An update on BIA-ALCL

BY SHADI GHALI

The author discusses the concerns and new restrictions on breast implants due to cases of breast implant associated-anaplastic large cell lymphoma – should we be worried?

Breast implants, first introduced in the 1960s, have continued to evolve, having survived a number of safety concerns. In the early 1990s the Food & Drug Administration (FDA) moratorium against silicone, and later the 2010 Poly Implant Prothese (PIP) implant scandal and later still, the 2015 Silimed ban, have all dented the image of silicone breast implants. The newest concern is with breast implant associated-anaplastic large cell lymphoma (BIA-ALCL). The first case was reported in 1997 by Keech and Creech [1] and in the last 10 years, there has been an exponential rise of cases, culminating in the 2016 classification of BIA-ALCL as a unique disease entity by the World Health Organization [2]. Suggested theories of the cause of BIA-ALCL include textured implant particulate, chronic allergic inflammation, and / or response to a biofilm. Research is ongoing in all these areas. In spite of this, breast augmentation with silicone implants continues to be one of the most common aesthetic operations performed worldwide [3].

BIA-ALCL presents most commonly with a late seroma (defined as a seroma presenting >1 year post-breast implantation) but can also present with a breast or axillary lump as well as firmness or pain. The presentation occurs on average eight years post implantation (range 2-28 years). It is important therefore not to dismiss late seromas but rather to investigate them by way of an ultrasound guided drainage and analysis of the fluid. Volumes of an effusion can range from 50 to 1000ml and are typically more viscous than a benign seroma, owing to the high protein content and cellularity. The fluid should be tested for atypical, monoclonal T-cells, which are CD30 positive and anaplastic lymphoma kinase (ALK) negative by immunohistochemistry and flow cytometry should be carried out to diagnose BIA-ALCL (nb: If CD30 is positive, it may or may not be BIA-ALCL, and cell block cytology and flow cytometry are required to make the diagnosis). Mammograms are not useful in making a diagnosis. In confirmed cases, PET scans may be performed to help stage the disease [4]. It is important to note that the majority of late seromas will not be BIA-ALCL. Additionally, benign fluid collections (CD30 negative with negative cytology) are not precursors to the development of BIA-ALCL, and to date there has not been a report of a patient with recurrent benign seromas that then converted to a CD30 positive effusion.

If a diagnosis of BIA-ALCL is made, the vast majority of patients can be cured. Recommendations for treatment include:

- Most cases are cured by the removal of the implant and the entire capsule surrounding the implant.
- The majority of patients require no additional treatment.
- Infrequently, patients will need to undergo chemotherapy, or radiation therapy when there is extracapsular disease that is unable to be excised [4].

As of February 2019, the Manufacturer and User Facility Device Experience (MAUDE) database of the FDA had received 457 cases of ALCL (initially reported as 660 cases but many were identified as duplicates or incomplete reports) [5]. Globally, 17 confirmed deaths have been reported, nine of which occurred in the USA.

The rate is no different between silicone and saline; it occurs in both cosmetic and reconstructive patients. The risk is only with textured implants and not smooth implants. The FDA reported that "there have been reports of BIA-ALCL in patients with smooth-surfaced implants and many reports do not include the surface texture of the implant at the time of diagnosis." As of the time of this publication it is known that a single case of smooth only BIA-ALCL was originally reported to the FDA; however, it was later determined that this was not accurate and the case was a mixed implant case, and the report to the FDA was amended (Feb 2019)* [6].

There seem to be geographical differences in the rates of BIA-ALCL worldwide [7]. This may be due to lack of awareness and / or different reporting and registries, but there may well be a genetic predisposition that is not yet fully understood. For instance, as of this time there are very few cases in Asian patients and very few cases in Germany relative to other European countries.

The FDA reports that the risk of developing ALCL is 1:3817 to 1:30,000 in their latest statement [8]. These risk assessments are changing on an on-going basis, but this is the most accurate information currently available.

Based on current data, the risk can be further explained by the texture grade of the implants as follows:

- Grade 1 (smooth only) – In global databases, there has not been a confirmed case of smooth only.
- Grade 2 (e.g. microtexture, Siltex and similar) – 1:82,000.
- Grade 3 (e.g. macrotexture, Biocell and similar) – 1:3200.
- Grade 4 (e.g. polyurethane) – 1:2800 **.

** 100% Silimed polyurethane implants that had a manufacturing defect and have now been withdrawn from the market (based on data from the Australian study in 2017 by Loch-Wilkinson et al. [9]

On the back of this emerging data, the French and Canadian regulators, as well as the Dutch Plastic Surgery Association, have suspended (or recommended suspension) of macro-textured and polyurethane implants. Rightly or wrongly, it is only a matter of

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time before more national regulators and / or national associations will likely follow suit. Thankfully no authority has recommended elective explantation of macro-textured or polyurethane implants from patients (as was the case with intact PIP implants) as the risk of doing so would no doubt far outweigh the risks of developing BIA-ALCL. When we consider risk for our patients, consider this:

- Average woman's risk of developing breast cancer in her lifetime is 12.5% (1 in 8) [10].
- Risk of death in a car accident in a lifetime is 0.14% (1 in 572) [11]
- Risk of death from complications from a cosmetic procedure is 0.002% (1 in 50,000) [12].
- Risk of developing BIA-ALCL associated with a breast implant is 0.003-0.0003% (~1 in 3817-30,000) [13].
- Risk of developing advanced BIA-ALCL with lymph node metastasis is approximately 0.0004% (~1 in 250,000) [14].
- Risk of developing BIA-ALCL and not resolved within three years is approximately 0.0002% (~1 in 500,000) [14].

Also consider the question; what implant would you recommend for a member of your family?

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(All links last accessed April 2019)

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