Case 3

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

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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
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”, pericystic neutrophils
„Cyst”, pericystic 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 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.

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 epitheloid 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

Paviour 2002/ Taylor 2003

CNGM

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

- Suppurative

- Tetracyclin is the drug of choice
CASE REPORT

Granulomatous Lobular Mastitis Following Drug-Induced Galactorrhea and Blunt Trauma

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

[Image from Wikimedia]
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