Cystic Neutrophilic Granulomatous Mastitis: A Review of 12 Consecutive Cases from a Canadian Centre

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**BACKGROUND:**
- Cystic neutrophilic granulomatous mastitis (CNGM) is an uncommon cause of mastitis and is associated with Corynebacterium. It was first described in reports from New Zealand and Australia in the early 2000s1, and it has subsequently been reported in North America by Renshaw and colleagues2.
- CNGM is characterized by neutrophilic and granulomatous inflammation surrounding clear cystic spaces (lipid droplets). Sparse clusters of bacteria may be seen in these cystic spaces with Gram stain1 (Images D-E).
- This infection appears to be associated with certain age groups, ethnicities, parity status, and with hyperprolactinemia (primary or secondary from drug exposure, such as phenothiazines)3,4.
- Current literature indicates that cases of granulomatous mastitis, previously considered idiopathic, are often associated with lipolysis Corynebacterium spp. infection, particularly C. kroppenstedtii5.
- It is clinically important to identify cases of CNGM to guide appropriate antimicrobial therapy with antibiotics such as doxycycline, which can penetrate fatty tissues6.
- There have been two cases of C. kroppenstedtii-associated granulomatous mastitis recently reported in British Columbia. Interestingly, both cases lacked the typical histologic pattern of CNGM7.
- Our series is the first comprehensive compilation of CNGM from a Canadian centre.

**OBJECTIVES:**
- To study the histopathologic and clinical features of CNGM in a Canadian setting.
- To determine the work-up required to identify microorganisms in cases of CNGM.

**METHODS:**
- A retrospective search of our electronic surgical pathology files for breast biopsies and excisions reported as demonstrating abscesses, acute, chronic, and/or granulomatous inflammation over a 20-year period was performed. Cases of post-surgical changes were excluded.
- Review of clinical records and surgical pathology slides was undertaken with a breast pathologist and infectious disease specialist.

**RESULTS:**

<table>
<thead>
<tr>
<th>Age</th>
<th>Ethnicity</th>
<th>Parity; last birth (yrs)</th>
<th>Past medical history</th>
<th>Presentation (laterality)</th>
<th>Original specimen</th>
<th>Additional specimens</th>
<th>Gram stains (pos/neg/total)</th>
<th>C&amp;S, PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>Caucasian; 2; 30</td>
<td>Hyperprolactinemia</td>
<td>Painful mass (R)</td>
<td>Lupumectomy</td>
<td>None</td>
<td>7/13</td>
<td>NP; NP</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>Chinese; 1; 7</td>
<td>Healthy</td>
<td>Painful mass (R)</td>
<td>Core</td>
<td>Lumpectomy</td>
<td>1/2</td>
<td>Neg; neg</td>
</tr>
<tr>
<td>3</td>
<td>A. 33 B. 35</td>
<td>Chinese; 1; 2</td>
<td>Gestational diabetes; performed breast feeding</td>
<td>A. Painful mass (R) B. Painful mass (L)</td>
<td>A. Core B. Core</td>
<td>A. FN (prior), excision (after) A. 2/2 B. 0/3</td>
<td>A. Positive for C. kroppenstedtii B. Neg; Neg; neg</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>Caucasian; 0; N/A</td>
<td>PCOS, DM2, obesity</td>
<td>Painful mass (L)</td>
<td>Core</td>
<td>Previous normal core</td>
<td>1/3</td>
<td>NP; NP</td>
</tr>
<tr>
<td>5</td>
<td>54</td>
<td>Caucasian; 2; 20</td>
<td>Hypothyroidism, hyperprolactinemia</td>
<td>Painful mass (L)</td>
<td>Core</td>
<td>None</td>
<td>1/1 (GMP)</td>
<td>NP; NP</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>Caucasian; 2; 12</td>
<td>Diabetes; smoker at presentation</td>
<td>Painful mass (R)</td>
<td>Core</td>
<td>Core, mastectomy</td>
<td>0/2 (core), 0/5 (mastectomy)</td>
<td>Neg; NP</td>
</tr>
<tr>
<td>7</td>
<td>25</td>
<td>Caucasian; 0; N/A</td>
<td>Healthy, ex-smoker</td>
<td>Mass (R)</td>
<td>Core</td>
<td>Excision</td>
<td>0/4</td>
<td>NP; NP</td>
</tr>
<tr>
<td>8</td>
<td>37</td>
<td>Venezuelan; 2; unknown</td>
<td>Healthy</td>
<td>Unknown (R)</td>
<td>Core</td>
<td>None</td>
<td>1/3 (GMS)</td>
<td>NP; NP</td>
</tr>
<tr>
<td>9</td>
<td>43</td>
<td>Caucasian; 3; 5</td>
<td>Healthy, performed breastfeeding</td>
<td>Pain (L)</td>
<td>Core</td>
<td>None</td>
<td>0/8</td>
<td>NP; NP</td>
</tr>
<tr>
<td>10</td>
<td>39</td>
<td>Caucasian; 3; 5</td>
<td>Choroidi-Marie-Tooth disease with ataxia</td>
<td>Pain (L)</td>
<td>Core</td>
<td>None</td>
<td>1/3 (Steiner stain positive)</td>
<td>Neg; NP</td>
</tr>
<tr>
<td>11</td>
<td>A. 32 B. 57</td>
<td>Caucasian; 1; unknown</td>
<td>Pregnant at 50 weeks</td>
<td>Healthy</td>
<td>A. Painful mass (R) B. Painful mass (L)</td>
<td>A. Core B. Core</td>
<td>A. FN, core, excisions A. 0/2 (core), 0/2 (excision) B. 0/3 (core), 0/3 (excision)</td>
<td>Aspirate from I&amp;D grew CoNS; Neg</td>
</tr>
<tr>
<td>12</td>
<td>57</td>
<td>Caucasian; 3; unknown</td>
<td>Unknown</td>
<td>Pain &amp; erythema (R)</td>
<td>Core</td>
<td>Previous core (non-specific inflammation)</td>
<td>0/1</td>
<td>NP; NP</td>
</tr>
</tbody>
</table>

**DISCUSSION:**
- CNGM, resulting in breast biopsy, is rare in our population; we identified 12 patients in a 20-year retrospective review of non-postoperative inflammatory breast pathology specimens.
- Two patients had multiple breast biopsies, showing early palisading granulomas followed by classic CNGM on subsequent biopsies. This suggests there is an evolution of morphological patterns with this infection (Images A-C).
- Similar to previous studies, our cohort included 1) patients of varied ethnicities, 2) most patients were parous (10/12), and 3) several had an endocrinopathy (5/12). Interestingly, two patients had bilateral disease and one patient demonstrated Gram positive cocci.
- Our study supports the previous recommendations of performing multiple Gram stains when suspicious CNGM: 1) 21/74 (28%) of Gram stained revealed organisms; 2) 9/23 (31%) of the repeatedGram stains were positive confirming the value of the additional workup; 3) 8/12 (67%) of patients demonstrated organisms on at least one of the specimens submitted.
- From this series, we have found that due to sparse distribution of the bacteria, it is crucial to: 1) test multiple blocks as this increases the probability of identifying the bacteria. In cases where there is only one block, it advisable to order a repeat gram stain as the bacteria are sometimes visible on deeper sections; 2) If an infection is suspected clinically, C&S should be sent to increase the chances of identifying the organisms and susceptibilities. If an infection was not suspected at presentation, but histopathology reveals neutrophilic or granulomatous inflammation, subsequent specimens should be sent for C&S.

**CONCLUSIONS:**
- CNGM may appear as palisaded granulomatous inflammation, without the expected ‘cystic’ pattern.
- Application of multiple Gram stains increases the ability to identify the causative bacterium.
- Recognition of CNGM in breast biopsies and collaborative communications are essential to direct appropriate therapy.

**REFERENCES:**


**CONTACT INFORMATION**

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