Current Breast Cancer Reports (2019) 11:332–334
https://doi.org/10.1007/s12609-019-00336-0

HOT TOPICS IN BREAST CANCER (K HUNT, SECTION EDITOR)

Update on Breast Implant-Associated Anaplastic Large Cell Lymphoma

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Published online: 7 November 2019

Abstract

Purpose of Review The US Food and Drug Administration issued a recall of textured breast implants in July 2019 secondary to their association with anaplastic large cell lymphoma. This brief review serves to summarize what is actually known about breast implant associated anaplastic large cell lymphoma.

Recent Findings Since the FDA's first preliminary report in 2011, there have been a reported worldwide total of 573 breast implant associated anaplastic large cell lymphoma (BIA-ALCL) cases, including 33 deaths. In addition to halting the implantation of textured implants, the July recall served to increase awareness and vigilance when caring for patients with a history of textured breast implants. Recommendations continue to be against voluntary implant removal.

Summary In the setting of the FDA recall, the importance of comprehensive counseling remains paramount. For patients with textured breast implants, it is vital to ensure patient awareness with thorough education on warning signs and the importance of follow-up.

Keywords Breast implant-associated lymphoma · Textured breast implants · Current guidelines · Pathogenesis · Diagnosis · Treatment

Introduction

On July 24, 2019, the US Food and Drug Administration (FDA) requested voluntary recall of textured breast implants and tissue expanders secondary to their association with breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) [1••]. The FDA first recognized the entity with the release of a preliminary report in 2011, which reviewed the findings of ALCL in 34 patients who had undergone augmentation mammoplasty. At that time, due to the small sample size identified out of the estimated 10 million women with breast implants worldwide, the association was poorly understood and there was not a means to identify a specific type of implant or an underlying cause of BIA-ALCL [2].

However, at the time of the July 2019 recall, the FDA's analysis was strengthened with the now reported worldwide total of 573 BIA-ALCL cases, including 33 deaths, that have been associated with textured breast implants [1••]. By raising understandable concern in both patients and providers, the FDA announcement provides an opportunity to revisit and strengthen public education and physician awareness of BIA-ALCL.

Background

The past decade has seen an ongoing increase in the number of women undergoing breast augmentation and as such, breast augmentation remained the top cosmetic surgical procedure at the end of 2018 [3]. With both smooth and textured implants on the market, it is important to recognize that most implants placed in the USA are smooth and, to-date, there are no well-documented reports associating smooth implants with ALCL. Since the first BIA-ALCL case report in 1997, the FDA, in conjunction with the American Society of Plastic Surgery and Plastic Surgery Foundation, initiated the Patient Registry and Outcomes For Breast Implants and Anaplastic Large Cell

This article is part of the Topical Collection on *Hot Topics in Breast Cancer*

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Lymphoma Etiology and Epidemiology (PROFILE) registry. Doren et al. [4] estimated the lifetime prevalence of BIA-ALCL to be 1 per 30,000 patients with a textured breast implant (< 0.01%). As the association became better defined, the National Comprehensive Cancer Network released the first edition of consensus guidelines for the diagnosis, staging, and treatment of BIA-ALCL in 2016 [5].

Pathogenesis

BIA-ALCL is a rare CD30(+), ALK(−) T cell lymphoma arising in the fibrous capsule of a breast implant [2]. The most common presentation is enlargement of the breast as the result of a seroma associated with the implant. Less commonly, the patient may present with a mass adjacent to the implant. Reported cases have shown equal distribution between textured implants placed for both reconstructive and cosmetic purposes [6••, 7••]. On average, BIA-ALCL develops 10 years following the index surgery, but BIA-ALCL should be considered and ruled out for any patient with textured implant presenting with seroma or mass as early as 1 year after surgery.

The pathogenesis of BIA-ALCL is likely multifactorial and may involve both infectious and inflammatory processes [8]. Hu et al. studied implant capsules using electron microscopy and bacterial rRNA profiling [9]. Contracted capsules from patients without BIA-ALCL frequently contained a biofilm colonized with Staphylococcus. Contracted capsules from patients with BIA-ALCL rarely harbored staphylococcus but were frequently colonized with Ralstonia species. Ralstonia is a gram-negative, aerobic bacteria that is similar to *Helicobactor pylori*, a bacterium linked to gastric lymphoma. BIA-ALCL has been linked to textured, but not smooth implants. Texturing provides a roughened surface which greatly increases the surface area of the implant to promote tissue ingrowth. The risk of BIA-ALCL has been shown to rise with increasing coarseness of the textured surface [10••, 11•].

Diagnosis and Management

Ultrasound is the most sensitive diagnostic tool for patients with symptoms or signs related to their implants, and computed tomography along with positron emission tomography are the most specific modalities for staging used after the diagnosis is established and prior to operative intervention [6••]. As outlined in Fig. 1 by Clemens et al. [12••], recommendations continue to be that any patient with a history of breast implants should undergo aspiration of a seroma or needle biopsy of a mass associated with the implant. The specimen must undergo CD30 immunohistochemistry, with abnormal CD30-positive cells supporting the diagnosis of BIA-ALCL [6••]. More specific than CD30-positivity alone, which is broadly associated with ALCL, the classical variant of BIA-ALCL is marked by the presence of the "hallmark cell," which exhibits an eccentric nucleus and a prominent, pale Golgi region [13].

After diagnosis of BIA-ALCL is established and further work-up complete, surgical excision of the surrounding implant capsule in its entirety, explantation of the implant, and removal of any disease or mass with negative margins remains the cornerstone of care. Event-free survival and overall survival has been found to be highest in patients with early detection and complete surgical excision when compared to patients who underwent limited operative intervention, chemotherapy, or radiation [2]. Current research does not support sentinel lymph node biopsy. However, if a patient presents with clinical lymphadenopathy, it is prudent to proceed with excisional biopsy of any concerning lymph nodes [2].

While rare, there have been reports of patients presenting late with disseminated disease. A multidisciplinary care team is crucial in the care of these patients, as multiple therapies, including adjuvant chemotherapy or radiation therapy in addition to surgery, may be indicated [6••].

Conclusion

The importance of provider-driven education to patients with textured implants is heightened in the setting of the July 2019 FDA recall. Patients will benefit most by comprehensive counseling, including clear descriptions of presenting signs and the importance of seeking medical evaluation for any new concern. Despite the fact that textured implants have now been recalled in the USA, the importance of informed discussion with patients pursuing breast augmentation, including discussion about BIA-ALCL, persists. Moving forward, as BIA-ALCL has unique data-collection points when compared with other breast malignancies, the ongoing provider-driven reporting of cases to the PROFILE registry remains critical.

Compliance with Ethics Guidelines

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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