An advanced case of breast implant-associated anaplastic large cell lymphoma

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ABSTRACT

Introduction: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare type of non-Hodgkin lymphoma that was first described in the literature in 1997. The most common clinical presentation of BIA-ALCL is a persistent seroma, which can be accompanied by breast swelling, asymmetry, or pain. Approximately 30% of patients present with a tumor mass. Case Report: A 66-year-old woman underwent bilateral mastectomies and immediate implant reconstruction for screen detected ductal carcinoma in situ (DCIS) of the right breast in January 2016. Four years later the patient presented with a right breast mass that developed over a period of weeks. Radiological and pathological investigations confirmed the presence of multifocal mass forming BIA-ALCL with axillary, sub-pectoral, and intra-mammary lymph node involvement. Following multi-disciplinary team (MDT) input, definitive was surgery and was also performed. En bloc resection of the right breast tumors and capsulectomy was performed in parallel with left breast explantation and capsulectomy. An axillary lymph node clearance of the right axilla was performed. The patient had an uneventful postoperative recovery and was discharged on post-operative day 5. Following MDT discussion the patient is awaiting adjuvant chemo/radiation therapy. Conclusion: All patients presenting with a delayed spontaneous seroma (>1 year after implantation) after placement of a textured implant should be investigated for BIA-ALCL. In the majority of cases explantation and total capsulectomy is curative and patients will have an excellent survival outcome.

Keywords: Anaplastic, Breast implant, Lymphoma

INTRODUCTION

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare type of non-Hodgkin lymphoma that was first described in the literature in 1997 [1]. The first case of BIA-ALCL described a 41-year-old woman with a CD30+ peripheral T-cell lymphoma mass surrounding a cosmetic textured-surface breast implant [1]. Since 1997 more than 500 cases of breast implant-associated anaplastic large cell lymphoma have been reported across 29 countries worldwide [2]. Breast implant-associated anaplastic large cell lymphoma was provisionally classified in the 2016 revision of the World Health Organization classification of lymphoid neoplasms [3]. In 2019, the U.S. Food and Drug Administration released a statement reporting the lifetime risk for breast implant ALCL is between 1 in 3817 and 1 in 30,000 women with textured breast implants [4]. The median...
interval from time of implant insertion to diagnosis of BIA-ALCL is between 7 and 10 years [5, 6]. The most common clinical presentation of BIA-ALCL is a persistent seroma, which can be accompanied by breast swelling, asymmetry, or pain [5]. Axillary lymphadenopathy has been reported in up to 15% of cases and approximately 20% of patients present with a mass around the implant [5, 7]. Small subsets of patients with BIA-ALCL present with cutaneous symptoms such as a skin rash or pruritis and others are diagnosed incidentally at the time of implant exchange or removal [8]. Given the novel and rare nature of BIA-ALCL clinical decision-making relies on retrospective series, case reports, and expert opinions. We present an interesting case of advanced BIA-ALCL in a 66-year-old woman.

CASE REPORT

A 66-year-old woman underwent bilateral mastectomies and immediate implant reconstruction for screen detected ductal carcinoma in situ (DCIS) of the right breast in January 2016. The patient requested to have a contralateral left breast risk-reducing mastectomy and immediate implant based reconstruction at the time of her surgery. The patient was counseled on the additional risks and null survival benefit of contralateral surgery prior to surgery. Following surgery the patient made an excellent recovery and was prescribed adjuvant hormonal manipulation in the form of an aromatase inhibitor.

The patient had expressed some discontent over the position of the left reconstructed breast as she felt the implant migrated laterally and attended a consultant plastic surgeon in January 2020. At this time clinical examination was normal. In April 2020, the patient presented to the emergency department with a red breast implant and palpable mass at the lateral edge of the implant. No effusion/seroma was appreciated. She was systemically well with mildly elevated inflammatory markers. An ultrasound was performed which revealed an ill-defined mass in the lateral right breast with associated axillary and internal mammary lymphadenopathy. A core biopsy was obtained which reported chronic inflammatory cells of indeterminate significance. Fine needle aspirate of the axillary node showed atypical lymphoid cells positive for CD30 and negative for ALK 1. Findings were reported with a seroma and cytological analysis revealed atypical lymphoid cells showing partial positivity with cutaneous lymphocyte-associated antigen (CLA) with the majority of cells being positive with the T-cell markers CD43, CD4, and MUM1. The tumor was strongly diffusely CD30 positive and ALK1 negative. The patient made an excellent post-operative recovery and was discharged on post-operative day 5. Following MDT discussion the patient will receive adjuvant chemotherapy/radiotherapy response as per MDT discussion. The right lateral tumor mass and anterior chest wall mass were resected en bloc with right capsulectomy. The aim was to achieve clear margins (R0 resection) without compromising pleural integrity. The anterior chest wall mass was adherent to the anterior ribs, however a plain of dissection was adequately achieved (Figures 2–7). The histopathology report of the right breast capsulectomy revealed multifocal nodular involvement of large markedly atypical lymphoid cells with the largest nodule measuring 10 × 3.5 cm. Skeletal muscle was focally involved at the deep margin and this was deemed non-improvable surgically. Two out of seven axillary lymph nodes showed involvement and partial nodal sinusoidal involvement by BIA-ALCL. Immunohistochemical studies showed atypical lymphoid cells showing partial positivity with cutaneous lymphocyte-associated antigen (CLA) with the majority of cells being positive with the T-cell markers CD43, CD4, and MUM1. The tumor was strongly diffusely CD30 positive and ALK1 negative. The patient made an excellent post-operative recovery and was discharged on post-operative day 5. Following MDT discussion the patient will receive adjuvant chemotherapy (CHOP regime) and radiotherapy with the aim of reducing the risk of loco-regional or systemic recurrence. Clinical review will be on a three monthly basis.

Three weeks after the patient was diagnosed, a second patient was diagnosed with BIA-ALCL in the same department. This patient presented more typically with a seroma and cytological analysis revealed atypical lymphoid cells positive for CD30 and negative for ALK1. Curative surgery in the form of a left capsulectomy was performed with no further treatment required.

Both cases illustrate the complex nature of the disease and how the clinical presentation can vary.

DISCUSSION

To the best of our knowledge this is the first documented case of BIA-ALCL in the Republic of Ireland. The primary risk factor for developing BIA-ALCL is exposure to textured implants. To date, there are no
Figure 1: T2-weighted MRI image of bilateral reconstructed breast. Red arrow points to right chest wall lymphoma mass.

Figure 2: Pre-operative image on the operating table of right reconstructed breast with right lateral tumor mass.

Figure 3: Right breast lateral tumor mass resected en bloc with right capsule.

Figure 4: Intra-operative image of dissection plane between tumor and chest wall.

reported cases in patients with smooth implants only [5, 7, 9]. The precise pathogenesis of BIA-ALCL is unclear with multiple hypotheses proposed. One such theory hypothesizes that the hosts’ T-cell (cytotoxic and helper) response to the particulate on the textured implant surface is a potential pathological driving force [10, 11]. Textured implants are different to smooth implants because they shed particulate matter. Macrophages auto digest this particulate to form foamy cells and secrete pro-inflammatory cytokines such as interleukin-1, interleukin-6, and tumor necrosis factor which in turn leads to T-cell chemotaxis and replication [12, 13]. An alternative theory of pathogenesis involves colonization of gram-negative bacteria in a biofilm surrounding the implant producing lymphocyte hyperplasia [14]. Both theories infer that the underlying pathological mechanism of BIA-ALCL is a result of aberrant reactive T-cell lymphoproliferation. From a cancer genomics perspective, activating somatic mutations in the JAK-STAT signaling pathway, SOCS1, TP53, and DNMT3A have been described in BIA-ALCL [15, 16]. Intriguingly germ line mutations in the JAK3 signaling pathway
have been identified in some patients with BIA-ALCL suggesting certain innate host factors may predispose to the development of BIA-ALCL [17]. Considering the novel nature of this disease, the pathogenesis and genetic drivers underlying BIA-ALCL are still unclear and further research is needed in this area.

BIA-ALCL has been described in women who have undergone breast implantation for cosmetic and reconstructive options. The most common clinical presentation is delayed seroma (>1 year after implantation) surrounding the implant, this occurs in two-thirds of patients [5]. The term seroma is incorrect in the context of this disease as a seroma by definition contains transudative fluid with a low protein count. The fluid surrounding the implant in BIA-ALCL contains liquefied and necrotic lymphoma cells with a high protein content, therefore the term effusion should be more accurately adopted [18]. Our case was unusual in that she presented with a tumor mass and skin changes overlying the reconstructed breast. No appreciable effusion was detected. Approximately 30% of patients present with a tumor mass which is usually palpable along the medial or lateral surface of the implant. In the case of our patient, the fixed tumor mass was palpable over the lateral border of the implant and increased in size over a period of weeks.

The National Comprehensive Cancer Network (NCCN) has outlined the diagnostic work-up required for BIA-ALCL [19]. Any effusion occurring greater than one year after implantation that is not readily explained by infection or trauma should be suspected for BIA-ALCL. Ultrasound guided aspiration of periprosthetic seroma fluid for microbiological analysis and cytology assessment is required. Magnetic resonance imaging of the breasts is required for assessment of implants integrity and tumor mass. In the case of mass forming BIA-ALCL, cytological aspirate assessment should be geared toward adenocarcinoma as well as lymphoma diagnoses [19]. Immunohistochemistry should be performed to determine the immunophenotype. CD30 is expressed in all cases of BIA-ALCL and ALK 1 is typically negative. CD30 is characteristic of BIA-ALCL but not specific as it also expressed in various other lymphoid malignancies [20]. If a tumor mass is detected pre-operatively, en bloc resection with clear margins is recommended. Patients presenting with an effusion require explantation and complete capsulectomy and this is curative for many patients [8, 19].

Breast implant-associated anaplastic large cell lymphoma is commonly regarded as having an indolent clinical course, and the majority of patients achieve complete remission with surgery alone [21]. A study conducted by Miranda et al. [22] reporting the long-term follow-up of 60 BIA-ALCL patients concluded that most patients achieve complete remission (72% and 93% for patients presenting with and without a mass, respectively). Advanced BIA-ALCL describes patients with bilateral breast disease, lymph node involvement, and visceral
metastasis. Complete remission rate for patients with lymph node involvement was 67% in a study conducted by Collins et al. in 2019 [21]. This cohort of patients require definitive surgery (explantation, capsulectomy, and tumor resection), chemotherapy, and radiotherapy to optimize survival outcomes [21]. The trajectory toward a poorer outcome for patients with advanced disease was attributed to a delay in diagnosis and definite surgery. Our case was diagnosed and underwent definite surgery within four weeks which will hopefully translate into a good outcome for the patient.

CONCLUSION
Breast implant-associated anaplastic large cell lymphoma is a rare condition that is gaining recognition and awareness due to continued research and publications in the area. All patients presenting with a delayed spontaneous seroma (>1 year after implantation) after placement of a textured implant should be investigated for BIA-ALCL. Seroma fluid should be aspirated and screened for lymphoma using CD30 immunohistochemistry and flow cytometry. In the majority of cases explantation and total capsulectomy is curative and patients have an excellent survival outcome.

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C Cullinane – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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