Antimicrobial treatment options for granulomatous mastitis caused by
Corynebacterium species

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Running Title: Treatment of mastitis caused by Corynebacterium spp.

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Abstract:

Background: Corynebacterium species are increasingly recognised as important pathogens in granulomatous mastitis. Currently there are no published treatment protocols for Corynebacterium breast infections. This study describes antimicrobial treatment options in the context of other management strategies used for granulomatous mastitis.

Method: Corynebacterium spp. isolated from breast tissue or aspirates stored from 2002-2013 were identified and determined to species level using MALDI-TOF, 16S RNA sequencing and rpoB gene targets. The minimum inhibitory concentrations (MIC) for 12 antimicrobials were performed by E-test for each isolate. Correlations of these with antimicrobial characteristics, choice of antimicrobial, and disease outcome were evaluated.

Results: Corynebacterium spp. from breast tissue or aspirates were confirmed in 17 isolates from 16 patients. Based on EUCAST breakpoints, Corynebacterium kroppenstedtii isolates (11) were susceptible to seven antibiotic classes but resistant to beta-lactam antibiotics. Corynebacterium tuberculostearicum isolates (4) were multi-drug resistant. Two non-lipophilic species were isolated; Corynebacterium glucuronolyticum and Corynebacterium freneyi, both with variable susceptibility to antimicrobial agents. Short course antimicrobial therapy was common (median six courses per subject, range 1-9). Patients with C. kroppenstedtii presented with a hot, painful breast mass and underwent multiple surgical procedures (median four, range 2-6).

Conclusion: The management of Corynebacterium breast infections requires a multidisciplinary approach and includes culture and appropriate sensitivity testing to guide antimicrobial therapy. Established infections have a poor outcome possibly because...
adequate concentrations of some drugs will be difficult to achieve in lipophilic granulomata.
Lipophilic antimicrobial therapy may offer a therapeutic advantage. The role of immunotherapy has not been defined.

Introduction

Granulomatous mastitis (GM) is a rare inflammatory condition which typically occurs in parous women of reproductive age (1). Clinically it can present as a breast mass with features similar to breast malignancy (2). Multiple infective and inflammatory conditions, including tuberculosis (TB), fungal infections, sarcoidosis, amyloidosis, and Wegener’s granulomatosis have been recognised but recently attention has been drawn to corynebacteria species as a specific pathogen in this disease. Typically corynebacteria breast infections are characterized by abscess formation, granulomatous inflammation and progression to sinus/fistula formation (3). This and other specific diagnoses should be excluded before a diagnosis of idiopathic granulomatous mastitis (IGM) is made (3–5).

Commonly it is the lipophilic species of the Corynebacterium genus that cause mastitis (3, 6–8). As such, a microbiological diagnosis can be challenging due to their fastidious growth requirements and prolonged incubation time (3, 7). It is likely that cases due to Corynebacteria are under-recognised or its relevance underappreciated when isolated from breast samples (5). Furthermore, most antimicrobials are hydrophilic with poor distribution to lipid environments, which has implications for efficacy of treatment (see Table 1).

Current knowledge about antimicrobial options to treat Corynebacterium mastitis is lacking.
Antimicrobial choices for these infections have largely been driven by non-standardized disc
testing, indicating broad susceptibility to a range of antimicrobial classes. Many patients undergo multiple surgical procedures and repeated short-courses of antimicrobials before symptoms abate months to years later suggesting this approach has little effect on the natural history of this disease (3, 9–11).

The aims of this study were; firstly to describe the *Corynebacterium* species isolated from cases of granulomatous mastitis; and secondly to describe antimicrobial treatment options for *Corynebacterium* breast infections with reference to their likely concentration at the site of infection. This is placed in the context of other suggested management strategies for granulomatous mastitis such as surgery and immunomodulator therapy.

**Materials and methods:**

**Case definition.** Cases were included if a *Corynebacterium* species was isolated from a specimen obtained by a sterile technique from a breast mass. Cases were excluded if there was any other cause found for the condition on histology or culture.

A database search of samples processed at Canterbury Health Laboratories (Christchurch, New Zealand) found a record of 27 isolates identified as *Corynebacterium* spp. from breast specimens from 2002-2013. Twenty isolates (two from the same patient) were from a sterile site (surgical tissue specimen or percutaneous aspirate) and able to be grown in culture.

**Microbiological investigations.** Each isolate was cultured on 5% sheep blood agar (Fort Richard Laboratories, Auckland, New Zealand) and incubated at 5% CO₂, 37°C. Colonies were identified by phenotypic characteristics and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) using the Bruker
Biotyper (Bremen, Germany). Accepted identification by MALDI-TOF was made on scores of \( \geq 2.0 \), otherwise samples were reanalysed after ethanol-formic acid extraction (12). The identification of all 20 isolates was confirmed by 16S RNA sequencing (13). Isolates established to be *Corynebacterium* spp. had *rpoB* gene PCR performed (14). The DNA sequences were compared to reference strains deposited in the GenBank database using the BLAST algorithm (15).

**Susceptibility testing.** The minimum inhibitory concentrations (MIC) for 12 antimicrobials (listed in Table 1) were performed by *E*-test (bioMerieux, Marcy l’Etoile, France). The antimicrobial selection was based on: published susceptibility data; empiric use in breast infections; and suitability for prolonged courses or in combination therapy (7, 16, 17).

Mueller-Hinton agar (Fort Richard Laboratories, Auckland, New Zealand) was used for the *E*-tests and incubated at 37 °C, 5% CO\(_2\). The plates were inoculated with a bacterial suspension in brain heart infusion (BHI) broth (Fort Richard Laboratories, Auckland, New Zealand) of turbidity equivalent McFarland standard 1 as per *E*-test manufacturer recommendations for *Corynebacterium*. European Committee on Antimicrobial Susceptibility Testing (EUCAST) *Corynebacterium* breakpoints were used for the interpretation of MICs (18). Non-species related breakpoints were used for amoxicillin-clavulanate and ceftriaxone.

**Clinical correlation.** The clinical notes of patients with confirmed *Corynebacterium* breast infection were reviewed to confirm the presence of a breast mass, a granulomatous reaction on histology and exclude any with alternative pathology. Basic demographic information, antimicrobial therapy, duration of treatment and outcome were recorded.
Results:

Identification of isolates. From the initial 20 isolates, three were reclassified to the genus Actinomyces, leaving 17 Corynebacterium isolates from 16 patients. Prior to the availability of MALDI-TOF MS and molecular techniques in our laboratory, identification combined phenotypic characteristics and biochemical profile (API-Coryne system, BioMérieux, France).

Ten patients had Corynebacterium kroppenstedtii isolated from breast specimens (one patient with C. kroppenstedtii isolated twice); four had Corynebacterium tuberculostearicum isolated; one Corynebacterium glucuronolyticum and one Corynebacterium freneyi.

Morphologically C. kroppenstedtii and C. tuberculostearicum had round, non-pigmented, non-hemolytic colonies (<1mm). C. glucuronolyticum colonies were large, white and mucoid whereas C. freneyi had large, yellow, wrinkled colonies.

Of the 17 isolates, six reliably scored ≥2.0 on MALDI-TOF and a further five ≥1.8. The remainder had values below the accepted score for reliable identification (<1.7). MALDI-TOF was unable to differentiate C. freneyi from C. xerosis.

16S rRNA gene sequencing was able to confirm species identification in 16 isolates with ≥98% similarity to the type strain of the species. The exception was C. freneyi which needed rpoB gene sequencing to differentiate from C. xerosis with a 98% gene similarity to the type strain.

Antimicrobial susceptibility. E-test MICs for the lipophilic C. kroppenstedtii and Corynebacterium tuberculostearicum were read at 24 and 48 hours, due to their slow growth. C. glucuronolyticum and C. freneyi E-test MICs were read at 24 hours.
The susceptibilities of *C. kroppenstedtii*, *C. tuberculostearicum*, *C. glucuronolyticum* and *C. freneyi* isolates are shown in Table 1. Based on EUCAST breakpoints for this genus, isolates of *C. kroppenstedtii* were susceptible to rifampicin, tetracycline, trimethoprim-sulfamethoxazole, linezolid and vancomycin and resistant to the beta-lactams (18). One isolate was multi drug-resistant. Isolates of *C. tuberculostearicum* were multi-drug resistant, only consistently sensitive to linezolid and vancomycin.

**Clinical correlation.** A pure growth of a *Corynebacterium* species was isolated from the initial breast specimen in 13 subjects. Of these, 12 presented with a new breast lesion (*C. kroppenstedtii* 10, *C. tuberculostearicum* 1, and *C. freneyi* 1) and one grew *C. tuberculostearicum* from a collection eight months after surgery. The one male patient in this series grew *C. glucuronolyticum* and an *Actinomyces spp.* from an acutely infected breast cyst. In two patients who had previous surgical intervention other bacteria were identified from the same sample (*C. tuberculostearicum* and *Staphylococcus lugdunesis; C. tuberculostearicum*, *Finegoldia magna* and *Staphylococcus aureus*). Gram positive bacilli were seen on microscopy of a direct Gram stain with 8/17 specimens. In most cases growth of corynebacteria was observed early in the clinical presentation, but repeated isolation was uncommon in successive specimens. Notably, only *C. kroppenstedtii* was isolated from specimens taken at a later date in two of the 10 patients. Mycobacterium culture had been requested in six of the 12 patients who presented with a new breast mass; these were all negative. No patient had fungal testing requested. Ten of the 16 patients, including the one male patient, were of NZ European or European ethnicity. The other ethnicities included Pacific Islander (n=2), Maori (n=2), African and East Asian. The median age was 42 years (range 21-71 years).
All 16 patients were referred to general surgery for management and 14 underwent fine-needle or open biopsy to exclude malignancy. Three patients had been seen by the infectious diseases team for advice on antimicrobial therapy once a microbe had been isolated. Empiric antimicrobial choice, treatment and outcome are showed in Table 2. Repeated short courses (5-7 day) of antimicrobial therapy was common (median six courses per subject, range 1-9). No patient had been treated with immunomodulator or antituberculous therapy.

Clinical information was available for nine of the ten patients from whom C. kroppenstedtii had been isolated. All presented with a single peripheral breast mass of up to four months duration that was hot, painful and swollen. Three subjects went on to develop bilateral breast disease with multiple breast abscesses on both sides. Two patients had an aspirate cultured from a secondary breast mass and no microbe was isolated. Granulomatous inflammation was reported on histology in four cases but no bacteria were seen on pathology samples. The median number of surgical interventions per patient was four (range 2-6). These included incision and drainage, fistulotomy and partial mastectomy.

Discussion

The role of Corynebacterium in invasive infections if often debated as most of these species are part of the endogenous skin flora. However, the link between Corynebacterium and granulomatous mastitis has periodically been reported since the publication of a case series by Taylor et al. in 2003 (6, 9, 10, 19). Growth in pure cultures and the isolation from sterile sites, as well as distinct histological findings from breast tissue samples, supports the
causative link (3, 20). In addition, Corynebacterium is a well-known cause of granulomatous mastitis in animals (21). In our series, all 12 patients who presented with a new breast mass had Corynebacterium spp. as a single isolate from a tissue or aspirate sample, further supporting the pathogenic role of these species in breast disease.

Corynebacterium identification and genus characterisation has become more reliable with the availability of MALDI-TOF and molecular techniques (7, 22, 23). To determine to a species level all isolates in this study, 16S rRNA and \( rpoB \) gene sequencing was used. MALDI-TOF reliably identified 6/17 isolates with reliability likely to improve as more strains are added to the Biotyper database.

As found in this study, strains of \( C. \) tuberculostearicum are often multi-resistant, demonstrating the macrolide-lincosamide-streptogramin B (MLSB) mechanism conferred by the \( ermX \) gene (24, 25). While data is limited, antimicrobial susceptibility by non-standardised disc diffusion has been performed on isolates of \( C. \) kroppenstedtii, reporting broad susceptibility to most classes of antimicrobials (9, 11). Isolates in this study, however, were largely resistant to penicillin by \( E \)-test though this could represent a selection bias with penicillin-sensitive strains treated. The variable Corynebacterium strain resistance suggests that correct species identification and antimicrobial susceptibility testing would ideally be performed for all isolates.

The presence of granulomatous inflammation should lead to consideration of further therapy. Corynebacteria survive in lipid-filled vacuoles surrounded by a reactive neutrophilic granulomatous infiltrate rather than in the inflamed tissue (3, 20). This inflammatory reaction can be rapid; in our series the development of granulomata were seen as early as a week from the start of clinical symptoms. In this environment, adequate tissue
concentrations for bactericidal activity may be achieved by agents that are highly lipophilic and have a high volume of distribution which include rifampicin, clarithromycin, trimethoprim-sulfamethoxazole and clindamycin (25, 26). In contrast beta-lactams and fluoroquinolones have low lipid solubility and therefore are expected to be less effective. However fluoroquinolones are used in other active granulomatous infection such as tuberculosis.

Short duration antimicrobial treatment did not appear to help clinical outcomes particularly once granulomatous inflammation was present. However, there were insufficient data to demonstrate that a long duration of treatment was beneficial, as in TB. Furthermore, as the selection of antimicrobial therapy was variable, outcome cannot be inferred from MIC results. For selection of an antimicrobial agent, results of sensitivity testing, MIC values and the agent’s pharmacological properties should be considered and evaluated in prospective studies. Immunomodulator therapy may be a useful therapeutic adjunct by modifying the initial immune response and granuloma formation (23). Corticosteroid therapy in IGM is increasingly used (27–29). Further studies looking into the impact of immunomodulator treatment in cases of granulomatous breast infections are needed, with particular caution if combined with an antimicrobial regime that includes rifampicin (30).

Surgical intervention, particularly for sampling of breast tissue and management of abscesses and fistulae, is necessary. Success when combining these procedures with antimicrobial therapy has been reported (9, 11). Ideally, prompt diagnosis will avoid consequent disfiguring complications.

In summary, the primary goal in any patient who presents with a non-puerperal breast mass is accurate diagnosis including exclusion of malignancy. This study suggests that a failure of
Empiric treatment of mastitis with beta-lactam antimicrobials should trigger further microbiological investigations. Given the poor outcomes seen with *Corynebacterium* mastitis treated with beta-lactam therapy, we suggest other antimicrobials are used as empiric therapy for atypical breast infections, for example doxycycline or trimethoprim-sulfamethoxazole. If granulomatous disease is present, it seems prudent to choose agents that are both active against *Corynebacterium* spp. and have physicochemical properties that would promote activity within the lipid-filled spaces. Preferred choices would include clarithromycin and rifampicin, which are also active in other granulomatous infections such as mycobacteria. Further clinical studies of antibiotic choice and duration of therapy are necessary. Oral corticosteroids, or other immunosuppressive agents, could be of benefit to slow the host immune response and therefore curtail the development of granulomatous disease once a microbiological diagnosis has been established, but again, further research is required.
References:


18. European committee on antimicrobial susceptibility testing. EUCAST. http://www.eucast.org/.


Table 1. Antimicrobial lipophilicity and antimicrobial susceptibilities for C. kroppenstedtii (n=11), C. tuberculostearicum (n=4), C. glucuronolyticum (n=1) and C. freneyi (n=1).

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>LogP EUCAST breakpoint</th>
<th>MIC50</th>
<th>MIC90</th>
<th>MIC Range (%) resistant</th>
<th>Isolate 1</th>
<th>Isolate 2</th>
<th>Isolate 3</th>
<th>Isolate 4</th>
<th>C. glucuronolyticum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>0.76</td>
<td>0.25</td>
<td>0.75</td>
<td>0.094 to 0.75</td>
<td>&gt;32</td>
<td>0.125</td>
<td>&gt;32</td>
<td>0.125</td>
<td>0.094 to 0.75</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>-2.1/ -1.5</td>
<td>0.19</td>
<td>0.38</td>
<td>0.064 to 0.5</td>
<td>&gt;32</td>
<td>0.064</td>
<td>&gt;32</td>
<td>0.094</td>
<td>0.047 to 0.38</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>3.24</td>
<td>0.023</td>
<td>0.023</td>
<td>&lt;0.016 to &gt;32</td>
<td>&gt;32</td>
<td>&gt;32</td>
<td>0.032</td>
<td>0.094</td>
<td>0.38 to 4.0</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>-4.4</td>
<td>0.75</td>
<td>0.75</td>
<td>0.38 to 1.0</td>
<td>0.75</td>
<td>0.5</td>
<td>0.38</td>
<td>0.75</td>
<td>0.38 to 0.38</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>-3.5</td>
<td>0.38</td>
<td>0.38</td>
<td>0.25 to 0.5</td>
<td>&gt;32</td>
<td>&gt;32</td>
<td>&gt;32</td>
<td>&gt;32</td>
<td>0.75 to 0.75</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>-1.8</td>
<td>0.75</td>
<td>4</td>
<td>0.125 to &gt;32</td>
<td>&gt;32</td>
<td>0.75</td>
<td>&gt;32</td>
<td>0.75</td>
<td>1.0 to 1.0</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>-0.81</td>
<td>0.19</td>
<td>&gt;32</td>
<td>0.094 to &gt;32</td>
<td>&gt;32</td>
<td>0.125</td>
<td>&gt;32</td>
<td>0.094</td>
<td>0.25 to 0.094</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>1.04</td>
<td>0.125</td>
<td>0.19</td>
<td>0.064 to &gt;32</td>
<td>&gt;32</td>
<td>&gt;32</td>
<td>0.5</td>
<td>0.75</td>
<td>0.125 to 0.047</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>2.77</td>
<td>0.006</td>
<td>0.006</td>
<td>&lt;0.006 to 0.008</td>
<td>0.125</td>
<td>0.047</td>
<td>0.032</td>
<td>0.064</td>
<td>&lt;0.002 to 0.004</td>
</tr>
<tr>
<td>Trimethoprim/Sulfamethoxazole</td>
<td>2.18/ 0.79</td>
<td>0.094</td>
<td>0.094</td>
<td>0.032 to 0.094</td>
<td>&gt;32</td>
<td>0.75</td>
<td>0.5</td>
<td>0.25</td>
<td>0.19</td>
</tr>
<tr>
<td>Antimicrobial</td>
<td>S0.64</td>
<td>S0.5, R&gt;2</td>
<td>0.38</td>
<td>0.5</td>
<td>0.25 to 0.5</td>
<td>(0)</td>
<td>0.5</td>
<td>0.75</td>
<td>1.5</td>
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<tr>
<td>Linezolid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>&gt;0.5</td>
<td>≤0.064</td>
<td>2.0</td>
<td></td>
<td>0.047 to 3.0</td>
<td>(18)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*non-species related EUCAST breakpoints

LogP values (26): The partition coefficient is the ratio of the concentration of the compound in octanol to its concentration in water and is a measure of lipophilicity. Antimicrobials with high LogP coefficients (>1) are preferentially distributed to lipophilic compartments.

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16
<table>
<thead>
<tr>
<th>No.</th>
<th>Age/sex</th>
<th>Ethnicity</th>
<th>Presentation</th>
<th>Histology</th>
<th>Empiric antimicrobial</th>
<th>Culture</th>
<th>Treatment</th>
<th>Susceptibility by E-test</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47/F</td>
<td>NZ European</td>
<td>R breast abscess for 4 months</td>
<td>Granulomatous mastitis</td>
<td>Ciprofloxacin* Clindamycin* Metronidazole</td>
<td>C. kroppenstedtii Isolated twice, 17 days apart</td>
<td>Doxycycline* ciprofloxacin*</td>
<td>R to penicillin</td>
<td>Right breast mass for 24 months, left breast IGM 5 years later.</td>
</tr>
<tr>
<td>2</td>
<td>35/F</td>
<td>Pacific Islander</td>
<td>Right breast mass with pain for 2 weeks</td>
<td>Acute and chronic inflammatory cells</td>
<td>nil</td>
<td>C. kroppenstedtii</td>
<td>Doxycycline*</td>
<td>R to penicillin</td>
<td>Recurrence with wound discharge for 25 months.</td>
</tr>
<tr>
<td>3</td>
<td>21/F</td>
<td>Maori</td>
<td>Recurrent bilateral breast lumps with 24 hr history of acute right breast abscess</td>
<td>Inflammatory cell infiltrate with granuloma</td>
<td>Flucloxacillin Roxithromycin Ciprofloxacin*</td>
<td>C. kroppenstedtii Isolated twice, 3 weeks apart</td>
<td>Flucloxacillin Ciprofloxacin* Amoxicillin-clavulanate* Cefaclor Doxycycline*</td>
<td>Two isolates with the same susceptibility profile. R to penicillin.</td>
<td>Recurrent bilateral breast abscesses treated for 4 months then loss to follow-up.</td>
</tr>
<tr>
<td>4</td>
<td>47/F</td>
<td>NZ European</td>
<td>Left breast mass for 1 month</td>
<td>Multifocal granulomatous inflammation &amp; micro-abscess formation (3 months later)</td>
<td>nil</td>
<td>C. kroppenstedtii</td>
<td>Amoxicillin</td>
<td>R to penicillin</td>
<td>Diagnosed as IGM. Left breast mass resolved six months later. Recurrent multifocal IGM three years later.</td>
</tr>
<tr>
<td>5</td>
<td>42/F</td>
<td>British European</td>
<td>Right breast abscess for 1 week</td>
<td>Acute inflammatory infiltrate</td>
<td>nil</td>
<td>C. kroppenstedtii</td>
<td>Clindamycin*</td>
<td>R to penicillin, ceftriaxone</td>
<td>Developed fistula, resolved 10 months later.</td>
</tr>
<tr>
<td>6</td>
<td>57/F</td>
<td>NZ European</td>
<td>Left acute breast abscess</td>
<td>Consistent with abscess</td>
<td>Flucloxacillin</td>
<td>C. kroppenstedtii</td>
<td>Flucloxacillin Ciprofloxacin Amoxicillin-clavulanate* Metronidazole</td>
<td>R to penicillin, ciprofloxacin, moxifloxacin</td>
<td>Repeated left breast drainage, left breast central duct excision 23 months later.</td>
</tr>
<tr>
<td>7</td>
<td>39/F</td>
<td>NZ European</td>
<td>-</td>
<td>-</td>
<td>C. kroppenstedtii</td>
<td>-</td>
<td>-</td>
<td>R to penicillin</td>
<td>-</td>
</tr>
<tr>
<td>No.</td>
<td>Age</td>
<td>Gender</td>
<td>Race</td>
<td>Breast Affected</td>
<td>Duration</td>
<td>Symptoms</td>
<td>Initial Treatment</td>
<td>Extended Treatment</td>
<td>Resistance</td>
</tr>
<tr>
<td>-----</td>
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</tr>
<tr>
<td>8</td>
<td>38/F</td>
<td>Pacific Islander</td>
<td>Large right breast abscess for 2 months</td>
<td>Diffuse acute inflammation</td>
<td>Flucloxacillin* Amoxicillin-clavulanate*</td>
<td>C. kroppenstedii</td>
<td>Flucloxacillin* Amoxicillin-clavulanate*</td>
<td>No resistance</td>
<td>Large draining cavity packed for 1 month. Resolved after 4 months.</td>
</tr>
<tr>
<td>9</td>
<td>34/F</td>
<td>African</td>
<td>Large left breast abscess for one week with fever</td>
<td>Ill-defined granulomata with giant cells</td>
<td>Amoxicillin-clavulanate Flucloxacillin</td>
<td>C. kroppenstedii</td>
<td>Doxycycline* Ciprofloxacin* Amoxicillin</td>
<td>R to penicillin, clarithromycin, ceftriaxone, ciprofloxacin, clindamycin, moxifloxacin.</td>
<td>Fistulotomy, partial mastectomy, resolution after 6 months.</td>
</tr>
<tr>
<td>10</td>
<td>41/F</td>
<td>South East Asian</td>
<td>Left breast abscess for 8 days</td>
<td>Acute inflammation</td>
<td>Flucloxacillin Cefazolin Gentamycin Clindamycin</td>
<td>C. kroppenstedii</td>
<td>Doxycycline*</td>
<td>R to penicillin, clarithromycin, ceftriaxone, ciprofloxacin, clindamycin, moxifloxacin.</td>
<td>Resolved after 3 months.</td>
</tr>
<tr>
<td>11</td>
<td>42/F</td>
<td>Pacific Islander</td>
<td>Large right breast abscess for two months</td>
<td>Granulomata surrounding lipid spaces with central micro-abscess formation</td>
<td>Flucloxacillin Amoxicillin-clavulanate*</td>
<td>C. tuberculostearicum</td>
<td>Flucloxacillin Amoxicillin-clavulanate*</td>
<td>R to penicillin, clindamycin</td>
<td>Chronic multi-focal right breast mastitis for 17 months.</td>
</tr>
<tr>
<td>12</td>
<td>51/F</td>
<td>NZ European</td>
<td>Right breast abscess for one week</td>
<td>No evidence of malignancy (previous L breast cancer)</td>
<td>Flucloxacillin</td>
<td>C. freneyi</td>
<td>Flucloxacillin Doxycycline*</td>
<td>R to penicillin</td>
<td>Separate abscess right breast 1 month later (same spp. isolated).</td>
</tr>
<tr>
<td>13</td>
<td>51/F</td>
<td>NZ European</td>
<td>Post-operative wound infection</td>
<td>Not performed</td>
<td>amoxicillin-clavulanate Flucloxacillin Cefazolin</td>
<td>C. tuberculostearicum, F. magne, S. aureus</td>
<td>Penicillin Metronidazole Cefazolin</td>
<td>Multiresistant strain</td>
<td>4 months wound care.</td>
</tr>
<tr>
<td>14</td>
<td>71/F</td>
<td>NZ European</td>
<td>Seroma post-surgery</td>
<td>Not performed</td>
<td>Nil</td>
<td>C. tuberculostearicum, S. lugdunensis</td>
<td>Flucloxacillin</td>
<td>Multiresistant strain</td>
<td>Resolved with drainage.</td>
</tr>
<tr>
<td>15</td>
<td>53/F</td>
<td>NZ European</td>
<td>Collection 8 month post</td>
<td>No evidence of recurrence</td>
<td>Flucloxacillin Ciprofloxacin*</td>
<td>C. tuberculostearicum</td>
<td>amoxicillin-clavulanate*</td>
<td>R to penicillin, clarithromycin,</td>
<td>Collection with chronic nipple discharge</td>
</tr>
<tr>
<td>Case</td>
<td>Gender</td>
<td>Age</td>
<td>Race</td>
<td>Location</td>
<td>Initial Diagnosis</td>
<td>Initial Antimicrobial</td>
<td>Result</td>
<td>Recurrence</td>
<td></td>
</tr>
<tr>
<td>------</td>
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<td></td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>43</td>
<td>NZ</td>
<td>European</td>
<td>Right chest wall abscess for 30 weeks</td>
<td>Clindamycin, tetracycline</td>
<td>Resolved after 12 months.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No clinical information available for case 7.

Empiric antimicrobial therapy defined as antimicrobials given prior to a positive Gram stain or microorganism isolated from specimen.

*Strain susceptible to antimicrobial based on in vitro E-test. Strain considered sensitive to doxycycline if susceptible to tetracycline. R = resistant (EUCAST breakpoint).