The microbial epidemiology of breast implant infections in a regional referral centre for plastic and reconstructive surgery in the south of France

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SUMMARY

Background: Breast implant infections are usually caused by Staphylococcus aureus and coagulase-negative staphylococci. Gram-negative bacilli are rarely reported to be involved in breast implant infections.

Methods: Thirty-seven cases of microbiologically confirmed breast implant infection managed from January 2008 to June 2012 in the study centre were reviewed, including 10 cases from the study centre itself and 27 cases from private clinics in the region.

Results: The prevalence of breast implant infection in the study centre was 0.74% of breast implantation, i.e., 3.23% in breast reconstruction for breast cancer and 0.27% in aesthetic breast augmentation (p = 0.0002). Of the 37 cases, 30% had undergone radiotherapy and 11% had undergone a lymph node dissection. S. aureus was identified in 18 cases, Gram-negative bacilli in 10 cases, coagulase-negative staphylococci in eight cases, anaerobic bacteria in eight cases, and streptococci in three cases. Pseudomonas aeruginosa was the second most commonly identified pathogen. Staphylococcus epidermidis was the most frequent coagulase-negative Staphylococcus species. In addition to Propionibacterium acnes and Actinomyces neuii, other facultative and strict anaerobic bacteria have not been reported before, e.g., Bacteroides thetaiotaomicron, Corynebacterium simulans, Dermabacter hominis, Finegaldia magna, and Peptostreptococcus harei. Seventy-percent of cases were treated by immediate implant removal. All cases treated only with antibiotics were treated with surgery at the second visit.

Conclusions: The microbiological epidemiology was noted by an increasing the proportion of Gram-negative bacteria and anaerobic bacteria detected with the advent of MALDI-TOF MS and molecular identification for diagnosis.

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1. Introduction

Breast implant infection is a complication after breast augmentation that occurs in 2–53% of cases.1,2 The incidence is higher in breast reconstruction after surgery for breast cancer than in aesthetic breast augmentation.2,4 In previous years, common pathogens of breast implant infection have been Staphylococcus aureus and coagulase-negative staphylococci.2 Atypical mycobacteria have been reported as pathogens involved in many breast implant infection outbreaks.5,9 Few studies have reported breast implant infections caused by Gram-negative bacilli.2,10

There are some well known risk factors for breast implant infection, including obesity, diabetes mellitus, renal failure, active skin disorders, and tobacco use. The risk is increased in patients undergoing mastectomy, axillary dissection, or chemotherapy, as well as those who have undergone prior radiation treatment, reoperations, operations lasting longer than 2 h, or drain placement.2

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The diagnosis of breast implant infection may be difficult in the absence of scar discharge, purulent flow, cellulitis, or abscesses. Despite improvements in the recognition of breast implant infections, management strategies vary widely across centres, particularly with regards to the choice and duration of antimicrobial treatment and when to remove the breast implants.1 However, some authors have reported one-time exchanges of the breast implants using antibiotics.11

The early and accurate identification of bacteria is a critical requirement for prompt and appropriate antimicrobial treatment of breast implant infections.12–13 The arrival of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) in the study centre has increased the speed and identification of the common and rare bacterial species involved in human infection.14

In this study, the clinical and microbiological features of breast implant infections managed in a regional referral centre for plastic/reconstructive surgery in the south of France were reviewed retrospectively.

2. Materials and methods

A review was performed of all breast implant infection cases managed from January 2008 to June 2012 in a regional referral centre for plastic/reconstructive surgery in the south of France. A total of 1350 breast implant surgeries were performed in the study centre during the study period, including 217 definitive implants for reconstruction and 1133 aesthetic breast augmentations. The study centre also supports patients with breast implant infections for whom the breast implant surgery was performed in private clinics in the region.

The following data were collected: patient clinical characteristics (i.e., age, comorbidities, use of tobacco, previous radiotherapy, adjuvant chemotherapy, and lymphadenectomy) and past surgical history (i.e., aesthetic or reconstruction, type of incision, and type of implant). The timing of onset of the infection, clinical signs, and microbiological results were also recorded. An acute breast implant infection was defined by the appearance of clinical signs ≤6 weeks after the implantation; a late breast implant infection was defined by the appearance of clinical signs >6 weeks after the implantation.1,2 The antimicrobial and/or surgical treatment approaches used in each case were reviewed. The treatment outcome was evaluated at 3, 6, 12, and 24 months after the end of treatment. This study was approved by the institutional research ethics board and written informed consent was obtained from each patient.

The diagnosis of breast implant infection was based on the patient’s medical history, including clinical evidence of infection from biological and/or radiological data, and at least two positive cultures from deep surgical or percutaneous biopsy samples to exclude contaminating bacteria, as described previously.15 After incubation, the bacteria were identified through MALDI-TOF MS (Bruker Daltonik), as described previously.16 Complete 16S RNA gene sequencing was performed for unknown anaerobic bacteria not identified by MALDI-TOF MS, as described previously.15,16 The antibiotic susceptibilities of bacterial isolates were determined and interpreted according to the recommendations of the French Society for Microbiology and the European Committee on Antimicrobial Susceptibility Testing (http://www.sfm-microbiologie.org/UserFiles/files/casfm/CASFM_EUCAST_V1_0_2014.pdf). The susceptibility of Staphylococcus epidermidis to methicillin was screened by agar diffusion using cefoxitin disks (BioRad, Marnes-La-Coquette, France).

The antimicrobial and/or surgical treatment approaches used and the final outcome of each case were reviewed. Treatment was considered successful when there was remission, i.e., the disappearance of all breast infection symptoms after the end of antibiotic treatment. Relapse was defined by the reappearance of active breast implant infection symptoms at any time following treatment.

Data analyses were performed using IBM SPSS Statistics, version 20.0 software (IBM Corp., Armonk, NY, USA). Proportions were compared using the Chi-square test or Fisher’s exact two-tailed test. A p-value of <0.05 was considered statistically significant.

3. Results

A total of 37 cases of microbiologically confirmed breast implant infection were managed in the study centre. Of the 37 breast implant infection cases, 14 (38%) had undergone breast implant placement for reconstruction after breast cancer and 23 (62%) had undergone placement for aesthetic breast augmentation. Forty-eight percent of patients with aesthetic breast augmentations had undergone repeat implant placement.

Ten breast implant infections involved patients from the study centre, representing 0.74% of breast implantations; these included seven cases (3.23%) of breast reconstruction for breast cancer and three cases (0.27%) of aesthetic breast augmentation. The prevalence of breast implant infection was significantly higher in the group of patients who had breast implants placed for reconstruction after breast cancer ($p = 0.0002$). Twenty-seven other breast implant infection cases were from private clinics in the region, including seven cases in breast reconstruction for breast cancer and 20 cases in aesthetic breast augmentation.

Silicone implants were used in 81% of cases, while saline serum implants were used in 19% of cases. In all 37 cases, the breast implants were inserted in the retromuscular space at the level of the periostium, through the inframammary fold in 50% of cases, through the mastectomy incision in 32%, and by axillary incisions in 18%.

The mean patient age was 44 ± 14 years (range 19–76 years). Eleven patients (30%) were tobacco users, 11 patients (30%) had undergone radiotherapy for breast cancer, four patients (11%) had undergone a lymph node dissection for breast cancer, one patient had diabetes mellitus, two patients were on immunosuppressive therapy and/or corticosteroid treatment, and one patient was HIV-positive (Table 1).

Sixteen cases (43%) occurred at <6 weeks after the implantation and 21 cases (57%) occurred >6 weeks after the implantation. The median onset to diagnosis was 330 days (range 3–6120 days). Most cases were paucisymptomatic and the main symptoms were purulent flow or scar distension, which was present in 17 of the cases (46%), followed by abscess in 11 cases (30%), local cellulitis in six cases (16%), and fever in seven cases (19%). Biological parameters of inflammation, i.e., a high leukocyte count (>12 × 10³/l) and/or a high plasma C-reactive protein level (>40 mg/ml), were recorded in five of the cases (13%). There were four complications of breast implant infection: one toxic shock syndrome associated with a breast implant infection due to Streptococcus pyogenes and three cases of chronic rib osteomyelitis.

Among the 17 species of bacterial isolate (N = 47) involved in breast implant infection, S. aureus was the most common, identified in 18 cases (49%), followed by Gram-negative bacteria in 10 cases (27%), coagulase-negative staphylococci in eight cases (22%), strict anaerobic bacteria in five cases (14%), facultative anaerobic bacteria in three cases (8%), and streptococci in three cases (8%). The five strict anaerobic bacteria identified in this study were Propionibacterium acnes, Bacteroides thetaiotaomicron, Finegoldia magna, and Peptostreptococcus harei, and the three facultative anaerobic bacteria identified were Dermabacter hominis, Corynebacterium simulans, and Actinomyces neuii.
Table 1
Breast implant infections: comorbidities, clinical and biological presentations, and related complications

<table>
<thead>
<tr>
<th>Pattern and type of breast implant prosthesis</th>
<th>Number of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aesthetic reasons</td>
<td>23</td>
<td>62%</td>
</tr>
<tr>
<td>Repeat implant placement for aesthetic</td>
<td>11</td>
<td>29%</td>
</tr>
<tr>
<td>Breast augmentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>14</td>
<td>38%</td>
</tr>
<tr>
<td>Silicone implant</td>
<td>20</td>
<td>54%</td>
</tr>
<tr>
<td>Saline serum implant</td>
<td>7</td>
<td>19%</td>
</tr>
<tr>
<td>Unknown type of breast implant</td>
<td>10</td>
<td>27%</td>
</tr>
<tr>
<td>Comorbidity of breast implant infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior radiotherapy</td>
<td>11</td>
<td>30%</td>
</tr>
<tr>
<td>Tobacco user</td>
<td>11</td>
<td>30%</td>
</tr>
<tr>
<td>Lymph node dissection</td>
<td>4</td>
<td>11%</td>
</tr>
<tr>
<td>Corticosteroid treatment or</td>
<td>2</td>
<td>6%</td>
</tr>
<tr>
<td>immunosuppressive treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
<td>3%</td>
</tr>
<tr>
<td>HIV</td>
<td>1</td>
<td>3%</td>
</tr>
<tr>
<td>Type of breast implant infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute infection (&gt;6 weeks)</td>
<td>16</td>
<td>43%</td>
</tr>
<tr>
<td>Late infection (&gt;6 weeks)</td>
<td>21</td>
<td>57%</td>
</tr>
<tr>
<td>Clinical and biological presentations of breast implant infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purulent flow or scar dissection</td>
<td>17</td>
<td>46%</td>
</tr>
<tr>
<td>Abscess</td>
<td>11</td>
<td>30%</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>6</td>
<td>16%</td>
</tr>
<tr>
<td>Fever</td>
<td>7</td>
<td>19%</td>
</tr>
<tr>
<td>Leukocytosis &gt;12x10^3/l or CRP &gt;40 mg/ml</td>
<td>5</td>
<td>13%</td>
</tr>
<tr>
<td>Complications of breast implant infection</td>
<td>4</td>
<td>11%</td>
</tr>
<tr>
<td>Toxic shock syndrome</td>
<td>1</td>
<td>3%</td>
</tr>
<tr>
<td>Rib osteomyelitis</td>
<td>3</td>
<td>8%</td>
</tr>
</tbody>
</table>

CRP, C-reactive protein.

*Pseudomonas aeruginosa* was identified as the second most common pathogen species of breast implant infection in this study. Seven (19%) of the breast implant infection cases were polymicrobial. Only one bacterium (*D. hominis*) out of the 47 bacterial isolates required identification by 16S rRNA gene sequencing. The bacterial species involved in the breast implant infections are shown in Figure 1.

All 18 of the *S. aureus* isolates were methicillin-sensitive *S. aureus* (MSSA). Of the eight coagulase-negative Staphylococcus isolates, only two *Staphylococcus epidermidis* were resistant to methicillin, whereas three *S. epidermidis* isolates, two *Staphylococcus lugdunensis* isolates, and one *Staphylococcus simulans* isolate were susceptible to methicillin.

Eleven cases (30%) of breast implant infection were treated with an antibiotic regimen without immediate implant removal; 26 cases (70%) were treated with immediate implant removal. Surgical debridement consisted of a fistulectomy and removal of the necrotic tissues, leaving only good quality tissues. The periosteam and perichondrium was later followed to avoid exposing the pleura and mediastinum.

All 11 cases treated initially with only antimicrobials were subsequently treated with surgery. One patient was treated with a one-stage prosthesis exchange and another patient was treated with a salvage attempt consisting of prosthesis removal and compartment cleaning. Both of these patients relapsed and required complete removal of the implant.

The main antibiotic treatment in the postoperative period was amoxicillin–clavulanic acid (22 cases), followed by a combination of ceftazidime or piperacillin/tazobactam and ciprofloxacin (eight cases), a combination of rifampicin–ofloxacin (four cases), co-trimoxazole (one case), a combination of co-trimoxazole and clindamycin (one case), and amoxicillin (one case). The mean
duration of antibiotic treatment was 44 ± 14 days (range 14–90 days). With regard to complications of breast implant infections, there were three cases of costal osteomyelitis, which were treated with 90 days of antibiotic therapy. New prostheses were successfully placed in 16 cases. The median time to the new placement was 228 days. The mean duration of follow-up was 331 ± 231 days (range 60–810 days). No relapses were observed during the follow-up period.

4. Discussion

This study investigated 37 cases of microbiologically proven breast implant infection that represented 2.74% of breast implantations managed during the study period of 4.5 years. The breast implant infection rate was found to be significantly higher in breast reconstruction after mastectomy for breast cancer than aesthetic breast augmentation in this series (6.45% vs. 2.03%, p = 0.001). Infection rates after aesthetic breast augmentation reported in the literature vary from 2% to 2.5%2,14,16 the average infection rate after mastectomy for breast cancer has been reported to be 5.8% (range 0–29%).7 Some authors have recorded a higher rate, ranging from 47% to 53% of breast implant procedures.16,19

With regard to the classical risk factors for breast implant infection, such as diabetes mellitus, tobacco use, and immunodeficiency,3,20 30% of cases in the present study had undergone radiotherapy and 11% had undergone a lymph node dissection for breast cancer. Nevertheless, the most important risk factor observed was repeat implant placement for aesthetic breast augmentation (29%). Breast implant infections are usually reported as early infections, frequently occurring at <6 weeks after the implantation.1 Surprisingly, it was found that 57% of cases in the present study occurred at ≥6 weeks after the implantation. This may be explained by the higher number of breast implant infections in patients presenting from the private clinics in the region (17 cases) compared to inpatients (five cases). No risk factor or bacterial species was identified that was significantly associated with the time elapsed between placement of the breast implant and infection.

*S. aureus* remains the most frequent pathogen identified in breast implant infection: 49% in the present study and 67% in the literature.21 However, Gram-negative bacilli that have been considered uncommon pathogens of breast implant infections were found in 27% of cases in the present series. A higher proportion (42–44%) of Gram-negative bacilli has been reported recently in breast implant infection after surgical reconstruction in patients with breast cancer.10,22 No significant difference in Gram-negative bacilli between breast implant infections after surgical reconstruction in patients with breast cancer compared with breast implant infections after aesthetic breast augmentation were found (3/14 vs. 7/23, p = 0.7099). It was found that Gram-negative bacilli breast implant infections were not significantly involved in late infections compared to acute infections (7/21 vs. 3/16, p = 0.4613).

Of the coagulase-negative staphylococci involved in breast implant infections, *S. epidermidis* was the most common pathogen, identified in 14% in the present series and in 19.2–67% in previous studies.10,21 A few cases of breast infection caused by *S. lugdunensis* after plastic surgery, e.g., mammoplasty and mastectomy for breast cancer, have been reported.14–25 Moreover, *S. simulans*, which was identified in one of the present breast implant infection cases, has not been reported in the literature.

Eight facultative and strict anaerobic bacteria involved in breast implant infections were identified in this study. Among them, *P. acnes* has been reported in 27.3% of breast implant infections.19 A few cases of breast implant infection caused by *A. neui*24 and *Corynebacterium* species have been reported.29 Nevertheless, breast implant infections caused by *B. thetaiotaomicron, C. simulans,* D. *hominis, F. magna,* and *P. harei* have not been reported. No association was found between bacterial species and the risk factors in this study.

The lack of a comparison with previous data on the microbial epidemiology of breast implant infections before the arrival of MALDI-TOF MS in the study centre to confirm this changing epidemiology of breast implant infection is one of the limitations of this study. Nevertheless, 98% of 47 bacterial species involved in breast implant infections in this series were identified by MALDI-TOF MS; only one bacterial species, *Dermabacter hominis,* required molecular identification. In addition, MALDI-TOF MS allowed the early and accurate identification of anaerobic bacteria involved in the cases of breast implant infection in this study; the technique has been used successfully in the identification of unknown anaerobic bacteria involved in osteoarticular infections in previous studies.13,20 Ninety-two percent of Staphylococcus isolates in this study were susceptible to methicillin, which is lower than the percentage reported in previous studies.13,21 In this study, the presence of Staphylococcus isolates resistant to methicillin and an increase in the proportion of Gram-negative and anaerobic bacteria were noted. We do not recommend specific empirical antibiotic treatment before bacterial species identification and the results of susceptibility testing are known.

Surgical removal of the implant is required in most cases of breast implant infection; a two-stage breast prosthesis replacement is usually recommended.2,21 Some studies have reported successful one-stage prosthesis exchange or salvage attempts, consisting of prosthesis removal and cleaning of the compartment.32–34 The reported success rate of early salvage followed by one-stage prosthesis exchange in cases of breast infection that are not too severe is in the range of 45% to 76.7%.32–34 Two of the cases in the present series treated by salvage without implant removal both relapsed and required complete implant removal. Due to the lack of randomized controlled trials, we do not recommend one-stage prosthesis exchange in severe cases of breast implant infection.

In conclusion, breast implant infection rates after cosmetic augmentation are low, unlike the higher rates after breast reconstruction following mastectomy for breast cancer. The most important risk factor observed was repeat implant placement for aesthetic breast augmentation. With regard to the microbiological epidemiology, an increasing proportion of Gram-negative bacteria and anaerobic bacteria detected with the advent of MALDI-TOF MS and molecular identification for diagnosis was noted. The remission rate for this condition is high, nevertheless severe and rare complications such as toxic shock syndrome and rib osteomyelitis may occur. Breast implant infections require a multidisciplinary approach to improve the prognosis, and the management consists of implant removal and antibiotics selected according to the microbiological surgical sample results.

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