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

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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 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 and further defined by the World Health Organization (WHO) classification of lymphoid neoplasms in 2016. The most common clinical presentation is with a seroma (fluid swelling) adjacent to the implant, or less commonly the development of a mass. 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. This demonstrates the need for caution where fluid cytology is found to be negative but
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, 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. 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.

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 Arbour 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 (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.

**Table 1**

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

**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.
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. 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.

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 preoperative 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)

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

REFERENCES