

Case 3

Joint Session Breast Pathology / Infectious Diseases Pathology: Infections of the breast

**31st European Congress of Pathology
Nice**

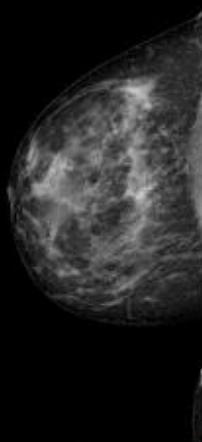
8 September, 2019

Clinical history 1

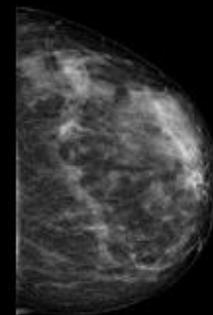
- 32-year-old female with a right breast erythema, swelling, pain and UO quadrant mobile mass about 5 cm in size.
 - 7 days of antibiotics (amoxicillin+clavulanate) without effect; 7 days 500mg cefuroxime bid – remission; 1 month later abscess formation
 - Mammography: negative (R1); Ultrasound: fluid between the layers (U2).
 - US-guided CNB (3 weeks after onset)
- (Pregnancy with cesarean section at term 4 years before.)

Mammography

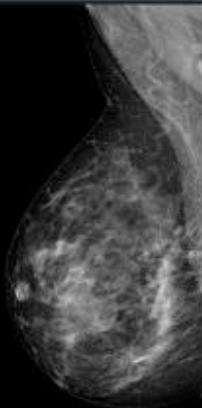
1: R CC (Series 2)



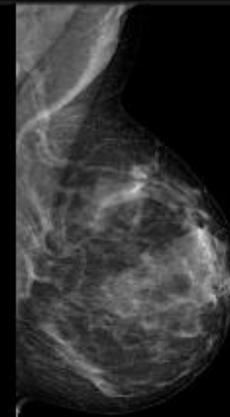
2: L CC



3: R MLO (Series 2)



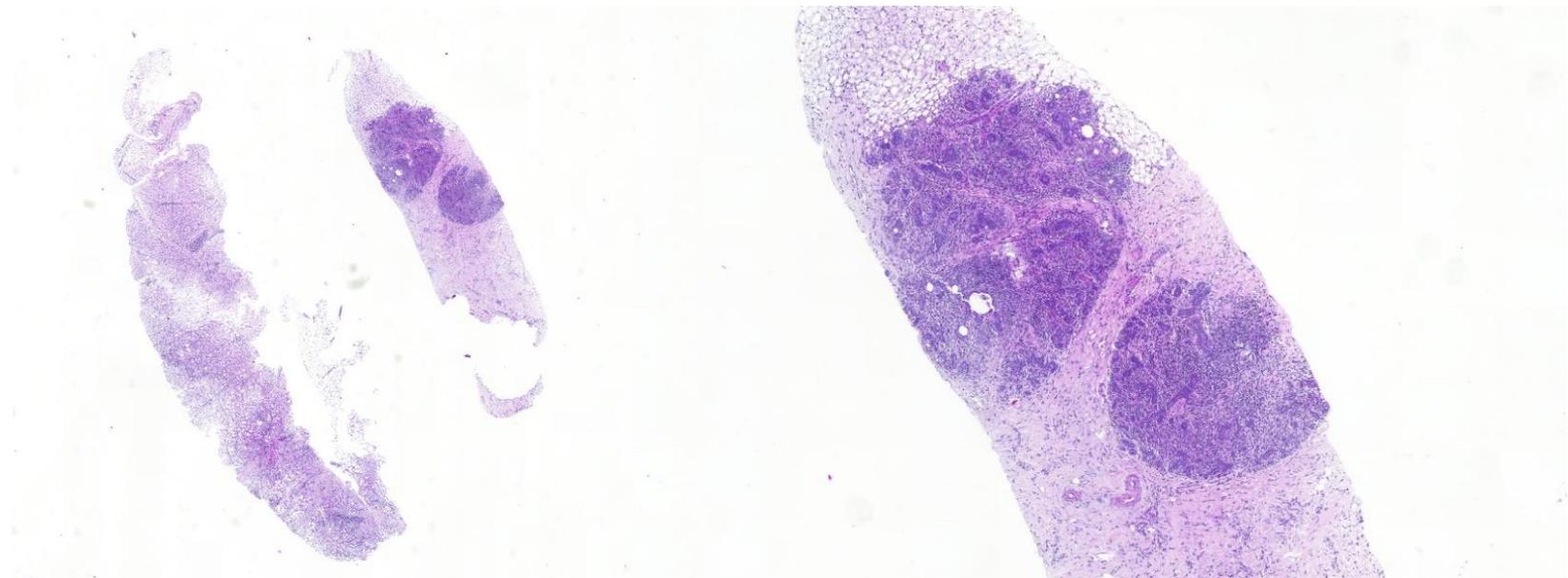
4: L MLO (Series 2)



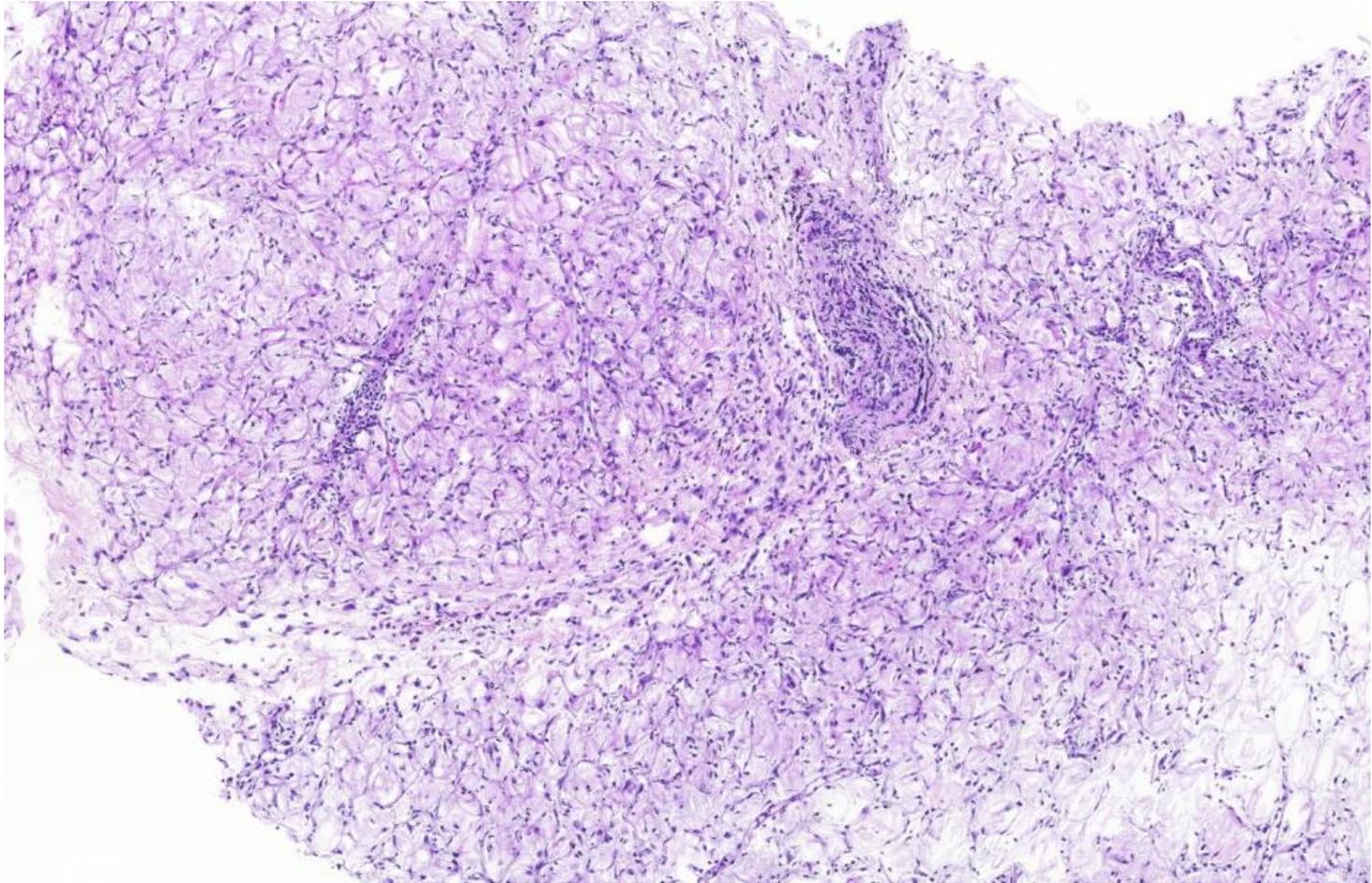
HE

x1.5

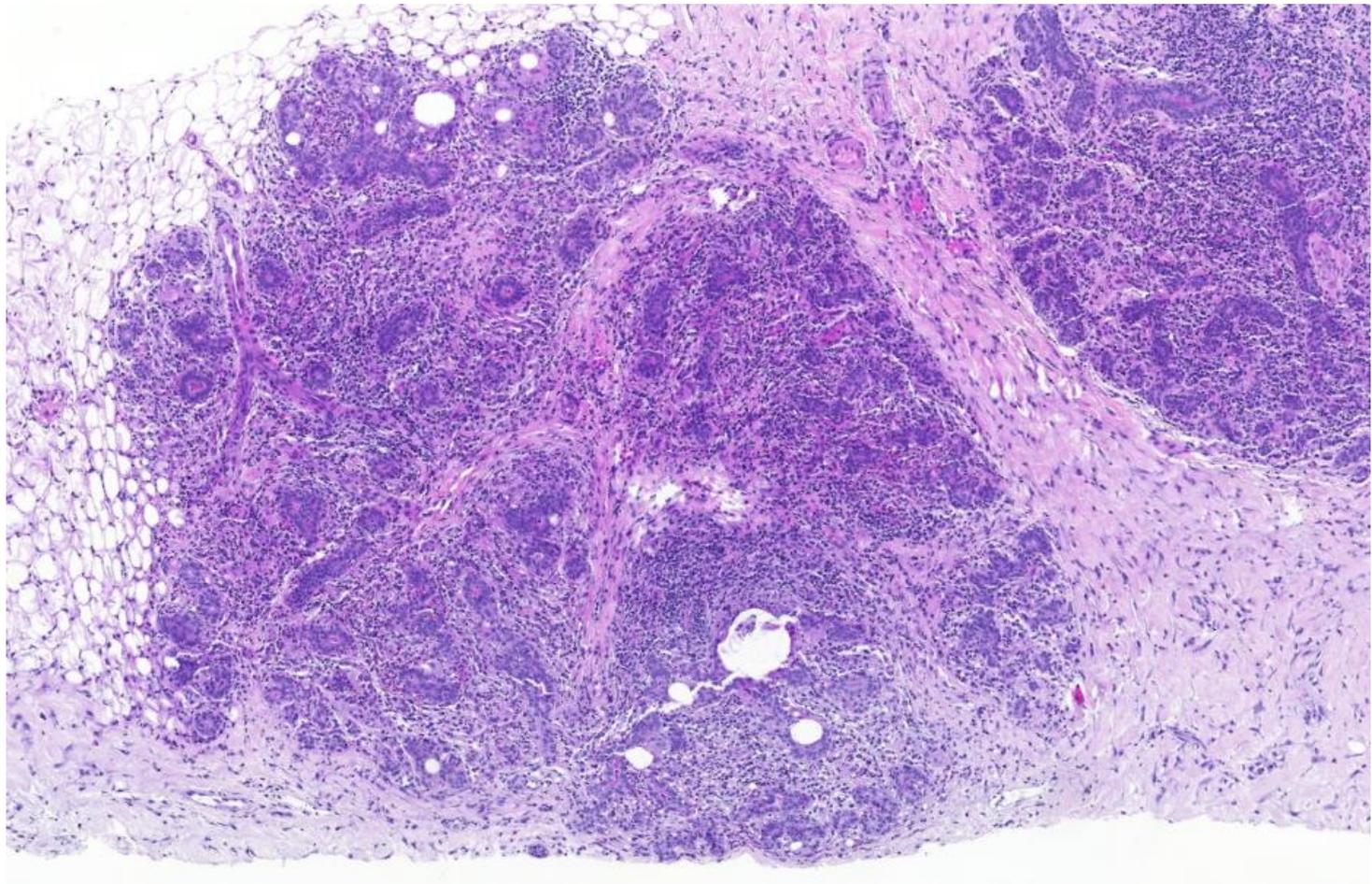
x5



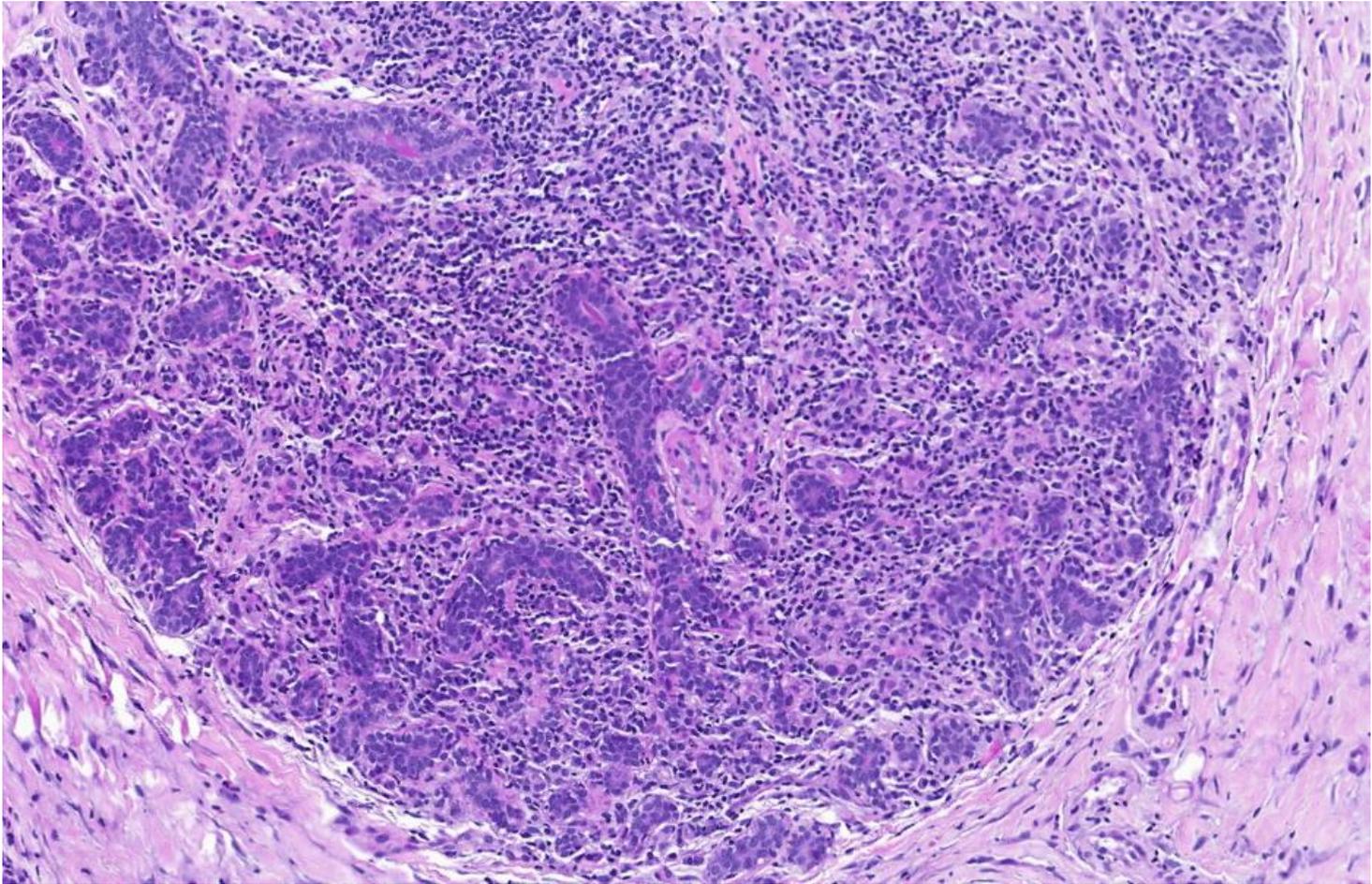
X10, adipose tissue, with few lymphocytes (left particle)



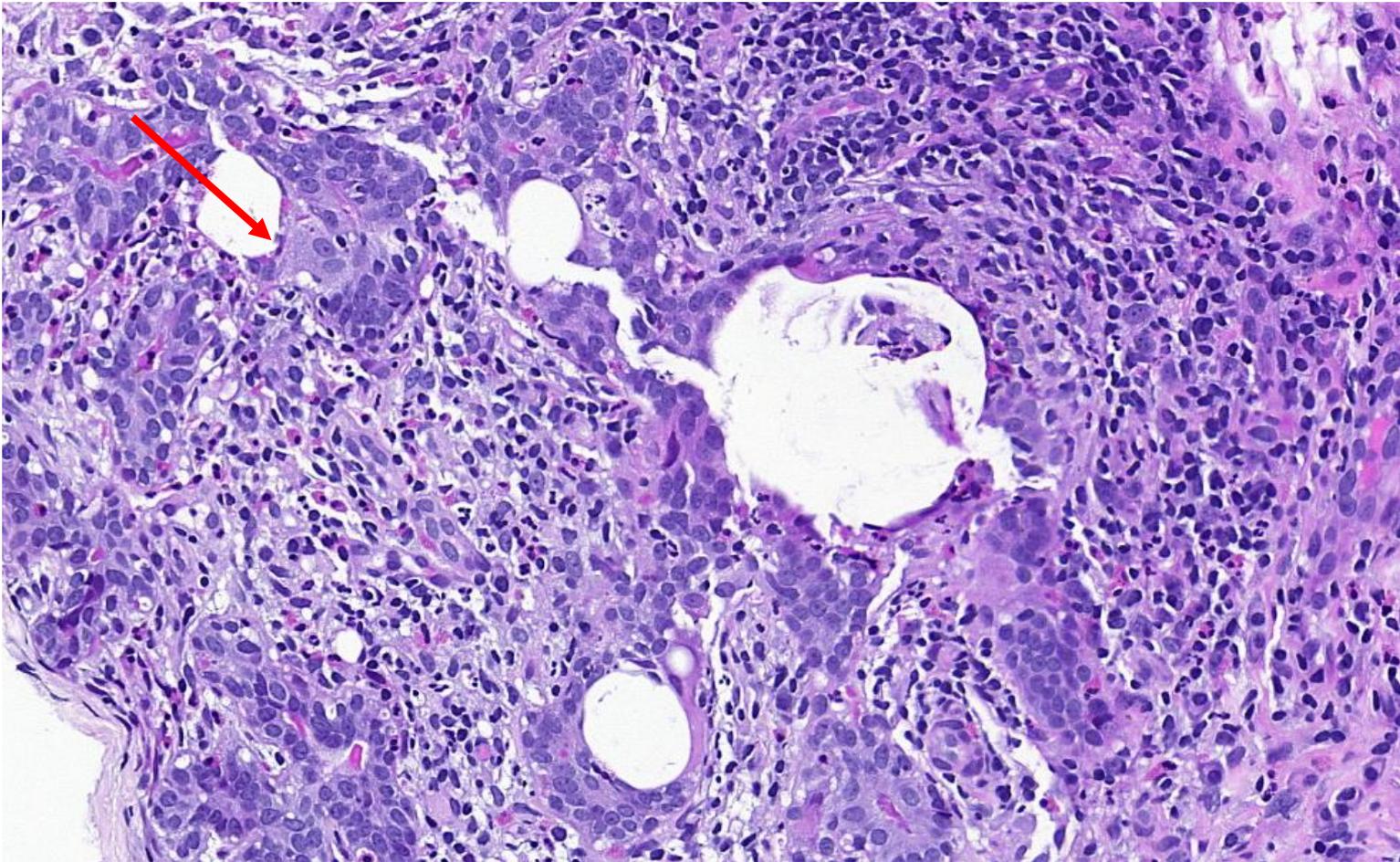
Lobulocentric infiltration (x10)



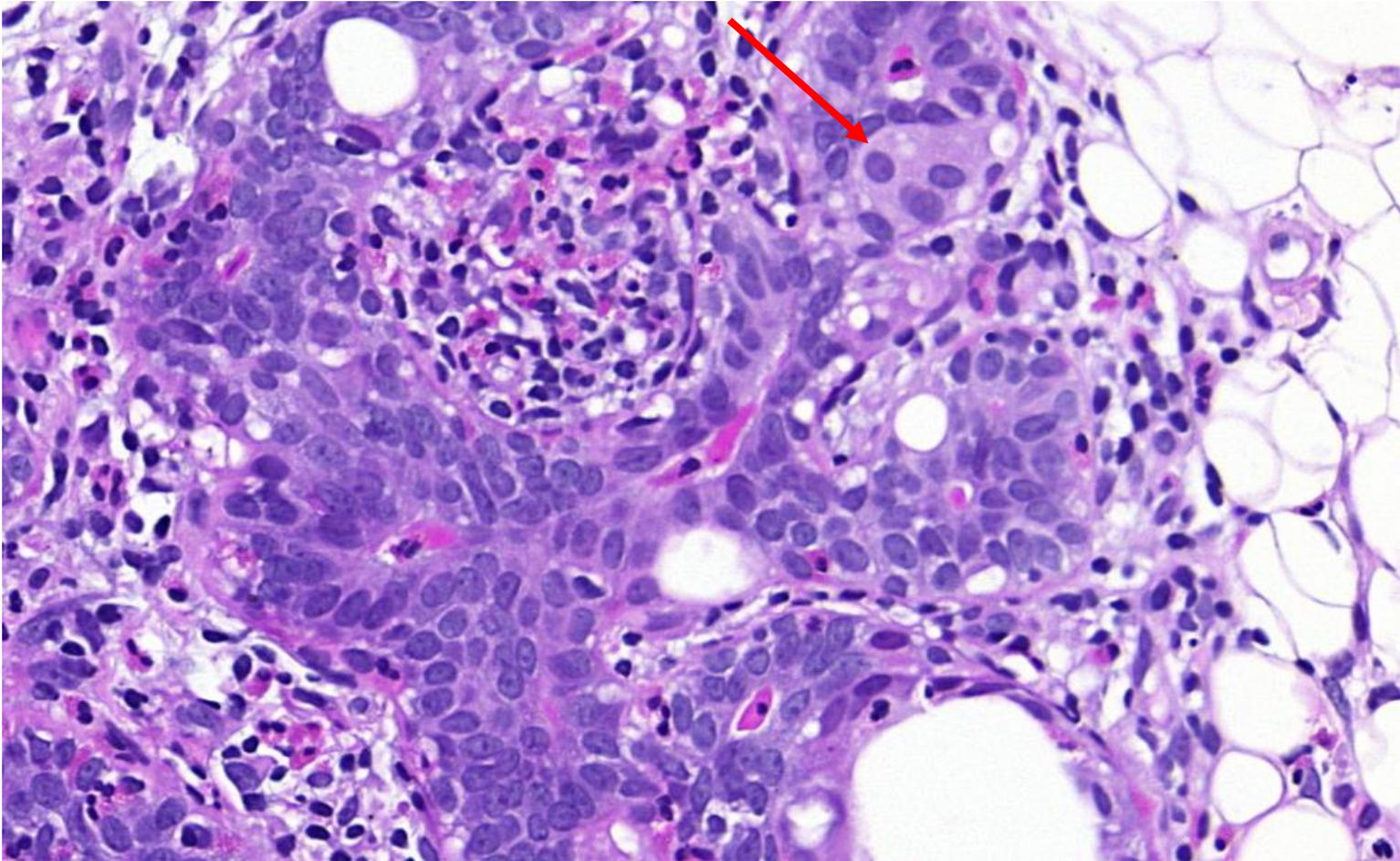
X20, mononuclear cells



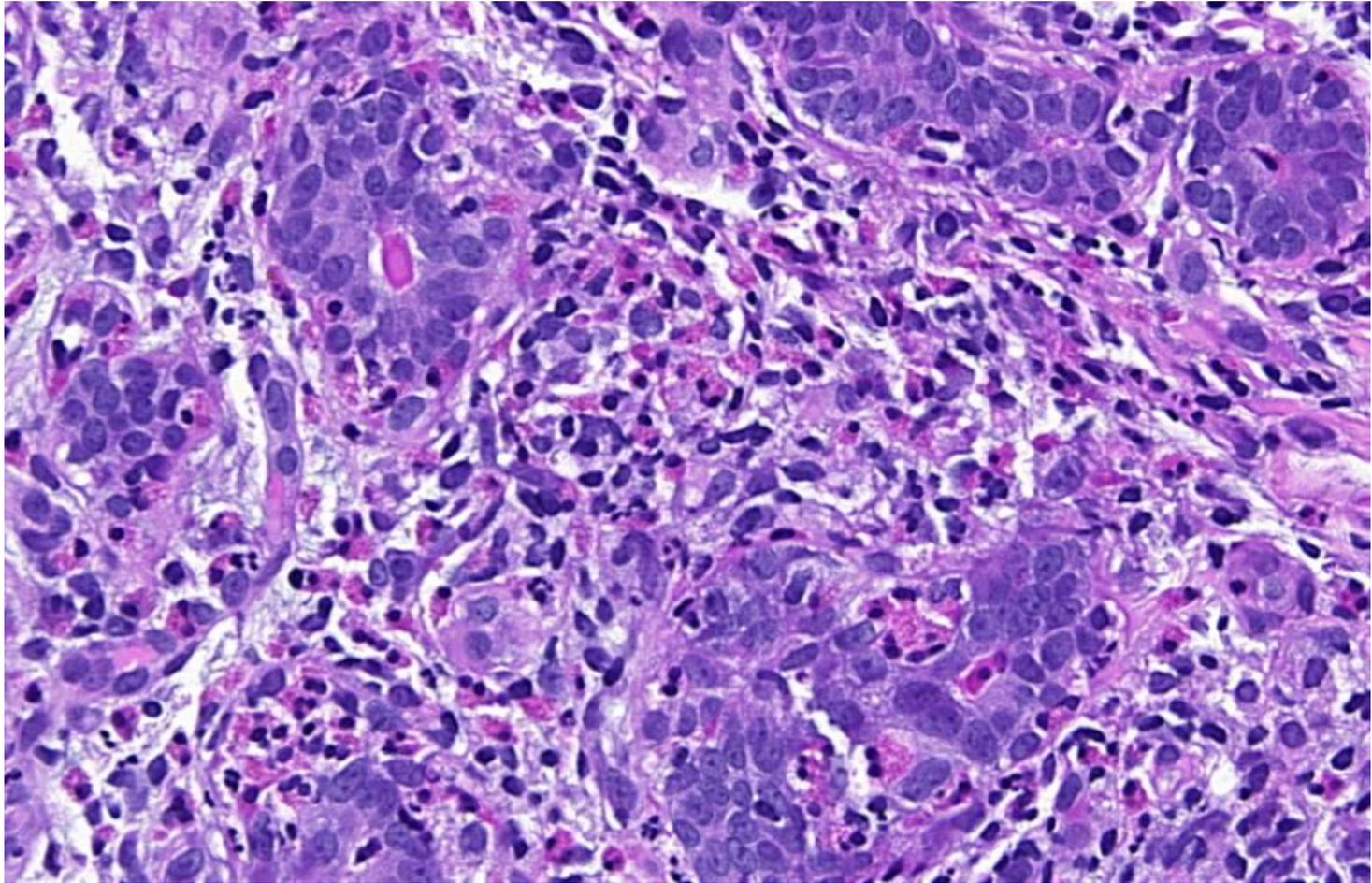
X70 (right particle); **giant cells**, „cysts”, mononuclears, eosinophils, few neutrophils



X70; **giant cells**, „cysts”, mononuclears,
eosinophils, few neutrophils



Tissue eosinophilia



CNB

- One core: dominantly adipous tissue
- Second core: inflammation, with predominantly lymphocytes, no granulomas, tissue eosinophilia, few neutrophils
- B2: inflammatory change (with mixed inflammatory cells and tissue eosinophilia); non-specific mastitis

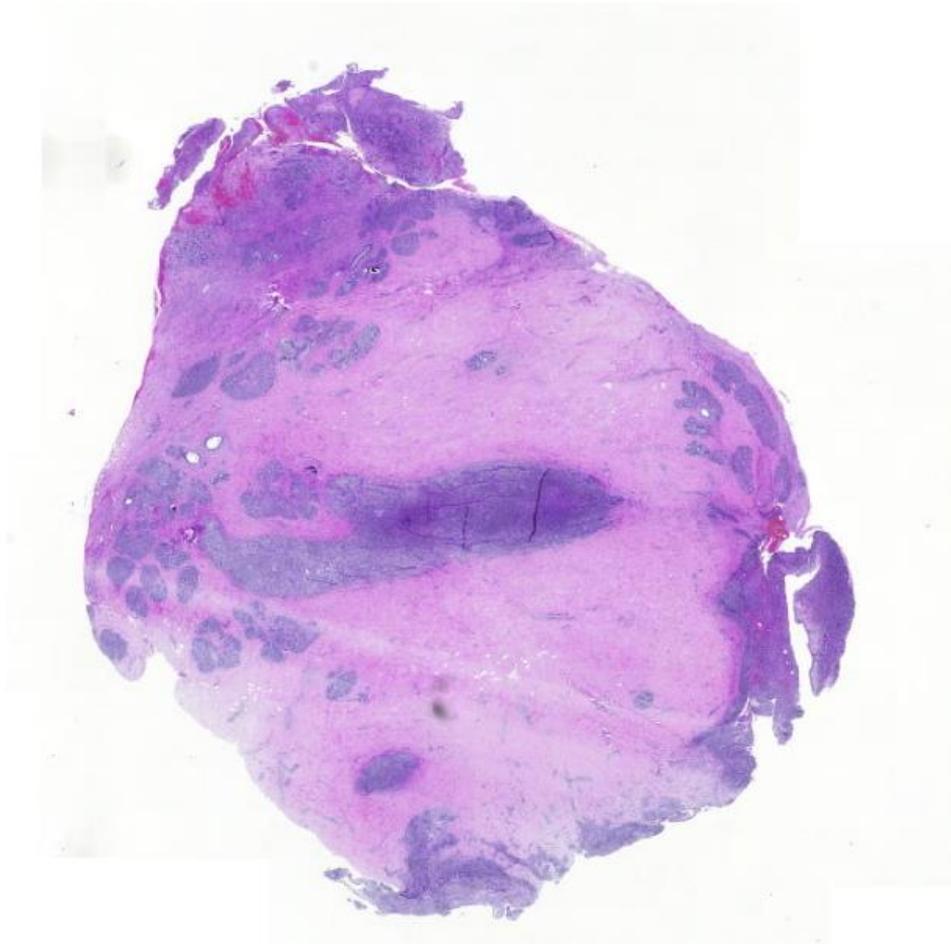
Clinical history 2

- Further antibiotics: cefuroxim (Zinnat)
- No effect, 3 weeks later still some discharge:
bacteriology

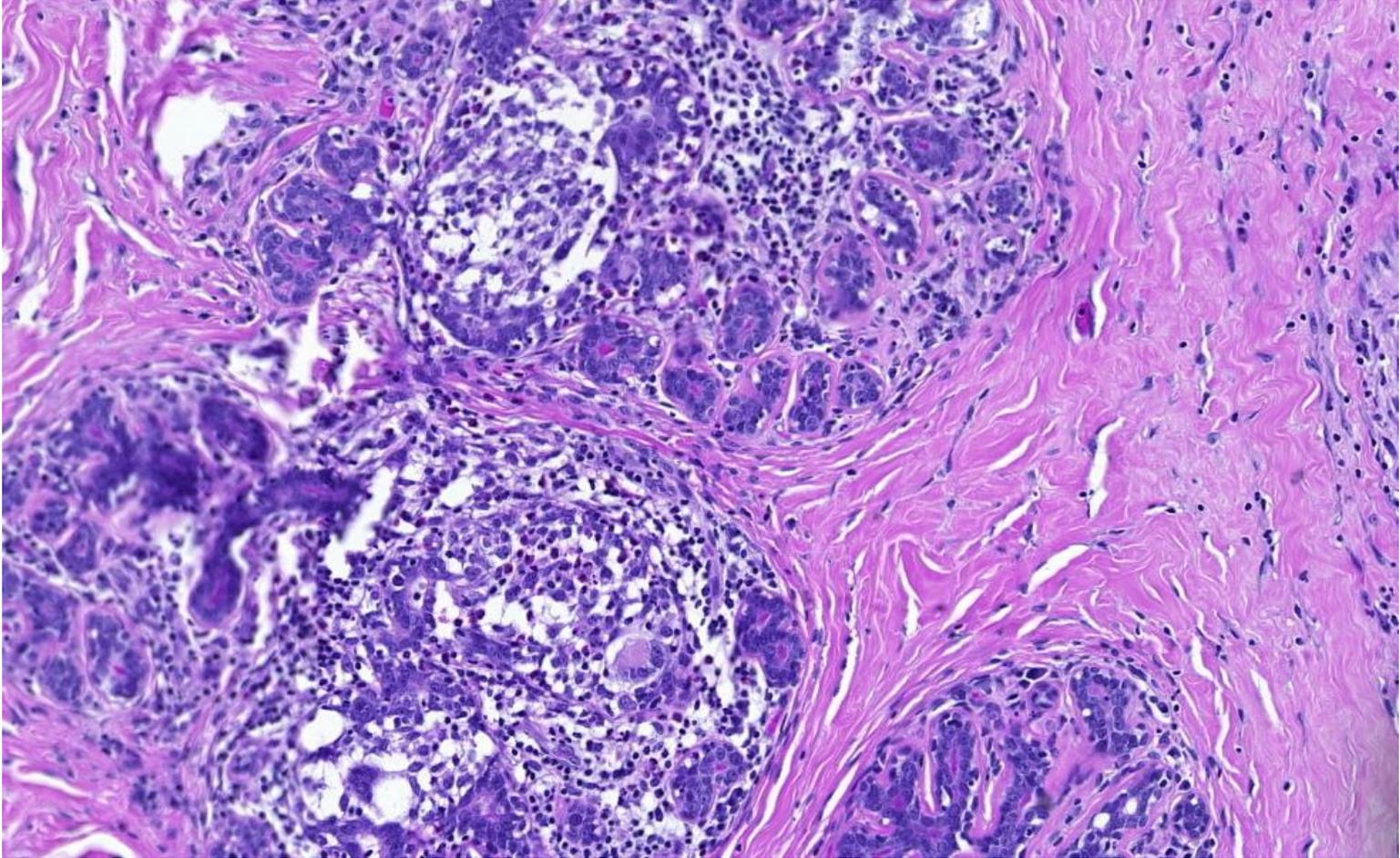
Bacteriology

- **Culture** from discharge: Coagulase negative Staphylococcus & **Corynebacterium jeikeum** (**resistant to** a number of antibiotics, incl. **tetracyclin**; sensitive to vancomycin and linezolid)
- **Probability of contamination**
- But **same flora in 3 consecutive** samples (2 discharges +1 surgical drainage sample with oozing pus (no histology))
- Vancomycin treatment (parenteral) initiated for the „abscess” (no fluctuation or signs of confluent suppuration)
- Fluid aspirated: **C. jeikeum cultured, Gram+ bacilli**
- 2.5 months after initial symptoms: **open surgical biopsy**

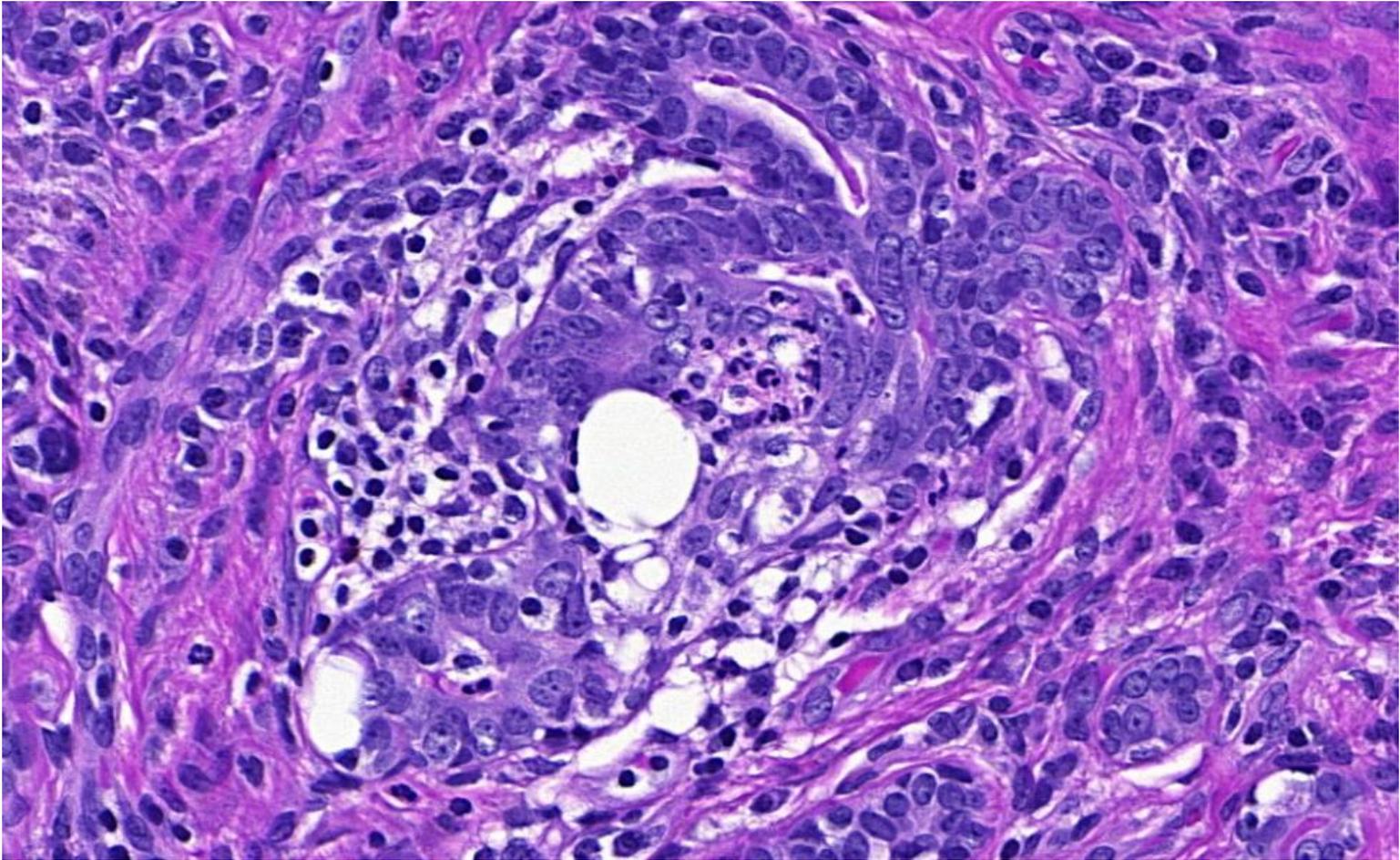
Excision x1



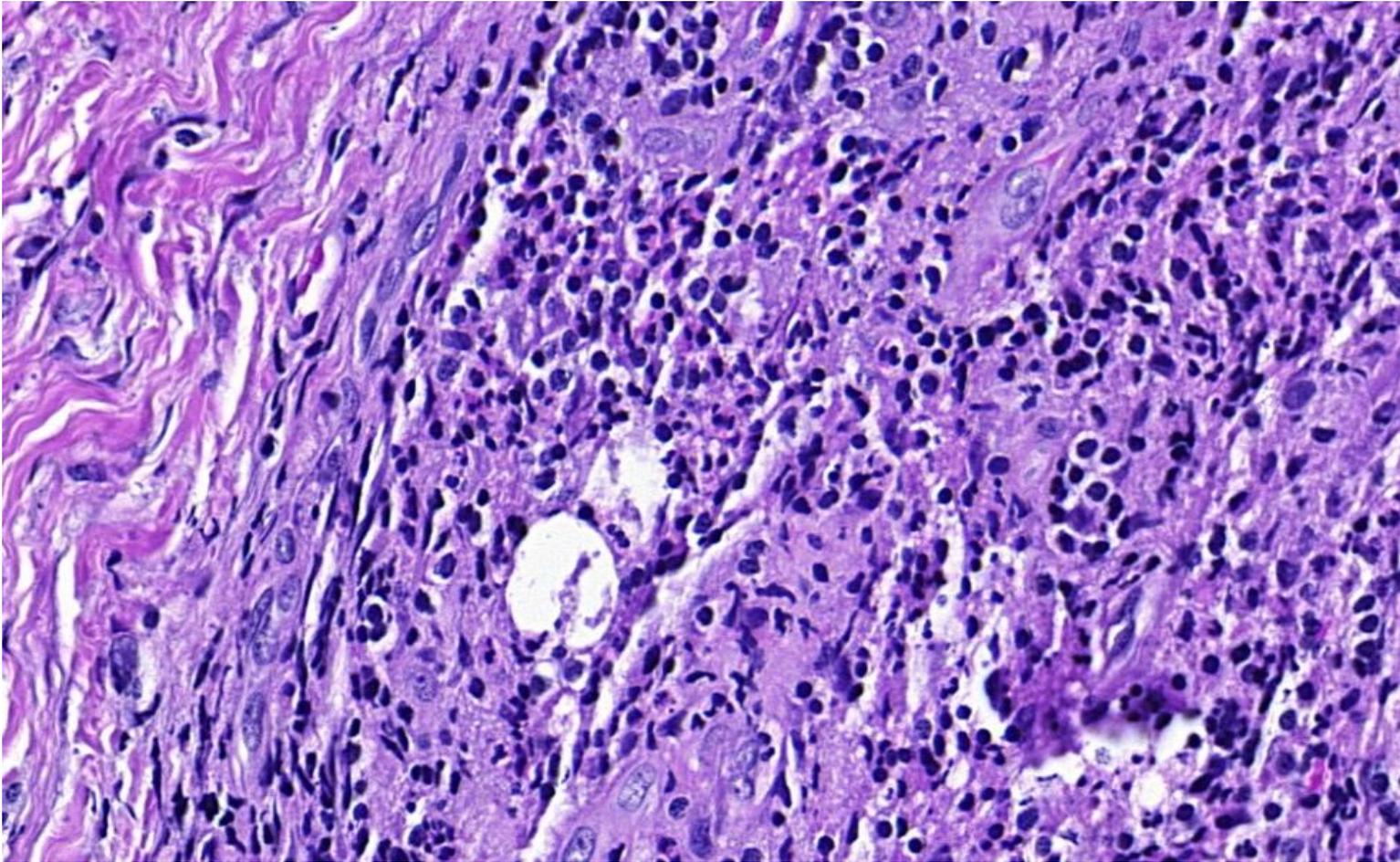
X25 Granulomas



„Cyst”, pericyclic neutrophils



„Cyst”, pericyclic neutrophils



Opinion

- Inflammation with granulomas & „cysts”, without intracystic neutrophils, but pericystic neutrophils, eosinophils and mononuclear cells, with *Corynebacterium jeikeum* as likely aetiology.
- In keeping with: **cystic neutrophilic granulomatous mastitis (CNGP)**

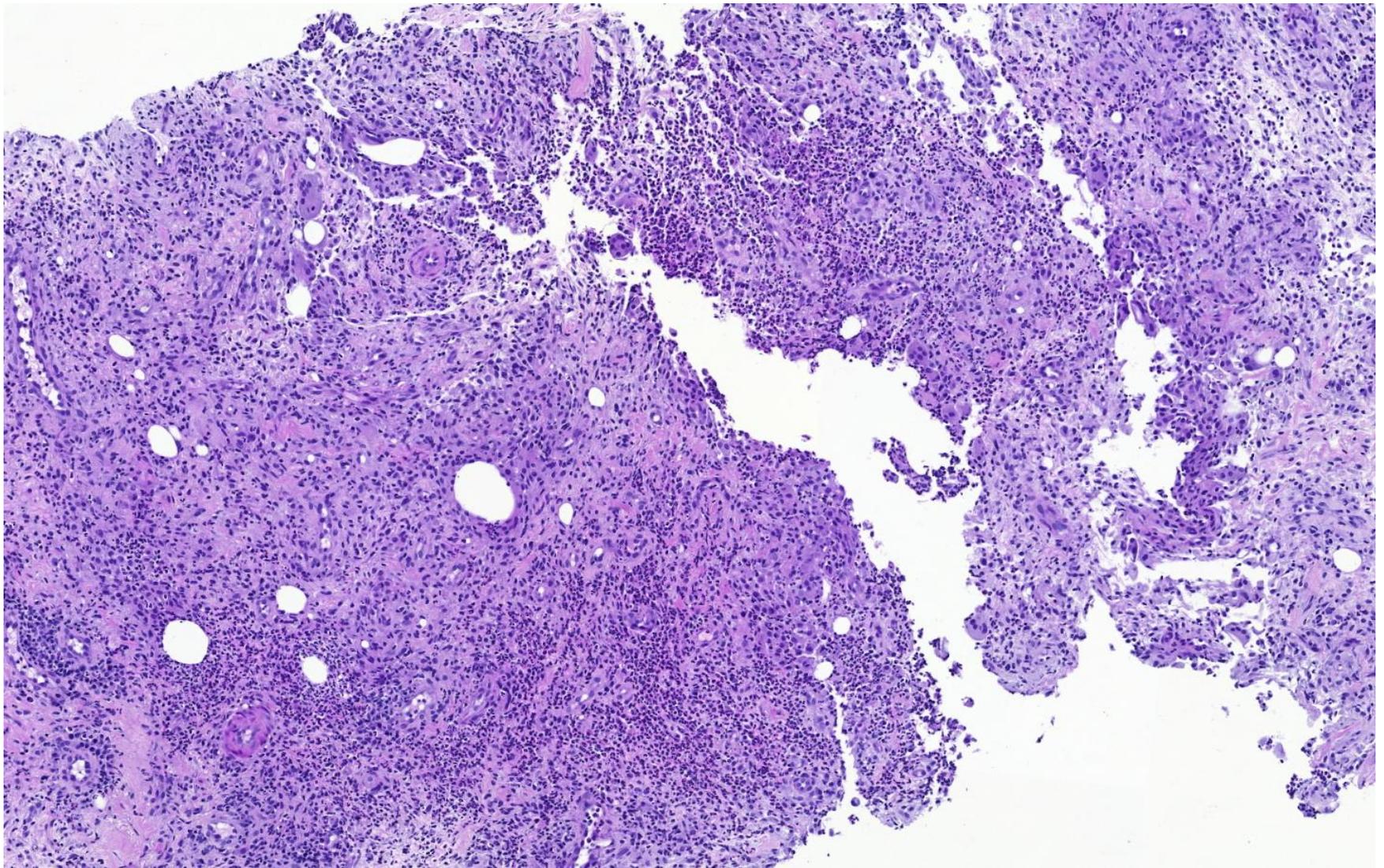
Further treatment

- Open surgery, continuous antiseptic washings and vacuum assisted drainage (negative pressure wound therapy – NPWT)
- VAC foil for 1 month
- Regression of inflammatory symptoms
- NED one year after

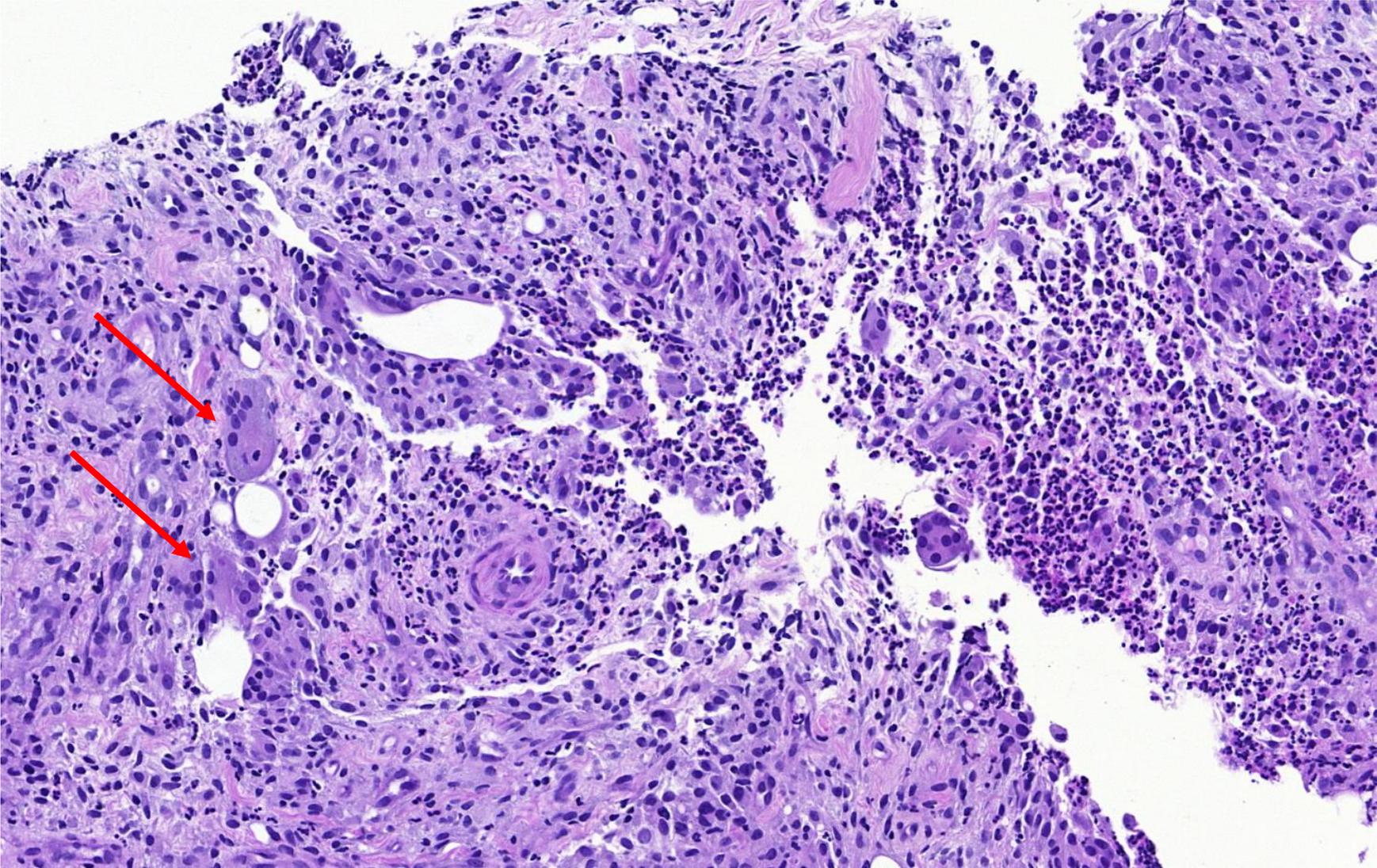
Another CNB case – a more typical one

Another CNB case – a more typical one

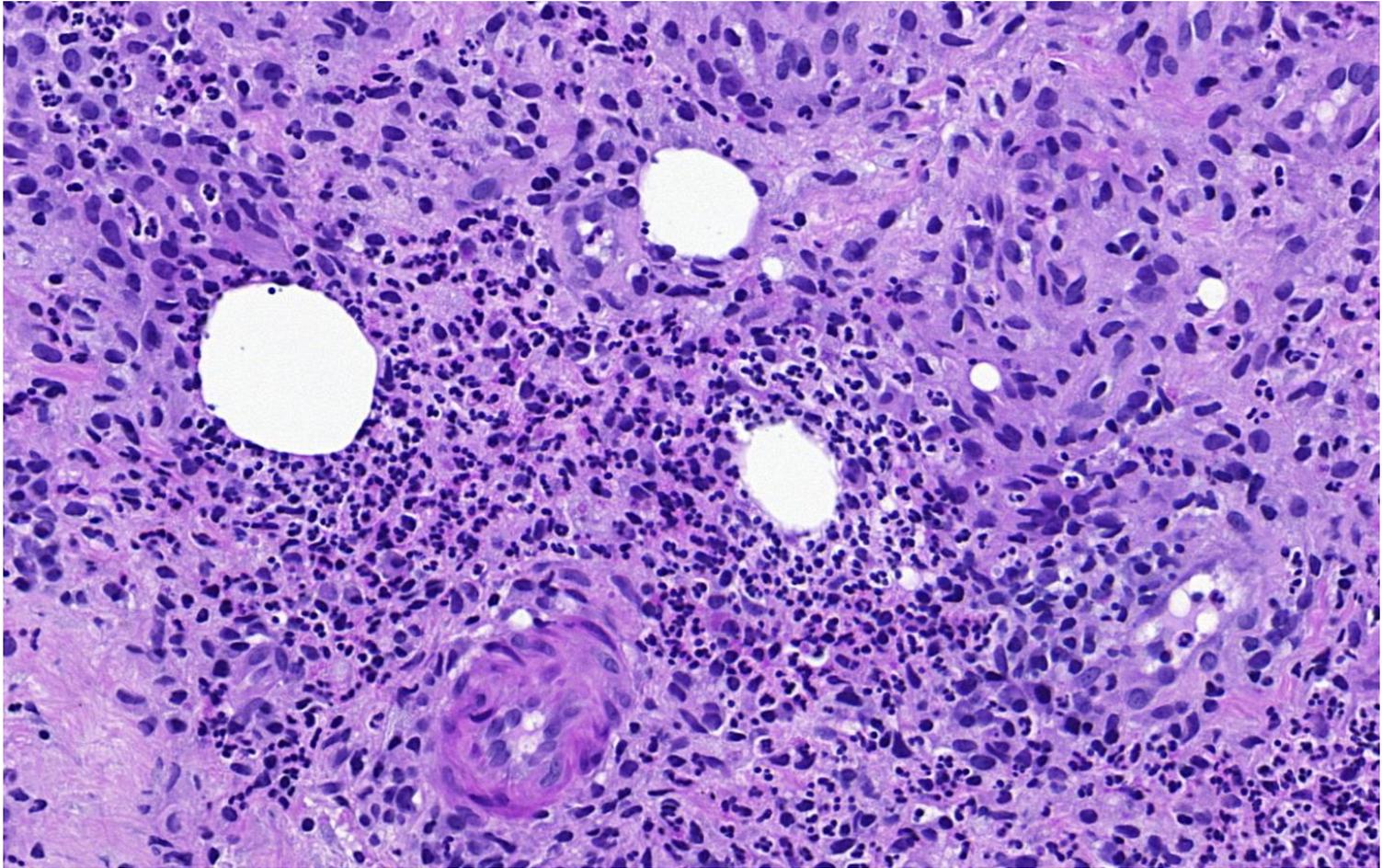
HE x18



HE x40



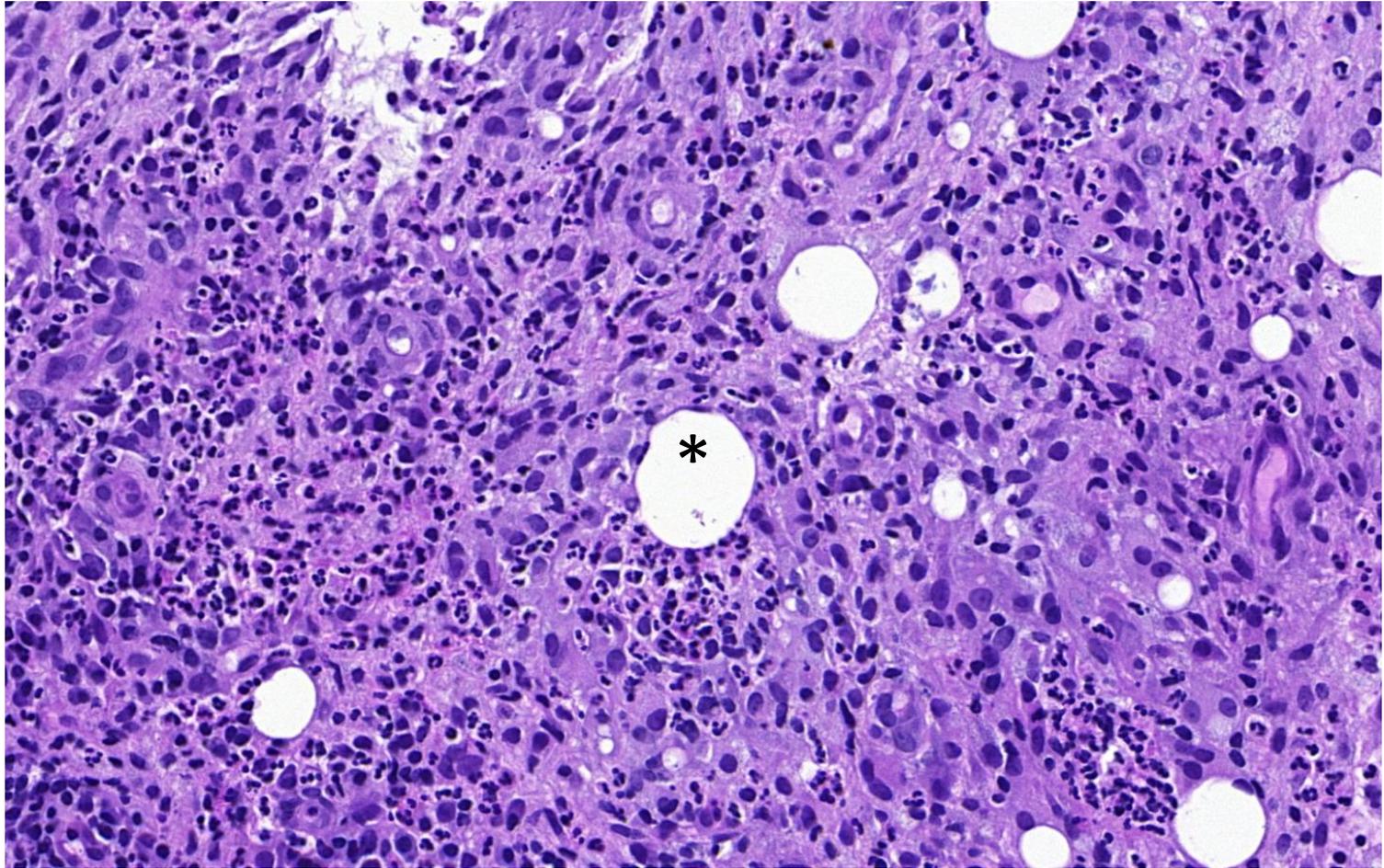
HE x70



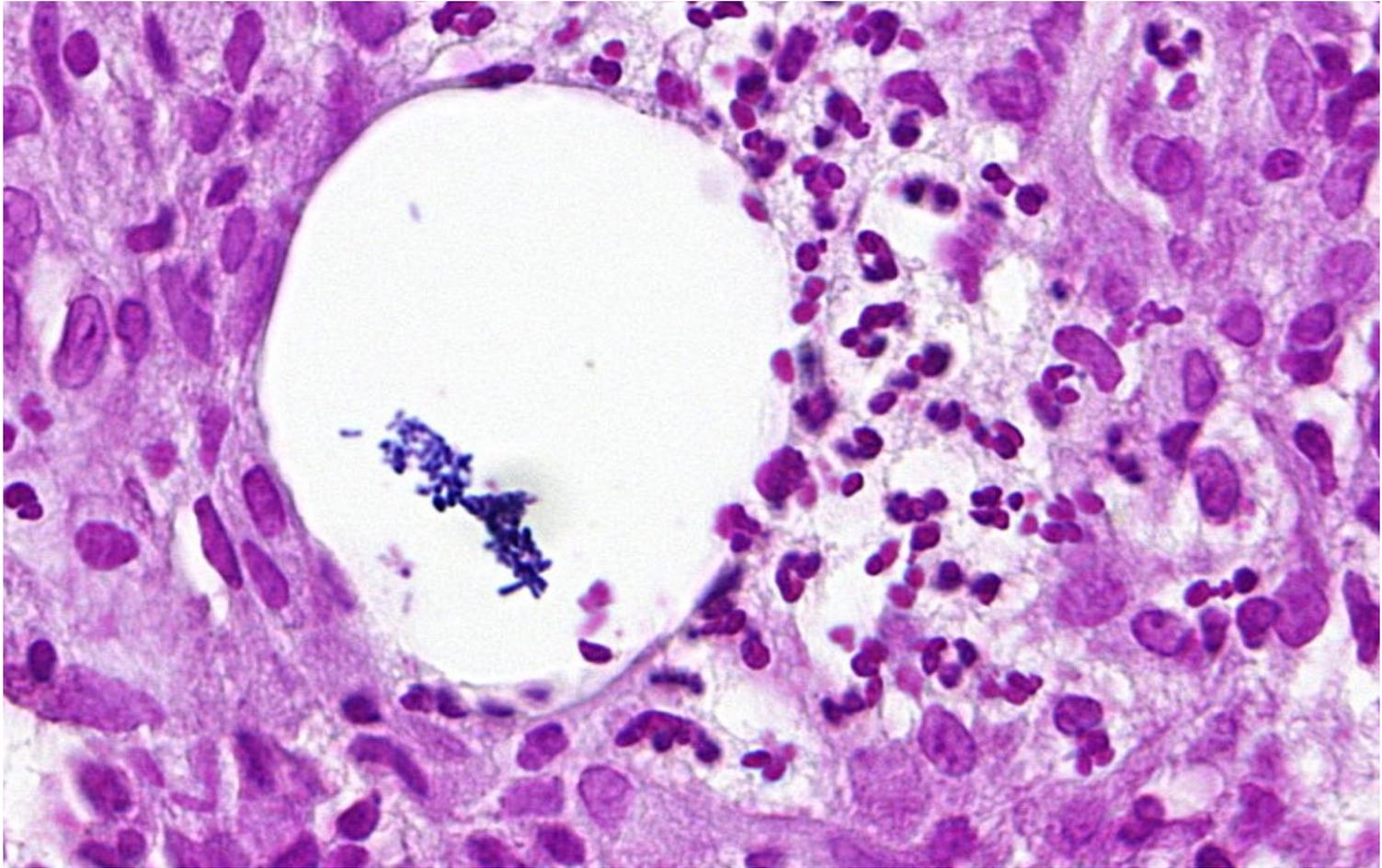
Cystic neutrophilic granulomatous mastitis

- Lipophilic corynebacteria are **difficult to grow**.
- The **organisms** are very **easy to miss by microscopy**. They are **rare** and **present only in the cystic spaces**.
- The **pattern of inflammation with cystic spaces is so distinctive** and the likelihood of identifying the organism is so low ... ([mycobacterial infection](#) has been **excluded**), **the diagnosis of corynebacterial infection** should seriously be **considered even in the face of a negative Gram stain** to avoid having patients return for multiple biopsies before appropriate antibiotic therapy is initiated.
- **Conclusion: Gram-positive bacilli infections have a distinctive pattern of inflammation in breast abscesses that can easily be overlooked. General pathologists should be aware of the distinctive features of this infection in breast abscesses and should **actively search for gram-positive bacilli in distinctive cystic spaces.****

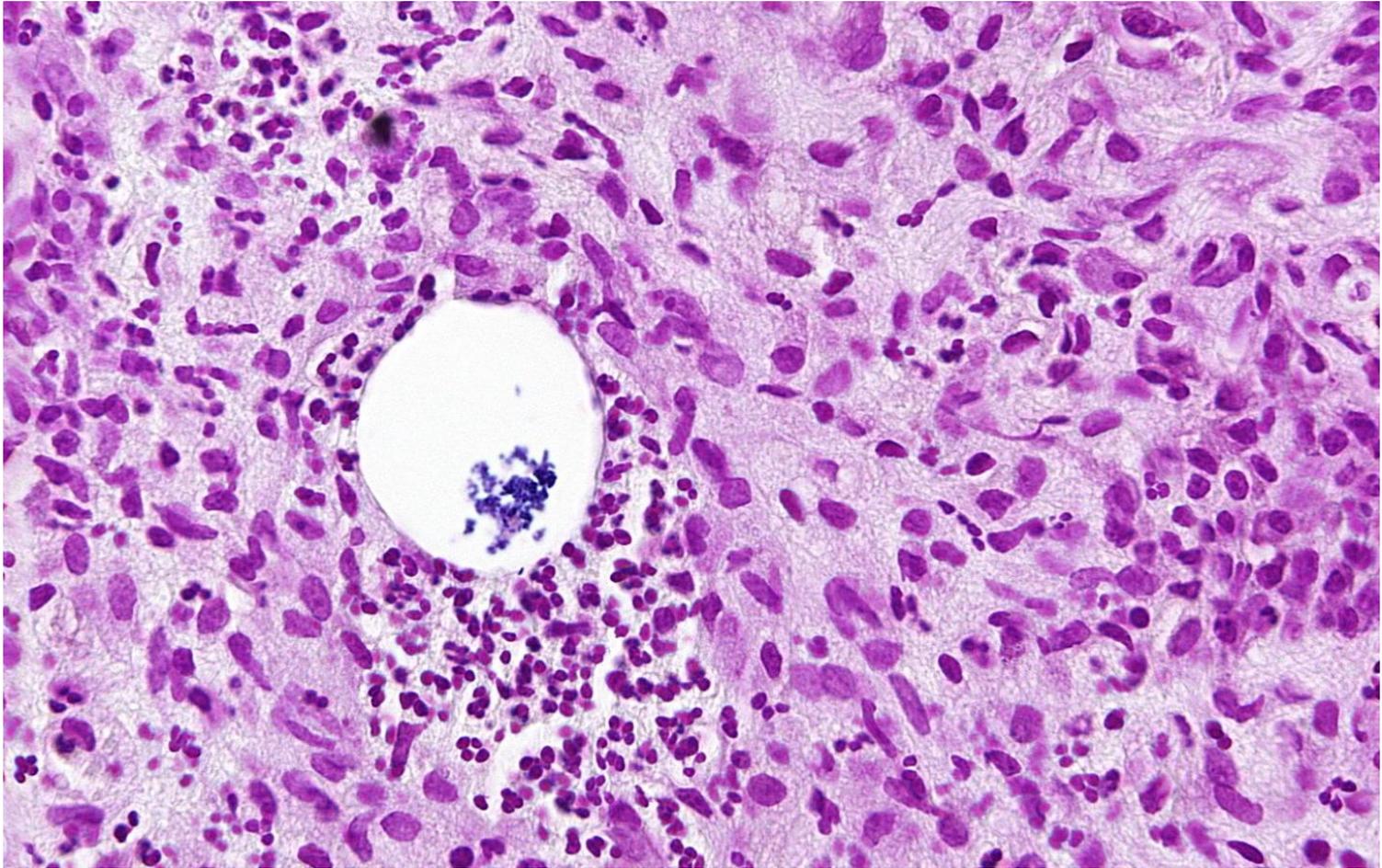
HE x70



Gram x250



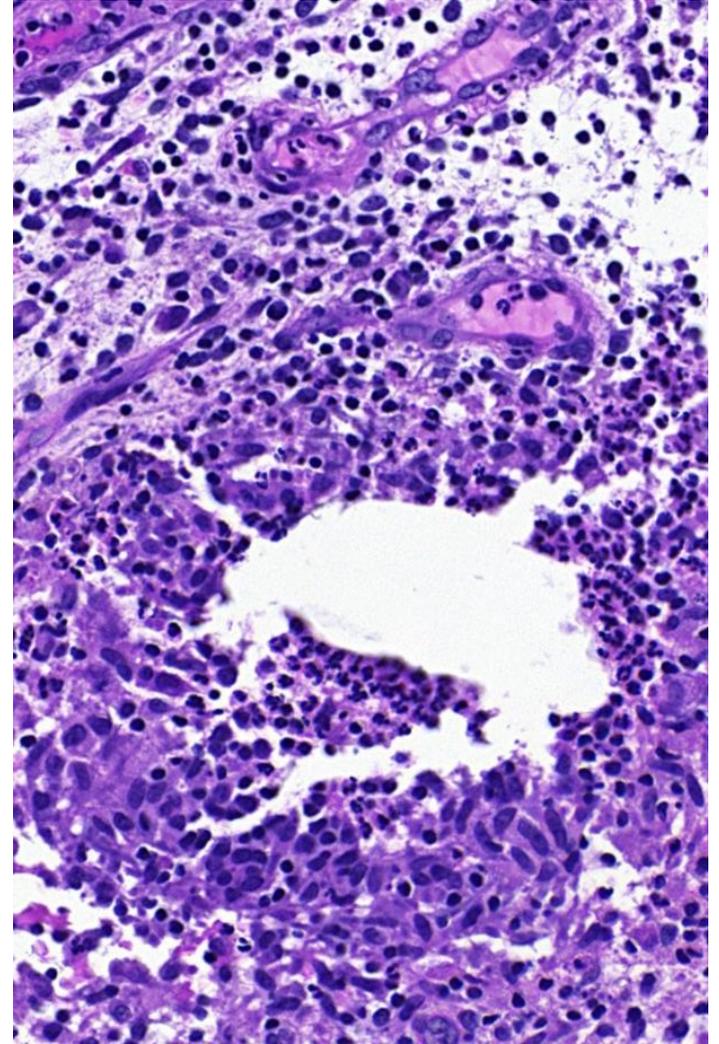
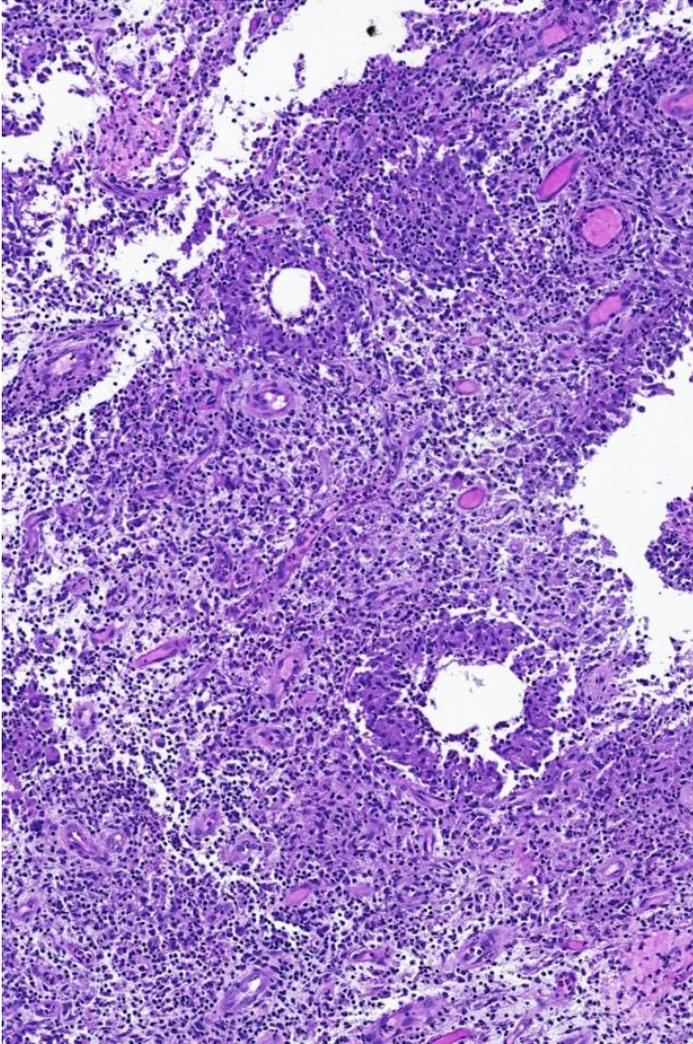
Gram x140



A 3rd typical case (excision: „abscess wall”)

x20

x70



Cystic neutrophilic granulomatous mastitis

- Gram positive bacteria present (or absent)
- **Corynebacterium** species as usual etiologic agent > *ex juvantibus tetracycline* therapy (prolonged: 2x100 mg for 2-4 weeks; CAVE: photosensitisation)
- **Granulomatous inflammation** is quite common with *Corynebacterium* infection, it **is not always present** (Renshaw AA, et al. Am J Clin Pathol 2011;136:424-7.)

First systemic description in breast

- Corynebacteria isolated from 24 women's breast tissue, pus or deep wound swabs during a period of 7 years
- Mean age: 31, mean parity 2.4; 8 breast feeding at presentation
- The lipophilic *Corynebacterium kroppenstedtii* was the most common

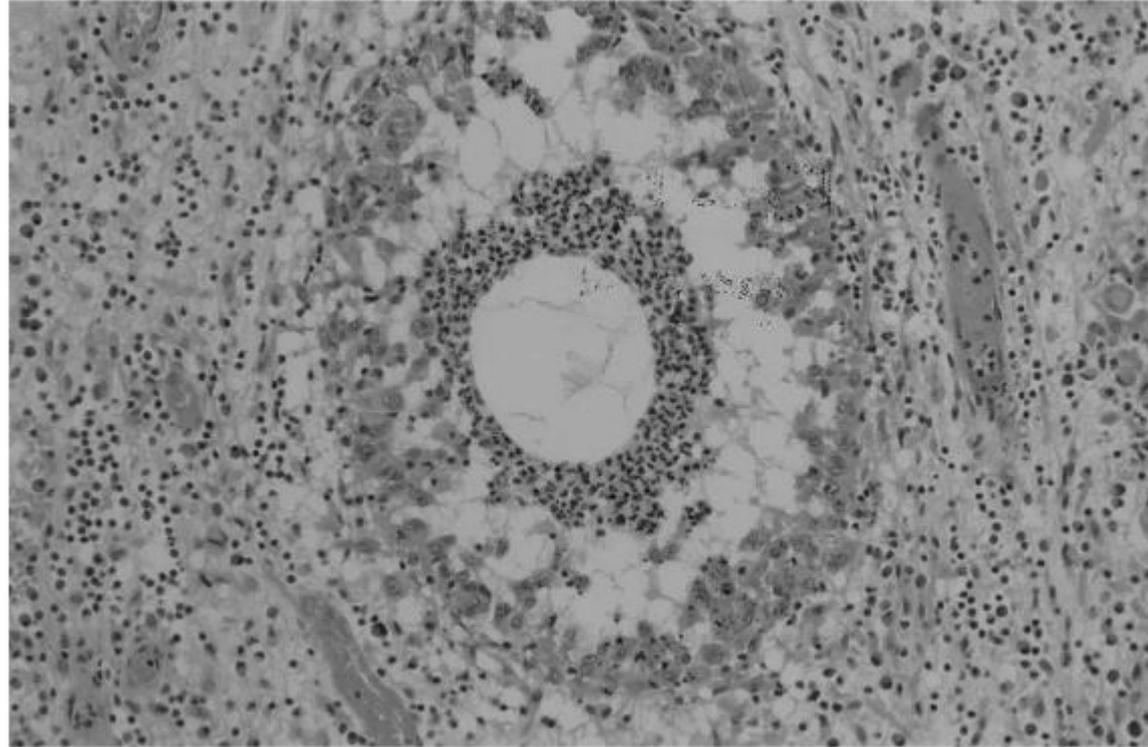
- Corynebacteria are normal flora (infection vs colonization vs contamination), but infection and causative nature is the most likely

First systemic description in breast

- 17 had specimens for **microscopy** (cytology or histology):
 - 12 acute and chronic inflammation with **granulomas**:
 - 9 lobulocentric reminiscent of lobular granulomatous mastitis
 - 2 ductectasia without lobulocentric granulomas
 - 1 unclassified (no breast epithelium in CNB)
 - 10 had **characteristic „suppurative lipogranulomas”**

The „suppurative lipogranulomas” (Fig 1)

- Outer cuff of epithelioid histiocytes + giant cells
- Central collection of PMNs
- Empty space (dissolved lipid?)
- Coryneform Gram-positive bacilli in the spaces (in 7/10 cases)



Suppurative granulomas associated with *Corynebacterium* infection

- **34** women with **inflammatory breast disease + microbiological specimens with corynebacteria isolated and/or histological specimens containing coryneform bacteria.**
- **27/34 (79%)** of the cases had histological and/or cytological evidence of **suppurative granulomas**, 14/34 cases also had Gram-positive bacilli (GPB), recognizable as coryneform bacteria, in histological sections. In all cases **the bacilli were confined to empty spaces, consistent with dissolved lipid, and were surrounded by neutrophils and, frequently, suppurative granulomas.**
- Granulomatous mastitis can be associated with corynebacteria infection, particularly infection by *C. kroppenstedtii*. The significance of this finding, which has previously been described in only a single case report, is discussed.

Taylor GB, Paviour SD, Musaad S, et al. A clinicopathological review of 34 cases of inflammatory breast disease showing an association between corynebacteria infection and granulomatous mastitis. *Pathology* 2003;35:109–119

Granulomatous mastitis

Kessler & Wolloch 1972

Idiopathic Lobular GM

Often peri- /postpartum inflammation
Lobulocentric chronic inflammation

- Suppuration?
- Steroid therapy favoured over surgery
- Many of these may represent „CNGM” – (difficult to culture or demonstrate the causative bacteria) - this may interfere with „literature review” results

Paviour 2002/ Taylor 2003

CNGM

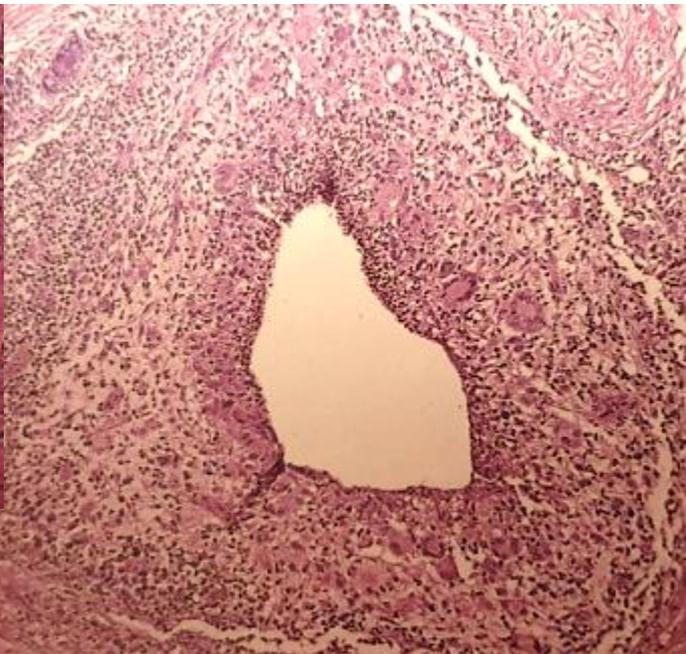
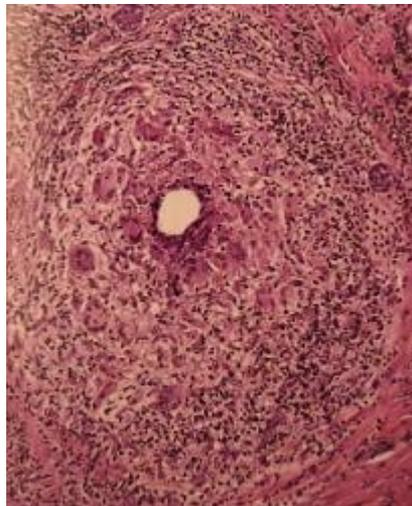
- Suppurative
- Tetracyclin is the drug of choice

CASE REPORT

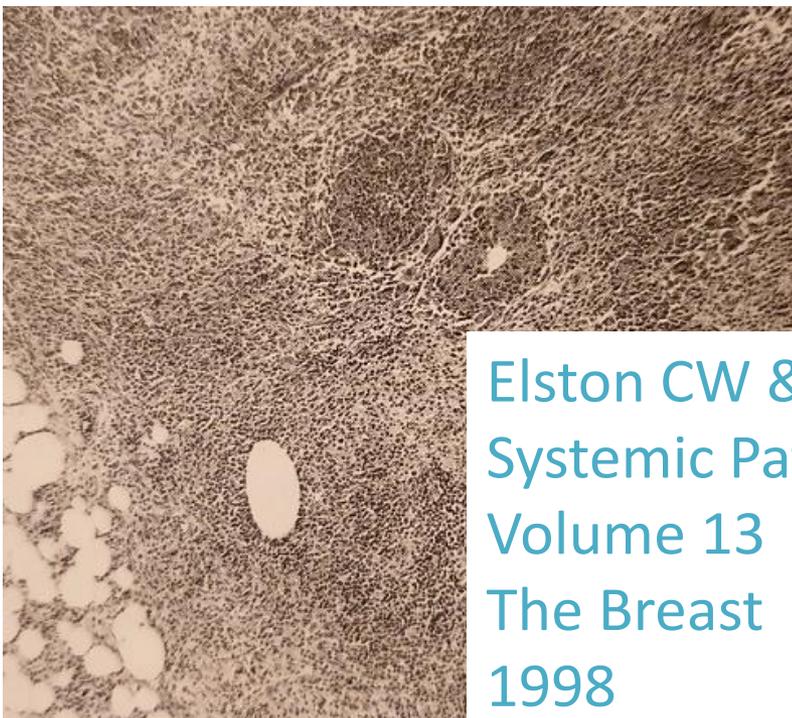
Granulomatous Lobular Mastitis
Following Drug-Induced
Galactorrhea and Blunt Trauma

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Departments of *Pathology and †Surgery, Bács-Kiskun County Teaching Hospital,
Albert Szent-Györgyi Medical University, Kecskemét, Hungary



Rosen's Breast
Pathology 3rd,
2009



Elston CW & Ellis IO
Systemic Pathology
Volume 13
The Breast
1998



Figure 3. Lobular distribution of the inflammation with granuloma formation in fibrous background tissue. (Hematoxylin and eosin; objective $\times 4$; original magnification $\times 13$.)

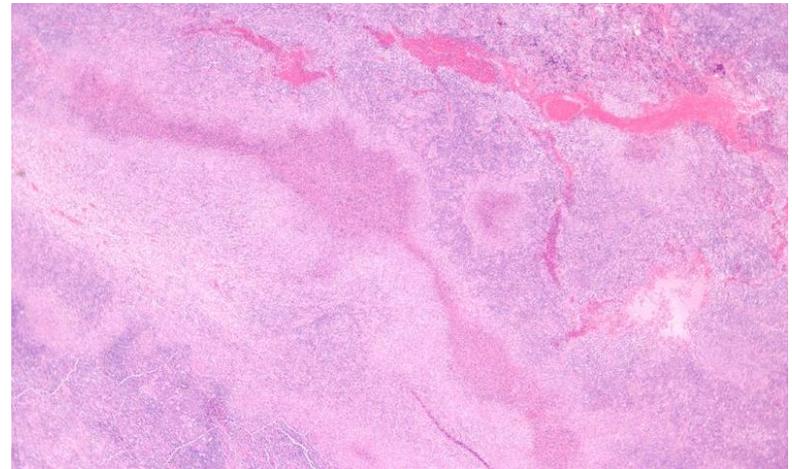
Granulomatous mastitis

Mycobacterial infections (AFB)

- If granulomatous – non suppurative (typically caseating necrosis)
 - *M. tbc* or *bovis*
- If suppurative, generally non granulomatous, but pseudocysts with neutrophils are often present
 - E.g. *M. chelonae*

Suppurative granulomatous infections

- Cat-scratch disease (bartonellosis)



Take home messages

- CGNM is now believed to represent a *Corynebacterium* infection associated mastitis
- The typical feature is the „suppurative lipogranuloma”
- Granulomas may be absent
- The ex juvantibus tetracycline may not always work
- „Idiopathic” lobular granulomatous mastitis may be identical with CGNM in many (or even more) cases