

# A case of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)

Clare McGenity  
Alyn L Cratchley

## Abstract

Breast implant associated anaplastic large cell lymphoma (BIA-ALCL) is a recognized but rare complication of breast implantation. This condition occurs with textured implants and on average, presents around 10 years post insertion. We report a case of BIA-ALCL and describe the histological and cytological examination findings. Furthermore, we discuss the condition in more detail, how this disease may be staged and the requirement for central registration.

**Keywords** BIA-ALCL; breast implant; complications; lymphoma; staging

## Case report

A female in her forties presented to the breast clinic with a swelling to one breast. A unilateral fluid collection, or seroma, was identified surrounding her breast implant. The patient had undergone breast augmentation with textured implants some years previously, but otherwise, the medical history was unremarkable.

An ultrasound-guided aspiration of the seroma fluid was sent for cytological assessment which revealed a mixture of lymphocytes and atypical lymphoid cells (Figure 1). The atypical cells were positive for CD30 on immunohistochemistry; however, clonality assessment failed. After multi-disciplinary discussion, the patient proceeded to bilateral en-bloc capsulectomies, of which the symptomatic side revealed four firm nodules present on the inner surface on macroscopic assessment, measuring up to 30 mm in diameter.

Histological examination of the nodules reveals areas of extravasated silicone, a foreign body giant cell reaction and patchy chronic inflammation suggestive of previous implant rupture (Figure 2a). A 'bluer' area of inflammation is identified at low power on the inner capsular surface (Figure 2a). At higher power this corresponds to a region of atypical lymphoid cells within the fibrinous exudate on the surface (Figure 2b), and focally extending deeper into the surrounding fibrous

**Clare McGenity** MBBS, Digital Pathology Fellow, Leeds Teaching Hospitals NHS Trust and University of Leeds, UK. Conflicts of interest: Dr McGenity is funded by Leeds Hospitals Charity.

**Alyn L Cratchley** MBChB FRCPath, Consultant Histopathologist, Leeds Teaching Hospitals NHS Trust, Leeds, UK. Conflicts of interest: none declared.

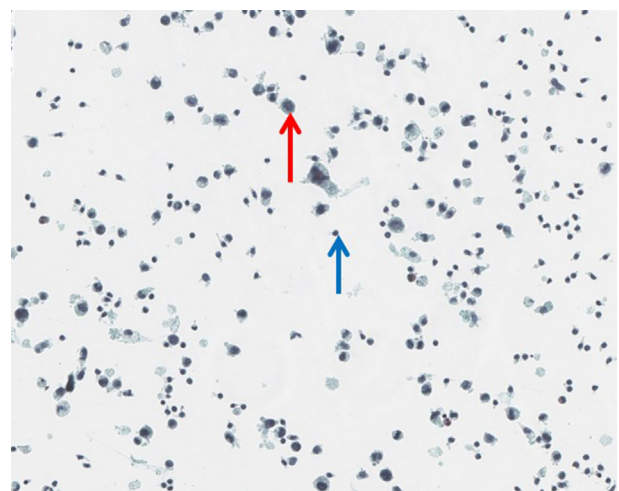
This Short Case is brought to you in association with the Pathological Society of Great Britain and Ireland. Each month we feature a Short Case written by a member of the Trainees' Subcommittee of the Pathological Society of Great Britain and Ireland. The Short Case includes a series of Test Yourself Questions at the end to check your understanding of the case. We hope you enjoy reading it.

**Pathological Society**  
Understanding Disease — Guiding Therapy

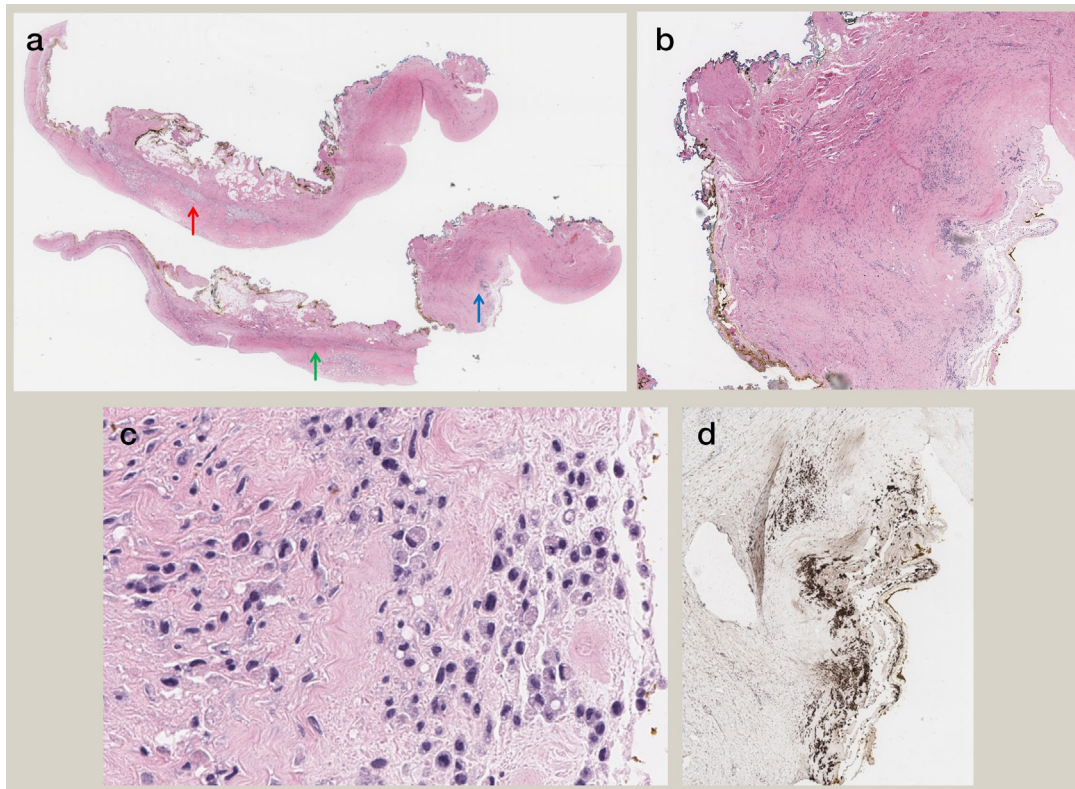
capsule. The cell population are discohesive, with large pleomorphic nuclei and plentiful cytoplasm (Figure 2c). Some of the nuclei are eccentric or have a horseshoe-shaped appearance. Immunohistochemistry of these atypical cells revealed CD30 positivity, in keeping with a diagnosis of BIA-ALCL (Figure 2d). The case was referred to our local haematological malignancy diagnostic service (HMDS) and the diagnosis confirmed by the presence of CD30+ atypical lymphoid cells with an aberrant T cell phenotype. Clonality again failed, but given the morphology and aberrant T cell phenotype, this was still considered diagnostic.

## Discussion

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a non-Hodgkin's T cell lymphoma, found in patients with a history of breast implantation. It is a relatively new entity first described in 1997<sup>1</sup> and further defined by the World Health Organization (WHO) classification of lymphoid neoplasms in 2016.<sup>2</sup> The most common clinical presentation is with a seroma (fluid swelling) adjacent to the implant, or less commonly the development of a mass.<sup>3</sup> As in this case, the first seroma fluid sample is the more likely to be diagnostic, with an increased false negative rate in subsequent samples.<sup>3</sup> This demonstrates the need for caution where fluid cytology is found to be negative but



**Figure 1** Cytology preparation, PAP stain. The red arrow demonstrates atypical lymphoid cells (ALCL). The blue arrow shows a normal lymphocyte for comparison.



**Figure 2** (a) Nodule showing extravasated silicone (red arrow), chronic inflammation (green arrow) and concerning blue area on capsular surface (blue arrow). (b) High power view of atypical lymphoid cells at the capsular surface. (c) Discohesive lymphoid cell population showing large pleomorphic nuclei with surrounding plentiful cytoplasm. (d) CD30 positive staining of the atypical lymphoid cells.

there is a high clinical suspicion of the disease. For a patient with a breast implant, the incidence of BIA-ALCL is estimated at one to three per million per year,<sup>3</sup> accounting for <1% of all malignant breast diagnoses.

In our case, the areas of atypical, pleomorphic lymphoid cells were patchy, with features elsewhere consistent with previous implant rupture. These pathological changes can be variable and sometimes very focal. Careful microscopic examination should be undertaken and the threshold for requesting additional blocks should be low, especially if there is high clinical index of suspicion. To aid in diagnosis, the atypical cells are uniformly and strongly positive for CD30 and are ALK negative. Additionally, it is important to note that these atypical cells can be variably positive for EMA (in up to 90%) which can be a potential diagnostic pitfall.

This condition is associated with textured breast implants and a linear relationship between surface area and roughness with bacterial attachment and growth has been shown.<sup>4</sup> The exact pathogenesis is not yet determined; however, it is postulated that chronic inflammation may cause T cell activation in this context, thereby increasing the risk of developing a T cell related malignancy.<sup>3</sup>

As a pathologist, it is important to note that BIA-ALCL is not staged by the same method as other haematological malignancies using the Ann Arbor classification. This disease behaves in a similar way to solid tumours and should therefore be staged using the adapted TNM staging system proposed by Clemens et al. in 2016<sup>5</sup> (Table 1). This provides better prognostic information on which to aid decisions on further treatment options (including radiological monitoring, radiotherapy or chemotherapy), patient follow up, and risk of recurrence.

**TNM staging for breast implant-associated anaplastic large cell lymphoma as proposed by Clemens et al<sup>5</sup>.  
Reproduced with permission of Wolters Kluwer Health**

TNM stage	Description
<i>Tumour extent</i>	
T1	Confined to effusion or luminal side of capsule
T2	Superficial infiltration luminal aspect of capsule
T3	Sheets or clusters of cells infiltrate thickness of capsule
T4	Lymphoma infiltrates beyond capsule into breast or soft tissues
<i>Lymph node</i>	
N0	No lymph node involvement
N1	One regional lymph node
N2	Multiple regional lymph nodes
<i>Metastasis</i>	
M0	No distant spread
M1	Spread to other organs / distant sites

**Table 1**

It is a requirement in the United Kingdom for all cases to be centrally registered with the Medicines and Healthcare Products Regulatory Agency (MHRA) through the Yellow Card Scheme.<sup>6</sup> It is also essential that the potential risks of this condition must be explained to patients prior to breast augmentation or reconstruction with an implant.<sup>7</sup>

## Conclusion

This case highlights BIA-ALCL as a rare but serious complication of breast implantation. These specimens require careful microscopic evaluation, with additional sampling required compared with a conventional capsulectomy specimen when there is a high index of suspicion, even in the context of a negative pre-operative cytology specimen. Staging is performed using the proposed TNM system, which more accurately reflects the course of the disease to the clinician and patient. ◆

## Practice points

- Be wary of negative cytology samples in the context of high clinical suspicion.
- BIA-ALCL can be very focal so careful microscopic examination is essential and consider taking additional blocks.
- The atypical cells are CD30+ and ALK-. A proportion can show EMA positivity.
- BIA-ALCL is staged as for carcinomas using the TNM staging system (albeit a TNM staging created specifically for these tumours rather than being the same as for primary breast carcinoma) rather than the Ann Arbor classification for lymphomas.
- All cases of BIA-ALCL must be reported to Medicines and Healthcare Products Regulatory Agency (MHRA)

## REFERENCES

- 1 Keetch Jr JA, Creech BJ. Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. *Plast Reconstr Surg* 1997; **100**: 554–5.
- 2 Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood* 2016; **127**: 2375–90. <https://doi.org/10.1182/blood-2016-01-643569>.
- 3 Jones JL, Hanby AM, Wells C, et al. National Co-ordinating Committee of Breast Pathology. Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL): an overview of presentation and pathogenesis and guidelines for pathological diagnosis and management. *Histopathology* 2019; **75**: 787–96. <https://doi.org/10.1111/his.13932>. Epub 2019 Oct 6. PMID: 31166611.
- 4 Jones P, Mempin M, Hu H, et al. The functional influence of breast implant outer shell morphology on bacterial attachment and growth. *Plast Reconstr Surg* 2018; **142**: 837–49.
- 5 Clemens MW, Medeiros LJ, Butler CE, et al. Complete surgical excision is essential for the management of patients with breast implant-associated anaplastic large-cell lymphoma. *J Clin Oncol* 2016 Jan 10; **34**: 160–8. <https://doi.org/10.1200/JCO.2015.63.3412>. Epub 2015 Nov 30. Erratum in: *J Clin Oncol*. 2016 Mar 10;34(8):888. DiNapoli, Arianna [corrected to Di Napoli, Arianna]. PMID: 26628470; PMCID: PMC4872006.
- 6 Medicines & Healthcare Products Regulatory Agency (MHRA). Breast implants, all types, makes and models – continue to report suspected cases of breast implant associated - anaplastic large cell lymphoma (MDA/2018/027). 2018, <https://www.gov.uk/drug-device-alerts/breast-implants-all-types-makes-and-models-continue-to-report-suspected-cases-of-breast-implant-associated-anaplastic-large-cell-lymphoma-mda-2018-027> (accessed 21 October 2020).
- 7 Joint Statement between ABS, BAAPS, BAPRAS & MHRA on BIA-ALCL. 2018. Accessed 21st October 2020: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/729612/180725\\_BIA-ALCL\\_Joint\\_Statement.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/729612/180725_BIA-ALCL_Joint_Statement.pdf).

## Self-assessment

**1. Which of the following is only identified in capsulectomy specimens containing BIA-ALCL? (Choose one option)**

- A. Silicone extravasation
- B. Foreign body giant cell reaction
- C. Atypical lymphoid cells with pleomorphic nuclei
- D. Chronic inflammation
- E. Fibrous capsule

Answer: C - Atypical lymphoid cells with pleomorphic nuclei

**2. Which are the most common clinical presentations of BIA-ALCL? (Choose two options)**

- A. Peau d'orange
- B. Mass in breast
- C. Mastalgia
- D. Nipple inversion
- E. Seroma fluid formation

Answer: B – Mass in breast and E – Seroma fluid formation