Fat Grafting after Implant Removal Due to Anaplastic Large Cell Lymphoma May Mimic Recurrence

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Breast cancer is the most commonly diagnosed cancer and the second cause of death from malignancy in women. In recent years an association between silicone implants used for breast enhancement or reconstruction and a distinct subtype of anaplastic large T-cell lymphoma was reported. Initially, breast implant-associated anaplastic large cell lymphoma (ALCL) was considered as only anecdotal, but in recent years its recognition has increased dramatically. According to U.S. Food and Drug Administration publications, more than 400 cases have been reported. Nonetheless, knowledge is sparse regarding the pathogenesis, diagnosis, treatment, follow-up, and especially the recurrence characteristics of the disease. We present a woman diagnosed with breast implant-associated ALCL who underwent a bilateral implant and periprosthetic capsule removal that resulted in breast deformity. The fat grafting that was used for reconstruction resulted in breast lumps that were suspected for recurrence of ALCL.

PATIENT DESCRIPTION

We previously described a healthy 51-year-old woman 11 years after breast augmentation with Allergan plc (Dublin, Ireland) textured silicone breast implants who was diagnosed with breast implant-associated ALCL [1]. The disease was presented as unilateral swelling of the right breast. Ultrasound examination revealed periprosthetic proteinaceous fluid collection and capsular thickening. Percutaneous fluid aspirations of the periprosthetic fluid showed yellowish serous fluid.

Cytology analysis of the aspirated fluid revealed atypical lymphoid cells suspicious for high grade lymphoma. Cellblock staining revealed that CD3, CD30, and CD45 were positive, while CD4, CD8, CD7, CD20, and ALK1 were negative. T-cell rearrangement was positive and demonstrated monoclonality. G-banding analysis revealed a female complex karyotype with multiple structural and numerical abnormalities. SNP array analysis demonstrated multiple copy number alternations as well as copy neutral loss of heterozygosity [1]. The patient underwent bilateral total capsulectomy, in which the capsule and the implants were removed as a whole. On the inner surface of the periprosthetic capsule, a fibrinoid material was observed. The pathology confirmed the diagnosis of anaplastic T cell lymphoma CD30 positive, ALK 1 negative, which was confined to the fibrinoid material next to the prosthesis. She was closely followed every 3 months for 2 years. During the postoperative period there was no clinical, laboratory, or imaging (PET/CT) signs of residual or recurrent lymphoma.

The patient was interested in improving her breast appearance. After consultation, reconstruction using fat grafting was favored. The lower abdomen was selected as a donor-site. Fat was injected at three levels: subglandular, breast parenchyma, and subdermal. To the left and right breast, 130 cc and 170 cc of fat were grafted, respectively. Six months after the graft, a small painful lump was felt in the right breast. On clinical examination, a tender palpable mass was found at the upper pole of the right breast. There was no lymphadenopathy or any other pathological findings. On breast sonography, the upper mentioned lesion appeared to be a benign mass. Mammography did not demonstrate any abnormalities. Due to the lack of data regarding the mammographic and sonographic presentation of breast implant-associated ALCL, recurrence an ultrasound guided fine needle aspiration was conducted. The cytology evaluation demonstrated microfragments of fat tissue with no evidence of tumor cells.

COMMENT

Breast implant-associated ALCL is a rare disease associated with breast implants. Regardless of whether the implant was used for cosmetic purposes or for post-mastectomy reconstruction, treatment guidelines are the same. According to the guidelines from the National Comprehensive Cancer Network, the surgical management of breast implant-associated ALCL should entail removing the breast implant, periprosthetic malignant effusion, and the periprosthetic capsule, as a whole [2]. Additional chemotherapy or radiotherapy might be indicated for selected cases. After implant removal, the breast may show signs of significant atrophy, emptiness, and ptosis, which might cause body image concern. The preferred method of breast reconstruction for such patients is currently under debate in the plastic surgery community. Unfortunately,

the literature reveals limited information on this issue. For suitable patients requiring a modest increase in volume or correction of breast deformities, fat grafting can be an attractive option. Subcutaneous fat can be suctioned from sites such as the abdomen, thighs, and buttocks. The fat cells are then isolated from the aspirate, injected into the defected area, and scattered in a layered fashion. Grafted fat that does not incorporate might present as fat necrosis, calcification lumps, or liponecrotic or oil cysts. The radiological image of these findings is usually distinguished by an experienced radiologist from lesions suspected for breast carcinoma.

Because of the small number of cases identified, short follow-up treatment, and scarce reported cases of recurrence, information is insufficient regarding the clinical and radiological profile of breast implant-associated ALCL. A search of the literature revealed 13 cases of breast implant-associated ALCL recurrence after treatment [Table 1]. Recurrence was described following various types of treatment including surgical removal of the implant and preprosthetic capsule, and some also received chemotherapy in addition to or instead of surgery. In a few patients, an implant exchange took place. Recurrence appeared as a solid mass/growth in the operated breast, as a persistent seroma, with involvement of local and distant lymph nodes, or as pleural and pericardial effusion. All recurrent cases occurred within 1 year of treatment.

The most sensitive and specific imaging modalities for detecting seroma around breast implants are ultrasound and magnetic resonance imaging (MRI). MRI is generally carried out in cases in which sonography yields unclear results and for staging. PET/CT is useful for disease staging after breast implant-associated ALCL diagnosis. .Surprisingly, implant-associated masses have been reported to be difficult to identify in any imaging studies [3].

Our patient underwent the recommended evaluation [4] for breast implant-associated ALCL suspected lesion. Ultrasound and a biopsy supported the diagnosis of a benign mass. A PET/CT conducted at a later date also confirmed the benign nature of the findings.

Due to limited experience with this disease, unjustified imaging modalities and biopsies may be performed to differentiating a post-surgical benign mass from breast implant-associated ALCL recurrence. The case presented here illustrates the knowledge gap regarding recurrence of breast lymphoma associated with breast implants. As more cases of the described malignancy are identified, the number of patients that undergo surgery and associated reconstruction will also increase. Therefore, dilemmas

Table 1. Characteristics of patients with recurrent breast implant-associated anaplastic large cell lymphoma

Published article	Age of patient, years	Implant procedure	ALCL presentation	Time until ALCL presentation	Initial treatment	Time of relapse	Relapse presentation
George EV et al. 2013	67	Breast reconstruction	Seroma	8 years	Capsulectomy and implant replacement	6 months	Mediastinal, para-aortic, and axillary lymph node involvement
Gaudet G et al. 2013	50	Breast reconstruction	Sub-cutaneous nodules	9 years	Chemotherapy	1 year	Pleural and pericardial effusions, a left lower lobe infiltrate and mediastinal lymphadenopathy
Taylor KO et al. 2012	58	Cosmetic	Seroma and mass	2 years	Capsulectomy and implant removal	Several weeks	Breast mass followed by metastases to the thoracolumbar spine and the right lung
Newman MK et al. 2008	52	Cosmetic	Seroma and a mass	14 years	Chemotherapy	3 months	Persistent seroma
Farace F et al. 2013	51	Breast reconstruction	Seroma	10 years	Subtotal capsulectomy and implant replacement	3 weeks	Intracapsular seroma, skin redness and febrile episodes
Popplewell L et al. 2004	62	Cosmetic	Seroma	30 years	Subtotal capsulectomy, implant removal, chemotherapy and radiation	5 months	Not available
Popplewell L et al. 2011	54	Cosmetic	Nodule	9 years	Implant removal and chemotherapy	2 weeks	Not available
Popplewell L et al. 2011	41	Cosmetic	Nodule	7.5 years	Chemotherapy, implant removal, and radiation	Not available	Breast nodule in the contralateral breast, axilla, and abdomen involvement
Carty MJ et al. 2011	57	Several cosmetic procedures	Mass with chest wall invasion and pleural thickening	8 years	Capsulectomy and implant and mass removal; chemotherapy and radiation	6 months	Recurrent disease on the left side with malignant pleural effusion and axillary metastases
Wu D et al. 2015	43	Cosmetic	Seroma amd implant rupture	Not available	Capsulectomy and implant removal	5 months	Supraclavicular mass, pleural and pericardial effusions and an enlarged right axillary lymph node
Lechner MG et al. 2012	43	Cosmetic	Seroma	Not available	Capsulectomy and implant removal	2 months	Axillary, supraclavicular, and mediastinal lymph node involvement and bilateral pleural effusions with lung infiltrates
Aladily TN et al. 2012	63	Breast reconstruction	Seroma and capsule contracture	10 years	Capsulectomy, implant removal, and chemotherapy	1 year	Breast mass
Aladily TN et al. 2012	47	Breast reconstruction	Seroma and a mass	10 years	Chemotherapy	1 year	Mass at the same site and seroma

ALCL = anaplastic large cell lymphoma

regarding treatment and diagnostic options are expected to increase.

CONCLUSIONS

Based on published data, we recommend delaying breast reconstruction for at least 1 year post-treatment of breast implant-associated ALCL. Furthermore, surgeons should be alert to the possibility of recurrence by monitoring seroma, lymphadenopathy, and solid growths in the breast. Although some of these findings may be benign secondary to fat injection, a high degree of suspicion in breast implant-associated ALCL patients is required due to the possibility of recurrence and the variability of its presentation.

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Capsule

Brain circuit visualization and manipulation

How are behaviorally relevant representations of the outside world initiated and manifested in the mammalian brain? **Marshel** and co-authors combined a channelrhodopsin with an improved holographic stimulation technique to examine activity in the mouse visual cortex, including its deep layers. Optogenetic stimulation of neurons previously activated by natural visual stimuli recreated the original activity and behavior. Neuronal population activity typically propagated from cortical layer 2/3 to layer 5 rather than in the reverse direction. Stimulation of a larger number of cells was required to initiate activity in layer 2/3 than in layer 5. This indicates differences in ensemble coding between the two layers.

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Capsule

An appetite for memory

The hippocampus serves a critical role in memory formation and cognition. Hippocampal lesions are among the earliest changes in Alzheimer's disease (AD); however, the molecular mechanisms responsible for these alterations remain unclear. Using autoptic brain samples from patients with AD and a mouse model of AD, **Tian** et al. showed that in the hippocampus, pathologic β-amyloid directly binds and inhibits the receptor for the "hunger hormone" ghrelin (GHSR1α). In the animal model, the binding blocked the GHSR1α-mediated dopamine receptor D1 (DRD1) activation, leading to synaptic plasticity impairments and memory loss. Simultaneous pharmacological activation of GHSR1α and DRD1 rescued synaptic plasticity and spatial memory in AD mice.

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Capsule

Changes in bone mineral density after prophylactic bilateral salpingo-oophorectomy in carriers of a *BRCA* mutation

Kotsopolus et al. addressed the question of what is the association of preventive oophorectomy with bone health in individuals with a *BRCA* mutation? In this cohort study of 95 women with a *BRCA* mutation, prophylactic oophorectomy was associated with a decline in bone mineral density, which was most apparent among women who were premenopausal at surgery. The reduction in bone muscle density was as follows: lumber spine: annual change -3.45%, femoral neck: -2.85%, total hip: -2.24%. Use of hormone therapy was associated with less bone loss. Although limited by the small sample size, these findings support targeted management strategies to maintain bone health in this high-risk population.

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