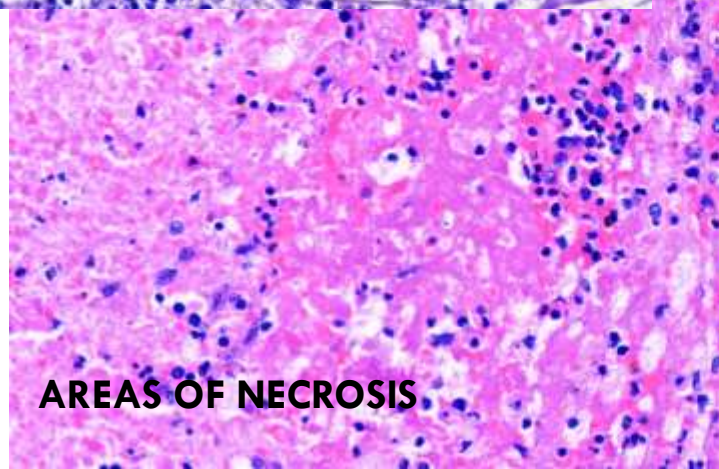


400 X



LV EMBOLI OF POORLY DIFFERENTIATED COMPONENT

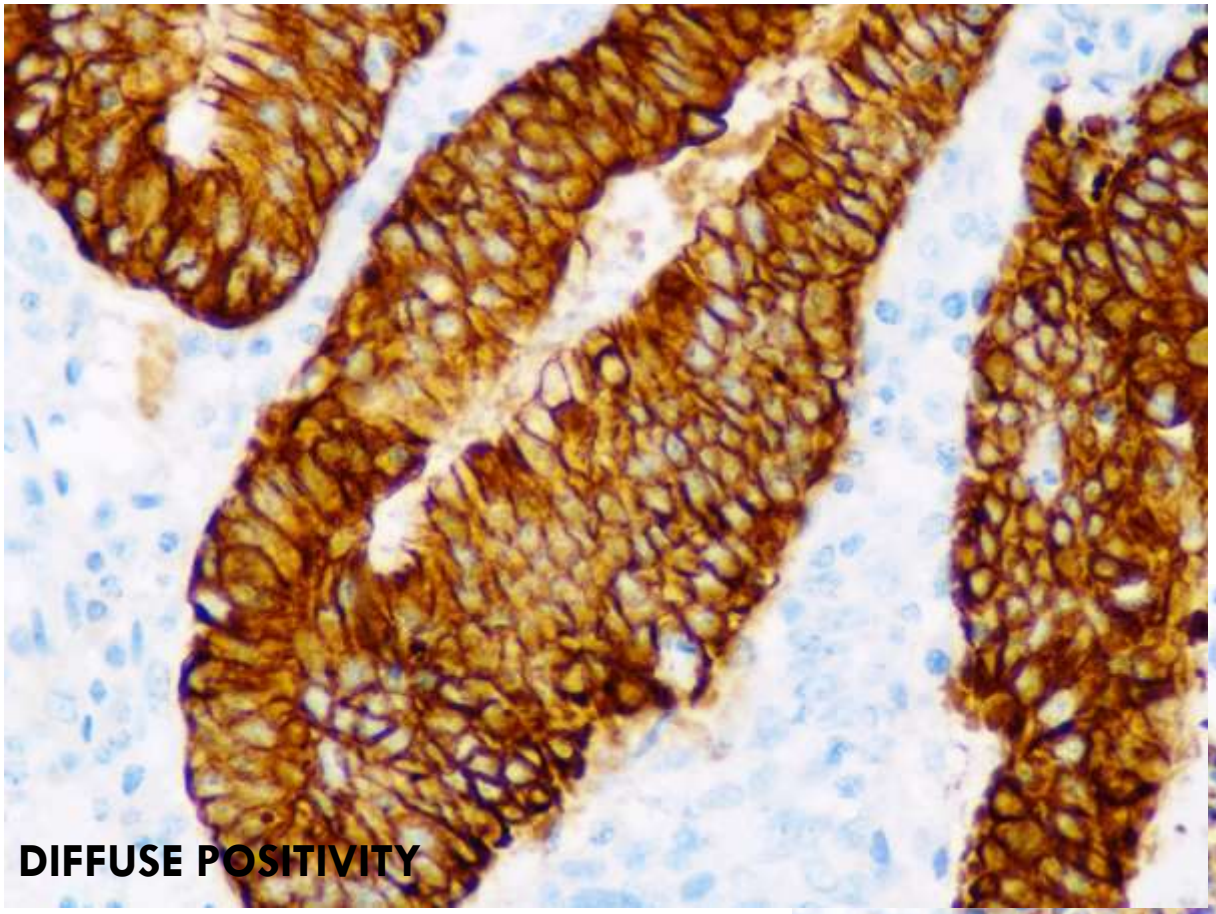




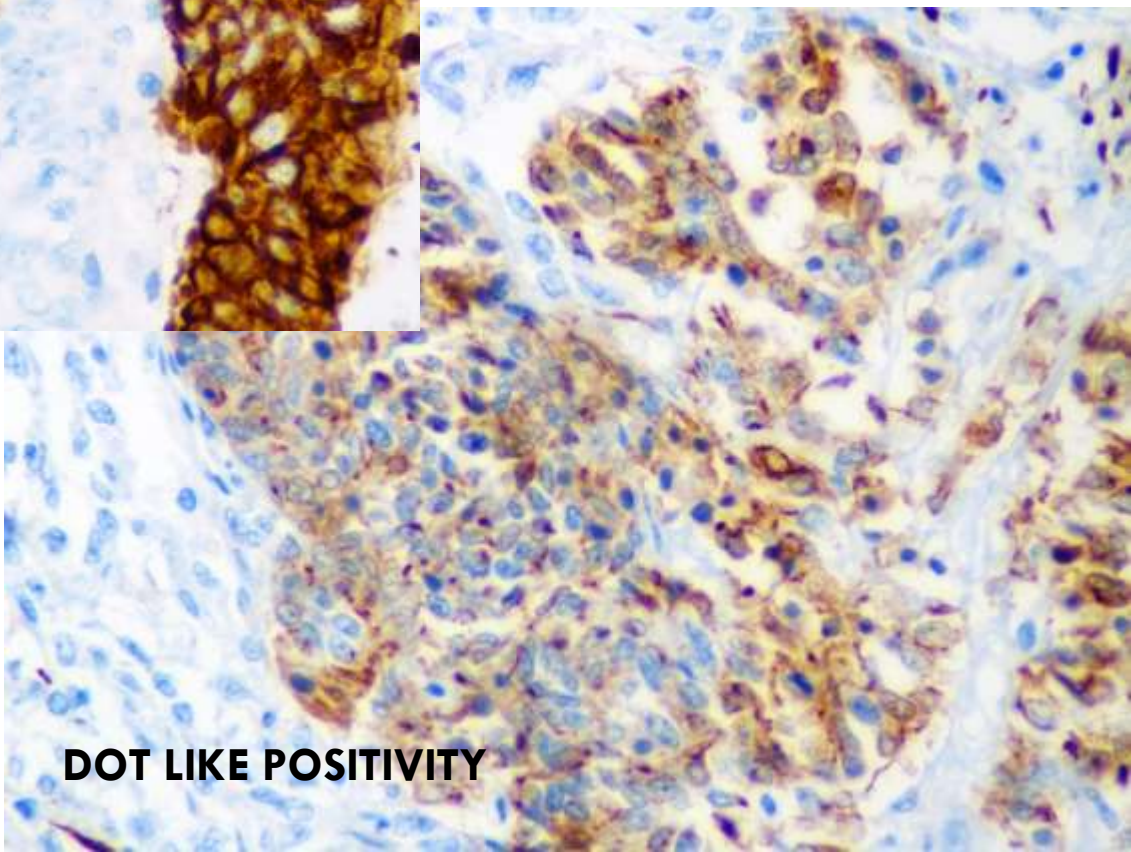
AREAS OF NECROSIS

400 X

Immunohistochemistry

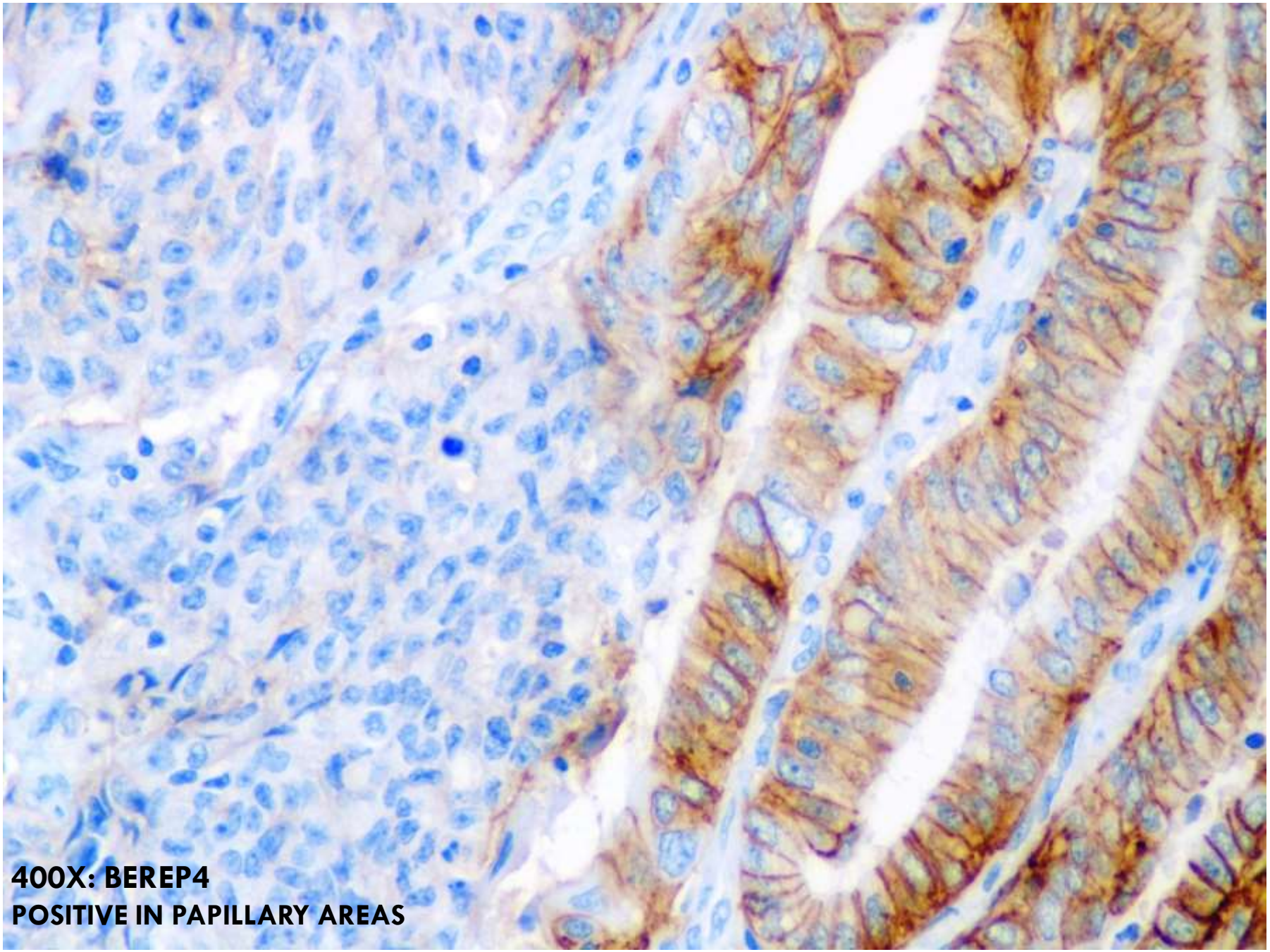


DIFFUSE POSITIVITY

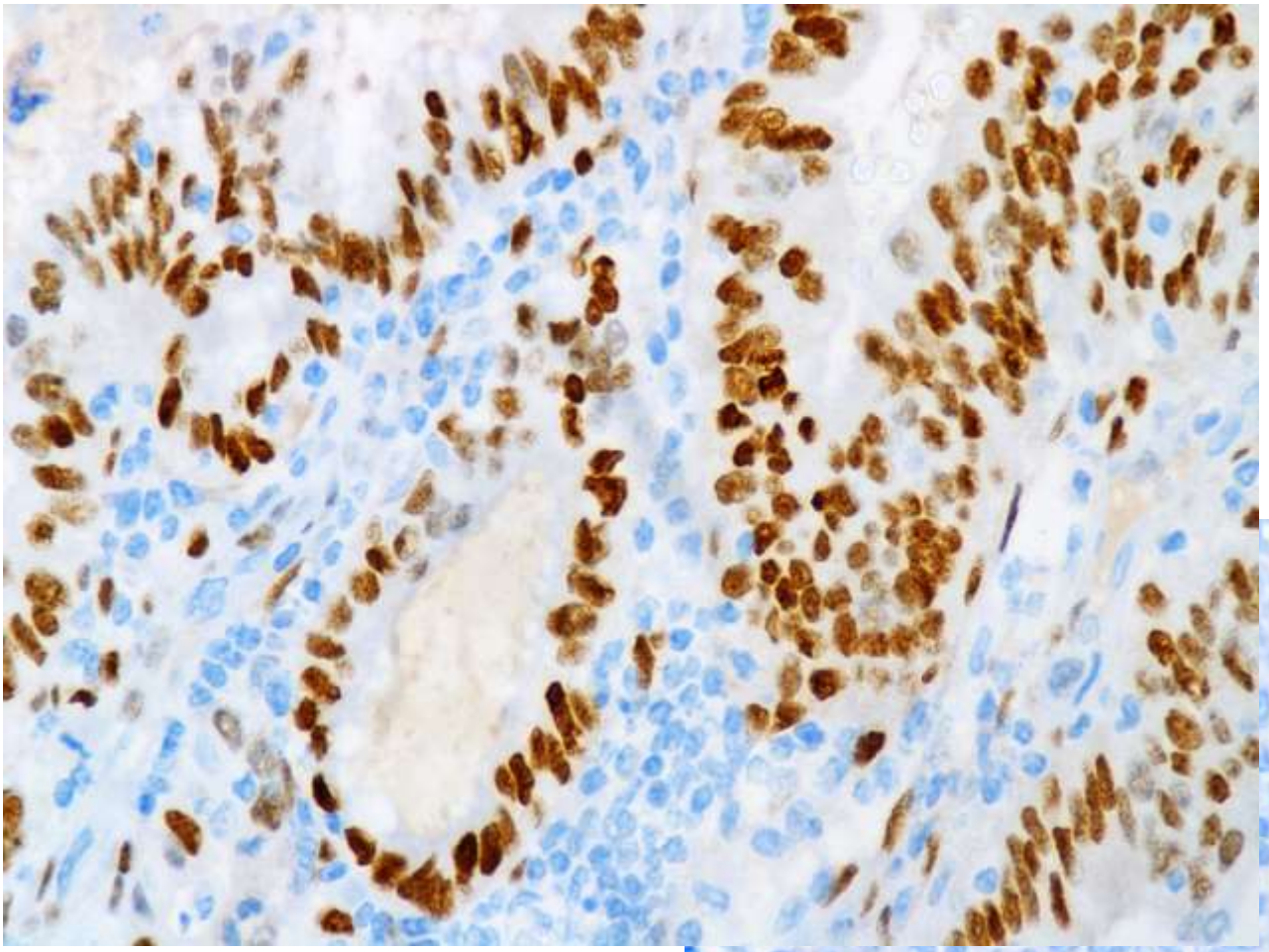


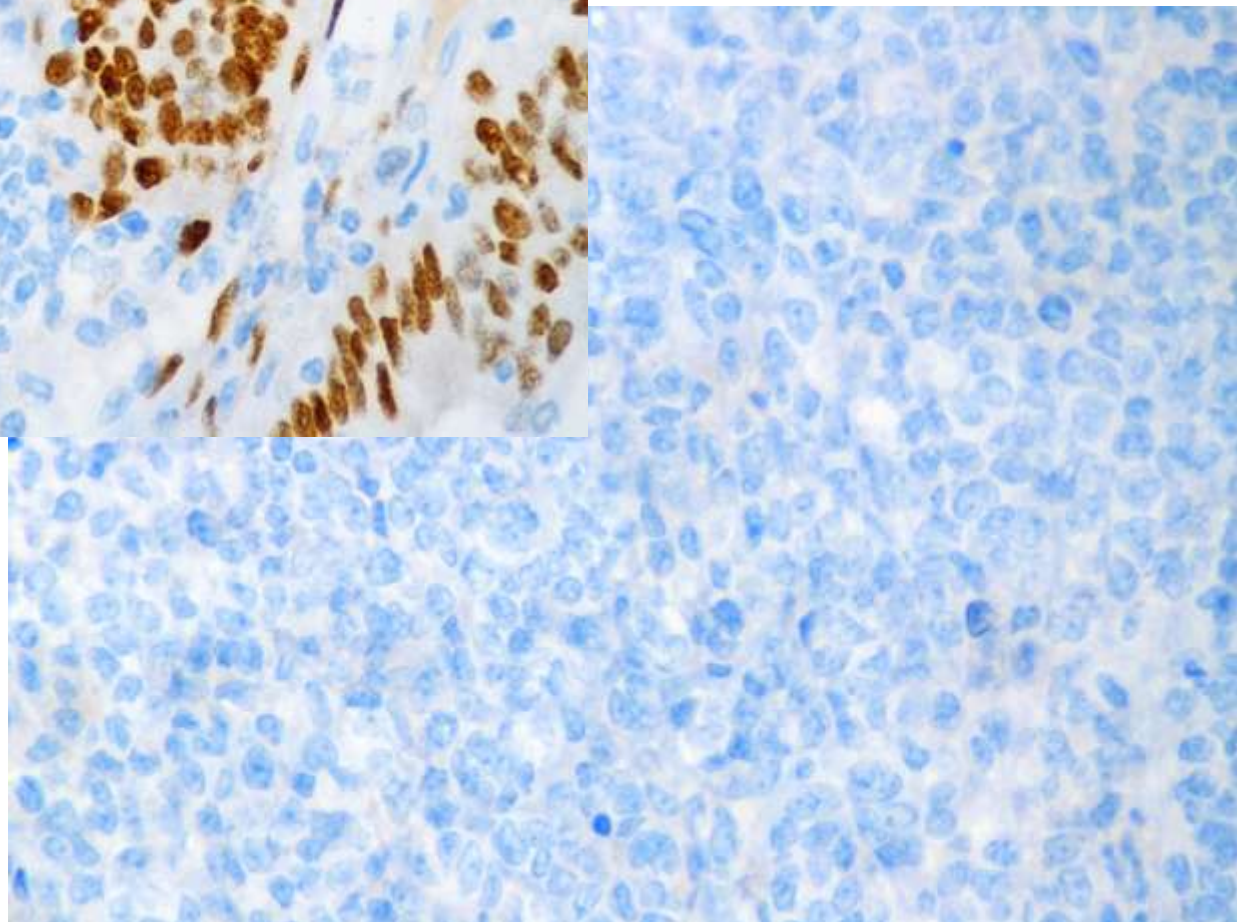
DOT LIKE POSITIVITY

400 X: CK

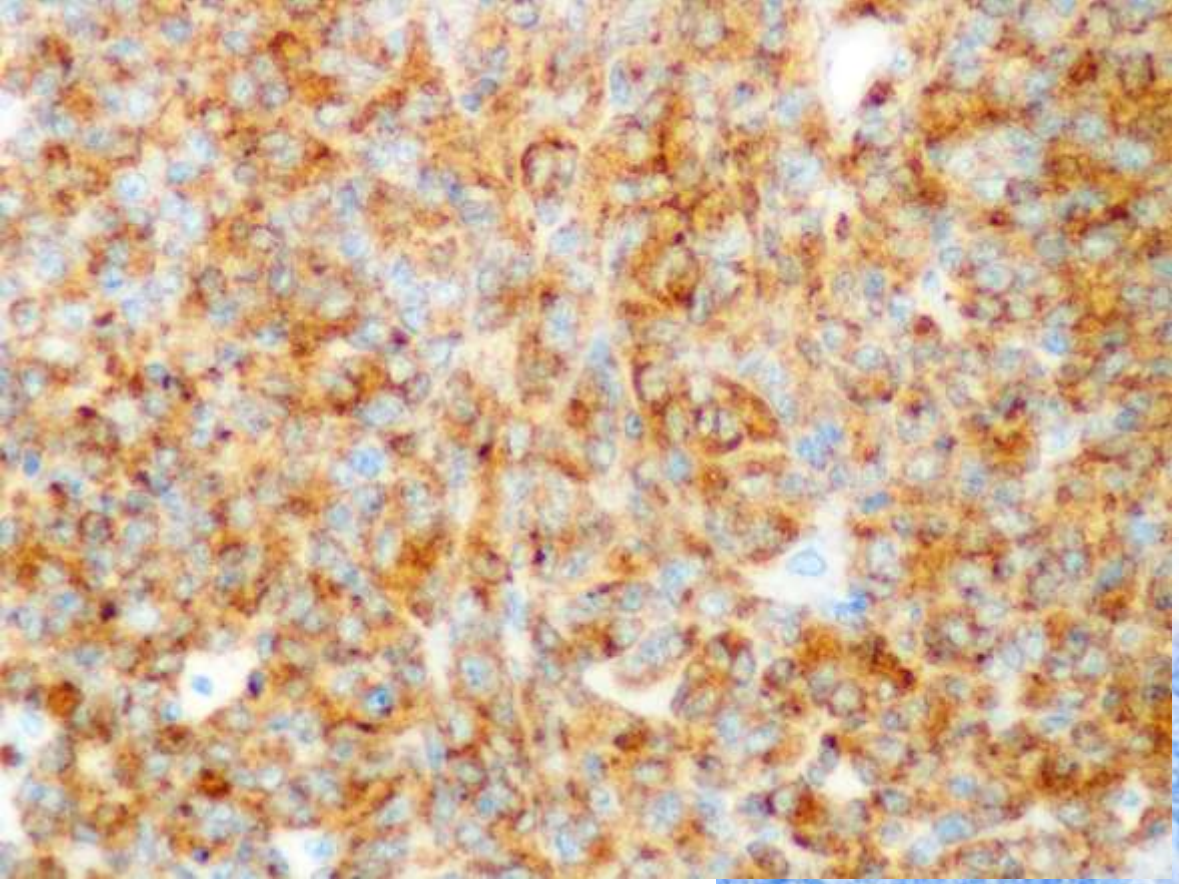


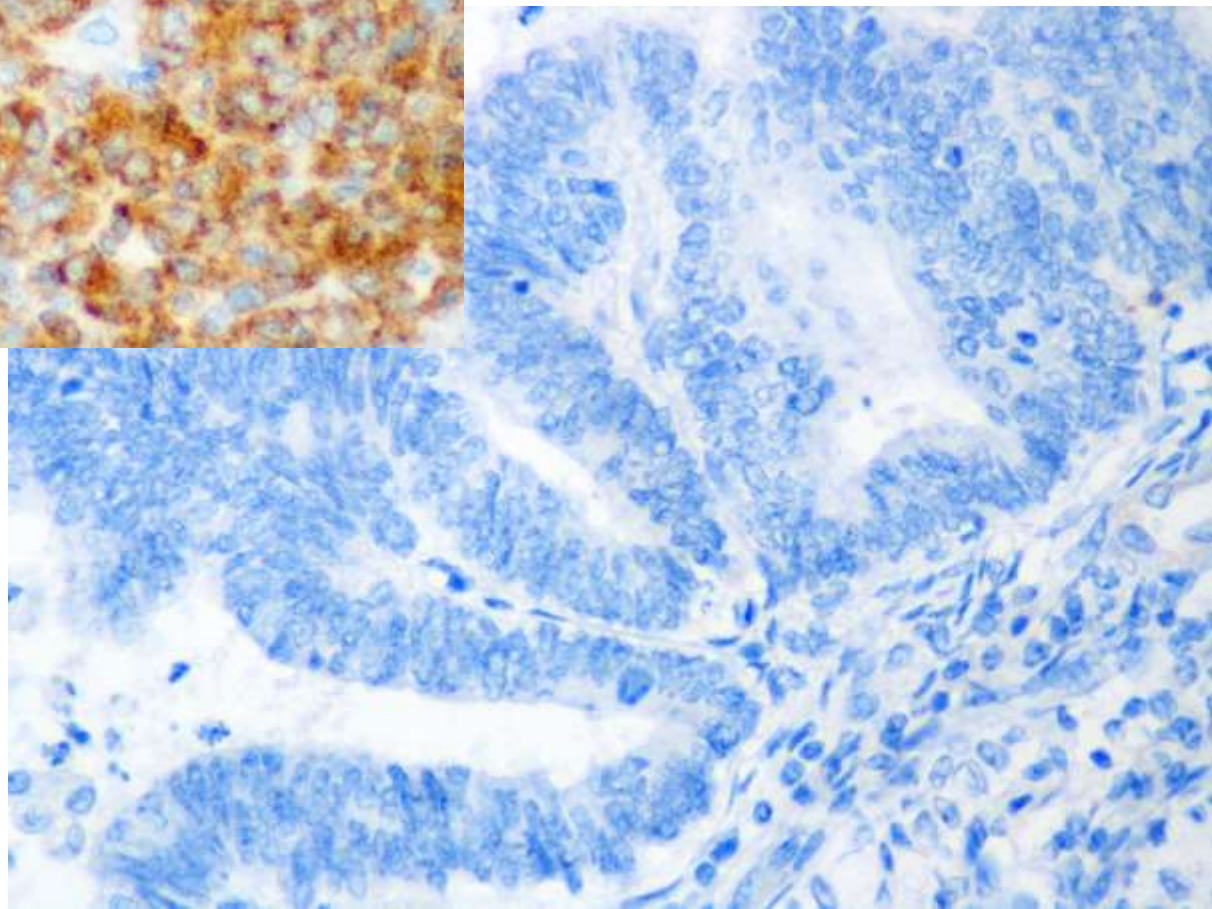
400X: BEREP4
POSITIVE IN PAPILLARY AREAS



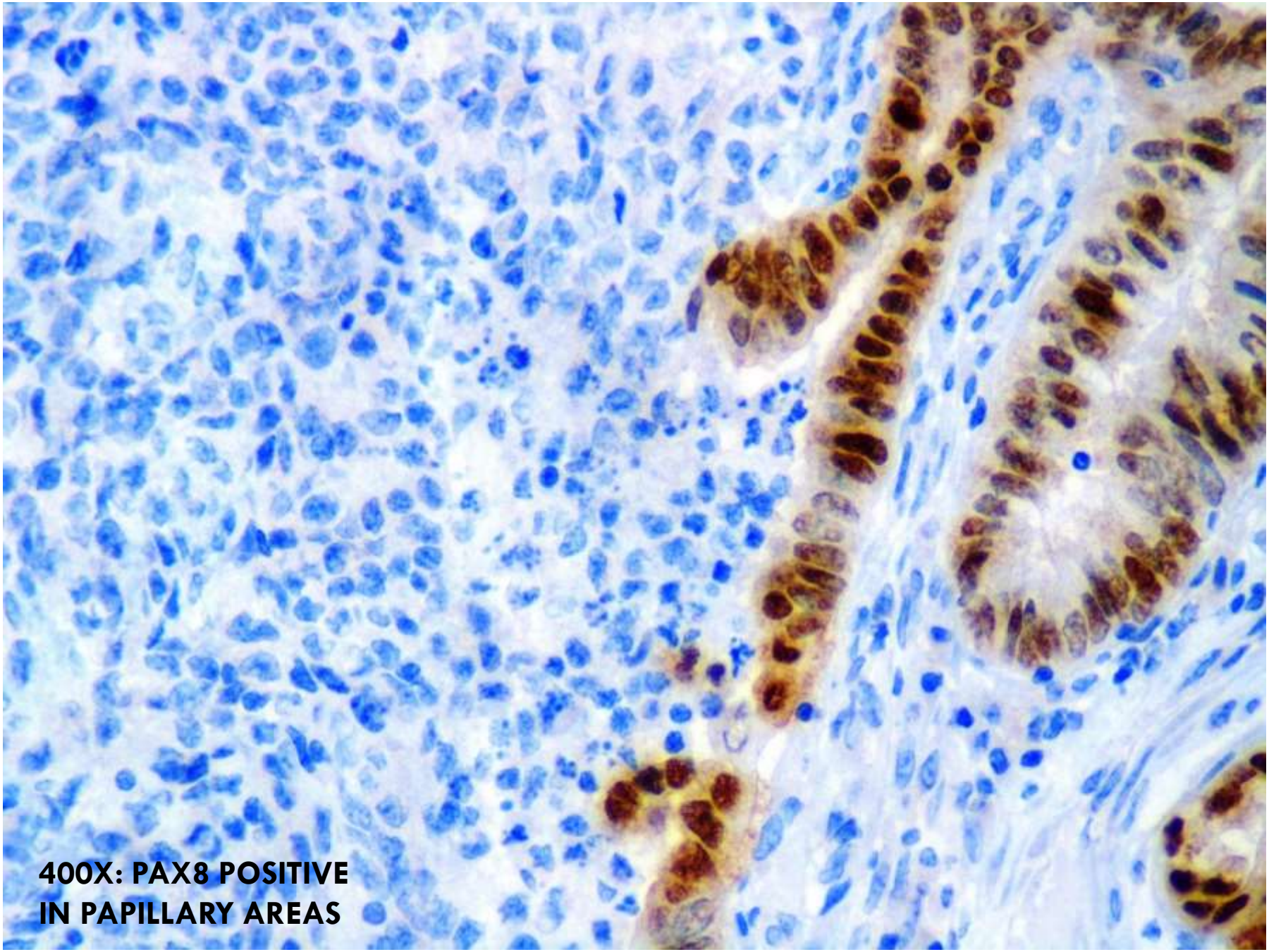


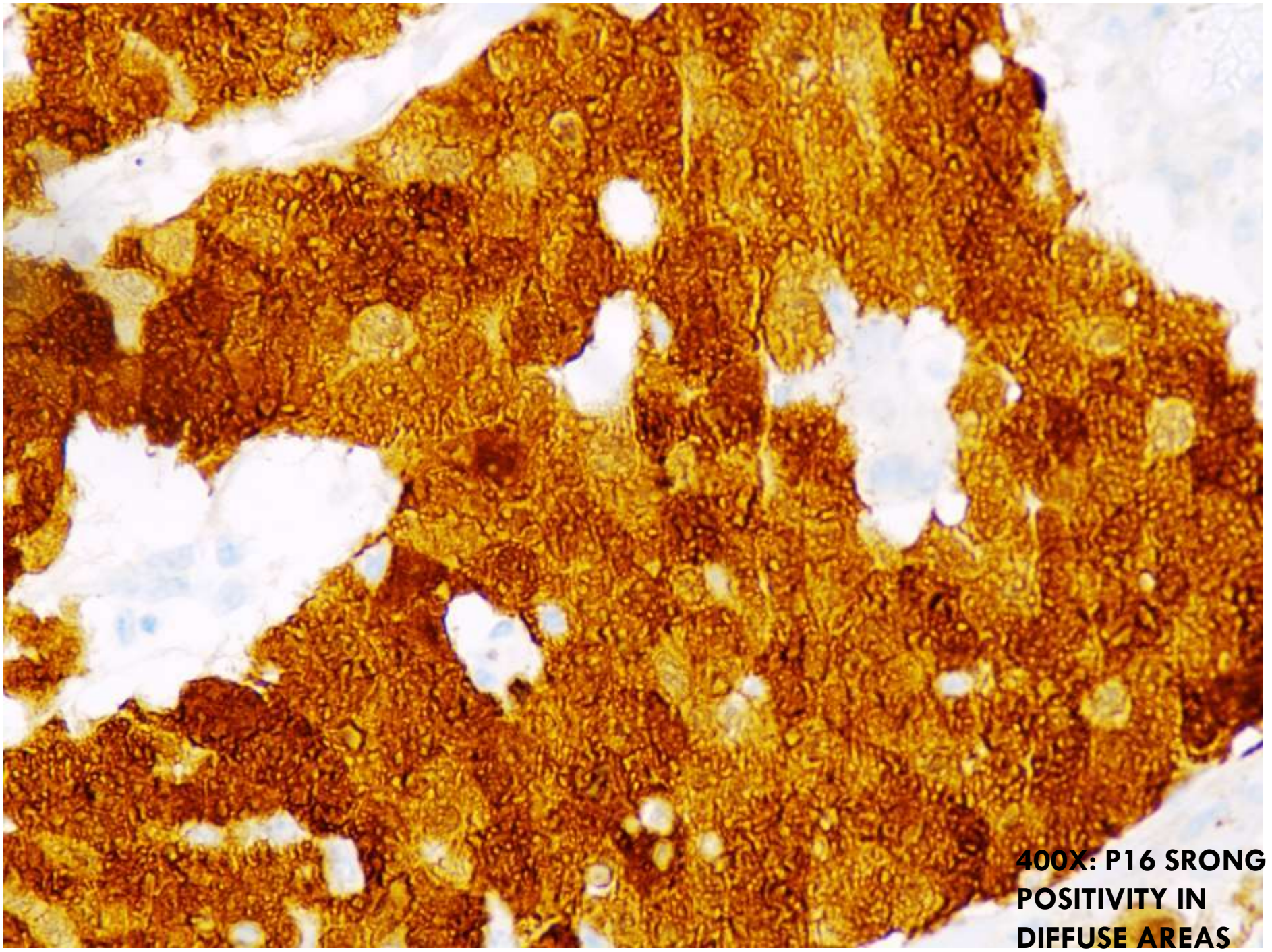
400X: ER POSITIVE IN PAPILLARY AREAS





400X: SYNAPTOPHYSIN POSITIVE IN DIFFUSE AREAS


400X: PAX8 POSITIVE
IN PAPILLARY AREAS


400X: P16 SRONG
POSITIVITY IN
DIFFUSE AREAS

Summary of Immunohistochemistry

- Poorly differentiated component was
  - Positive for synaptophysin and P16
  - CK show dot like positivity
  - Negative for ER and PAX8

  Large cell neuroendocrine carcinoma

- Papillary component was
  - Positive for ER and PAX8
  - CK and BEREP 4 are also diffusely positive
  - Negative for synaptophysin and p16 (patchy)

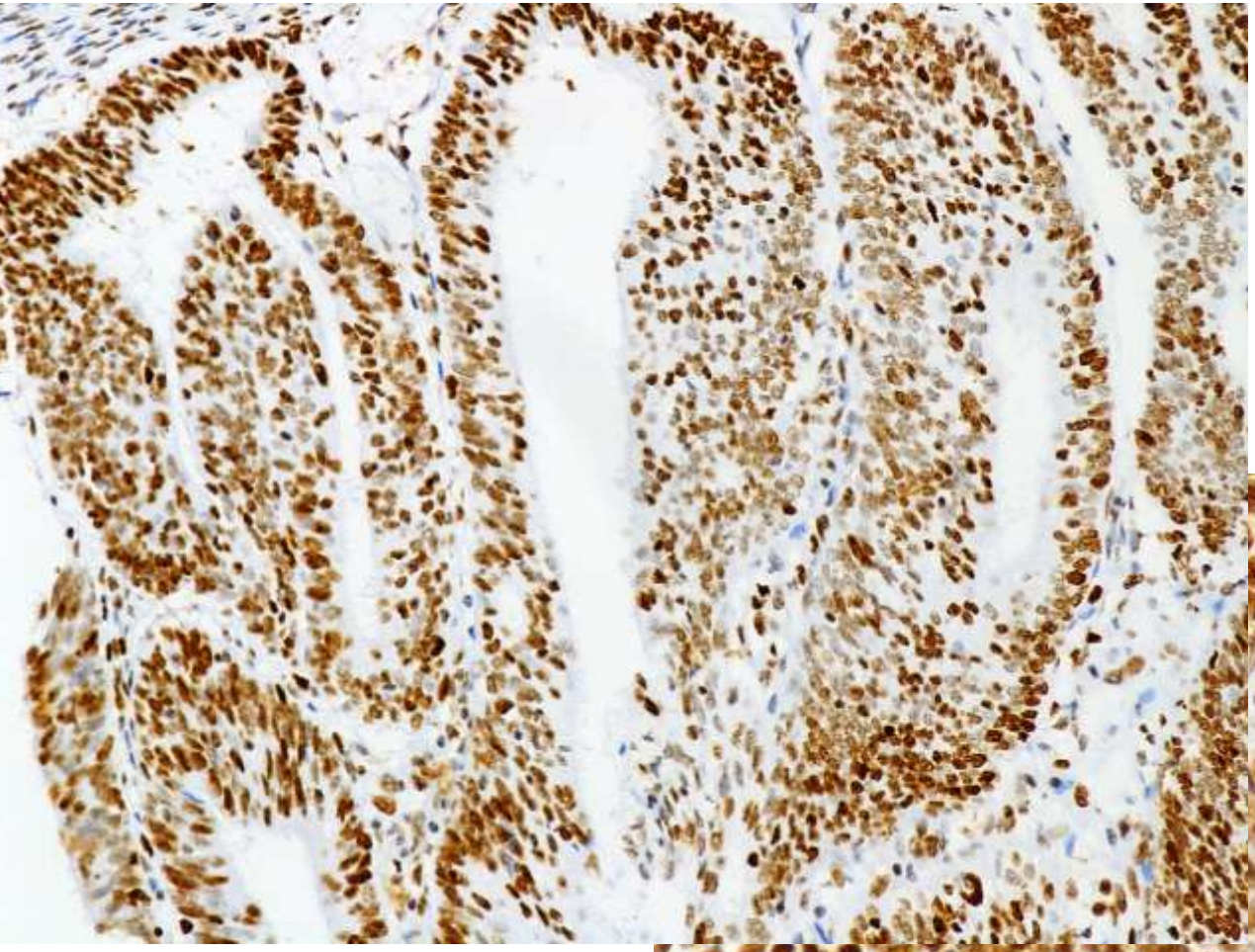
  Endometrioid adenocarcinoma

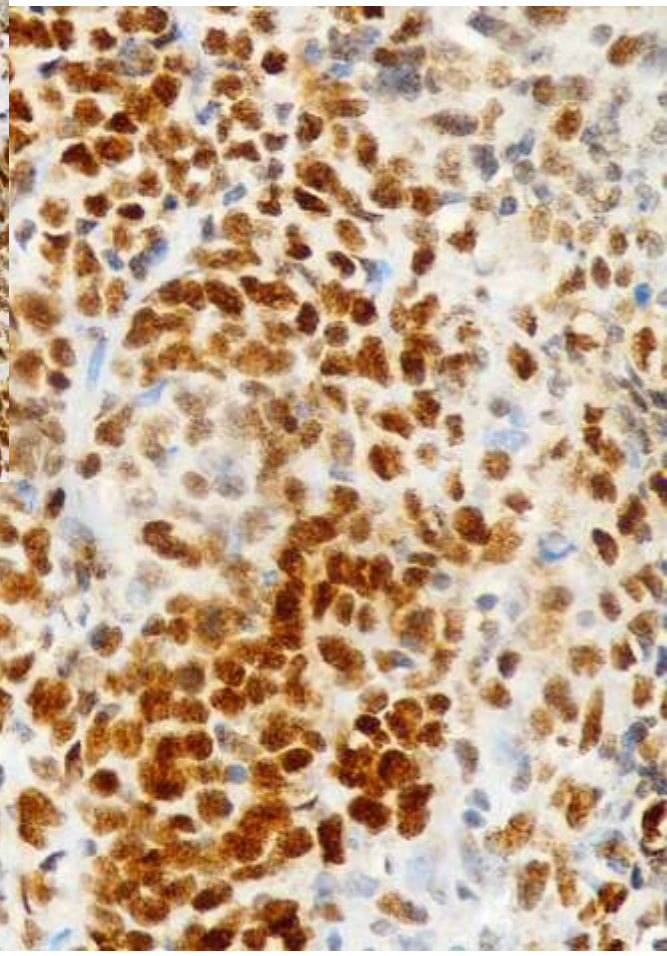
Diagnosis

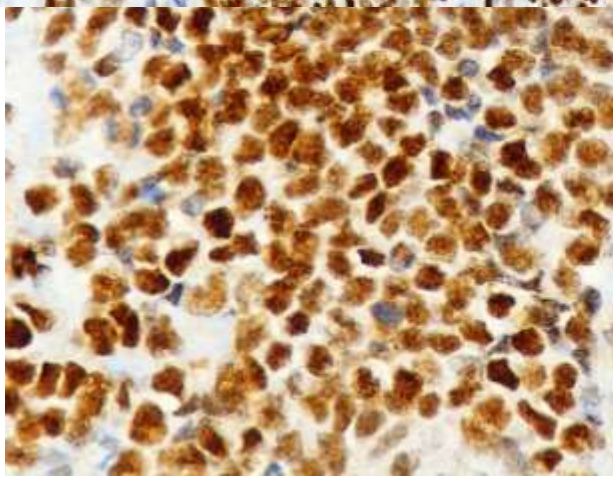
- Collision tumour : Large cell neuroendocrine carcinoma and Grade 1 Endometrioid carcinoma

Further ancillary Testing

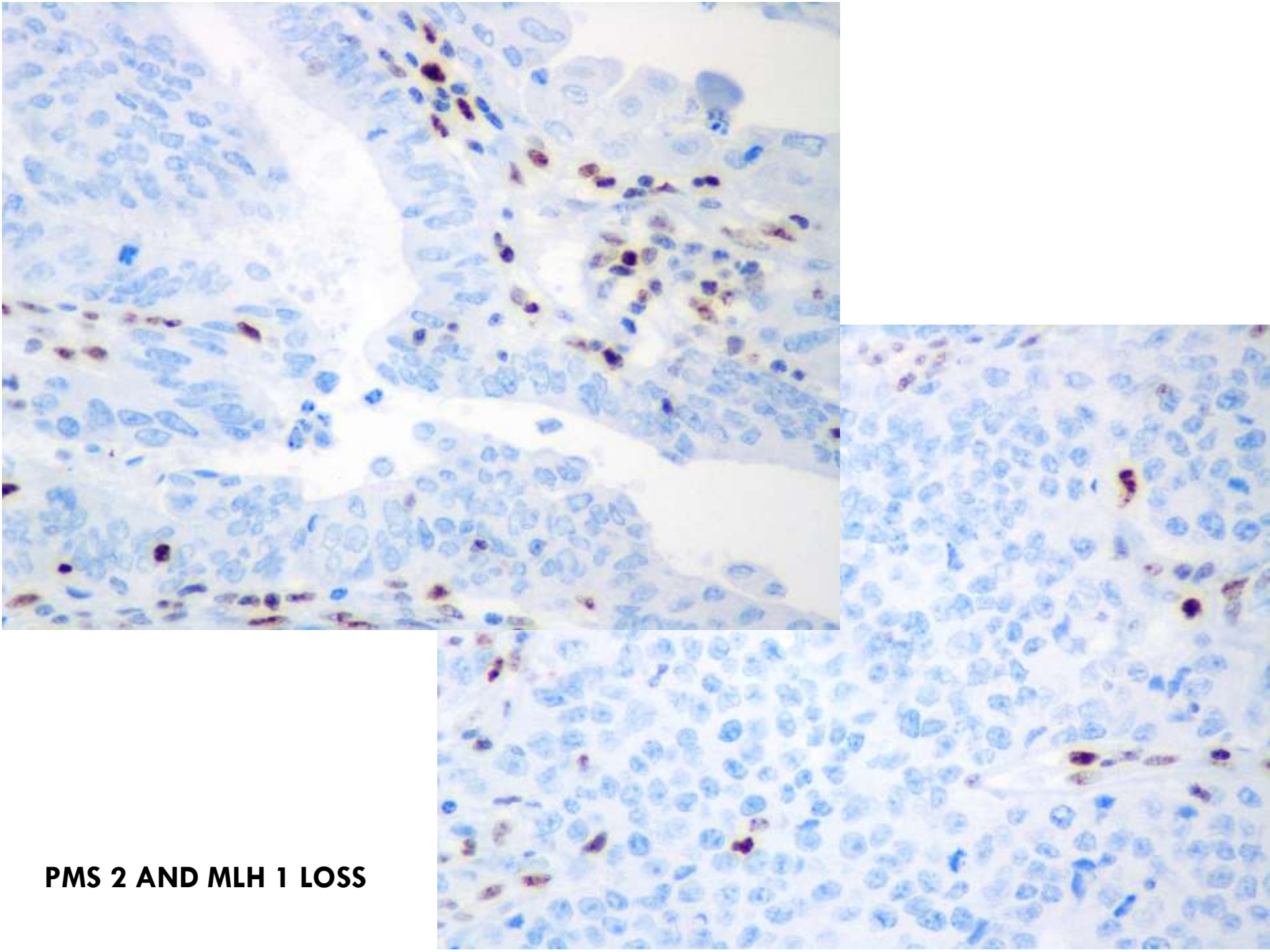
- On MMR testing both component were MMR deficient
  - Loss of PMS 2 and MLH 1
  - Intact MSH2 and MSH6







MSH2 AND MSH 6



PMS 2 AND MLH 1 LOSS

Discussion

- Collision tumors are defined by the presence of cancers of different histopathological origin at the same anatomical organ or site
- Important implications, both for the patient and possibly in terms of cancer risks and predisposition

J Med Cases. 2018;9(9):309-312

- Several reports determined that collision tumors of the uterine corpus were mainly composed of two distinct tumors
  - Endometrial carcinoma (endometrioid or serous adenocarcinoma)
  - Mesenchymal tumor (leiomyosarcoma or endometrial stromal sarcoma)

J Clin Diagn Res. 2017 Feb; 11(2): ED20–ED22

S.No	Components			Age	Ref
	Adenocarcinoma	Sarcoma	Other		
1	Endometrioid	Endometrial stromal sarcoma		73	1
2	Papillary Serous	Leiomyosarcoma		55	12
3	Endometrioid	Endometrial Stromal Sarcoma		36	13
4	Endometrioid	Endometrial Stromal Sarcoma		55	13
5	Endometrioid	Endometrial Stromal Sarcoma		59	13
6	Papillary Serous Endometrioid		Malignant Mixed Mullerian tumour	70	3
7	Hepatoid carcinoma		Carcinosarcoma	68	5
8	Endometrioid adenocarcinoma	Endometrial stromal sarcoma high grade		47	4
9	Endometrioid adenocarcinoma	Endometrial stromal sarcoma high grade		85	4
10	Endometrioid Adenocarcinoma		Malignant Rhabdoidtumour	49	6
11	Serous carcinoma	Heterologous sarcoma		72	11
12	Endometrioid adenocarcinoma	Homologous sarcoma		67	11
13	Adenocarcinoma	Leiomyosarcoma		55	10
14	-	Endometrial stromal sarcoma	Squamous cell carcinoma	60	Our case

[Table/Fig-5]: List of collision tumours of uterus and their components reported in literature till date [1,3-6,10-13]

- Very rare case report are describing the collision of neuroendocrine carcinoma and endometrioid carcinoma

Journal of Cancer Research Updates, 2012, 1, 39-43

Large cell neuroendocrine carcinoma

- An uncommon malignancy
- Aggressive tumors
- Perimenopausal or postmenopausal women with a mean age of 60 years
- Abnormal uterine bleeding is the most frequent initial complaint

- Large polygonal tumor cells, with organoid, trabecular, or cordlike growth patterns.
- Peripheral palisading, necrosis, vesicular nuclei, and frequent mitotic figures and apoptotic bodies
- Synaptophysin M.C expressed NE marker
- Diffuse p16 positivity
- Usually PAX-8, TTF-1, and CD117 negative
- Microsatellite instability is seen in many cases

NECa : a diagnostic challenge

- LCNECa is most likely under-reported
- In most cases reported, a distinct high grade component was recognized but was originally interpreted as
  - Solid component of endometrioid carcinoma
  - Undifferentiated carcinoma

Am J Surg Pathol . 2016 May ; 40(5): 577–586

- LCNECa is distinguished from FIGO grade 3 endometrioid carcinoma
  - Architectural pattern
  - Expression of at least one NE marker
- LCNECa from undifferentiated carcinoma
  - based solely on the percentage of tumor cells expressing at least one NE marker in >10% of tumor cells

- Several explanations that have been proposed for the co-occurrence of endometrioid adenocarcinoma with neuroendocrine tumors of the endometrium
  - Divergent differentiation of a common progenitor tumor
  - Dedifferentiation of a differentiated tumor
  - True collision tumor

- In this case also there were two distinct component
- 90% of tumour show large cell neuroendocrine morphology
- Only 10% tumour was of endometrioid morphology of low grade
- It is essential to differentiate and report this entity because NEC component needs to be treated with different treatment approach

- Endometrioid adenocarcinoma grade 1 has a good prognosis
- Treatment plan is according to grade and stage
- Therapy for NEC : Little data exists due to rarity
- Aggressive tumour
- Warrants aggressive therapy, including chemotherapy and radiation therapy
- Our case also recevied chemotherapy and radiotherpy

THANK YOU