Cystic Neutrophilic Granulomatous Mastitis
An Underappreciated Pattern Strongly Associated With Gram-Positive Bacilli

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Abstract

Although granulomatous lobular mastitis is associated with gram-positive bacilli such as Corynebacterium, this association is not well known. We report 3 cases of mastitis caused by gram-positive bacilli.

All 3 abscesses were suppurative with distinct enlarged cystic spaces in which rare gram-positive bacilli were identified. Two cases were also granulomatous. Cultures in all 3 cases were negative. All 3 patients recovered after biopsy and tetracycline-based therapy.

Infection in the breast by gram-positive bacilli is associated with a distinct histologic pattern, including cystic spaces in the setting of neutrophilic/granulomatous inflammation that can be recognized and should prompt careful search for the organism within enlarged vacuoles.

Breast abscesses are not uncommon and are associated with a variety of infectious organisms, particularly bacteria.1-8 In most cases, these bacterial infections are associated with nonspecific acute and chronic inflammation and reactive changes. While many bacteria are easily cultured from tissue specimens, some organisms can be harder to grow, and a small percentage of cultures from breast abscesses remain negative.3,6-7 In 2003, Taylor et al9 reported a landmark series of 34 breast abscesses with distinct histologic features that were associated with Corynebacterium infection. Most cases were granulomatous, but all cases had a suppurative component with distinct vacuoles that were thought to represent dissolved lipid. Organisms were identified by Gram stain in 16 cases, but in every case, the organisms were rare, often missed on initial review of the Gram stain, and found only within the vacuoles. Although corynebacteria were identified by culture in every case, it was noted that culture of Corynebacterium can be difficult and may not be possible without special culture techniques, including the use of 1% polysorbate (Tween) 80.

Despite this excellent study,9 appreciation of the distinct features of Corynebacterium infection in breast abscesses is not well recognized. We were unable to find a citation of this report in any standard breast pathology or general pathology textbook. To help bring this recognizable histologic pattern to the attention of the general pathology community, we report 3 additional cases of breast abscesses with the same suppurative inflammation with vacuoles and granulomas associated with gram-positive bacilli.
**Case Reports**

Case 1 involved a 54-year-old woman with a dominant 4- to 5-cm mass in the 4 o’clock position of the left breast. There was no history of trauma. The patient had an open biopsy and was given a diagnosis of suppurative and granulomatous mastitis. Initial interpretation of the Gram stain was negative, but on review, gram-positive bacilli were identified in a single cystic space. Fungal and acid-fast stains were negative. The patient underwent 2 subsequent debridements during the next 2 months, but the process did not heal. Cultures from all 3 procedures were negative. Eventually, she was treated with tetracycline for 4 weeks, and the mass eventually resolved.

Case 2 involved a 22-year-old woman with a red, indurated mass 2 weeks after undergoing nipple piercing. Open biopsy revealed neutrophilic, granulomatous inflammation with large cystic spaces. A Gram stain was initially interpreted as negative, but review showed gram-positive bacilli in a single cystic space. Fungal and acid-fast stains were negative. Cultures were negative. She was treated with doxycycline for 2 weeks, and the lesion resolved.

Case 3 involved a 27-year-old woman with a breast abscess of unknown etiology. A debridement was performed. A diffuse, neutrophilic infiltrate was present with distinct cystic spaces. No granulomas were identified. Initial Gram stains were negative. Repeated Gram stain showed rare gram-positive rods in a single cystic space. Fungal and acid-fast stains were negative. The patient’s condition improved with tetracycline therapy for 4 weeks.

None of the 3 women were pregnant or lactating. Cultures were sent directly from the operating room. The length of time from excision to immersion in formalin is not known. Gram stain was performed with a Brown and Brenn tissue Gram stain.

**Histologic Features**

The histologic features in all cases were similar. All 3 contained neutrophilic inflammation with cystic spaces and granulation tissue. In addition, discrete, well-formed granulomas were present in 2 cases. In some areas, the granulomatous inflammation became more diffuse and had central neutrophilic necrosis. Discrete cystic spaces were identified in the neutrophilic areas within the granulomas and within diffuse sheets of neutrophils. These spaces were larger than the surrounding adipose cells. The Gram stain showed gram-positive bacilli in a single cystic space in each case.

**Discussion**

Our purpose here is to bring to the attention of the general pathology community the excellent article by Taylor et al. on *Corynebacterium* infection in the breast. In that report, Taylor et al. described 5 patterns of inflammation: granulomatous lobular mastitis; granulomatous lobular mastitis and duct ectasia; acute mammary duct ectasia with suppurative granulomas; granulomatous inflammation, not otherwise specified; and inflammation, not otherwise specified. While granulomatous inflammation is quite common with
Corynebacterium infection, it is not always present. However, in every case in which organisms were identified, there were distinct enlarged vacuoles within neutrophilic inflammation, and the organisms were present in only 1 cystic space. We believe that pathologists should recognize that granulomatous and neutrophilic inflammation with cystic spaces is a distinct pattern of Corynebacterium infection.

Although we were able to identify gram-positive bacilli in each of our cases, we were unable to grow the bacteria in any case. This is not uncommon, as Taylor et al.9 point out. Nevertheless, while these bacteria may represent Corynebacterium, other gram-positive bacilli, such as Propionibacterium or Clostridium species could not be ruled out. However, the histologic features we report are similar to those described by Taylor et al.9 In addition, to our knowledge, the most common bacterium that has been documented to have granulomas associated with it in breast abscesses is Corynebacterium.10 Finally, there are also several other case reports describing cases of Corynebacterium infection in the breast,11-14 suggesting that this is not an uncommon pathogen in this site.

Regardless of the exact species, recognition of this pattern of gram-positive bacillus infection is important for several reasons. First, many gram-positive species such as Corynebacterium are hard to grow. Lipophilic corynebacteria are fastidious organisms that are difficult to grow without special media, specifically media containing 1% Tween 80.9 Many laboratories, including our own, do not usually use this medium, and, as a result, the cultures in all of our cases were negative. Therefore, if the organisms are not identified by pathology, the fact that the inflammation is bacterial rather than idiopathic may not be recognized, and the patient may not be appropriately treated. In 1 of our cases, the infection was difficult to eradicate until tetracycline-based therapy was initiated. In the series by Taylor et al.,9 the average patient underwent more than 2 procedures and the process took more than 1 year to resolve. In addition, granulomatous reactions are traditionally thought to be more common with mycobacterial infection in the breast15 and in noninfectious inflammation of the breast16 than with bacterial infection. It is important to ensure that acid-fast stains are performed in every case because some mycobacteria can be variably gram-positive. Given the difficulty that may occur in trying to culture some mycobacterial infections, clinicians may elect to...
try a course of treatment for mycobacteria in cases in which bacteria are not identified.

Second, the organisms are very easy to miss. Initial review of the Gram stain in 10 of the 16 cases reported by Taylor et al\(^9\) was negative, and, in our hands, initial review in all 3 cases was negative. There are good reasons that these organisms are often missed. They are rare and present only in the cystic spaces, not the inflammation in between. A pathologist who is unaware of this pattern of inflammation may easily look for organisms in the wrong parts of the slide.

Finally, because the pattern of inflammation with cystic spaces is so distinctive and the likelihood of identifying the organism is so low in many laboratories, once the possibility of a mycobacterial infection has been excluded, should the pathologist raise the possibility of gram-positive bacillus or even corynebacterial infection even in the face of a negative Gram stain? We think this should seriously be considered, if for no other reason than to avoid having patients return for multiple biopsies before appropriate antibiotic therapy is initiated.

We conclude that 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.

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References


