

## **Anaplastic Large Cell Lymphoma (ALCL)**

ALCL is an extremely rare subtype of non-Hodgkin's lymphoma that can affect different tissues, including the breast. It has been reported in women with and without breast implants and population-based studies estimate an overall incidence of between 0.1 and 0.3 per 100,000 women<sup>i</sup>. The French National Cancer Institute reported 18 cases in women with implants with an incidence of 0.7-1.17 per 100,000<sup>ii</sup>. However, even this small risk may be of concern to women with breast implants.

ALCL was first described in 1985 but only classified as a distinct disease in 1994. The first case of ALCL that was associated with breast implants was reported in 1997, however, there are no prospective epidemiological studies linking ALCL with breast implants and a causative link has not been established. In 2011 the FDA released a notice about a possible association between breast implants and ALCL<sup>iii</sup>. The most recent literature review, published in 2015 by Gidengil et al<sup>iv</sup>, identified 54 cases of breast implant associated ALCL. Brody et al, have recently published the largest analysis with 173 cases worldwide<sup>v</sup>. These were derived from published and unpublished case reports, although they may have included some duplications.

The commonest presenting symptom for breast-implant associated ALCL is the formation of a delayed unilateral seroma, not usually associated with any other manifestations. Only occasionally was it associated with tenderness, a lump or capsular contraction. Cases have been reported in the absence of a peri-prosthetic fluid collection in association with capsular contraction or a mass or as a cutaneous nodule. Where ALCL is associated with breast implants, CD30-positive cytokeratin-negative malignant cells are found infiltrating the periprosthetic capsule on histological analysis, or in the aspirated fluid collection surrounding the implant. Both saline and silicone filled implants have been identified in case reports.

Treatment depends on the stage of presentation but may include removal of the implant and capsulectomy alone. In others it may be combined with chemotherapy and less commonly radiotherapy. Of note is that implant-associated ALCL tends to follow a less aggressive course than in women who develop the disease who do not have implants.

Silicone and saline breast implants remain safe for use in both cosmetic breast augmentation and breast reconstruction. Although ALCL is an extremely rare disorder increased awareness and vigilance is required for ALCL in the differential diagnosis of late seroma following previous implant reconstruction surgery or breast augmentation.

## **Guideline for the suggested management of late seromas, occurring more than 6-months post breast augmentation**

A differential diagnosis of late periprosthetic fluid collection includes trauma, double capsule formation, synovial metaplasia, infection, biofilm formation, inflammation, implant rupture, malignancy, ALCL and idiopathic causes. Patients with a non-resolving periprosthetic fluid collection should be further evaluated.

This should be discussed with patients as a framework for their management, but may include alternative approaches to balance risks of complications and of inadequately treating the condition and to meet informed consent requirements.

1. Exclude infection. Unless there are overt signs of infection fluid samples should be taken prior to commencement of antibiotics to improve the chance of culturing an organism.
2. USS to document any peri-implant fluid collection of over 20cc. USS guided needle aspiration of any fluid, to be sent for culture (aerobes, anaerobes, fungi), and cytology with Wright Giemsa stain. If this stain is positive, cell block should be sent for CD30, ALK. Should start 5-day course of prophylactic antibiotic immediately post-aspiration.
3. Assess for any palpable mass in breast or capsule, palpable nodes adjacent to the breast or in the axilla. If present, biopsy is required.
4. If cytology or the biopsy is positive for CD30, ALK, atypical lymphoid hyperplasia, other lymphoproliferative disorder or ALCL discuss at Breast MDT and Haematology MDT and report the case to the MHRA. Exclude systemic disease. Patient likely to require initial resection of abnormal tissue with complete capsulectomy.
5. The most accurate and definitive diagnostic method of recurrent late seroma is surgical exploration with direct visual examination of the entire periprosthetic capsule, and biopsy of any nodular, shaggy, or thickened areas of capsule combined with random biopsies of the entire capsule.
6. If surgical exploration is undertaken take further seroma fluid for repeat cytology and culture. If clinically suspicious or abnormal areas of capsule are present (or if a diagnosis has been made from cytologic examination of the fluid), complete capsulectomy, drainage, and removal of implants without replacement must be considered<sup>vi</sup>.

## **Samples required to evaluate for possible ALCL.**

Any samples should be sent immediately to the lab and must include details of implant related symptoms such as seroma or mass with a request to 'investigate for possible anaplastic large cell lymphoma'. Test required: H&E stain, Wright-Giemsa stain, cell block immunohistochemistry including CD30, and ALK

1. If serous fluid/seroma is present: Send at least 10cc of serous fluid in a universal pot.
2. If abnormal breast tissue or abnormal capsule tissue is present: Send at least 1cc and place in a formalin sample pot.

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i de Jong D, Vasmel WL, de Boer JP, et al. Anaplastic large-cell lymphoma in women with breast implants. JAMA 2008;300: 2030–2035.

ii Rapport de l'INCA (<http://www.e-cancer.fr/toutes-les-actualites/84-linstitut-nationaldu-cancer/9373-avis-dexperts-sur-les-lymphomes-anaplasiques-a-grandes-cellulesassocies-a-un-implant-mammaire>).

iii U.S. Food and Drug Administration. Anaplastic large cell lymphoma (ALCL) in women with breast implants: Preliminary FDA findings and analyses. January 2011 Available at: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/default.htm>. Accessed February 17, 2011.

iv Gidengil CA, Predmore A, Mattke S, et al. Breast Implant–Associated Anaplastic Large Cell Lymphoma: A Systematic Review. Plast Reconstr Surg. 2015;135: 713-720.

v Brody GS, Deapen D, Taylor CR, et al. Anaplastic large cell lymphoma occurring in women with breast implants: Analysis of 173 cases. Plast Reconstr Surg. 2015;135:695–705.

vi JB Tebbetts. Diagnosis and management of seroma following breast augmentation: an update. Plast Reconstr Surg. 2011 Jul;128(1):17-25