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Frequency of reoperation in patients who underwent breast reconstruction using Allergan implants after an interview about breast implant-associated anaplastic large cell lymphoma

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Background In recent years, breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) has emerged as an important concern. At our institution, patients who received breast reconstruction using Allergan implants were informed individually about BIA-ALCL. The present study analyzed correlations between patients' level of satisfaction with their breast shape and whether they chose to undergo reoperation (implant removal or replacement).

Methods Breast reconstruction with Allergan implants was performed between December 2014 and April 2018. In total, 107 patients were interviewed, excluding those who had died, were unreachable, or had already undergone reoperation. The mean follow-up period was 53 months (range, 26–73 months).

Results After the interviews, 68 patients postponed reoperation, 29 had their implant replaced, and 10 had their implant removed. Nearly one-fifth (18.9%) of patients who were satisfied with their breast shape (13 out of 69) underwent reoperation due to anxiety over ALCL. Meanwhile, 68.4% of patients who were not satisfied due to capsular contracture or scar contracture (26 out of 38) underwent reoperation. Sixteen of the 30 patients who received postoperative radiotherapy (53.3%) chose to undergo reoperation.

Conclusions Satisfaction with the cosmetic outcomes of implant placement played a meaningful role in patients' decisions to undergo reoperation. This tendency may be linked to postoperative radiotherapy, which is a major contributor to complications such as contracture. Nonetheless, a substantial proportion of patients who were satisfied with the outcomes chose to undergo reoperation due to concerns regarding ALCL.

Keywords Allergan / Breast implant-associated anaplastic large cell lymphoma / Reoperation

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INTRODUCTION

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) was first identified in 1997. The announcement of the provisional entity of BIA-ALCL by the World Health Organization (WHO) in 2016 raised anxiety among patients who had undergone breast plastic and reconstructive surgery with textured implants. The Korean media also started to cover this issue in late 2018. The Korean Society of Plastic and Reconstructive Surgeons and the

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Ministry of Food and Drug Safety have officially recognized the issue of BIA-ALCL and have managed and conducted long-term follow-up of cases of implant-associated abnormalities. BIA-ALCL is more closely associated with the use of Allergan products than with the use of other types of textured implants. Therefore, all individuals who received breast reconstruction at our institution using Allergan textured implants were informed of BIA-ALCL. Three ALCL cases have been reported in Korea, with no known deaths. Our institution interviewed each individual who received Allergan implants and analyzed how frequently they requested reoperation. We investigated the correlations among implant-associated complications after breast reconstruction, patients' level of satisfaction with their breast shape, and the frequency of reoperation (implant removal or replacement). We also analyzed the correlation between postoperative radiotherapy (PORTx), which affects breast shape, and the desire for reoperation.

METHODS

In total, 117 patients received immediate breast reconstruction with Allergan implants at our institution between December 2014 and April 2018. Among them, we interviewed 107 individuals, excluding those who had died (3 patients), were unreachable (1 patient), or had already undergone reoperation (6 patients). The mean follow-up period was 53 months (range, 26–73 months), the average age was 47.8 years old, and the average body mass index was 23.2 kg/m^2. The methods of the operations were an extended latissimus dorsi muscle flap with an Allergan implant in 78 cases, and direct-to-implant (DTI) reconstruction using an Allergan implant in 29 cases.

The interviews with the patients were conducted during outpatient visits, and patients with more than 6 months remaining before their next scheduled outpatient visit were requested to visit earlier. Each interview was conducted by one plastic surgeon and included the following information. First, the cause of BIA-ALCL and the relationship between BIA-ALCL and the implant (Allergan) used in the patient were explained. Second, it was clarified that prophylactic removal without suspicious symptoms is not recommended. Additionally, surgery is not recommended if there is no discomfort in the surgical site, capsular contracture of Baker grade I or II, or if the patient does not want it. Third, surgery is recommended when there is a shape abnormality in the surgical site, discomfort due to breast animation deformity, or capsular contracture of Baker grade III or IV.

The 107 patients were thoroughly informed of the risks and effects of reoperation during their BIA-ALCL interview. They decided either to postpone reoperation or to replace or remove the implant. In patients who underwent reoperation, we conducted a comparison between those with worsened capsular contracture or scar contracture caused by PORTx and those who were satisfied with their breast shape. We studied the frequency of reoperation according to the operation method, patients' satisfaction with their breast shape, and whether the patient received PORTx, which is the most important factor that causes deformation of the breast. Thirty patients received PORTx (Table 1), of whom 15 received 33 fractions (6,040 Gy), seven received 35 fractions (6,500 Gy), two received 30 fractions (6,000 Gy), one received 27 fractions (4,860 Gy), and one received 5 fractions (4,000 Gy). Four patients received PORTx at other institutions (CLINAC IX; Varian Medical Systems, Inc., Palo Alto, CA, USA).

In all cases, the reoperation procedure focused on removing both the Allergan implant and the double capsule. If the patient wished to have the implant replaced with another product, the regions with capsular contracture and scar contracture were corrected. The dual plane was corrected in cases where the Allergan implant was inserted by replacing it with a new implant (BellaGel microtexture round implant, Hansbiomed Co. Ltd., Seoul, Korea or Mentor smooth round implant, Mentor Worldwide LLC, Irvine, CA, USA) after fixing the pectoralis major muscle to the chest. In cases with a prepectoral plane, implants were inserted in the same plane after correcting areas of contracture. All patients who underwent implant replacement received acellular dermal matrix (ADM) (MegaDerm, L&C Bio, Seongnam, Korea or BellaCell/Surederm, Hansbiomed Co. Ltd.).

The cosmetic results after reoperation were evaluated based on the four classes defined according to the Harris method [1]. Two plastic surgeons evaluated the shape of patients' breasts after surgery at each outpatient visit, with satisfaction levels of excellent, good, fair, or poor (Table 2).

All statistical results were calculated using the R statistical pack-

Table 1. Number of patients who received adjuvant therapy

Adjuvant therapy	No. of patients
None	45
Chemotherapy	32
Radiotherapy	2
Chemotherapy + radiotherapy	28
Total	107

Table 2. Distribution of patients according to satisfaction

	Patients	Postponed reoperation	Implant replacement	Implant removal
Excellent or good	69	56	9	4
Fair or poor	38	12	20	6
Total	107	68	29	10

Values are presented as number only.
$P < 0.001$.

age (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria). To detect significant covariates associated with the frequency of reoperation in patients who underwent breast reconstruction using the Allergan implants, we used a multiple linear regression model. A difference was considered statistically significant if the P-value was <0.05.

RESULTS

The number of patients with each breast cancer stage based on the American Joint Committee on Cancer 8th edition classification was 23 with stage 0 (21.4%), 32 with stage 1 (29.9%), and 36 with stage 2 (33.6%). Altogether, 85.0% of patients had stage 0-2 disease (Table 3). Twenty-seven patients had implants smaller than 100 cc (25.2%), 30 had implants between 100 and 199 cc (28.0%), 28 had implants between 200 and 299 cc (26.1%), 12 had implants between 300 and 399 cc (11.2%), and four patients had implants with a volume of 400 cc or above (3.7%). Six patients underwent bilateral implant placement (5.6%) (Table 4).

Table 3. Number of patients by breast cancer stage (the AJCC 8th edition classification)

Breast cancer stage	No. of patients
Stage 0	23
Stage 1	32
Stage 2	36
Stage 3	9
Stage 4	4
Other (no cancer)	3
Total	107

AJCC, American Joint Committee on Cancer.

Table 4. Number of patients by implant size

Implant size	No. of patients
<100 cc	27
100–199 cc	30
200–299 cc	28
300–399 cc	12
≥400 cc	4
Bilateral	6
Total	107

As of June 2021, out of 107 patients who had BIA-ALCL interviews, 68 (63.5%) postponed reoperation, 29 (27.1%) had their implants replaced, and 10 (9.3%) had their implants removed.

Of the 78 patients who received breast reconstruction using an extended latissimus dorsi muscle flap and Allergan implant, 51 (65.3%) decided to postpone reoperation, 21 (26.9%) had their implant replaced, and six (7.7%) had their implants removed. Among the 29 patients who received DTI reconstruction, 17 (58.6%) decided to postpone reoperation, eight (27.6%) had their implants replaced, and four (13.8%) had their implants removed (Table 5).

Among the 69 patients who were satisfied with their breast shape, 56 (81.1%) decided to postpone reoperation, nine (13.0%) underwent replacement surgery, and four (5.8%) underwent removal surgery. Out of the 38 patients who were not satisfied with their breast shape, 12 (31.6%) decided to postpone reoperation, 20 (52.6%) had their implants replaced, and six (15.8%) had their implants removed (Table 4).

Of the 77 patients who did not receive PORTx, 54 (70.1%) decided to postpone reoperation, 15 (19.5%) had their implants replaced, and eight (10.3%) had their implants removed. Among the 30 patients who received PORTx, 14 (46.7%) postponed reoperation, 14 (46.7%) had their implants replaced, and two (6.7%) had their implants removed (Table 6).

Among the 53 patients who received breast reconstruction using an extended latissimus dorsi muscle flap and Allergan implant, but did not receive PORTx, 39 patients were satisfied with their cosmetic outcomes and 14 were not. Six of the 39 satisfied patients decided to undergo reoperation, as did nine out of the 14 dissatisfied patients (Fig. 1). Meanwhile, among the 25 patients who received

Table 5. Number of patients by operation method

	Patients	Postponed reoperation	Implant replacement	Implant removal
LD implant	78	51	21	6
DTI	29	17	8	4
Total	107	68	29	10

Values are presented as number only.
LD, latissimus dorsi muscle flap; DTI, direct to implant.
P=0.626.

Table 6. Number of patients by radiotherapy method

	Patients	Postponed reoperation	Implant replacement	Implant removal
Without RTx (none & CTx)	77	54	15	8
With RTx (RTx & RTx+CTx)	30	14	14	2
Total	107	68	29	10

Values are presented as number only.
RTx, radiotherapy; CTx, chemotherapy.
P=0.022.

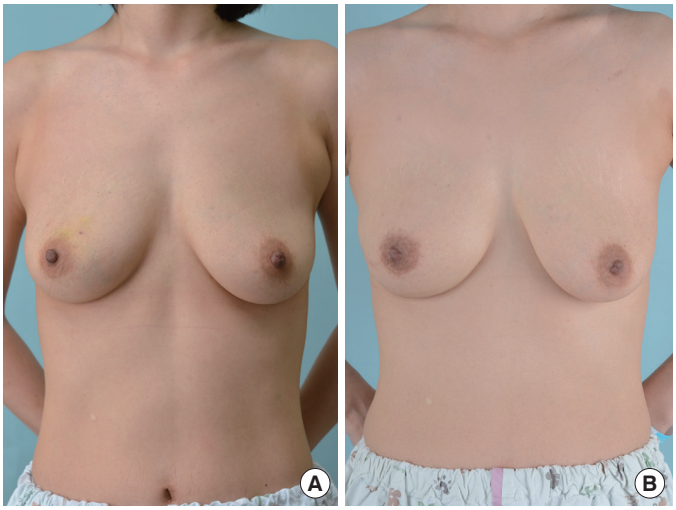

Fig. 1. Latissimus dorsi muscle flap with an Allergan implant, no postoperative radiotherapy. The patient was 39 years old, had right breast cancer (T2N1M0), and underwent breast reconstruction using an extended latissimus dorsi muscle flap and Allergan implant, but did not receive postoperative radiotherapy. Photographs were taken (A) preoperatively and (B) at 4 years postoperatively.

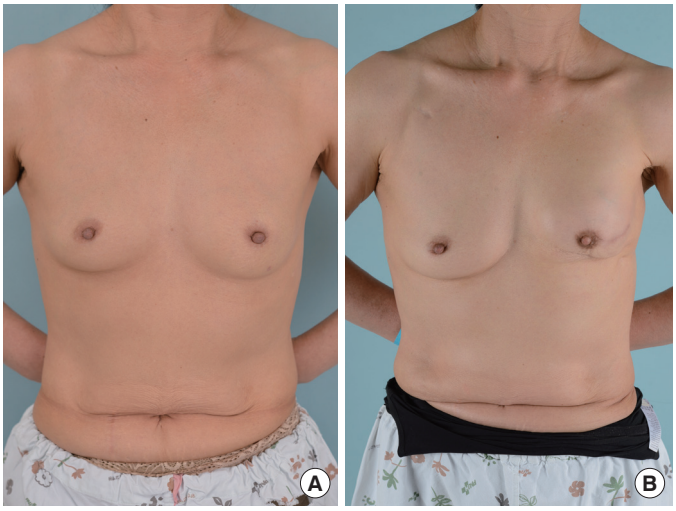

Fig. 2. Latissimus dorsi muscle flap with an Allergan implant, with postoperative radiotherapy. The patient was 56 years old, had left breast cancer (T2N2M0), underwent breast reconstruction using an extended latissimus dorsi muscle flap and Allergan implant, and received postoperative radiotherapy. Photographs were taken (A) preoperatively and (B) at 3 years postoperatively.

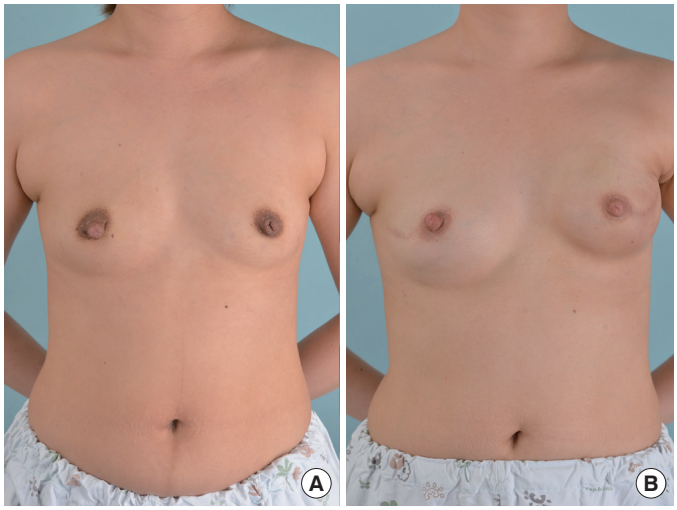

Fig. 3. Direct-to-implant with an Allergan implant, with postoperative radiotherapy. The patient was 58 years old, had bilateral breast cancer (T2N2M0), underwent breast reconstruction using direct-to-implant Allergan implants, and received postoperative radiotherapy in the left breast. Photographs were taken (A) preoperatively and (B) at 3 years postoperatively.

Table 7. Outcomes in cases using an extended latissimus dorsi muscle flap and Allergan implant (78 cases)

	Without RTx (none & CTx)	Reoperation	With RTx (RTx & RTx+CTx)	Reoperation
Good	39	6	9	1
Bad	14	9	16	11
Total	53	15	25	12

Values are presented as number only.
RTx, radiotherapy; CTx, chemotherapy.
P < 0.001.

Table 8. Outcomes in patients who underwent direct-to-implant reconstruction (29 cases)

	Without RTx (none & CTx)	Reoperation	With RTx (RTx & RTx+CTx)	Reoperation
Good	18	4	3	2
Bad	6	4	2	2
Total	24	8	5	4

Values are presented as number only.
RTx, radiotherapy; CTx, chemotherapy.
P = 0.055.

breast reconstruction using an extended latissimus dorsi muscle flap and Allergan implant and received PORTx, nine patients were satisfied with their cosmetic outcomes and 16 were not. One of the nine satisfied patients and 11 of the 16 dissatisfied patients decided to undergo reoperation (Table 7, Fig. 2). Among the 29 patients who underwent DTI reconstruction with an Allergan implant, 24 did not receive PORTx. Among them, 18 were satisfied with their breast shape, while six were dissatisfied, and four cases in each group underwent reoperation. Among the five DTI Allergan implant cases who received PORTx, three were satisfied with their breast shape while two were dissatisfied, and two patients in each group underwent reoperation (Table 8, Fig. 3).

DISCUSSION

From August 2012 to March 2018, a total of 186 cases of BIA-ALCL were reported in the US. The median time from implantation of any device to BIA-ALCL diagnosis was 11.0 years [2]. A more recent long-term cohort study at a single institution, the Memorial Sloan Kettering Cancer Center in the US, studied a cohort of patients who underwent reconstruction with macro-textured breast implants from December 1992 to December 2017. The overall risk of BIA-ALCL in the cohort was 1 of 355 women [3]. This outcome is higher than the risk of 1:30,000 suggested by the study of Doren et al. [4] conducted between 1996 and 2015 of patients reconstructed with textured implants, raising awareness among plastic surgeons.

Textured implants show good cohesion to the breast tissue and promote the stability of the breast pocket, reducing the frequency of reoperation by lowering the risk of capsular contracture [5-7]. Thanks to these benefits, the use of textured implants had been gradually increasing in the US, peaking in 2016 when the WHO announced BIA-ALCL. Since it takes an average of 10 years for the condition to develop after implantation, it is expected that the number of BIA-ALCL cases will likely peak around 2026 [8].

The Korean Society of Plastic and Reconstructive Surgeons established a referral system by connecting select primary institutions with tertiary institutions designated as BIA-ALCL specialized institutions, for patients who show suspected BIA-ALCL symptoms after using Allergan implants, such as sudden occurrence of a seroma or tumor 1 or more years after reconstruction. The primary institution may refer patients to specialized institutions for pathology examinations (37 institutions nationwide) or to designated intensive care tertiary institutions (41 institutions nationwide) for the diagnosis and treatment of BIA-ALCL. Patients who received implantation surgery are advised to immediately see a plastic surgeon if they experience sudden changes in breast size, pain, or a lump, and to receive annual check-ups if they have no symptoms. In 2021, Kim et al. [9] reported a case with a history of spontaneously resolved late seroma, which underscores the importance of guiding patients to visit the hospital at the proper time.

The common factors associated with BIA-ALCL occurrence are the use of a textured breast implant, activation of the immune system at the surgical site as shown by the formation of a biofilm, and a genetic predisposition for JAK/STAT activation [10]. The treatment of BIA-ALCL varies according to the stage of ALCL. At stage 1, a complete cure is possible with implant removal and total capsulectomy, while stage 2–3 patients require systemic treatment including chemotherapy, radiotherapy, and brentuximab vedotin [10]. At the moment, no medical society has recommended preventive implant removal; instead, patients are advised to be checked regularly by plastic surgeons [10].

This study found a double capsule in all patients who underwent reoperation involving a total capsulectomy. One patient received ADM reinforcement of a tear in the pleura that occurred during removal of the capsule on the chest wall during total capsulectomy. The case was consulted with a cardiothoracic surgeon and no abnormal opinion was found during follow-up. Special attention is required when removing a capsule that is firmly attached to the chest wall, because aggressive capsulectomy could injure the pleura and cause further complications such as pneumothorax [11]. The decision to perform preventive removal of an Allergan implant and total capsulectomy without any suspected BIA-ALCL symptoms should be made cautiously, considering potential postoperative infection and pleural injury. Each of the six patients who underwent reoperation before the BIA-ALCL announcement is being closely followed after their individual interviews, as they have some capsule remaining in their chest wall (base) and it is not possible to rule out the potential of BIA-ALCL occurrence.

The total number of patients who underwent breast reconstruction using Allergan implants was 117, of whom we interviewed 107 patients with the exception of 10 patients who had the implant removed, had died, or were not possible to reach. A majority (78 cases) of them had undergone total mastectomy using an extended latissimus dorsi muscle flap and Allergan implant, most of those who received an implant and extended latissimus dorsi muscle flap had an implant smaller than 200 cc, and half as many patients received radiotherapy as did not. Twenty-nine patients underwent total mastectomy and DTI; most of them did not have plans for radiotherapy before the operation, but five ultimately received PORTx. In all patients who received DTI reconstruction, dual-plane ADM was used.

Most of the 38 patients (out of 107 who were analyzed) who were not satisfied after the initial reconstruction due to a shape deformity or contracture had already been considering reoperation, and 26 of them decided to undergo reoperation triggered by the BIA-ALCL announcement (replacement: 20, removal: 6). Fifty-six of the 69 patients who were satisfied with their breast shape decided to postpone reoperation, and 13 patients underwent reoperation (replacement: 9, removal: 4) simply due to anxiety regarding BIA-ALCL even though they did not have any suspected symptoms such as delayed seroma.

Contracture and deformation occurred most frequently after PORTx, which is the largest risk factor for deformation of the breast shape after reconstruction. Sixteen of the 30 patients who received PORTx chose to undergo reoperation, a relatively high percentage. Twenty-five of these patients had undergone a procedure using a latissimus dorsi muscle flap, of whom 12 underwent reoperation. However, four of the five patients who received PORTx after DTI underwent reoperation due to capsular contracture after PORTx, which is a predictable result.

In conclusion, 18.8% (13 out of 69) of Allergan implant reconstruction patients had the implant replaced or removed due to

anxiety over ALCL, even though they expressed satisfaction with their breast shape during the interview, while 68.4% (26 out of 38) of patients who were dissatisfied due to capsular contracture or scar contracture caused by PORTx had their implants removed or replaced. This outcome shows that patients who were dissatisfied with their breast shape were more likely to undergo reoperation, in combination with their anxiety over BIA-ALCL.

NOTES

Conflict of interest

Su Bong Nam 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.

Ethical approval

The study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital (IRB No. 05-2021-173) and was performed in accordance with the principles of the Declaration of Helsinki.

Patient consent

The patients provided written informed consent for the publication and the use of their images.

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