Breast implant-associated squamous cell carcinoma

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Breast implant-associated squamous cell carcinoma (BIA-SCC) is a rare but serious disease that originates from the lining of the breast implant capsule. Alongside BIA-anaplastic large cell lymphoma, the U.S. Food and Drug Administration issued a safety communication in 2022 regarding BIA-SCC to alert healthcare providers and patients. Although only a few cases have been reported, the high mortality and poor prognosis associated with BIA-SCC underscore the severity of the disease. This review discusses the current knowledge of BIA-SCC, including its pathogenesis, diagnostic methods, and treatment options based on reported cases.

**Keywords** Breast implants / Carcinoma, squamous cell / Capsules

**INTRODUCTION**

Nearly 30 years after the initial use of a textured surface breast implant in 1968, the first case of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) was reported in 1997 [1]. With the increasing number of case reports concerning BIA-ALCL, the U.S. Food and Drug Administration (FDA) issued a safety communication in 2011 about the potential link between ALCL and breast implants, and established a registry for physicians to collect scientific data on ALCL [2]. In 2016, the World Health Organization recognized BIA-ALCL as a distinct type of T-cell lymphoma, which has helped to raise global awareness [3]. However, beyond BIA-ALCL, other malignant conditions associated with implants, such as B-cell lymphoma and squamous cell carcinoma (SCC), have been identified over the past decade [4-6]. In this review, we provide an overview of BIA-SCC, which has recently been highlighted in a U.S. FDA safety communication [7].

**ETIOLOGY AND EPIDEMIOLOGY**

BIA-SCC differs from primary SCC of the breast as it originates from the breast implant capsule. The pathogenesis of BIA-SCC is believed to be associated with chronic inflammation or irritation of the inner lining of the breast implant capsule, which has undergone squamous metaplasia [8]. The squamous epithelial cells are thought to arise from either metaplasia of the breast ductal cells or transformation of the capsular cells [9].

The incidence of BIA-SCC is extremely low, with its prevalence being 3.3 times lower than that of primary SCC in breast parenchyma. When comparing the risk of BIA-SCC to BIA-ALCL in patients with textured implants, it is 180 times lower [10]. According to a 2023 U.S. FDA safety communication, there have been 19 cases of SCC that developed in the capsule surrounding the breast implant. The mean age at diagnosis was 55.8 years, and the average time after implantation was 22.7 years. While all cases of BIA-ALCL have been diagnosed in patients with textured implants, there are patients with BIA-SCC who had smooth implants (Table 1) [11]. Additionally, reported cases of BIA-SCC have occurred not only after cosmetic breast augmentation but also following implant-based breast reconstruction [6].

**DIAGNOSIS**

Similar to BIA-ALCL, symptoms of BIA-SCC include unilateral swelling, erythema, and late seroma. However, patients with BIA-SCC typically present with breast pain and enlargement, and may also experience regional lymph node enlargement [6,12]. Capsular contracture and extracapsular spread are common at the time of...
En bloc capsulectomy and explantation of silicone and saline implants are essential before surgery to rule out distant metastasis. Given that a significant number of patients exhibit extracapsular spread and had invaded adjacent structures by the time of diagnosis, it is recommended to obtain more than 50 mL for cytology and more than 10 mL for flow cytometry immunophenotyping. The aspirated fluid should be tested for CK5/6 and p63, using flow cytometry to identify squamous cells and keratin (Table 1). In addition to ultrasound, magnetic resonance imaging (MRI) should be performed to evaluate the capsule and rule out any masses. Any suspicious mass lesions should be biopsied and sent for pathology to confirm dysplastic keratinized epithelium of the capsule and to conduct immunohistochemical evaluations [6]. Positron emission tomography-computed tomography (PET-CT) is performed to evaluate the extent of disease.

**Table 1. Comparison between BIA-SCC and BIA-ALCL**

<table>
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<tr>
<th></th>
<th>BIA-SCC</th>
<th>BIA-ALCL</th>
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<tbody>
<tr>
<td>Average postoperative period</td>
<td>&gt; 20 yr</td>
<td>10 yr</td>
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<tr>
<td>Typical symptoms</td>
<td>Unilateral enlargement and pain</td>
<td>Unilateral swelling and pain</td>
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<tr>
<td></td>
<td>Erythema</td>
<td>Erythema</td>
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<tr>
<td>Mass with extracapsular spread</td>
<td>Late seroma</td>
<td>Late seroma</td>
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<tr>
<td>Implant type</td>
<td>Textured and smooth surface</td>
<td>Textured surface</td>
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<tr>
<td></td>
<td>Silicone and saline</td>
<td>Silicone and saline</td>
</tr>
<tr>
<td>Immunostaining</td>
<td>CK5/6+, p63+</td>
<td>CD30+, ALK-</td>
</tr>
<tr>
<td>Treatment</td>
<td>En bloc capsulectomy</td>
<td>En bloc capsulectomy</td>
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<td></td>
<td>Explantation</td>
<td>Explantation</td>
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<td>Mastectomy at an advanced stage</td>
<td>Chemotherapy</td>
<td>Radiation</td>
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<tr>
<td>Prognosis</td>
<td>Poor</td>
<td>Good</td>
</tr>
</tbody>
</table>

BIA, breast implant-associated; SCC, squamous cell carcinoma; ALCL, anaplastic large cell lymphoma.

**DISCUSSION**

Most late seromas following breast implantation are associated with benign capsular conditions, including synovial metaplasia, capsular epithelialization, late hematoma, and double capsules [9]. However, while most capsules remain benign, some may undergo fibrotic changes and develop masses, including BIA-ALCL, which accounts for 6% to 9% of patients with late seroma [18,19]. Both plastic surgeons and patients are increasingly aware of the risk of BIA-ALCL, particularly in patients with textured surface implants [20]. In 2022, 11 years after its initial safety communication about BIA-ALCL, the U.S. FDA issued another safety communication. This update reported on cases of SCC and various lymphomas found in the capsules surrounding breast implants. On March 8, 2023, the U.S. FDA provided additional information on 19 cases of BIA-SCC, including details from the first reported case in 1992 to the most recent one in 2023 [9,12]. Patients with BIA-SCC are more likely to experience symptoms such as breast swelling or enlargement and pain, whereas late seroma is commonly observed in BIA-ALCL cases. Additionally, most BIA-SCC cases had progressed to extracapsular spread and had invaded adjacent structures by the time of diagnosis, leading to extensive surgery and a poor prognosis.

Unlike BIA-ALCL, which exclusively involves textured-surface implants, there are four cases (21%) of BIA-SCC in patients with smooth-type implants. It remains uncertain whether a specific type of implant acts as a source of chronic inflammation or irritation that could lead to the development of BIA-SCC. BIA-SCC has been diagnosed in patients who have undergone implantations not only for aesthetic breast augmentation but also for reconstruction following mastectomy.

Surgeons must be vigilant for both BIA-ALCL and BIA-SCC in patients presenting with symptoms such as breast pain, enlargement, late seroma, or capsular mass, and should conduct appropriate evaluations. Ultrasound and/or MRI are recommended to assess the potential presence of these malignancies. If late seroma is observed around the implant, periprosthetic fluid should be collected via ultrasound-guided aspiration for cytological analysis and cultured to exclude infection. In cases where a mass-like lesion is present, the patient should undergo a biopsy. Immunohistochemical staining for CD30 and ALK is necessary to diagnose BIA-ALCL, and staining for CK5/6 and p63 is crucial to rule out BIA-SCC. Additionally, flow cytometry should be performed on the specimens to analyze T-cells, B-cells, squamous cells, and keratin, aiding in the differential diagnosis. Given that a significant number of patients exhibit extracapsular spread at the time of diagnosis, a PET-CT scan may be advisable before surgery to rule out distant metastasis.

Although BIA-SCC is a rare disease, its aggressive nature can lead to significantly high mortality rates. Currently, data on BIA-SCC are scarce due to a limited understanding of the disease entity, and cases are believed to be underreported. However, the number of re-
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reported cases has been increasing over the past few years as recognition of this serious disease grows. Increased sharing of data and information about BIA-SCC by healthcare providers could enhance awareness of the disease and potentially improve treatment outcomes in the future.

NOTES

Conflict of interest
Han Gyu Cha is an editorial board member of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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