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Short communication

EUSOMA position regarding breast implant associated anaplastic large cell lymphoma (BIA-ALCL) and the use of textured implants

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ABSTRACT

During the last two decades the number of breast implants used in aesthetic, oncologic and risk reducing surgery has increased substantially mainly due to the improvement and confirmed safety of these devices. Since identification of the first case of anaplastic large cell lymphoma associated with a breast implant (BIA-ALCL) 20 years ago, there has been an increase in the number of reports of this very rare disease, demonstrating a clear association with breast implants. Whilst the majority of cases are localised and cured by implant removal and full capsulectomy, a small percentage require chemotherapy and the mortality rate is very low. The evidence linking BIA-ALCL to implant surface texturing, as the majority of cases were diagnosed in patients with textured implants, has raised concerns about the long term safety of these devices resulting in patient and regulatory authority concerns globally. We hereby present the current published knowledge about the link between BIA-ALCL and implant surface texture and a review of current regulatory and professional body advice across Europe, which may enable a better understanding of this rare disease, how to manage and ultimately prevent it. We conclude by giving EUSOMA recommendation, towards the unnecessary change in attitudes towards implant based surgery, according to the most recent available published evidence as long as patients are properly informed about the risk of BIA-ALCL.

1. Background

The number of women around the world with breast implants in 2017 was estimated to be approximately 10 million [1] while the prevalent number of women with breast cancer was calculated to be around 1,6 million in 2018 [2]. In many countries use of implants for breast augmentation is the leading cosmetic procedure. Use of implants for post mastectomy reconstruction is the leading reconstructive technique in the cancer and risk reducing settings in many countries [3].

Since the introduction of silicone breast implants in the sixties several issues have been raised regarding their safety. The first was the possible relation of silicone gel with auto-immune diseases resulting in a temporary ban imposed by the FDA and followed in parts of Europe between 1992 and 2006, until this association was scientifically refuted [4]. In 2010 the French medical oversight agency (ANSM) decided to suspend the use of Silicone-filled breast implants, produced by Poly Implant Prothese (PIP) due to the presence of silicone gel which was not certified for use in humans and also due to their more frequent rupture rate [5]. In 2015 the selling of Silimed implants was suspended following contamination reports in a manufacturing facility in Brazil.

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In 1992 the first case of ALCL, an extremely rare, Non-Hodgkin lymphoma of T-cell origin, associated with a breast implant was reported in the literature [6]. In 2008 the first epidemiologic study was published [7] and in 2015, 173 cases were reported in the literature [8]. In 2016 BIA-ALCL was included in the World Health Organization's lymphoma classification as a new entity [9]. Despite the absence of definitive epidemiological causal evidence, existing data strongly suggests that BIA-ALCL is associated with the use of breast implants, and may be associated predominantly with the use of textured rather than smooth coated implants.

Various causal factors have been suggested such as a local inflammatory response, promoted by silicone-derived products or specific bacterial species adherent to the textured prosthesis surface (biofilm), possibly via a chronic auto-immune response. Toxic products related to the production of breast implants have been implicated as direct mutagens [10].

The lymphoma most often presents as a late onset seroma (by definition more than 1 year after implant placement and on average, 10 years after placement), with malignant alterations confined to the periprosthetic fluid or much less frequently as a tumorous mass. Diagnosis is confirmed by seroma aspiration and identification of CD30 positive large atypical cells (ALK negative). As long as the lymphoma remains confined to the seroma cavity, the outcome is excellent following simple removal of the implant and full capsulectomy. If capsular invasion is identified, adjuvant chemotherapy is mandatory. In rare cases where dissemination of the disease is identified the outcome is poor even with systemic treatment although to date, the number of such deaths is extremely small internationally [10], estimated at ~2% by the FDA in 2017.

2. Actual situation

Accurate estimations of the incidence of this rare entity have been difficult to calculate due to the sporadic reporting of cases. The first epidemiologic study in 2008 by de Jong et al. demonstrated an 18 fold relative risk for women with implants versus those without, of developing a BIA-ALCL [7]. This risk estimate was updated in 2018 to a value 10–20 times higher with a prevalence rate of 1 in every 12000 women with textured implants (82%) [11]. The total number of reported cases in the research literature, is likely to be around 250, by 2018, but the exact number is difficult to confirm due to reporting overlaps from literature reviews (Table 1). Numbers globally may be higher as not all cases are published in academic journals and National registration databases, if available, may show higher numbers (the FDA for example). Of reported cases, the majority, but not all cases, are linked to textured implants. The FDA report in 2017 of 414 reported cases of BI-ALCL received data on surface type in 272 cases, with 242 linked to textured implants and 30 linked to smooth surfaced implants (12% smooth).

Since 2016 reporting of BIA-ALCL is mandatory in many countries. There has been rising concern among scientific societies and health authorities on how best to tackle the problem, but two important actions are consistent by all countries:

1. That the risk of BIA-ALCL must be communicated to patients before they undergo implant surgery [12] (cosmetic or reconstructive) when giving informed consent and
2. The inclusion of all cases in a National prospective registry [13,14].

In December 2018 Allergan a leading global biopharmaceutical company, and the main company selling textured implants in Europe, announced that the company has suspended sales of textured breast implants and tissue expanders and is withdrawing any remaining supply in European markets. The withdrawal decision follows a compulsory recall request from Agence Nationale de Sécurité du Médicament (ANSM), the French regulatory authority. The suspension of sales stems from the expiration of the company's CE Mark for these products. ANSM is planning to review evidence relating to implant use in early February and is presently advising clinicians preferentially use smooth surfaced implants [15].

This decision has had an immediate impact across Europe with several subsequent actions from scientific societies and health authorities within different countries (Table 2) aiming at minimizing the risk for patients. It is important to state however that the available data from different countries is, in the majority of cases, a collection of reported cases and difficult to accept as a true incidence value due to the absence of a reliable denominator. The most reliable data available to date because it is based in robust population registries are the Dutch the US and the Australian and New Zealand (Table 1) [1,16,17].

3. EUSOMA position

This dilemma will certainly persist due to the fact that the risk seems to be associated with textured implants in general and not only to a specific brand. Textured implants have seen an expansion in their use due to their lower rate of capsule formation and reduced likelihood of implant rotation, which is critically important where anatomically shaped implants are used to restore a more

Table 1
Breast Implant-Associated Anaplastic Large Cell Lymphoma. (Summary of published multiple case series, mainly National Registries. Single case reports have not been included).

Reference	Data Source	Study period	Case number	Reason	Mean age	Mean time to diagnosis (years)	Type of implant	Lifetime prevalence in women with textured implants
de Boer Jama Oncology 2018 [16]	Dutch National Pathology Registry	1990–2016	32	65% cosmetic 45% reconstructive	59	13	Textured 82%	1/12000
Dachevsky The Breast J 2017 [13]	MSKCC Registry	2010–2016	11	20% cosmetic 80% reconstructive	54	10	All known -textured	
Loch-Wilkinson PRS 20175 [17]	Australia and New-Zealand Registry	2007–2016	55	69% cosmetic 21% reconstructive	47	7.5	All known - textured	1/3800-1/60000 Depending on type of implant
Doren EL PRS 2017 [1]	US retrospective data	1996–2015	100	49% cosmetic 51% reconstructive	53	10	All known - textured	1/30000
Johnson EJSO 2017 [14]	UK Scientific Societies cooperation	2012–2016	23	56% cosmetic 44% reconstructive	52	10	All known -textured	
			221		**±50**	**±10**	**Textured**	**Variable ±1/30000**

Table 2
Country recommendations towards BIA-ALCL and attitudes towards textured implants by January 2019.

Country	National Regulatory Board	Report mandatory	Recommendation towards all textured implants	Scientific Societies Ministry of Health Recommendations	Withdraw of Textured Implants by Allergan	Still using other brands textured implants	Estimated Rates of BIA-ALCL (per implant placed)	Recommendatios for early diagnosis
AUSTRIA	Österreichisches Register für Medizinprodukte-MP	NO	NO	NO	Unknown	YES	1/20000	YES
BELGIUM	Federal Agency for Medicines and Health Products, FAMHP	NO	YES	NO	YES	YES	Unknown	YES
BULGARIA	Bulgarian Drug Agency, Direction “Market control and inspections”	YES	NO	YES	YES	YES	Unknown	YES
DENMARK	Danish Medicines Agency	YES	YES	YES	YES	YES	Unknown (7 reported cases)	YES
ICELAND	Lyfjastofnun Íslands	YES	YES	YES	YES	YES	Unknown (None reported)	YES
IRELAND	Health Products Regulation Association, HPRA	NO	NO	NO	NO	NO	1/25000	YES
ITALY	Ministry of Health (Dec 18.2018)	YES	NO	YES	YES	YES	1/2227	YES
FINLAND	Social and Health Ministry	YES	NO	NO	YES	Unknown	Unknown (8 reported cases)	YES
FRANCE	Agence nationale de sécurité du médicament et des produits de santé (ANSM)	YES “LYMPHOPATH”	YES	YES	YES	NO	1/8928	YES
GERMANY	Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM	YES	NO	NO	YES	YES	Unknown (7 reported cases)	NO
GREECE	National Medicines Agency	NO	NO	YES	YES	YES	Unknown	YES
LATVIA	State Agency of Medicines of Latvia	YES	NO	NO	YES	YES	1/300000	YES
POLAND	The Office for Medicinal Products, Medical Devices and Biocidal Products	YES	NO	YES	YES	YES	Unknown (3 reported cases)	YES
PORTUGAL	INFARMED	YES	NO	NO	YES	YES	Unknown	YES
SPAIN	Agencia Espanola de Medicamentos y Productos Sanitarios - AEMPS	YES	NO	NO	NO	YES	Unknown	YES
SWEDEN	Läkemedelsverket	YES	NO	NO	NO	YES	Unknown	YES
SWITZERLAND	Swiss Medics	YES	NO	YES	YES	YES	1/4500	YES
UK	Medicines and health care products regulatory authority (MHRA)	YES	NO	YES	YES	YES	1/24000	YES

natural 'tear drop' shaped breast following mastectomy. The vast majority of implants in Europe are textured and in the setting of breast reconstruction, implant based surgery cannot be easily replaced by other techniques. It is therefore important that we stay alert regarding new developments as more evidence becomes available. It is also critical that patients with existing implants are given appropriate advice and support at this time of uncertainty and women considering implant surgery are fully informed of the most recent updates.

According to the evidence available, Eusoma recommends that, for the moment, textured implants can safely continue to be used with patient's fully informed consent, and that women that have these type of implants already in place don't need to remove or substitute them, which would undoubtedly cause harm to many tens of thousands of women, to prevent an exceptionally rare, largely curable and currently poorly understood disease.

Conflicts of interest

The authors declare they have no conflict of interest.

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