Perspective from the United Kingdom on Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

Nigel S. G. Mercer, ChM, FRCS, FRCPCH, FFFMLM

Abstract
Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare disease known to be associated with textured breast implants. The most up-to-date incidence in the United Kingdom is 1:24,000 and 45 confirmed cases have been reported since the first UK case was reported in 2012 and there has been one confirmed death as a result of BIA-ALCL. How the regulatory framework in the United Kingdom works and shapes the information, which must be given by surgeons to patients contemplating breast augmentation, for any reason, is discussed. In addition, the approach to informing patients with breast implants in situ is discussed. It is surgeons’ duty to inform all prospective patients that there is a risk of BIA-ALCL. Not to do so in the United Kingdom would be likely to leave surgeons open to legal action by patients who develop the disease.

Plastic surgeons and breast surgeons must all now be aware of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), a rare non-Hodgkin lymphoma, which is associated with breast implants.

The causation is yet to be understood but, as yet, no cases of BIA-ALCL have been reported in patients who have a history of only smooth implants and it is known to be very rare in patients of Asian extraction. Textured breast implants have been in use for almost three decades and, with time from the index carcinogenic mutation to presentation thought to be in the region of 8-10 years for BIA-ALCL, there has yet to be a reasonable explanation as to why we were not seeing this disease from the 1990s onwards. Any deaths caused by earlier cases of BIA-ALCL would have been reported as being associated with tumor in the implant capsule, regional nodes or metastases, yet it appears none was reported despite other forms of ALCL being recognized pathologic entities. It, therefore, seems likely that BIA-ALCL is a “new” tumor and was designated as such by the World Health Organization in 2016.1 The Scientific Committee on Health Environment and Emerging Risks (SCHEER) published advice in 2017 regarding a potential connection between textured breast implants and BIA-ALCL (BIA-ALCL is defined as CD30 positive and ALK negative) and they recommended an in-depth evaluation.2 As yet, we do not know why we have not seen the tumor before despite the use of textured implants for almost 3 decades. For example, have there been any changes in the production of the surface coating of implants in the last 10-15 years or other changes to production, which might shed light on the issue?

Dr Mercer is a plastic surgeon in private practice in Bristol, UK.

Corresponding Author:
Dr Nigel Mercer, 58 Queen Square, Bristol BS1 4LF, UK.
E-mail: nmercer1@me.com; Twitter: @NigelMercer
International Monitoring

Every country has a governmental body equivalent to the Food and Drug Administration (FDA) in the United States. In the United Kingdom, that body is the Medicines and Healthcare products Regulatory Authority (MHRA). All these international regulatory bodies liaise closely with each other over issues such as BIA-ALCL, because sharing of information at every level is essential in rare diseases such as this. A review of the literature by the FDA showed that the first reported case was in 1997 and between then and May 2010, 34 unique cases were reported internationally.3,4 The first case was reported in the United Kingdom in 2012.5

MHRA Advisory Notices/Guidance

MHRA first issued a Medical Device Alert about the risk of ALCL and breast implants in February 2011 (MDA/2011/017) and subsequently published a webpage dedicated to BIA-ALCL on July 26, 2017, which was updated on November 26, 2018. As of September 2018, MHRA has received 57 reports of potential ALCL cases associated with breast implants, but only 45 of those cases have met the WHO diagnostic criteria for BIA-ALCL. There have been three reported deaths but only one of these was confirmed to have been from BIA-ALCL. The others do not meet the WHO diagnostic criteria. The incidence of BIA-ALCL in the United Kingdom has been estimated by MHRA to be in the order of 1:24,000 based on reported cases and the numbers of implants known to be sold into the market in the United Kingdom.6 This compares well with the incidence of 1:20,110 recently calculated in a slightly different way by the European Association of Plastic Surgeons (EURAPS) and presented by Professor Santanelli at the London Breast Meeting in September 2018.7

The UK competent authorities have not felt it necessary to take regulatory action other than issuing alerts at this level of incidence but consider it is essential patients are informed BIA-ALCL can occur when being counseled and consented for breast implant surgery for either cosmetic or reconstructive indications. It has been stressed that patients undergoing postcancer reconstruction must be warned very early in the conversation of the risk. To have been the unlucky 1:8 woman to have developed a breast cancer, requiring sometimes arduous treatment, may well change the patient’s perception of risk when told their reconstruction carries a 1:24,000 risk of developing a second, different cancer, known to be associated with an implant, when there are other alternatives available for reconstruction. Lay members and patient advocates on MHRA’s Plastic, Reconstructive and Aesthetic Surgery Expert Advisory Group (PRASEAG) have been very clear on this, in that the current risk of BIA-ALCL stated by MHRA should be quoted very early in the process of advising any patient seeking breast augmentation for any reason. It is of deep professional concern to still be hearing from patients that they are not being informed of BIA-ALCL by some surgeons and businesses providing cosmetic surgical services, possibly because the surgeon has decided that the level of risk is low and so it is not worth worrying the patient and potentially putting them off surgery, especially if they are seeking a cosmetic augmentation.

The Montgomery Ruling and Advising Patients Seeking to Undergo Breast Augmentation of Any Indication

If the surgeon or business has decided that the risk is so low that they do not need to warn the patient, they need to be reminded the law on consent for medical procedures changed in the United Kingdom in 2015 as a result of the Montgomery Ruling. This ruling by the Supreme Court was retrospective to the time the injury happened to the patient in 2006.8 Before this ruling, the law stated that the information given to a patient in consenting them to undergo a medical procedure was dependent on what a “responsible body of medical men” thought it would be reasonable for the patient to know, by using the Bolam Principle. The Montgomery Ruling made it clear that times have changed and we now live in a digital age where patients have a wide range of resources available to them to be able to help them make decisions. Now, quite rightly, the onus is on the doctor to provide the level of information a “Reasonable Patient” would expect. A good “rule of thumb” is to give the patient the same information that you, as a doctor, would wish to receive. If there is any risk of cancer or catastrophe, doctors would wish to know and so would our patients.

It is also very important that such information is given to the patient at the outset and not hidden away at the end of the discussion or consenting process. The ruling also means every treatment option available to a patient must be explained to them. The surgeon can no longer offer only one type of implant and one “pocket.” In explaining every treatment option, the surgeon has to discuss the relative merits of each and describe the complications associated with each option before providing the patient time to make up their mind, which, if any, choose.

If the patient chooses an option the surgeon does not provide or is not trained to perform, there is a legal duty to refer the patient on to a surgeon who does and they must not try to persuade the patient to accept an option they have already discarded. In English Law, patients are entitled to make a poor decision, provided they have “competence” to make that decision and are fully informed of the risks. The surgeon, however, is not obliged to provide a
treatment if they feel it would be inappropriate on medical grounds to do so.

**Patients Who Have Breast Implants In Situ**

The question then remains; what do we tell patients who have breast implants in situ?

It is beholden on us, as doctors, to warn patients with a breast implant in place, who come to see us for any reason, there is a new disease identified and what symptoms and signs they should look out for. If the patient does not know what sort of implant they have in situ, they should be advised to contact their original surgeon. Some surgeons have decided to contact past patients to inform them of the risk. Indeed, a medical malpractice insurer in the United Kingdom has informed a surgeon that they will not indemnify the individual if a past patient takes action for developing BIA-ALCL if no attempt has been made to contact past patients. However, the General Data Protection Regulation (GDPR), which is now in force in the United Kingdom and throughout the European Union, makes this problematic. Many patients are young when they undergo cosmetic augmentation and are very likely to have changed address. Some reconstructive patients may have succumbed to their original disease and some may have moved on following their treatment. It would be a GDPR breach if the notification went to the wrong individual and any “remedy” awarded by the courts would potentially lead to a significant financial penalty. The GDPR are less than year old and, whilst the law on breaching patient confidentiality is much as it was before its introduction, the financial penalties for breaking the regulations are massively increased (4% of turnover or €20 million, whichever is greater).

Every surgeon and business providing breast implant surgery should consider what approach to take and formulate a well-reasoned policy, probably with legal input.

The MHRA, FDA, and international regulators agree that there is no indication for screening asymptomatic patients. It would be impossible to draw fluid off for cellular analysis where there is none and, in any case, a small percentage of circulating lymphocytes are CD30 in normal fluids. There is, by the same token, no current evidence that patients should have breast implants removed prophylactically but if a “worried well” patient asks advice they must be given the pros and cons of removal and of watchful waiting. This is because we now know the average time from implant to developing BIA-ALCL is in the region of 8 years, and it is strongly recommended that all patients are advised of the need for vigilance and regular follow-up throughout and probably beyond 10 years. If a patient undergoes an exchange of implant, from the data from multiply implanted patients, the entire capsule may need to be excised but that remains a subject for discussion. From our current understanding of the disease, there may no longer be a place for capsulotomy or partial capsulectomy when an implant is removed, whether it is replaced or not. This is likely to be an area where more guidance is needed in coming months.

**How Long Should We Keep Patient Records?**

This is a very difficult question and the answer often quoted of 7 years is laying a surgeon open to legal challenge, because we know the time for implant to BIA-ALCL presenting is a mean of 8 years at present. The new Medical Device Regulations (MDR), which will be applicable in 2020, have a requirement for health institutions to store and keep (preferably by electronic means) the unique device identifiers (UDI) of class III implantable devices they have supplied, such as breast implants. Additionally, health institutions will be required to provide patients with implant cards. Surgeons would be well advised to scan the records of every patient, who undergoes a breast implant under their care, to be able to access their medical record indefinitely. Again, under the GDPR regulations, individual, identifiable information must be destroyed as soon as it is no longer needed, but it is clear that it may be needed many years in the future for these patients. The GDPR regulations stipulate that a written policy needs to be set out and a copy given to each patent. In addition, every patient who undergoes a breast implant procedure must be strongly advised their details should be registered on the Breast and Cosmetic Implant Register (www.digital.nhs.uk/Breast) and Cosmetic Implant Registry FAQ (for Patients v0.4). Only in that way can accurate data be collected and patients contacted if problems arise in the future. We must remember that there has been a question raised against breast implants at least every decade since they were introduced.

**Advice for Members From Professional Associations**

The Association of Breast Surgeons, the British Association of Aesthetic Plastic Surgery, and the British Association of Plastic, Reconstructive and Aesthetic Surgery, whose members perform a very significant proportion of the breast implant procedures performed in the United Kingdom, published a joint statement, in conjunction with MHRA, in July 2018, for their members to follow when counseling and consenting patients for breast implantation for cosmetic or reconstructive indications. It also includes
advice on how to investigate patients who present with potential symptoms of the disease.\textsuperscript{11}

**Advice for Members for Patient Advocacy Groups**

Patient advocacy groups are represented on the Breast Implant Registry (BIR) Steering Group and there is close collaboration and information sharing between the PRASEAG and the BIR. It is essential that patient advocacy groups are part of the process so that it is clear that nothing is being hidden. What we as surgeons would want to know, patients also want to know and the Montgomery ruling now gives that requirement legal force in the United Kingdom.

**Reporting of Cases**

BIA-ALCL is a rare disease and, for this reason, international cooperation in investigating the disease is essential. There are approved guidelines for investigating suspected cases and these must be followed but they will vary between countries, but hopefully only until consensus can be agreed. In the meantime, surgeons, radiologists, and pathologists must make themselves aware of what is required in their jurisdiction. It is essential for patient safety that we do not miss cases because, whilst BIA-ALCL is an indolent disease at the outset, diagnostic delay and inadequate treatment will lead to unnecessary deaths. All cases should be reported to your haemo-oncology multidisciplinary team and the treatment plan should be agreed with them. Consensus has already determined an en bloc resection of the whole capsule and implant is required to be effective.\textsuperscript{12} A smooth implant may be re-inserted, but patients should be warned that the safest option is not to have another implant. No cases of BIA-ALCL have yet been reported in patients who have a history of only smooth implants, but we are not yet in a position to say that any breast implant is completely “safe.” Stating that an implant is “safe” may provide false reassurance because every surgical procedure, whether it involves an implant being inserted into the body or not, carries some element of risk, whether fully understood or not. This is why regulators use the term “acceptably safe” to indicate that not all risks can be known for every medical device in every circumstance because, over time, completely unpredicted complications may occur.

Breast implants are not lifetime devices and revision surgery may be required for a variety of reasons. Textured, cohesive implants were initially introduced to reduce the risk of movement, capsular contracture, and gel migration after rupture. At the time, these developments were seen as beneficial, reducing these complications and clinical practice adapted accordingly. However, in common with other implanted medical devices, new information and potential risks have emerged, which have meant revisiting the balance of benefit versus risk over time. It is a surgeon’s professional and legal responsibility to ensure that they have explained to prospective patients all the current information on the benefits and risks of breast augmentation and that other, as yet unknown, problems may appear over time. The surgeon must also check that the information has been understood and retained by the patient so that they can decide for themselves whether or not to have surgery.\textsuperscript{13}

**Sharing Information**

International cooperation is essential when new, rare diseases develop to ensure as much information is gathered and analyzed, by those best placed to do so and this information then needs to be shared in an open and transparent way in the best interests of patients, while respecting their confidentiality. This includes breaking down of some traditional rivalries between research groups and the commercial interests of manufacturers. For example, MHRA cooperates closely with their international counterparts and it is this type of collaboration, which is required between all the stakeholders involved. To ensure a free and complete flow of important information, it is essential that, when professional bodies or other organizations receive registration of cases, they should also ensure the case is also reported to the relevant regulatory authorities, either directly or by the original reporter.

While encouraging reporting is essential, on a cautionary note, there can be significant problems with sharing patient identifiable data across international boundaries. To avoid them suitable, anonymization should be undertaken to avoid any legal consequences, because patient confidentiality laws vary across international boundaries and this needs to be considered carefully. Therefore, if UK clinicians submit data to international registries, it is essential that they have informed consent from the patient before any identifiable data are shared, especially when tissue and cytology samples are being requested. In UK, for example, MHRA while expecting all cases to be reported would wish all patient identifiable data to be redacted or encrypted when histology reports are sent to them. On a final note, it is of paramount importance that treatment is not delayed, because of information sharing issues, because diagnosis and treatment planning must take priority.
Centralization of Care of Those Who Develop BIA-ALCL

BIA-ALCL remains a rare disease and so the generic experience of treating it will be patchy at best. In addition, the whole diagnostic and treatment pathway is complex, requiring haemo-oncology and breast cancer level surgical skills. In that light, centralizing the care of these individuals in centers equipped to deal with complex cancers would seem most appropriate, especially if they are not adequately treated by surgery and need immunotherapy. The specialist centers chosen should have specialist breast oncology and hematology services, including access to PET scanning, hemo-pathology, oncological and reconstructive breast services as well as hemo-oncological expertise, including both breast and hemo-oncology MDTs. Centers will need to be centrally designated by the NHS. In the case of the United Kingdom, that would mean treatment in expert NHS cancer centers. With the numbers of cases presenting with the disease being very low at present, perhaps there should be four national centers in the British Isles, one each for; the south of England/London; Wales/Midlands; Scotland/north of England; Ireland?

CONCLUSION

In today’s world, “doctors do not know best” when it comes to the information a patient is given, especially when contemplating a cosmetic or reconstructive breast implantation. It is essential that prospective and existing patients are given information they can understand about the risk of BIA-ALCL so they are able to make an informed decision about what to do. As doctors, we have a “duty of candour” to our patients and withholding this information would be a breach of that duty. It is essential that we inform our patients of the risk of BIA-ALCL and that we cooperate at all levels to increase our understanding of this new disease. Definitive treatment guidelines have not been given in this article because they will change with time and experience across jurisdictions but a link to the NCCN guidelines is included in the bibliography. It is essential that surgeons performing breast implant surgery are “au fait” with the current guidelines for investigation and treatment of suspected and proven cases of BIA-ALCL in their jurisdiction.

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