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Breast-Implant Associated Anaplastic Large Cell Lymphoma: A Case Report

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Abstract

The Food and Drug Administration (FDA) released a statement in the beginning of 2017 regarding a rare cancer, Anaplastic Large Cell Lymphoma (ALCL) that has been related to textured breast implants and resulted in nine deaths. The first case of Breast Implant-Associated ALCL (BIA-ALCL) was published in 1997. This entity is more recently recognized and has been provisionally classified in the 2016 revision of the World Health Organization classification of lymphoid neoplasms. Here we report a case of a 58 year old woman with history of sub glandular silicone implants for bilateral breast augmentation 25 years ago, with complaints of bilateral breast pain and found to have bilateral Baker Grade III capsular contracture, and a suspicious chest wall lesion on imaging. Patient underwent removal of bilateral breast implants and total capsulectomies. The capsule and all associated abnormal lesions were sent for excisional biopsy. Microscopic examination revealed breast implant-associated anaplastic large cell lymphoma on the left side. On immunohistochemistry the lymphoma cells were positive for CD3 (subset), CD4, CD7, CD30, and CD43, and negative for CD2, CD5, CD8, CD68 and ALK1; supporting the diagnosis of breast implant-associated anaplastic large cell lymphoma. No lymphoma cells were identified in the submitted sections of right breast capsule which was confirmed by CD30 stain. This diagnostic workup proves it to be a Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) which is an uncommon peripheral T- cell lymphoma arising around textured-surface breast implants.

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Keywords

Anaplastic Large Cell Lymphoma; Breast Implants; Textured Implants; Peripheral T-Cell Lymphoma; BV Plus CHP Chemotherapy

Introduction

In 2016 about 290,000 women in the United States had breast augmentation using implants about third of these women received them for reconstruction after breast cancer [1]. The Food and Drug Administration (FDA) released a statement in early 2017 concerning a rare cancer ALCL that has been linked to breast implants and is associated with nine deaths [1]. This entity is more recently recognized and has been provisionally classified in the 2016 revision of the World Health Organization classification of lymphoid neoplasm [2,3].

Case Report

A 58-year-old Spanish woman with no significant past medical history presented to her primary care at Harbor-UCLA Medical Center with pain in her bilateral breasts with radiation to left arm for 3 months. The patient had a history of bilateral sub-glandular silicone implants placed over 25 years ago. The patient had no personal history of cancer. On examination: both breasts were firm and distorted cosmetically, consistent with Baker Grade III capsular contracture. However, there was no evidence of palpable mass or lymphadenopathy, no nipple retraction or skin changes. There was bilateral 3 cm scar on lateral breast corresponding to previous surgery. A diagnostic mammogram and ultrasound were performed that demonstrated a 3.6×0.8 cm oval, parallel-hypoechoic area adjacent to the implant with indistinct margins in the left breast involving 8 O'clock, 9 O'clock and 10 O'clock position and was located 13 centimeters from the nipple; most likely inflammatory in origin. Additionally, there were multiple enlarged left axillary lymph nodes measuring 1.7×1.5 cm. The findings were consistent with BI-RADS Category 4A (Suspicious Abnormality). On further investigation a magnetic resonance imaging of the chest without contrast revealed a rim enhancing heterogeneous fluid collection centered near the left 3rd costochondral articulation; most suggestive of an abscess that was further confirmed by biopsy. For diagnostic workup, patient also underwent ultrasound-guided biopsy of the enlarged left axillary lymph nodes that showed a normal lymph node architecture without evidence of lymphoma or malignancy. Given the concern for possible mass, patient was transferred to breast surgery team to rule out malignancy or any infectious process. Due to uncertain etiology of patient symptoms and long history of implants, patient was consented for capsulectomy and implant removal. The surgical procedure was performed and was uneventful. The explanted capsules and implants were sent to pathology for analysis. It was revealed that both the implants were textured; the capsules were extensively covered with thick, chalky-

white deposits. The usual manufactures' imprint on the implant was not visible. Microscopic examination on hematoxylin and eosin stain on the left breast capsule revealed large, pleomorphic cells with abundant cytoplasm; admixed with dense fibrotic scar (Fig. 1). On immunohistochemistry, these lymphoma cells were positive for CD3 (subset), CD4, CD7, CD30, and CD43; and negative for CD2, CD5, CD8, CD68 and ALK1 (Fig. 2-5). The morphology and immunohistochemical stains confirm the diagnosis of breast implant-associated anaplastic large cell lymphoma in the left breast. Also there were no lymphoma cells identified in the sections of right breast capsule which was further confirmed by CD30 stain.

With the appropriate diagnosis, the patient was sent to a medical oncologist for treatment options. A Positron Emission Tomography-Computed Tomography (PET/CT) scan was ordered and was positive for metastatic disease with multiple FDG uptake on lymph nodes in the bilateral neck, bilateral axilla, mediastinum, sternum, right anterior upper ribs, in the pleural fat above the right diaphragm, inguinal nodes and the left gluteus muscle. Based on the pathologic findings and in conjunction with PET/CT imaging, an advanced stage disease of TNM IV was determined. The patient is currently undergoing chemotherapy with Brentuximab Vedotin (BV) plus Cyclophosphamide, Doxorubicin and Prednisone (CHP). A follow-up PET/CT scan for surveillance is scheduled.

Figure 1: High power view of anaplastic large lymphoma cells (400×).

Figure 2: Immunohistochemistry CD30 positive in lymphoma cells (400×).

Figure 3: Immunohistochemistry ALK negative in lymphoma cells (400×).

Figure 4: Immunohistochemistry CD3 positive in lymphoma cells (400×).

Figure 5: Immunohistochemistry CD4 positive in lymphoma cells (400×).

Discussion

Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) is an uncommon peripheral T-cell lymphoma arising around textured-surface breast implants. The pathogenesis of BIA-ALCL is poorly understood. Available evidence suggests that BIA-ALCL develops in the setting of implant-induced chronic inflammation [4-6]. One proposed mechanism implicates chronic T-cell stimulation with local antigenic drive in the development of lymphoma [7]. The immune system's response to chronic inflammation surrounding the breast implant may lead to genetic degeneration and dysplasia in a genetically susceptible patient [5,8]. BIA-ALCL typically manifests as a seroma or fluid collection but may present with a discrete mass originating from the fibrous capsule around the implant [9]. A systematic review and structured expert panel was organized by Kim et al., to advise clinicians when BIA-ALCL may be suspected. The panel agreed that there was an association between implants and ALK-negative ALCL and that a delayed or recurrent seroma beyond 6 months should be investigated with aspiration and cytologic analysis or flow cytometry to rule out infection and lymphoma [10].

Morphologically, the tumor is comprised of large, pleomorphic cells with abundant cytoplasm, and horseshoe-shaped nuclei with prominent nucleoli [11,12]. On immunohistochemistry, BIA-ALCL demonstrates strong and uniform membranous expression of CD30 and lacks Anaplastic Lymphoma Kinase (ALK) expression. Other T-cell antigens are expressed variably, with the most common being CD4 (80 to 84%), CD43 (80 to 88%), CD3 (30 to 46%), CD45 (36%), and CD2 (30%) [12]. Expression of CD5, CD7, CD8, or CD15 is rare. [12] While the diagnosis is based upon the presence of positive CD30 staining on immunohistochemical analysis of the peri-capsular fibrous tissue or fluid surrounding the capsule, CD30+ cells can often occur in the context of normal inflammation; and this finding must be in addition to large anaplastic morphology on cytology, a single T-cell clone, and correlated to the patient's presentation before a final diagnosis of BIA-ALCL is made with a combination of immunohistochemical analysis and clinical judgment [13]. There are no rearrangements involving the ALK gene on chromosome 2p23 in BIA-ALCL [3].

Treatment options to date consist of surgical therapy including implant removal and capsulectomy versus surgical and systemic therapy with or without radiation, typically indicated if the patient has classic B symptoms [14-16]. In the largest series of patients with lymph node involvement (n = 14), the 5-year overall survival was 75% for those with lymph node involvement compared with 97.9% in those without lymph node involvement at presentation.

Recently in November 2018 the US Food and Drug Administration (FDA) approved Brentuximab Vedotin (BV) for the treatment of adult patients with previously untreated systemic anaplastic large cell lymphoma or other CD30-expressing Peripheral T-cell Lymphomas (PTCL) in combination with Cyclophosphamide, Doxorubicin and Prednisone

(CHP). This has a superior progression-free survival and overall survival, compared with patients who received standard treatment with Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (CHOP) [17].

Conclusion

Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) is an uncommon peripheral T- cell lymphoma arising around textured-surface breast implants [18]. Complete surgical removal of the entire capsule is critically important because retained scar capsule has been associated with disease recurrence and progression. Peri-prosthetic effusions occurring more than one year following breast implant placement should be aspirated and examined for lymphoma, including CD30 immunohistochemistry and flow cytometry. The FDA recommends reporting all confirmed cases to improve the understanding of this rare disease.

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