Breast Cancer

In Pregnancy

Maria J Merino MD,

NCI,

Breast cancer in pregnancy

- Pregnancy associated breast cancer is defined as cancer of the breast diagnosed during pregnancy, up to 1 year after delivery or at any time while the patient is lactating.
- Breast cancer is the second most common cancer during pregnancy after carcinoma of the uterine cervix.
- Together, these two malignancies account for about 25% of the cancer diagnosed during pregnancy.
- Overall prognosis of patients with (PABC) is worse because they may present with advanced disease. Stage for stage and age, prognosis is similar.

PABC

- Undetermined
  - Two coincidental processes?
  - Changes in hormonal mileu favor tumorigenesis
  - Are molecular alterations are the same in BC and PABC?

- Known:
  - 3% of all breast cancers
  - Delay in diagnosis:
    - Prior studies report delays of 6 months. Now delays between 1-3 months

- Clinical examination is difficult.
- Common sign is the presence of a painless tumor mass misdiagnosed as benign.
- discharge or milk rejection sign.
- Mammograms difficult to interpret, high false negatives
- Larger tumors
- Positive Lymph nodes at diagnosis (53-74%)
- Negative ER, PR

PABC

- 24 patients
- Age: 21-38 (32m)
- Location

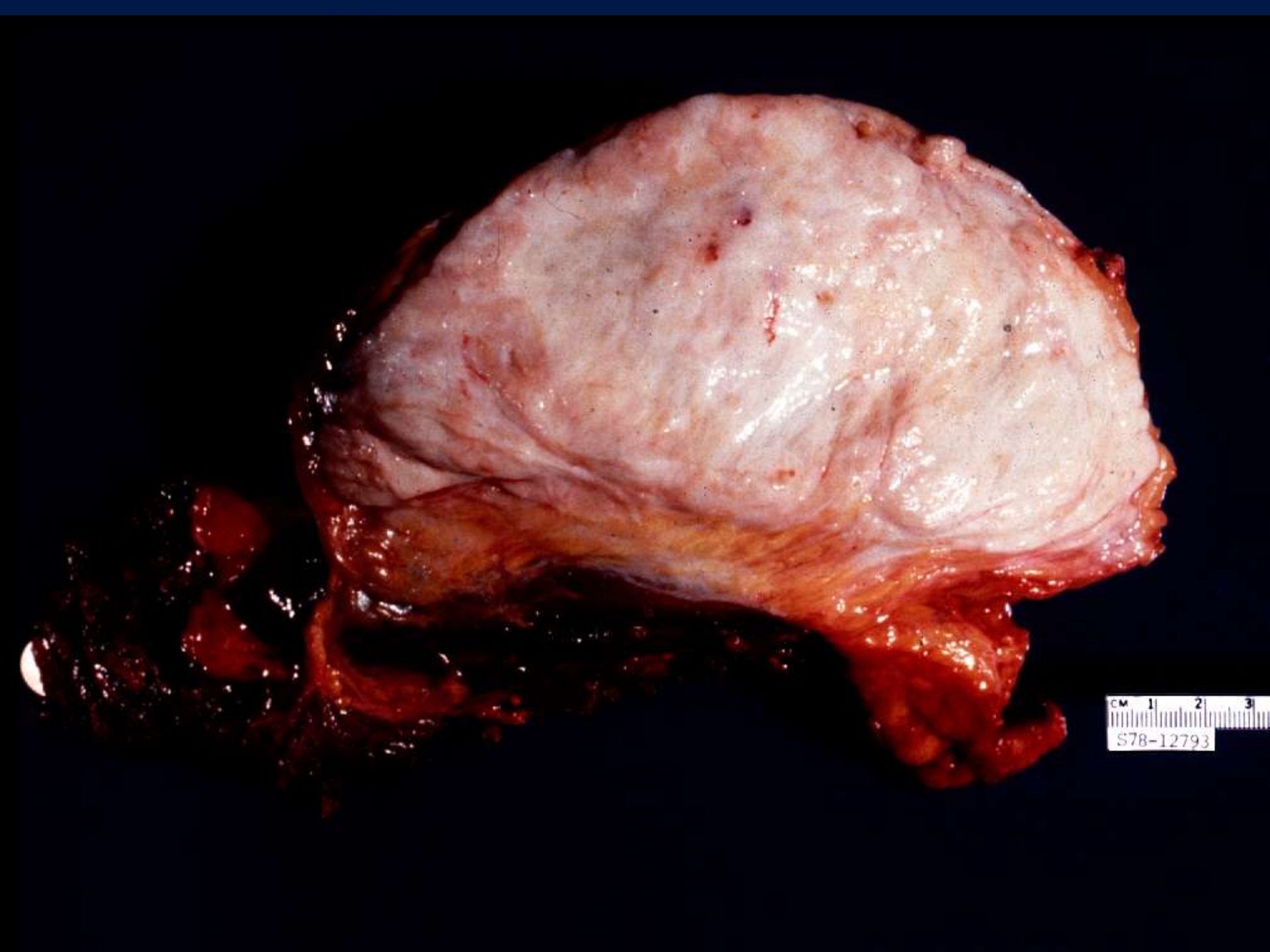
  Right breast 9, Left breast 15
- Lymph node metastasis at presentation

  Present…10 (41%)

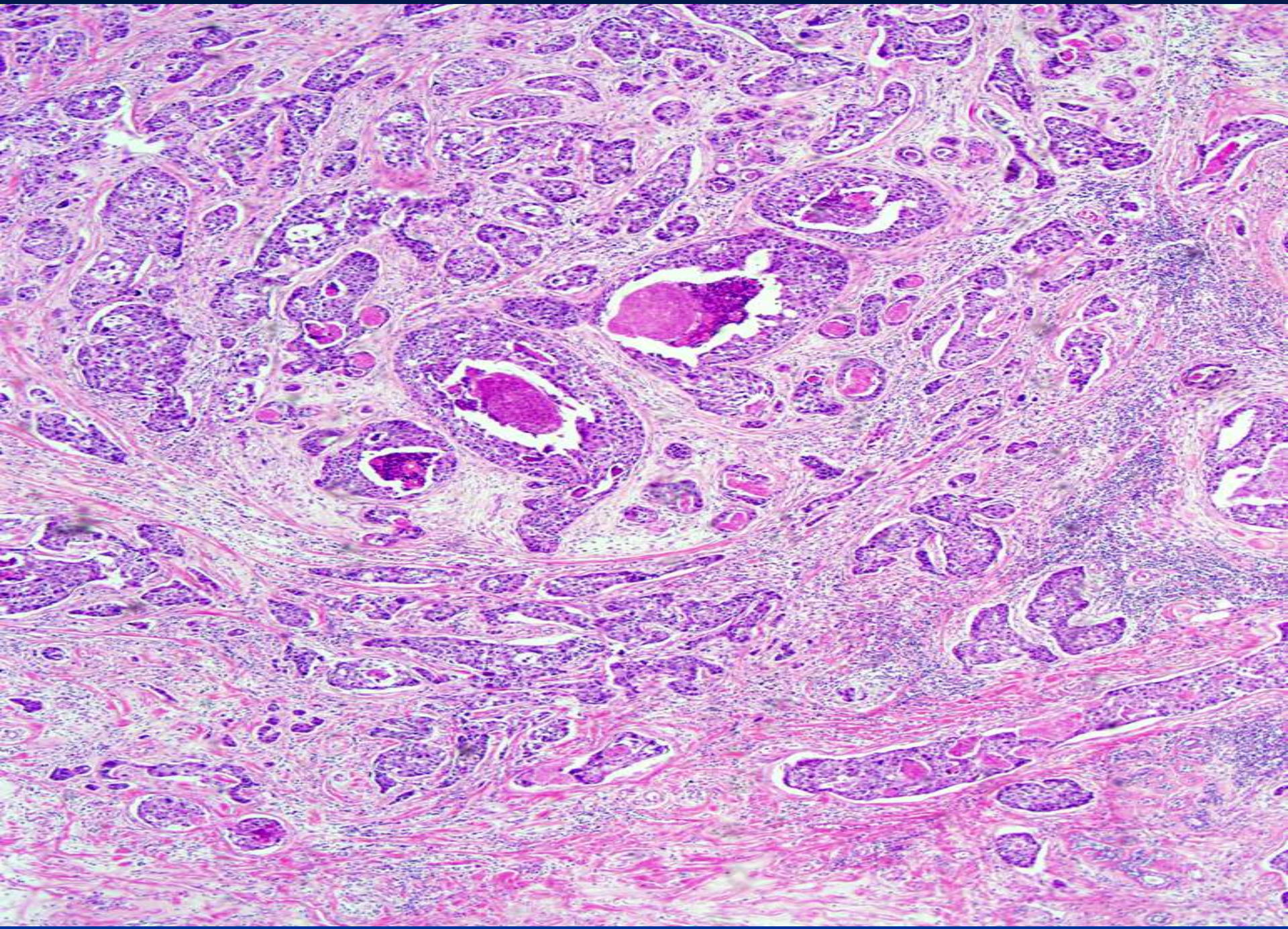
  Absent…14

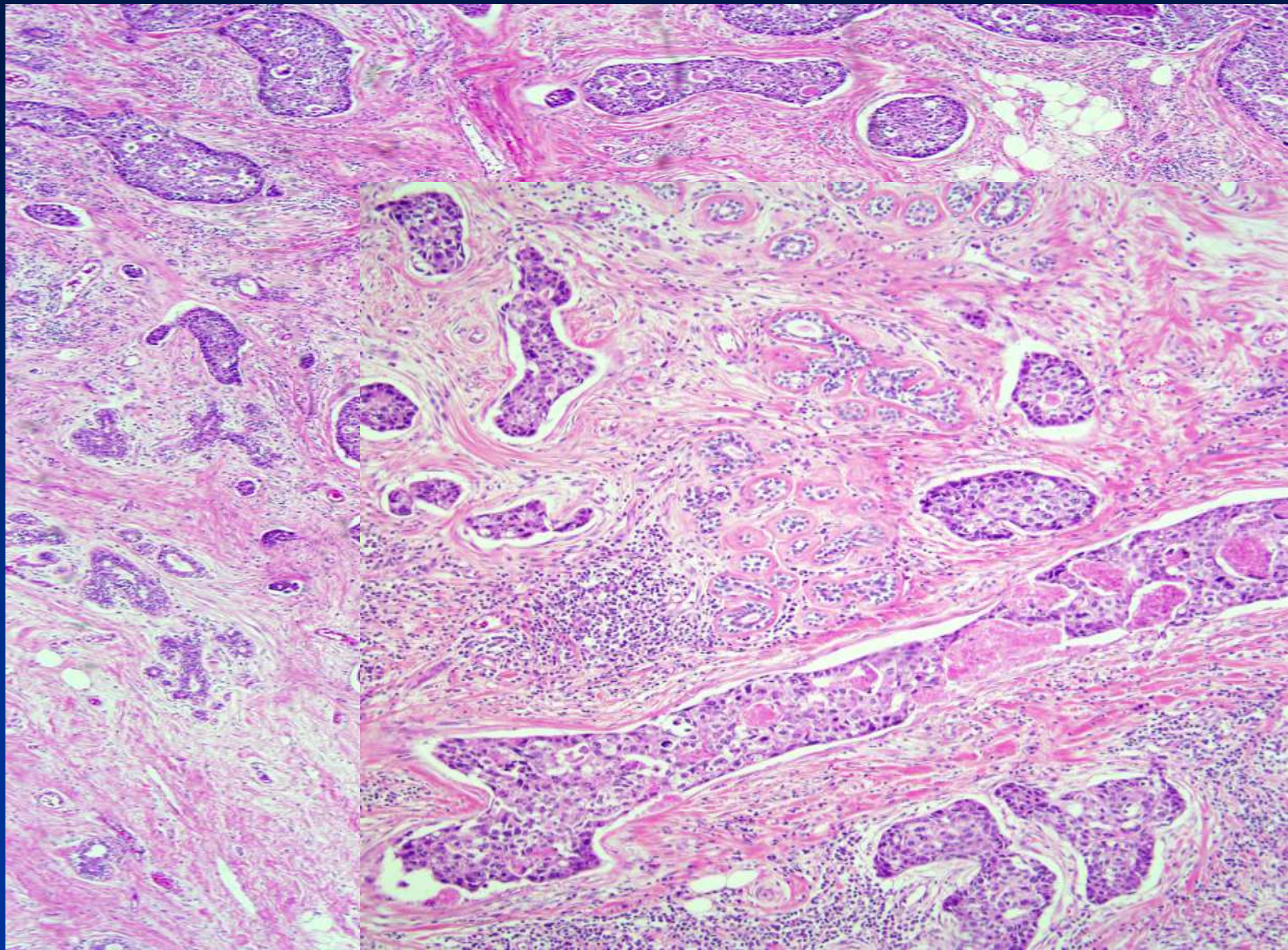
PABC

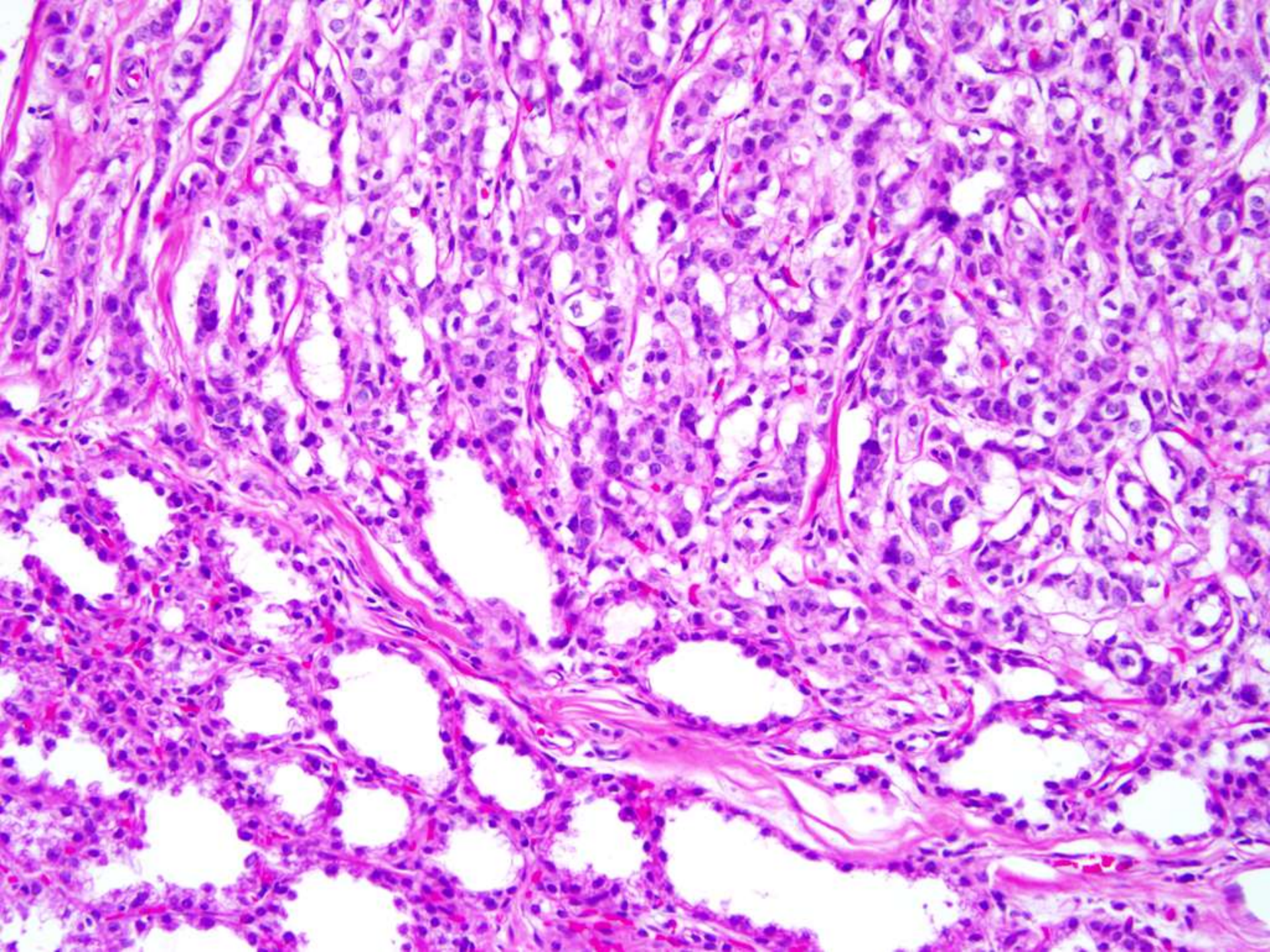
- Stage
  - Stage I…3
  - Stage II…18
  - Stage III…2
  - Stage IV…1
- Tumor size: 1- 5.5cm

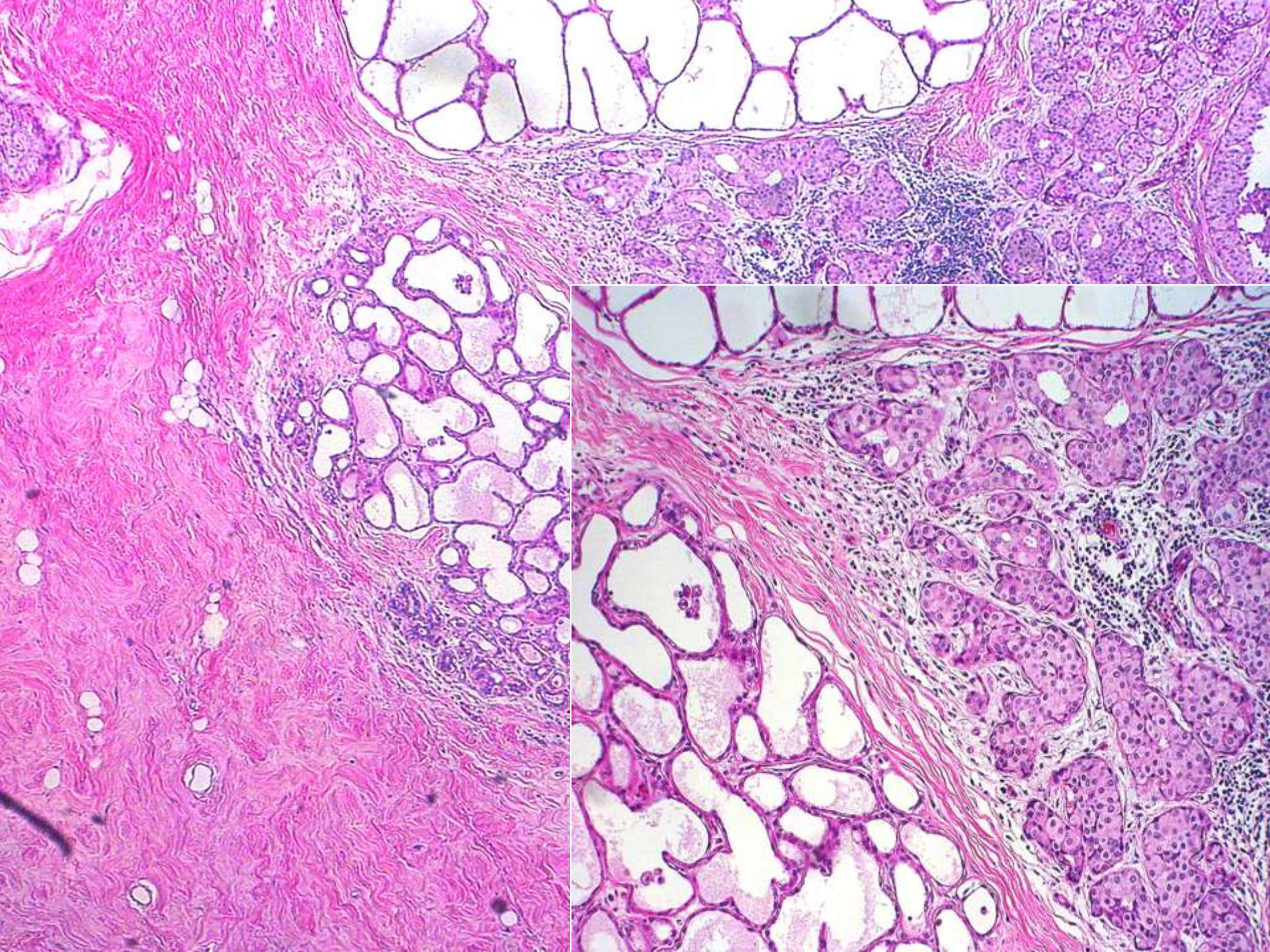

CM 1 2 3
S78-12793

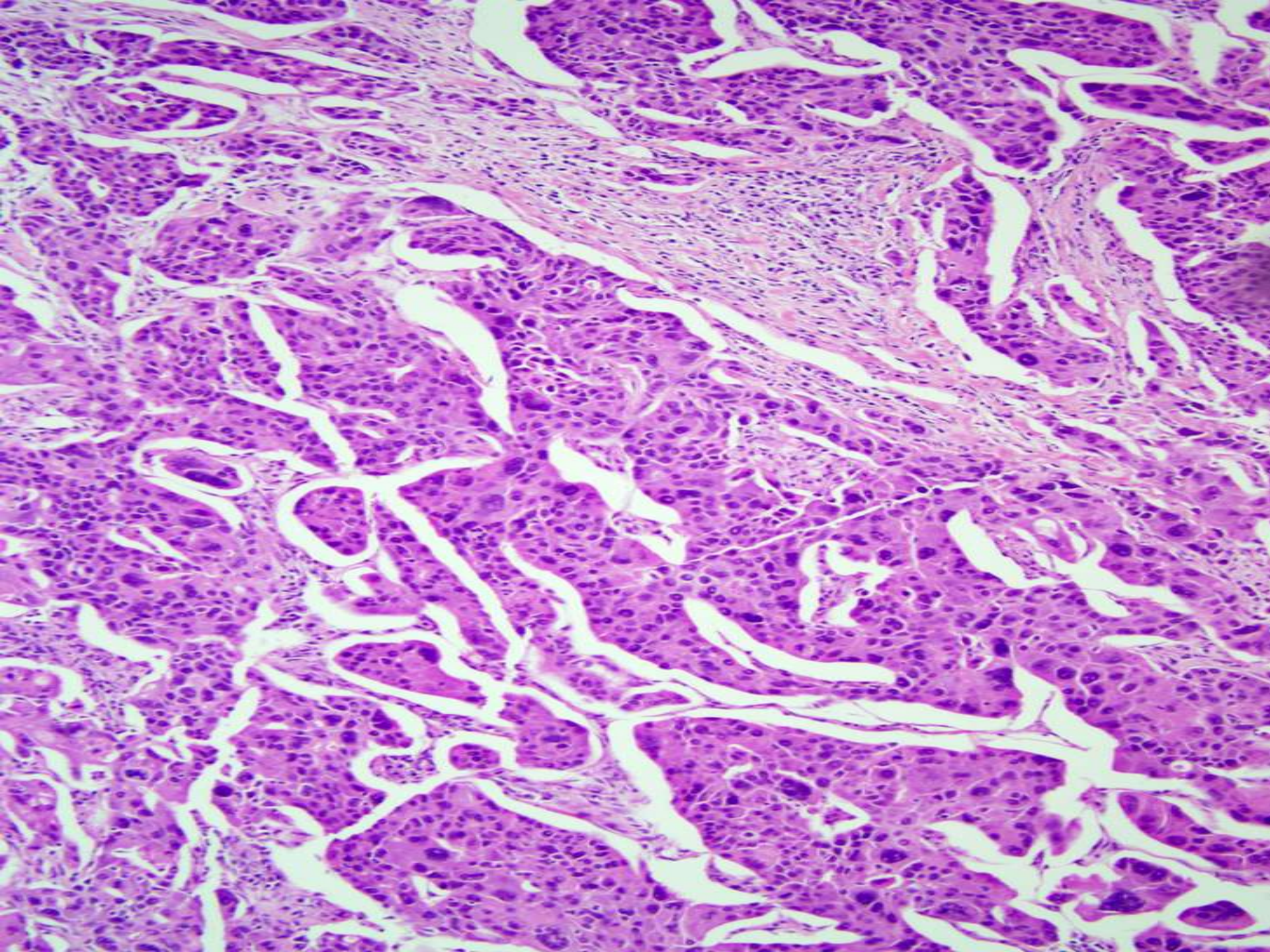
- Histological type:
  - -Infiltrating duct carcinoma…21
  - -Lobular carcinoma……..2
  - -Inflammatory carcinoma……1
- Tumor grade
  - -Well differentiated…..0
  - -Moderately differentiate….18
  - -Poorly differentiated…….6
- Nuclear grade
  - -1…0
  - -2….11
  - -3….13







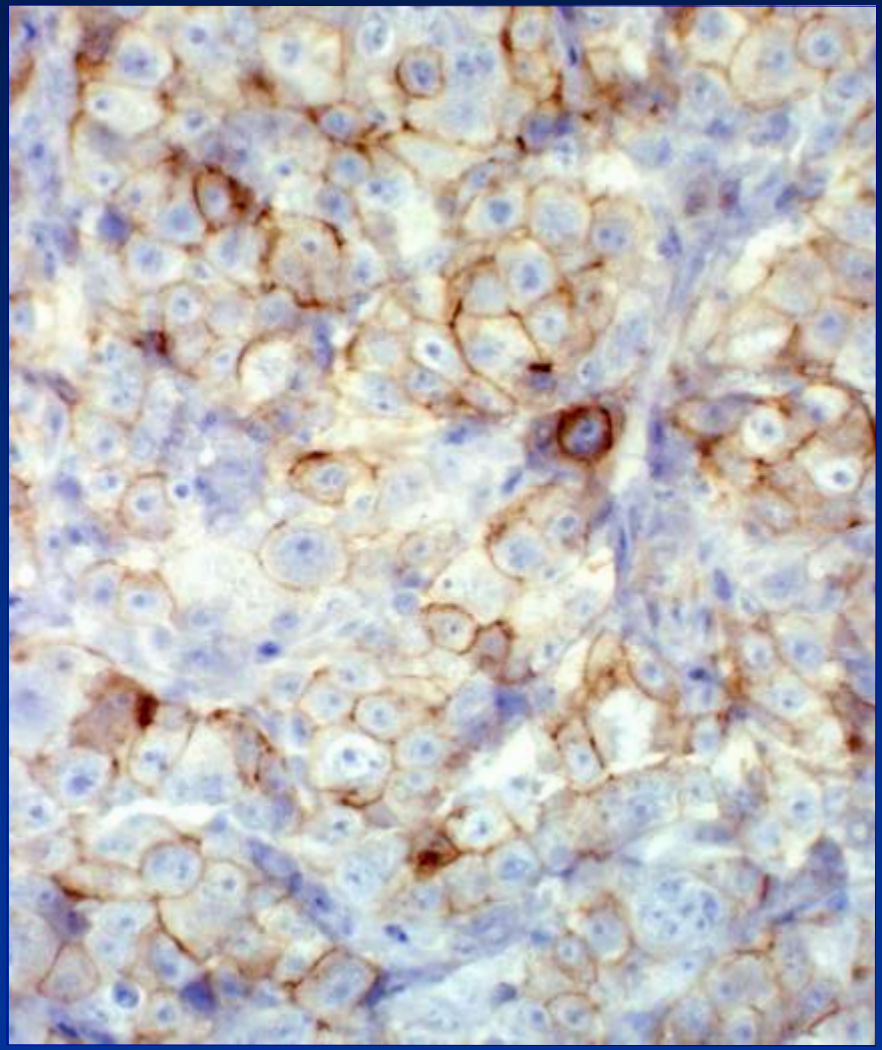




Markers

- ER……..10/11 (91%) negative
- PR……10/11 (91%) negative
- Her 2…….8/11; 4(3+) 50%; 4(2+) CISH-
- P53…… 5/11(46%)
- MIB1……..11/11 (100%), 40-90% of the Cells stained.

Her 2 neu



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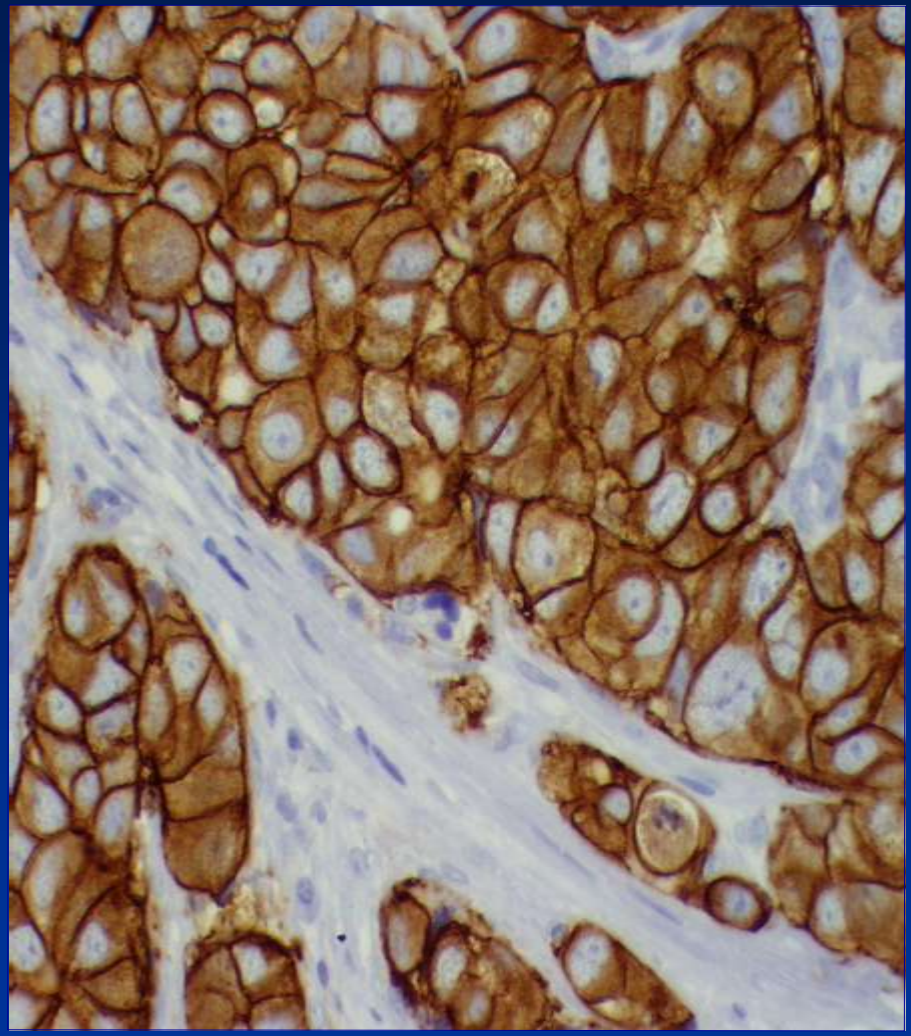

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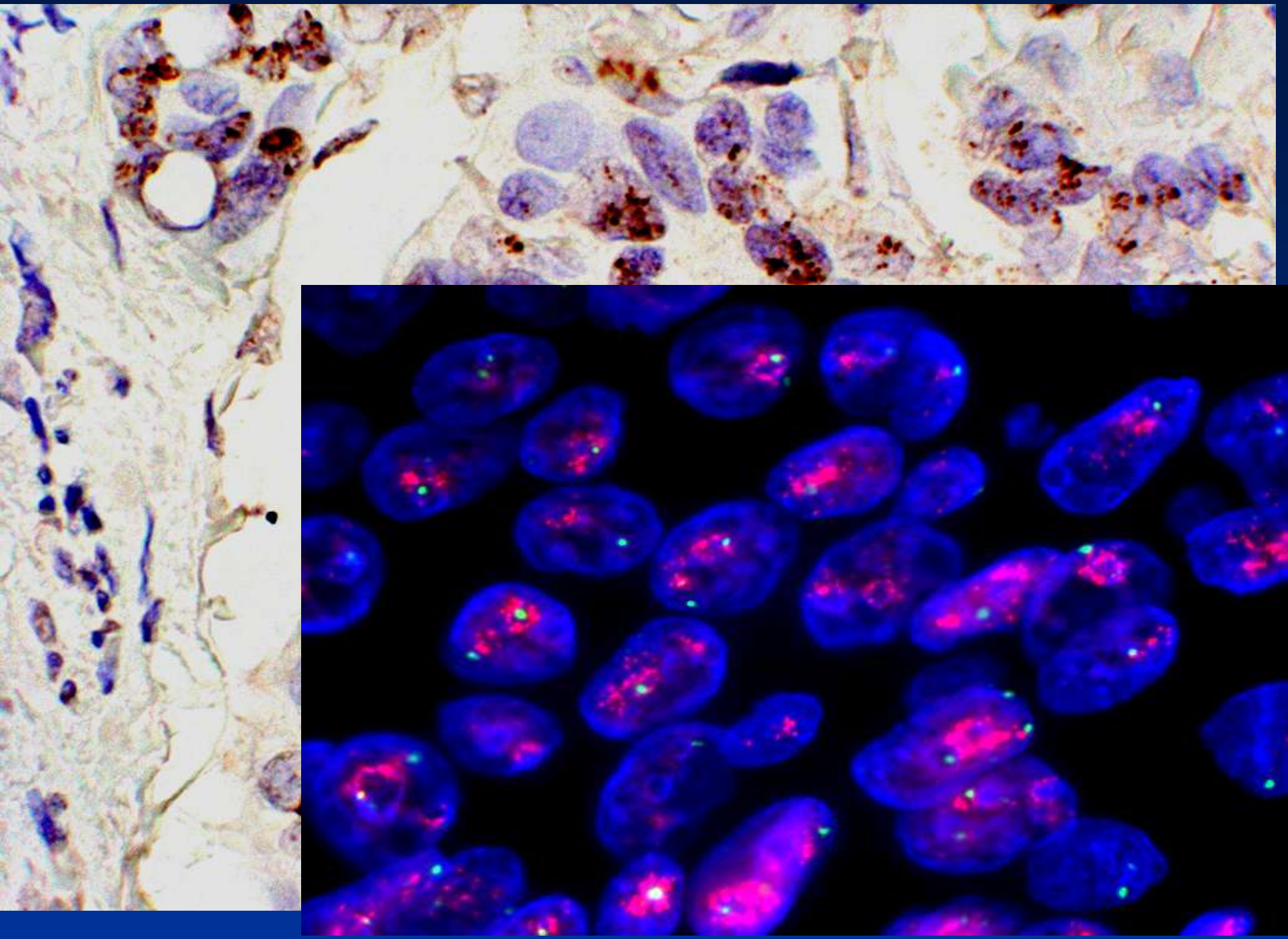

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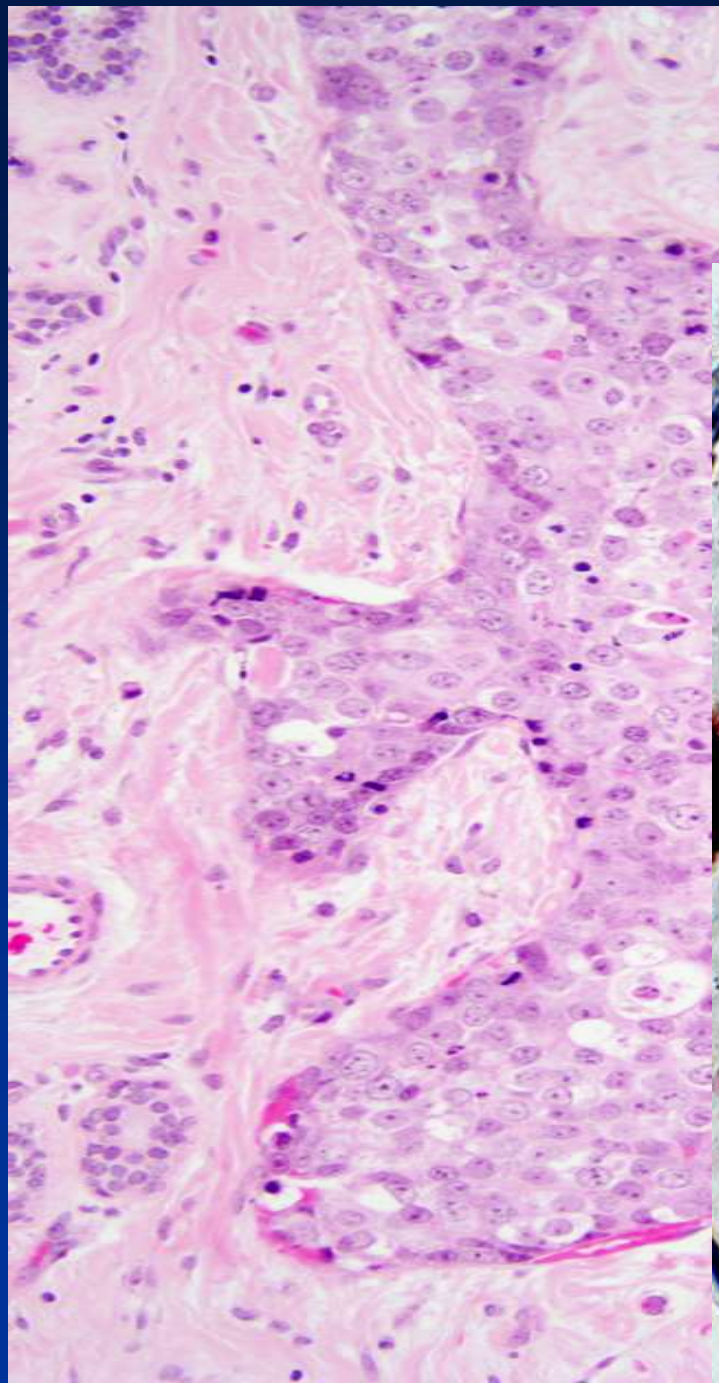
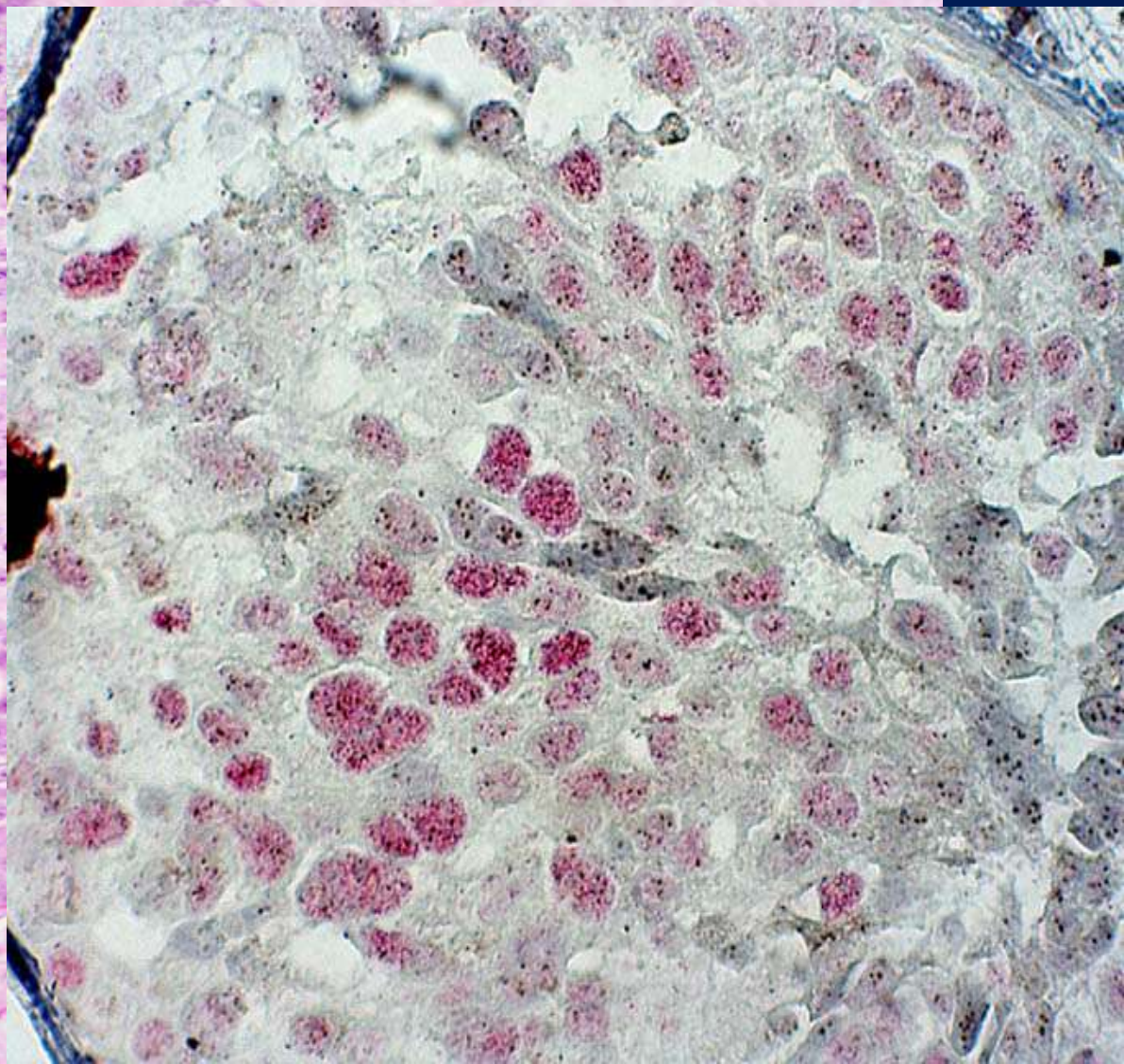




Loss of Heterozygosity

Genomic DNA from microdissected formalin-fixed paraffin embedded tissues was used to analyze loss of heterozygosity (LOH) on:

TP53, BRCA1, BRCA2, PTEN and NM23 genes. The results were correlated with other prognostic markers and with clinico-pathologic characteristics of the tumors.

Loss of Heterozygosity

- P53 gene (TP53 and D17S799)
- NM23 (17q21-17q22)
- PTEN (10q23.3, D10S1173, D10S1765)
- BRCA1 (17q21 (D17S1323, D17S855)
- BRCA2 13q12.1 (D13S290, D13S310, D13S217)

Primers	*Gene*	*INFORMATIVE*		*LOH*	
		n	Percentage	*n*	Percentage
D10S1173	PTEN	9/17	53%	4/9	44%
D10S1765	PTEN	10/17	59%	6/10	60%
Overall PTEN	PTEN	11/17	64%	7/11	63%
D17S799	P53	5/17	29%	4/5	80%
TP53	P53	14/17	82%	9/14	64%
Overall P53	P53	15/17	88%	9/15	60%
D17S1818	Her2	8/17	47%	5/8	62%
D17S855	BRCA-1	11/7	65%	6/11	54%
D17S1323	BRCA-1	4/17	23%	1/4	25%
Overall BRCA-1	BRCA-1	12/17	70%	6/12	50%
D13S290	BRCA-2	11/17	65%	2/11	18%
D13S310	BRCA-2	10/17	59%	2/10	20%
D13S217	BRCA-2	11/17	65%	2/11	18%
Overall BRCA-2	BRCA-2	13/17	76%	3/13	23%
NM23	NM23	10/17	59%	4/10	40%

Results

- High incidence of LOH in NM23, BRCA I, BRCA 2, p53 and PTEN
- LOH at BRCA1 correlated with tumor size >2cm and advanced stage
- LOH at NM23 correlated with + LN's and early recurrences
- LOH at BRCA2 correlated with high tumor grade
- LOH at PTEN correlated with >2cm, +LN's and ER,PR negative

Follow up

- Local and distant relapse occurred in 50% of the cases with a median of 27 months.
- The overall survival ranged between 3 months to 15 years. Eight patients (53%) died within 6 years, 2 are alive with disease after 5 years, and 5 were free of disease 10 years .
- *The reported overall survival in PABC cancer patients ranges from 37 to 51% at 5 years and 29% at 10 years and this proportion is statistically lower than that found in women younger than 40 years.* *Woo J, 2003 Arch Sur*

Treatment

- Surgery
  - Mastectomy
  - Lumpectomy
  - Sentinel node evaluation
- Chemotherapy
  - After first trimester of pregnancy
  - Tamoxifen: fetal abnormalities

Prognosis

- When matched for age and stage, the 5-year survival rates were 57% in pregnant women and 56% in nonpregnant women (Nugent and O'Connell). In
- In another the 5-year survival rate was 82% in both pregnant (n = 22) and nonpregnant (n = 103) women who were node-negative. Among node-positive patients, the survival rates were 47% in the pregnant group (n = 47) and 59% in the nonpregnant group (n = 63).

Conclusions

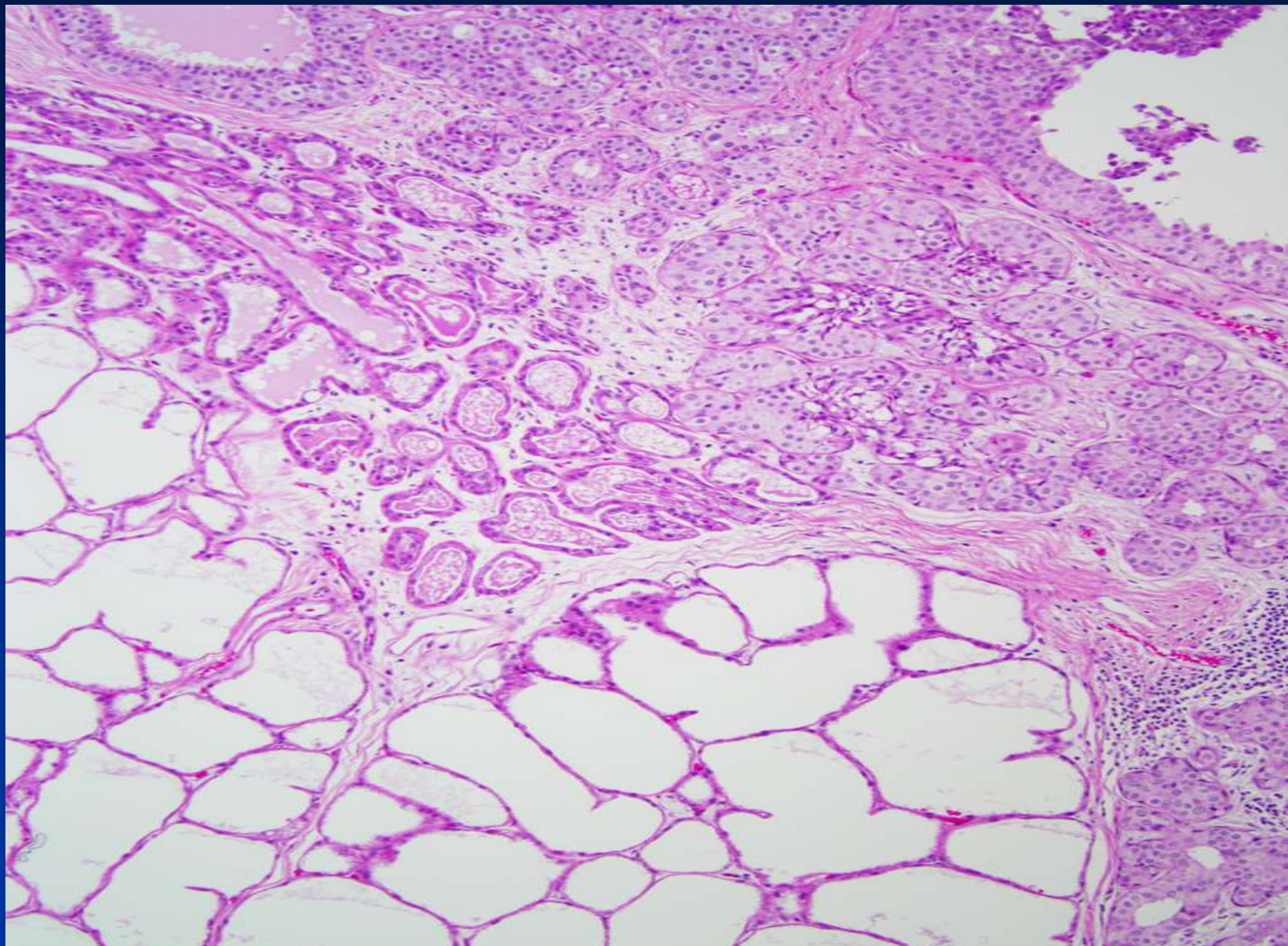
- Breast ca in pregnancy is rare
- Shorter delays in diagnosing PABC
- Advanced stage
- High incidence of positive nodes when compared to the non-pregnant population
- High grade tumors with prominent vascular invasion
- Early diagnosis is important to improve progosis
- ER, PR neg
  - Ishida et al reported 70% ER-negative and 71% PR-negative tumors in a group of pregnant and lactating women vs 39% and 32%, respectively, in age-matched controls.

- Frequent LOH in NM23, BRCA1 and BRCA2 p53 and PTEN.
  - Studies of 292 women diagnosed as having breast cancer before age 40 years, known *BRCA1* and *BRCA2* carriers were more likely to develop cancer during pregnancy.

Kirsti Ottem Langeland
Breast Cancer patient

- It is unclear if these differences are entirely due to delayed detection or if the increased vascularity of the breast during pregnancy, high circulating levels of hormones, and immune-suppressed state of pregnancy accelerate the course of cancer.

MARKERS	*LOH at PTEN*		*p* value
	N / informative	%	
TP53	5/7	71%	*p=0.43*
Her-2	3/7	43%	*p=0.46*
BRCA-1	4/7	57%	*p=0.55*
BRCA-2	2/7	28%	*p=0.21*
NM-23	2/7	29%	*p=1.0*



Peritoneal Gliomatosis produced by ovarian teratomas.

Nogales FF,Oliva HA

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140.Carcinoma in situ of the Fallopian tube associated with cervical carcinoma. Case report.Mendez JA, Bedoya JM Jr, Matilla A, Nogales F Jr, Galera H.Int J Gynaecol Obstet. 1976;14(4):353-5.