

Anaplastic large cell lymphoma associated with double-lumen breast implants: A case report and review of the literature

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BACKGROUND: Breast implant-associated anaplastic large cell lymphoma (ALCL) is commonly associated with diagnostic delay due to the insidious nature of presentation with late periprosthetic fluid collection, mass or locoregional adenopathy.

CASE PRESENTATION: A 75-year-old woman with a remote history of right breast cancer treated with modified radical mastectomy and immediate reconstruction with a double-lumen silicone implant presented 13 years later with volume asymmetry. The implant was removed and a saline implant was placed. Five years later, she presented with acute onset of right breast enlargement and pain. Ultrasound revealed an associated periprosthetic fluid accumulation. Cytology showed anaplastic lymphoma kinase-negative, CD30-positive ALCL without associated systemic disease. The patient was treated with implant removal and total capsulectomy.

CONCLUSION: Due to the insidious presentation of ALCL, a high index of clinical suspicion must be maintained when evaluating patients for delayed presentation of volumetric discrepancy. Treatment typically entails implant removal. Indications for additional systemic treatment include extracapsular spread of ALCL or presence of a periprosthetic tumour.

Key Words: Anaplastic large cell lymphoma; Breast implant; Capsulectomy; Periprosthetic capsule; Late seroma

The association between breast implants and primary lymphoma of the breast has garnered growing concern since 1995 (1). Primary lymphoma of the breast only constitutes 0.4% to 0.5% of all breast malignancies (2-4). Anaplastic large cell lymphoma (ALCL) is a T cell lymphoma with an incidence of three per 100 million per year in the United States (4-7). The first reported case linking ALCL to textured saline implants dates back to 1997 (8-10). Approximately 91 cases of breast-implant associated ALCL have been documented since that time and, in contrast, it is believed that five to 10 million breast implants have been placed for reconstructive or aesthetic purposes worldwide (3). The pathogenesis of breast-implant associated ALCL remains elusive.

Breast implant-associated ALCL presents as a site-specific lymphoma associated with devices of varying size, surface characteristics and pocket location. The median time between breast implant placement and diagnosis of ALCL is eight years, with a range from one to 23 years (11). In 2011, the United States Food and Drug administration alerted the public that women with breast implants have a very low but increased risk for developing ALCL (2,3). However, to date, no case

has reported a link between ALCL and double-lumen breast implants. In contrast to single-lumen silicone implants, double-lumen devices consist of an inner lumen of silicone surrounded by an outer lumen of saline (12). In 2005, these double-lumen implants were removed from the market due to high rupture rates (13). We present a case of double-lumen breast implant-associated ALCL to add to the current understanding of ALCL and to discuss management options.

CASE PRESENTATION

The patient was a 75-year-old Caucasian woman who underwent right modified radical mastectomy and immediate reconstruction with a 390 mL McGhan[®] Style 153 (Inamed Corporation, USA) double-lumen silicone implant in 1986. She remained well until 2008, when a right-sided seroma developed. Examination revealed a Baker grade III capsular contracture of the right breast with associated superior displacement of the implant. The left breast had grade III ptosis and was larger in volume than the right, which was attributed to weight gain following reconstruction (Figure 1). Magnetic resonance imaging (MRI) revealed no evidence of implant rupture and no associated periprosthetic masses; however, a periprosthetic fluid accumulation was noted.

To correct the volumetric asymmetry, she underwent right implant removal, inferobasilar capsulotomy with repositioning of the inframammary fold, and placement of a 540 mL Natrelle[®] (Natrelle Corporation, USA) textured, round saline implant. The patient was satisfied with her overall cosmetic outcome, and noted improvement in volume and symmetry.

In 2015, five years after the saline implant had been placed, the patient presented with acute right breast pain, erythema, swelling and gross volumetric discrepancy. The patient was referred for diagnostic ultrasound and image-guided needle aspiration. Cytology revealed anaplastic lymphoma kinase (ALK)-negative, CD30-positive anaplastic large cell lymphoma (Figure 2). Positron emission tomography computed tomography (PET-CT) showed no evidence of distant metastatic disease



Figure 1 Preoperative photographs demonstrating a new-onset right-sided late seroma with right Baker grade III capsular contracture with associated superior displacement of the implant

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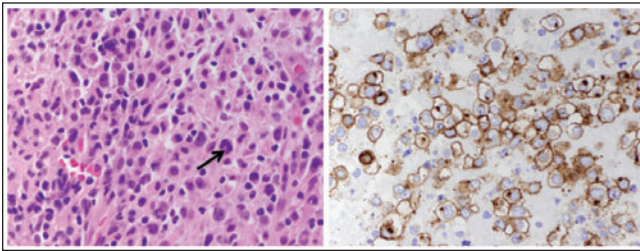


Figure 2) Cytology. Periodic acid-Schiff-stained capsulectomy specimen (left) revealing horseshoe-shape hallmark cells of anaplastic large cell lymphoma (arrow). CD30-stained breast cyst fluid (right) showing membrane-associated labelling of malignant cells

with the exception of small, stable pulmonary nodules. The patient was treated with urgent right implant removal and total capsulectomy. The capsule was noted to be thickened and adherent to the underlying implant (Figure 3). The case was reviewed in the authors' multidisciplinary breast tumour board. Given the lack of systemic illness and low risk of overall disease progression no further adjuvant therapy was recommended (14). Surgical pathology confirmed a thick fibrous capsule with associated large cell lymphoma. No isolated mass was identified in the periprosthetic capsule or surrounding tissue. The patient declined further reconstruction and is considering contralateral breast reduction for symmetry. The patient remains disease free 13 months from her diagnosis and treatment. Subsequent surveillance imaging has not identified any disease progression and she continues to be monitored in the University of Virginia VA Breast Center (Charlottesville, Virginia, USA).

DISCUSSION

Primary lymphoma of the breast is a rare disease that constitutes <1% of non-Hodgkin lymphomas (2,15). The majority of breast lymphomas are of B cell origin, and <10% are of T cell lineage (2,6). ALCL accounts for only 6% of all T cell lymphomas (2). Breast-implant associated ALCL was first described in 1997 (10), with recent literature citing an absolute risk ranging from 1 in 500,000 to 1 in 3,000,000 in patients with breast implants per year (9,16). All reported cases of breast-implant associated ALCL have been anaplastic lymphoma kinase (ALK)-negative (and CD30-positive), whereas systemic ALCL can be ALK-positive or ALK-negative (2). Prognosis differs dramatically between the systemic ALCL and breast-implant associated ALCL, with the former being more clinically aggressive and the latter being indolent (1,2).

The pathogenesis of ALCL remains unclear, although many hypotheses have been proposed, including response to particles of textured implants, presence of biofilm or chronic bacterial contamination, presence of capsular contracture, an immune reaction to silicone and a possible genetic predisposition (3,4). Brody et al (4) concluded that there was no association between the type of implant and the risk of breast-implant associated ALCL. The authors suggested a multifactorial inflammatory etiology for the disease process. However, it remains unclear why inflammatory signalling in the periprosthetic microenvironment leads to the development of ALCL, whereas elsewhere, the same process typically leads to less aggressive B-cell lymphomas (4).

Recent studies describe a possible mechanism involving chronic T cell stimulation with local antigenic drive that ultimately leads to lymphoma (3). Currently, there are no published cases linking ALCL to smooth surface devices (4). Compared with smooth implant capsules, textured implant capsules contain more T helper 17 (Th17) cells, which are classically associated with inflammation (4). Th17 cells produce interleukin-17, causing acute inflammation to perpetuate into the chronic state, eventually leading to capsular contracture (17). These T cells are also present in primary cutaneous ALCL (4). Based on these findings, Kadin et al (18) postulated that breast-implant associated ALCL may be related to cutaneous ALCL in terms of morphology and cytokine profiles.

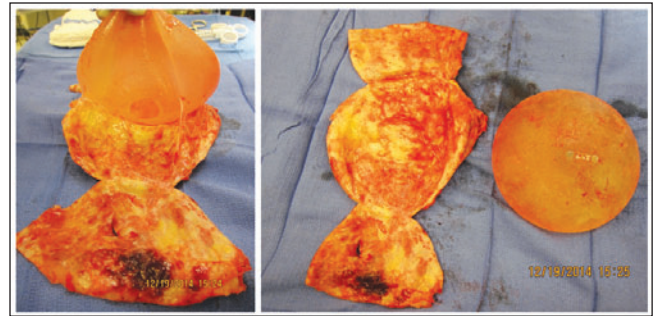


Figure 3) Periprosthetic capsule and 540 mL Natrelle (Natrelle Corporation, USA) textured, round saline implant associated with anaplastic large cell lymphoma at the time of total capsulectomy and device removal. Thickened capsule from right breast adherent to the Natrelle textured, saline implant (left). Fibrotic and densely adherent periprosthetic capsulectomy specimen separated from the implant (right)

Our case illustrates the development of ALCL associated with a double-lumen breast implant, which has, to date, not been reported. The McGhan® Style 153 (Inamed Corporation, USA) double-lumen silicone implant was removed from the market in 2005 secondary to high rupture rates, likely due to fold flaws causing prosthetic shell failure (13). During the removal of the double-lumen device in our patient, the implant was noted to be intact without evidence of rupture or silicone gel extravasation. The device was textured, and the manufacturing process for texturing breast implants has been implicated in the deposition of silicone granules within the peri-prosthetic capsule (4). Proponents of a chronic inflammation theory link the deposition of silicone granules with chronic inflammatory pathway activation (4). However, liquid silicone injections and other non-breast silicone prostheses are typically associated with granuloma formation, and no cases of ALCL have been reported with non-breast silicone prostheses (4). In contradistinction, proponents of textured implants commonly reference the animal work of Oppenheimer et al (19), which showed that implantation of smooth surface silicone implants resulted in soft tissue sarcoma formation, whereas textured surface implants did not. Given the contradictory nature of the current literature, further research is required to elucidate the risk factors of breast implant-associated ALCL.

In a recent retrospective review of 63 cases of breast implant associated ALCL, Hart et al (20) reported that implant surface characteristics were reported in 26 cases. Of the 26 cases for which surface characteristics were reported, 24 were associated with textured silastic surfaces while the remaining two were associated with smooth polyurethane surfaces. Of the 26 patients with surface characteristics, 24 were textured Silastic surfaces while the remaining two were with polyurethane surfaces. Multiple manufacturing techniques are available for surface texturing, including the 'lost-salt' processing technique used by Allergan Biocell® (Allergan Medical Corporation, USA) as well as Inamed, McGhan, PIP, and Nagor; the imprint-based technique used in the Mentor Siltex® surface (Mentor Corporation, USA) and laser etching technique used by Dow Corning (Dow Corning Corporation, USA) (21). The Biocell® surface texture is manufactured by placing a sized chunk into uncured silicone, followed by a bed of fine granular salt before curing, after which the salt is removed by rinsing the cured surface in water, which produces the characteristic granular wells. The Mentor Siltex® surface is manufactured in similar fashion except after placing the chunk into uncured silicone mix, the chunk is imprinted by placing it into textured polyurethane foam, which produces its characteristic surface features. When compared with scanning electron microscopy, the Mentor Siltex® surface demonstrates a flat peaked, nodular surface with 40 µm to 100 µm depth, whereas the Allergan Biocell® surface demonstrates an irregular surface of cuboid shaped wells with a greater depth of 100 µm to 200 µm (21). In the literature review reported by Hart et

al (20), in all cases of implant-associated ALCL in which the manufacturing process was identified, the manufacturing process was associated with a 'lost-salt'-based processing technique.

The clinical presentation of implant-associated ALCL is heterogeneous – patients can present with a seroma or a palpable mass. Patients who present with a seroma and no associated mass tend to have a more indolent course compared with patients who present with a distinct periprosthetic tumour (15). The age of diagnosis ranges from four to 29 years, and the latency period varies from three months to 25 years postinsertion of implants (5,15). Such diversity of presentation and demographics makes it difficult to establish clear guidelines for diagnosis and management. Beatriz et al (22) recently reported data regarding the sensitivity and specificity of imaging studies used in patients with implant-associated ALCL. For detecting an effusion, ultrasound was most sensitive (84%) and PET was most specific (83%). For detecting a mass, MRI was most sensitive (82%) while ultrasound and CT were equally specific (100%). In her initial presentation for volume asymmetry in 2008, our patient's MRI evaluation did not detect any focal masses; however, periprosthetic fluid was noted.

The patient in the present report presented with a right breast periprosthetic fluid collection. She underwent image-guided fine-needle aspiration and core biopsy. Cytology and histology confirmed the diagnosis of ALCL. Subsequent PET-CT failed to identify signs of systemic disease. She received surgical treatment only, with unilateral implant removal and total capsulectomy. Hart et al (20) conducted a meta-analysis of 63 cases and found no definitive pattern of treatment, with patients receiving surgery alone, surgery and radiation, surgery and chemotherapy, surgery with chemoradiation, or chemotherapy alone. In 2011, Kim et al (14) conducted a multidisciplinary panel in an attempt to create a structured approach to breast implant-associated ALCL. The panel agreed that a recurrent seroma occurring six months or more after implant insertion should undergo aspiration and cytological analysis. They also concurred that implant removal and capsulectomy would effectively prevent recurrence of disease, and adjuvant chemoradiation should not be offered to patients with capsule-confined ALCL (14). In a recent long-term follow-up study involving 60 patients, Miranda et al (10) concluded that "most patients with breast implant-associated ALCL achieved complete remission and had excellent disease progression-free survival". The authors recommended implant removal and capsulectomy alone for patients with an effusion and no focal mass. Due to the more aggressive nature of the disease, patients presenting with a discrete mass may benefit from systemic therapy in addition to surgery. Systemic therapy includes chemotherapy, radiation or both (23). Currently, there are insufficient data regarding implant replacement or contralateral breast treatment following surgical treatment of the affected breast (1,5).

CONCLUSION

Breast-implant associated, ALK-negative ALCL has emerged as a distinct clinical entity. The rarity of this disease contributes to the paucity of data regarding its pathogenesis, epidemiology and biology. The present case report aims to add to the current pool of knowledge regarding the pathogenesis of implant-associated ALCL. While the current literature suggests a multifactorial cause of the disease, a definitive etiology has yet to be defined. Further research is critical for the effective prevention, timely diagnosis and standardized treatment of breast implant-associated ALCL. Our patient first presented with a late periprosthetic fluid collection 13 years following initial breast reconstruction with a textured, double-lumen device. She underwent implant exchange and subsequently developed an additional periprosthetic fluid collection five years later, which ultimately was diagnosed as ALCL. Due to the insidious presentation of ALCL, a high index of clinical suspicion must be maintained when evaluating patients for delayed presentation of volumetric discrepancy.

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