

Breast Lesions during Pregnancy and Post-Partum Period

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I have no relevant financial interests to disclose

Outline



3 cases

- Breastfeeding
- Breast milk
- Lactational and pseudolactational changes without and with atypia
- Secretory carcinoma
- Lactational mastitis
- Breast abscesses (lactational vs. non-lactational)
- Squamous metaplasia of lactiferous ducts
- Duct ectasia
- Galactocele
- Pregnancy associated breast cancer
- Differential diagnosis of granulomatous mastitis



Benefits for baby

Reduces the risk of:

- ♥ Gastroenteritis (Diarrhoea & vomiting)
- ♥ Chest infection
- ♥ Diabetes
- ♥ Ear infection
- ♥ Eczema & asthma
- ♥ Urine infections

Improves:

- ♥ Response to immunisations
- ♥ Mouth formation
- ♥ IQ



Benefits for mum

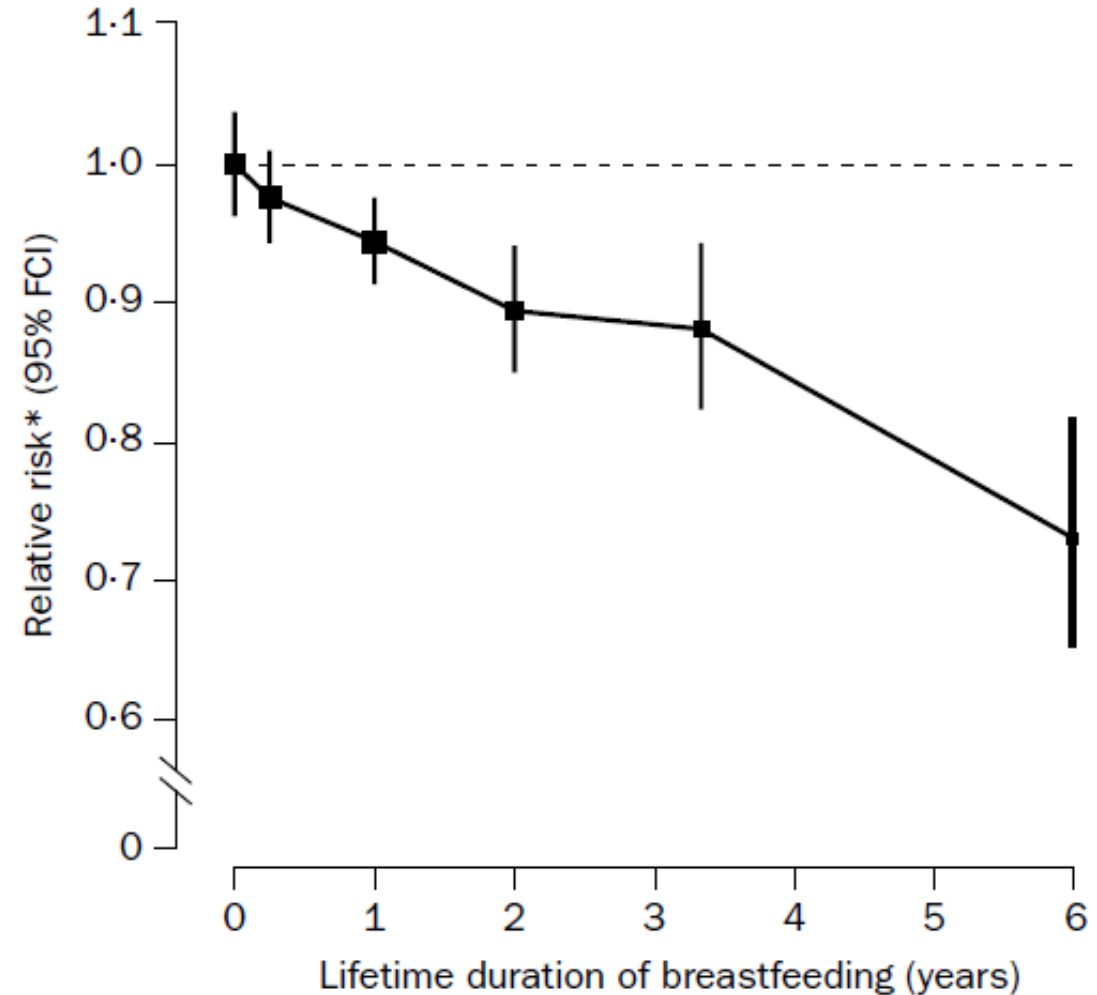
Reduces the risk of:

- ♥ Breast cancer
- ♥ Reduces the risk of ovarian cancer
- ♥ Reduces the risk of osteoporosis

Improves:

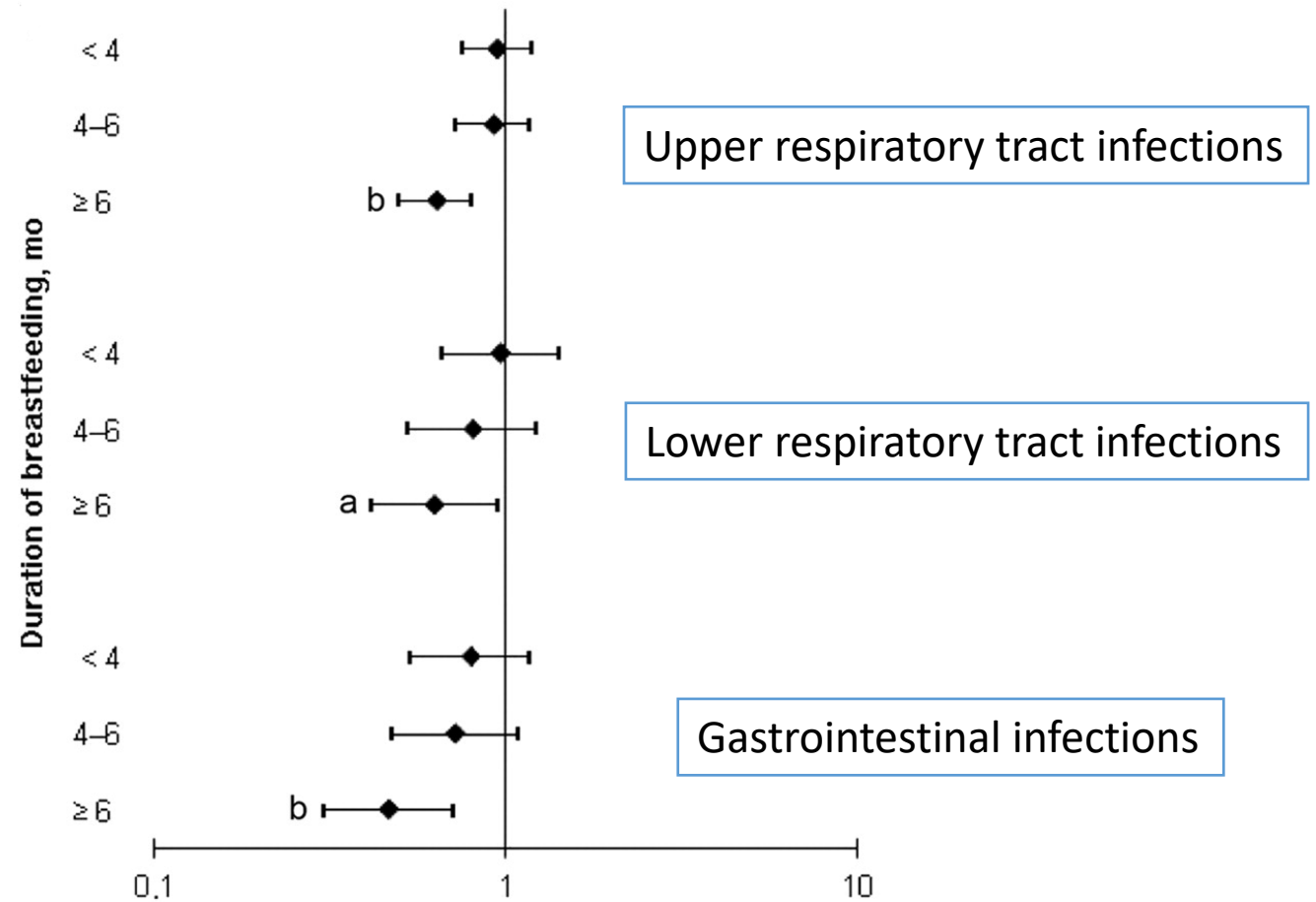
- ♥ Return to pre-pregnancy weight

- **Breastfeeding decreases risk for breast cancer in mom**
- The relative risk of breast cancer declines with increasing parity and duration of breastfeeding



Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet. 2002 Jul 20;360(9328):187-95.

- **Breast milk offers protection from infections to babies**
- There are bioactive components in breast milk:
 - IgA and other immunoglobulins
 - Immune cells
 - Cytokines
 - Growth factors (such as EFG and Erythropoietin)





American Academy of Pediatrics



DEDICATED TO THE HEALTH OF ALL CHILDREN®

"The American Academy of Pediatrics recommends that infants be exclusively breastfed for about the first 6 months with continued breastfeeding along with introducing appropriate complementary foods for 1 year or longer. WHO also recommends exclusive breastfeeding up to 6 months of age with continued breastfeeding along with appropriate complementary foods up to 2 years of age or longer"

Breast milk composition

	Human milk*	Cow's milk 	Formula 
Protein	0.9 to 1.2 g/dL	3.3 g/dL	1.9 g/dL
Fat	3.2 to 3.6 g/dL	3.3 g/dL	3.6 g/dL
Lactose	6.7 to 7.8 g/dL	5.4 g/dL	7.0 g/dL
Energy estimates	65-70 kcal/dL	66.7 kcal/dL	67.6 kcal/dL

- The most abundant proteins are casein, α-lactalbumin, lactoferrin, secretory IgA (sIgA), lysozyme, and serum albumin
- Compositional changes occur (during feedings, nocturnally, etc)
- Human milk provides the normative standard for infant nutrition

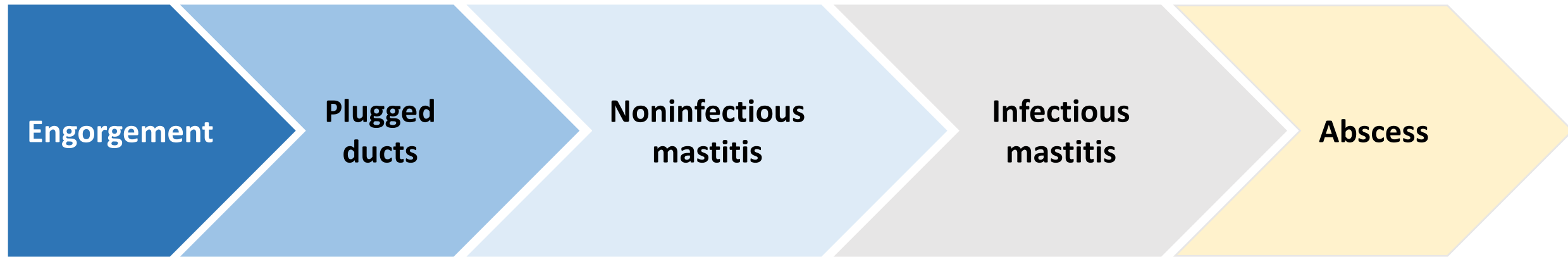
Human milk microbiota

- Breast milk was long assumed to be sterile
- Growing body of evidence that there is breast milk microbiota
 - Numerous bacteria in milk obtained under sterile conditions

Genera	Species
<i>Acinetobacter</i>	<i>A. calcoaceticus</i>
<i>Bifidobacterium</i>	<i>B. breve</i> , <i>B. adolescentis</i> , <i>B. bifidum</i> , <i>B. longum</i> , <i>B. animalis</i> , <i>B. catenulatum</i>
<i>Enterococcus</i>	<i>E. faecalis</i> , <i>E. faecium</i> , <i>E. durans</i> , <i>E. hirae</i> , <i>E. mundtii</i>
<i>Escherichia</i>	<i>E. coli</i>
<i>Gemella</i>	<i>G. haemolysans</i>
<i>Klebsiella</i>	<i>K. oxytoca</i>
<i>Kocuria</i>	<i>K. kristinae</i>
<i>Lactobacillus</i>	<i>L. rhamnosus</i> , <i>L. crispatus</i> , <i>L. gasseri</i> , <i>L. fermentum</i> , <i>L. plantarum</i> , <i>L. brevis</i> , <i>L. oris</i> , <i>L. animalis</i>
<i>Lactococcus</i>	<i>L. lactis</i> ssp. <i>lactis</i>
<i>Leuconostoc</i>	<i>L. mesenteroides</i> , <i>L. citreum</i> , <i>L. fallax</i>
<i>Propionibacterium</i>	<i>P. acnes</i>
<i>Pseudomonas</i>	<i>P. synxantha</i> , <i>P. fluorescens</i>
<i>Rothia</i>	<i>R. mucilaginosa</i>
<i>Serratia</i>	<i>S. proteomaculans</i>
<i>Staphylococcus</i>	<i>S. aureus</i> , <i>S. epidermidis</i> , <i>S. haemolyticus</i> , <i>S. hominis</i> , <i>S. pasteurii</i> , <i>S. warneri</i>
<i>Streptococcus</i>	<i>S. salivarius</i> , <i>S. mitis</i> , <i>S. gallolyticus</i> , <i>S. australis</i> , <i>S. vestibularis</i> , <i>S. parasanguis</i> , <i>S. pneumoniae</i>
<i>Weissella</i>	<i>W. cibaria</i> , <i>W. confusa</i>
Other bacterial genera detected but not assigned to species	
<i>Corynebacterium</i> , <i>Sphingomonas</i> , <i>Granulicatella</i> , <i>Bradyrhizobium</i> , <i>Prevotella</i> , <i>Ralstonia</i> , <i>Actinomyces</i> , <i>Clostridium</i> , <i>Veillonella</i>	
Data taken from [12–14,29,30,114].	

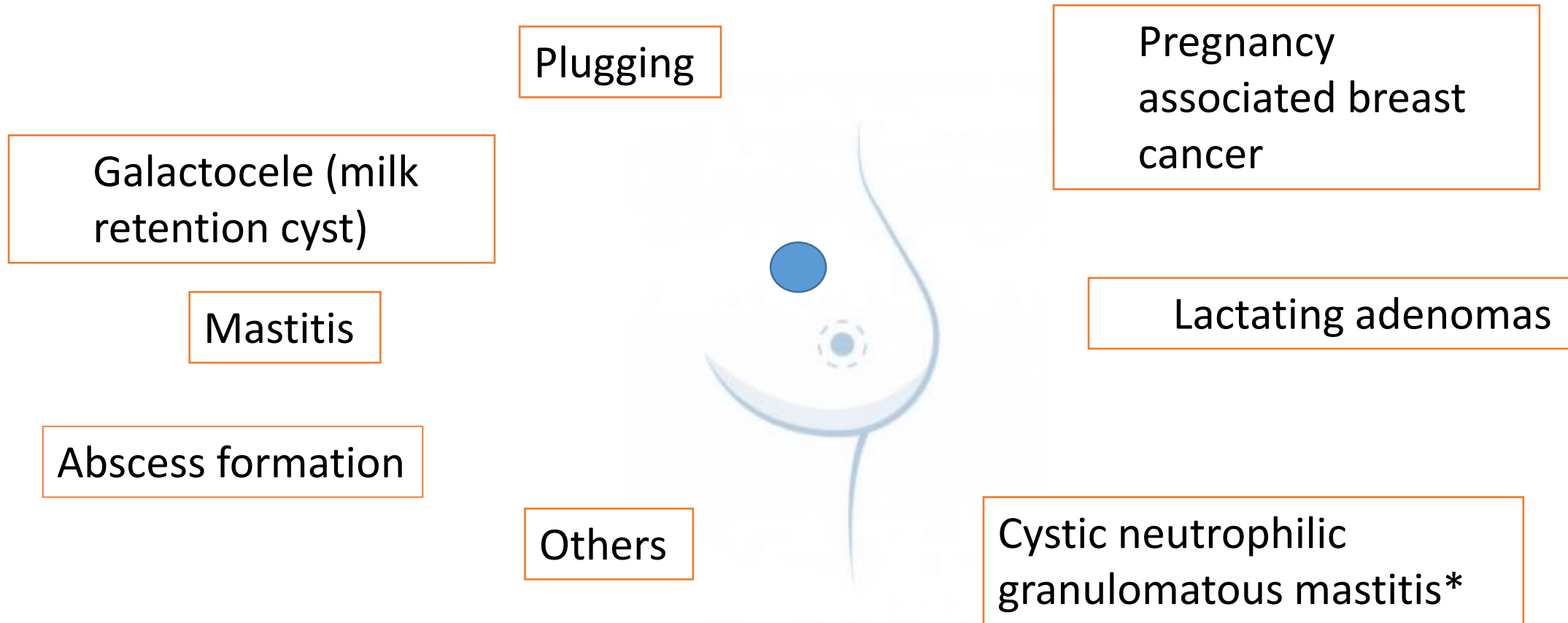
McGuire MK, McGuire MA. Got bacteria? The astounding, yet not-so-surprising, microbiome of human milk. *Current Opinion in Biotechnology* 44:63-68, 2017.

There are many benefits of breastfeeding but there are also some associated risks

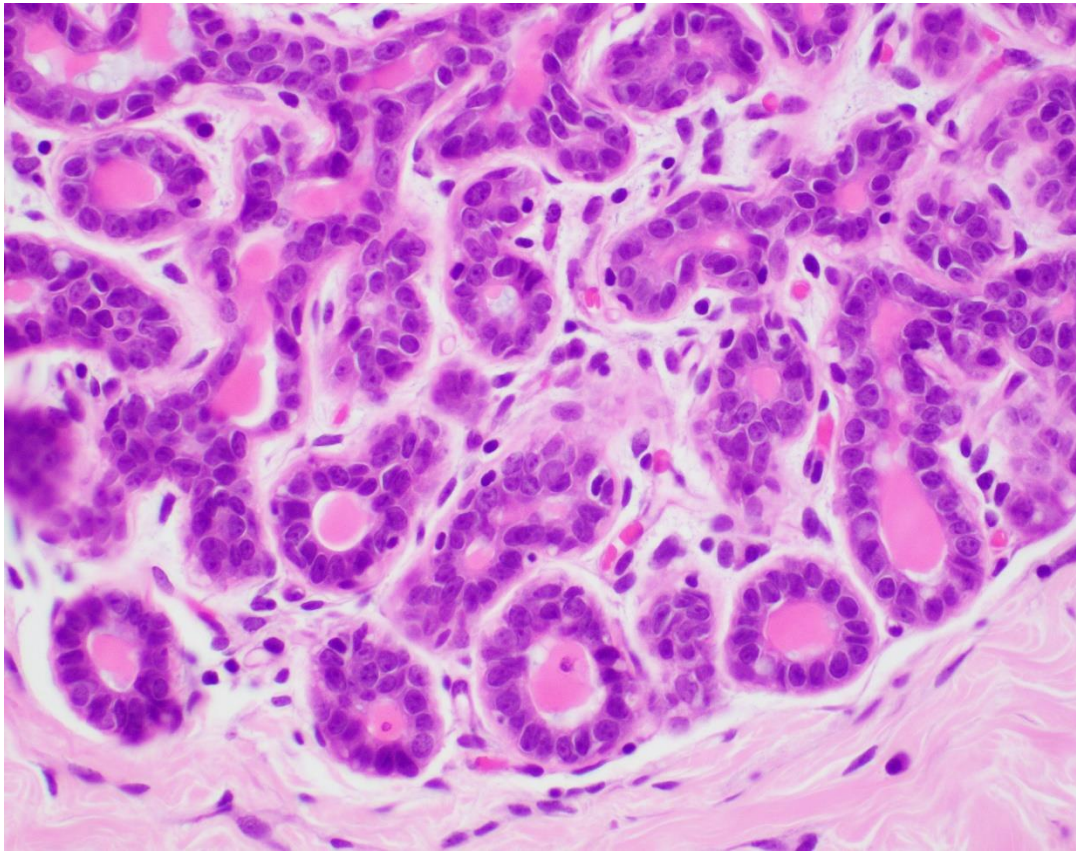


- Lactational mastitis
 - It is most common in the first three months of breastfeeding
 - Initially, engorgement occurs because of poor milk drainage
 - May be related to nipple trauma

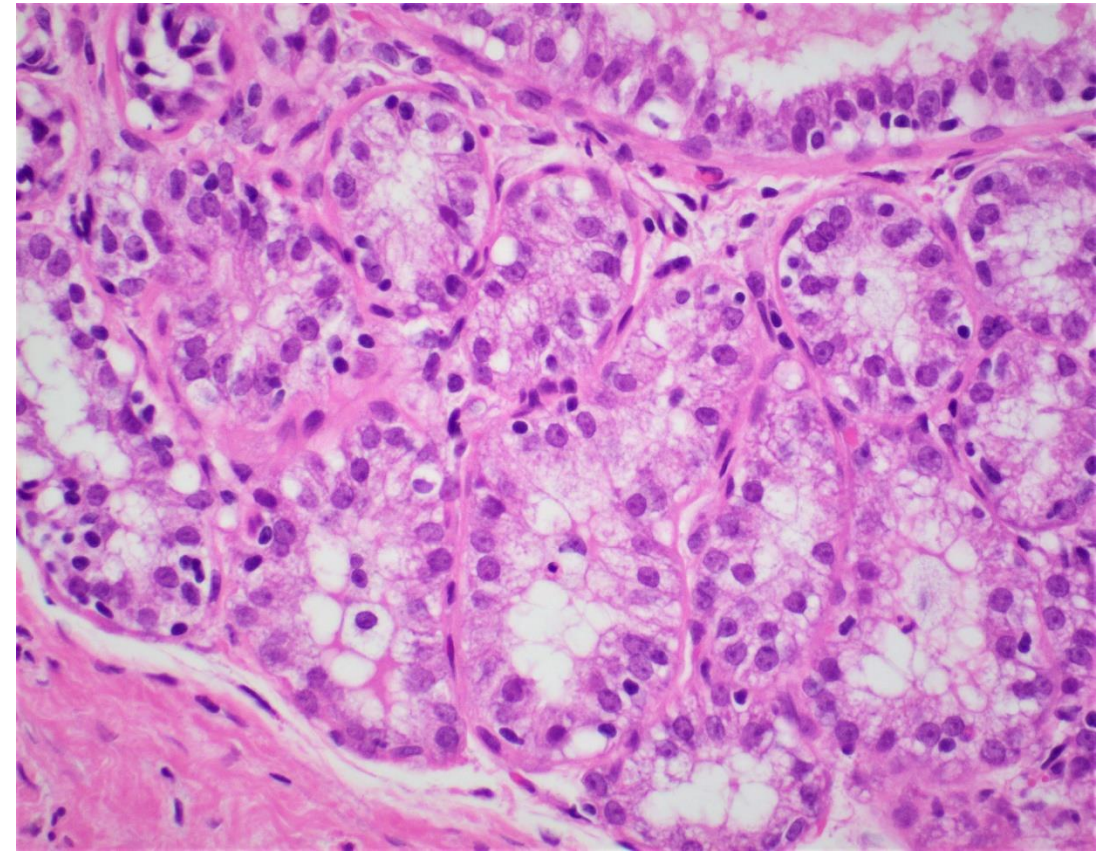
Differential diagnosis for a breast lump during pregnancy and postpartum period



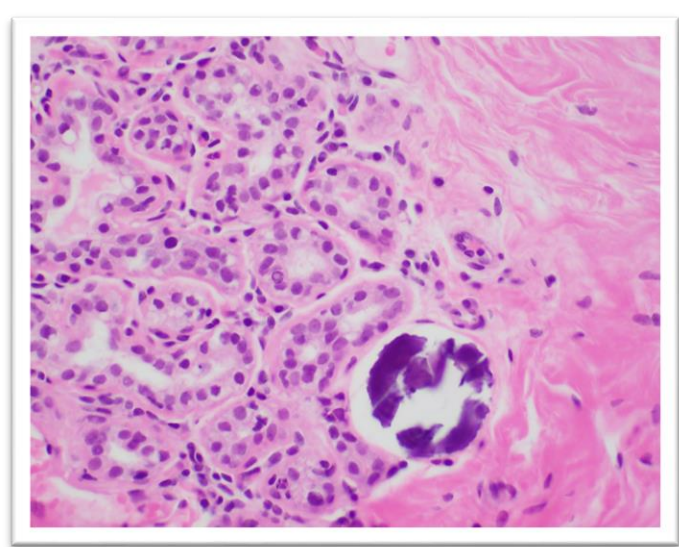
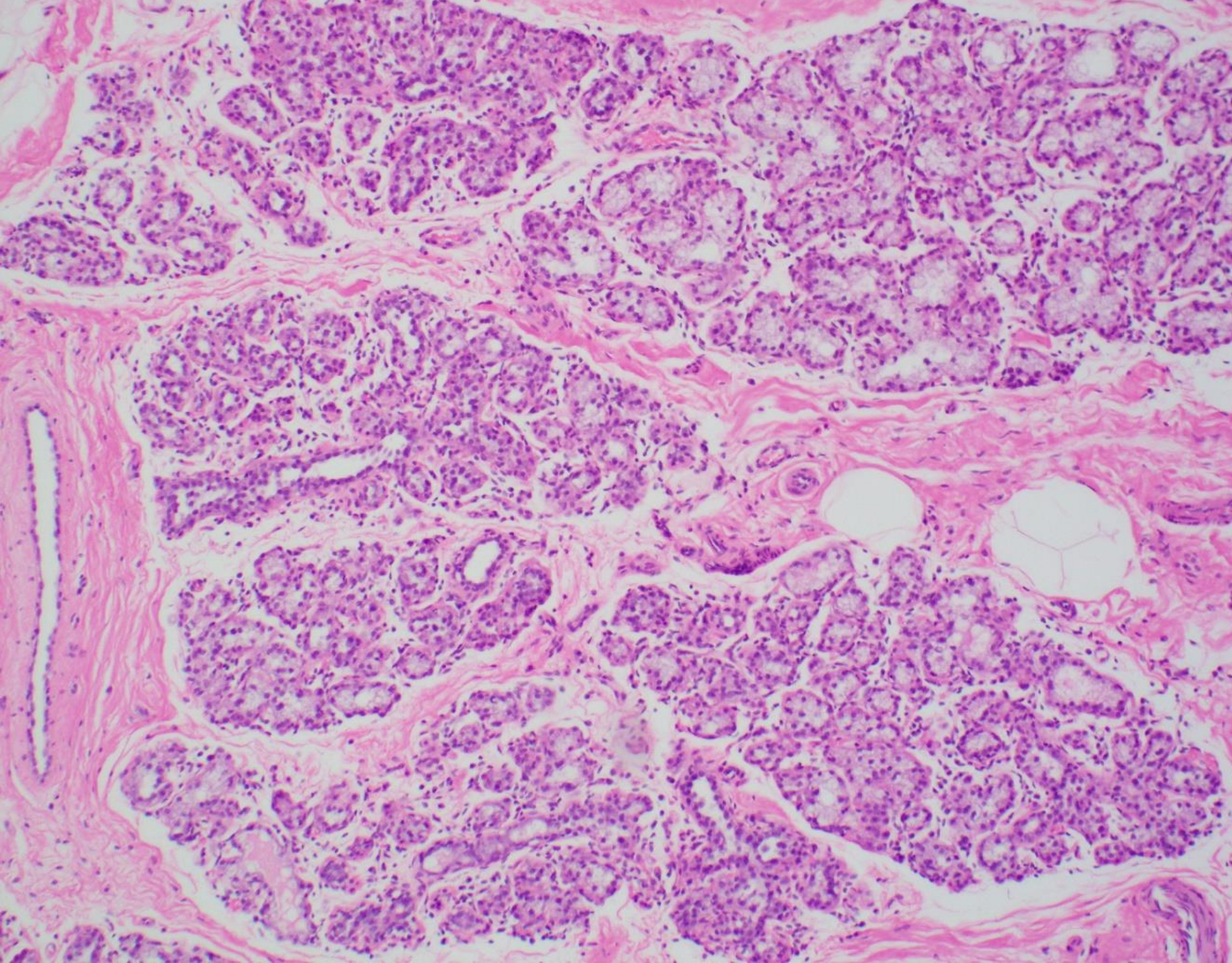
- Pregnancy related changes in breast start at time of first missed menstrual period (2nd - 4th week)
- Epithelial cells accumulate cytoplasmic organelles to sustain postpartum lactation
- Glands have dilated lumina and contain secretory vacuoles



Uninvolved lobule

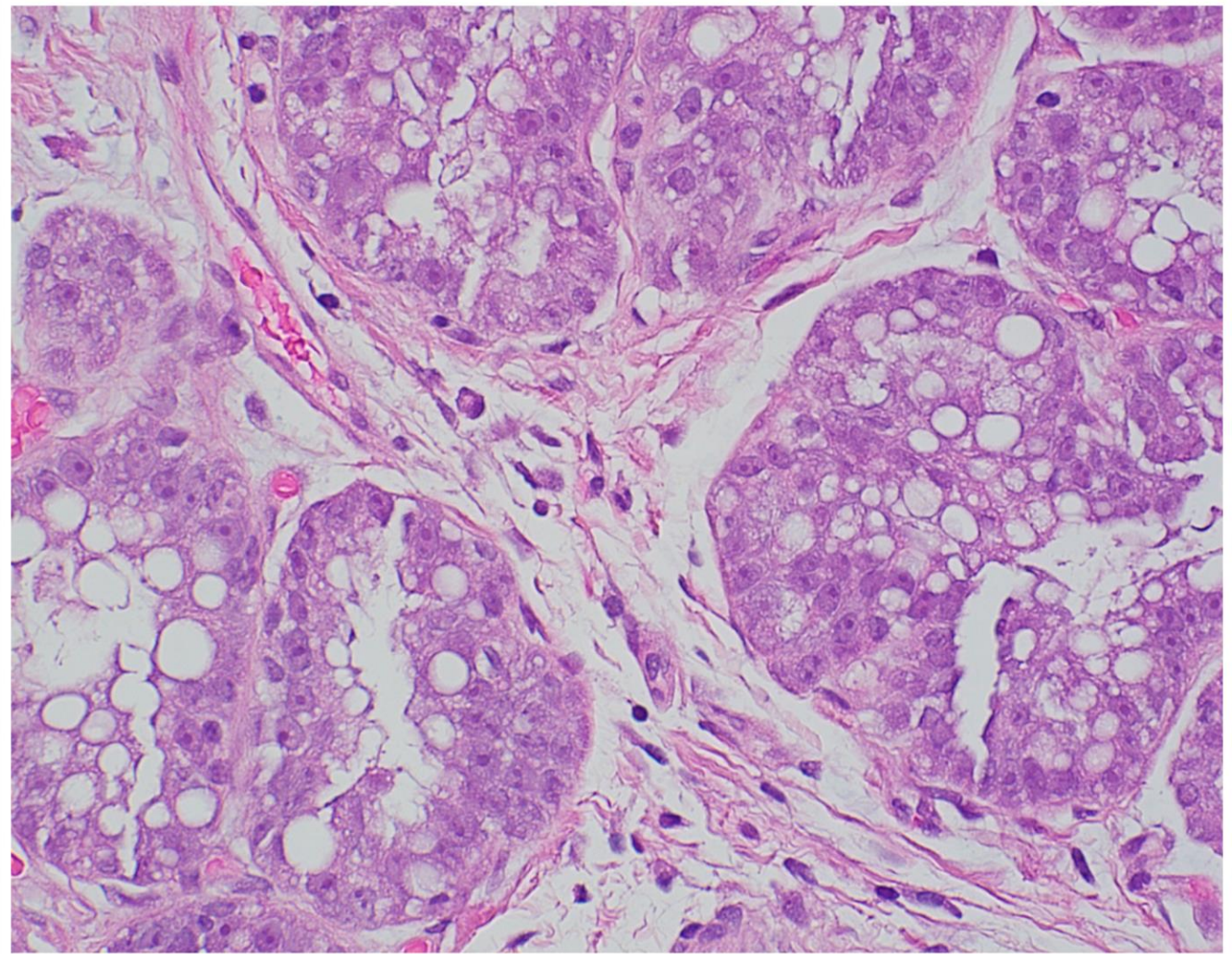
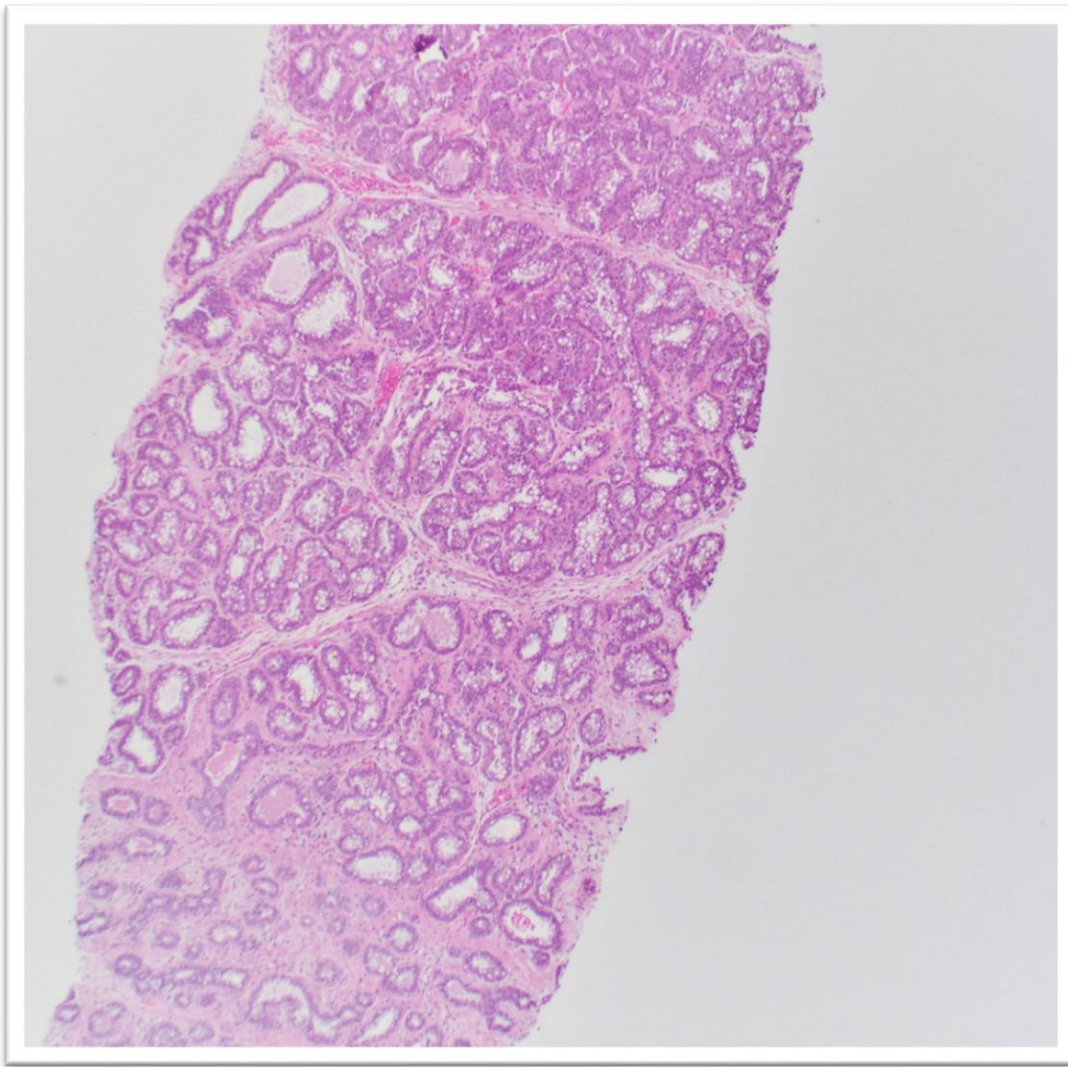


Lactational changes



Lactational changes are uneven throughout the breast and also involve ectopic breast tissue and pre-existing lesions

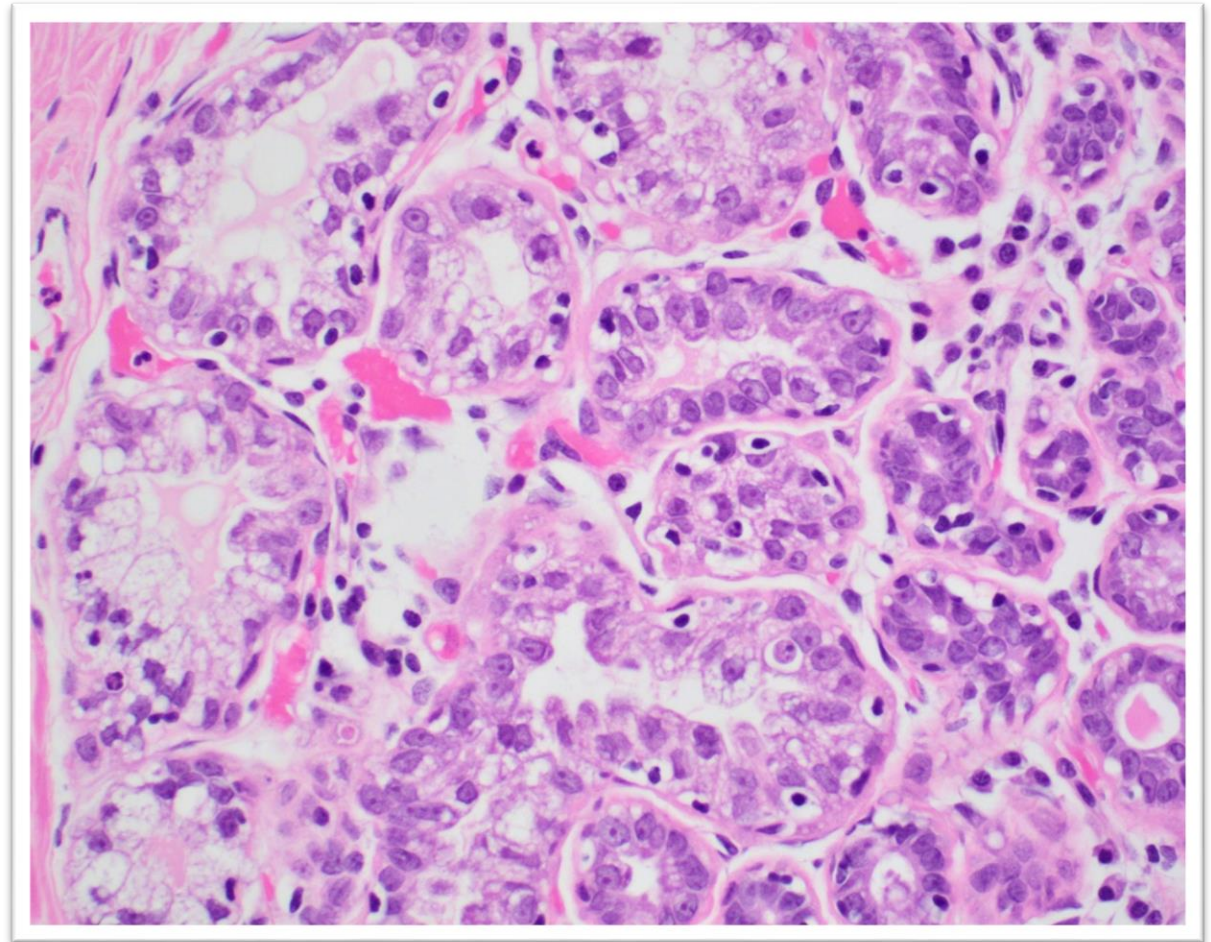
May show calcifications, often described as punctate on imaging (bilateral or unilateral)

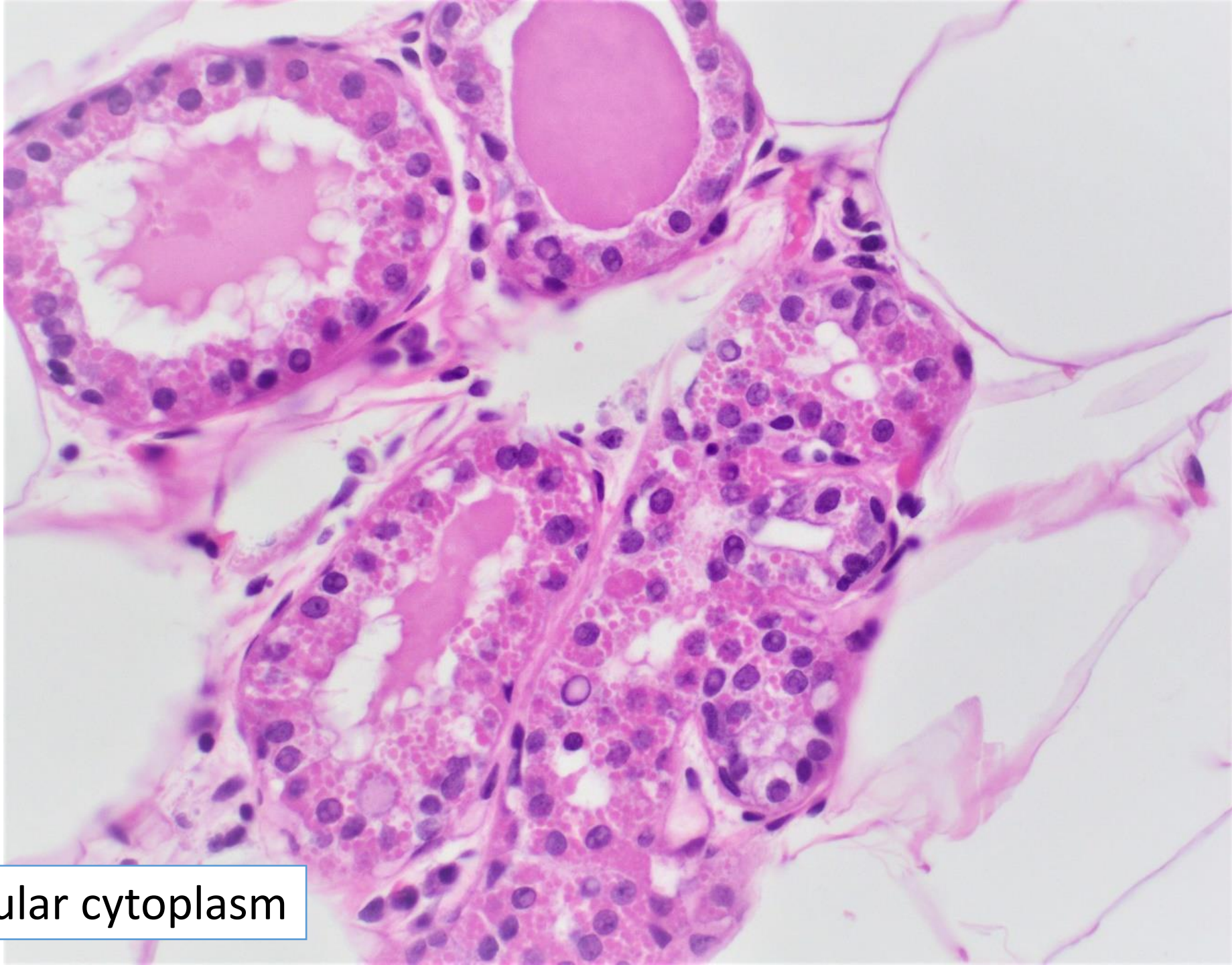


Lactating adenoma commonly occurs in the breast but can be found elsewhere along the milk line. It presents as painless slow growing mass in late pregnancy or early lactation. It usually regress spontaneously. Presence of atypia may be challenging to assess.

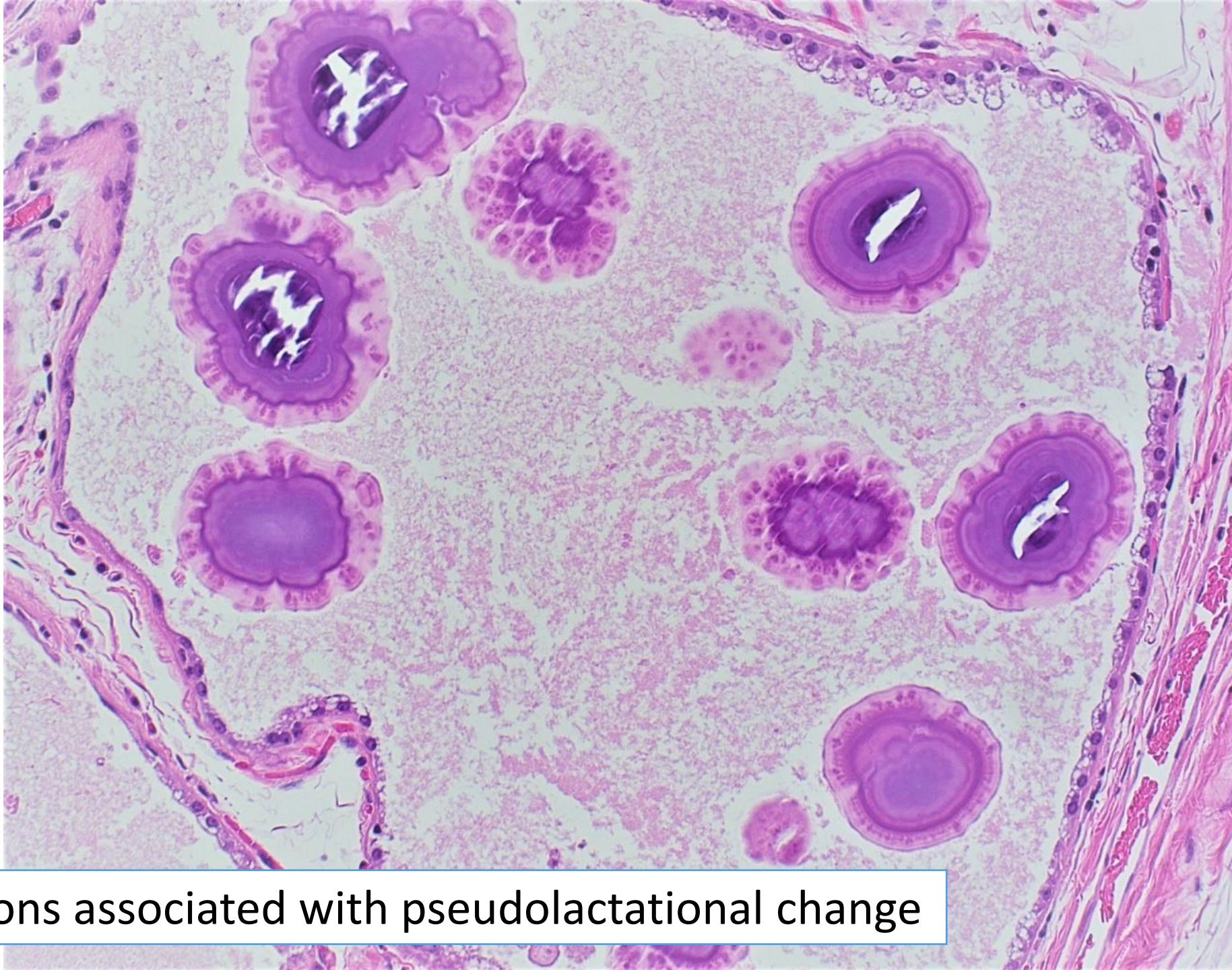
Pseudolactational change is very similar to lactational changes histologically

- Focal finding in 1.7% to 3% of specimens
- Pseudolactational changes occur in women who are not currently pregnant or lactating
 - May occur in nulliparous women
 - Hormonal, anti-psychotic, and anti-hypertensive medications may be associated





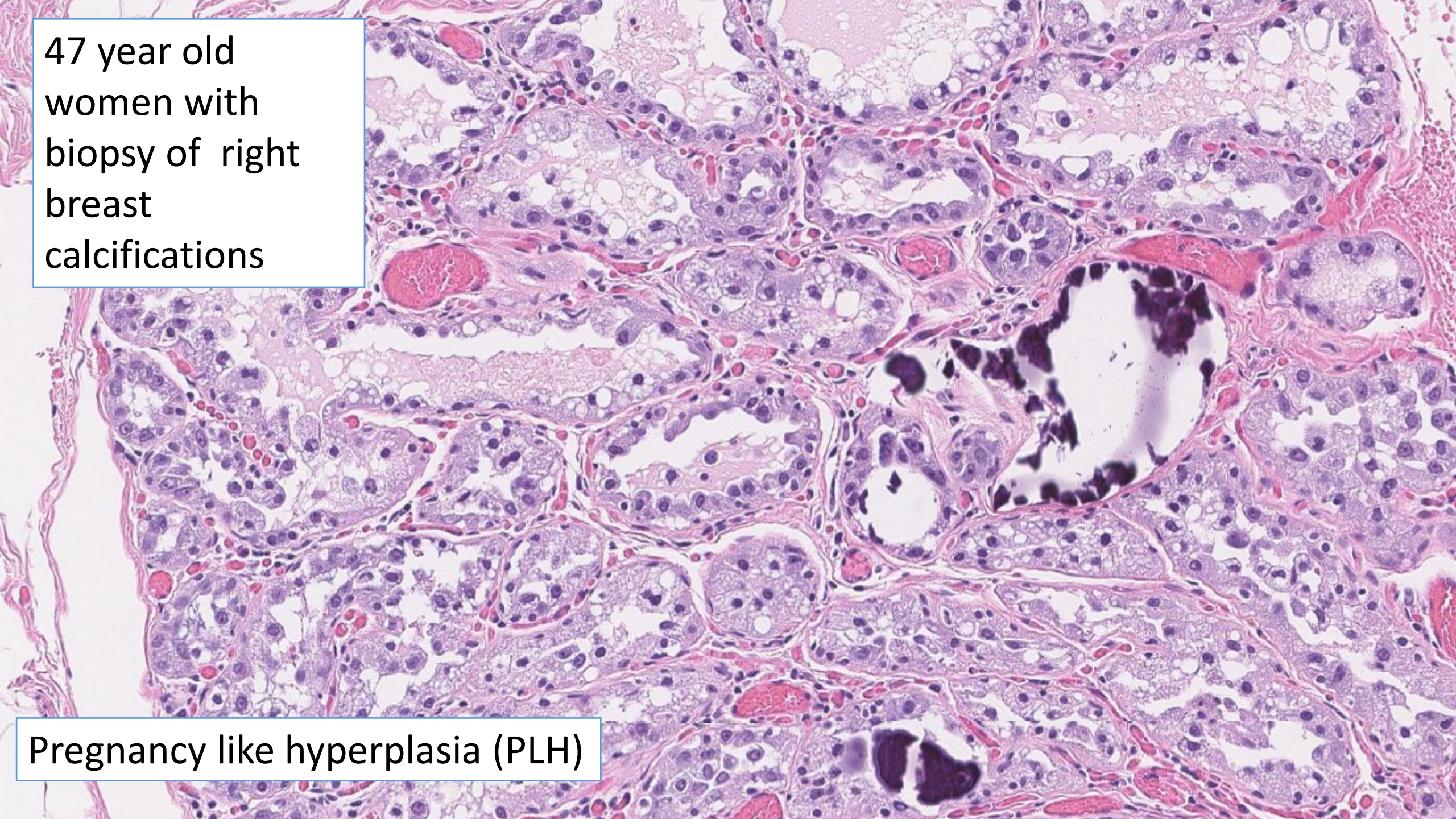
Pink granular cytoplasm

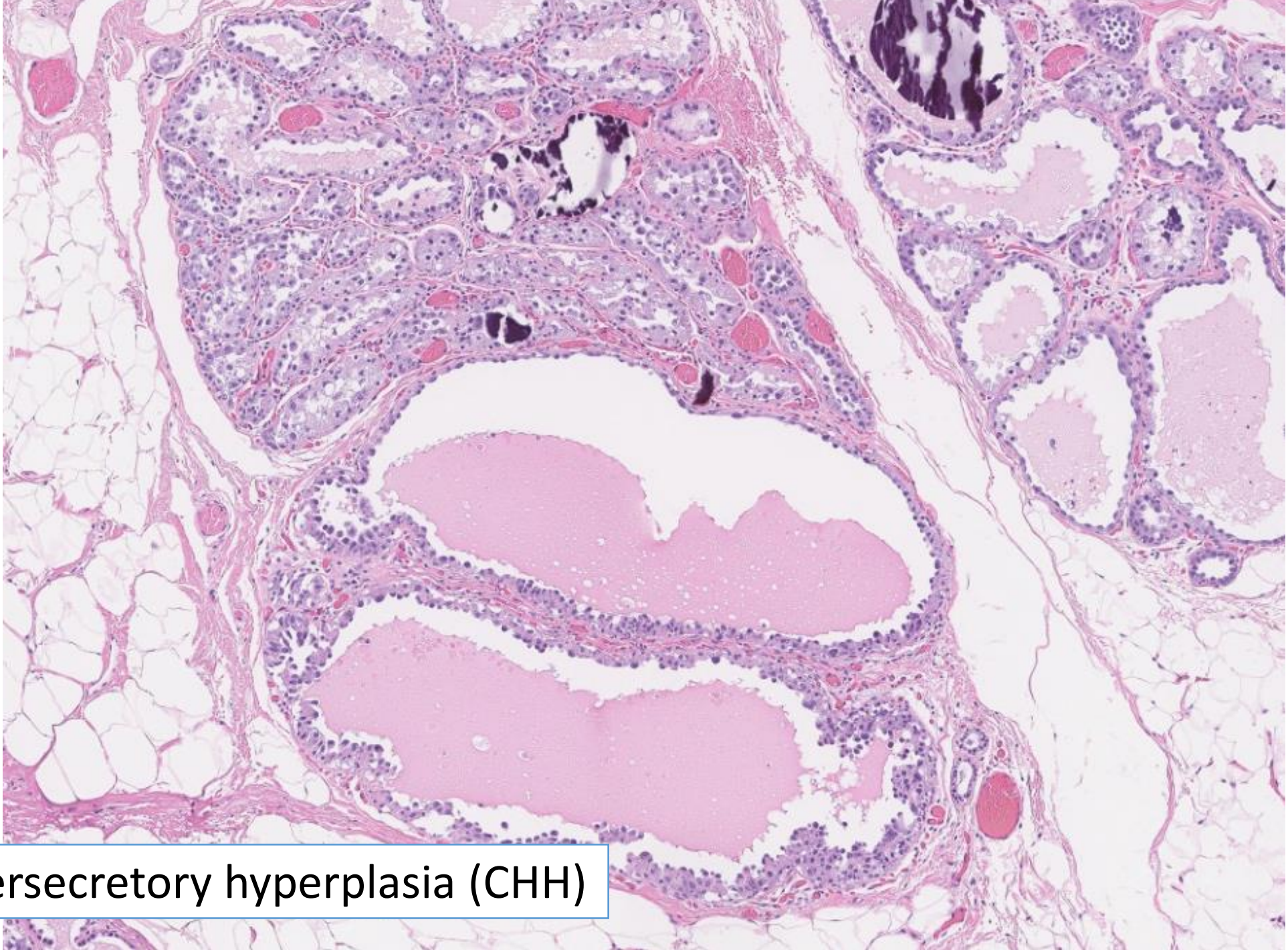


Calcifications associated with pseudolactational change

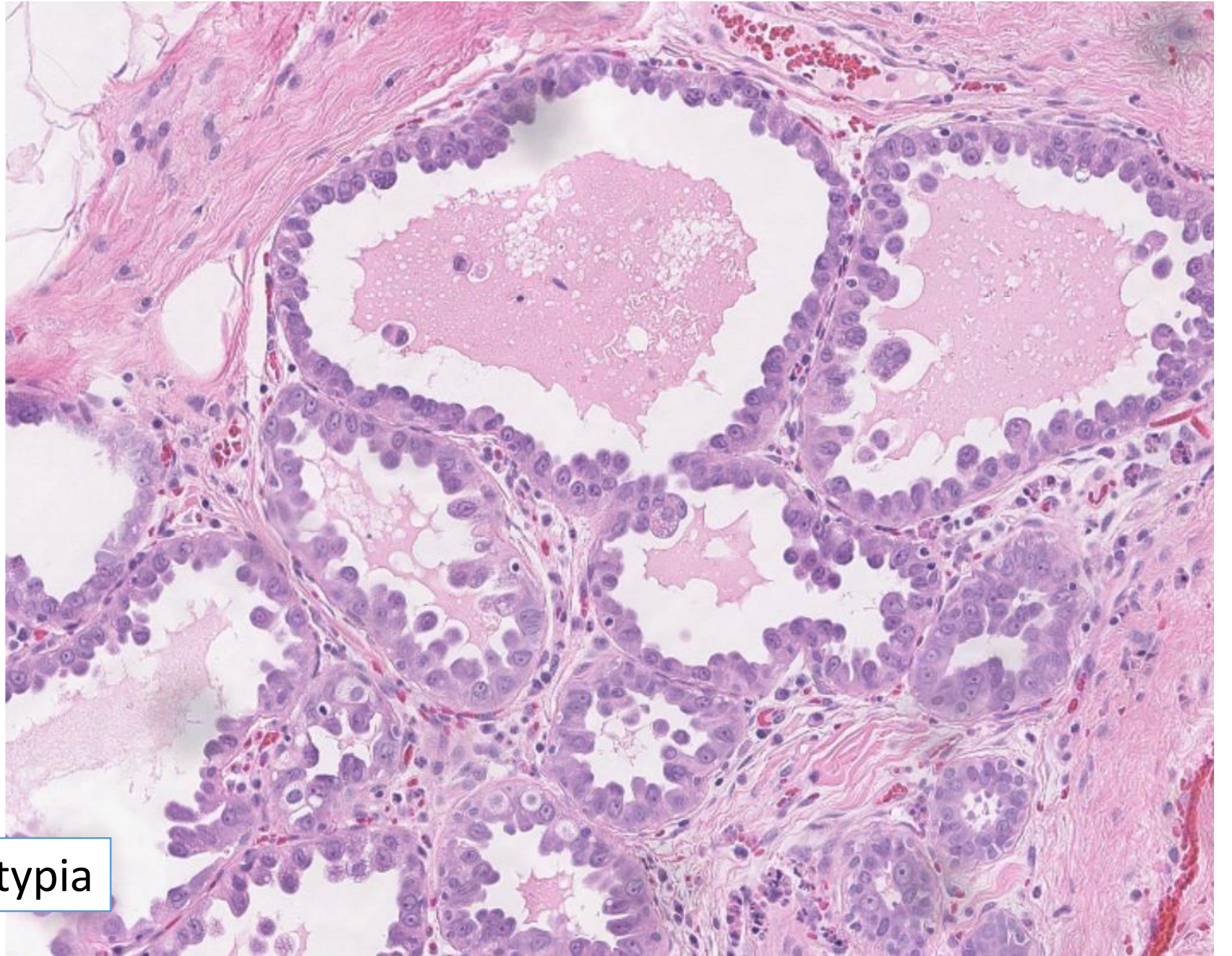
47 year old
women with
biopsy of right
breast
calcifications

Pregnancy like hyperplasia (PLH)

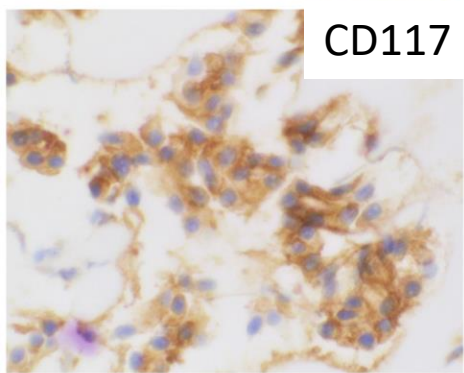
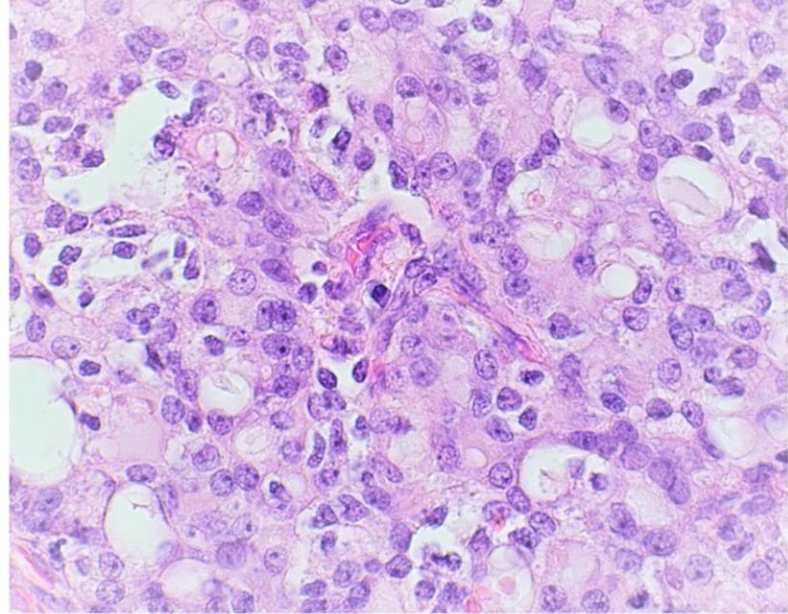




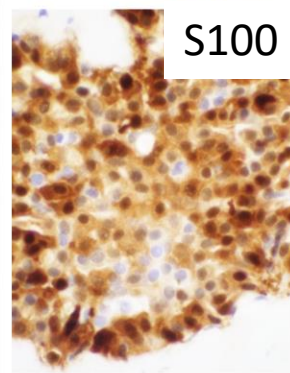
Cystic hypersecretory hyperplasia (CHH)



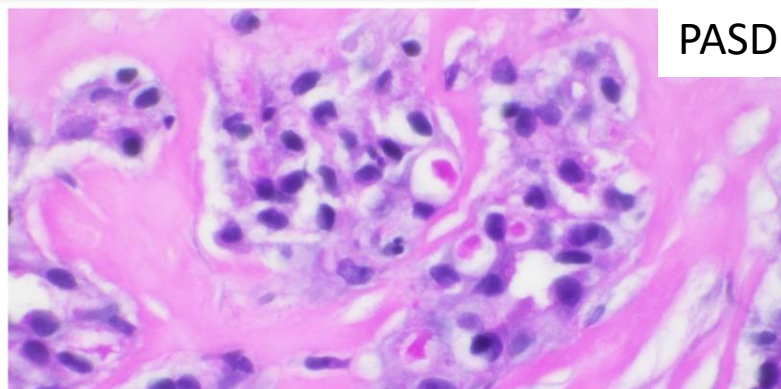
PLH, CHH with atypia



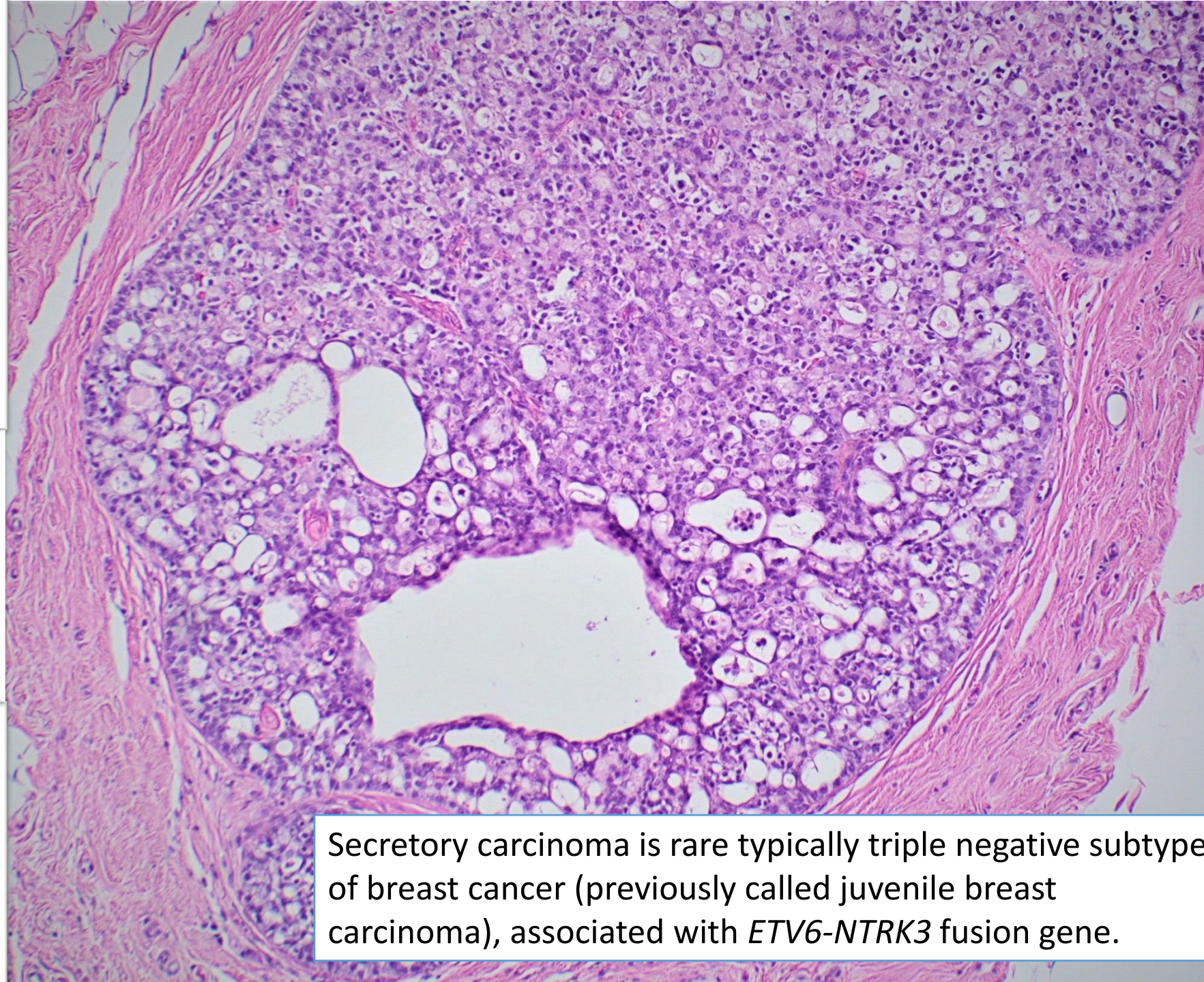
CD117



S100



PASD



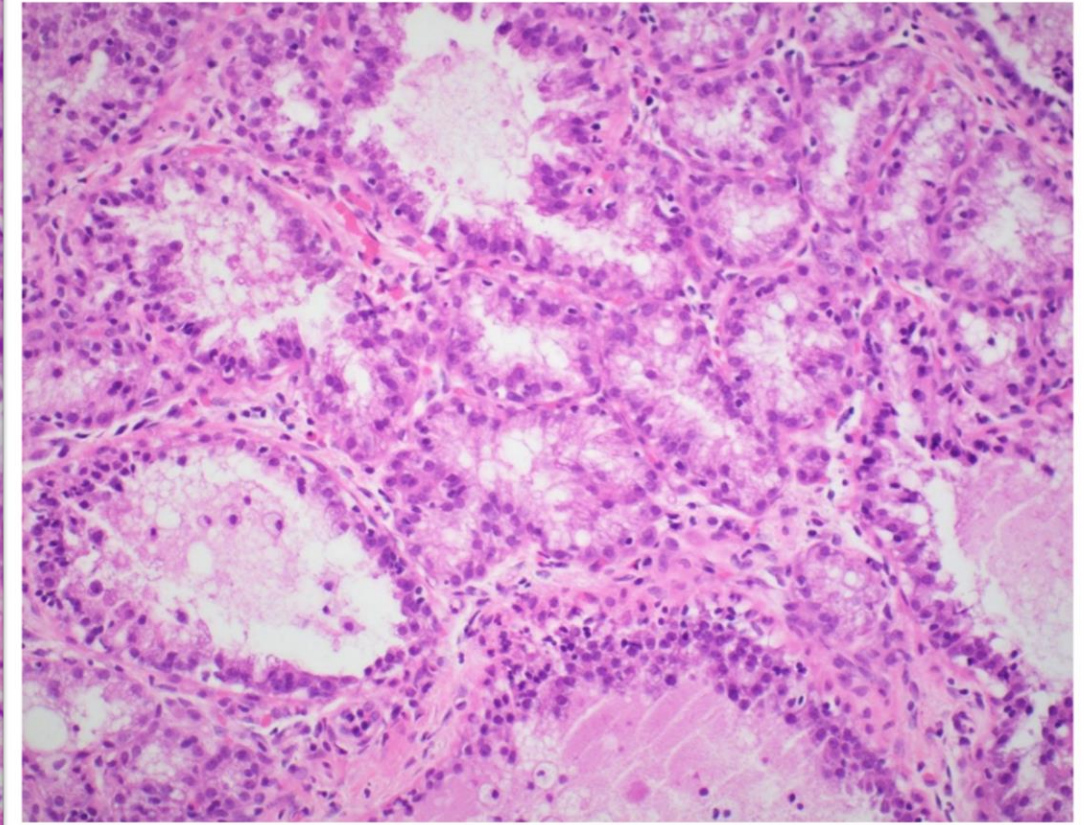
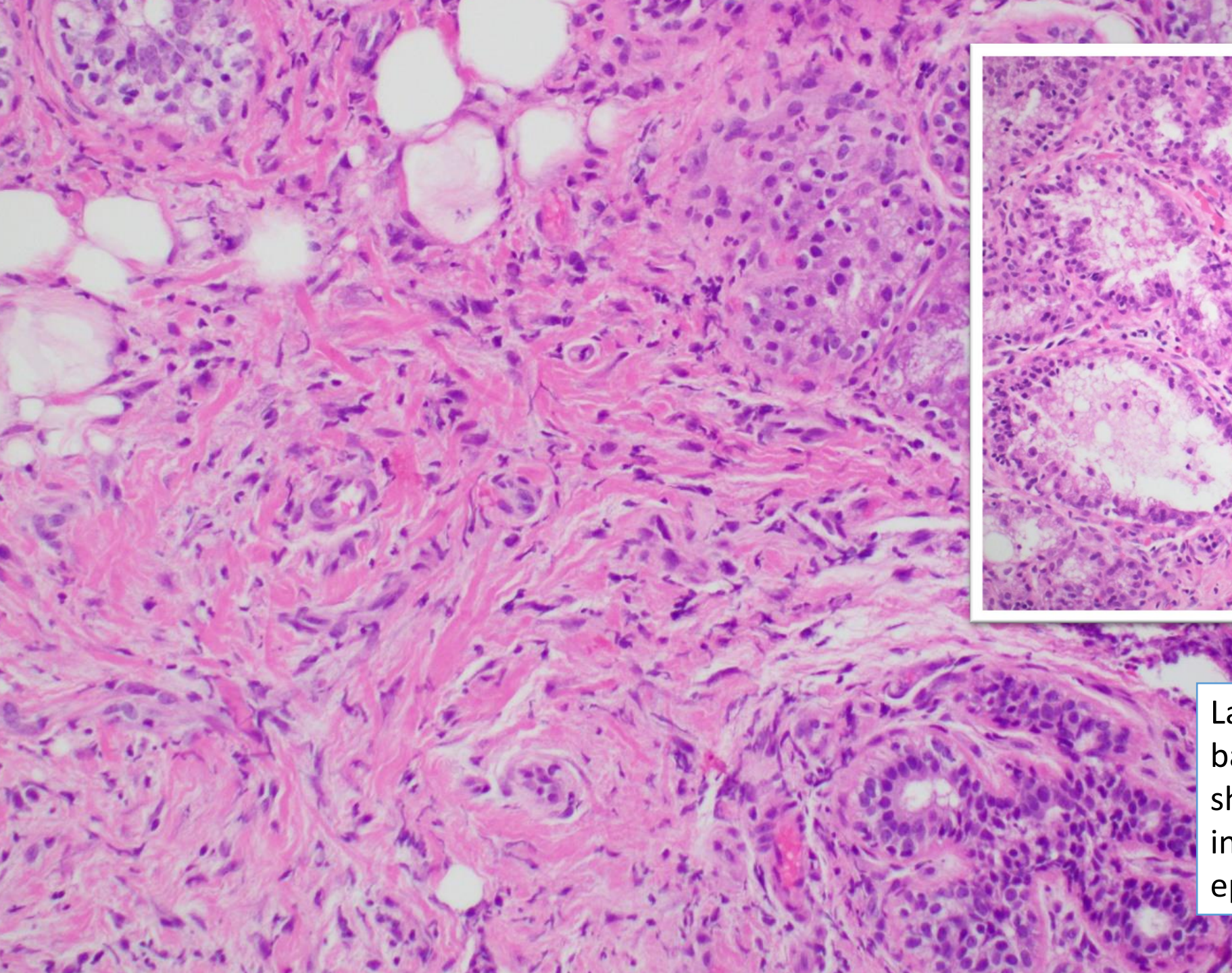
Secretory carcinoma is rare typically triple negative subtype of breast cancer (previously called juvenile breast carcinoma), associated with *ETV6-NTRK3* fusion gene.

Case presentations with differential considerations

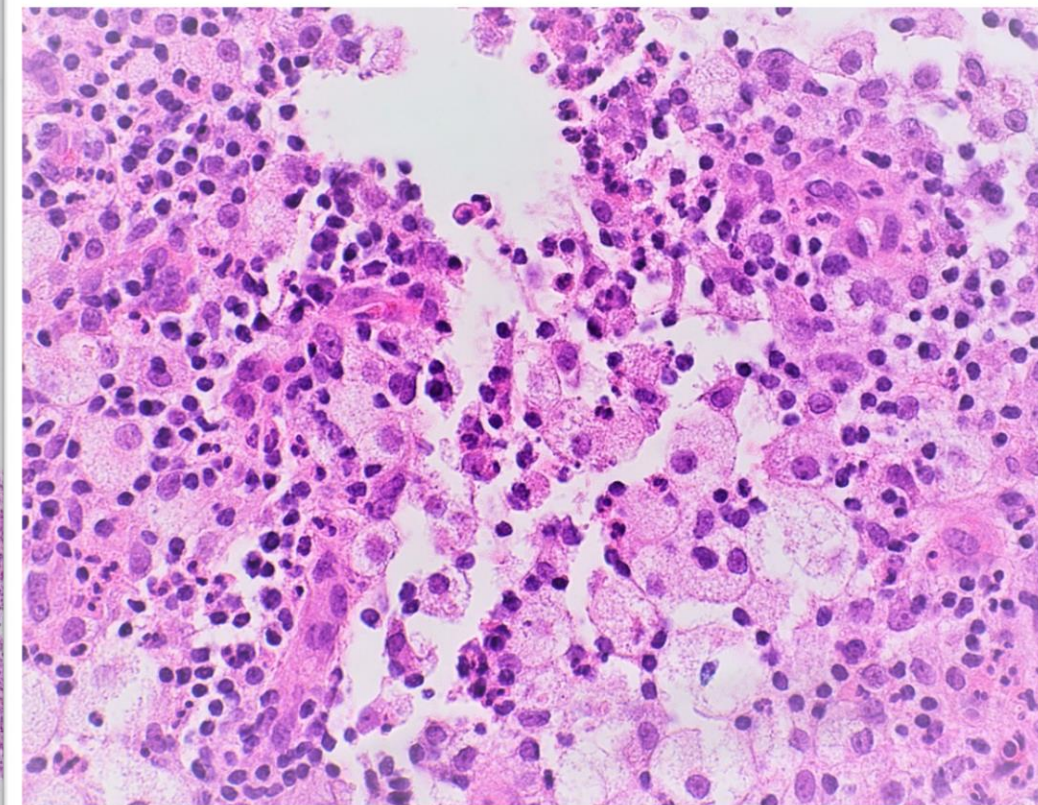
Three cases

Case 1. 32 year old female, 3 months postpartum, currently breastfeeding

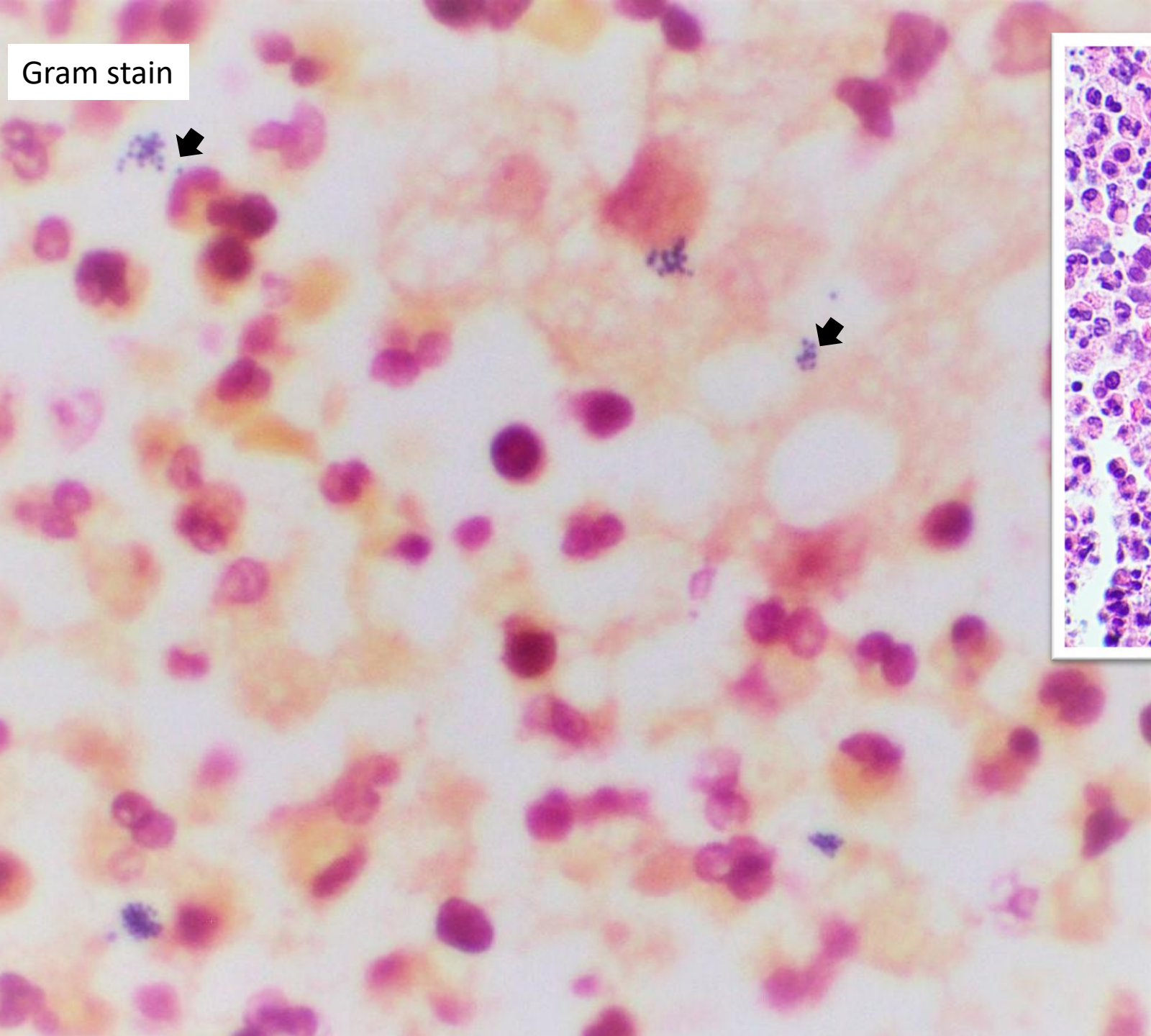
- Past medical history of lupus
- History of present illness:
 - Patient developed mastitis 1 month post partum, the infection cleared but she was left with a lump, she developed mastitis 2 more times and took antibiotics
 - Although the infection appeared to clear the lump got bigger and more painful each time
 - Imaging showed right breast with multiple round masses with an aggregate measurement of 6.2 cm, thickening of the overlying skin and multiple punctate calcifications
- Biopsy was performed



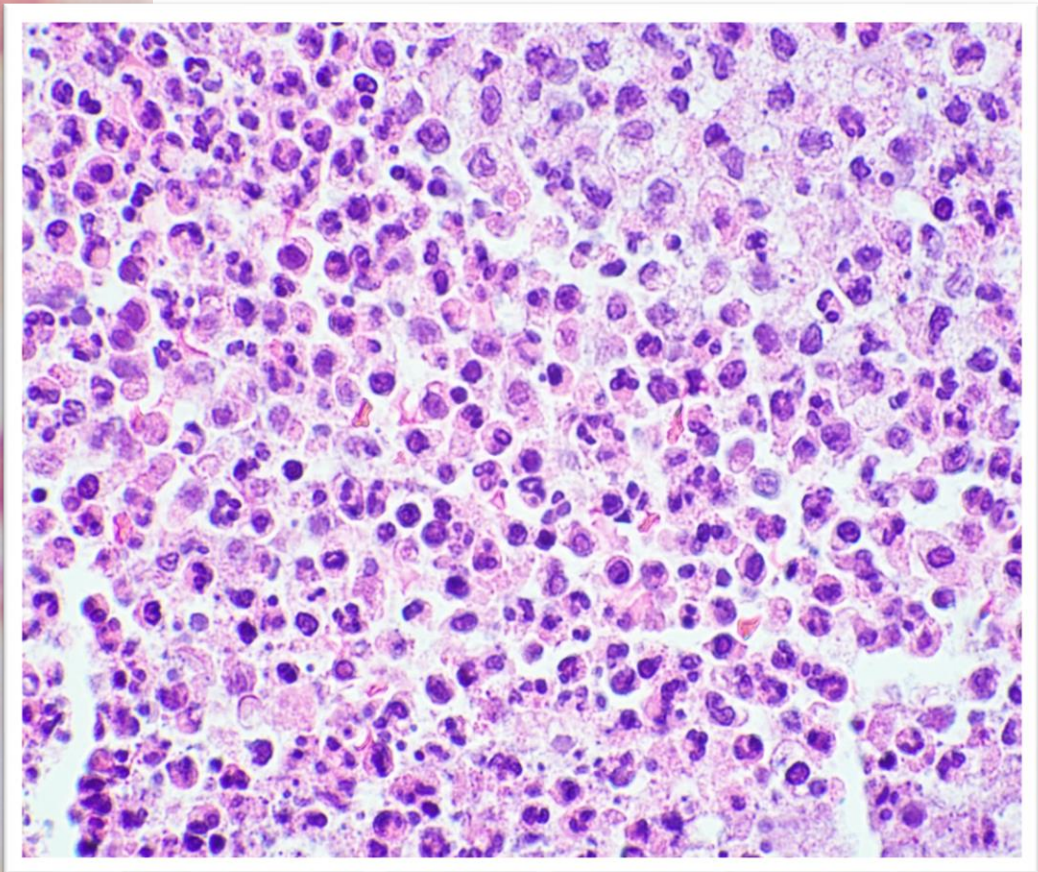
Lactational changes in the background epithelium showing infiltrating inflammatory cells without epithelial atypia



Prominent acute and chronic inflammation with abscess formation



Gram stain



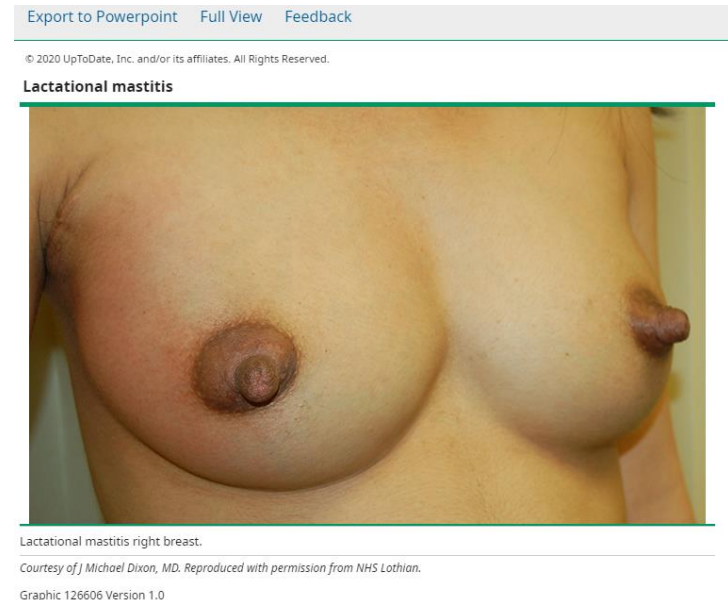
The performed GMS and AFB stains were negative

Case follow up

- Biopsy diagnosis:
 - Acute mastitis with abscess formation
 - No atypia or malignancy identified
- The patient was referred for surgical management
- Microbiologic work-up:
 - Aerobic wound cultures grew *Staphylococcus aureus*
 - Clindamycin and erythromycin and penicillin resistant
 - Anaerobic, acid fast bacillus and fungal cultures were negative
- Follow up of 5 months showed no recurrences after treatment

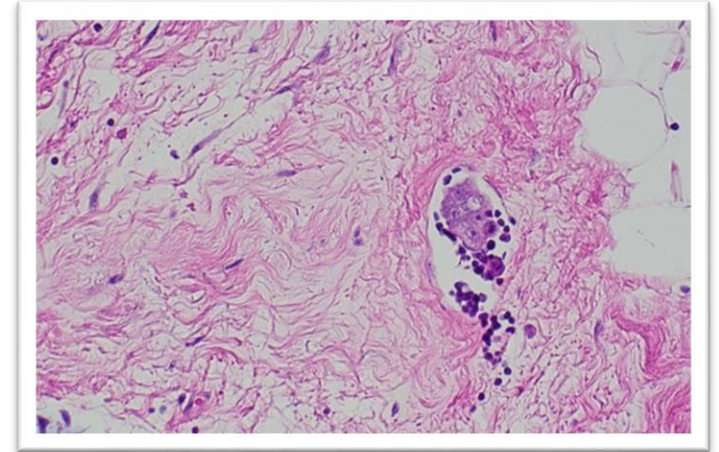
Lactational mastitis

- Typical presentation is a sudden onset breast pain and erythema usually unilateral and localized to a specific quadrant of the breast
 - Flu like symptoms, headache, fatigue, fever, tachycardia
- Frequency:
 - Common during lactation (about 1 to 33% of women)
 - Only 1-3% develop an abscess
- Risk factors:
 - Diabetes mellitus
 - Galactostasis
 - Nipple injury
 - Primiparous presentation



Inflammatory breast cancer is on the differential diagnosis for lactational mastitis

- Breast cancer is in the differential if mastitis does not resolve with appropriate treatment
- Inflammatory type of breast cancer shows redness or bruising, swelling, itchiness and unusual tenderness in one breast
- It typically does not produce a noticeable lump



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Inflammatory breast cancer



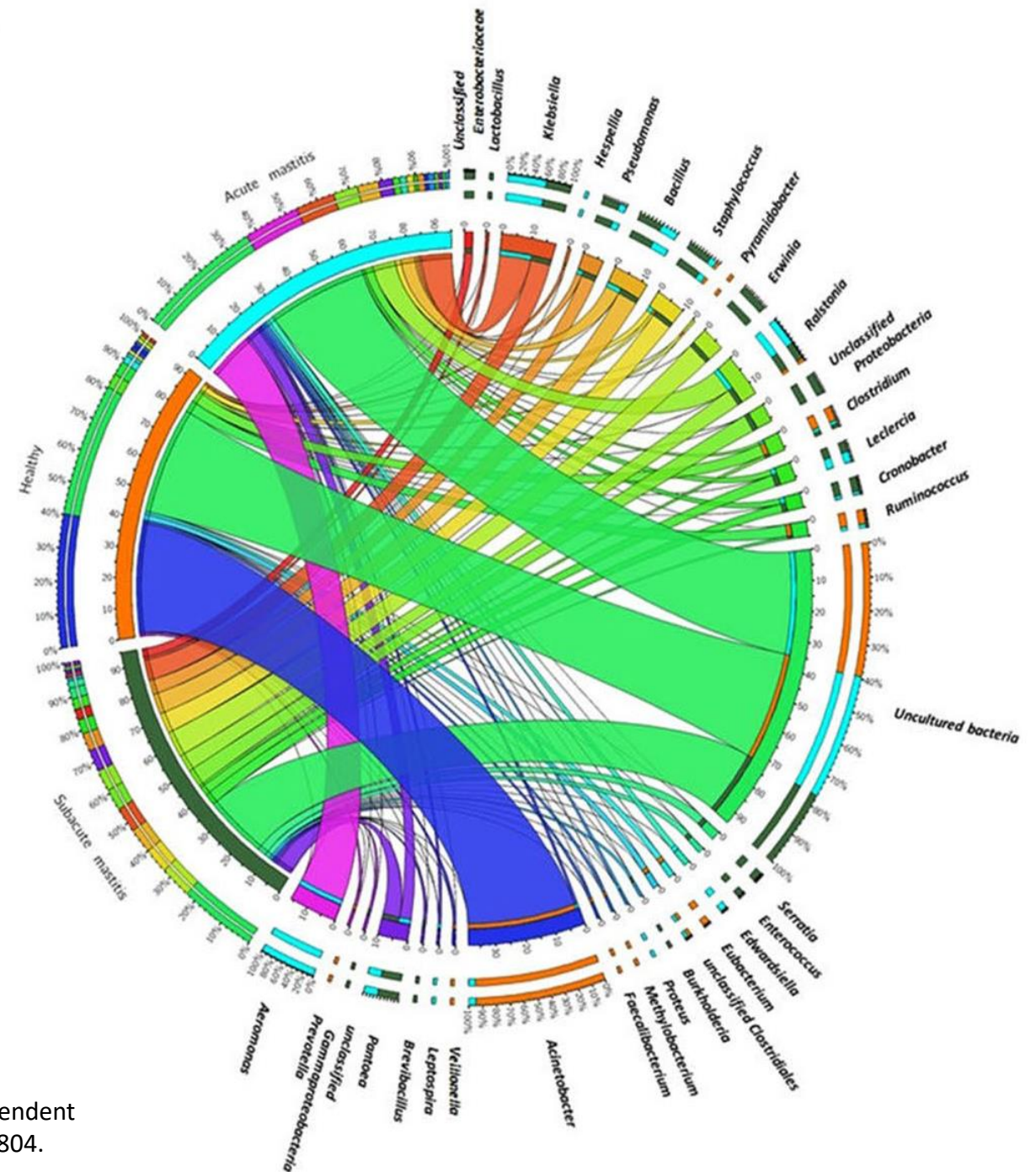
It is important to rule out inflammatory breast cancer if a suspected breast infection does not respond to antibiotics.

Courtesy of Michael J Dixon, MD.

Graphic 65383 Version 3.0

Implicated infectious organisms in lactating women

- Acute mastitis is most often associated with *Staphylococcus aureus* species infections
- *Staphylococcus epidermidis* being the dominant species in the microbiome of women diagnosed with subacute mastitis
- Circos plot of the top most abundant bacterial genera from healthy milk samples and from subacute and acute mastitis milk samples



Treatment and role of imaging

Management of lactational mastitis consists of symptomatic treatment to reduce pain and swelling (nonsteroidal inflammatory agents, cold compresses) and complete emptying of the breast



Management of infective lactational mastitis (lactational mastitis with persistent symptoms beyond 12 to 24 hours, with fever) consists of the above measures in addition to administration of antibiotic therapy with activity against *S. aureus*



If there is no clinical improvement within 48 to 72 hours, evaluation with ultrasound imaging to determine if there is an underlying abscess should be pursued

Imaging of breast abscesses

- Ultrasonographic guidance in abscess drainage
- Sonographic appearance of abscess demonstrate irregular hypoechoic mass or cyst, fluid level and internal echogenic debris
 - Galactoceles can have similar appearance on imaging but there are no clinical symptoms of infection such as pain or redness
 - Differential diagnosis also includes neoplasms, biopsy may be indicated to exclude that

Lactating breast abscess with skin compromise

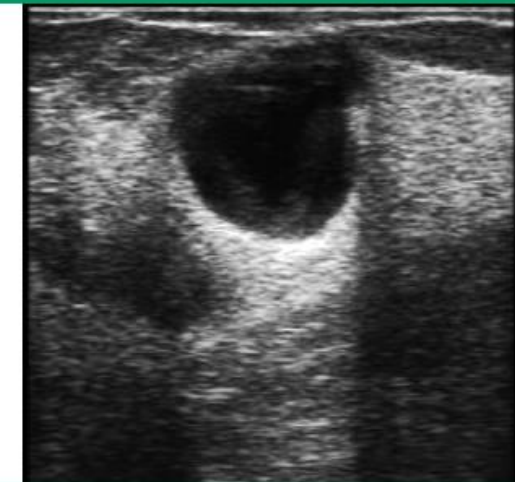


When the overlying skin is thinned or necrotic, the best procedure is incision and drainage.

Courtesy of Michael J Dixon, MD.

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Ultrasound appearance of a breast abscess



This image shows an abscess in the breast using ultrasound.

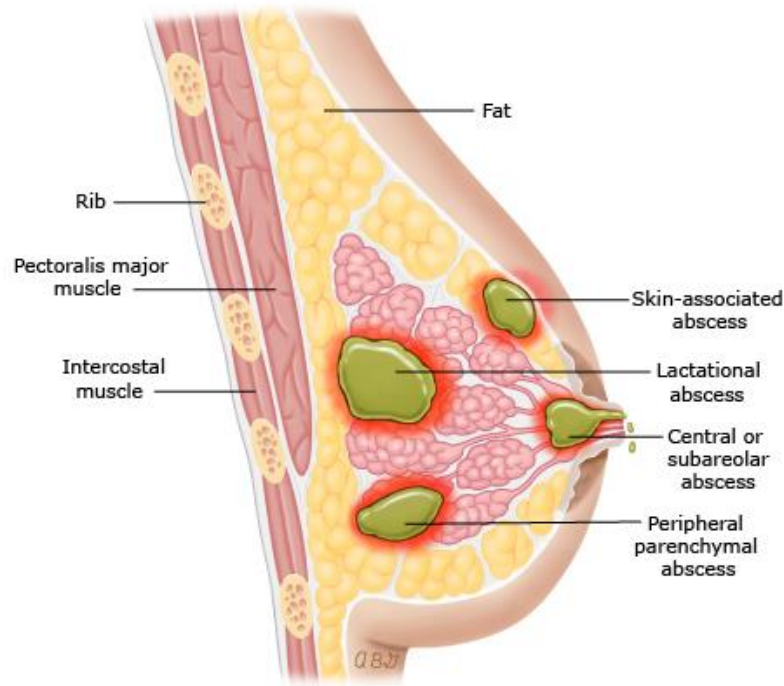
Courtesy of Michael J Dixon, MD.

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There are lactational and nonlactational breast abscesses

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Common sites and types of breast infection



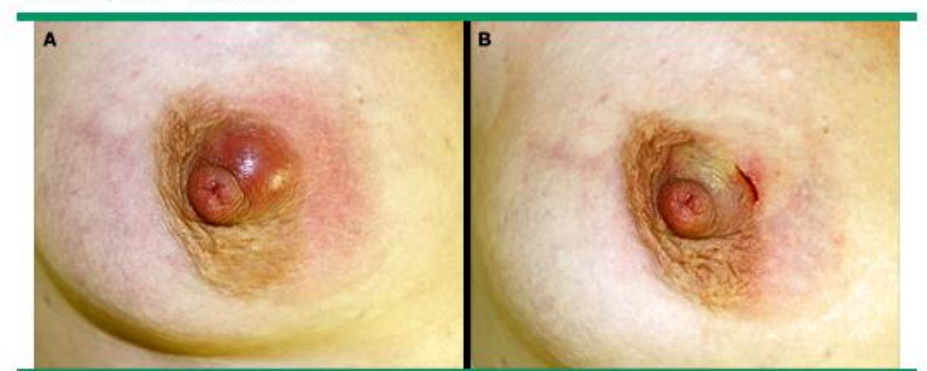
Mastitis refers to inflammation of the breast tissue that may or may not be accompanied by infection. This drawing depicts the most common types and locations of breast infections.

Graphic 68275 Version 2.0

- Only about 14% of primary breast abscesses are lactational [*World J Surg.* 2009 December ; 33(12): 2582–2586]
- Lactational abscesses are not usually at the nipple
- Non-lactational breast abscesses:
 - Breast abscess that occurs in a woman who is not pregnant or breastfeeding
 - Skin associated
 - Peripheral (away from the nipple)
 - Idiopathic granulomatous mastitis
 - Central (near or behind the nipple)
 - Periductal mastitis

Periductal mastitis or squamous metaplasia of lactiferous ducts (SMOLD)

Periareolar abscess

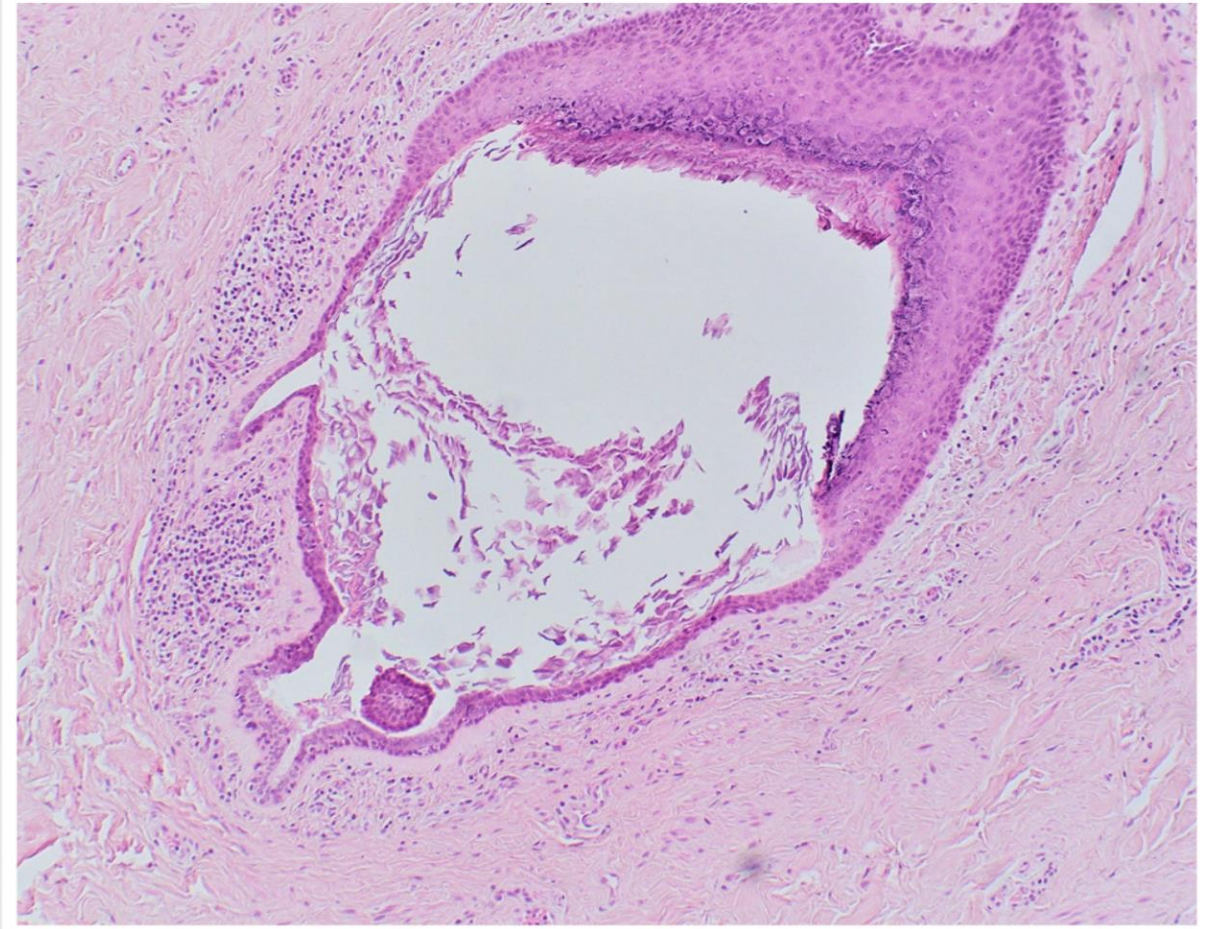


Periareolar abscess. Large incisions are not necessary for the drainage of a breast abscess.

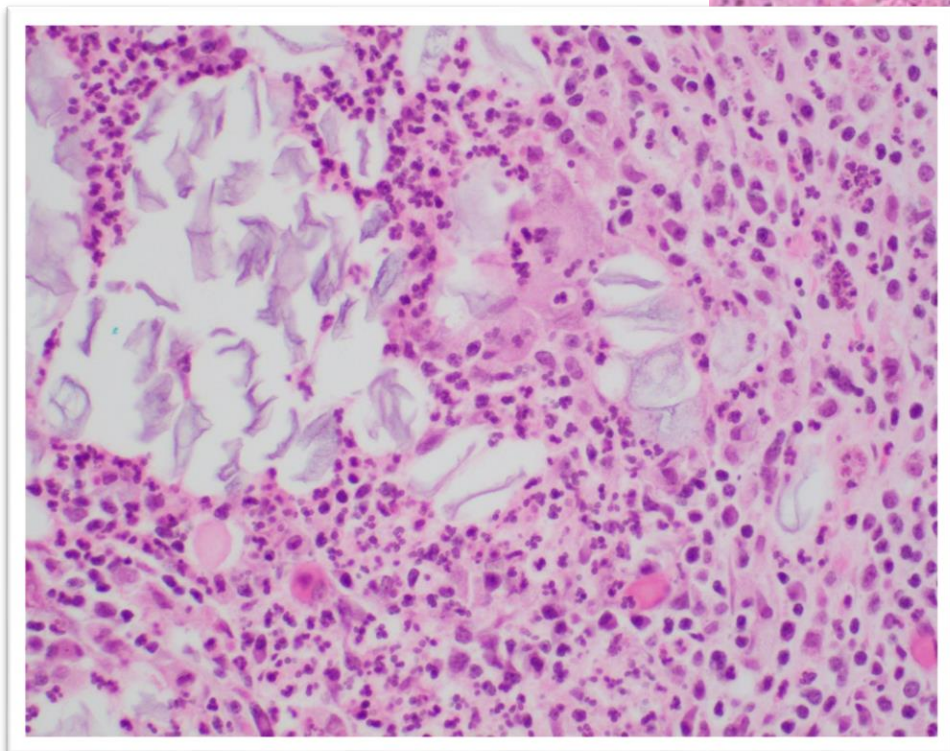
Courtesy of Michael J Dixon, MD.

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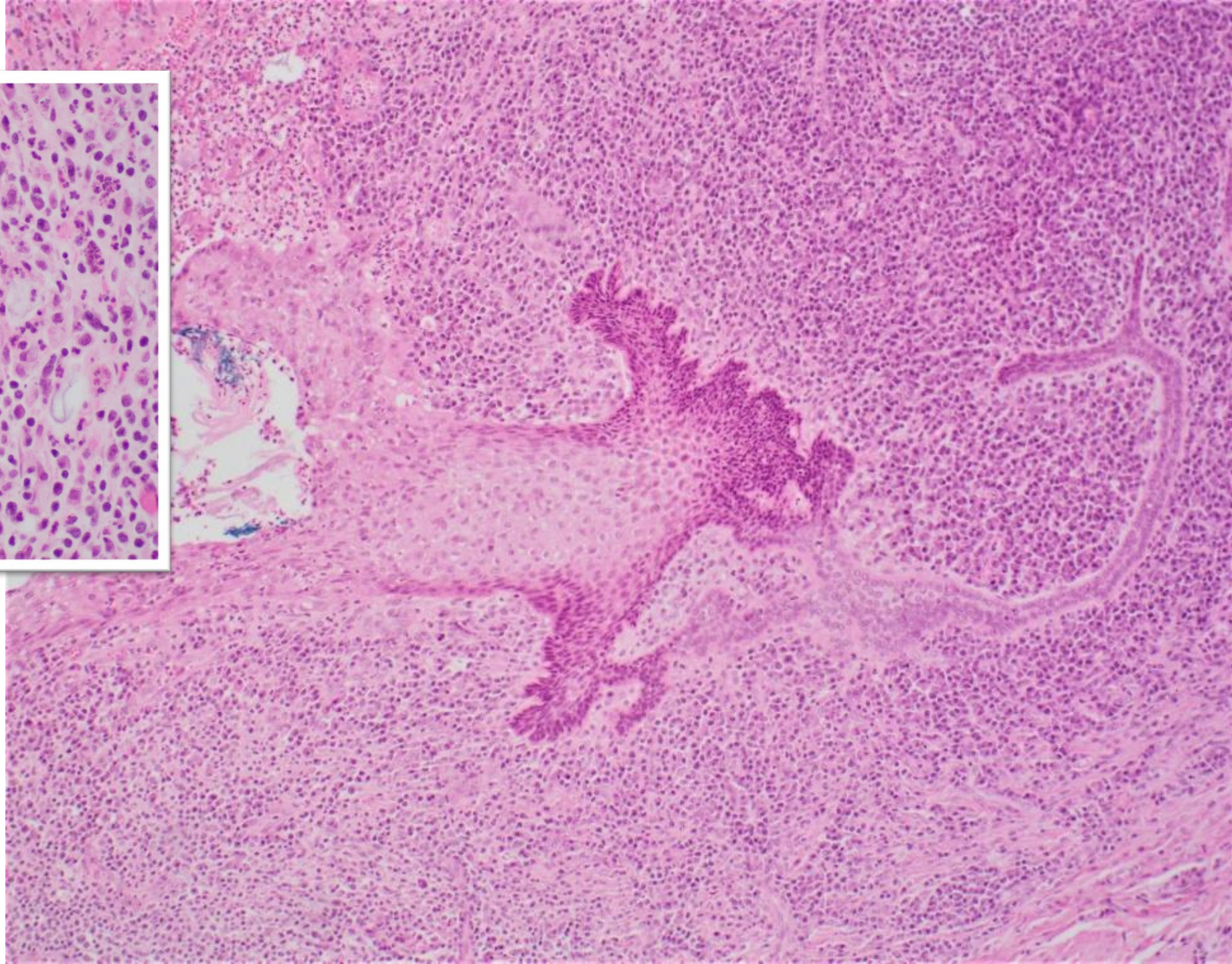
- Women or men, wide age range
- Patients usually present with painful erythematous subareolar mass, abscess or fistula
 - Clinically mistaken for recurrent abscess after multiple ineffective treatments with incision, drainage and antibiotics
 - Can have secondary bacterial infection
- Strongly associated with **smoking**
- Treatment: surgical excision of affected duct, smoking cessation



Keratin plug blocking lactiferous ducts
Periductal inflammation



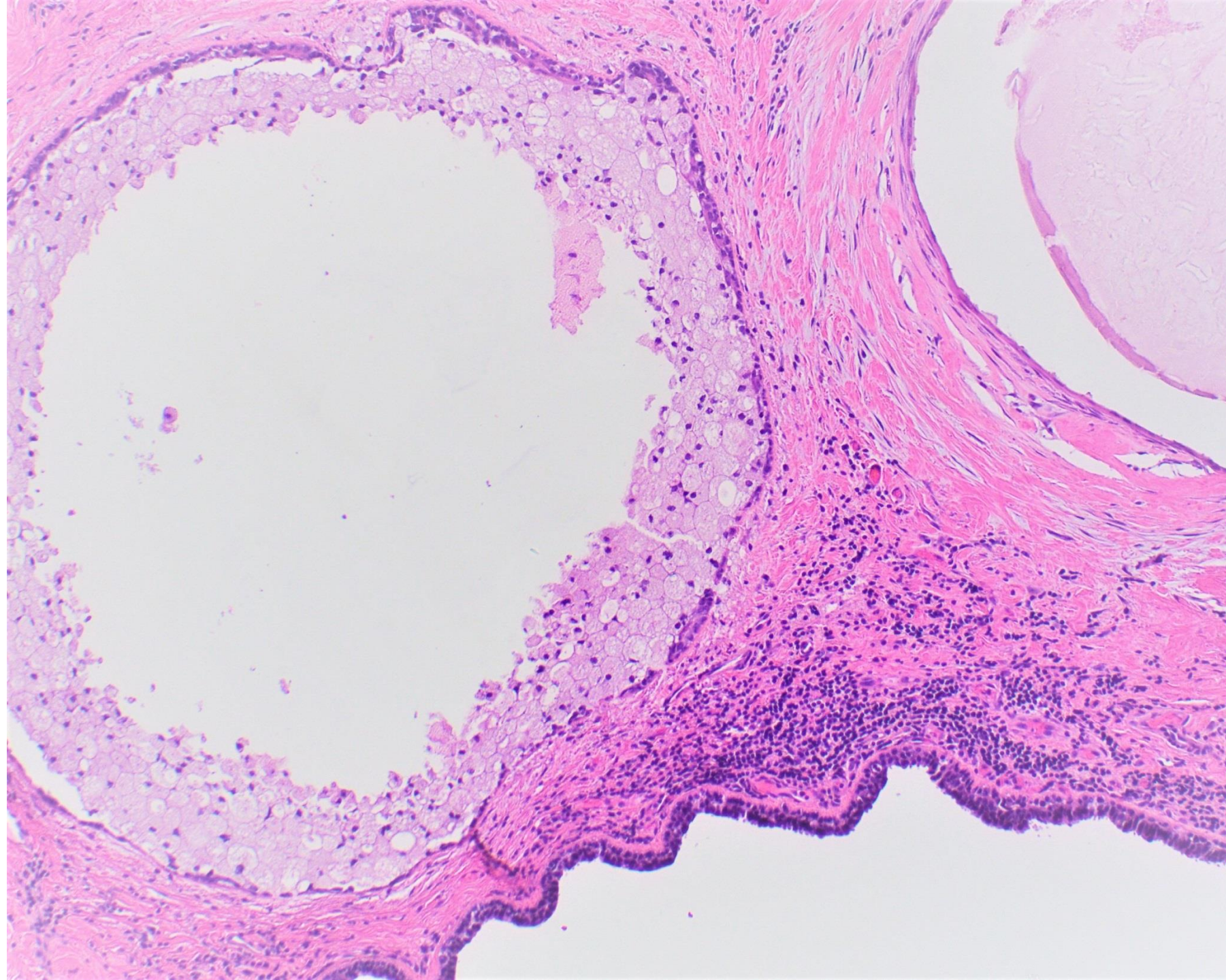
- Duct rupture and inflammation
- Abscess formation

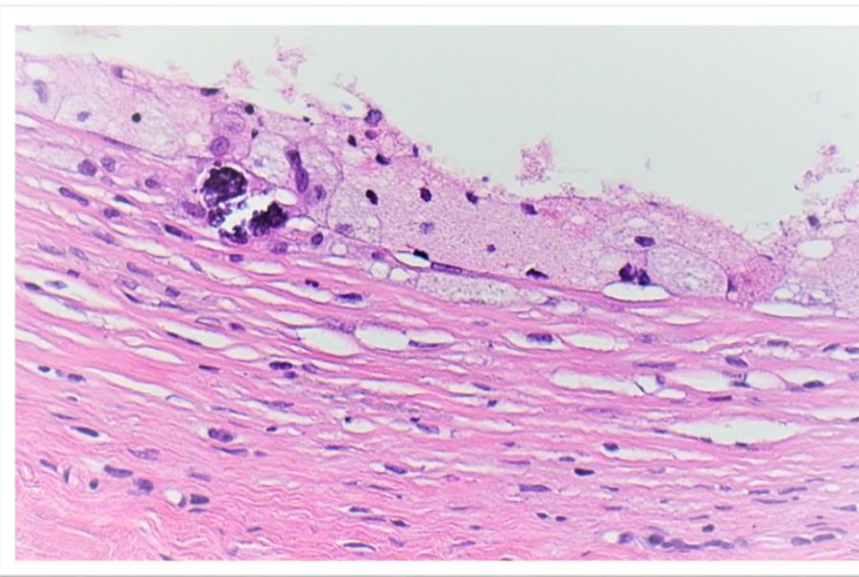
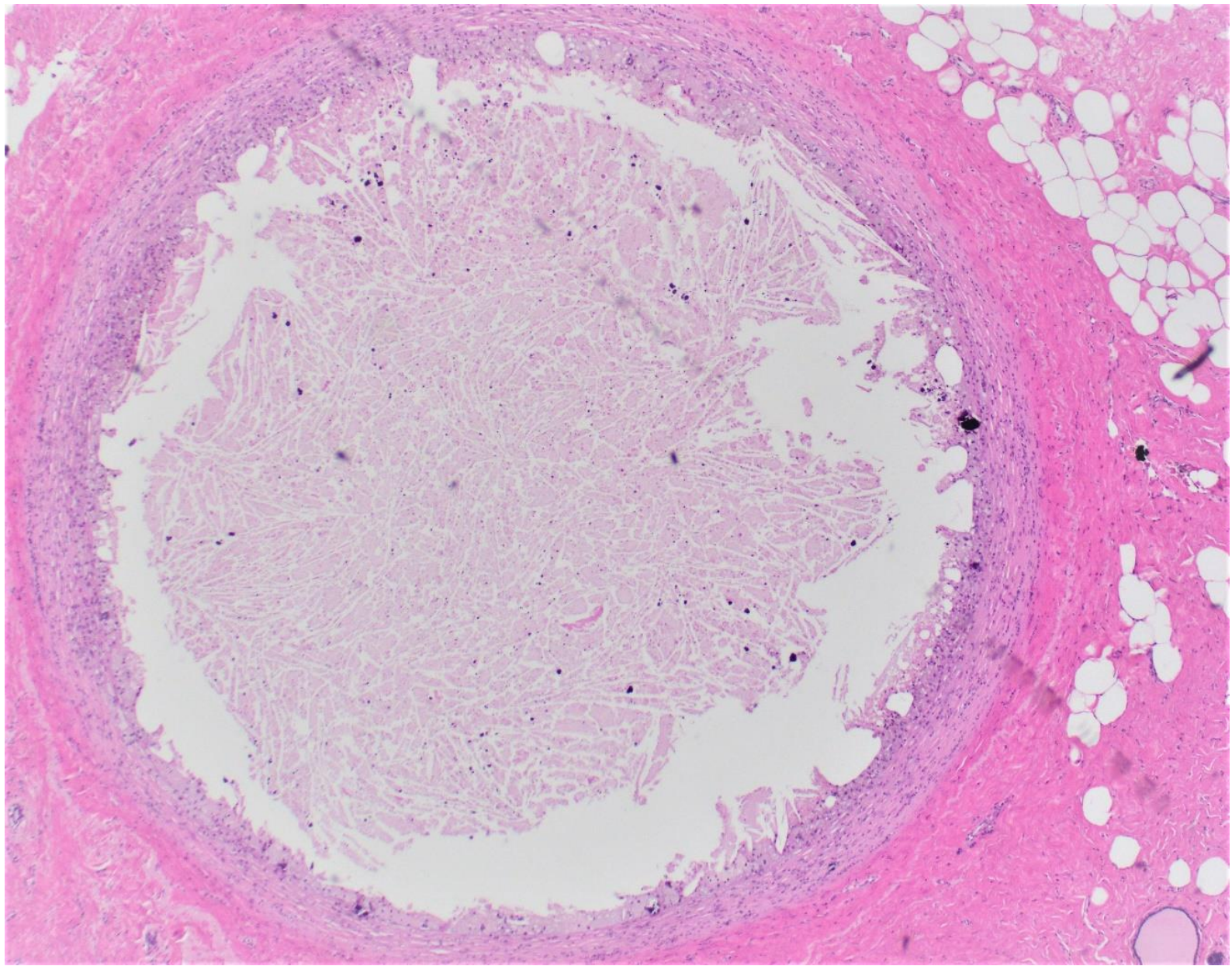


What is the difference between SMOLD and duct ectasia?

- Duct ectasia usually occurs in perimenopausal and postmenopausal women
- Involves extralobular and retroareolar ducts, and can be bilateral
- Symptoms:
 - Pain, nipple discharge, inversion or mass
 - Frequently asymptomatic
- Etiology: Not well understood but some believe that it may be related to stasis, atrophy, inflammation and duct obstruction

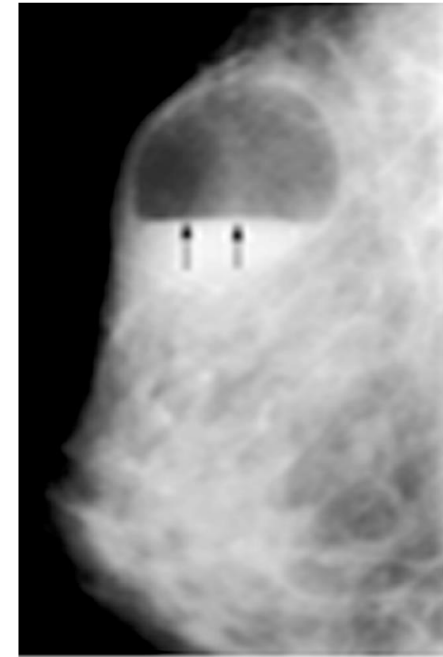
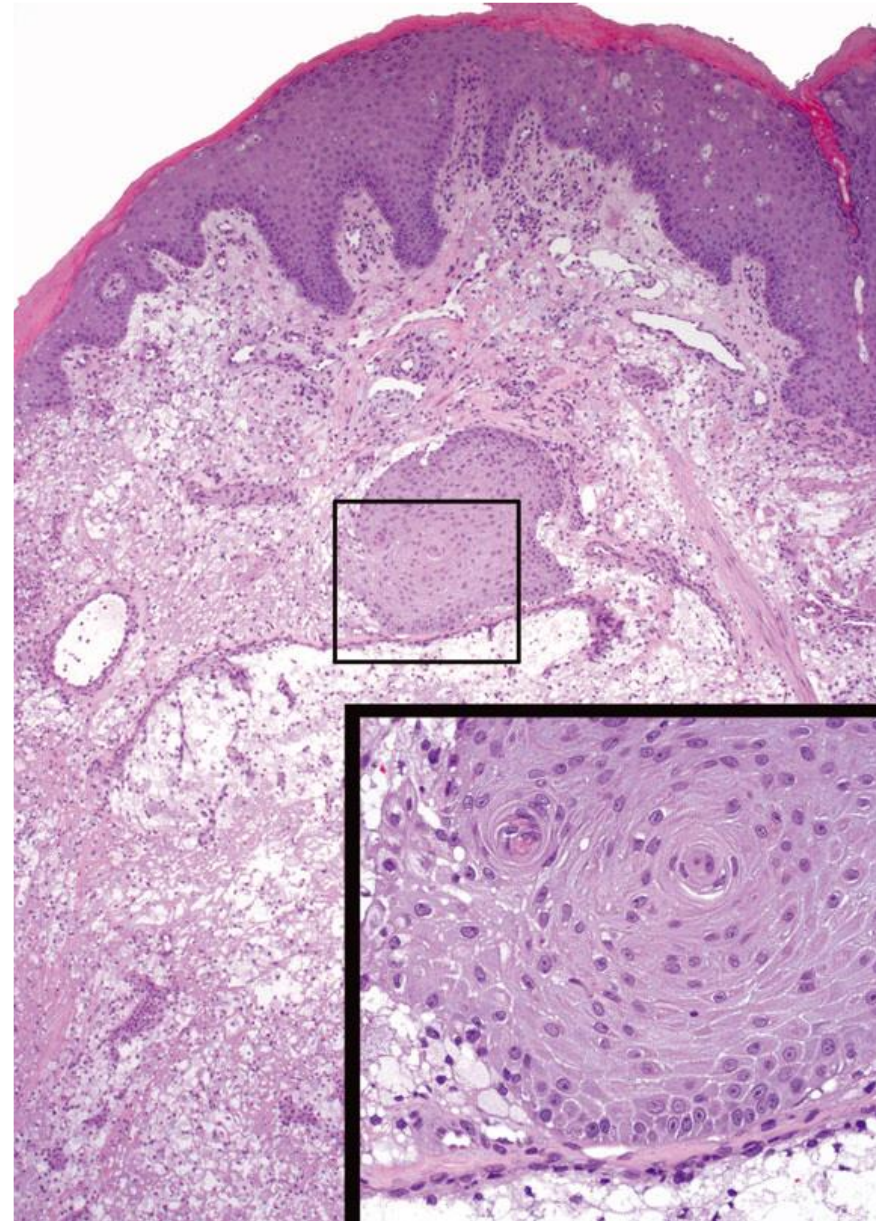
- Duct dilatation
- Periductal inflammation & fibrosis
- Foamy histiocytes (luminal and stroma)
- Obliteration of the duct's lumen can also be seen (garland sign)





Galactocele (also called lacteal cyst or milk cyst)

- Cyst caused by abnormal milk drainage
- Histology:
 - Cystic extension of duct, surrounded by inflammatory response and fibrosis
 - Lumen contains milk
 - Stromal inflammatory response, fat necrosis or xanthogranulomatous reaction
- Benign painless palpable mass often subareolar
 - Mostly detected after a few weeks or months from the time the patient stopped breast feeding, or during lactation or during the 3rd trimester of pregnancy
 - Aspiration may be curative



Mammogram showing an oval circumscribed cystic mass (arrows) with fat-fluid level

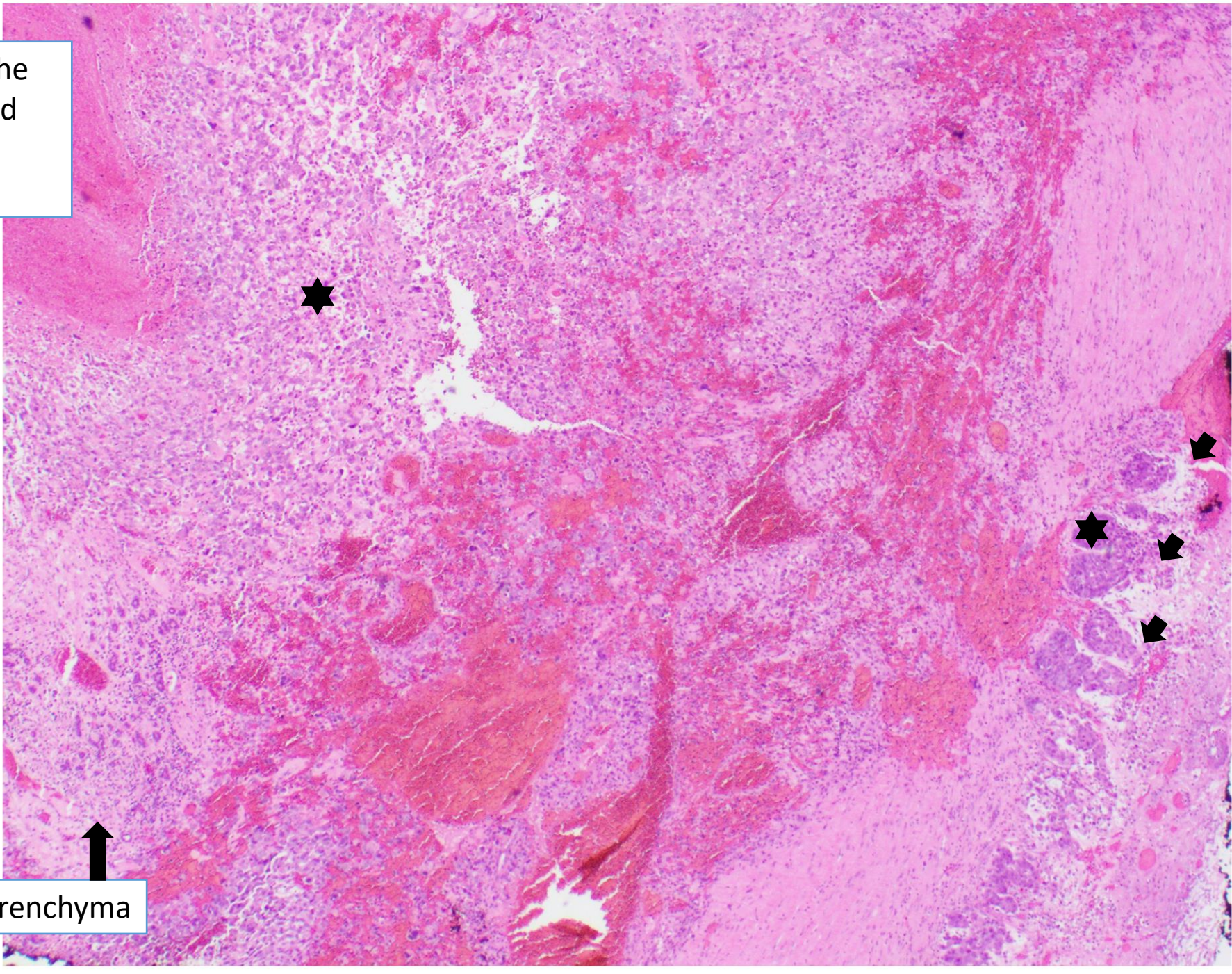
Case summary

- Benign changes and infections are likely explanations of breast lumps in lactating women
- Women are predisposed to infectious mastitis secondary to breast engorgement and nipple injury that occurs during breastfeeding
 - Staphylococcus aureus is often identified in acute mastitis
 - Lactational abscess are typically away from the nipple
- SMOLD is associated with smoking
 - Abscesses are usually subareolar

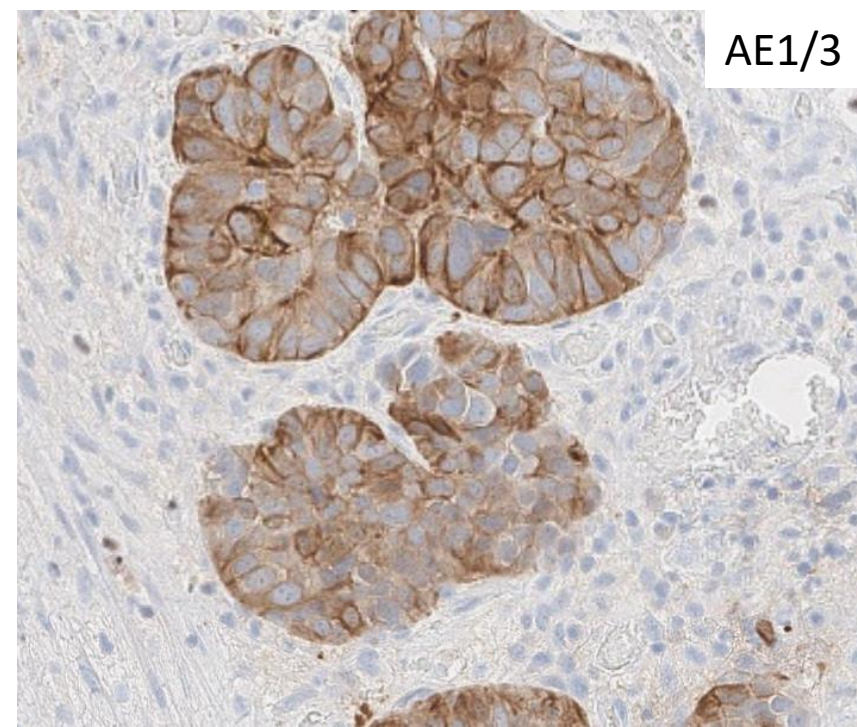
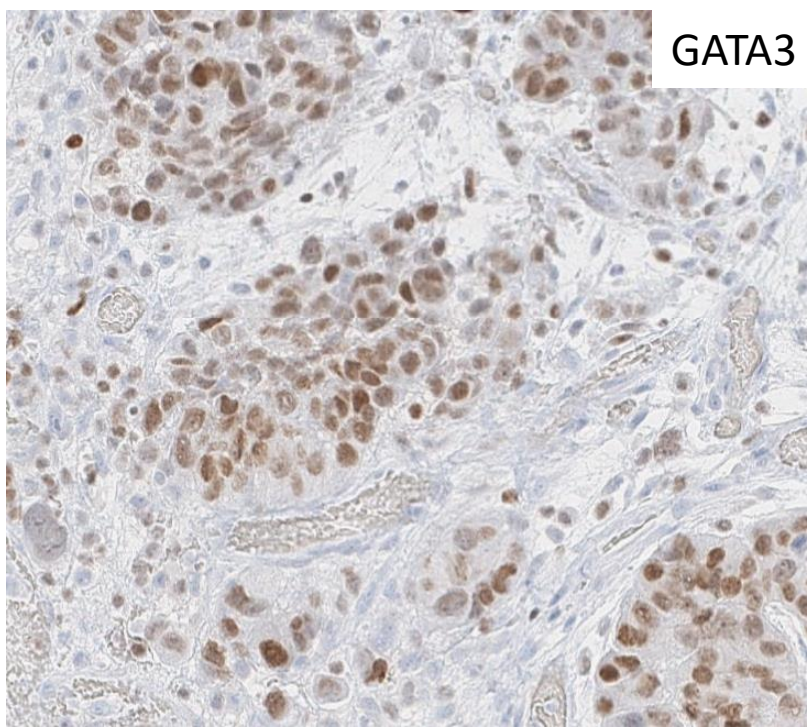
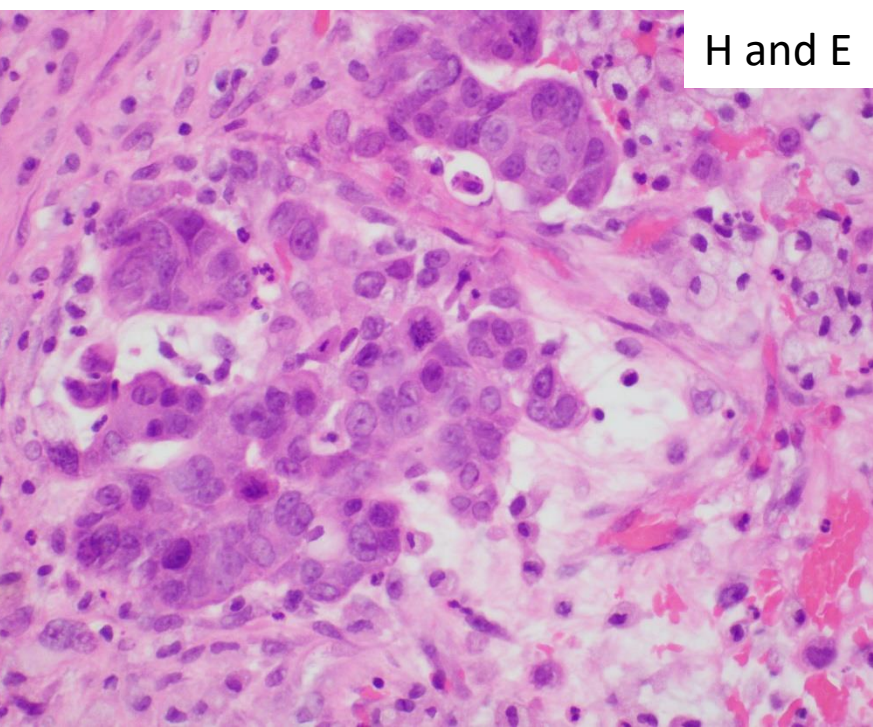
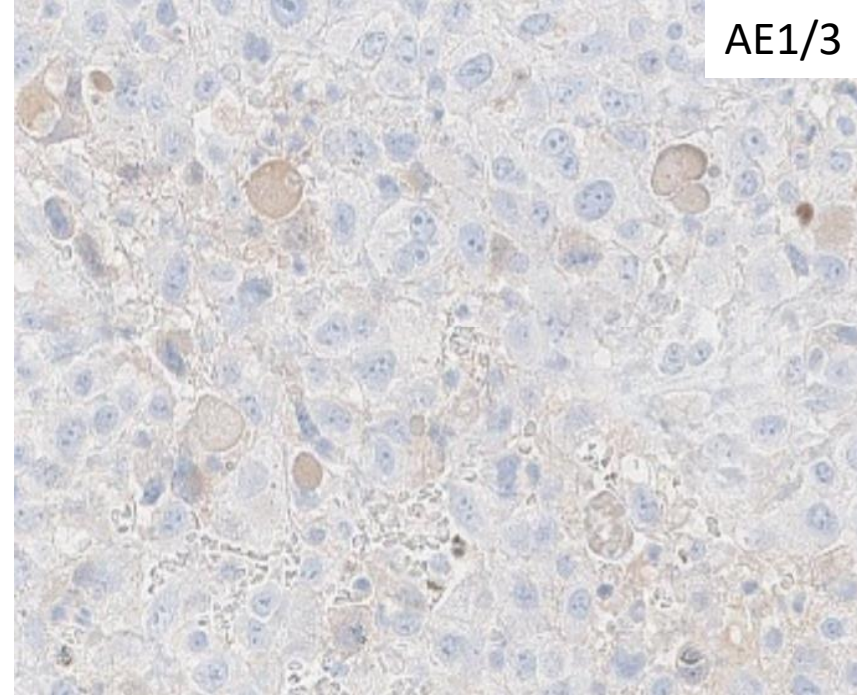
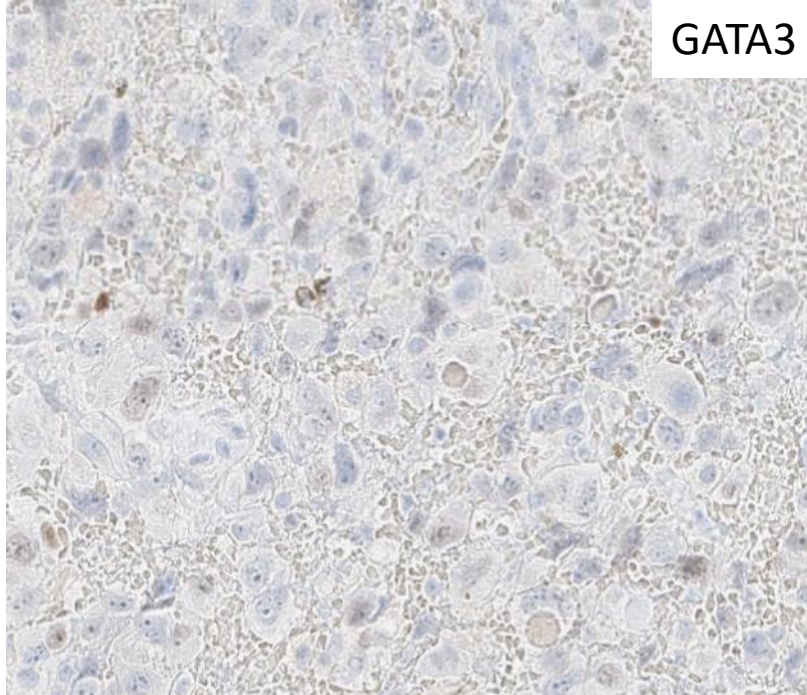
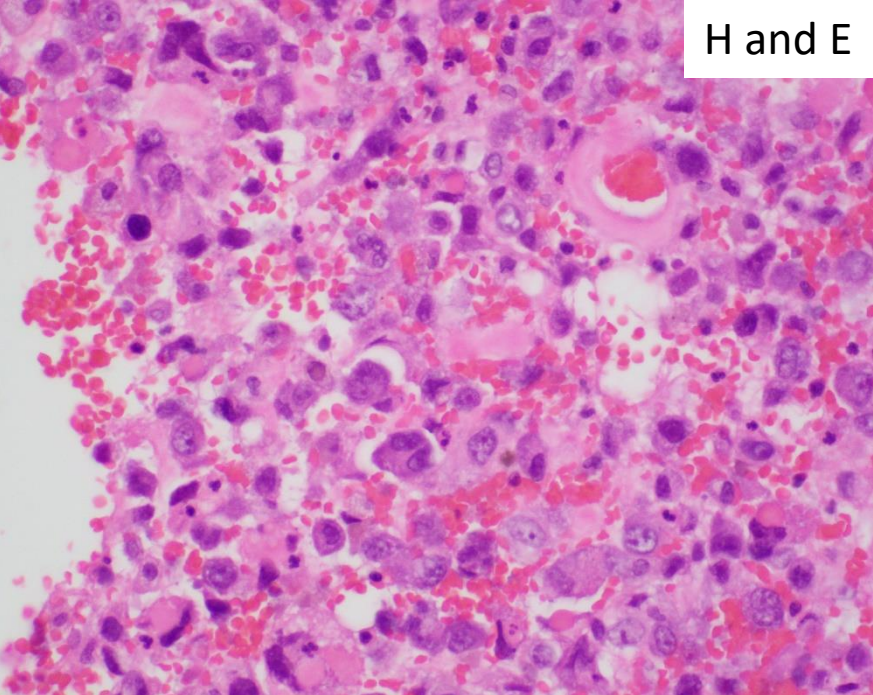
Case 2. 33 year old female, currently breast feeding (three and half months postpartum)

- Additional history:
 - Patient presented with breast pain of 3 months duration that developed soon after she gave birth
 - She was treated with antibiotics
 - Thought to clinically represent a recurrent breast abscess but multiple aspirations showed no growth on cultures
 - Currently with a 10 cm rapidly growing mass, breast erythema and pain and decreased milk production on the affected side
- Breast incisional biopsy was performed (about 2 months after presentation)

Majority of the tissue showed necrosis and hemorrhage



Residual breast parenchyma



Pregnancy associated breast cancer (PABC)

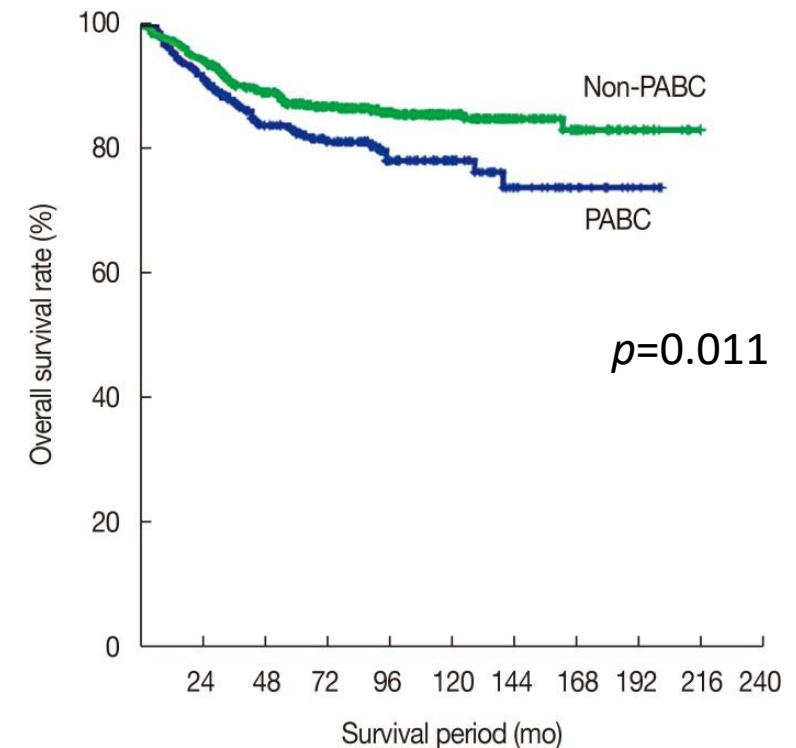
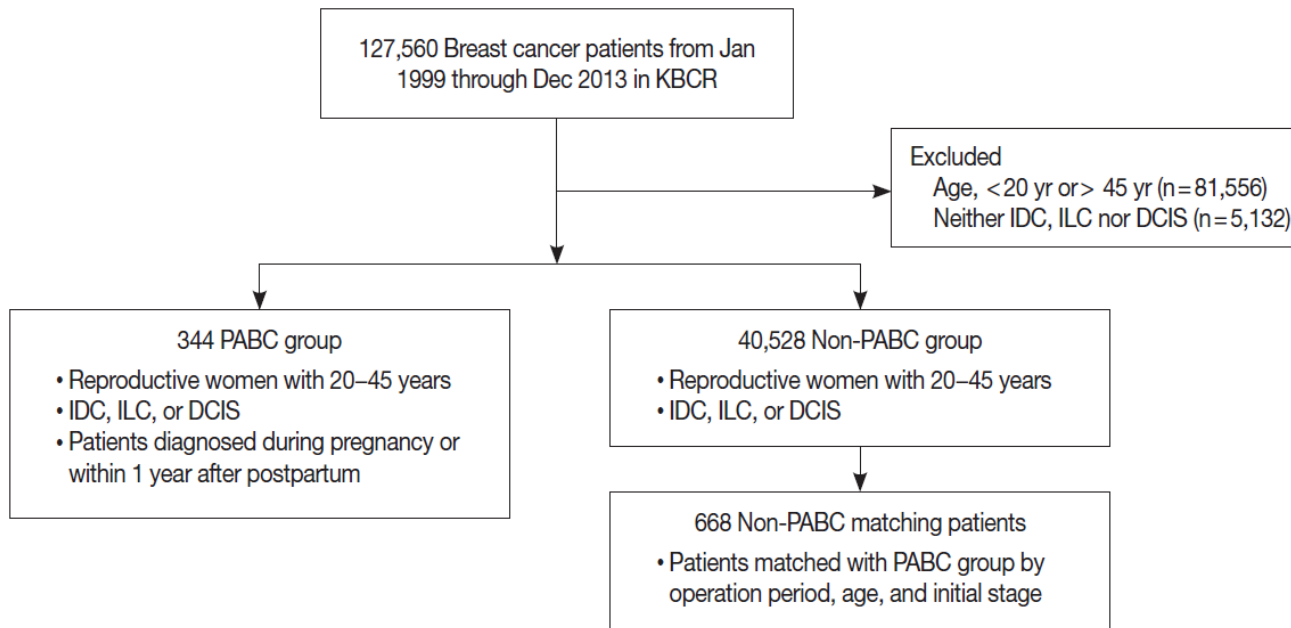
- Diagnosis of poorly differentiated carcinoma, Nottingham grade 3
- Tumor was associated with ulcerated overlying epidermis
- ER and PR were negative, unknown HER2 status (consultation case)
- This tumor represents a pregnancy associated breast cancer (PABC)
 - Defined as breast cancer diagnosis during pregnancy or in the first postpartum year

PABC



- 15 to 35 per 100,000 deliveries
 - One of the most common cancers in pregnancy worldwide
 - The frequency may be increasing because of delayed childbearing
 - Pregnancy itself may transiently increase an individual woman's risk of developing breast cancer, despite its long-term protective effect
- Termination of pregnancy is no longer routinely recommended
- Diagnosis is often delayed
 - PABC tends to be diagnosed at an advanced stage

Poor outcomes for women with PABC



10-year survival rate for PABC patient was 76.4% and non-PABC was 85.1%

Breast carcinoma in pregnant women: assessment of clinicopathologic and immunohistochemical features

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Affiliations + expand

PMID: 12942575 DOI: [10.1002/cncr.11614](#)

- 39 patients whose breast carcinoma was detected during pregnancy (n=38) or post-partum period (n=1)
 - Mean gestational age was 18 weeks (range of 2 to 37 weeks)
- Patients were 24 to 44 years (mean age of 33 years)
- Presentation self-discovered palpable masses (n=32), bloody nipple discharge (n=1), and diffuse erythema (inflammatory carcinoma) (n=1)

Histopathologic features

- All tumors were invasive ductal carcinomas
 - Extensive DCIS with microinvasion (n=1)
 - Metaplastic features (n=2)
 - Size 0.1 to 13.5 cm (mean of 4.5 cm)
- Differentiation:
 - 84% were poorly differentiated
 - 16% were well or moderately differentiated
- 61% of tumors had LVI

TABLE 1
Clinical Stage of Disease in Pregnant Women at Presentation

AJCC stage	No. (%)
I	2/39 (5)
II	19/39 (49)
III	16/39 (41)
IV	2/39 (5)

AJCC: American Joint Committee on Cancer. cancer staging manual, 5th ed.

TABLE 3
Immunohistochemical Analysis of Breast Carcinoma Occurring during Pregnancy

Prognostic marker	No. positive (%)
ER	7/25 (28)
PR	6/25 (24)
ER and PR	4/25 (16)
HER-2/ <i>neu</i>	7/25 (28)
p53	12/25 (48)
High Ki-67	15/25 (60)

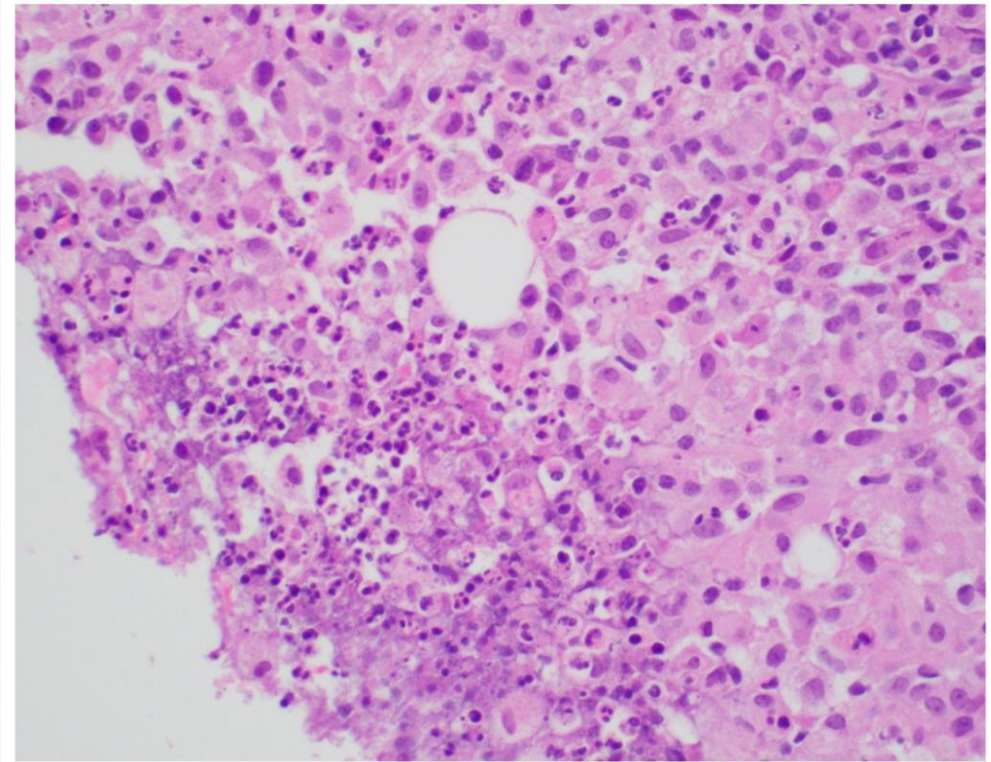
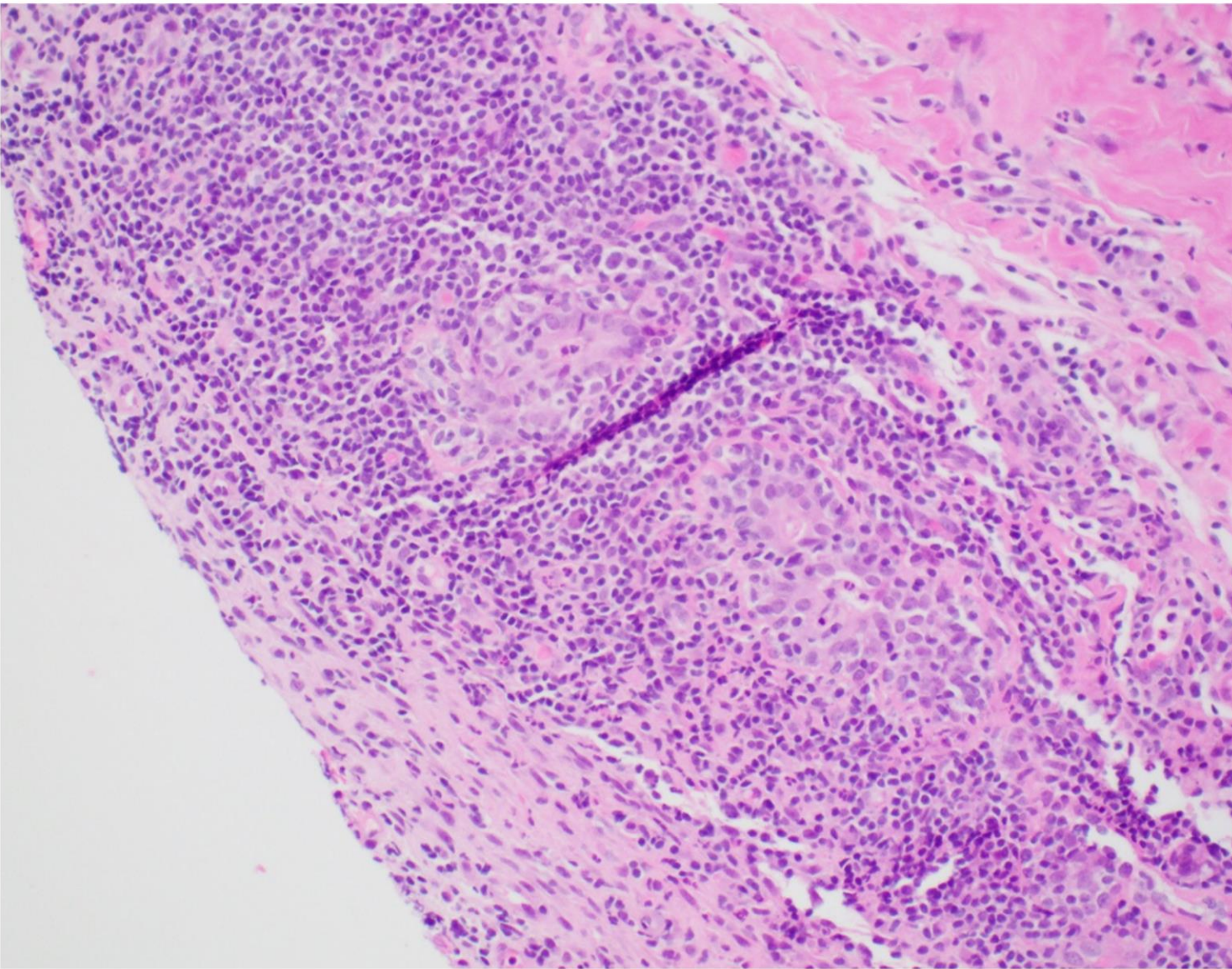
ER: estrogen receptor; PR: progesterone receptor.

Case summary

- Antibiotic unresponsive breast lumps in lactating women may need biopsy to rule out cancer
- Pregnancy associated breast cancer is one of the most common cancers in pregnancy worldwide
 - Probable increase in frequency because of delayed childbearing age
 - The diagnosis is often delayed because benign changes in pregnancy and lactation are more common
 - PABC is often estrogen receptor negative poorly differentiated cancer with lymphovascular invasion, positive lymph nodes and advanced clinical stage
 - PABC may be associated with poor outcome

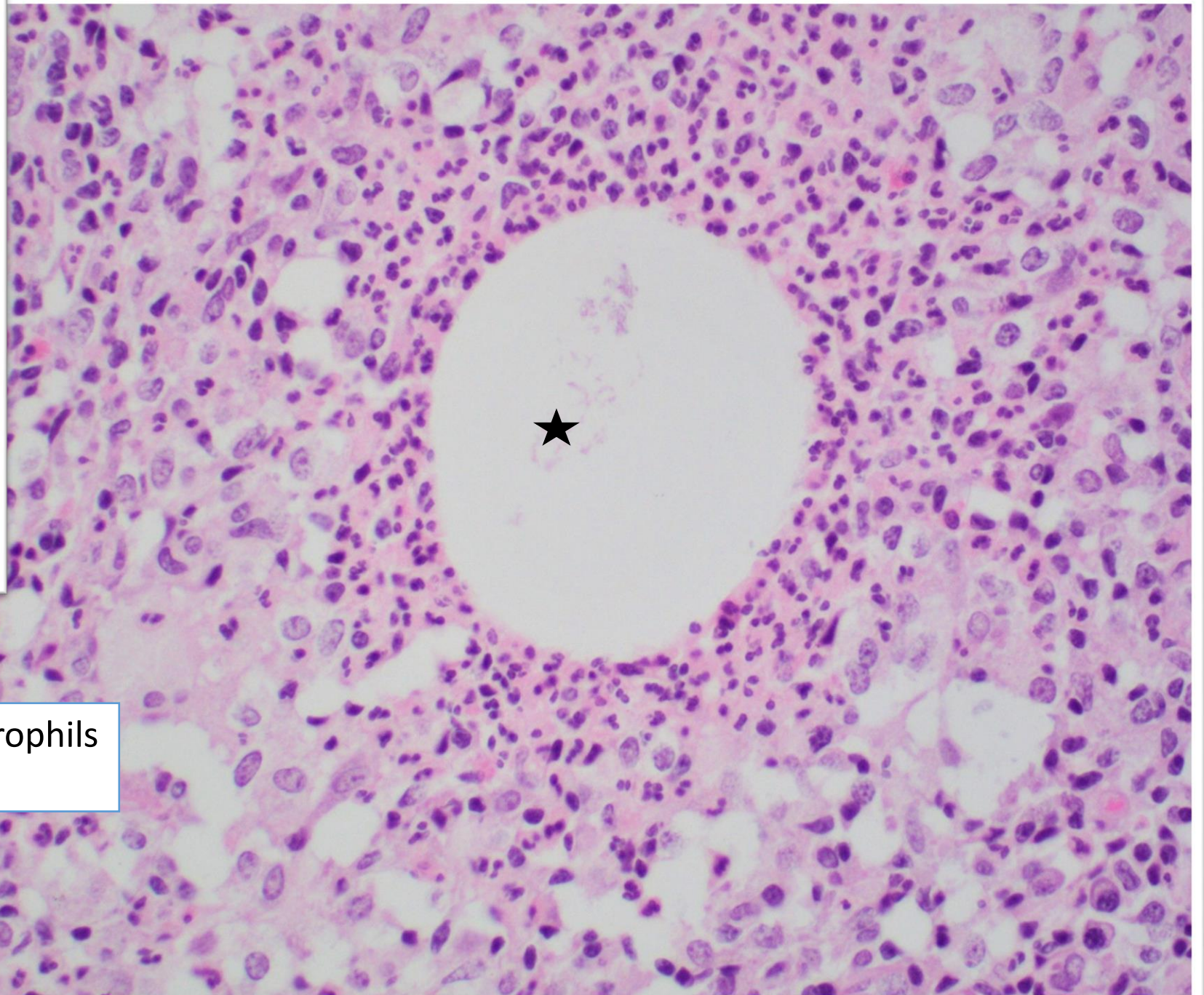
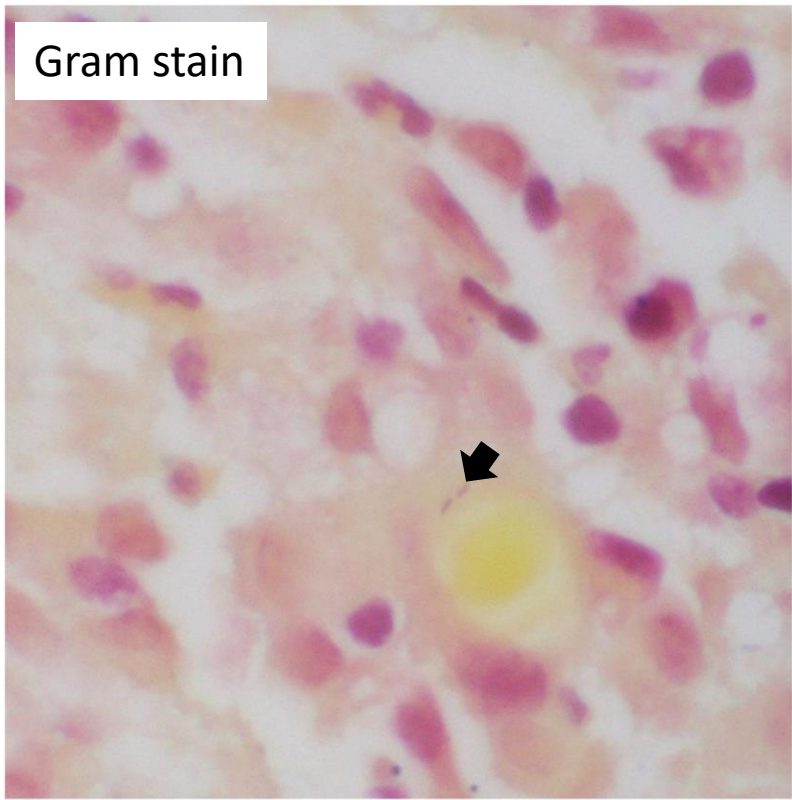
Case 3. 41 year old woman, had a baby 3 years prior

- Additional history: noticed pain while exercising in the right breast and over the course of 3-4 months developed a large mass
- No breast trauma
- Patient is not currently breastfeeding
- Biopsy was performed



Inflammation around lobules
Neutrophilic microabscess

Gram stain



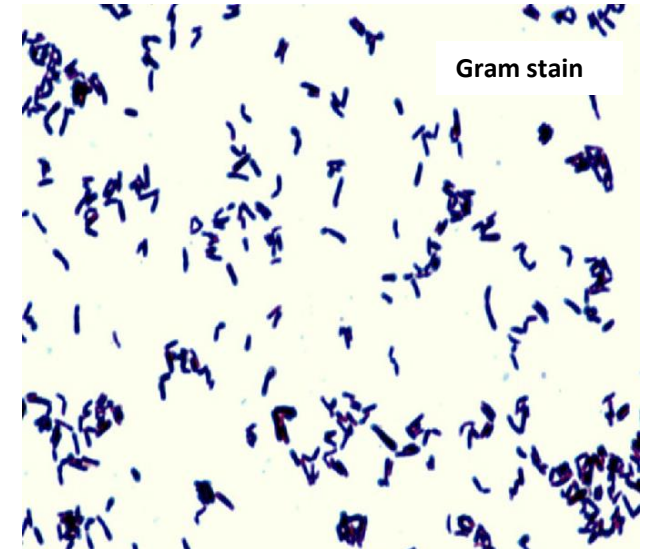
Cystic spaces surrounded by neutrophils
Abundant epithelioid histocytes

Case follow up

- The patient was managed surgically with debridement after initial biopsy showing granulomatous mastitis with features consistent with cystic neutrophilic granulomatous mastitis
- Aerobic and anaerobic wound cultures grew *Corynebacterium kroppenstedtii*
- The patient was placed on long term doxycycline therapy
- Changes resolved about 4 months after surgical management

Cystic neutrophilic granulomatous mastitis

- Most patients are women, parous or currently pregnant
- Association with *Corynebacterium* species, especially *Corynebacterium kroppenstedtii*
 - Microbiologic evidence can be difficult to obtain
 - Lipophilic bacteria
- Prolonged antibiotic therapy required for complete resolution



Cystic Neutrophilic Granulomatous Mastitis

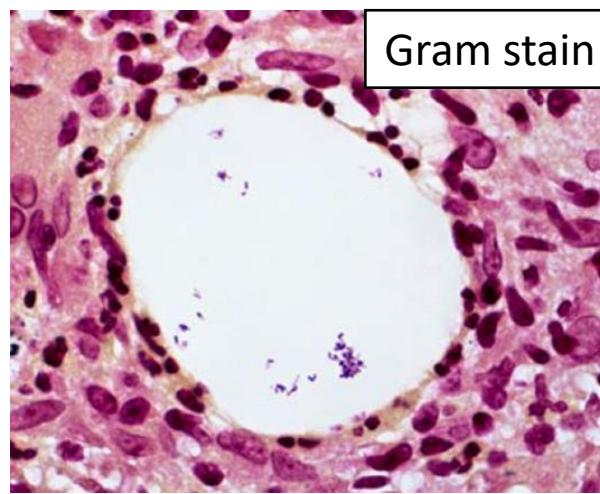
Further Characterization of a Distinctive Histopathologic Entity Not Always Demonstrably Attributable to Corynebacterium Infection

Timothy M. D'Alfonso, MD, Tracy-Ann Moo, MD,† Elizabeth K. Arleo, MD,‡
Esther Cheng, DO,* Lilian B. Antonio, BS, MPH,* and Syed A. Hoda, MD**

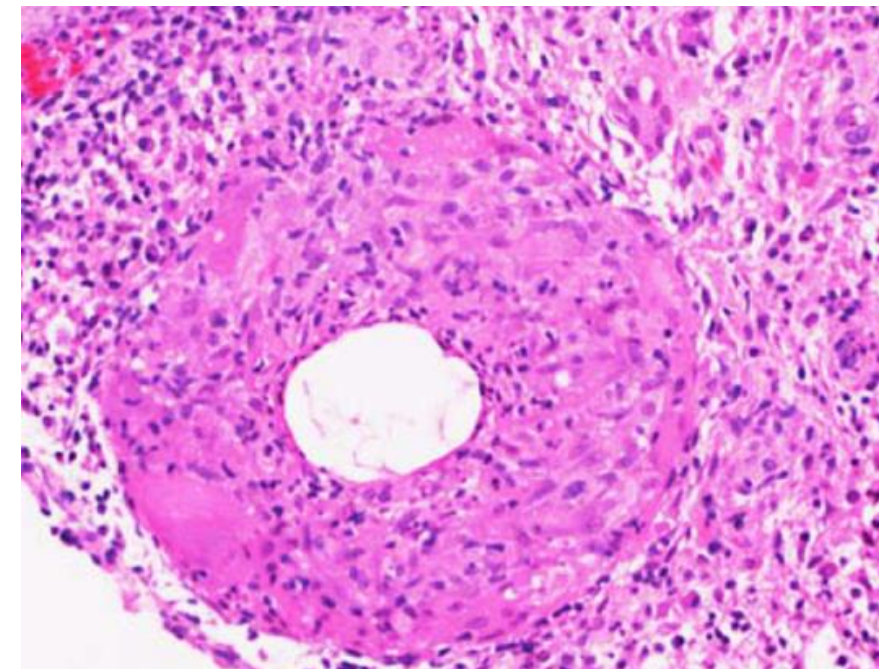
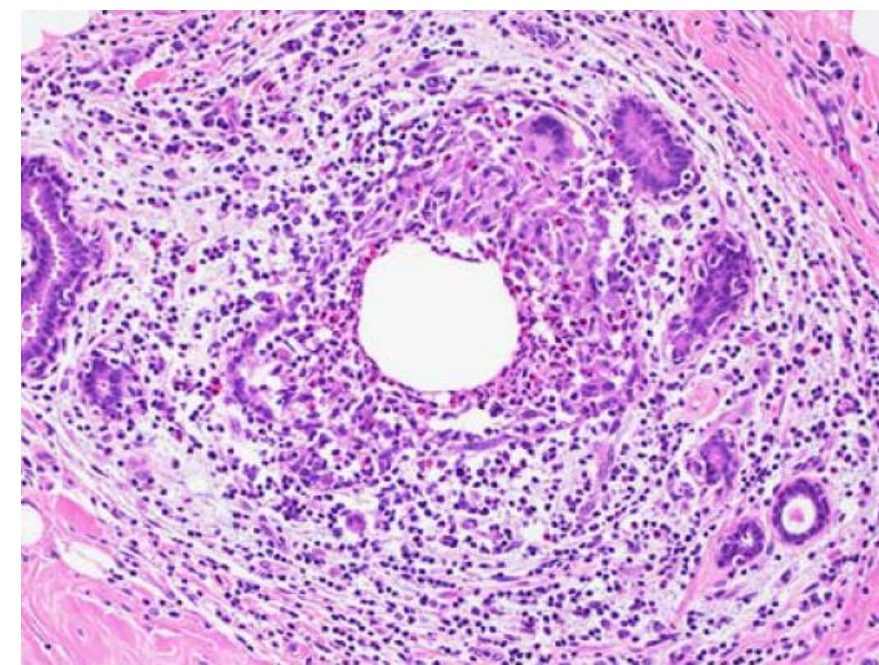
TABLE 2. Clinical Characteristics and Treatment for Cases of CNGM

Characteristic	n = 12 (%)
Age (median, range) (y)	34, 25-49
Laterality	
Left	6 (50)
Right	6 (50)
Presentation	
Palpable abnormality	12 (100)
Pain	6 (50)
Breast erythema	7 (58.3)
Nipple inversion	2 (16.7)
Nipple discharge	0 (0)
Treatment	
Antibiotics only	5 (41.7)
Antibiotics and steroids	1 (8.3)
Antibiotics and surgery	6 (50)

Characteristic histologic findings



- Lobulocentric inflammation:
 - Epithelioid histiocytes, giant cells, lymphocytes, plasma cells, and neutrophils
- Clear vacuoles (all <1mm) in the center of granulomas surrounded by neutrophils
- Neutrophilic microabscesses were present in 11/12 cases
- Granulomatous inflammation maybe extensive and confluent
- Gram-positive bacilli were identified in 5/12 cases
 - Present in the cystic vacuoles
 - Only 1 case showed abundant bacteria
- Negative AFB and GMS stains

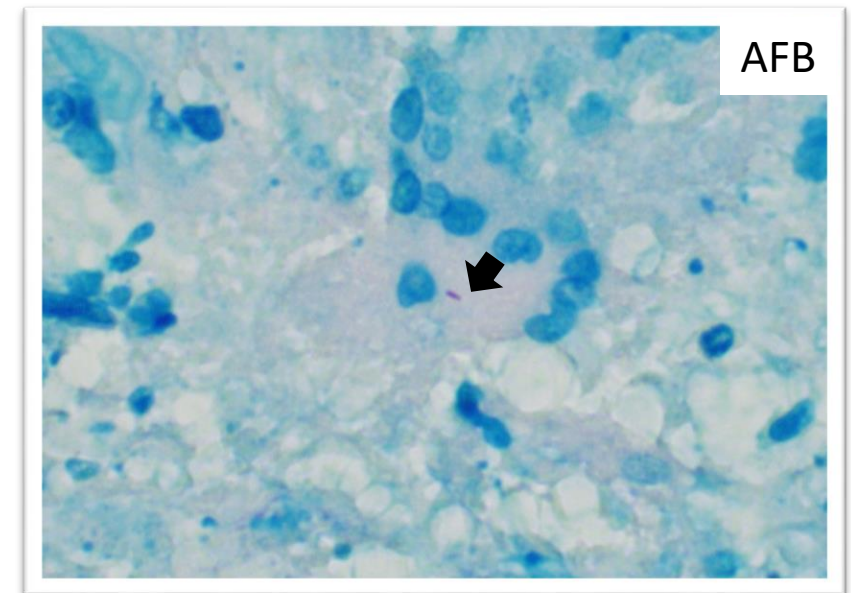
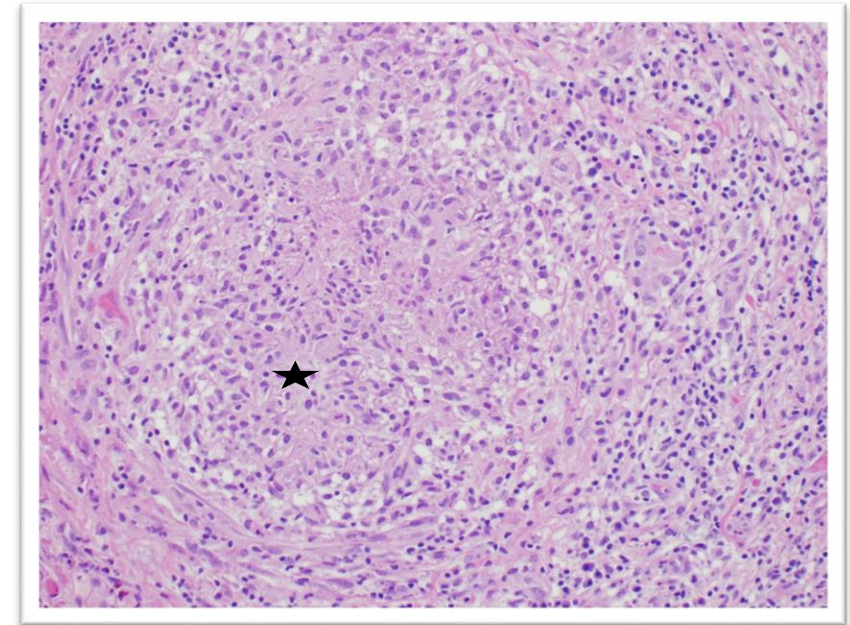


Treatment and course

- Microbiologic work up
 - A total of 9 microbial culture specimens from 6 patients were taken from breast wound or abscess tissue and showed no growth
 - 16S rDNA PCRs was unsuccessful (n=1)
- Follow up:
 - Draining sinuses developed in 5 cases
 - For all patients, significant resolution of symptoms ensued between 2 weeks and 6 months

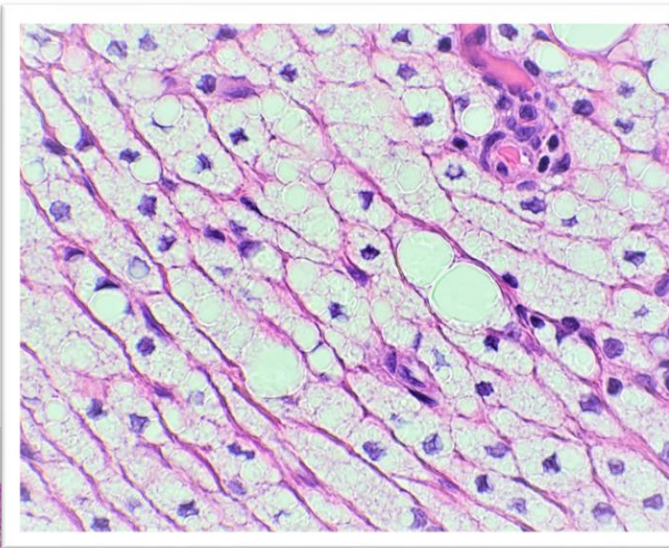
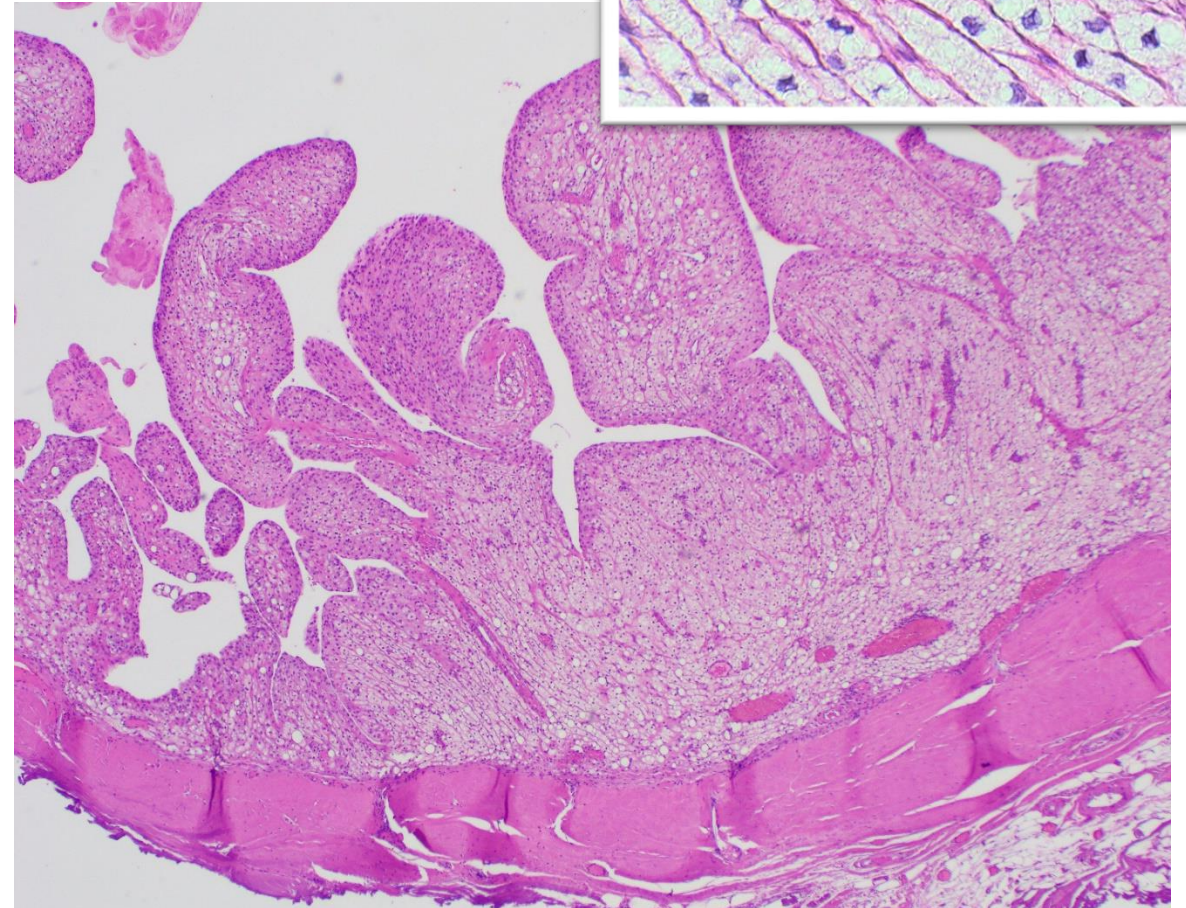
Differential diagnosis

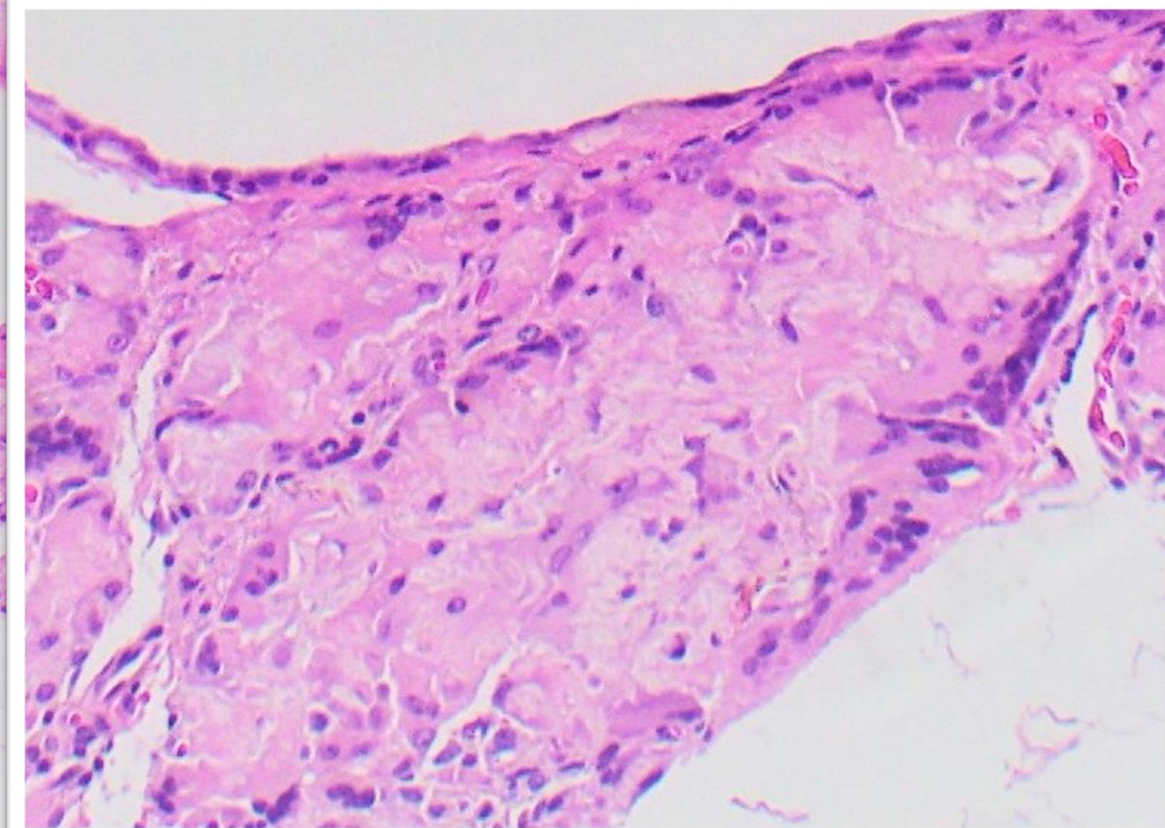
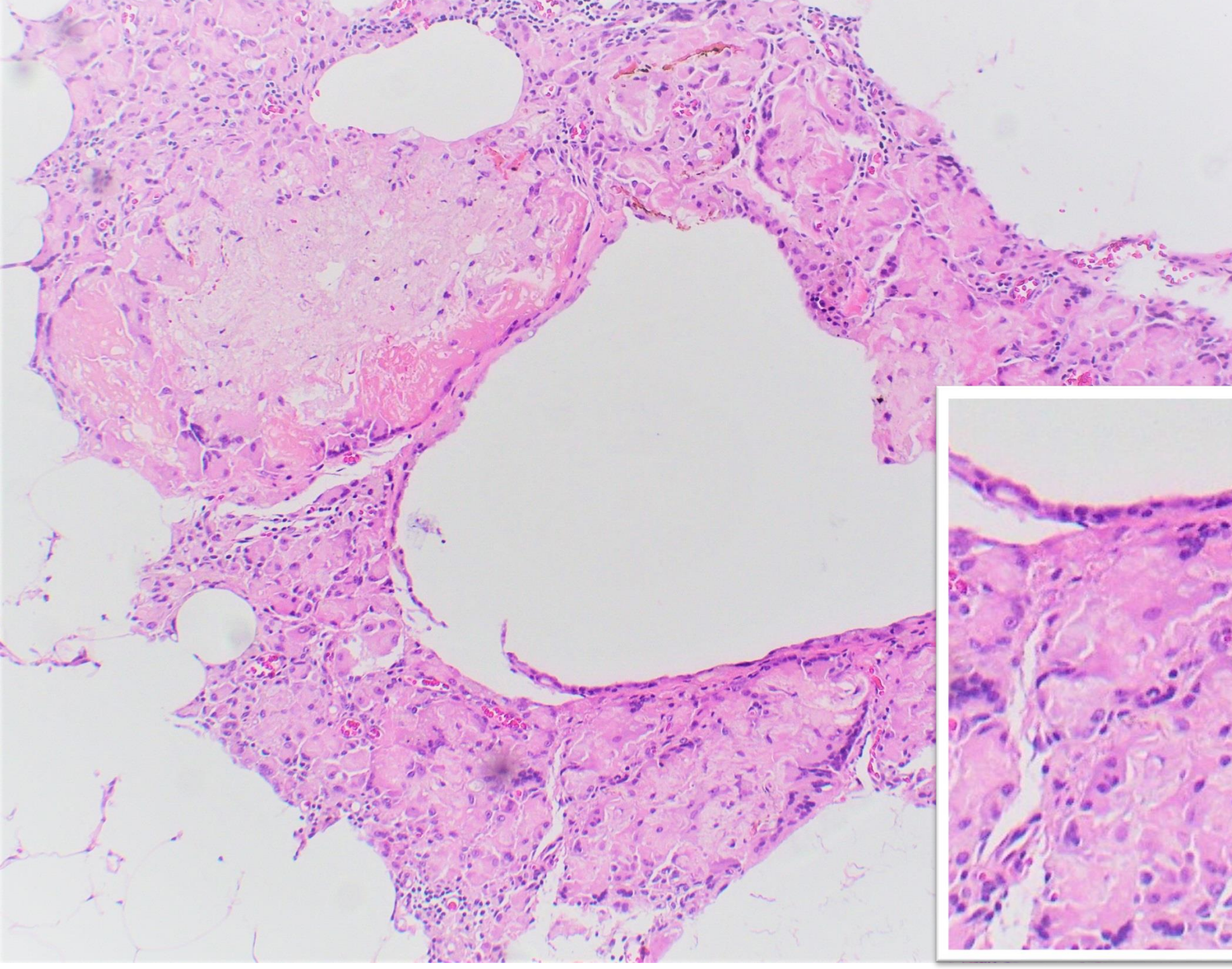
- Granulomatous mastitis due to other causes:
 - Infection (bacterial, fungal, parasitic)
 - Tuberculosis mastitis is very rare and shows caseating granulomas not typically associated with lobules
 - Foreign body reaction
 - Fat necrosis
 - Autoimmune diseases (granulomatosis with polyangiitis, sarcoidosis)
 - Granulomatous lobular mastitis (diagnosis of exclusion)



Foreign body giant cell reaction

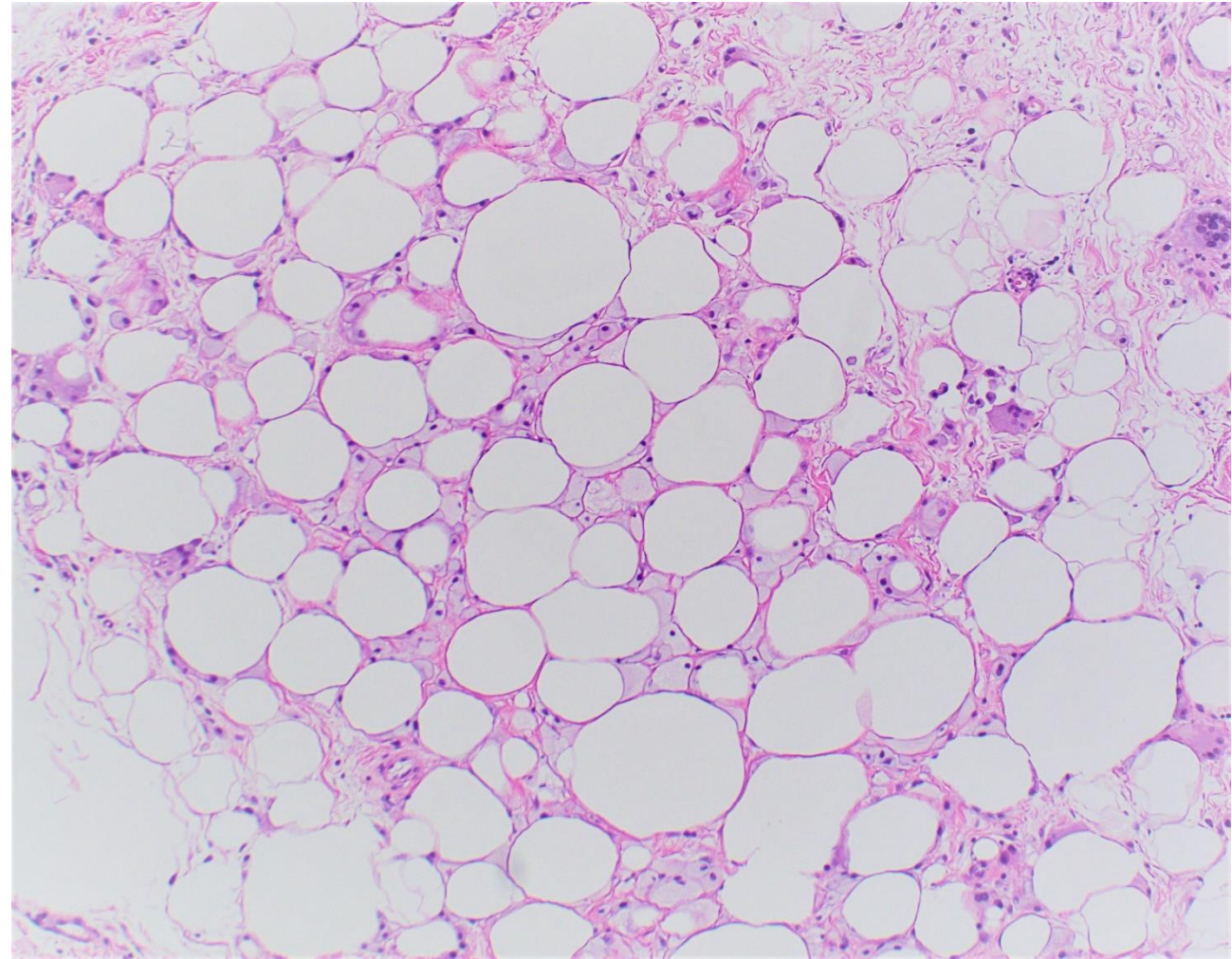
- Silicone gel implants are used for breast reconstruction or augmentation
- Leak or rupture causes local scarring, infection and disfigurement
- There is tissue reaction with birefringent material and foreign body giant cells in lymphoid background
- It may cause painful enlarged axilla caused by silicone migration





Fat necrosis

- Necrotic adipose tissue with foamy histiocytes, chronic inflammatory cells and multinucleated giant cells
 - Hemorrhage, cystic change, varying degrees of fibrosis and calcifications in later stages
- Can present a clinical and radiographic mass lesion
- Most described in perimenopausal women after trauma, surgery or biopsy
 - Causes: Trauma, iatrogenic, radiation



Case summary

- Cystic neutrophilic granulomatous mastitis has characteristic histologic findings and is association with *Corynebacterium* infection:
 - Neutrophilic microabscesses
 - Clear vacuoles surrounded by neutrophils and granulomatous inflammation
 - Gram stain may help to identify bacteria in the clear vacuoles
- Tuberculosis, fungal and parasitic infections are rare in breast
- Granulomatous inflammation in breast is most commonly associated with fat necrosis, silicone material, or foreign body

Conclusions

- The most common explanation for breast lump during pregnancy and postpartum period are benign changes:
 - Plugged ducts, galactoceles, lactating adenomas or infections (mastitis and abscess)
- Lactational mastitis is associated with *Staphylococcus aureus* infection
- Cystic neutrophilic granulomatous mastitis is associated with *Corynebacterium* infections, which may be seen on tissue gram stain (also it is difficult to culture)
- Pregnancy associated breast cancers (PABC) are often high grade receptor negative ductal carcinomas that have poor outcome and delayed diagnosis

Thank you

