Breast implant-associated anaplastic large-cell lymphoma (BIA-ALCL) is a rare but serious complication in patients with breast implants. Patients are at risk of BIA-ALCL whether they receive breast implants for cosmetic reasons or for reconstructive purposes after surgery for breast cancer or prophylactic mastectomy. During the past decade, an increased number of reports have addressed BIA-ALCL. Herein, we describe BIA-ALCL in a transgender woman. The patient received breast implants as part of her gender transition and was diagnosed with BIA-ALCL 20 years later. The patient underwent several revisional operations in the 20 years after her primary breast surgery to treat unexplained pain with low-grade fever, severe capsular contracture (Baker grade III-IV), and several instances of implant rupture. In July 2016, the patient presented to our office with "late-onset" periprosthetic seroma 5 years after her last revisional breast surgery. She was diagnosed with BIA-ALCL without capsular invasion based on results of cytologic analysis of the periprosthetic seroma and histologic evaluation of the periprosthetic capsule. This diagnosis was verified further by results of immunohistochemical testing, which indicated expression of CD30 and T-cell markers in the periprosthetic seroma only. Our intentions with this case report are to demonstrate that all patients who undergo breast implantation, including transgender women, are at risk of BIA-ALCL and to highlight the importance of cytomorphologic and immunohistochemical screening of seroma fluid in patients with late-onset periprosthetic seroma.

Level of Evidence: 5

Breast implant-associated anaplastic large-cell lymphoma (BIA-ALCL) is a rare variant of T-cell non-Hodgkin lymphoma that occurs in the periprosthetic fluid or capsule of women who undergo breast implantation.1-4 BIA-ALCL is included as a (provisional) entity in the 2016 nomenclature of the World Health Organization.5 When limited to the periprosthetic seroma or capsule, BIA-ALCL has an indolent clinical course, and explantation and capsulectomy may be adequate treatments.6 However, in approximately 10% of patients with BIA-ALCL, lymphoma dissemination occurs, which necessitates high-dose systemic chemotherapy and poses a risk of adverse prognosis.7 The pathogenesis of BIA-ALCL likely is multifactorial and associated with characteristics of the textured implant, features of the implant-related microbial biofilm (eg, its density and composition), and local immune response.8-11

Approximately 200 cases of BIA-ALCL have been described worldwide; these cases have occurred in the context of cosmetic augmentation (54%-57% of all cases) or breast reconstruction after cancer related or prophylactic surgery (43%-45%).12,13 Herein, we highlight a unique at-risk population by describing a transgender woman with BIA-ALCL.

Table 1. Implant-Related Surgical Procedures in a Transgender Woman

<table>
<thead>
<tr>
<th>Year</th>
<th>Age, y</th>
<th>Procedure</th>
<th>Reason for Procedure</th>
<th>Side of Surgery</th>
<th>Type of Prosthesis</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>38</td>
<td>Neomammaplasty with implantation</td>
<td>Male-to-female gender transition</td>
<td>Bilateral</td>
<td>Nagor GFXa textured gel-filled implants; 460 cc; placed bilaterally</td>
<td>NA</td>
</tr>
<tr>
<td>1999</td>
<td>39-40</td>
<td>Explantation and reimplantation</td>
<td>Pain in left breast; low-grade fever</td>
<td>Left</td>
<td>Rofilb highly cohesive textured gel-filled implant; 460 cc; placed unilaterally on left side</td>
<td>Elevated erythrocyte sedimentation rate; small hypoechoic structure, interpreted as postoperative seroma, on preoperative ultrasound examination of left breast</td>
</tr>
<tr>
<td>2012</td>
<td>52</td>
<td>Explantation, capsulectomy, and reimplantation</td>
<td>Baker grade 3 capsular contracture; bilateral implant rupture</td>
<td>Bilateral</td>
<td>Allergan Natrelle Inspira SoftTouchc textured gel-filled implant; 490 cc; placed bilaterally</td>
<td>Bilateral rupture of breast implants on preoperative ultrasound examination; results of postoperative pathology analysis of periprosthetic capsules indicated foreign-body reaction related to silicone particles; absence of T-lymphocytes that tested positive for CD3 or ALK</td>
</tr>
<tr>
<td>2015</td>
<td>56</td>
<td>Explantation and reimplantation</td>
<td>Implant rupture in right breast</td>
<td>Right</td>
<td>Allergan Natrelle Inspira SoftTouchc textured gel-filled implant; 490 cc; placed unilaterally on right side</td>
<td>No abnormalities of left breast; implant rupture and intracapsular hyperechoic seroma of right breast on preoperative ultrasound examination</td>
</tr>
<tr>
<td>2016</td>
<td>56</td>
<td>Explantation and capsulectomy</td>
<td>Progressive late-onset periprosthetic seroma of the left breast</td>
<td>Left</td>
<td>None</td>
<td>Results of cytopathologic assessment of periprosthetic seroma collected peroperatively indicated T-lymphocytes that tested positive for CD3 and ALK; diagnosis of seroma-associated BIA-ALCL</td>
</tr>
</tbody>
</table>

BIA-ALCL, breast implant-associated anaplastic large-cell lymphoma; NA, not applicable. aNagor Ltd., Cumbernauld, Glasgow, UK. bRofil, Breda, the Netherlands. cAllergan, Parsippany-Troy Hills, NJ.

CASE PRESENTATION

In July 2016, a 56-year-old transgender woman presented to our outpatient clinic with rapid enlargement of the left breast. Approximately 20 years prior to presentation, she had received bilateral breast augmentation with silicone-filled textured implants and penile inversion vaginoplasty as part of a gender transition. These procedures were performed in a single surgical session by a past staff physician of the Plastic Surgery Department of the VU Medical Center (Amsterdam, the Netherlands). The patient subsequently underwent multiple revisional breast surgeries to treat unexplained pain and low-grade fever, severe capsular contracture (Baker grade III-IV), and implant rupture (Table 1).

“Late-onset” periprosthetic seroma, (ie, after more than one year after implantation) of the left breast was noted on our examination and was confirmed by ultrasonographic findings (Figure 1). Unilateral explantation of the Natrelle Inspira SoftTouch device (textured, gel-filled, 490 cc; Allergan, Parsippany-Troy Hills, NJ) and complete capsulectomy were performed. Seroma fluid and capsular tissue were obtained for analysis at the VU University.
Histologic findings of the capsular tissue showed presence of a small collection of atypical lymphoid cells adherent to the inner surface of the fibrous capsule. No infiltrating component of the tumor was observed, despite lymphohistiocytic inflammatory infiltrate in the capsule tissue. Large atypical lymphoid cells were abundant in the seroma fluid. Immunocytologic results on the cytological preparations, were positive for CD30, CD2, and CD3 and negative for CD4, CD8, TIA1, granzyme B, ALK1, EBER, and B-cell markers, which confirmed the diagnosis of ALK-negative BIA-ALCL (Figure 2). We conducted a retrospective analysis of all available histologic specimens, including an immunohistochemical examination of capsular tissue excised at the patient’s revisional breast surgery 4 years before presentation. Our findings indicated absence of lymphoma localization at that time.

Results of a complete standardized hemato-oncologic work-up, involving positron emission tomography-computed tomography, demonstrated lack of dissemination, suggesting stage 1E lymphoma. The patient underwent explantation of the contralateral right breast implant; no oncologic treatment, such as chemotherapy or radiotherapy, was indicated. In accordance with international recommendations, follow-up was conducted in collaboration with the Departments of Hemato-oncology and Plastic and Reconstructive Surgery of the VU Medical Center (Amsterdam, the Netherlands). The patient was in complete remission 10 months postoperatively.

DISCUSSION

In a case-cohort epidemiologic risk assessment conducted in the Netherlands from 1990 to 2005, our group found an odds ratio of 18.2 for ALCL in women with breast implants; the estimated absolute risk was 1:300,000 to 1:1,000,000. In recent years, plastic surgeons and pathologists have become more aware of BIA-ALCL, which has yielded in an increasing apparent incidence of this disease. The number of cosmetic breast augmentations with macrotextured implants also has grown, but in view of the increasing market shares of these products, specific risk assessments in relation implant characteristics await further study. Therefore, the true incidence of BIA-ALCL may be increasing and may exceed current estimates. Transgender women have not formally been included in risk assessments of BIA-ALCL. To our knowledge, the current report is only the second description of BIA-ALCL in a transgender woman with breast implants.

The prevalence of gender dysphoria in the general population is 1:10,000, and an estimated 60% to 70% of individuals who undergo male-to-female transition require breast implantation. (Cross-sex hormone therapy adequately enlarges the mammary glands in 30%-40% of transgender women.) Therefore, BIA-ALCL may be diagnosed more frequently in transgender women in the coming years.

CONCLUSIONS

Physicians must recognize that all patients with breast implants, including transgender women, are at risk of BIA-ALCL. Cytohistologic and immunohistochemical analysis of aspirated seroma fluid constitute the most sensitive screening and diagnostic approach for patients with breast implants who present with late-onset periprosthetic seroma.
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REFERENCES

Figure 2. Histocytologic and immunohistochemical analyses of seroma-associated BIA-ALCL. (A) Lymphoma cells with abnormal (kidney- or horseshoe-shaped) nuclei in hematoxylin and eosin (H&E) staining (original magnification x200). (B) Enlarged atypical lymphoid cells were abundant in the seroma fluid and had adhered to the capsule (H&E-staining, original magnification x200). (C) Tumor cells stained with anti-CD30 in seroma fluid, showing brown chromogen (original magnification x400). (D) Tumor cells stained with anti-CD3 antibodies in seroma fluid (original magnification x400).