Value of GATA-3 expression in diagnosis of metastatic breast carcinoma

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INTRODUCTION

Globally, about 1.3 million new cases of breast carcinoma are diagnosed annually, it is overtaking cervical carcinoma as the most frequent malignancy diagnosed in women.

(Panieri et al., 2012)

In Egypt, Breast cancer is the most prevalent cancer among Egyptian women and constituting 17.5 % of total malignancies.

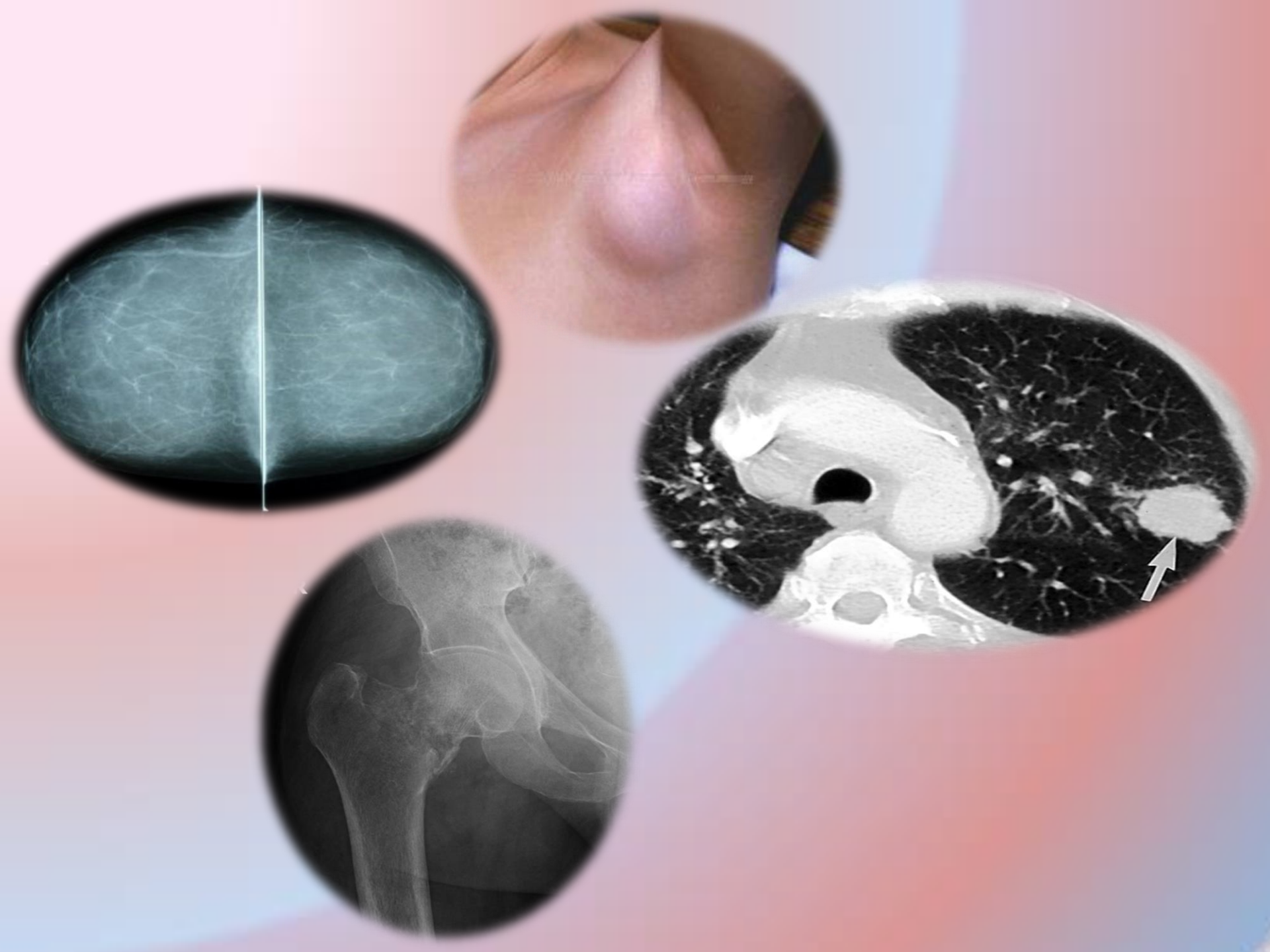
(Mokhtar et al., 2007)

Management and prognosis of invasive breast carcinoma does not depend any more on pure morphology only.

It also includes the IHC features of tumor based on its content of ER, PR and HER 2.

Breast cancers are categorized into the following main molecular groups:

- Luminal cell-like tumors, luminal A and B.
- Her2 positive tumors.
- Basal cell-like or “triple-negative”.



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Occult Breast Cancer Presenting With Axillary Metastases

Updated Management

Paul L. Baron, MD; Michael P. Moore, MD; David W. Kinne, MD; Frank C. Candela, MD; Michael P. Osborne, MD, MS; Jeanne A. Petrek, MD

Arch Surg. 1990;125(2):210-214. doi:10.1001/archsurg.1990.01410140088014.

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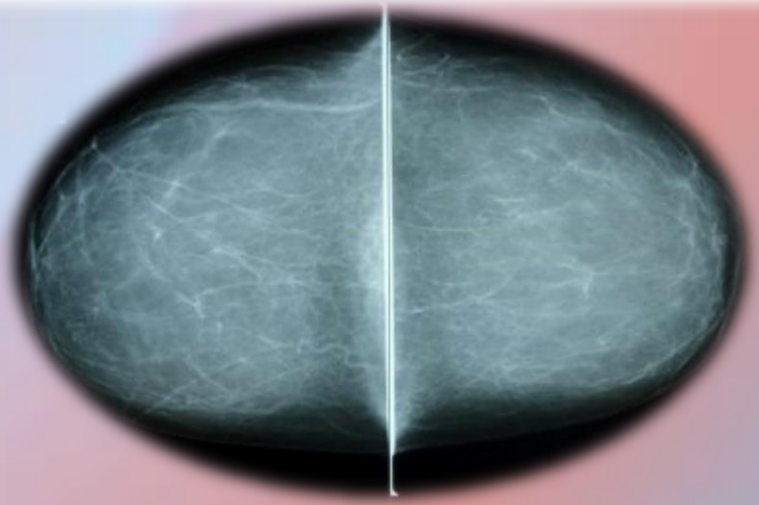


Estrogen receptor (ER), Gross cystic disease fluid protein-15 (GCDFP-15) and mammaglobin (MGB) are the most commonly used immunomarkers for identifying breast primary in tumors of unknown origin.

Identification of metastatic breast carcinoma of primary origin can be challenging, as positive ER and PR staining is frequently detected in both breast and gynecologic tract carcinomas.

Moreover, the reported sensitivities for GCDFP-15 and mammaglobin are 35% and 50% respectively. But both are usually not expressed in high-grade breast carcinomas

GATA-3

(GATA-binding protein-3) belongs to a family of transcription factors (GATA-1 to GATA-6).

These transcription factors bind with high affinity to the G-A-T-A nucleotide sequence in target gene and share a steroid-hormone-receptor super family C4 zinc-finger DNA binding motif

Several studies reported high GATA-3 expression in breast and urothelial carcinomas.

GATA-3 is supposed to be a useful immuno-histochemical marker for breast cancer identification.

AIM OF THE WORK

To evaluate GATA-3 expression in the various immunohistochemical subtypes of invasive breast carcinoma.

To evaluate GATA-3 utility in diagnosing the origin of metastatic carcinoma where primary breast cancer is suspected.

MATERIAL AND METHODS

Material and methods

Total

- 85 cases

Primary breast cancinoma (60 cases)

- 20 cases ER positive [luminal (A and B) subtype].
- 20 cases Her2 positive subtype.
- 20 cases Triple negative subtype.

Metastatic adenocarcinoma (25 cases)

- All metastatic cases had previous history of breast carcinoma

- **All cases were evaluated for the following data:**

I- Clinical data:

- Archival files of the patients were examined to record:
- Age and sex of the patient.
- Available surgical data.

П- Pathological data:

- Data concerning histopathologic features were obtained by examination of Haematoxylin and Eosin stained sections of 5 µm thickness, which were prepared from paraffin blocks.

Immunohistochemical study:

- **Primary antibody:**

- GATA-3 antibody; clone (L50-823) –CMC48970001 was obtained from Cell Marque, CA, USA.
- Mouse monoclonal antibody.
- Prediluted for immunohistochemical staining.

- **<u>Immunohistochemical procedure:</u>**

  GATA-3 labeling was performed on the BenchMark XT autostainer (Ventana) using DAB as chromogen and hematoxylin as counter-stain.

Evaluation of immunohistochemical results :

Only nuclear staining was considered for GATA-3 positive labeling and the extent of staining was scored on a scale of (0 to 4+):

4+ (>75%)

3+ (>50%–75%)

2+ (>25%– 50%)

1+ (>5%–25%)

0 (0–5%) **(Liu et al., 2012 and Miettinen et al., 2014)**

N.B: Any intensity of staining with greater than 5% distribution was considered positive.

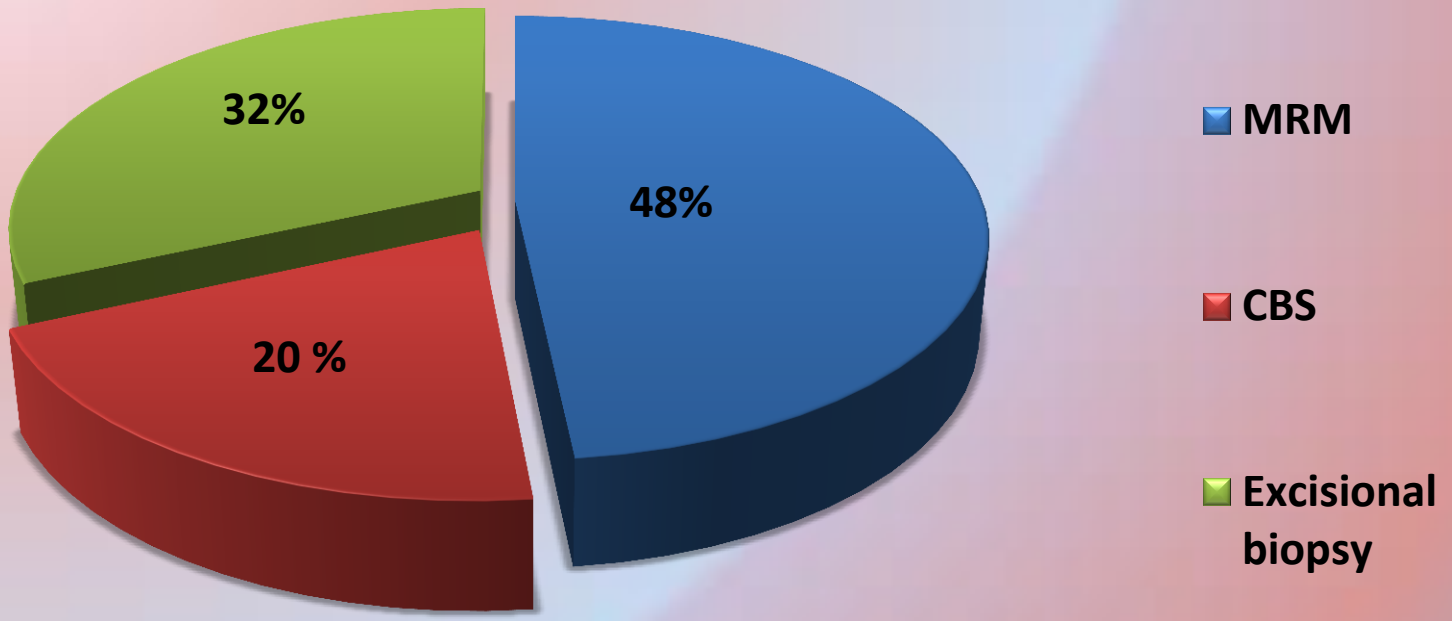
(Albergaria et al., 2009)

RESULTS

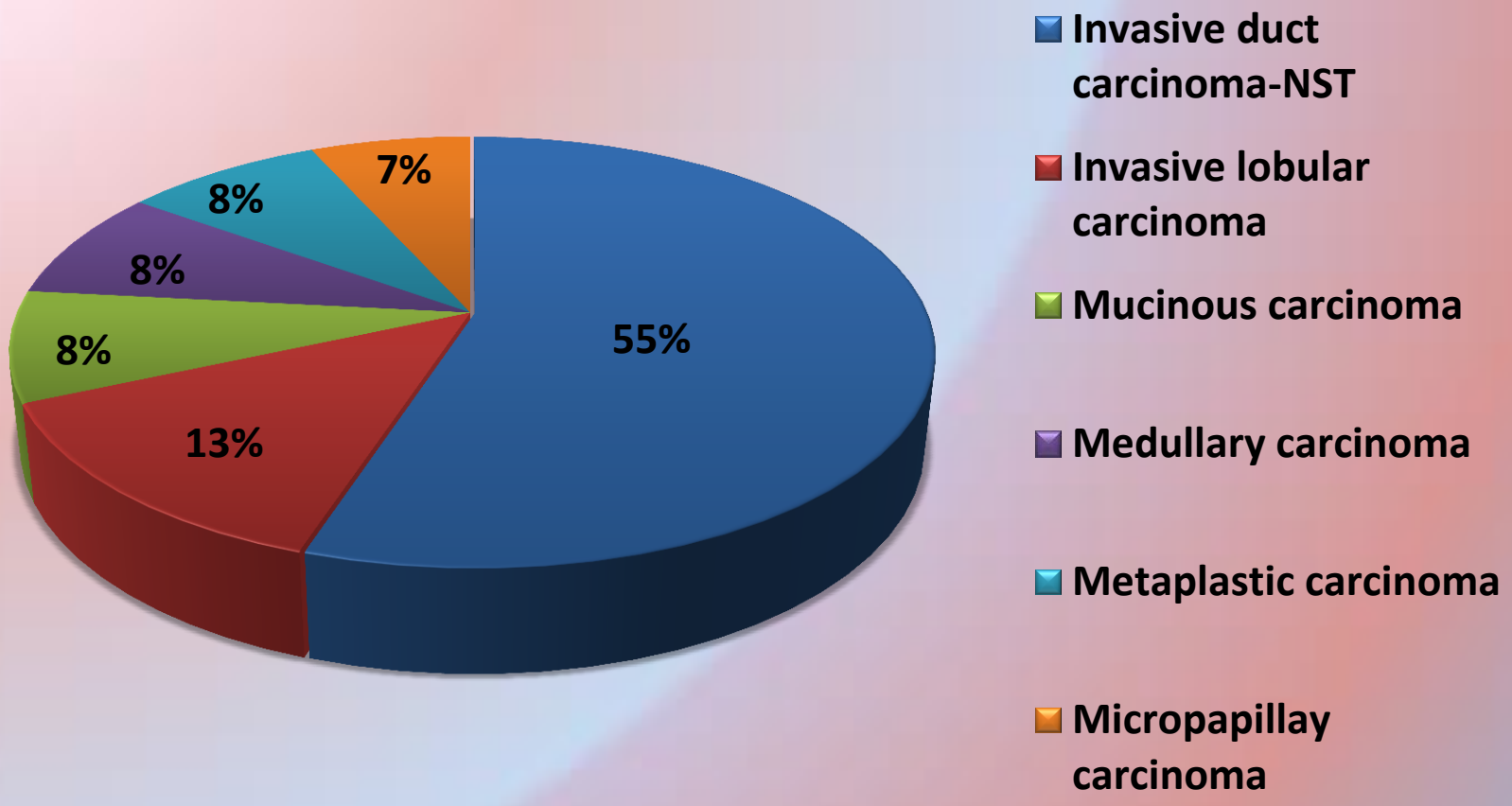
Demographic data of the studied cases

Gender	Number	Percentage	
Female Male	83 2	98 2	
Age (years)	Mean	SD	Range
	53.5	10.5	23-76

The types of surgical specinems of the primary breast carcinomas



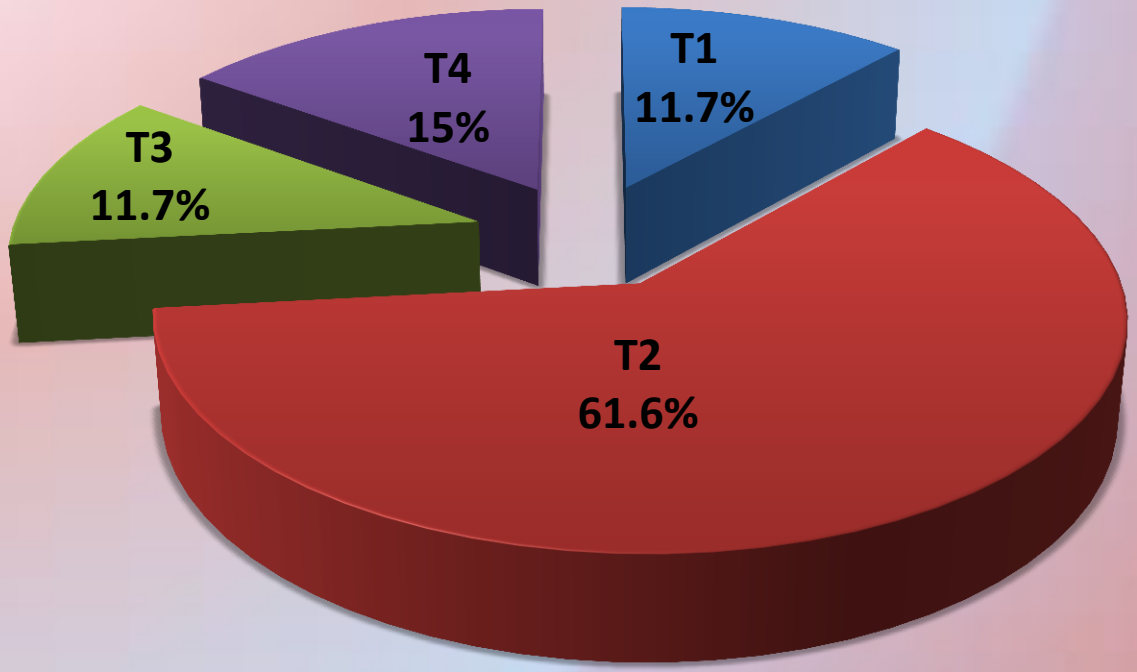
Morphological types of the primary breast carcinoma in the studied cases



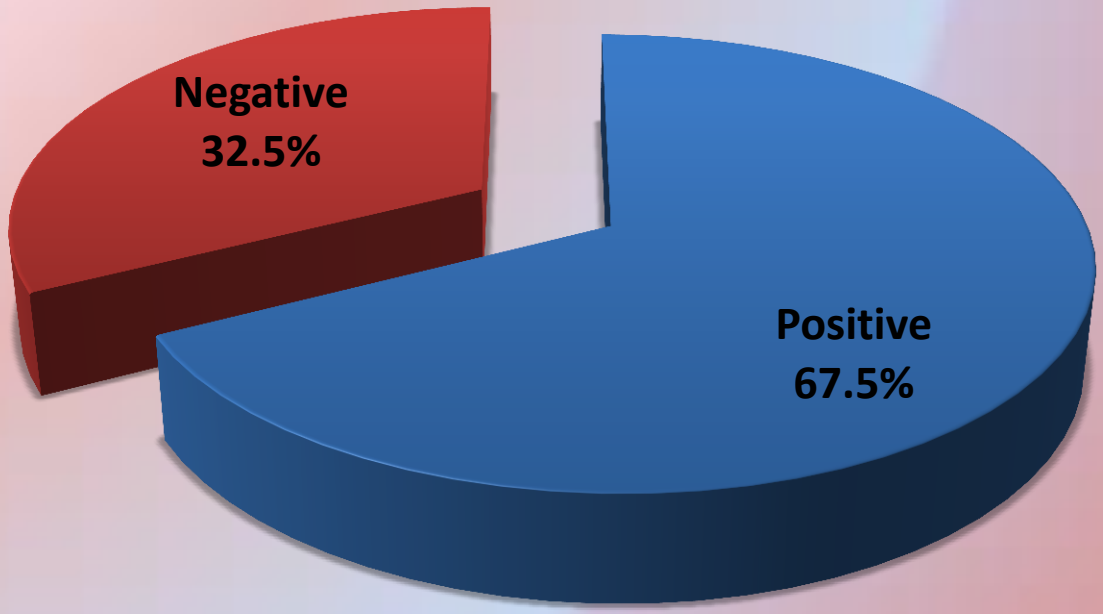
The grade of primary breast carcinoma in the studied cases

Tumor grade	Number	Percentage
G1	6	10
G2	36	60
G3	18	30
Total	60	100

Tumor size of primary breast carcinoma of the studied cases



Lymph node status in primary breast carcinoma specimens

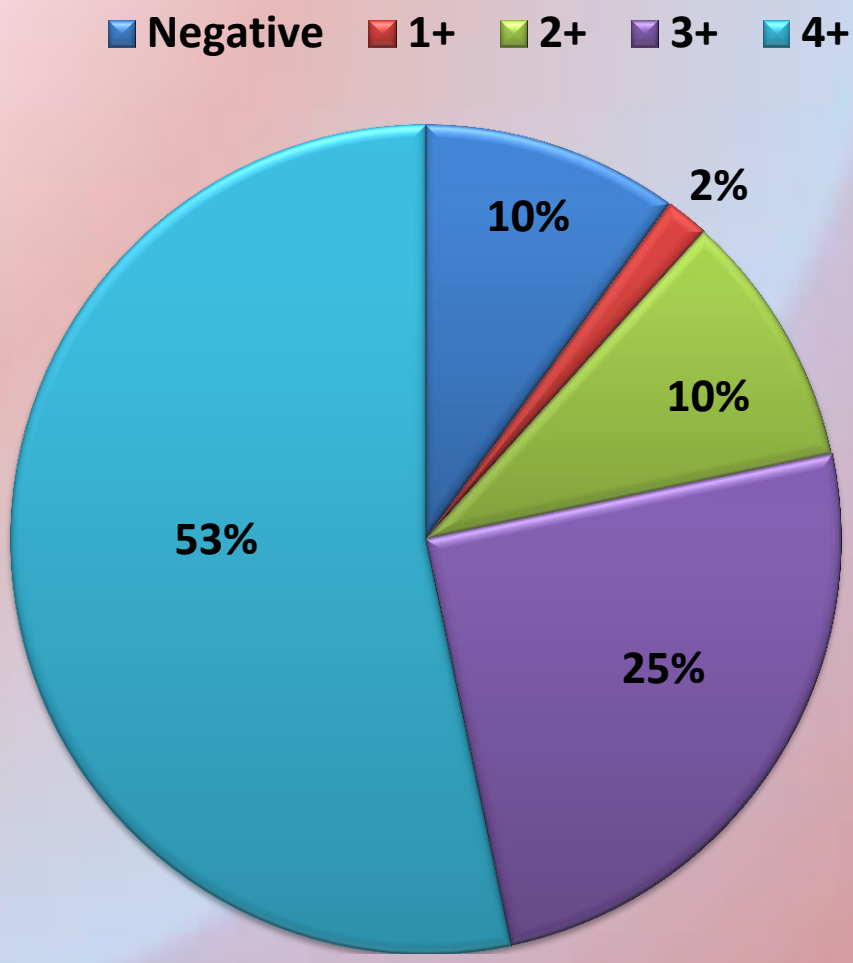


Site of metastatic deposits

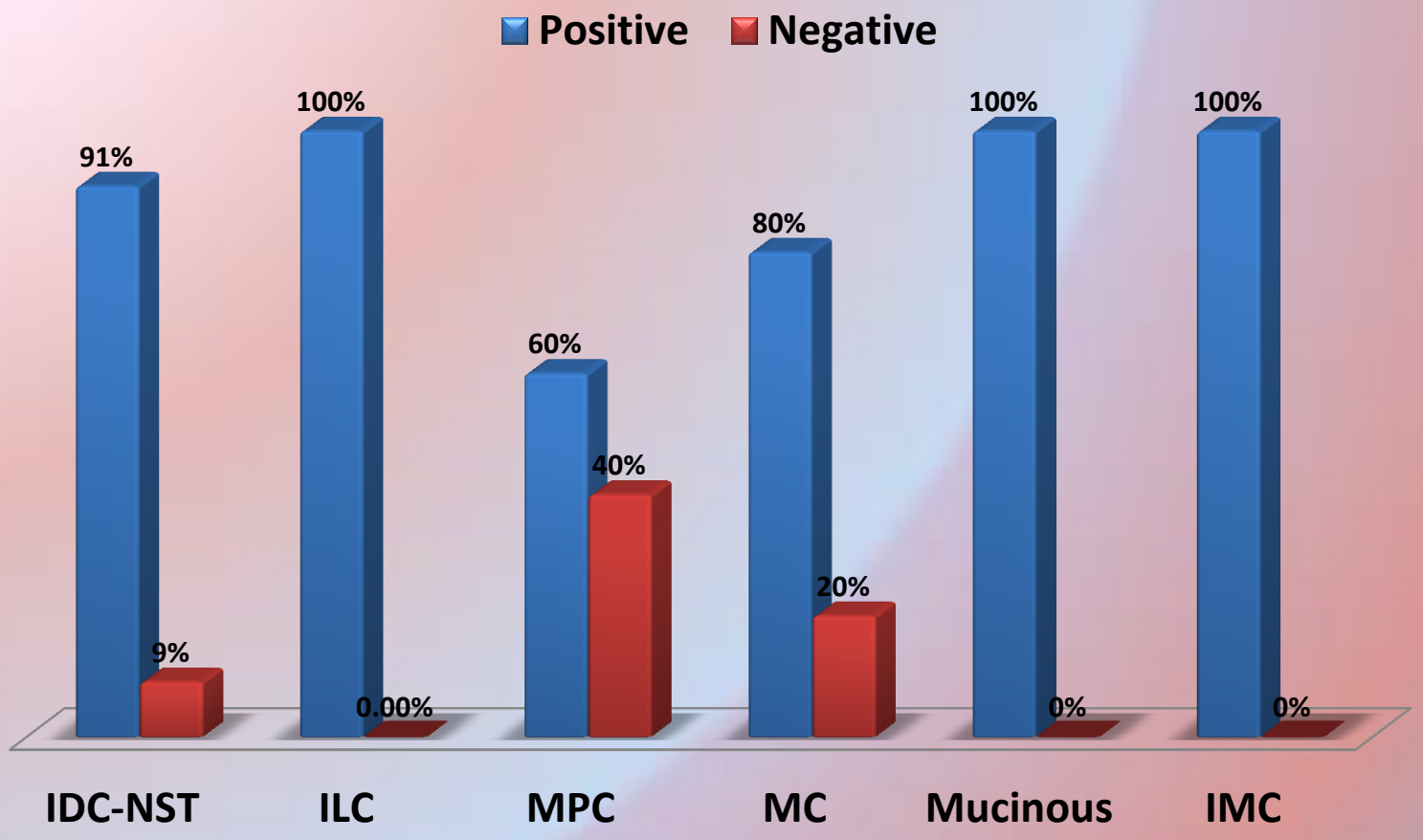
Site	Number	Percentage
Pleural effusion	4	16
Colonic deposits	4	16
Bone	4	16
Liver	4	16
Ovary	3	12
Ascites	1	4
Brain	1	4
Adrenal gland	1	4
Thyroid gland	1	4
Endometrial curettage	1	4
Urinary Bladder	1	4
Total	25	100

IMMUNOHISTOCHEMICAL RESULTS

GATA-3 expression in primary breast carcinomas

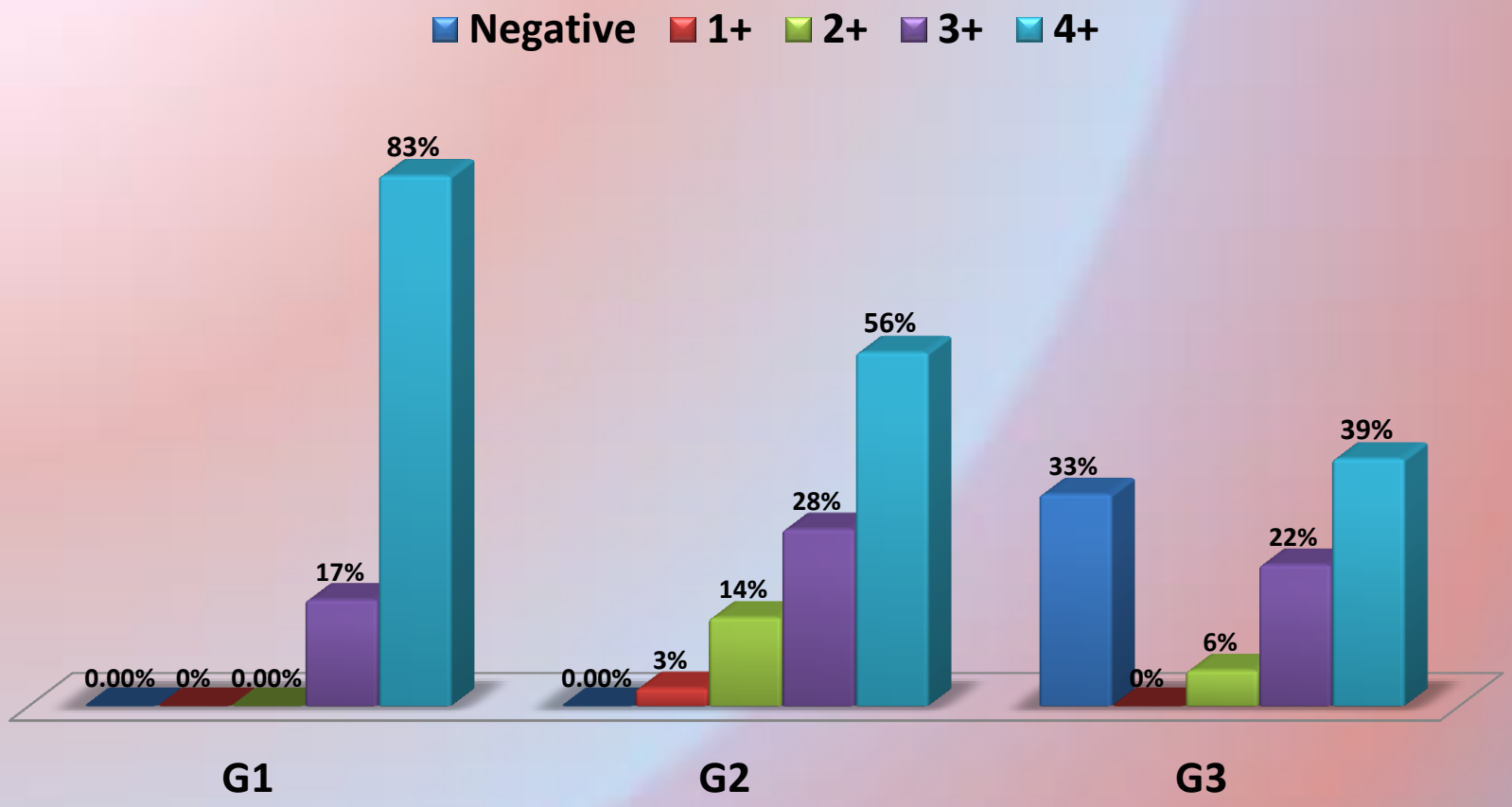


GATA-3 expression in different morphologic types of primary breast carcinoma



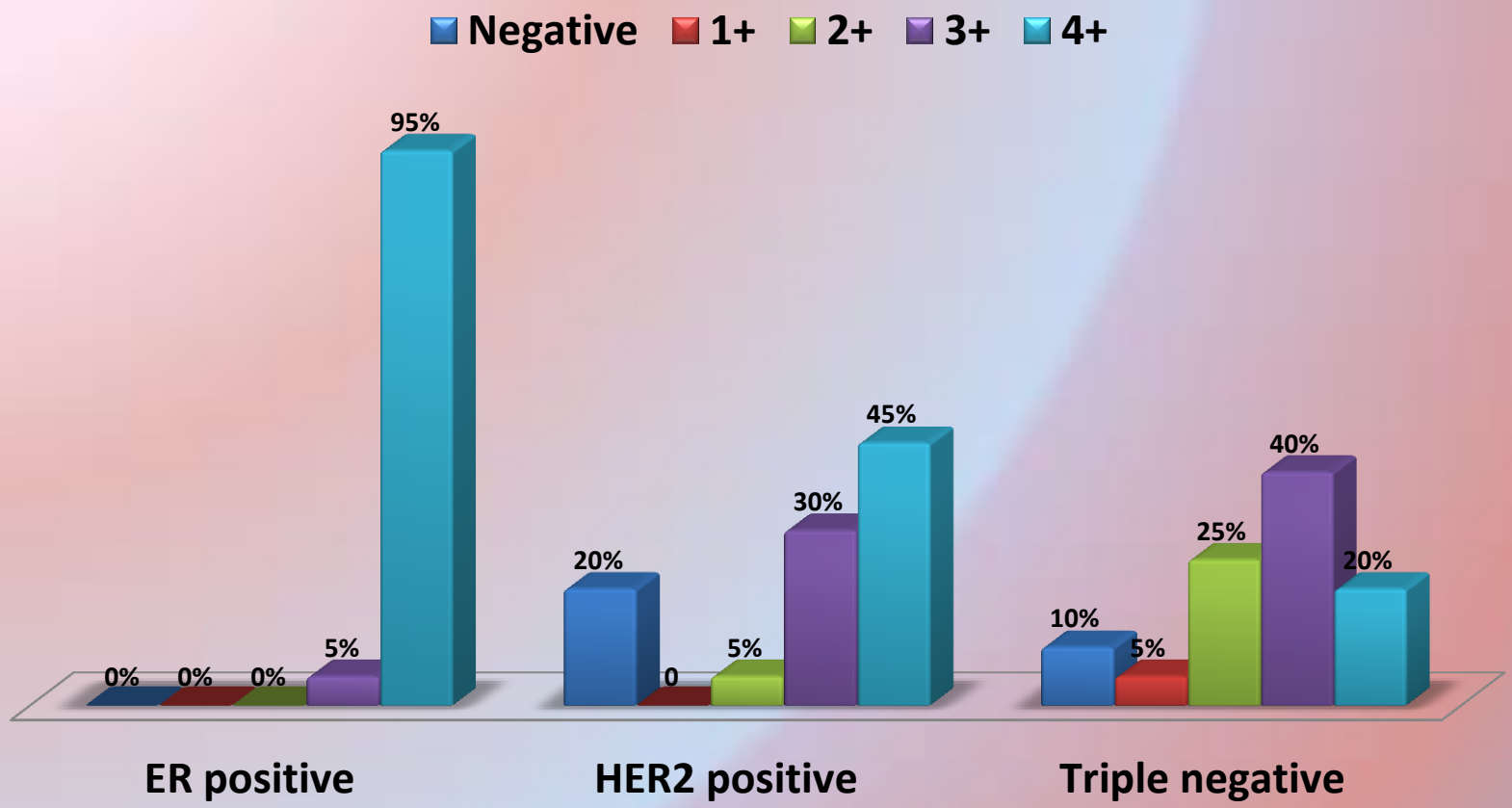
P value > 0.05 not significant

GATA-3 expression in different grades of primary breast carcinomas



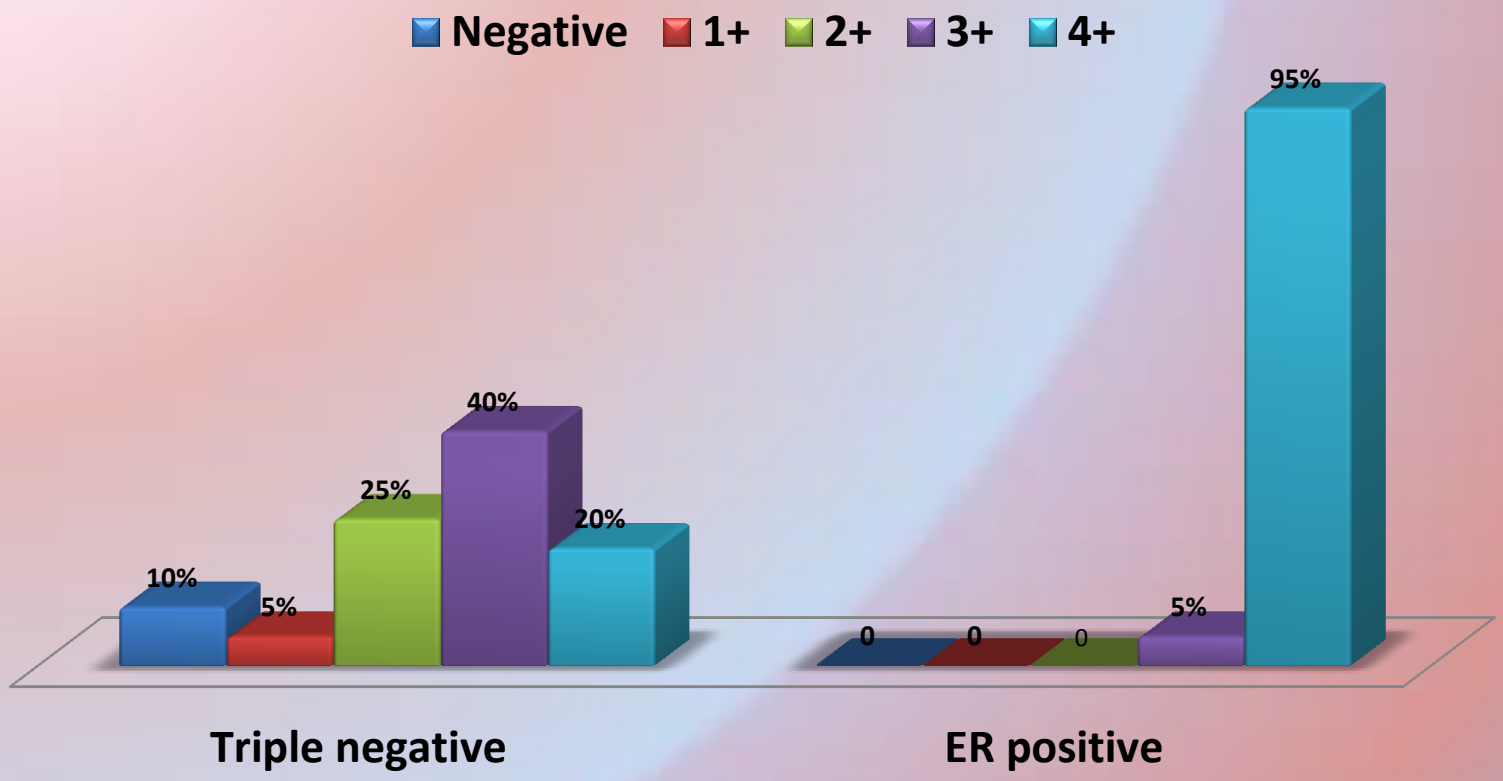
P value <0.05 significant

GATA-3 expression in different molecular subtypes of primary breast carcinoma cases



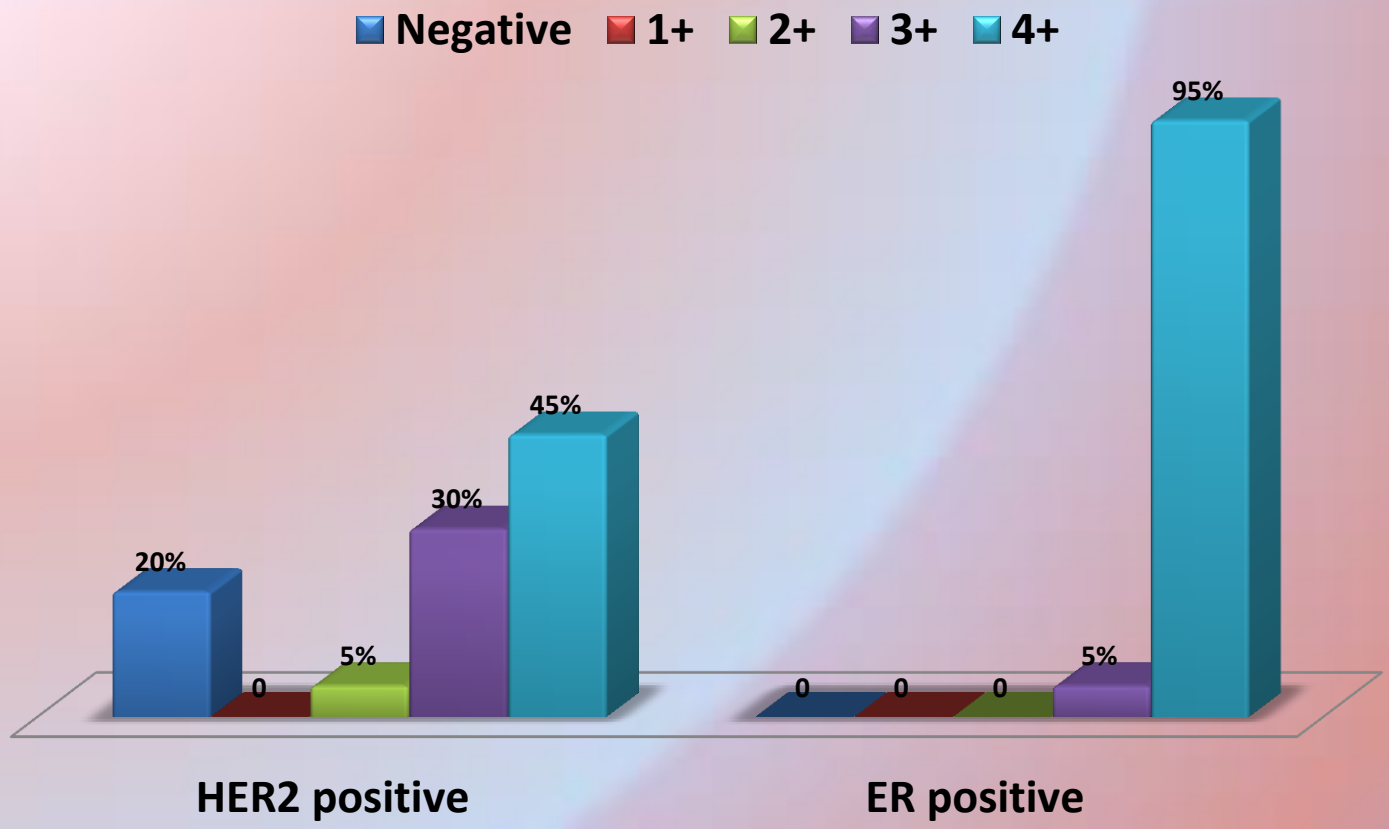
P value <0.001 highly significant

The difference between triple negative and ER positive molecular subtypes as regards GATA-3 expression



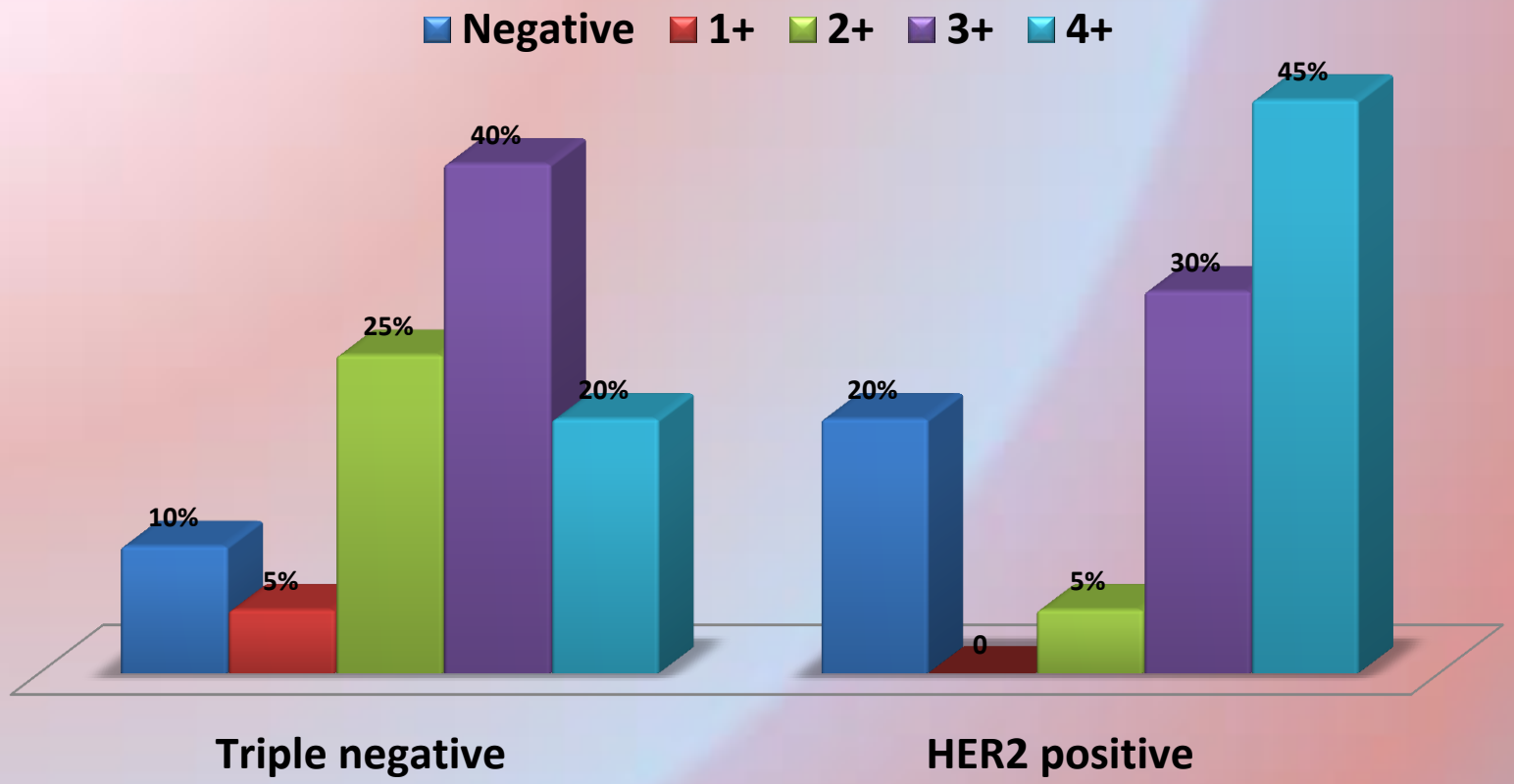
P value <0.001 highly significant

The difference between HER2 positive and ER positive molecular subtypes as regards GATA-3 expression



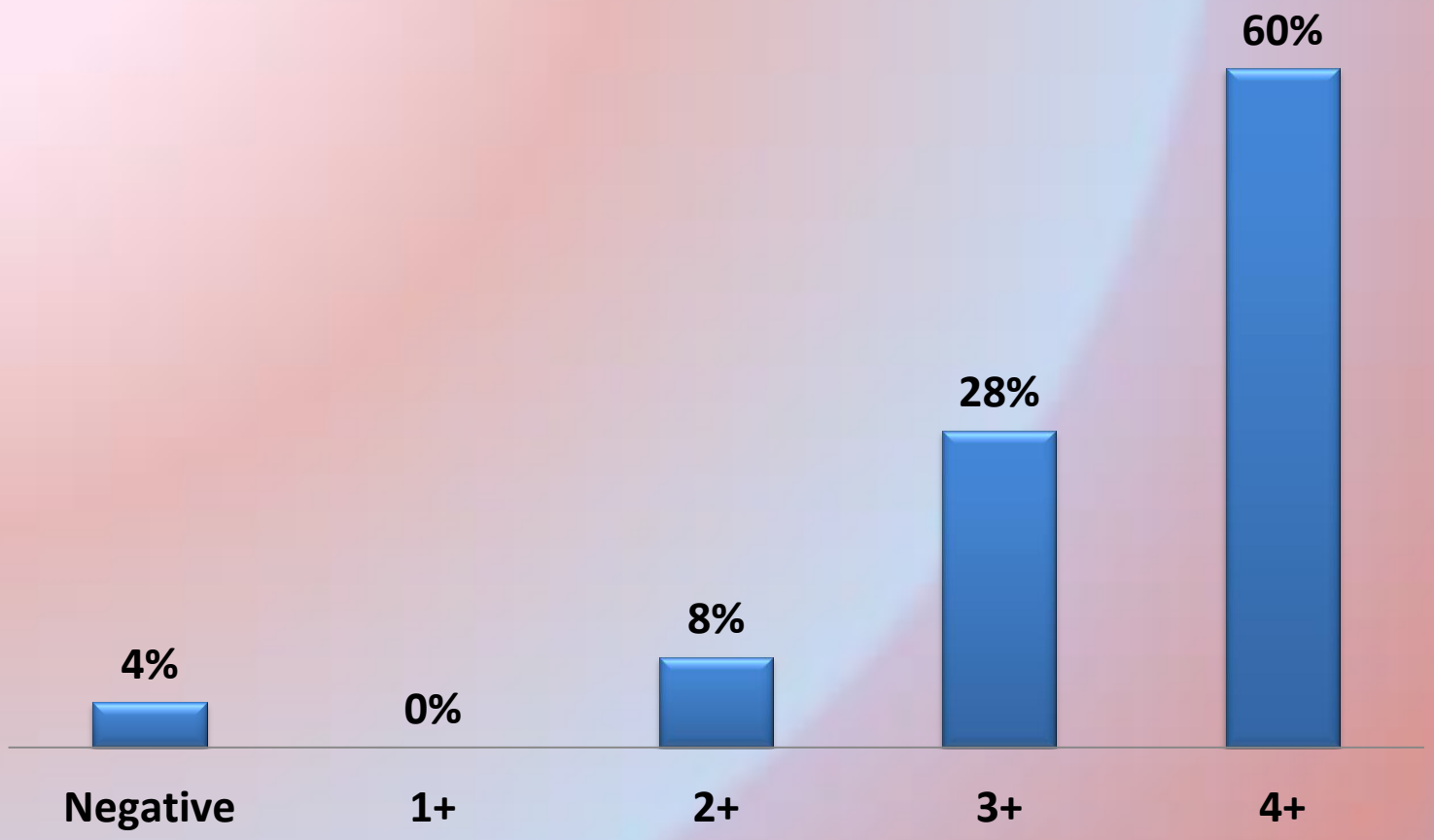
P value <0.05 significant

The difference between triple negative and HER2 positive molecular subtypes as regards GATA-3 expression

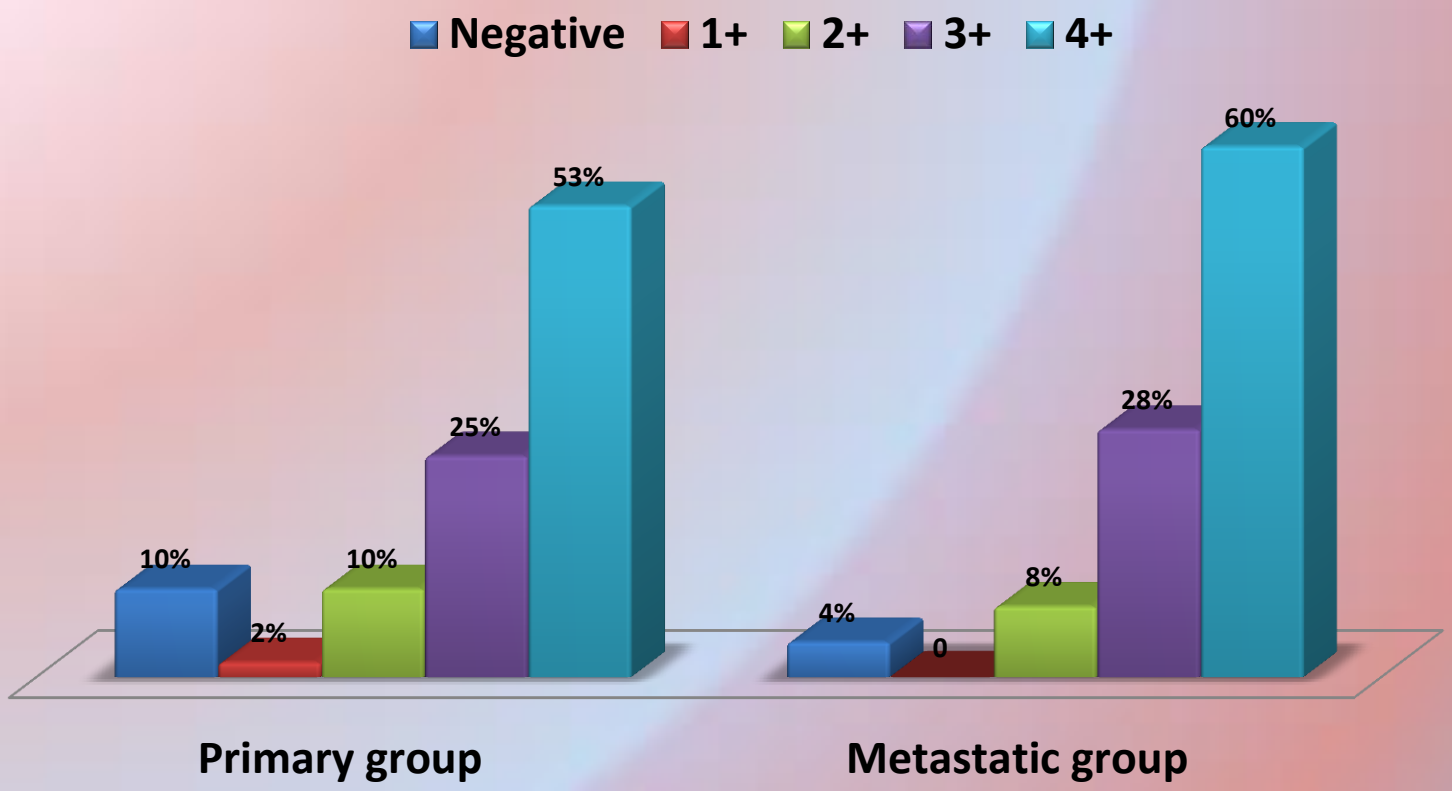


P value > 0.05 not significant

GATA-3 expression in metastatic group

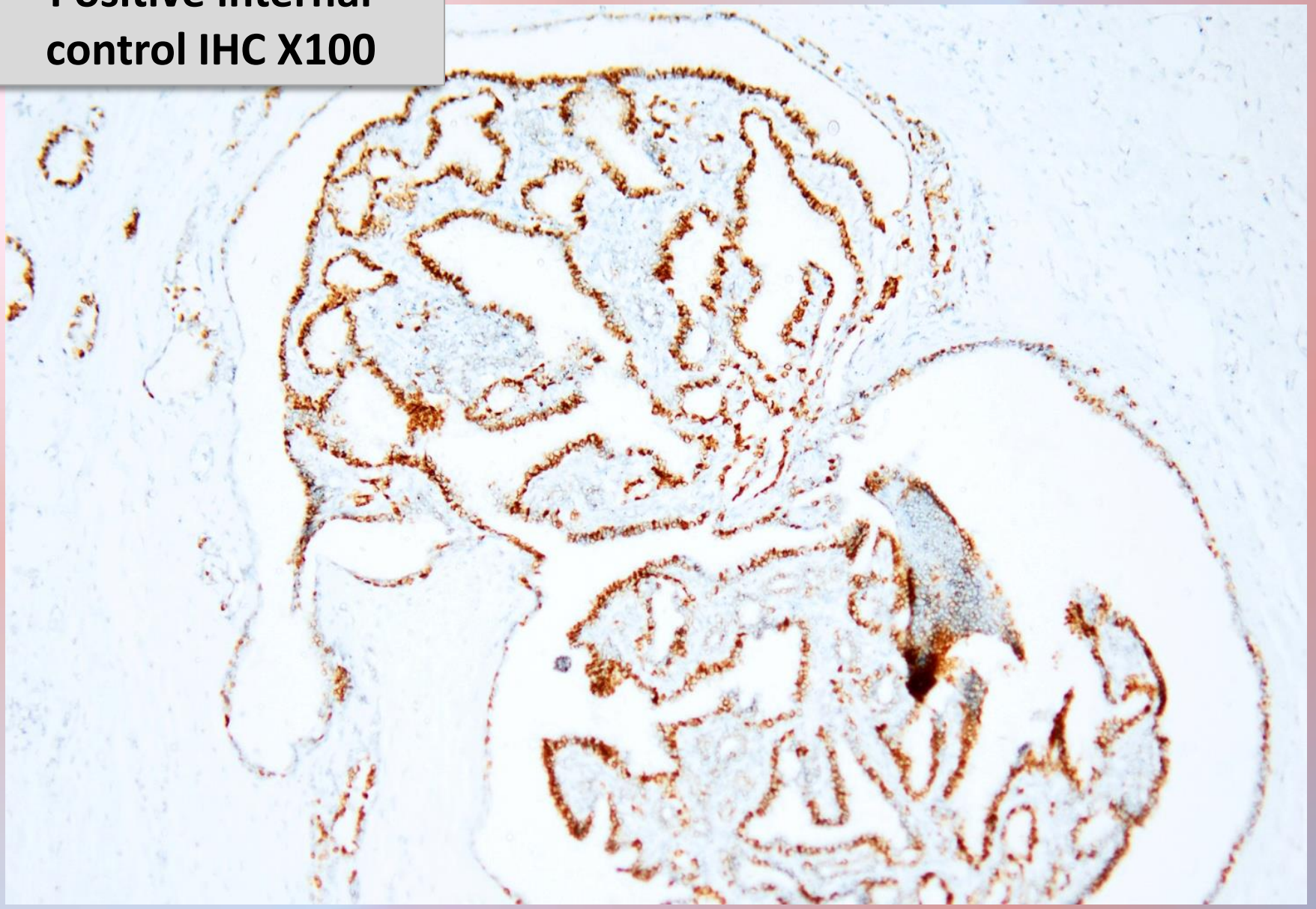


The difference between primary breast carcinoma cases and metastatic cases as regards GATA-3 expression



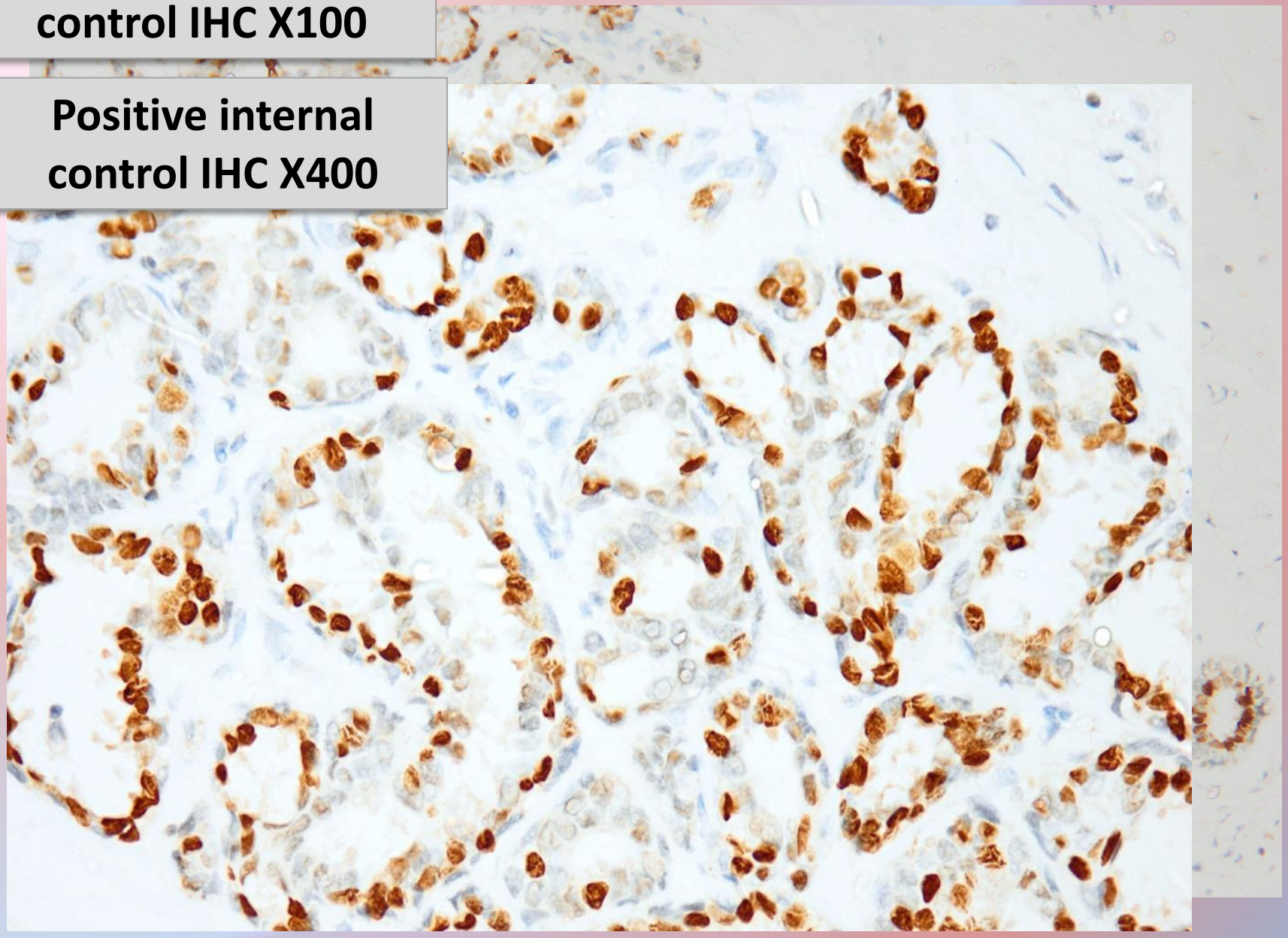
P value > 0.05 not significant

Positive internal control IHC X100

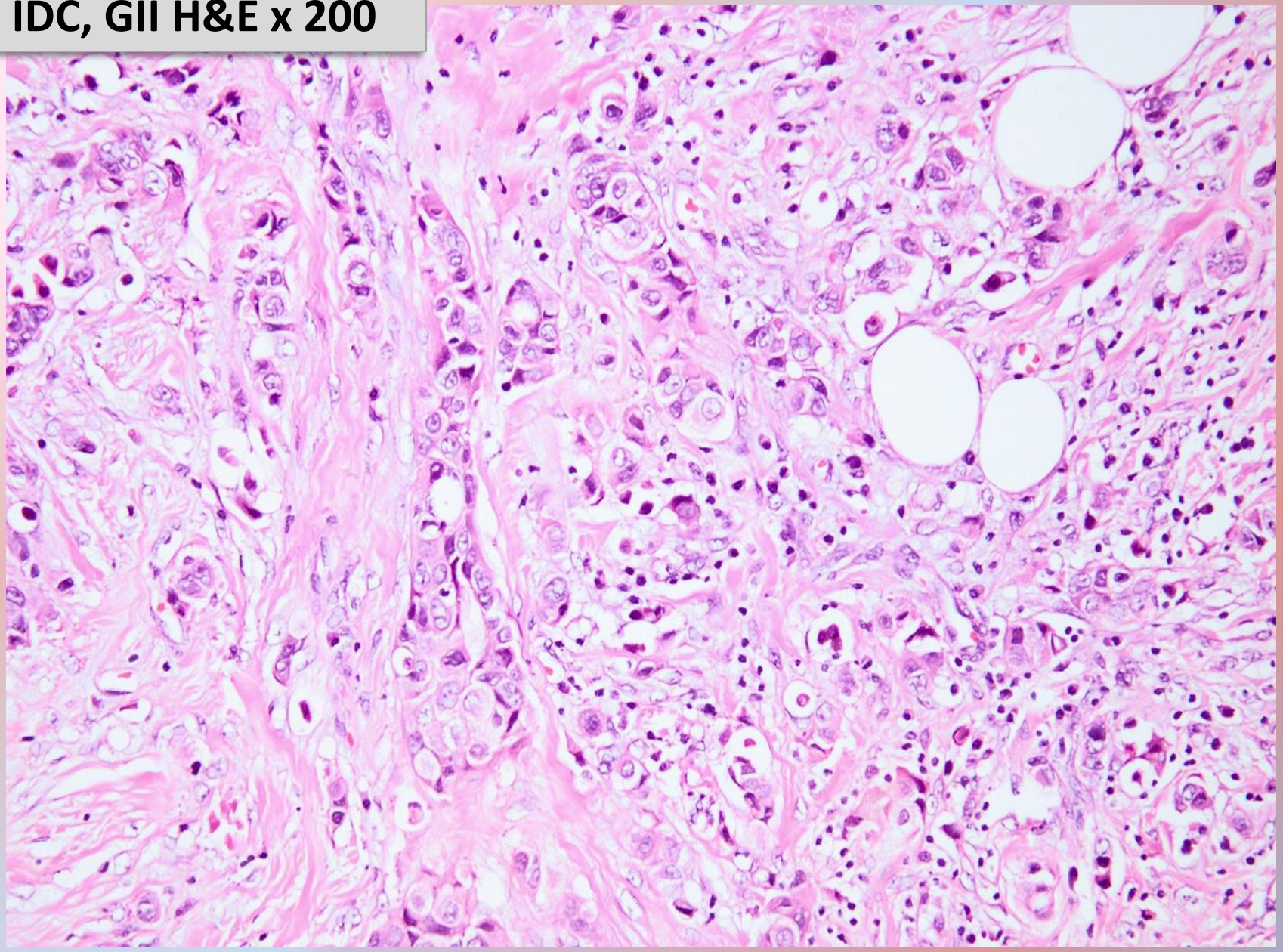


Positive internal control IHC X100

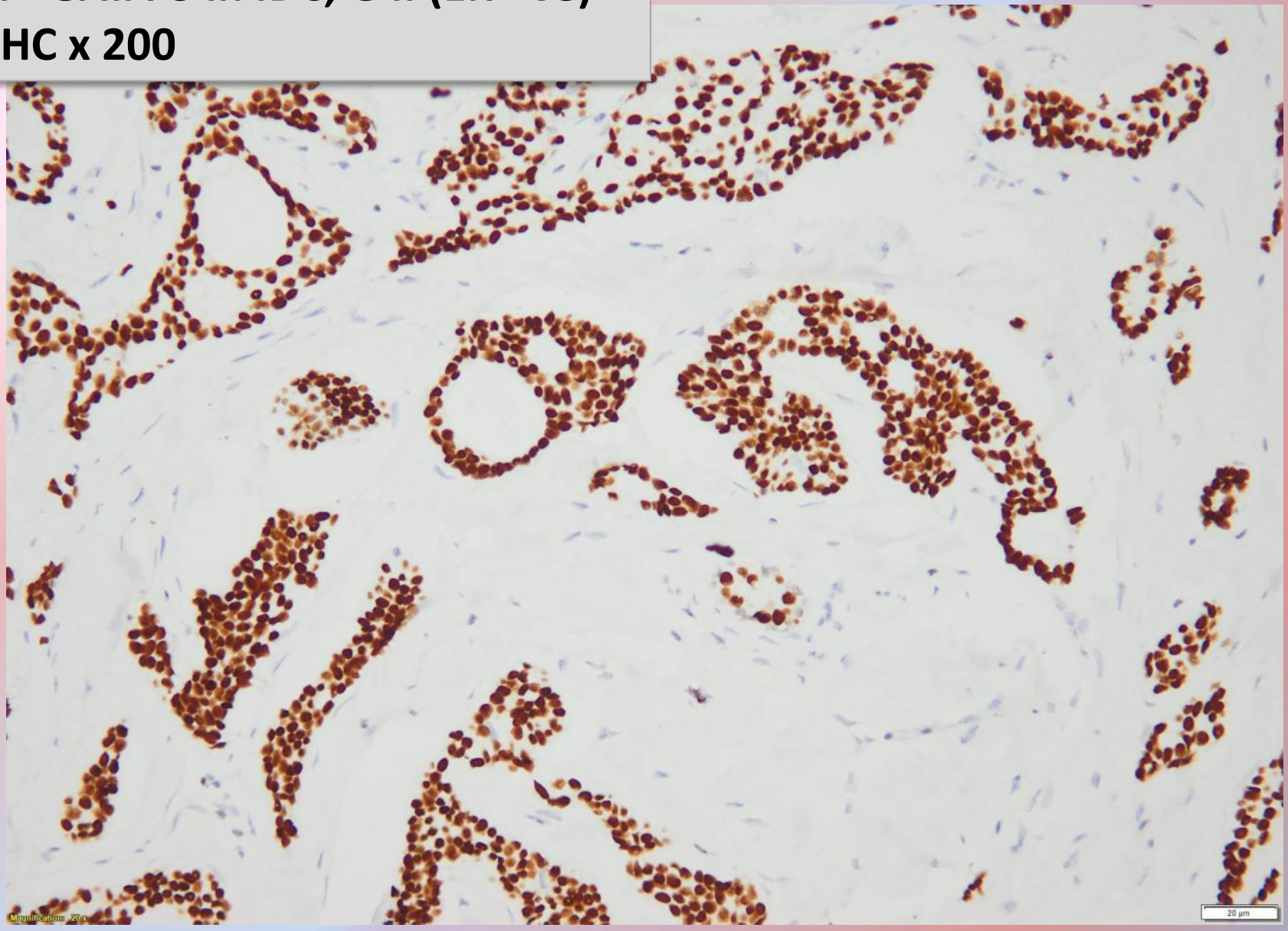
Positive internal control IHC X400



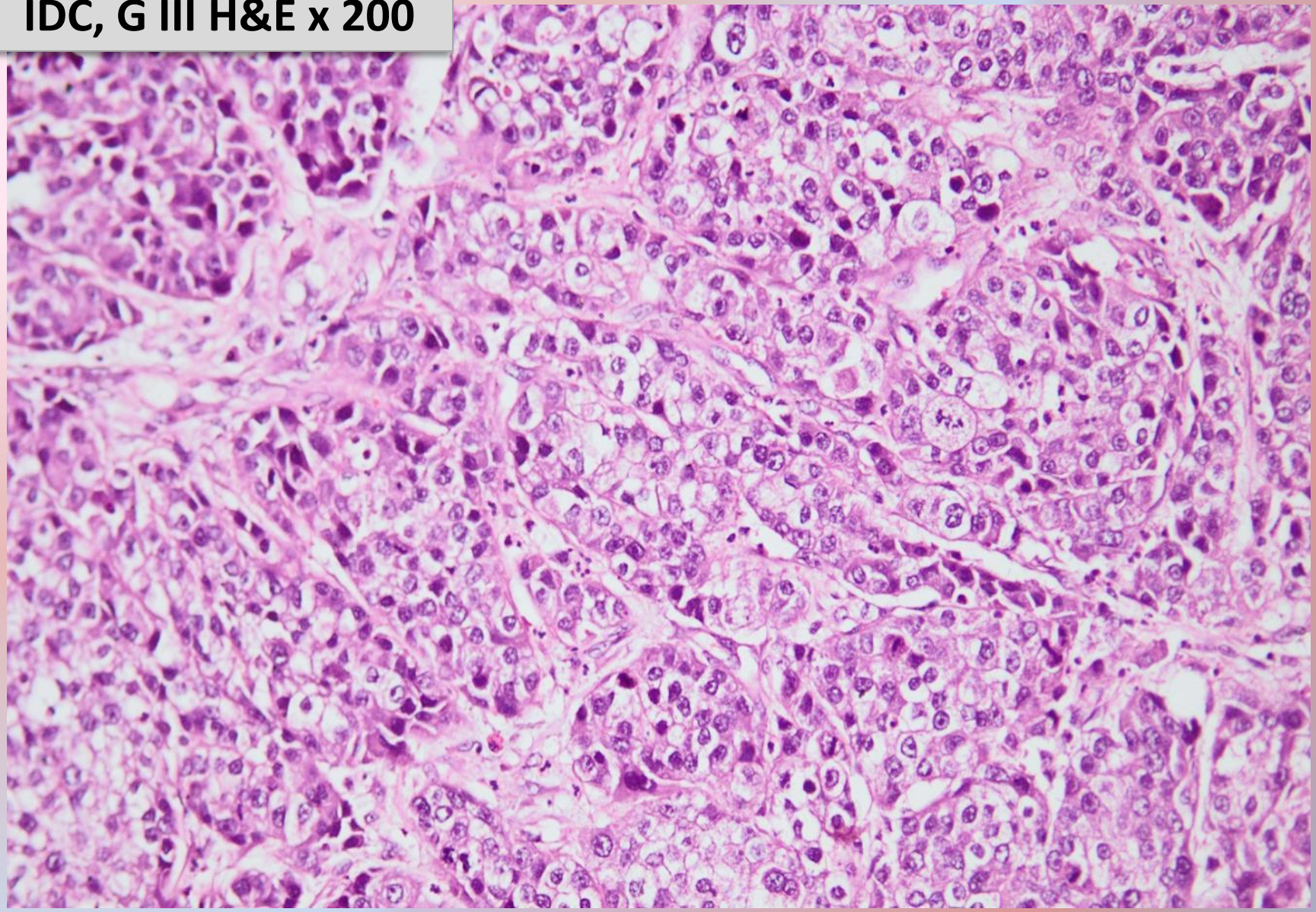
IDC, GII H&E x 200



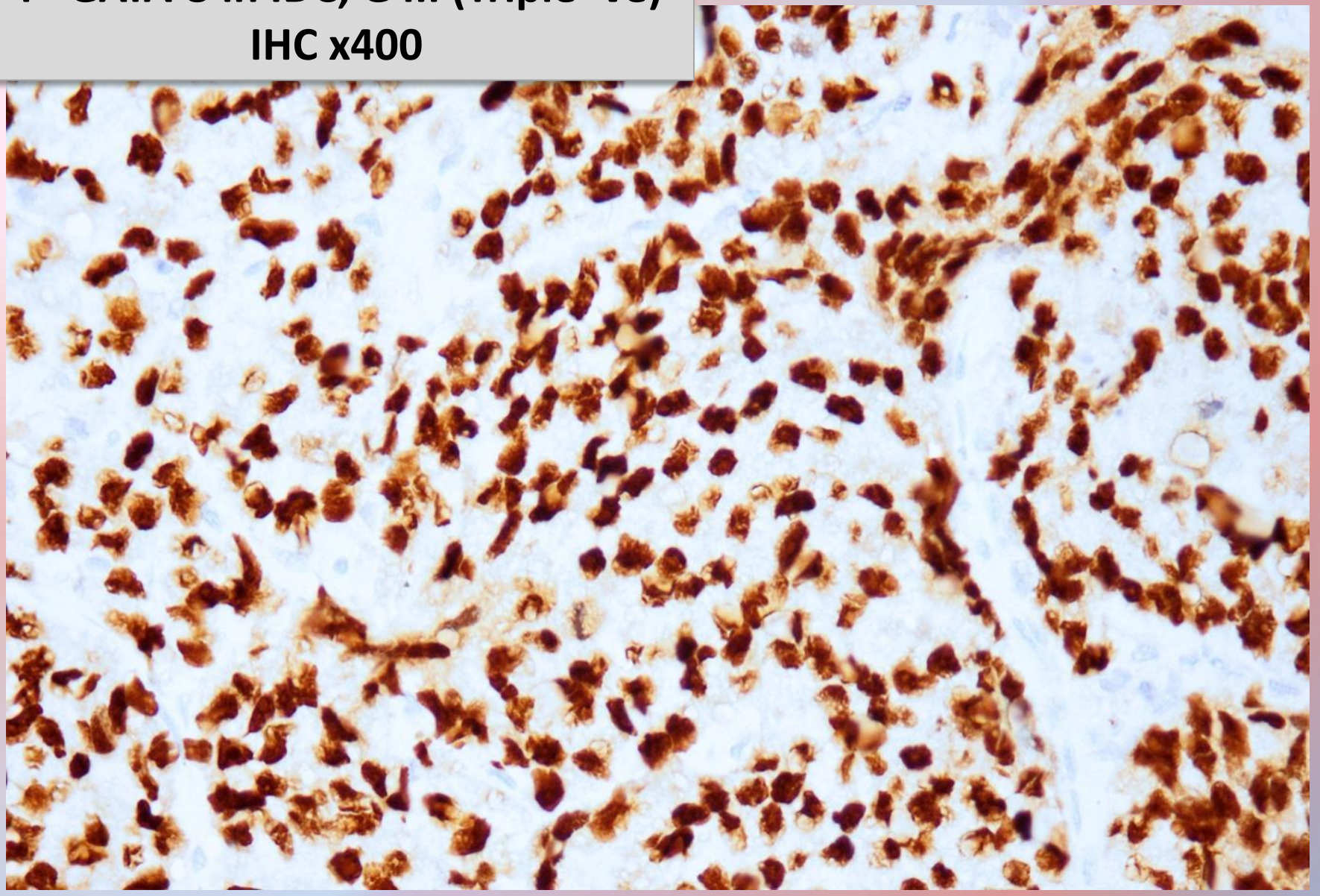
4+ GATA-3 in IDC, G II (ER +ve)
IHC x 200



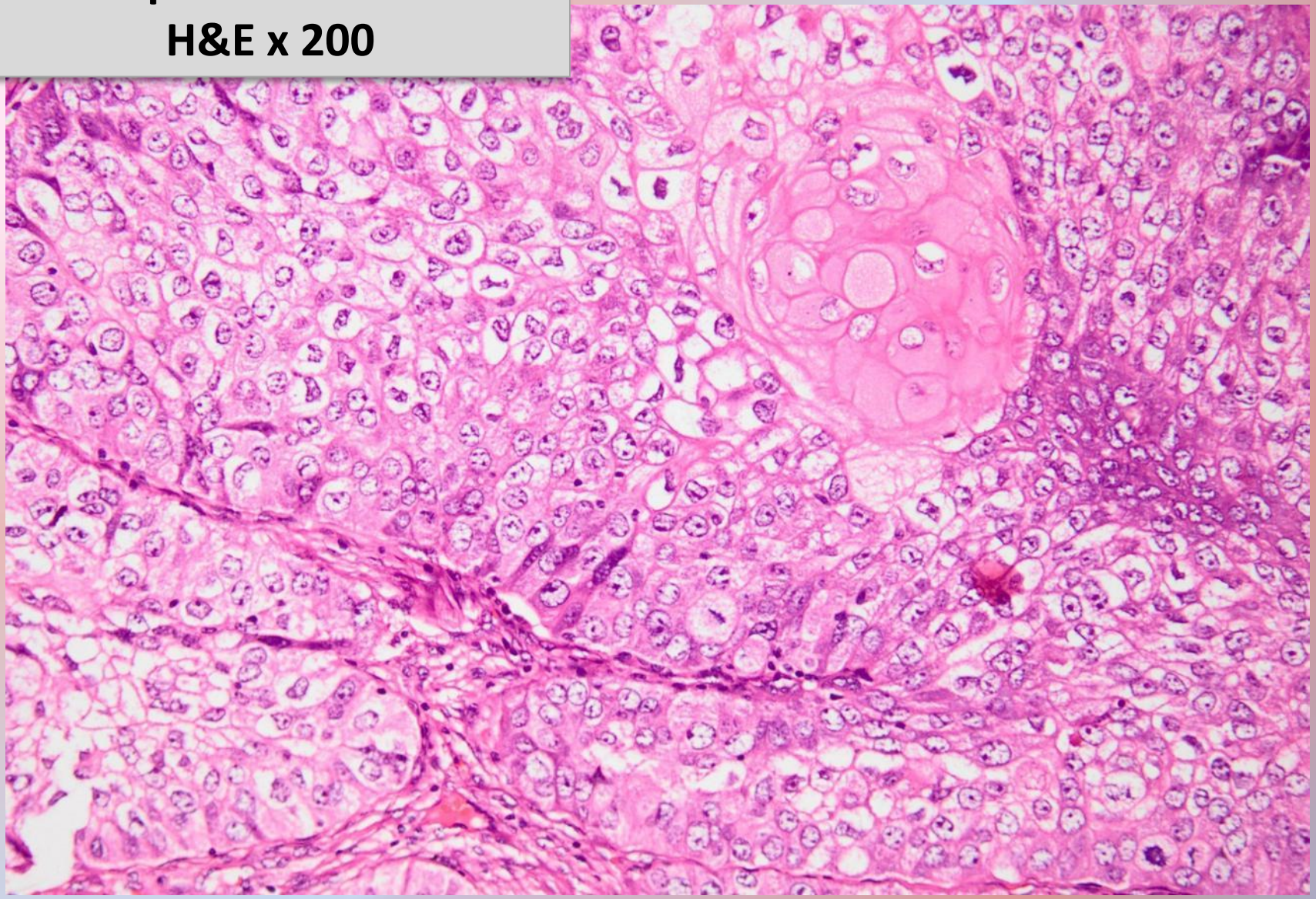
IDC, G III H&E x 200



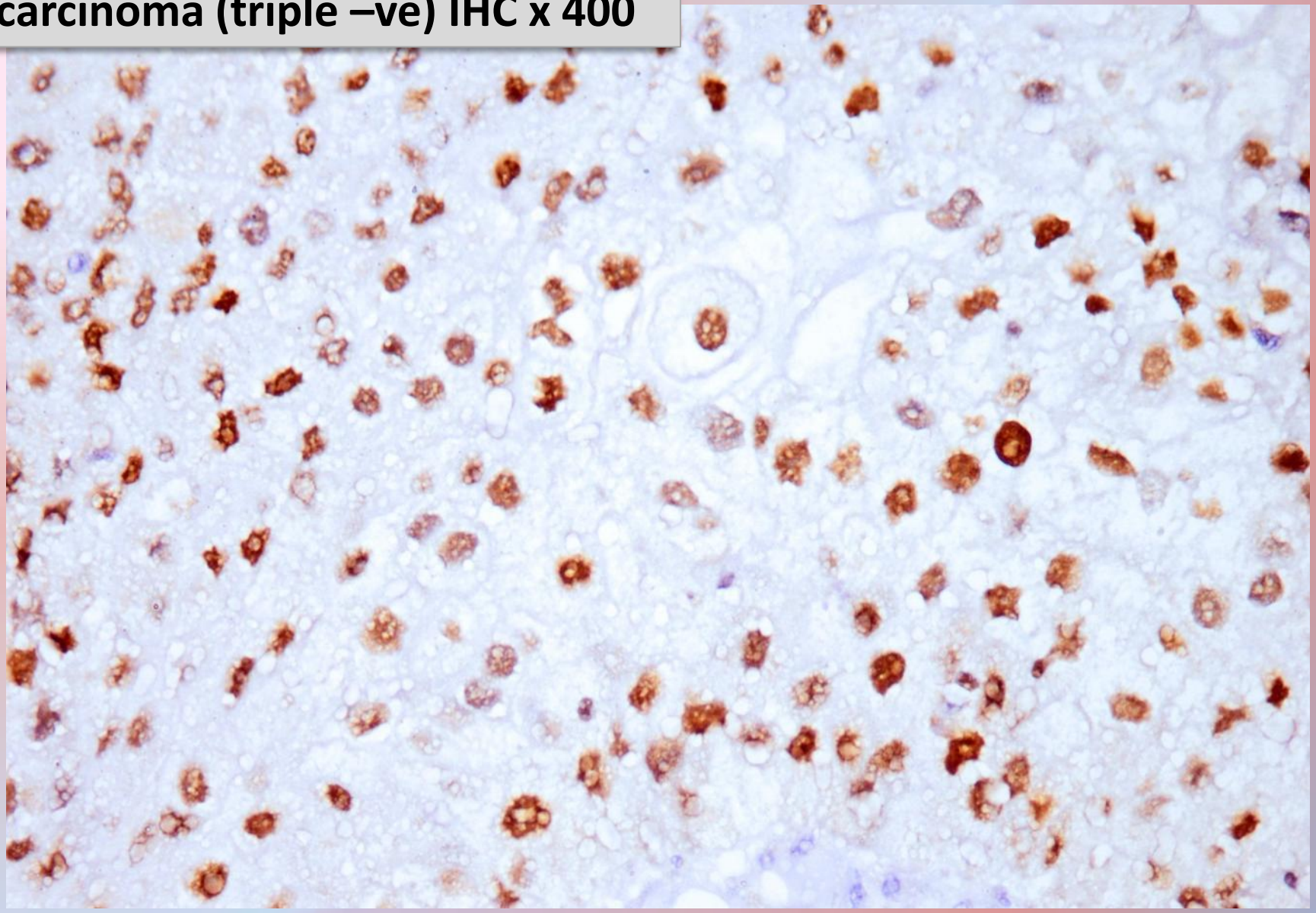
4+ GATA-3 in IDC, G III (Triple -ve)
IHC x400



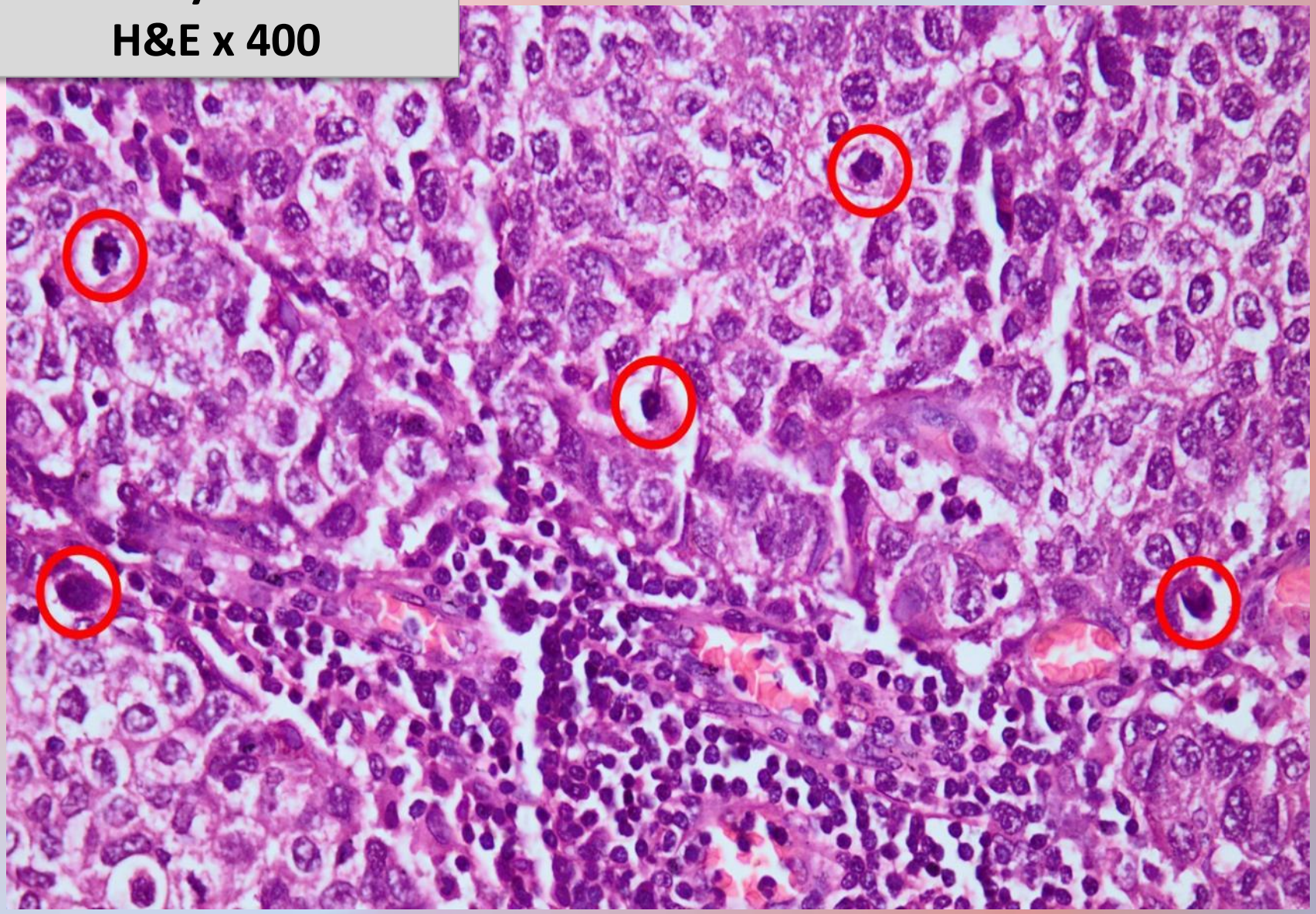
Metaplastic carcinoma
H&E x 200



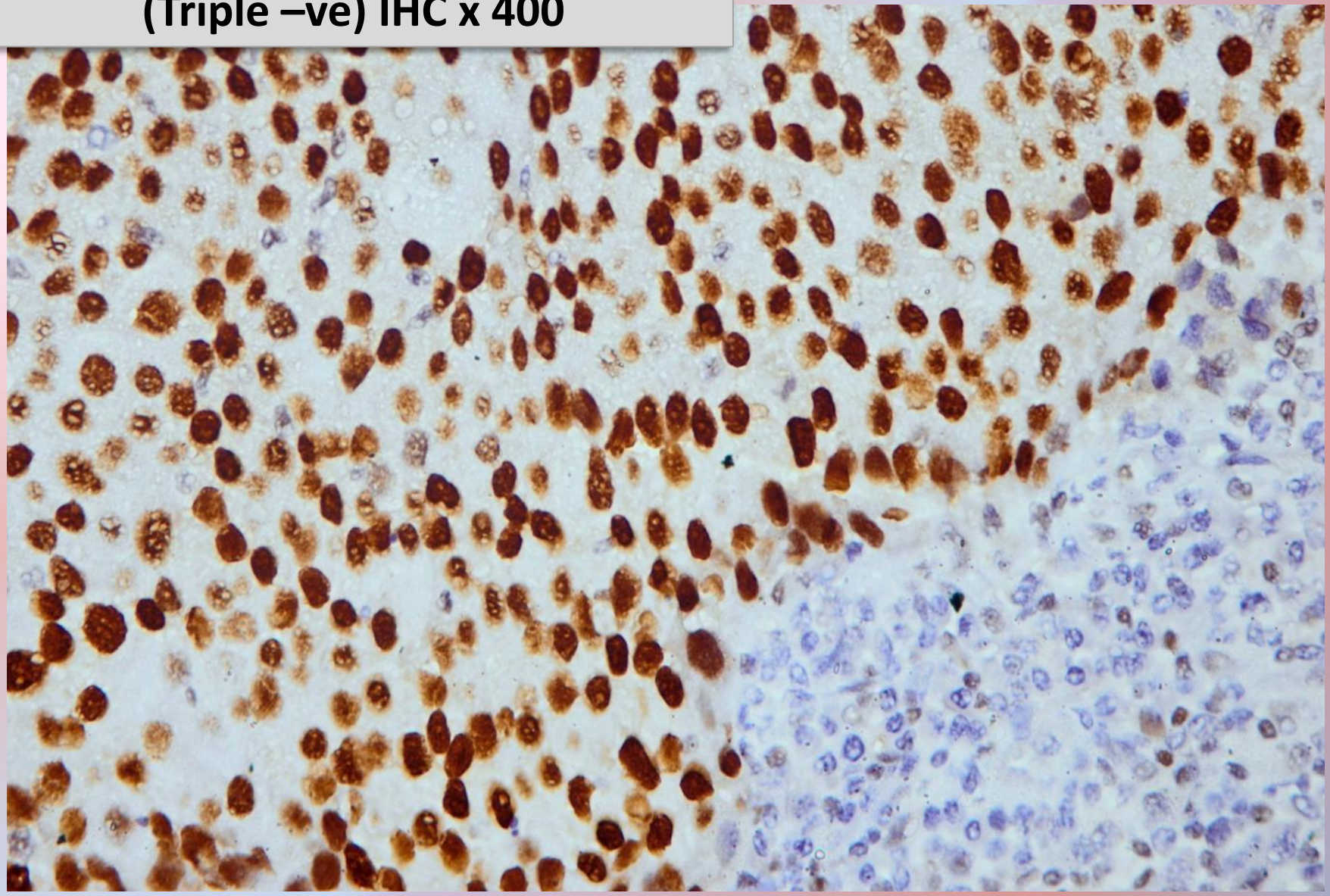
3+ GATA-3 in metaplastic carcinoma (triple –ve) IHC x 400



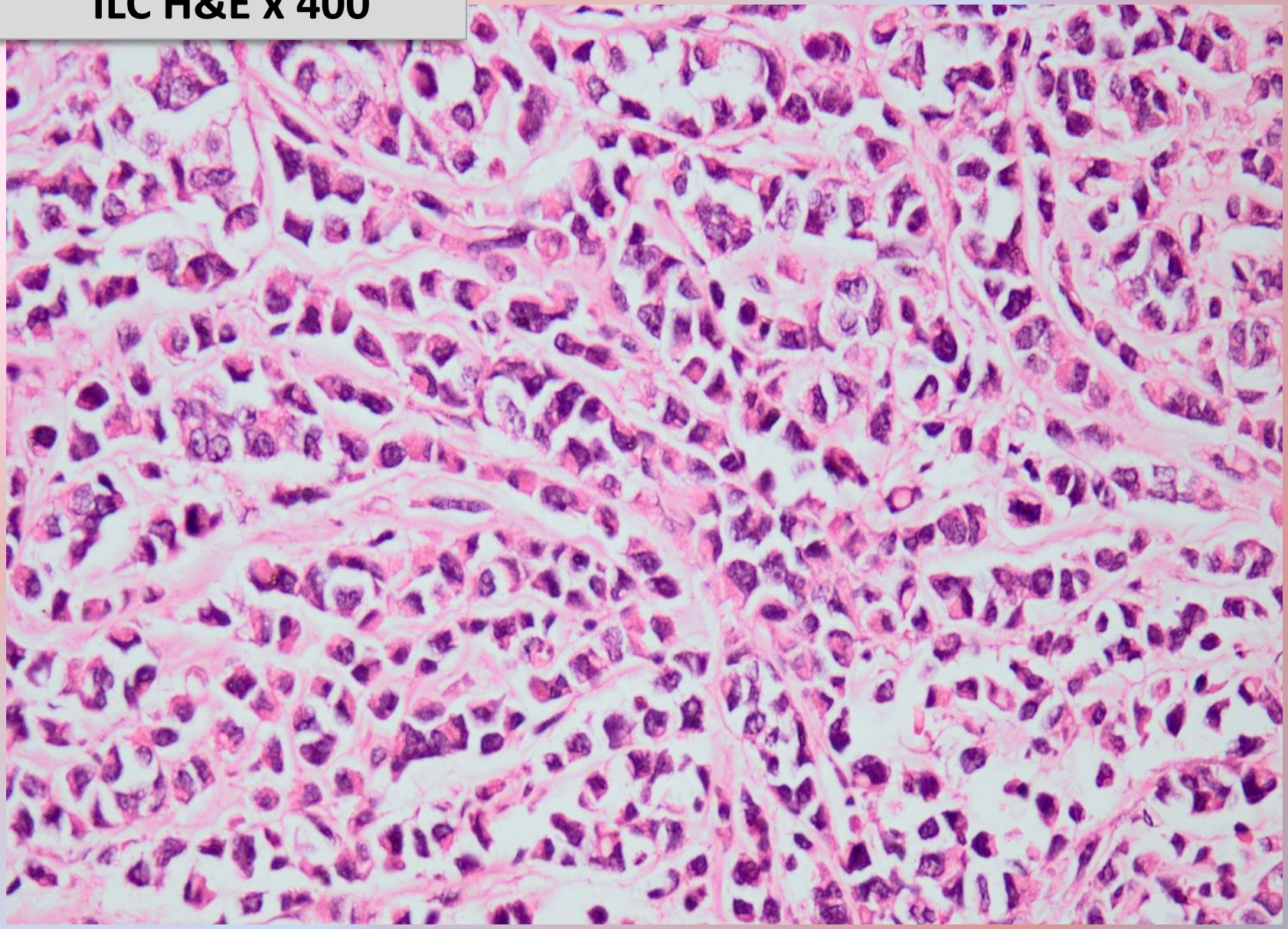
Medullary carcinoma
H&E x 400



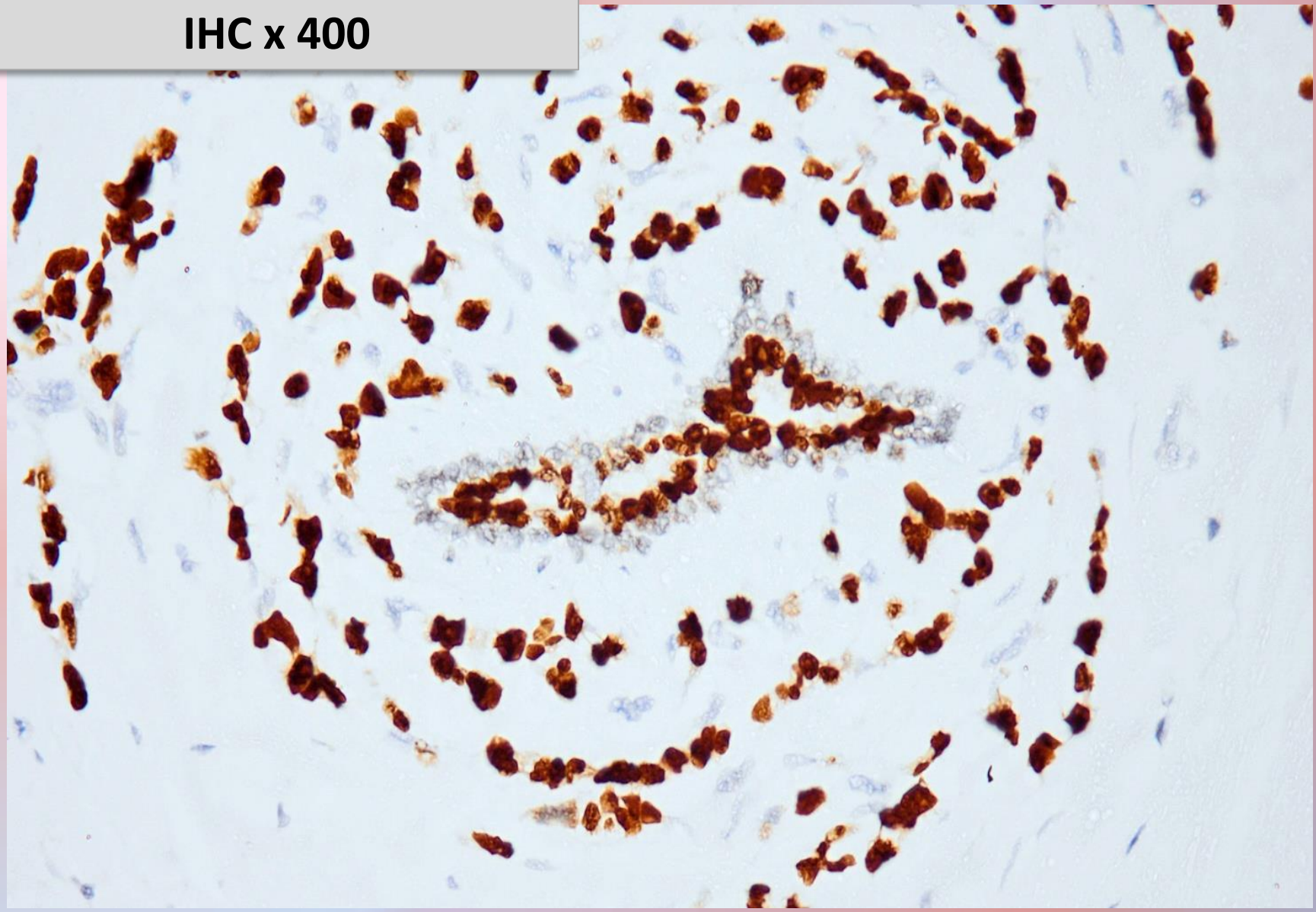
4+ GATA-3 in medullary carcinoma (Triple –ve) IHC x 400



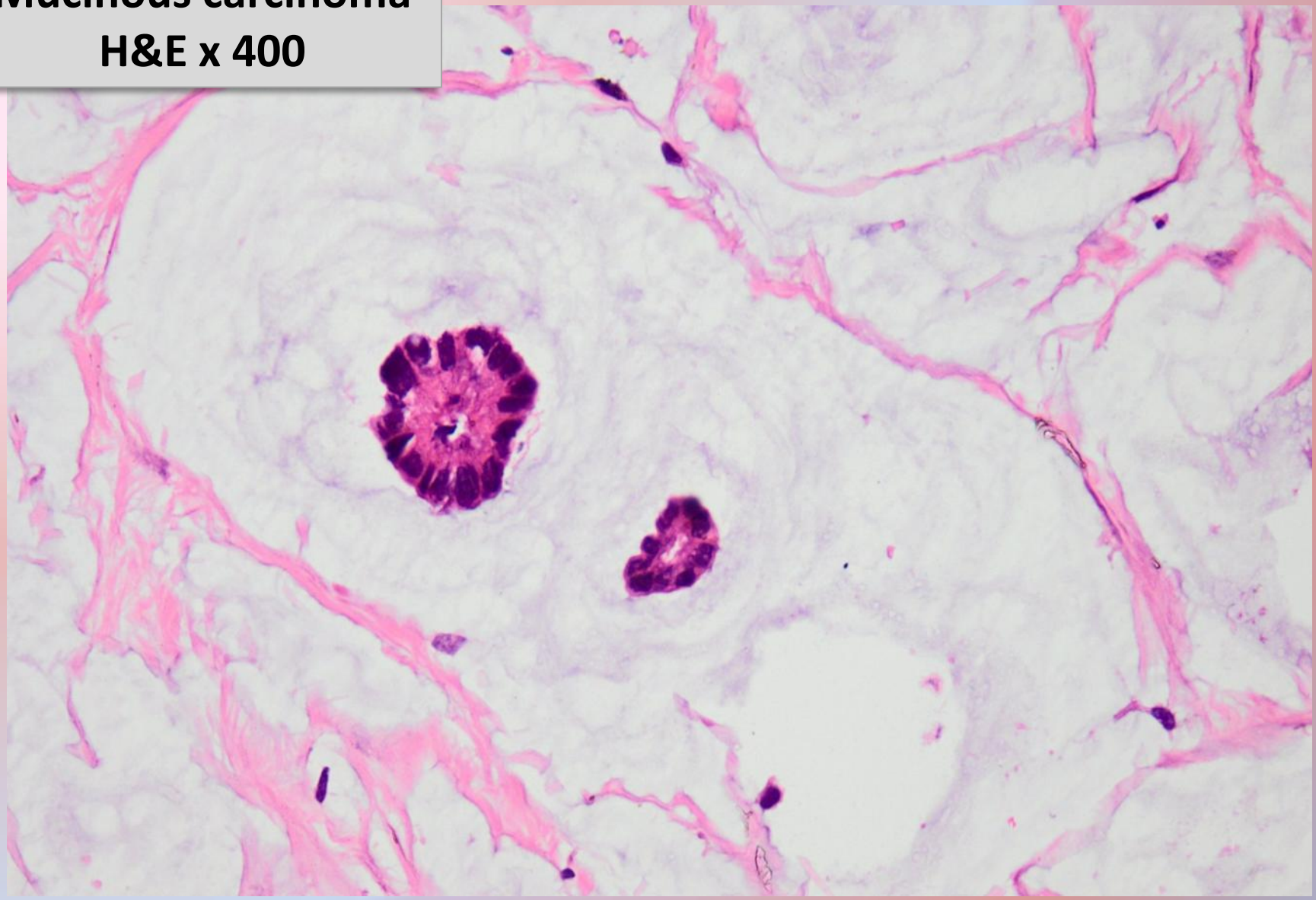
ILC H&E x 400



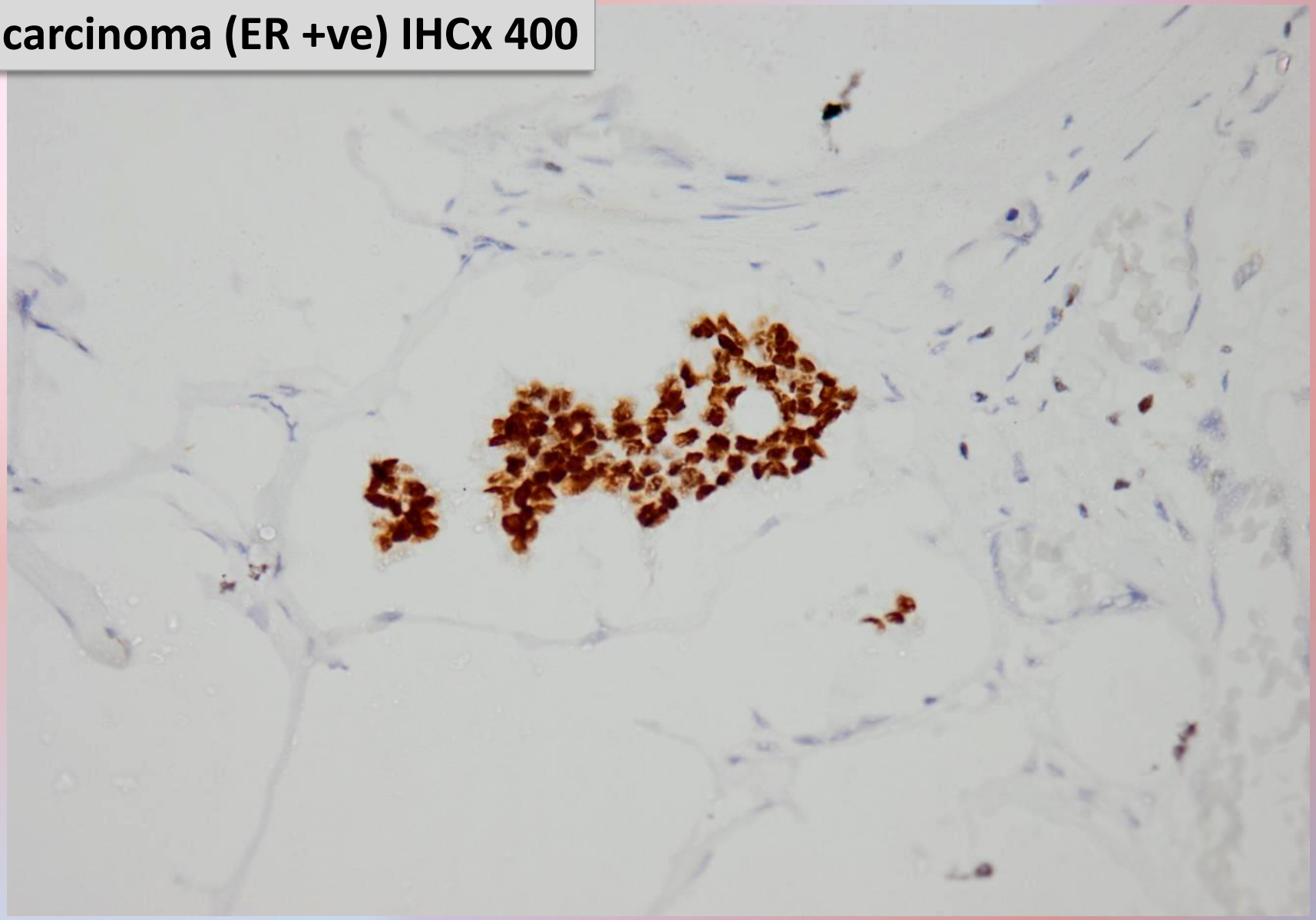
4+ GATA-3 in ILC (ER +ve)
IHC x 400



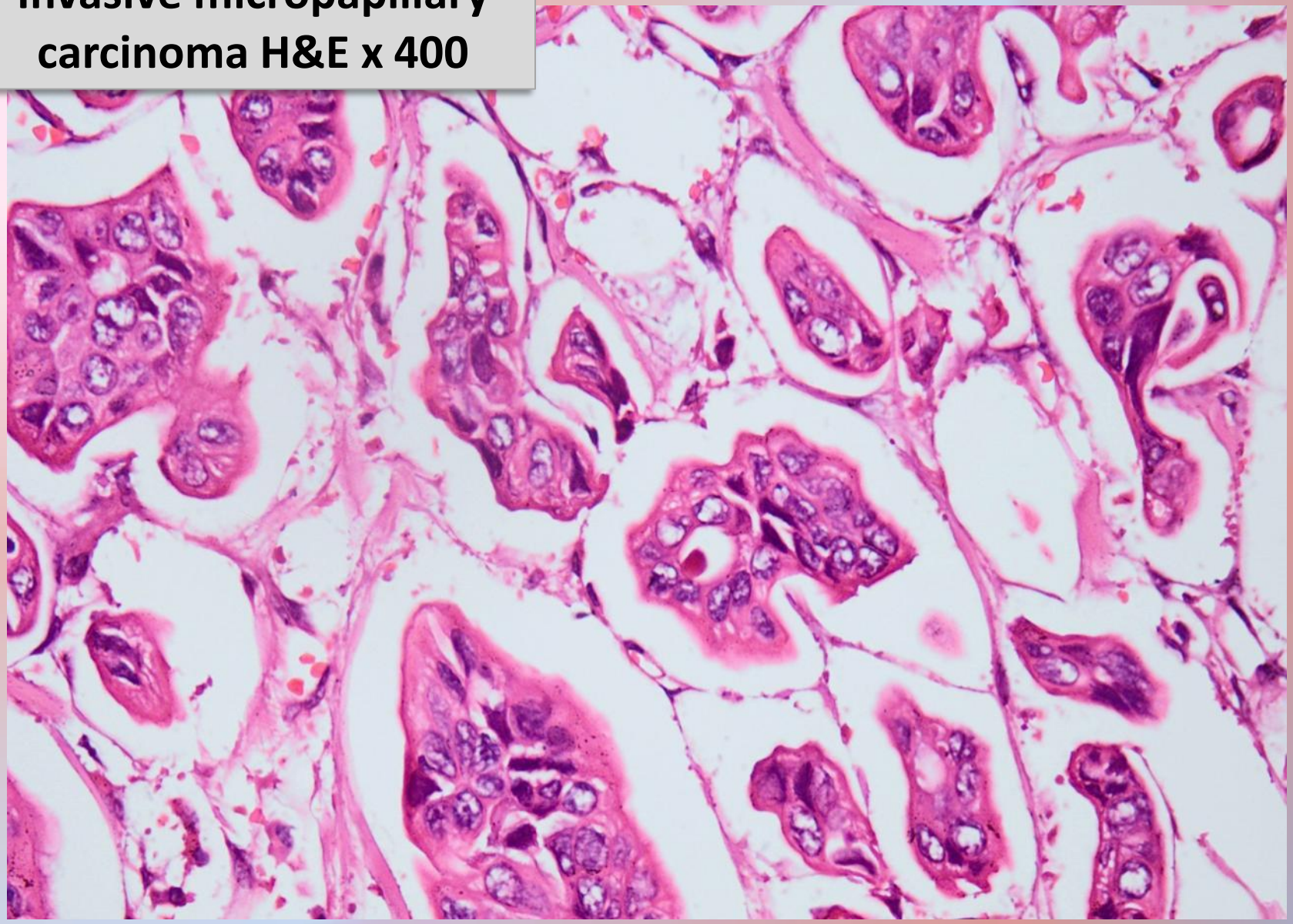
Mucinous carcinoma
H&E x 400



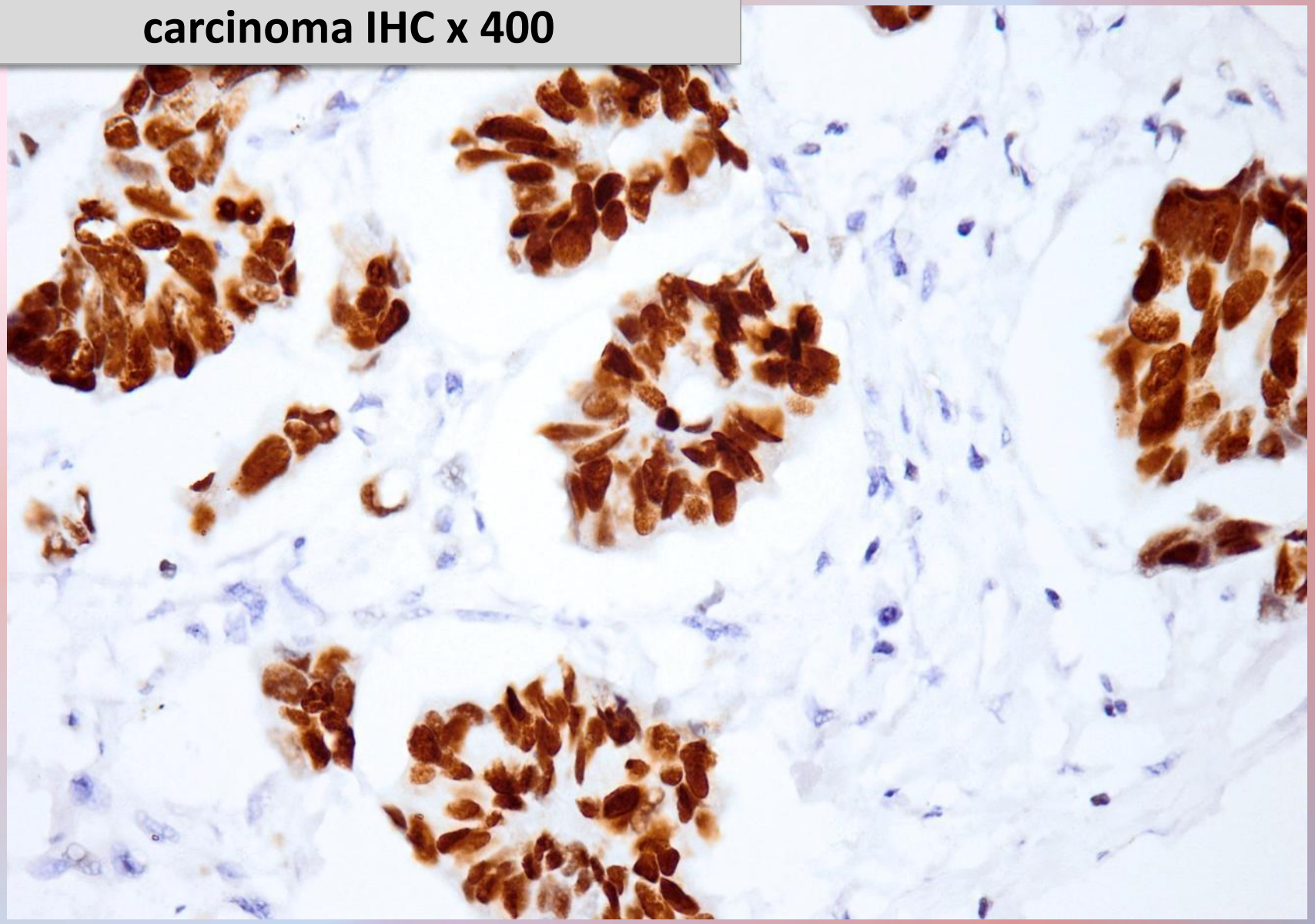
4+ GATA-3 in mucinous carcinoma (ER +ve) IHCx 400



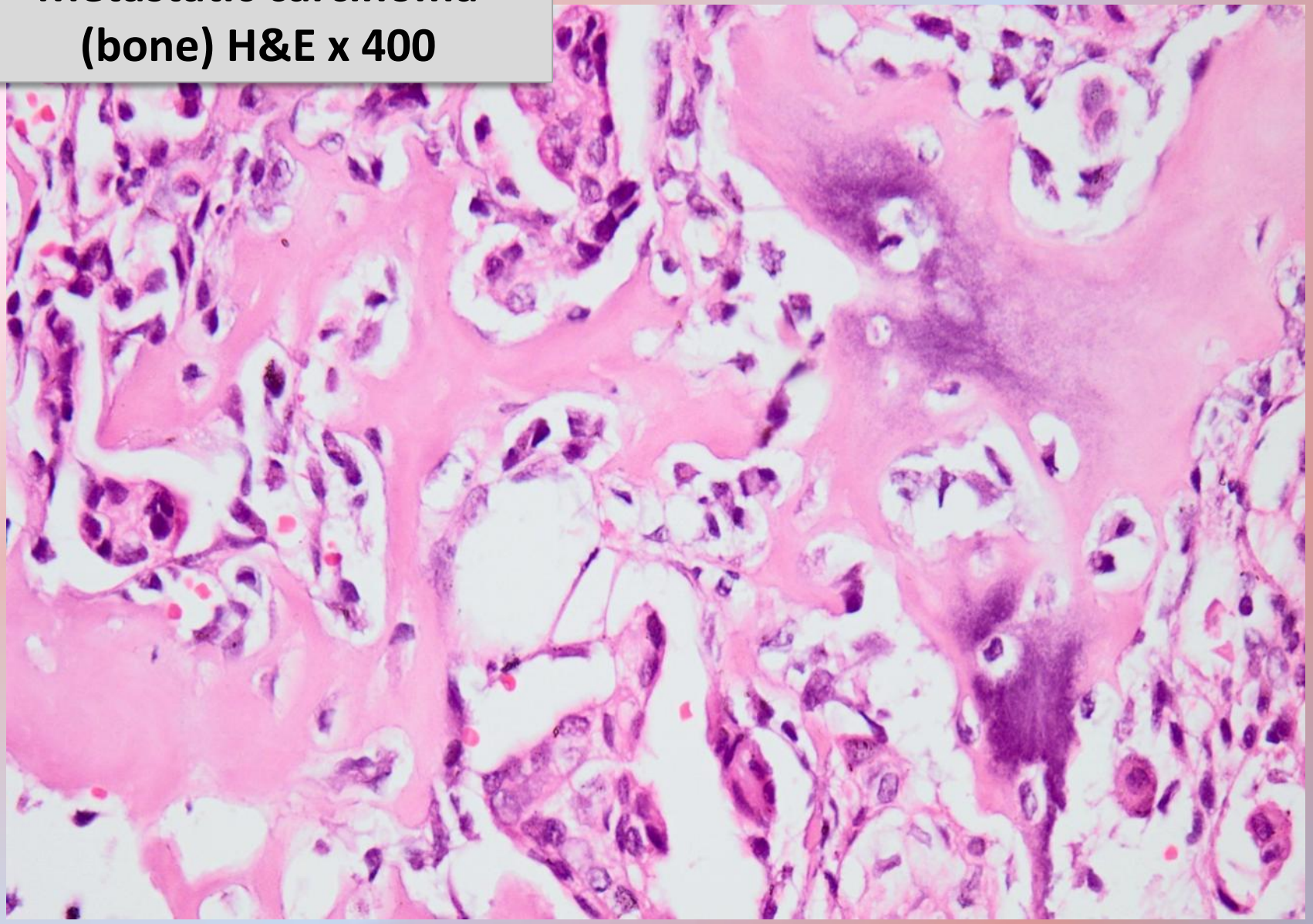
Invasive micropapillary carcinoma H&E x 400



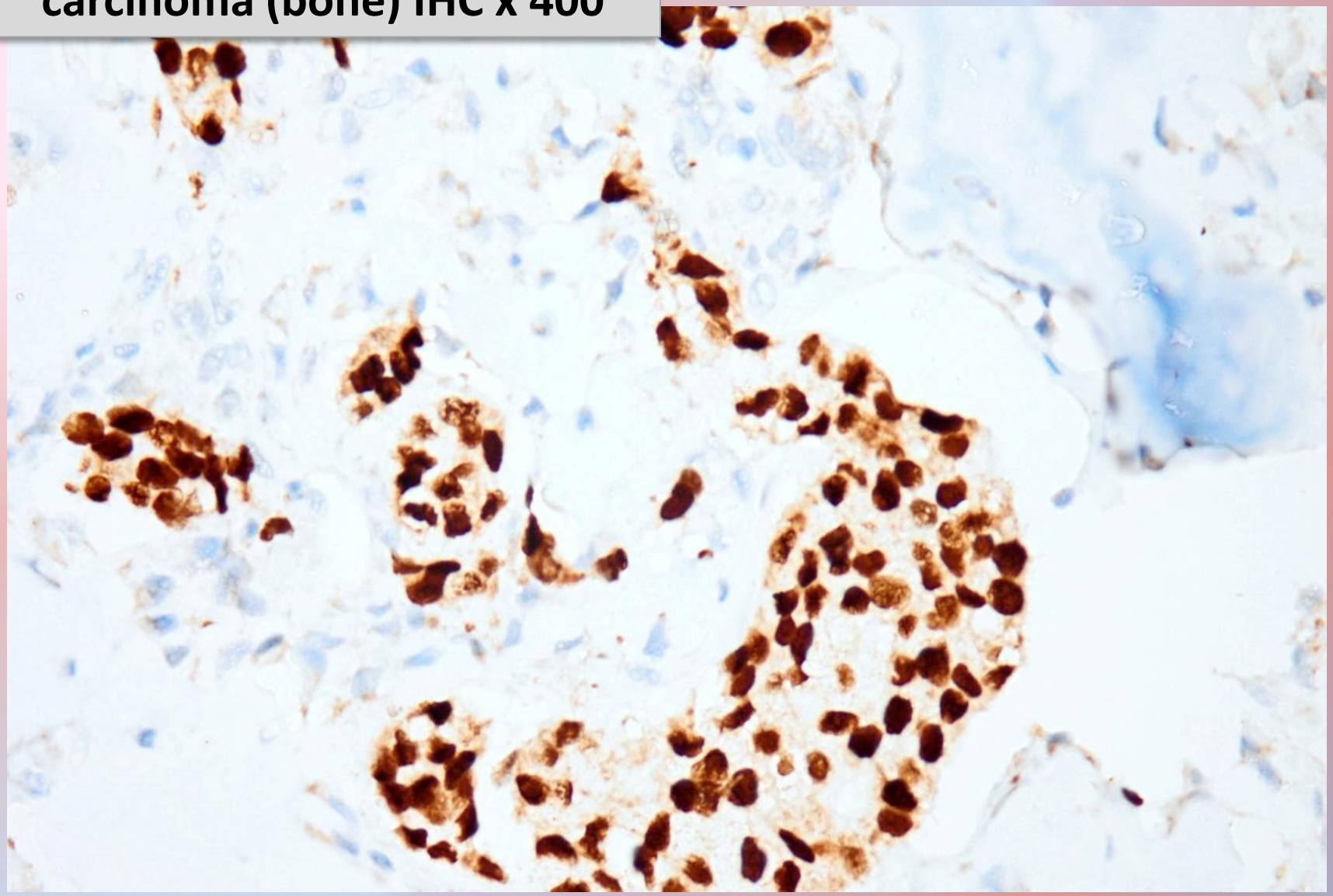
4+ GATA-3 in invasive micropapillary carcinoma IHC x 400



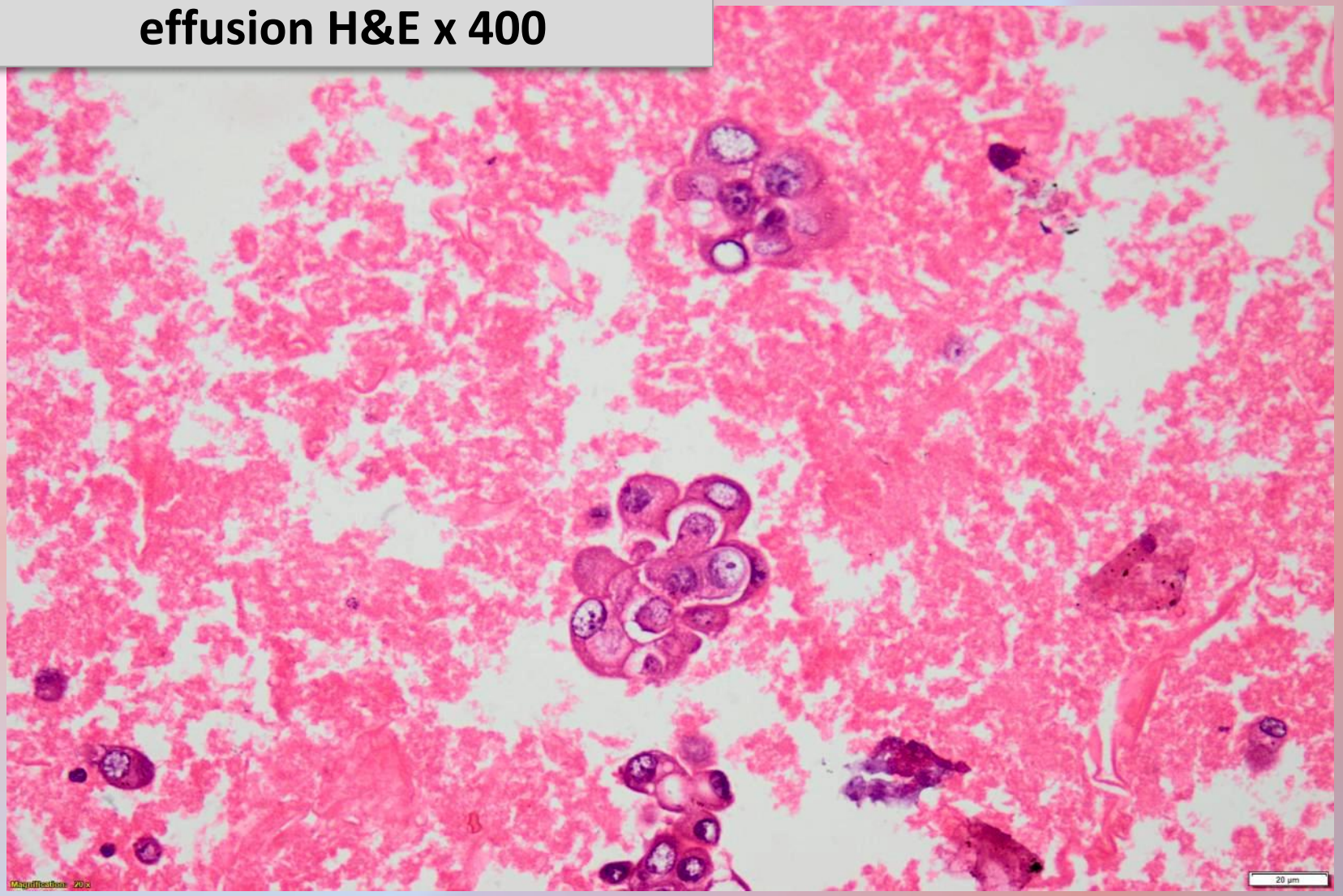
Metastatic carcinoma (bone) H&E x 400



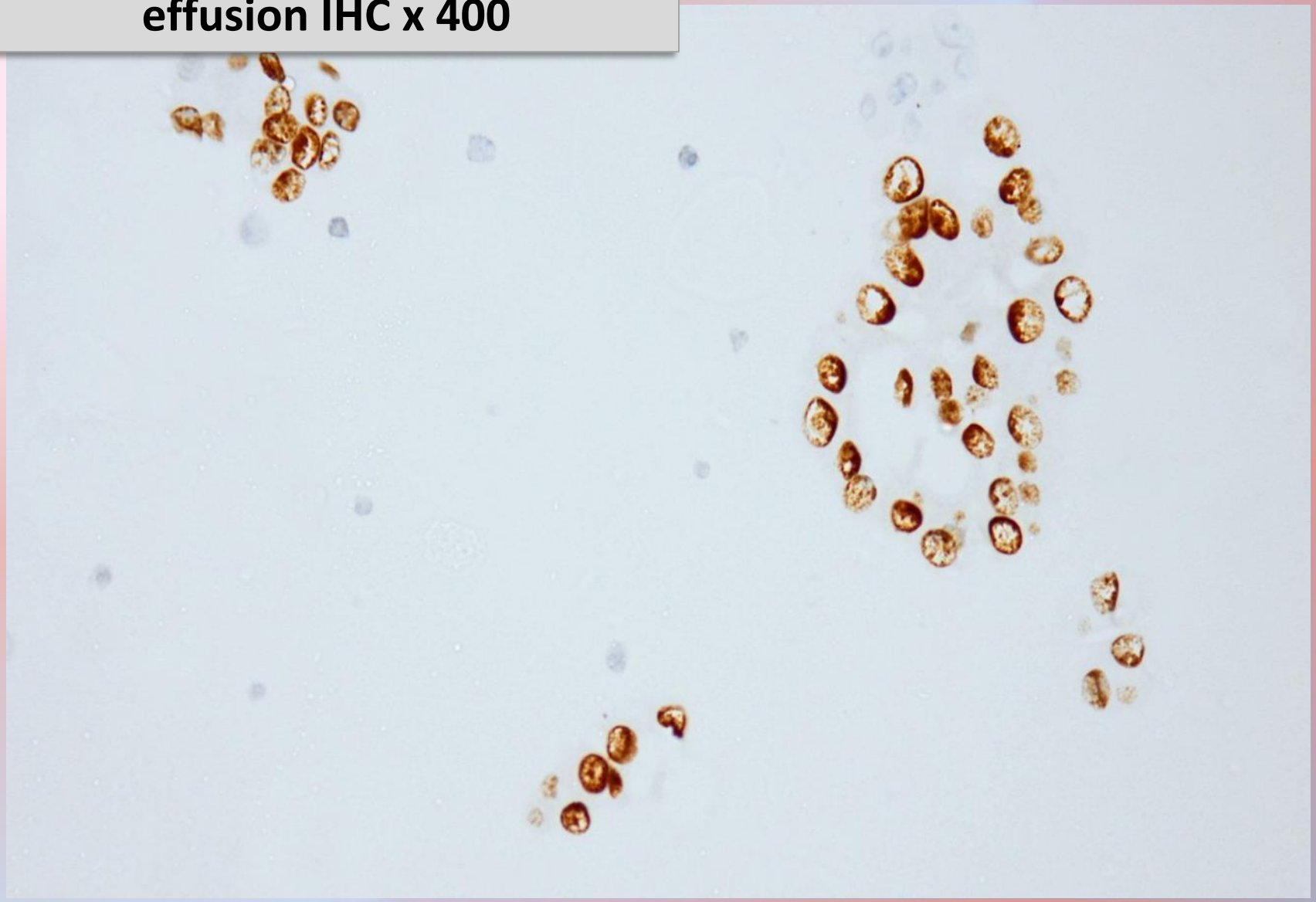
4+ GATA-3 in metastatic carcinoma (bone) IHC x 400



Cell block of malignant pleural effusion H&E x 400

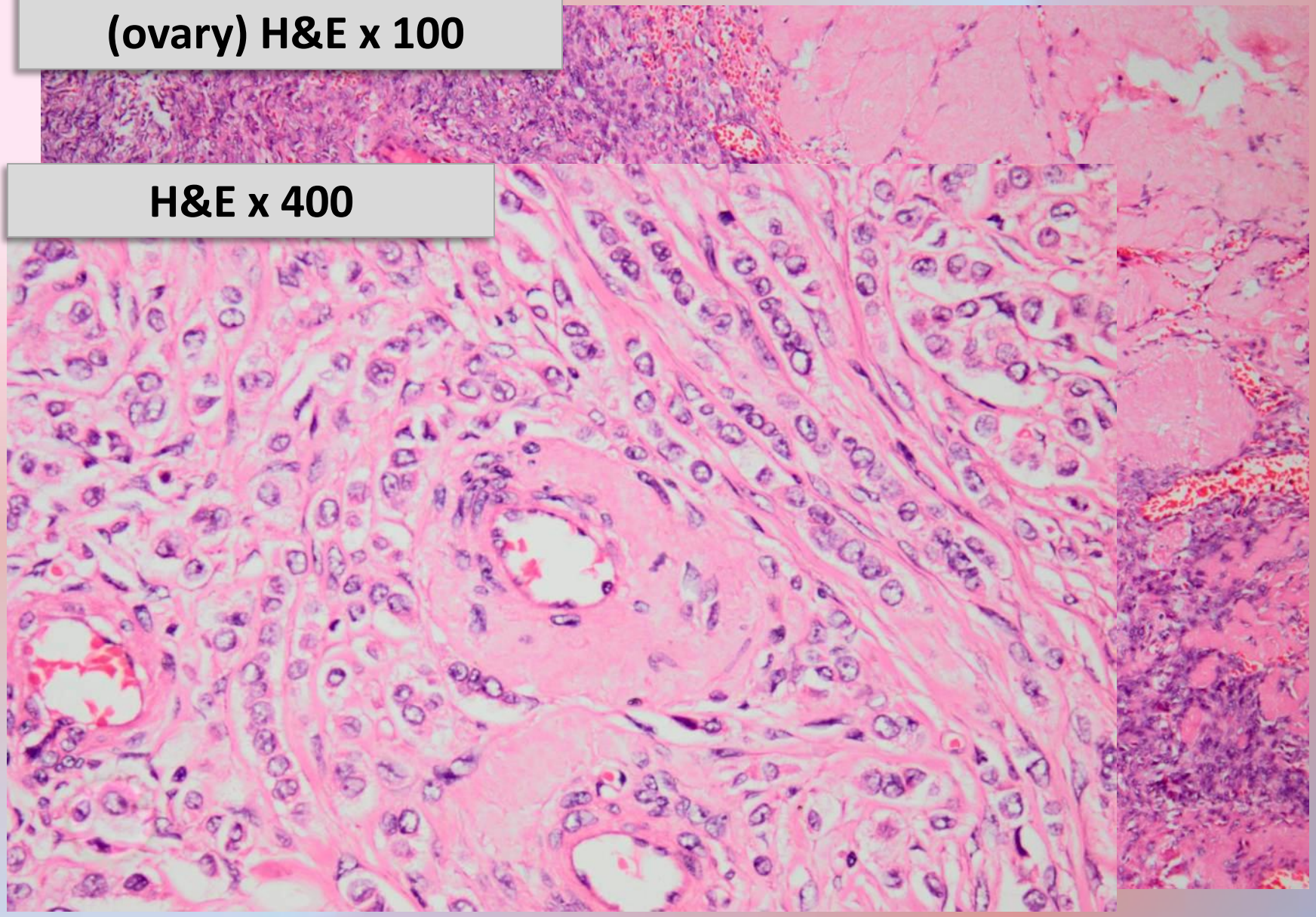


4+ GATA-3 in malignant pleural effusion IHC x 400

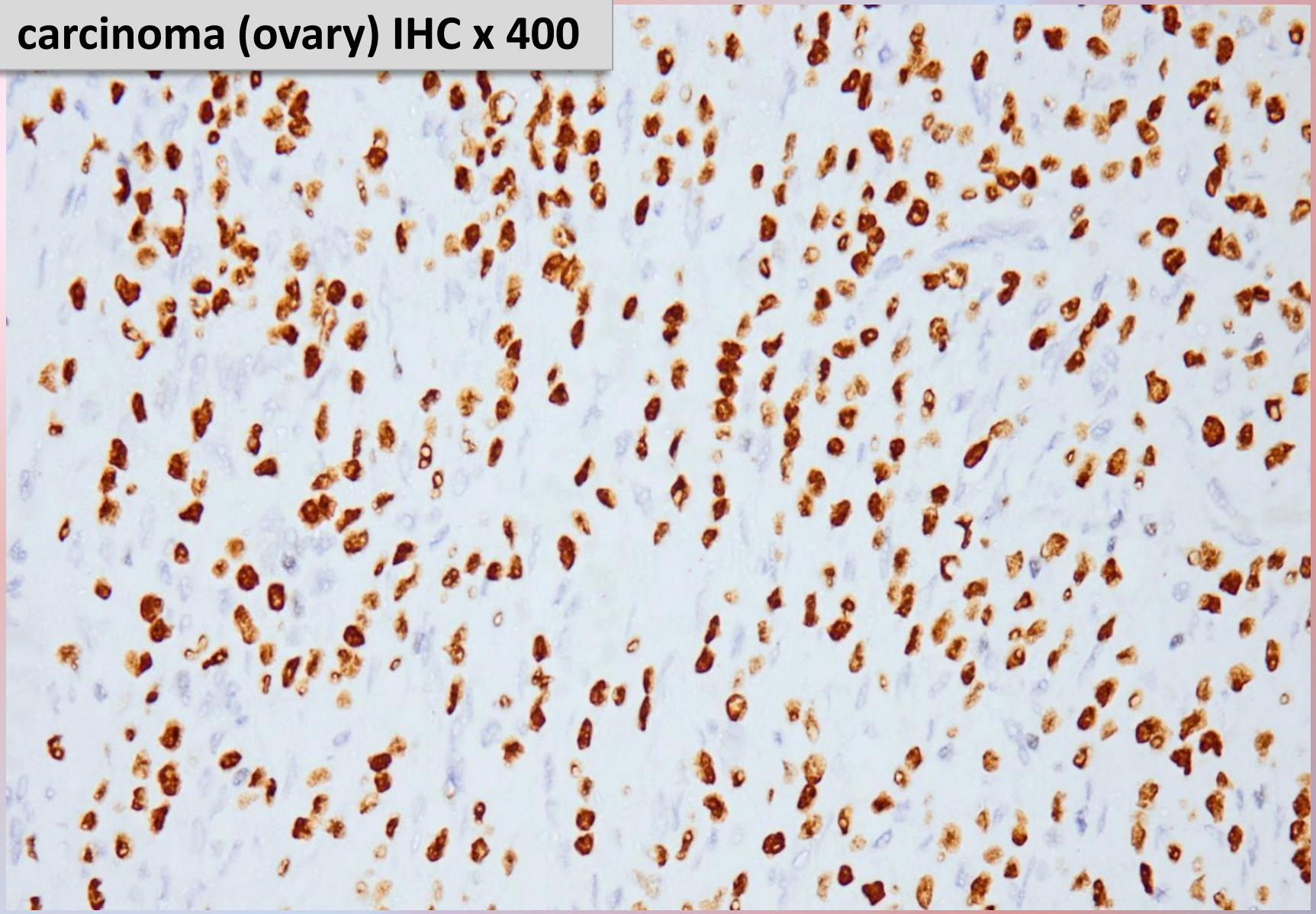


Metastatic carcinoma (ovary) H&E x 100

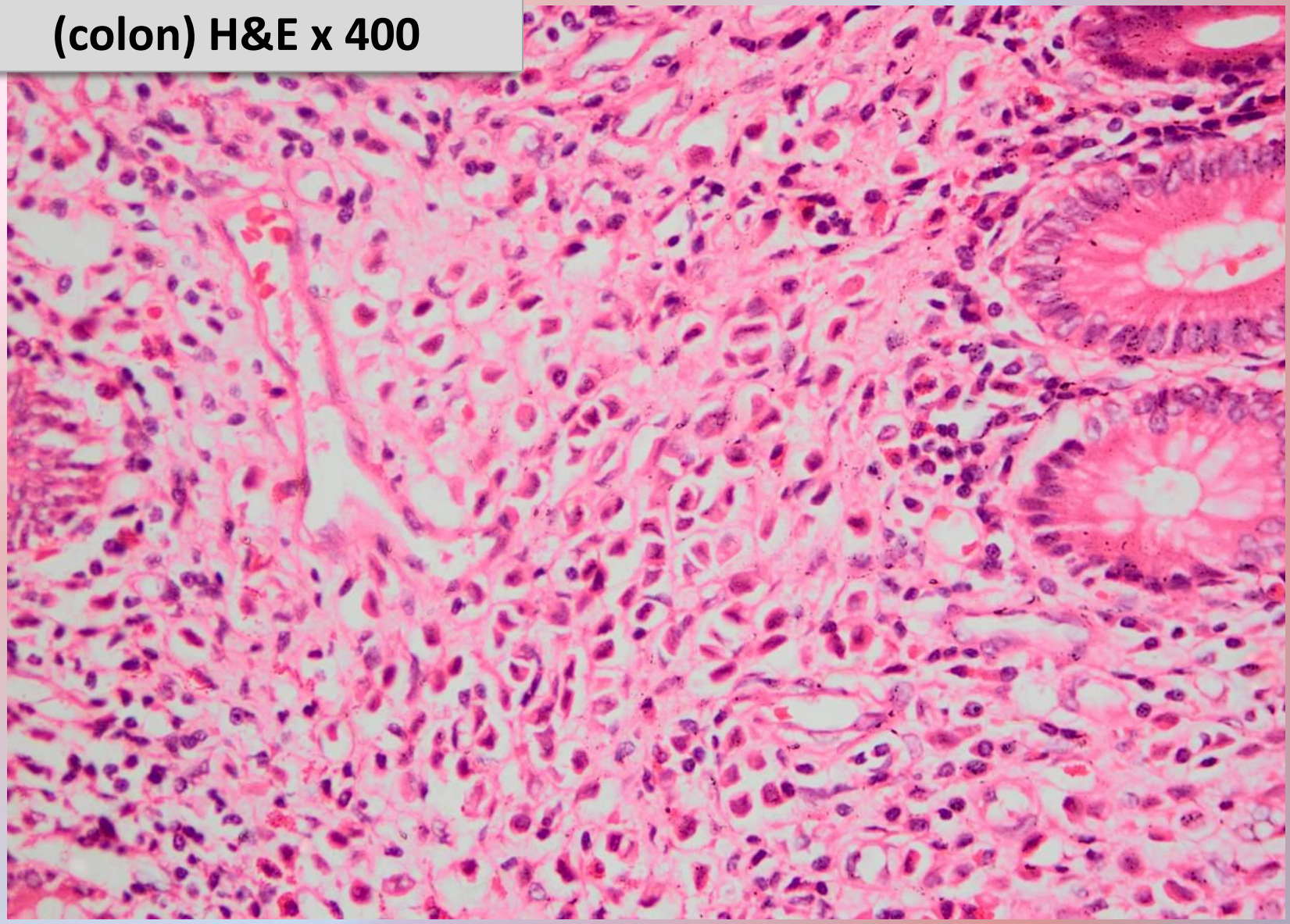
H&E x 400



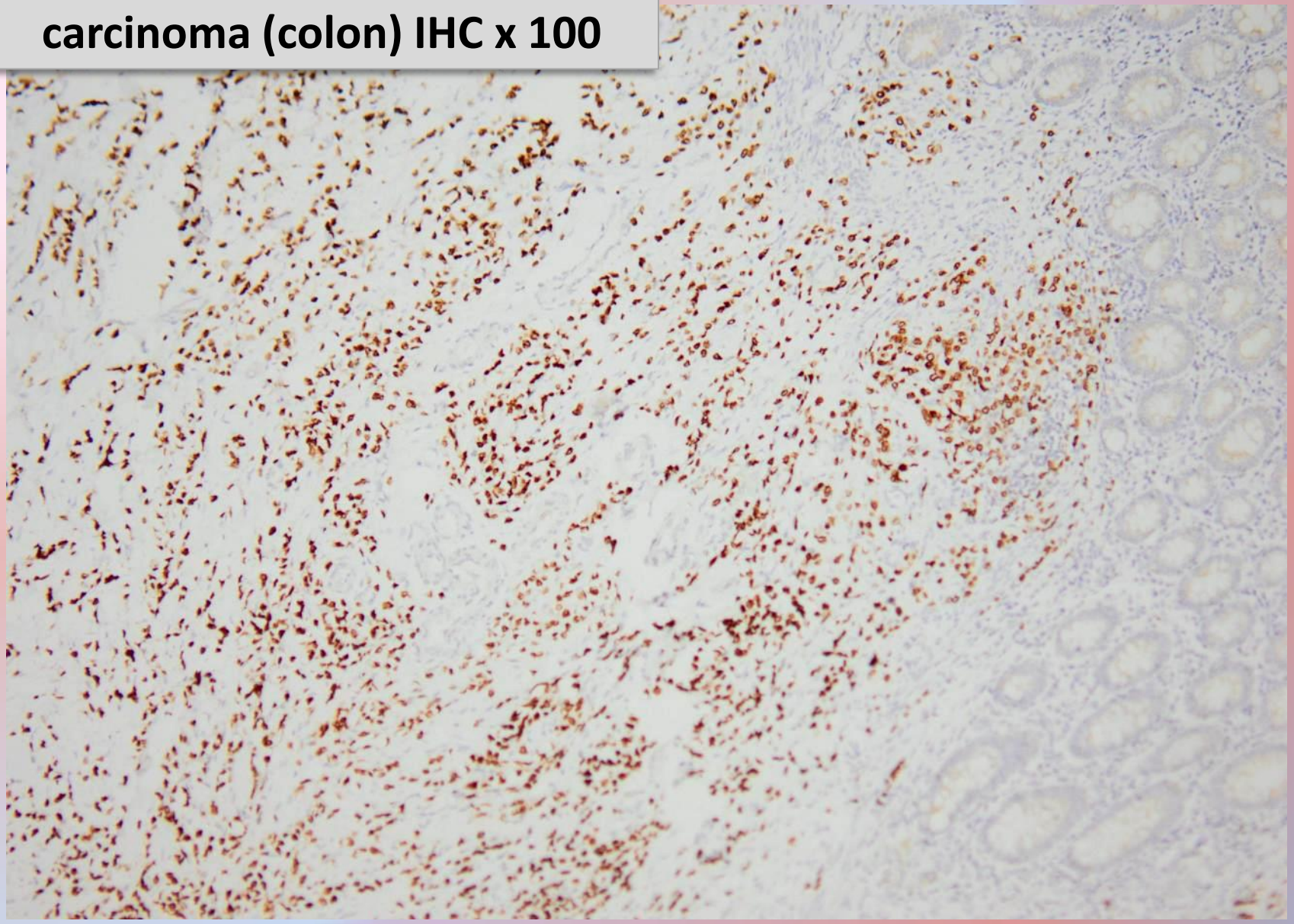
4+ GATA-3 in metastatic carcinoma (ovary) IHC x 400



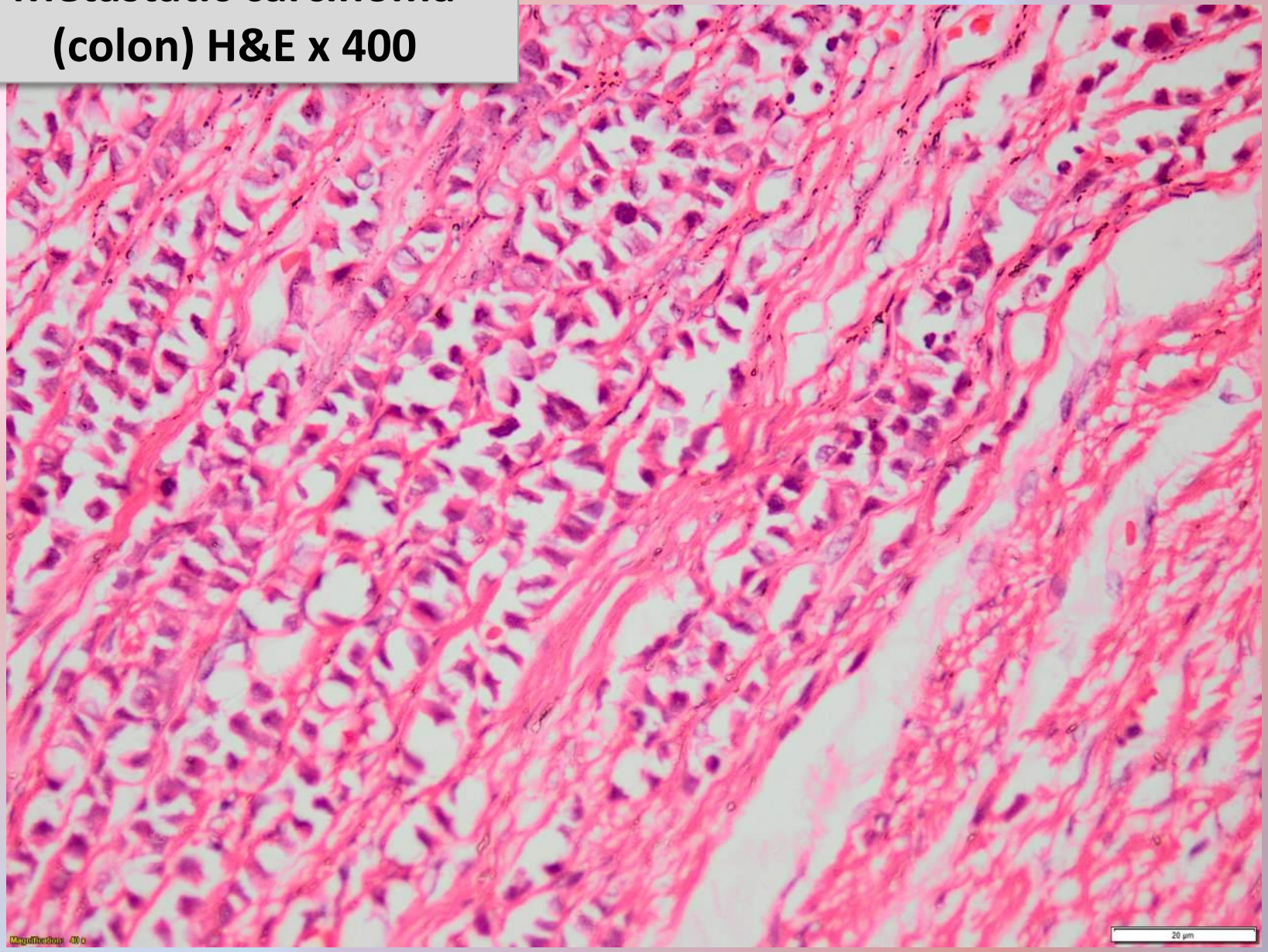
Metastatic carcinoma (colon) H&E x 400



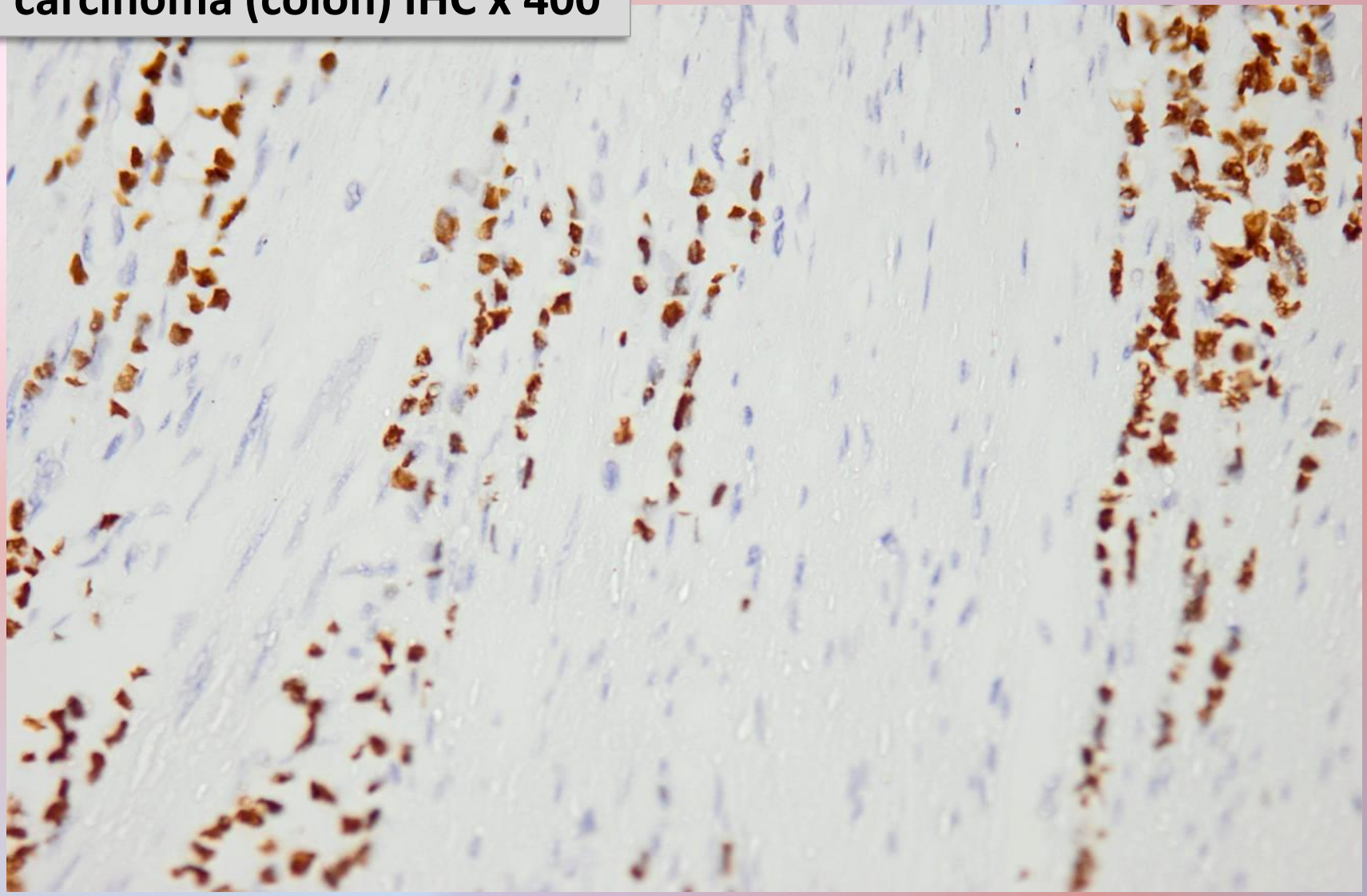
4+ GATA-3 in metastatic carcinoma (colon) IHC x 100



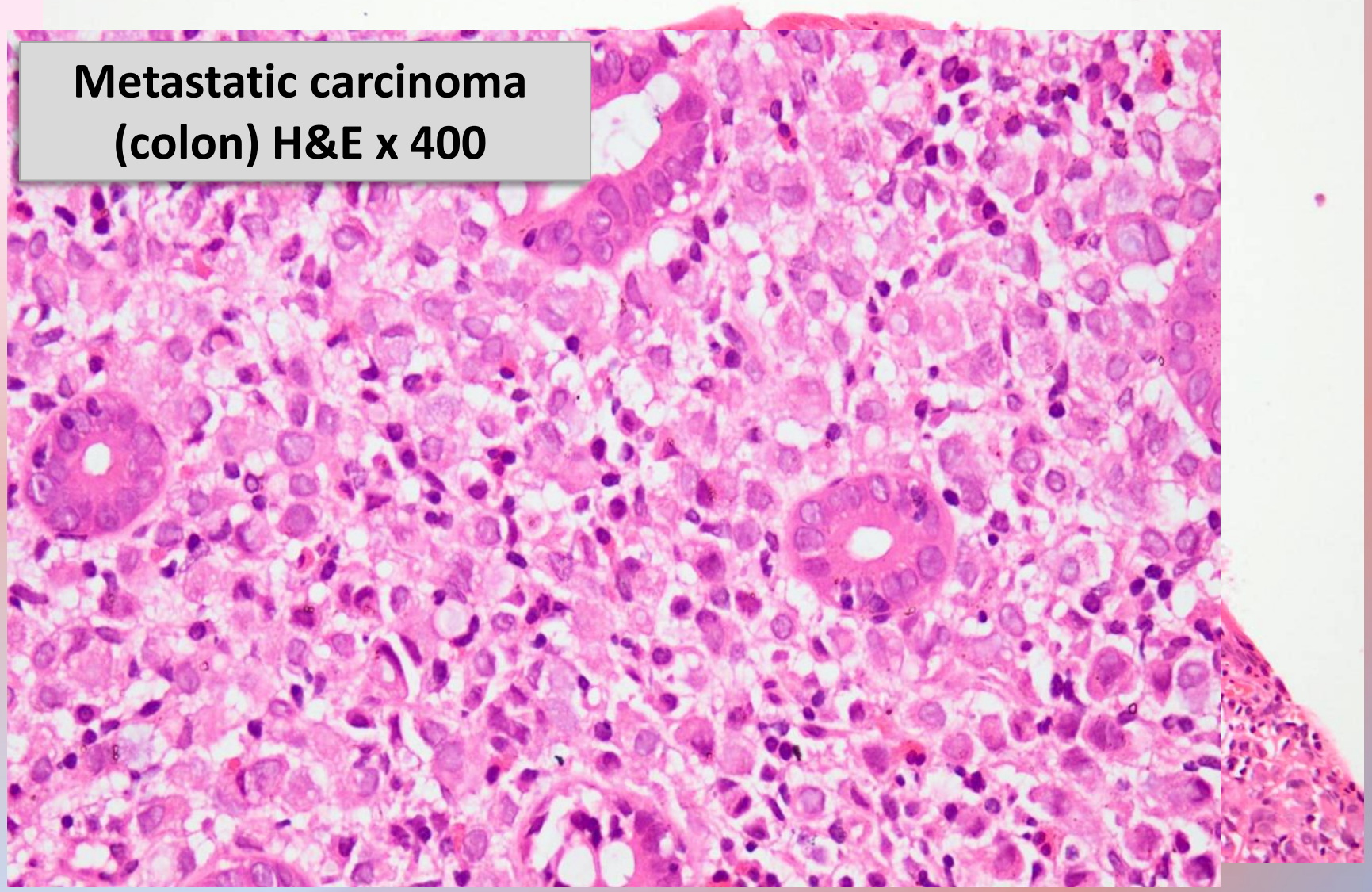
Metastatic carcinoma (colon) H&E x 400



3+ GATA-3 in metastatic carcinoma (colon) IHC x 400

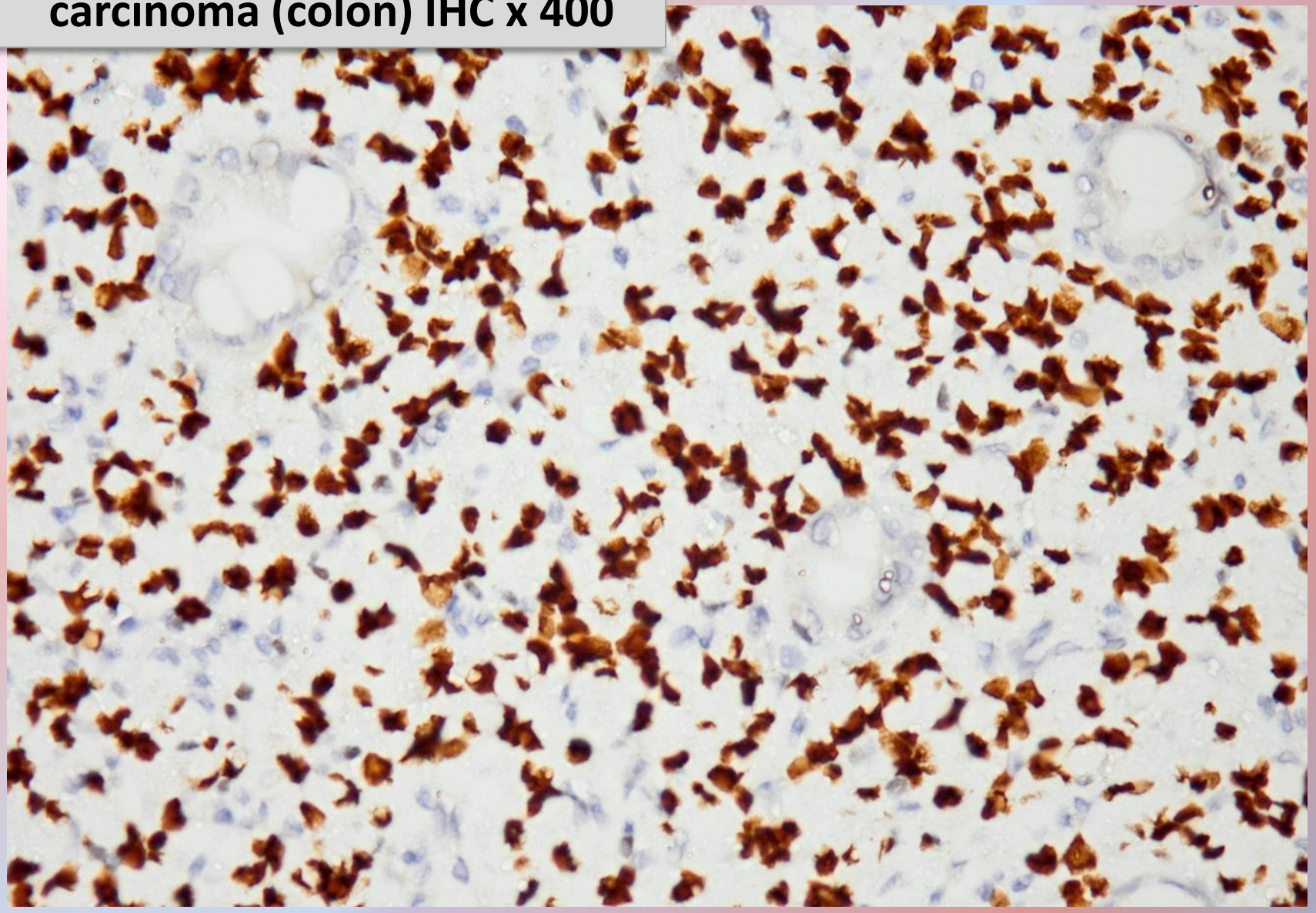


Another case of metastatic carcinoma (colon) H&E x 200

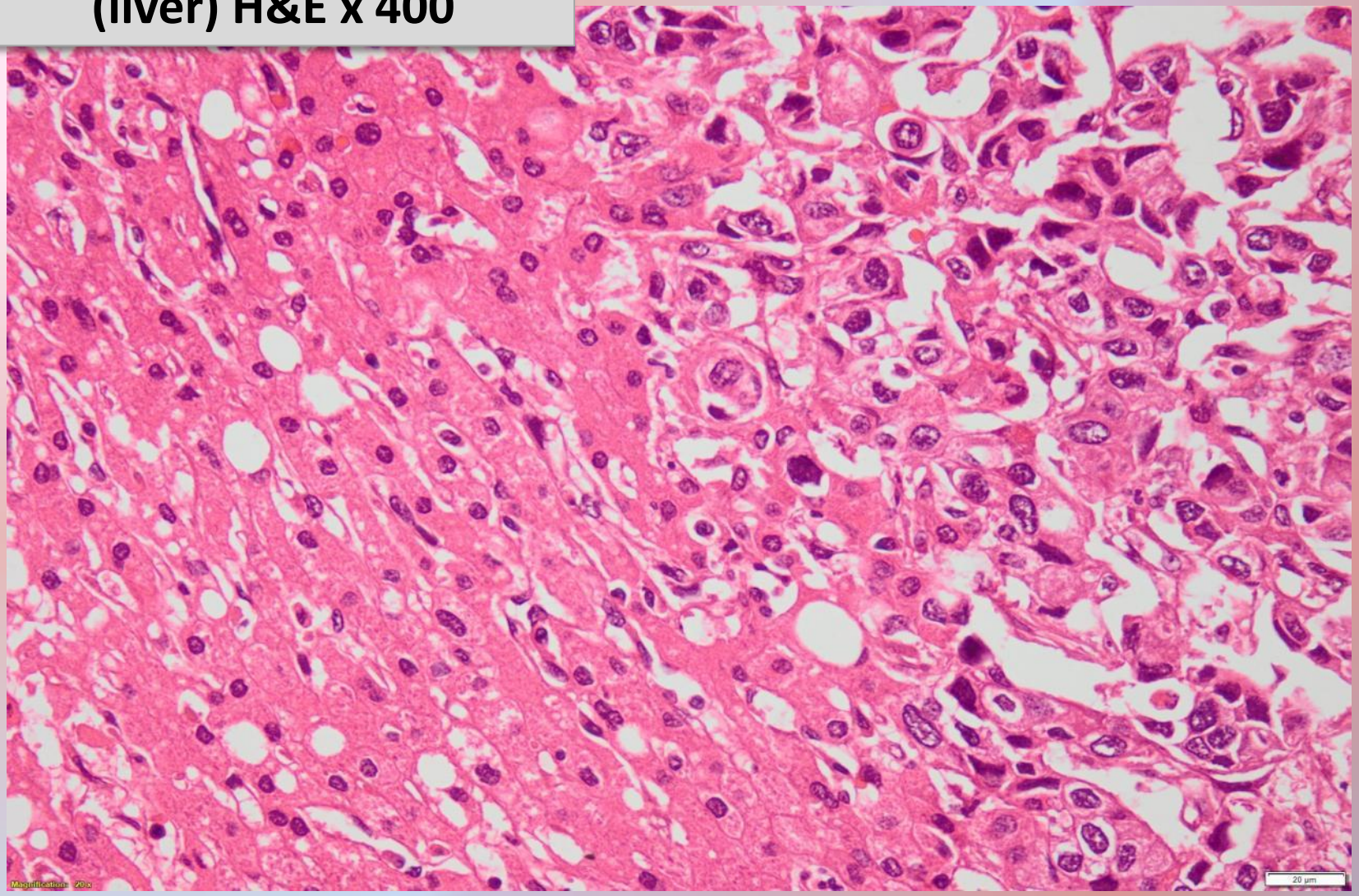


Metastatic carcinoma (colon) H&E x 400

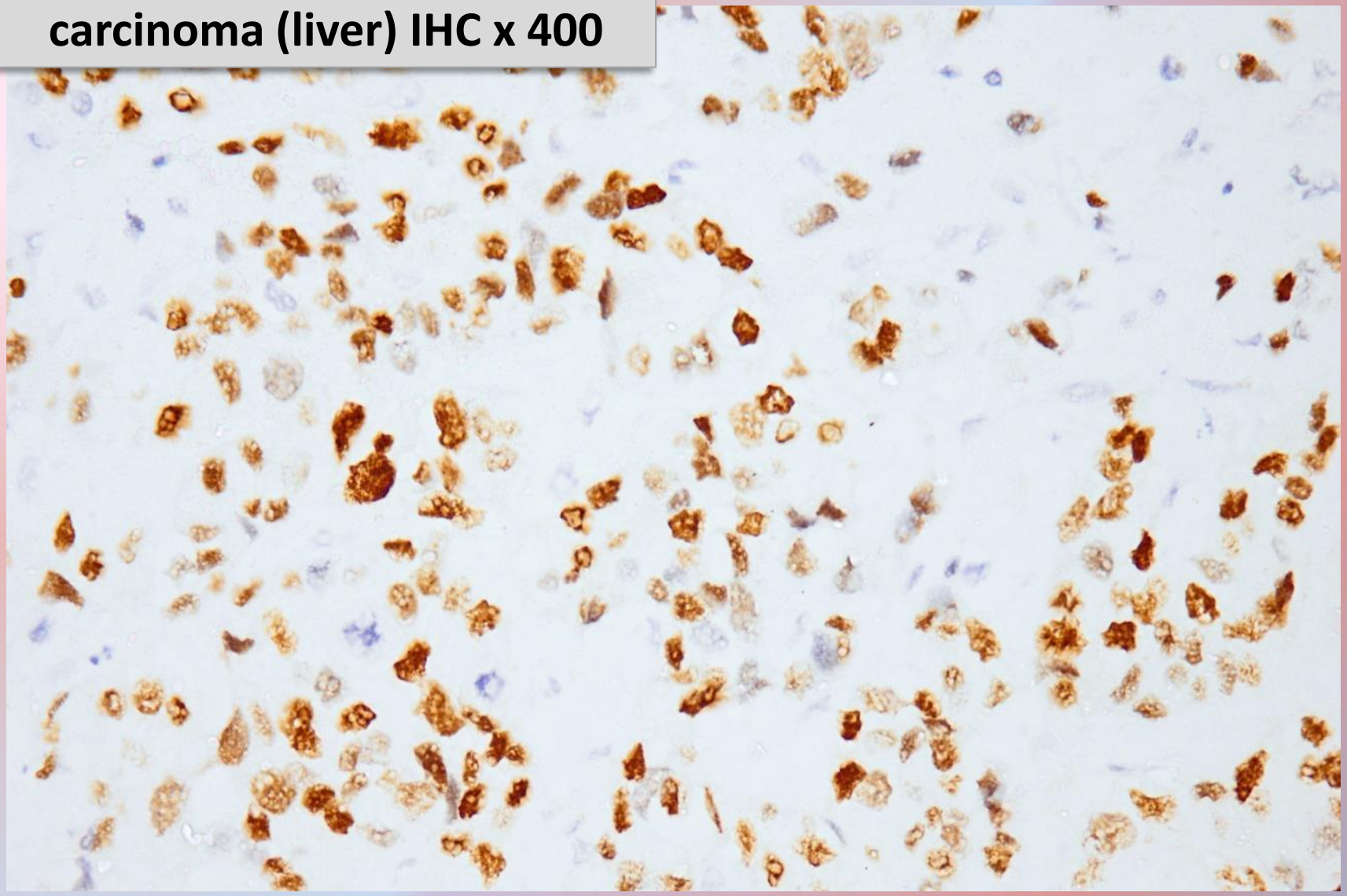
4+ GATA-3 in metastatic carcinoma (colon) IHC x 400



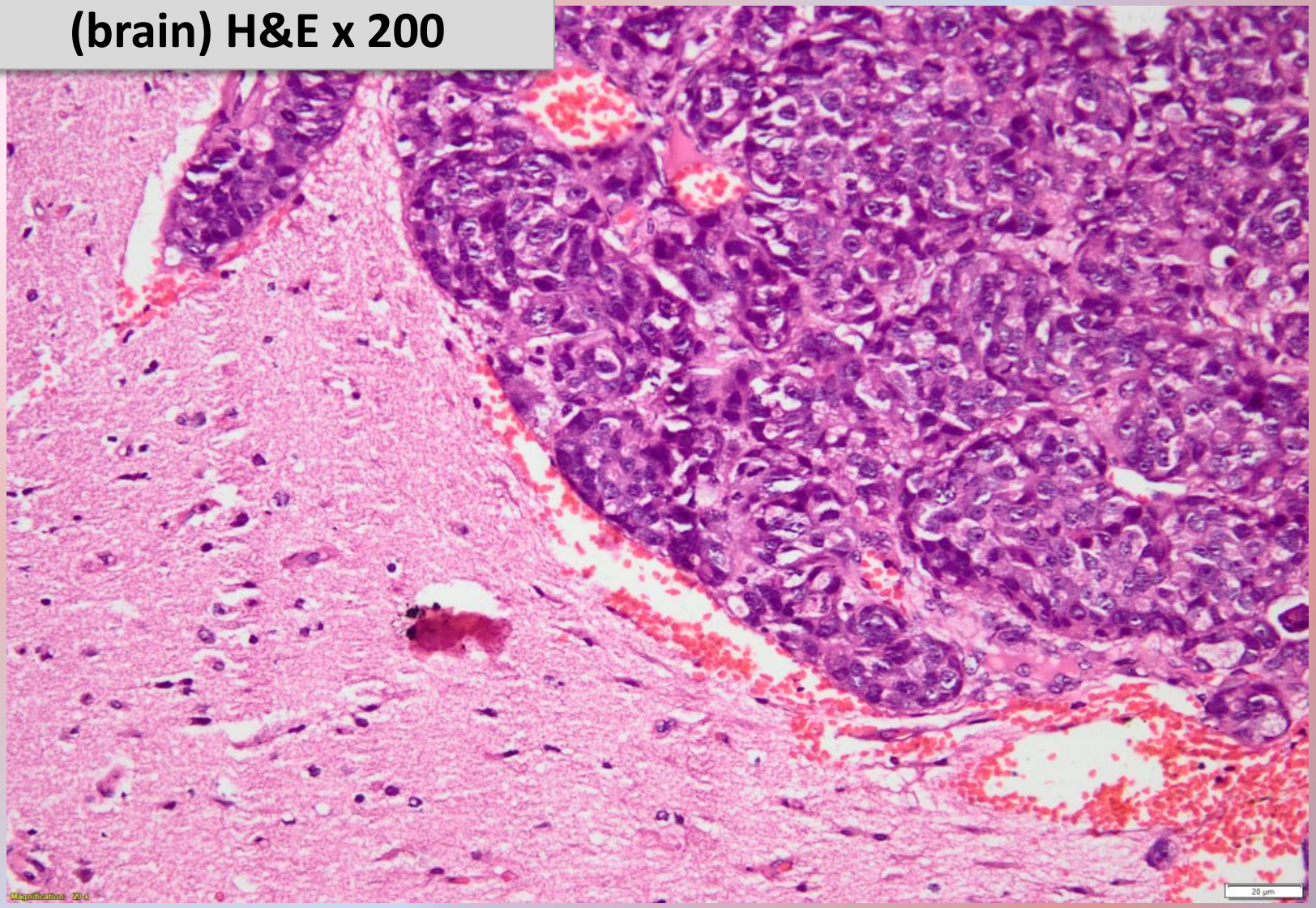
Metastatic carcinoma (liver) H&E x 400



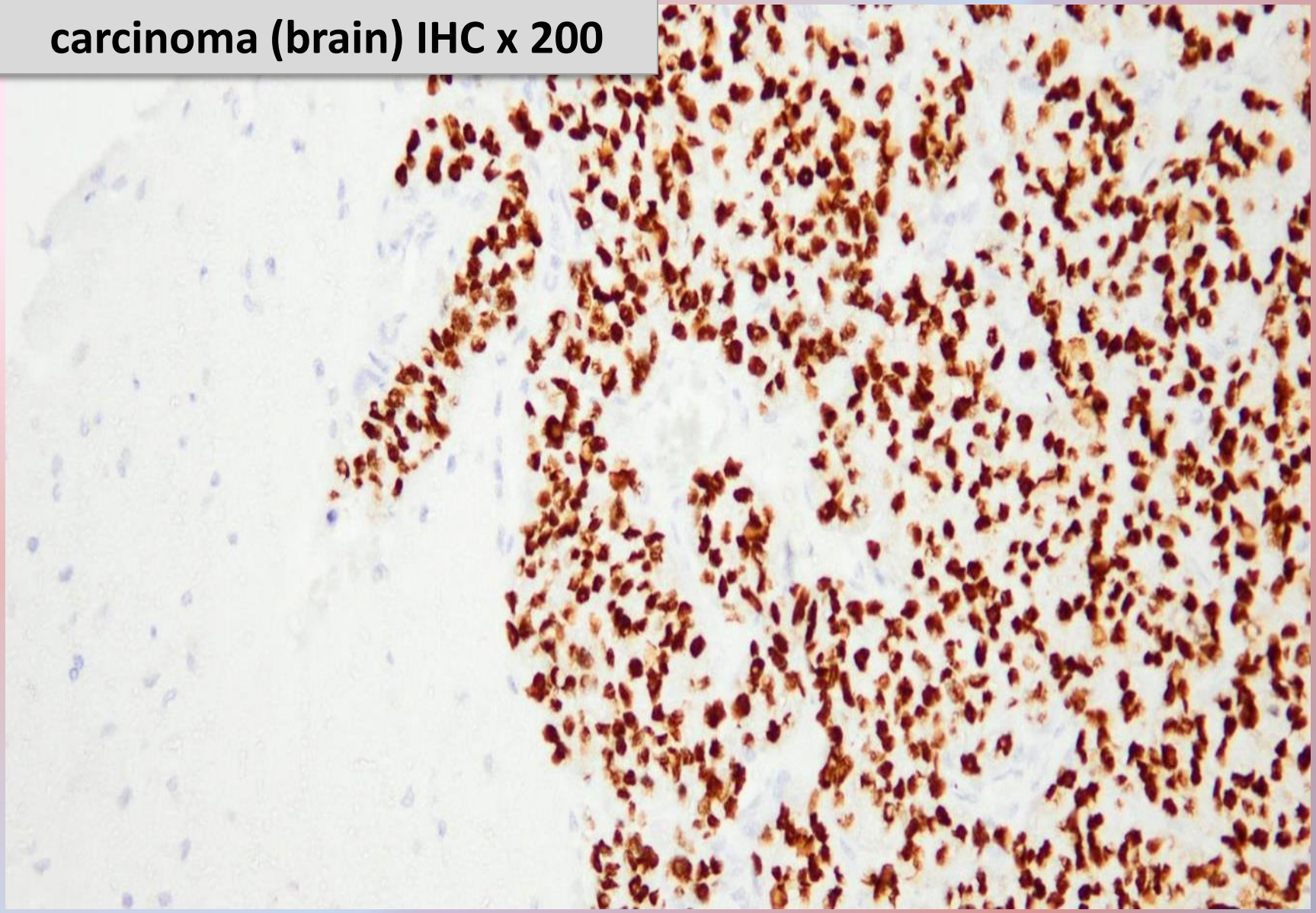
3+ GATA-3 in metastatic carcinoma (liver) IHC x 400



Metastatic carcinoma (brain) H&E x 200

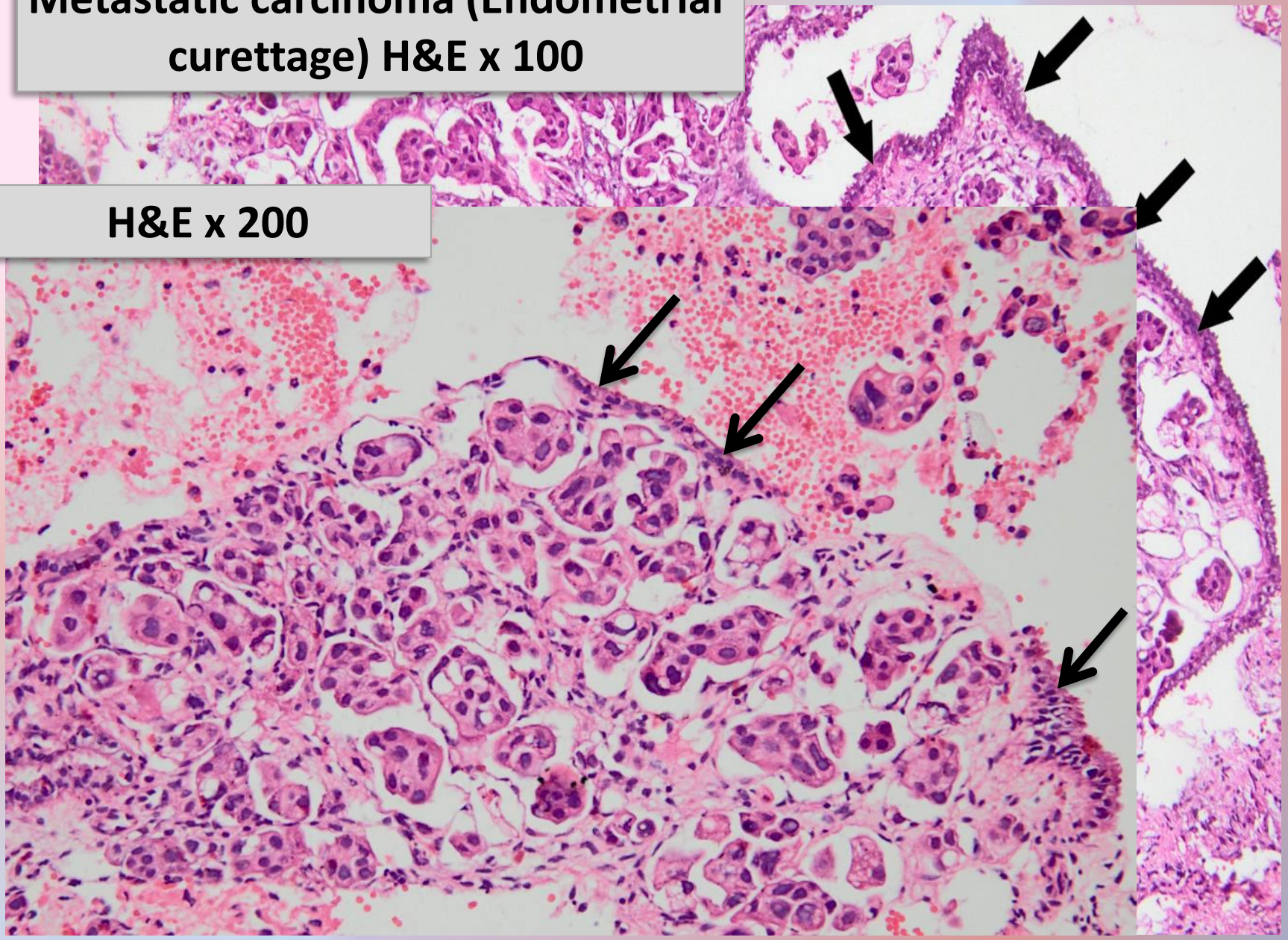


4+ GATA-3 in metastatic carcinoma (brain) IHC x 200

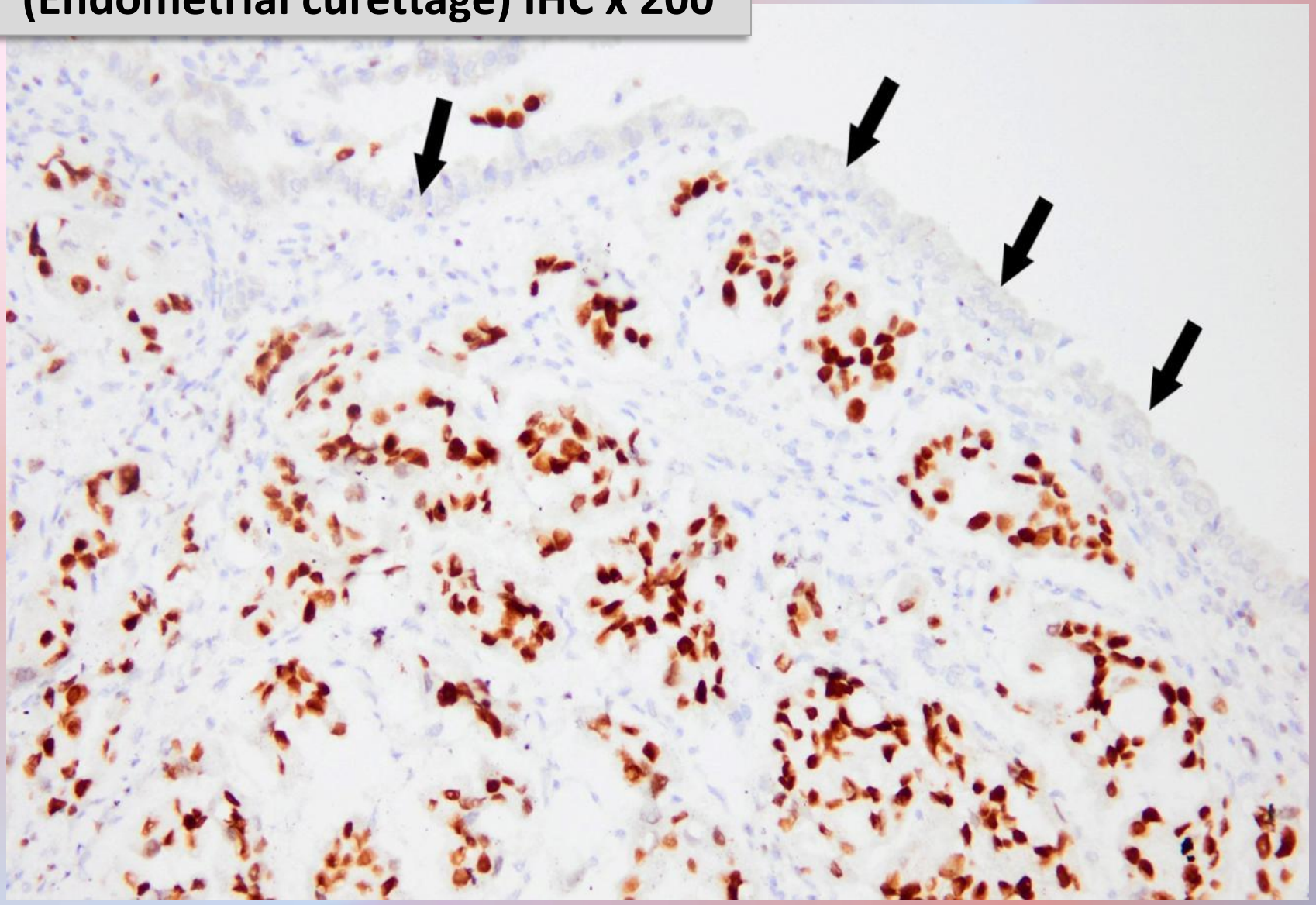


Metastatic carcinoma (Endometrial curettage) H&E x 100

H&E x 200

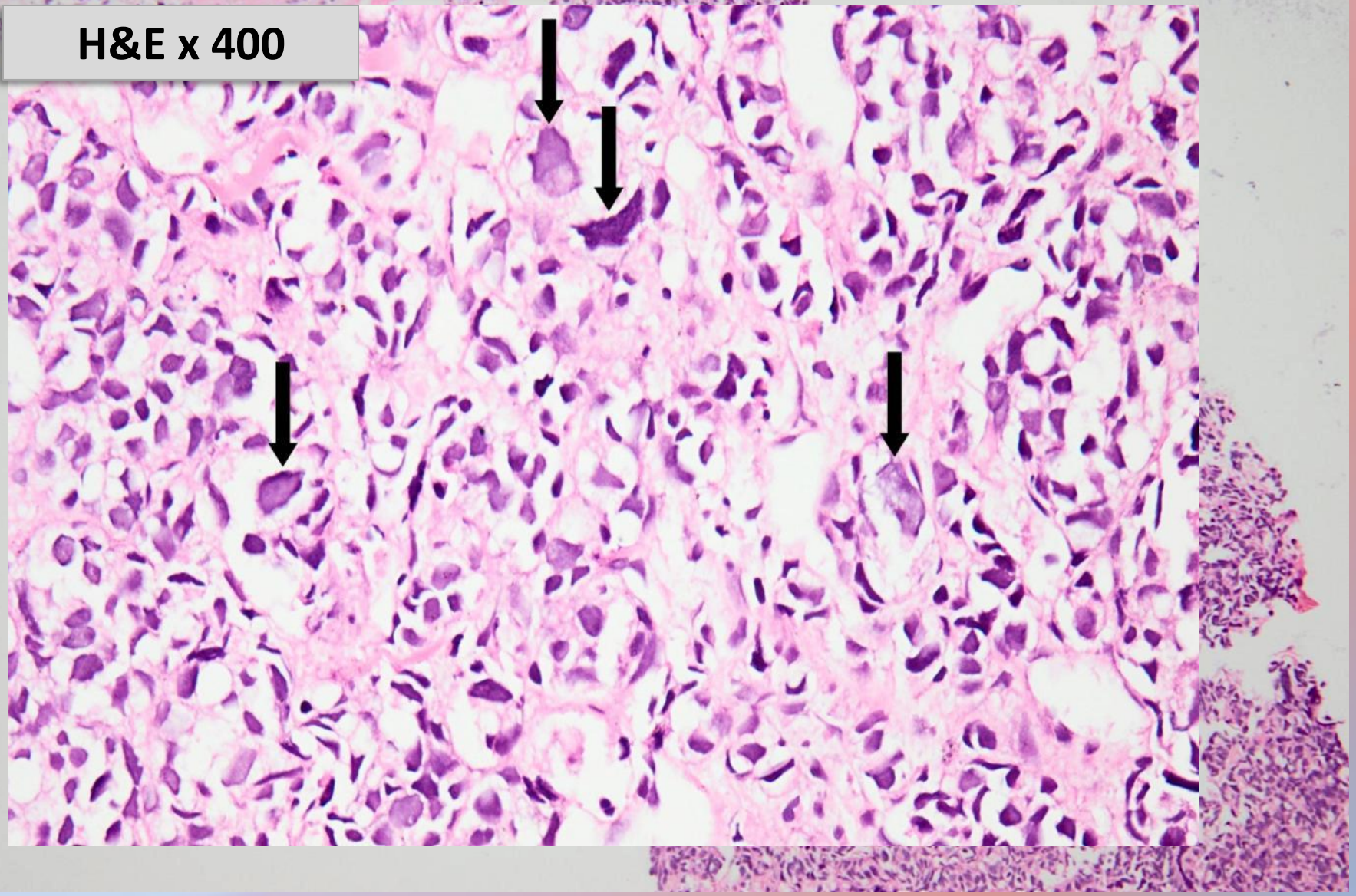


4+ GATA-3 in metastatic carcinoma (Endometrial curettage) IHC x 200

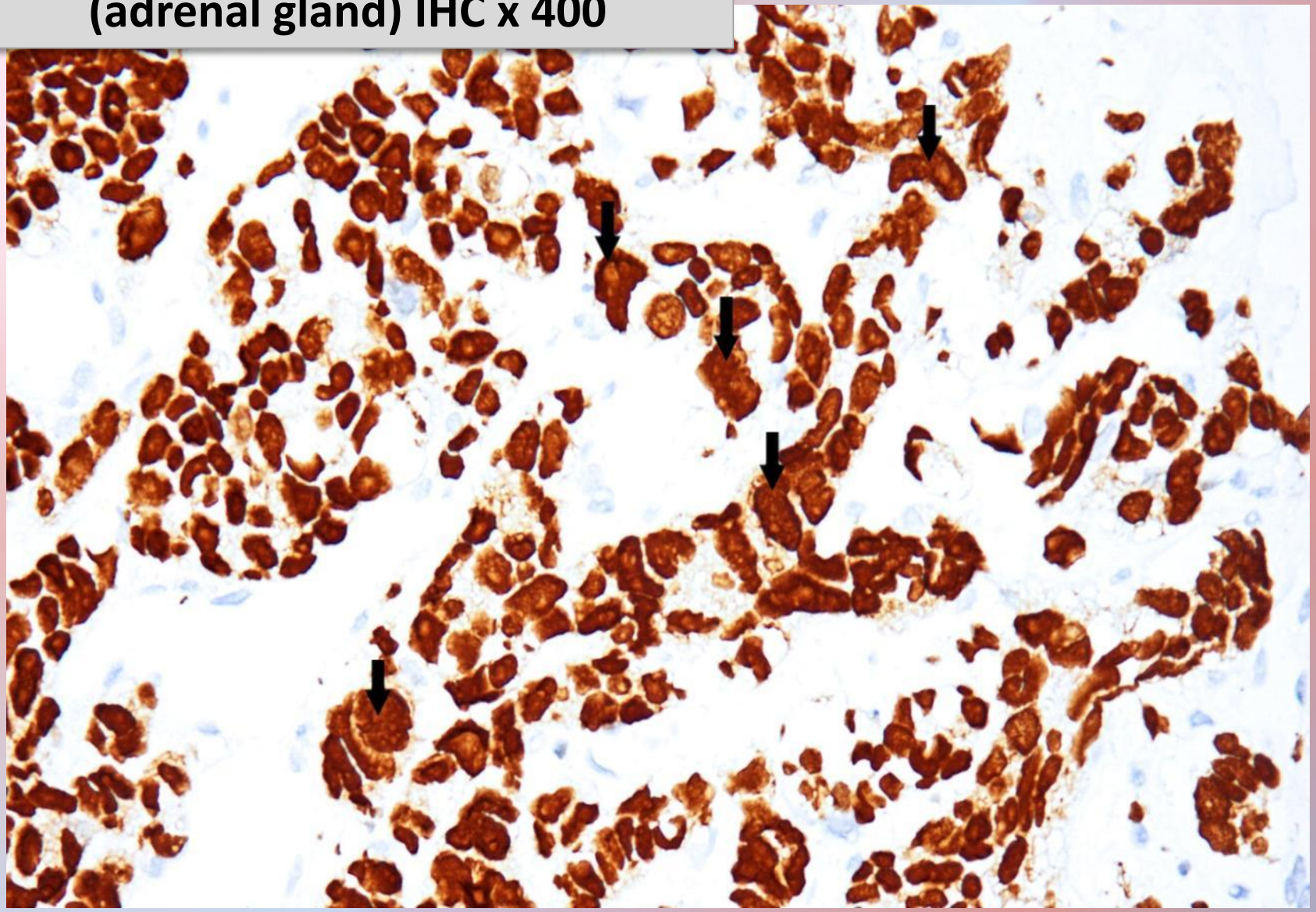


Metastatic carcinoma (adrenal gland)
H&E x 100

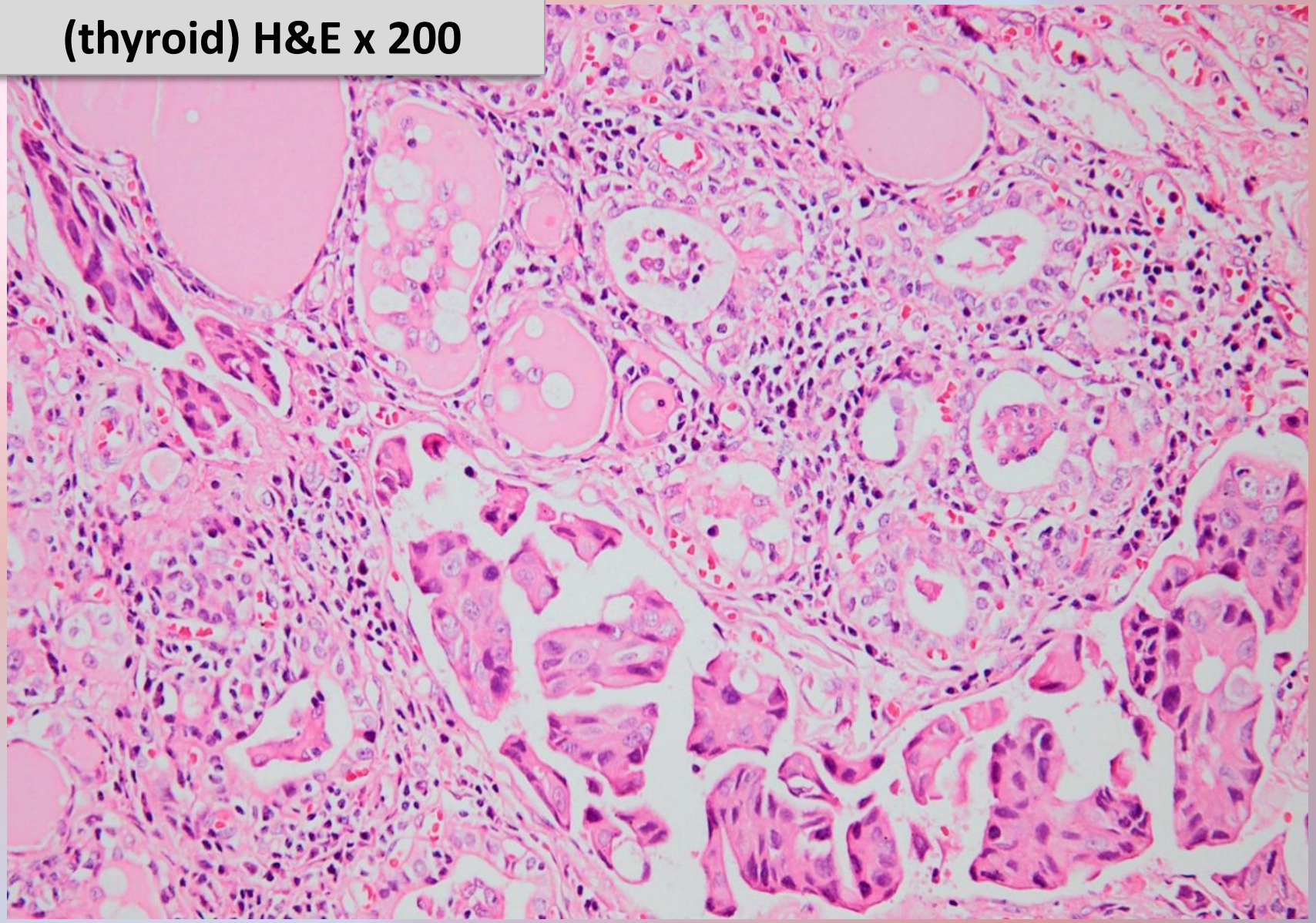
H&E x 400



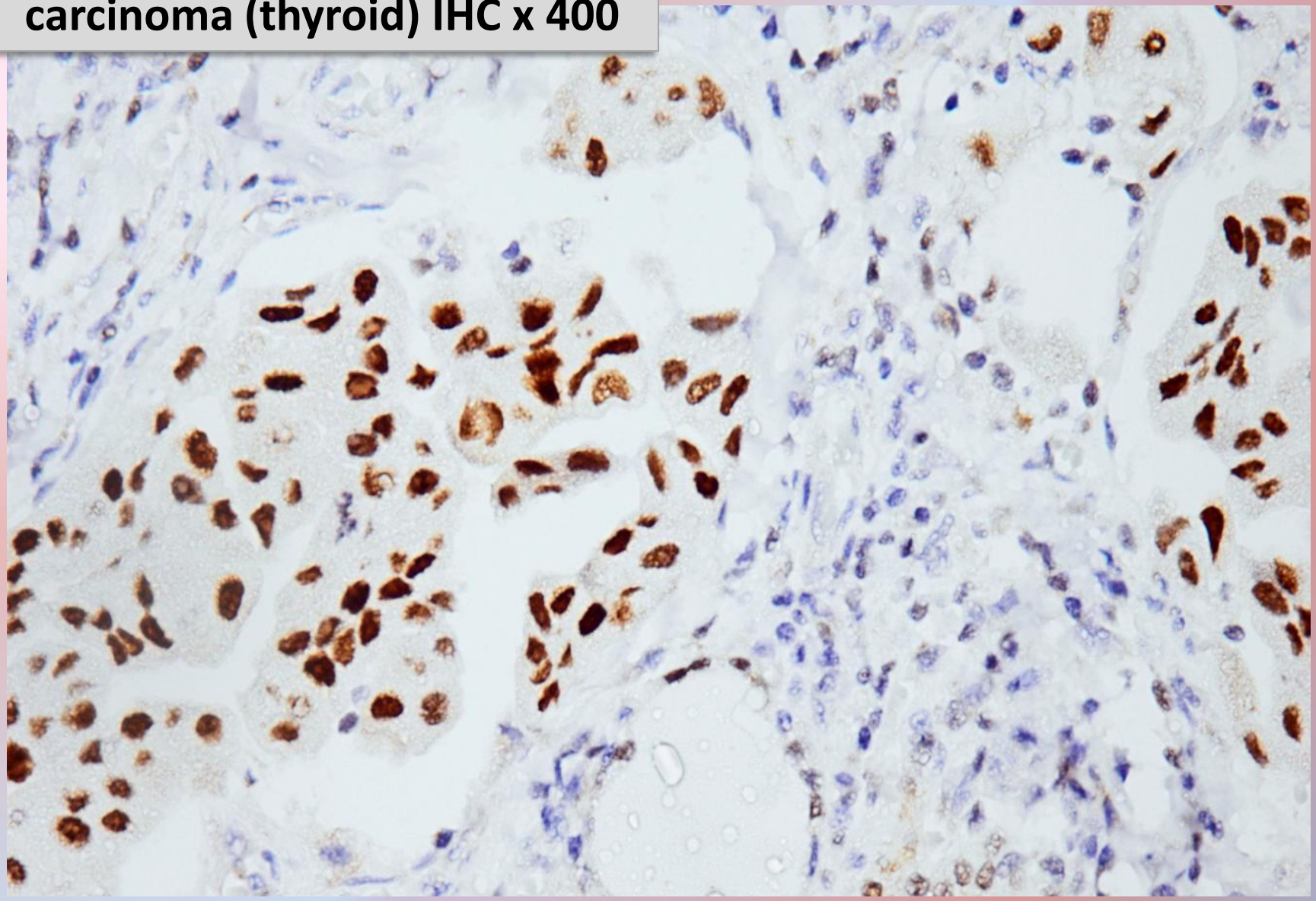
4+ GATA-3 in metastatic carcinoma (adrenal gland) IHC x 400



Metastatic carcinoma (thyroid) H&E x 200



4+ GATA-3 in metastatic carcinoma (thyroid) IHC x 400



CONCLUSION

GATA-3 is expressed in different morphologic and immunohistochemical subtypes of breast carcinoma

GATA-3 is a promising breast specific marker in identification of metastatic breast carcinoma when presenting in unusual sites, especially metastatic ER-negative breast carcinomas

GATA-3 may be a useful addition to IHC panels used in the differentiation between metastatic ER-positive carcinomas

RECOMMENDATIONS

GATA-3

Useful breast-specific marker to be incorporated in IHC panel in metastasis of unknown primary; when metastatic breast carcinoma is a consideration

Useful marker to be integrated in IHC panel for identification of metastatic breast carcinomas from other metastatic ER-positive carcinomas

Further studies are needed to compare the relative diagnostic sensitivity of GATA-3 in comparison to GCDFP-15 and MGB in metastatic breast carcinomas particularly in triple negative cases


Thank you