Actinomyces Species Isolated from Breast Infections


Actinomyces is a chronic, invasive, progressive, and often relapsing granulomatous infection caused by Gram-positive, facultatively anaerobic, rod-shaped bacteria belonging to the genus Actinomyces. Classical actinomycosis in humans is typically caused by Actinomyces israelii and is characterized by deep invasive abscess formation, tissue fibrosis, and draining sinuses affecting cervicofacial, thoracic, abdominopelvic areas (1). A number of more recently described Actinomyces species and Actinomyces-like organisms have been associated with less invasive superficial soft tissue infections and are isolated from abscesses at various anatomical sites (2–4).

Breast infections are frequently encountered in primary care and breast clinic settings. They can occur in the parenchyma of the breast or the overlying skin and may be in lactating or nonlactating breasts (5). Lactating breast infections are usually caused by Staphylococcus aureus (6). The microbial etiology of nonlactating breast infections, particularly those which are chronic or recurrent, is more variable, often polymicrobial, and predominantly anaerobic (5, 7). A study of nonpuerperal breast infections has demonstrated that, when culture methods are used which enhance recovery of fastidious anaerobic organisms, almost 25% of recurrent breast abscesses (8 of 33 patients) and 10% of primary breast abscesses (2 of 19 patients) involved Actinomyces species (7). However, primary Actinomyces infection of the breast, first described by Ammentorp in 1893 (8), is generally considered to be rare. A clinical review from 1994 reported 19 cases described in the English language literature (9). Diagnosis of Actinomyces breast infection was often made following surgical intervention, although the method of diagnosis was not specified. Duration of symptoms was reported to range from 1 to 8 years, with two-thirds of the patients presenting with recurrent abscesses. The remaining third of the patients were reported to have examination findings suggestive of malignancy. Most of the patients received extensive surgical treatment, with 11 patients undergoing a mastectomy, presumably for management of infection, as only 3 mastectomies were performed on patients with suspected malignancy. Subsequent to this review, case reports and studies have been published describing a further 27 breast infections caused by Actinomyces species.

Actinomyces breast infection is likely to be underascertained in routine clinical practice, as these fastidious organisms are notoriously difficult and laborious to identify using conventional laboratory methods (2–4). Subsequently, there is a risk that cultures of Actinomyces species are simply identified morphologically as diphtheroids and dismissed as skin commensals, even when grown from an abscess sample. However, new methods of identification, such as matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS), allow rapid and reliable identification of many bacteria, including Actinomyces-like organisms (10–12). MALDI-TOF MS and similar technologies are increasingly being adopted by routine diagnostic laboratories worldwide (13).

We present a series describing all cases of Actinomyces species isolated from breast infections at the Edinburgh Breast Unit over an 8-year period from 2005 to 2013 (Table 1). In addition, we include data about Actinomyces species isolated from breast samples which were referred to the Anaerobe Reference Unit, Cardiff, Wales, between 1988 and 2014 (Fig. 1). We then summarize the findings of case reports describing breast infections caused by Actinomyces species published since the review from 1994 (9) (Table 2).

(The abstract was presented as a poster at the Association of Breast Surgery Conference in Liverpool, May 2014.)

MATERIALS AND METHODS

Bacterial isolates. Review of electronic records of breast fluid aspirates received between 2005 and 2013 at the microbiology laboratory at the

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### TABLE 1
Cases of *Actinomyces* species isolated from breast infections at the Edinburgh Breast Unit over an 8-year period from 2005 to 2013

<table>
<thead>
<tr>
<th>Case</th>
<th>Year</th>
<th>Age (yr)/sex</th>
<th>Risk factors/PMH</th>
<th>Type of breast infection</th>
<th>MALDI-TOF MS identification (p score)</th>
<th>Molecular identification (16S sequencing)</th>
<th>Coinfecting organisms</th>
<th>No. of infections</th>
<th>Previous potential <em>Actinomyces</em> isolate not identified as such by laboratory</th>
<th>Comments on outcome (including antibiotic treatment, surgery, resolution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2013</td>
<td>36/F Nil</td>
<td></td>
<td>Left breast abscess</td>
<td><em>A. radingae</em> (2.0234) <em>A. europaeus</em> (1.972)</td>
<td><em>A. radingae</em> and <em>A. europaeus</em> Yes (Peptoniphilus sp.)</td>
<td>1 Yes</td>
<td>No</td>
<td>Good response to drainage and clindamycin</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2013</td>
<td>52/F Diabetes</td>
<td></td>
<td>Right breast inframammary fold abscess</td>
<td><em>A. europaeus</em> (1.779)</td>
<td><em>A. europaeus</em> No</td>
<td>1 No</td>
<td>No</td>
<td>Abscess aspirated and patient treated with flucloxacillin; complete resolution 3 mo later</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2013</td>
<td>36/F Nil</td>
<td></td>
<td>Left breast abscess</td>
<td><em>A. odontolyticus</em> (2.006)</td>
<td><em>A. odontolyticus</em> No</td>
<td>2 No</td>
<td>First isolate initially reported as diphtheroid of doubtful significance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2013</td>
<td>26/F Nil</td>
<td></td>
<td>Left breast abscess (infected epidermoid cyst)</td>
<td><em>A. neuii</em> (2.3314)</td>
<td><em>A. neuii</em> No</td>
<td>1 No</td>
<td>No</td>
<td>Chronic breast lump slowly increasing in size over 8 mo, initially investigated as potential malignancy; core biopsy revealed changes consistent with chronic abscess and purulent aspirate grew <em>A. odontolyticus</em></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2013</td>
<td>41/F Nil</td>
<td></td>
<td>Left breast abscess</td>
<td><em>A. radingae</em> (2.0348)</td>
<td><em>A. radingae</em> Yes (multiple anaerobe species) 7 (over 10 yrs)</td>
<td>Yes (sample from 2012 with diphtheroids and anaerobes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2013</td>
<td>19/F Smoker/hidradenitis suppurativa</td>
<td></td>
<td>Breast abscess</td>
<td><em>Actinomyces</em> species (closest sequence, <em>A. odontolyticus</em>)</td>
<td><em>Actinomyces</em> species (closest sequence, <em>A. odontolyticus</em>) No</td>
<td>1 No</td>
<td>Breast abscess drained; patient treated with amoxicillin-clavulanic acid for 1 wk with apparent resolution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2012</td>
<td>34/F Smoker</td>
<td></td>
<td>Left and right breast abscesses</td>
<td><em>A. radingae</em> (1.829)</td>
<td><em>A. radingae</em> Yes (Actinobaculum schaellei and multiple anaerobe species)</td>
<td>8 No</td>
<td>Multiple recurrences of breast abscesses over a period of 12 mo treated with aspirations and short courses of antibiotics (mostly combinations of flucloxacillin, amoxicillin-clavulanic acid and metronidazole); referred for mammary fistula and total duct excision of right breast</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2012</td>
<td>46/F Diabetes/smoker/hidradenitis suppurativa</td>
<td></td>
<td>Breast abscess</td>
<td><em>A. neuii</em> (2.076)</td>
<td><em>A. neuii</em> No</td>
<td>2 Yes (sample from 2011 with diphtheroids and anaerobes)</td>
<td>Abscess drained and patient treated with antibiotics; previous episode in 2011 treated with amoxicillin-clavulanic acid and metronidazole</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Results

**Lothian cases.** Over an 8-year period (2005 to 2013), we identified 11 cases of breast infections at our center caused by *Actinomyces* species (Table 1) and one case with the *Actinomyces*-like organism *Actinobaculum schaali*. The predominant *Actinomyces* species isolated from our subgroup of patients were *Actinomyces europaeus* \((n = 5)\), *A. neuii* \((n = 3)\), and *A. radingae* \((n = 3)\). Identification using MALDI-TOF MS was attempted for 11 isolates, and all of these correlated at the species level with the definitive molecular identification, with p scores ranging from 1.779 to 2.331. Confirming organisms were present in half of these cases \((n = 6)\) and...
usually were unidentified anaerobes. Ten of 12 cases (83%) had chronic, recurrent infections ranging from 2 to 8 episodes (mean, 2.8 episodes), some recurring over many years. Three patients had hidradenitis suppurativa, 6 patients were smokers, 4 patients were diabetic, and 3 patients had a combination of risk factors. No patients in our cohort had a lactational breast abscess, and there was no record of any patients having had a nipple piercing.

Case 5 in particular highlights the difficulties associated with diagnosing and managing *Actinomyces* breast infections. This patient had 7 episodes of breast infection and abscess formation over a 10-year period, treated with short antibiotic courses. Cultures of aspirated abscess material repeatedly failed to grow organisms or were reported to grow diphtheroids of uncertain significance. Following a positive growth of *A. radingae*, the patient received a 3-month course of antibiotics and has since had no further relapses (almost 2 years later).

**UKARU cases.** Over a 26-year period (1988 to 2014), 61 isolates identified as *Actinomyces* species from breast infections were referred to the United Kingdom Anaerobe Reference Unit (UKARU) from United Kingdom hospitals (Fig. 1). Although *Actinomyces* species are not considered true anaerobes, the UKARU has developed extensive expertise over many years regarding *Actinomyces* species. This expertise was driven largely by a referral demand from users for advanced identification of clinically relevant isolates initially categorized as anaerobic Gram-positive rods or anaerobic coryneforms. It is likely that the cases listed here represent only a small proportion of United Kingdom cases, as referral of isolates to the unit is not mandatory. Unfortunately, a further limitation of the referral process is that clinical information is not available for many of these cases; however, a small number (*n* = 5) state either recurrent or previous breast abscesses. One case worthy of particular mention states “recurrent breast abscess for 11 years,” from which *A. radingae* was isolated.

**Literature review cases.** Fifteen cases of *Actinomyces* breast infection were identified on literature review between 1994 and 2013, with another 12 cases (7, 14) found prior to 1994, not included in the review by Jain et al. (9) (Table 2). This paper therefore reports 27 published cases of *Actinomyces* breast infection in addition to the 19 reported in 1994, although clinical details are only available for 17 of these 27 cases. There was no clearly predominant *Actinomyces* species. Five cases reported coinfecting anaerobes (17, 24), and one case reported coinfecting *Staphylococcus aureus* (20), with no mention of coinfecting organisms in 11 of 17 cases. Seven cases were recurrent infections, and a range of different treatment combinations were required to reach abscess resolution. This ranged from 2 to 3 weeks of oral antibiotics to incision and drainage with prolonged antibiotics for 2 to 6 months; the most extreme treatment was tumorectomy of the breast (22). As with our cohort of patients, prior to the diagnosis of *Actinomyces* breast infection, some patients had been repeatedly treated without success (14, 17, 20).

**Combined cases.** The *Actinomyces* species most commonly isolated from breast infections according to a combined table of cases (Table 3) (*n* = 102) are *A. neuii* (*n* = 19), *A. europaeus* (*n* = 18), *A. turicensis* (*n* = 16), *A. radingae* (*n* = 15), and *A. odontolyticus* (*n* = 10). These species mostly belong to the group of *Actinomyces* species generally considered to be less invasive, although it is noteworthy that, in the Lothian and United Kingdom cohorts, *A. radingae* was isolated from those cases with the greatest number of relapses. The distribution of *Actinomyces* species broadly reflects previous findings regarding superficial *Actinomyces* soft tissue infections (2–4), although these studies did not look specifically at breast infections.

Within the NHS Lothian and the published cases, 48% (*n* = 14) presented clinically with an abscess, 33% (*n* = 9) presented with a breast mass, 10% (*n* = 3) presented with a fistula, and 7% (*n* = 2) presented with periductal mastitis. There was an average of 2.8 episodes of infection per patient in the NHS Lothian cases. Within the published cases, excluding case 1 who had numerous yearly episodes of recurrent infection for 23 years, there was an average of 1.5 episodes of *Actinomyces* breast infection per patient.
DISCUSSION

Humans and animals are the natural reservoirs of *Actinomyces* species, which until recently have not been found to exist freely in nature (29). Their normal habitat is the mucosal membranes of the oropharynx, gastrointestinal tract, and female genital tract. They are inherently low in virulence and may rely on the presence of copathogens, such as anaerobic bacteria, to enhance pathogenicity (1). Disruption of the mucosal barrier is the usual precursor to infection with *Actinomyces* species and, in the breast, the ductal system may serve as a portal of entry. Actinomycosis of the breast usually presents as a chronic, recurrent abscess which in some cases can be difficult to distinguish from inflammatory carcinoma (9, 15, 26). Fistulas and purulent or bloody discharge from sinuses may occur, which may discharge sulfur granules (26). In advanced prolonged cases, fibrosis with architectural distortion of the breast tissue is present on mammography (15).

The pathogenesis and true pathogenic role of various *Actinomyces* species isolated from breast infections and the treatment required for this has not been clearly defined. This is further complicated by the uncertain etiology of different types of chronic abscess-forming inflammatory conditions involving the breast from which *Actinomyces*-like organisms can be isolated, such as granulomatous lobular mastitis, hidradenitis suppurativa, and periductal mastitis. Granulomatous lobular mastitis presents as a peripheral inflammatory mass which may simulate malignancy or infection. Patients with this condition often develop multiple and recurrent abscesses. It has been suggested that the *Corynebacterium* spp. play a part in this condition, (30) but antibiotics effective against these organisms rarely lead to resolution of disease; thus, they may not have a major etiological role. Hidradenitis suppurativa is an inflammatory disease of unclear etiology which commonly affects the axilla and groin and can also affect the skin of the lower half of the breast, resulting in recurrent episodes of abscess formation (31). Recent evidence suggests that anaerobic actinomycetes may be involved in the disease process, especially when lesions are more severe (32). Periductal mastitis is a condition linked to cigarette smoking (33) in which the subareolar ducts are damaged and become infected, often by anaerobic bacteria (34). Women may present with subareolar inflammation, abscesses, and fistulas (35). Smoking has consistently been identified as a risk factor for primary breast abscess and its recurrence (5, 35, 36). Other factors, such as diabetes mellitus, obesity, African-American origin, and nipple piercing, have less consistently been associated with breast abscesses (5, 35).

Despite finding 12 cases over 8 years at our center, which is comparable to the number of cases described in the medical literature over the same time period, we suspect that there were many missed identifications. During the 8-year study period, we found another 15 cases in Lothian where potential *Actinomyces*-like organisms were isolated from recurrent breast abscesses, but further identification was not attempted and a report was sent out describing diphtheroids of doubtful or uncertain significance. In addition, 4 of our 12 culture-positive cases had previous samples with isolates of potential *Actinomyces*-like organisms reported as diphtheroids of doubtful significance. This supports the assumption that *Actinomyces* breast infections may easily go undiagnosed in routine clinical practice. *Actinomyces* species are slow to grow and notoriously difficult to identify using conventional laboratory methods, often requiring reference laboratory referral for reliable identification. When *Actinomyces* species do grow on culture, they can resemble other diphtheroid-like Gram-positive rods, such as *Corynebacterium* species, many of which are considered to be part of normal skin flora. *Actinomyces* species which are isolated from breast abscess samples may therefore be presumptively identified in the laboratory as diphtheroids based on their morphology and reported as diphtheroids of doubtful or uncertain significance. However, laboratories are increasingly adopting new methods of identification, such as MALDI-TOF MS (13), which allow rapid and increasingly reliable identification of this problematic group of organisms (10–12). Indeed, most of the cases in Lothian were identified after 2012, which is shortly after our laboratory started using MALDI-TOF MS. With 10 cases diagnosed in 2 years of using MALDI-TOF MS compared to 2 cases over 7 years without MALDI-TOF MS, it is clear that ease of identification is a major factor in the increased recognition of *Actinomyces* breast infections in our clinical setting. The Anaerobe Reference Unit (ARU) has seen a similar increase in the number of isolates referred to them, with more isolates (n = 26) referred to them over the last 3 years of the recorded period than had been referred over the first 20 years (n = 25). Based on information from referring laboratories, this increase is almost certainly driven by an improvement in the identification of *Actinomyces* species due to increased use of MALDI-TOF MS. Subsequently, laboratories unfamiliar with these organisms refer them to the ARU for confirmation of identification, susceptibility testing, and clinical advice.

Our results support previous findings that *Actinomyces* species can be reliably identified using MALDI-TOF MS (10–12), with all 12 of our tested isolates identified to the species level, as confirmed by molecular testing. Five isolates were correctly identified to the species level by MALDI-TOF MS despite identification scores only reaching genus-level confidence (ie, a p score of <2.0). This is keeping with recent evidence suggesting that the cutoff for species-level identification could be reassessed and perhaps lowered to a p score of ≥1.7 for this group of organisms (10, 12).

We have modified the approach to how organisms from breast samples are identified in Lothian. Breast abscess samples now receive anaerobic incubation for 5 days along with prolonged *Actinomyces* cultures when clinical details mention chronic or recurring infection. Any Gram-positive bacillus growing from a breast abscess sample is identified using MALDI-TOF MS and should no longer be reported as a diphtheroid of uncertain significance without an attempt to identify the organism.

The primary management of breast abscess is drainage along with antibiotic therapy appropriate for the underlying cause of the abscess (31). When *Actinomyces* species are isolated, longer courses of antibiotics should be considered. Treatment of classical, invasive actinomycosis, typically caused by *Actinomyces israelii* and to a lesser extent *A. gerencseriae, A. meyeri, A. odontolyticus,* and *A. viscosus/naeslundii* (2, 4, 37), involves prolonged antibiotic therapy. Textbooks commonly advise 2 to 6 weeks of intravenous (IV) penicillin followed by 6 to 12 months of oral penicillin or amoxicillin (38). However, there is evidence that shorter antibiotic courses of under 3 months may be sufficient in some cases (39), particularly those caused by less-invasive *Actinomyces* species, such as *A. europaens, A. funkei, A. neuii, A. radngiae,* and *A. turicensis* (2–4, 37, 40). Even shorter 7- to 14-day courses of oral antibiotics are typically used when treating breast infections, but this is likely to be insufficient for *Actinomyces*-associated breast infections, and longer courses, in addition to surgical drainage,
<table>
<thead>
<tr>
<th>Case</th>
<th>Country</th>
<th>Year</th>
<th>Age (yr)</th>
<th>Risk factors/PMH</th>
<th>Clinical description</th>
<th>Organism</th>
<th>Method of identification</th>
<th>Coinfecting organisms</th>
<th>No. of infections</th>
<th>Comments on outcome (including antibiotic treatment, surgery, resolution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>USA</td>
<td>1987</td>
<td>29</td>
<td>Severe peridental disease</td>
<td>Hard 5 × 4 cm left breast mass</td>
<td><em>A. meyerii</em></td>
<td>Not specified</td>
<td>Diverse anaerobes</td>
<td>1–3 episodes every yr for 23 yrs</td>
<td>Surgical debidement with ampicillin, doxycycline for 4 mo</td>
</tr>
<tr>
<td>2</td>
<td>USA</td>
<td>1987</td>
<td>36</td>
<td>Recurrent peridental abscesses</td>
<td>Hard 4 × 4 cm right breast mass</td>
<td><em>A. meyerii</em></td>
<td>Not specified</td>
<td>Diverse anaerobes</td>
<td>5 recurrences over 3 yrs</td>
<td>Surgical debidement with tetracycline, doxycycline for 4 mo</td>
</tr>
<tr>
<td>3</td>
<td>Brazil</td>
<td>2000</td>
<td>66</td>
<td>Diabetes</td>
<td>5-yr history of a mass in the left breast; nipple discharge, cutaneous fistulas</td>
<td>Actinomyces species</td>
<td>Histopathologic examination; culture of abscess 4 yrs before isolated <em>Actinomyces</em> sp.</td>
<td>None mentioned</td>
<td>2</td>
<td>Abscesses and fibrous tissue drained and resected; responded to 2 mo of IV penicillin followed by oral amoxicillin for 6 mo</td>
</tr>
<tr>
<td>4</td>
<td>Italy</td>
<td>2005</td>
<td>27</td>
<td>Nil</td>
<td>Unilateral right mastitis, palpable 5-cm nodular lump just beside the right areola</td>
<td><em>A. viscosus</em></td>
<td>Culture positive; biochemical tests</td>
<td>None mentioned</td>
<td>1</td>
<td>One wk of an unspecified antibiotic with no response; then oral amoxicillin-clavulanic acid followed by surgical drainage and excision of the lesion with no further antibiotics; resolution after 6 yrs follow-up</td>
</tr>
<tr>
<td>5</td>
<td>UK</td>
<td>2007</td>
<td>33</td>
<td>Bilateral nipple piercings removed 6 mo prior to presentation; on 5mg prednisolone for ulcerative colitis smoker</td>
<td>3-wk history of right breast pain, swelling, and offensive nipple discharge</td>
<td><em>A. turicensis</em></td>
<td>Culture positive; confirmed with 16S rDNA restriction analysis</td>
<td>Mixed anaerobes</td>
<td>3</td>
<td>Aspiration and amoxicillin-clavulanic acid for 7 days; worsening symptoms and three more attempts to aspirate over the following 2-wk period; incision and drainage with full excision of abscess wall, followed by ceftriaxone and oral metronidazole for 3 wks; complete resolution at follow-up 8 wks later</td>
</tr>
<tr>
<td>6</td>
<td>UK</td>
<td>2007</td>
<td>38 (male)</td>
<td>Ex-smoker</td>
<td>Right axillary and left subareolar abscess with nipple discharge for 7 mo; left axillary abscess drained 18 mo before</td>
<td><em>A. radingae</em> (isolated from subareolar abscess)</td>
<td>Culture positive; confirmed with 16S rDNA restriction analysis</td>
<td>Heavy growth of anaerobes (from right axillary abscess)</td>
<td>3</td>
<td>Incision and drainage of abscesses; oral amoxicillin and fusidic acid for 6 wks; recurrence of <em>A. radingae</em> followed by a prolonged course of oral ciprofloxacin and rifampin with eventual resolution</td>
</tr>
<tr>
<td>7</td>
<td>France</td>
<td>2009</td>
<td>48</td>
<td>Pregnant</td>
<td>Inflammatory breast mass (15 mm); clinically and radiologically interpreted as carcinoma</td>
<td><em>A. naeii</em></td>
<td>FNA showed granulomas; culture positive; confirmed with genetic amplification</td>
<td>None mentioned</td>
<td>1</td>
<td>Treated with 3 wks of oral amoxicillin with resolution</td>
</tr>
<tr>
<td>8</td>
<td>Iran</td>
<td>2009</td>
<td>30</td>
<td>Nil</td>
<td>A few days’ history of sudden painful and swollen left breast with multiple fistula formation</td>
<td><em>A. israelii</em></td>
<td>Morphology on culture</td>
<td>None mentioned</td>
<td>1</td>
<td>Responded to treatment with oral erythromycin for 6 mo</td>
</tr>
<tr>
<td>Country</td>
<td>Year</td>
<td>Age</td>
<td>Timeline</td>
<td>Description</td>
<td>Microbes and Pathology</td>
<td>Outcome</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>UK</td>
<td>2010</td>
<td>70</td>
<td>3 mo post-partum</td>
<td>History of tenderness and induration in the right breast</td>
<td>Not isolated on culture</td>
<td>Histopathologic examination, Staphylococcus aureus on skin swab, treated with oral penicillin, little improvement, further treatment with imipenem, amoxicillin-clavulanic acid, and metronidazole had little effect, finally treated for over 12 mo with oral clindamycin, with resolution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iran</td>
<td>2010</td>
<td>48</td>
<td>Psychiatric problem</td>
<td>2-mo history of non-tender mass in the left breast</td>
<td>Not isolated on culture</td>
<td>Histopathologic examination, None mentioned</td>
<td>Treated with 4 wks of IV penicillin, followed by oral amoxicillin for 4 mo; fully resolved at 2-yr follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>2010</td>
<td>46</td>
<td>Nil</td>
<td>Recurrent abscess with fistulas</td>
<td>A. neuii, Not specified</td>
<td>None mentioned, Recurrent abscesses</td>
<td>No improvement with antibiotics; tumorectomy of the breast; no recurrence after 6 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>2010</td>
<td>48</td>
<td>Nil</td>
<td>Painful erythematous fluctuating left breast lump</td>
<td>A. neuii, Culture positive; confirmed with 16S rRNA sequencing</td>
<td>None mentioned</td>
<td>Resolved with surgical debridement and a course of oral penicillin V</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switzerland</td>
<td>2011</td>
<td>67</td>
<td>Aortic valve replacement 2 mo before</td>
<td>History of painful 12-cm swelling and hyperemia of the left breast</td>
<td>A. europaeus, Culture positive; confirmed with 16S rRNA and 16S rDNA sequencing</td>
<td>Mixed anaerobic flora</td>
<td>3 wks of oral amoxicillin-clavulanic acid followed by 15 mo amoxicillin; at 3 mo, three sinuses formed; resolved at follow up 6 mo later with scar formation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>2012</td>
<td>50</td>
<td>Nil</td>
<td>6-mo history of intermittently discharging 6 × 4 cm right breast mass</td>
<td>A. israelii, Sulfur granules; morphology on culture</td>
<td>None mentioned</td>
<td>No information</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>2012</td>
<td>61</td>
<td>Diabetes</td>
<td>6-mo history of 5 × 6 cm mass in left breast</td>
<td>Not isolated on culture</td>
<td>Histopathologic examination, None mentioned</td>
<td>Treated with unspecified antibiotics; doing well on follow-up</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>India</td>
<td>2012</td>
<td>32</td>
<td>Nil</td>
<td>3-wk history of 7 × 8 cm right breast mass</td>
<td>Not isolated on culture</td>
<td>Histopathologic examination, None mentioned</td>
<td>Resolved after a course of unspecified antibiotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>2013</td>
<td>40</td>
<td>Nil</td>
<td>2-wk history of 3-cm tender right breast mass with overlying erythema</td>
<td>A. odontolyticus, Not specified</td>
<td>None mentioned</td>
<td>Cefalexin for 1 wk with resolution after 2 wks of oral penicillin V</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PMH, past medical history.
Ref, reference.
Two cases from 1987 that were not detailed in the 1994 review are included.
may be required to prevent recurrences. *Actinomyces* species are susceptible to many beta-lactam antibiotics, with penicillin and amoxicillin generally regarded as first-choice options (38, 41). However, due to the common presence of coinfecting, beta-lactamase-producing organisms, treatment options should ideally include beta-lactamase-stable antibiotics, such as amoxicillin plus clavulanic acid (41), at least for the initial 2 weeks of treatment. Isolates referred from Lothian were removed from this column to avoid double counting. Two Lothian cases had two different species spp. isolated. Data were gathered from Tables 1 and 2, Figure 1, and reference 7.

### References

Actinomyces Species Isolated from Breast Infections


