




# First Case Report of Breast Implant Associated-Anaplastic Large Cell Lymphoma from India: Are We Ready?

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## Abstract

Breast implant associated-anaplastic large cell lymphoma (BIA-ALCL) has become a hot topic in recent plastic surgery and oncology forum. Its cases have been on the rise since its first emergence more than two decades ago. This condition is less known and management guidelines are still evolving. BIA-ALCL was seen recently with a classical presentation in one of our patients, who underwent immediate reconstruction with a macro-textured silicone implant following breast cancer surgery. We want to add the first case report from India to the global information database. There are still unanswered questions in its management, and we wish to highlight the same to make way for further research. With the rise in aesthetic and reconstructive implant surgeries, the knowledge of BIA-ALCL must expand among oncologists, radiologists, and pathologists for early identification and treatment for better patient outcomes.

## Keywords

- ▶ breast implant associated-anaplastic large cell lymphoma
- ▶ breast implant lymphoma
- ▶ BIA-ALCL in India

## Introduction

BIA-ALCL is a distinct type of T-cell lymphoma and is strongly associated with textured implants with grade 3 or 4 surfaces.<sup>1</sup> There have been roughly 1,148 cases worldwide since the first case was reported in 1997.<sup>2,3</sup> In Asia, there have been four cases reported to date from Japan, Thailand, South Korea, and Taiwan.<sup>4–6</sup> We report the first case of BIA-ALCL from India. Cordeiro et al calculated the risk as 0.311 per 1000 person-year in a single center study.<sup>7</sup> The recent NCCN guidelines (2019) give a detailed protocol for assessing and managing the patient.<sup>8</sup>

In this article, we intended to summarize the recent updates and raise a few pertinent questions to our community for further debate, discussion, and action.

## Case Report

A 53-year-old female patient presented to our center previously with infiltrating ductal carcinoma of the right breast. She underwent mastectomy with sentinel lymph node biopsy and immediate right breast reconstruction with latissimus dorsi musculocutaneous pedicled flap and macro textured implant (Nagor extra-high profile silicone cohesive gel-filled,

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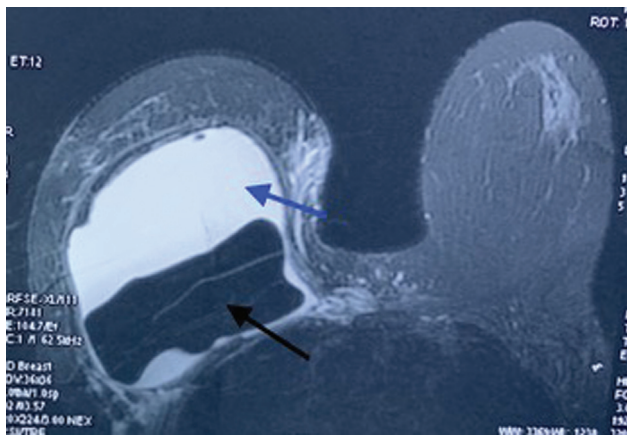
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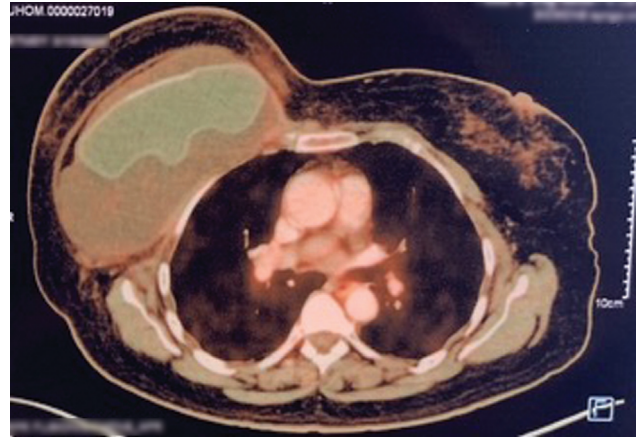
**Fig. 1** Image showing sudden enlargement of reconstructed right breast extending above her upper pole. The implant could be palpated separately, along with the cystic consistency of the breast.

GFX-EHP, GC Aesthetics, Glasgow) followed by adjuvant chemotherapy. Her sentinel lymph nodes were free of tumor. Now, 6 years later, she again presented to us with a sudden increase in the size of the reconstructed breast over 10 days. As she had recently had mammography, there was a suspicion of an implant rupture. On evaluation, she had a non-tender cystic enlargement of the right breast (→**Fig. 1**). The MR mammogram and ultrasound revealed an extensive fluid collection around the intact implant with no enlarged lymph nodes in the axilla and no solid tumor in the capsule (→**Fig. 2**). The PET scan did not show avid isotope uptake in the capsule or axilla (→**Fig. 3**). Ultrasound-guided diagnostic aspiration of peri-implant fluid was performed, and the same was sent for cell block to cytopathology.

The fluid was centrifuged, and cytospin smears were prepared; both air dried, and wet fixed smears were made



**Fig. 2** Magnetic resonance mammogram showing T2-weighted image of the implant in the center (black arrow) with surrounding fluid (blue arrow). No nodules were seen in the capsule, and no lymphadenopathy in the axilla.



**Fig. 3** PET scan of the right breast with normal uptake in the capsule and axilla.

and stained with MGG (May Grunwald Giemsa) and Pap (Papanicolaou) stain, respectively. On examination, the smears were cellular and composed of large pleomorphic cells arranged in a dispersed pattern. These cells were 1.5- to 5-fold more significant than small, mature lymphocytes, with pleomorphic nuclei, prominent nucleoli and moderate to abundant vacuolated cytoplasm (→**Fig. 4A**).

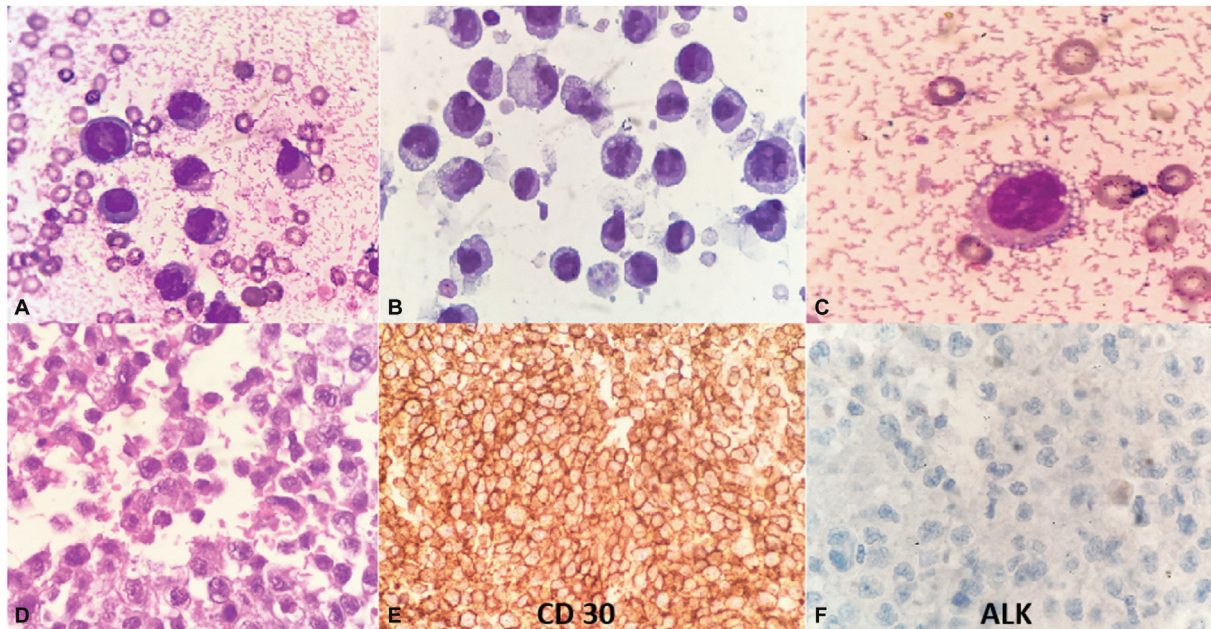
A cell block was prepared from the smears and stained with hematoxylin and eosin (H and E). The hallmark cells with kidney-shaped or horseshoe-shaped nuclei were seen (→**Fig. 4B**). A few mononucleated and multinucleated cells were seen. Subsequent immunocytochemistry (ICC) revealed atypical cells which were immunopositive for CD45 and CD30 but negative for cytokeratin (CK), CD3, CD20, CD4, CD2, CD8, CD79a, and ALK (alkaline phosphatase). Based on the above findings, ALK-negative anaplastic large cell lymphoma was diagnosed.

She underwent en bloc capsulectomy and removal of implant. The capsule was intact but adherent to the ribs on the posterior aspect and some fluid spillage could not be prevented (→**Figs. 5 and 6**). The capsule was removed entirely, and the cavity was thoroughly washed and closed with a drain (→**Fig. 7**). The fibrous tissue adhered to the implant surface and was sent for culture, which was found to be sterile (→**Fig. 8**).

The mastectomy scar and implant capsule were sent for histopathology. The sections prepared from scar mastectomy showed only chronic inflammation with no evidence of malignancy. The capsule cavity was lined by palisaded histiocytes, granulation tissue, and mixed inflammatory infiltrates composed of lymphocytes, plasma cells, and eosinophils and a few neutrophils along with variably sized fibrotic nodules scattered throughout the cavity.

Immunostaining for CD30, ALK, and CD68 was performed on a section from capsule and the cells were negative for CD30 and ALK, whereas CD68-positive histiocytes were present in the inflammatory infiltrate (→**Fig. 9**).

The patient was staged as IA as per the TNM classification.



**Fig. 4** (A) Pleomorphic cells with prominent focal nucleoli and a moderate amount of focally vacuolated cytoplasm (MGG,1000x). (B) The hallmark cells with horseshoe-shaped nuclei (arrow) (Pap, 1000x). (C) Neoplastic cells showing large multilobulated nuclei, moderate to abundant cytoplasm (MGG,1000x). (D) Cellblock section showing pleomorphic cells lying in a dispersed fashion (H and E,1000x). (E) Malignant cells with strong positive staining for CD30 on the cell membrane and Golgi region (CD30,1000X). (F) Neoplastic cells are negative for ALK (ALK, 1000x).

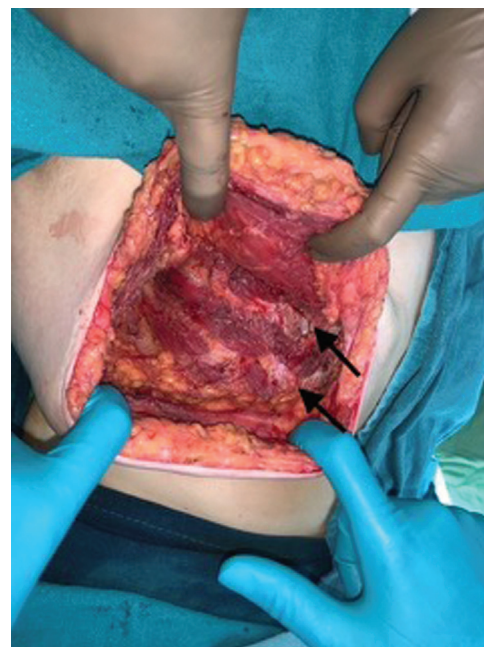
The case was discussed with international faculty and oncology colleagues. The consensus was only to do a close follow-up of the patient as per the NCCN recommendation. The patient has been followed up for 5 months until recently and remains well and disease free.

To investigate whether the Indian Plastic Surgery fraternity is ready to deal with this serious issue, we conducted a survey of our Indian plastic surgeons on BIA-ALCL. In a survey of 450 Indian plastic surgeons, we found that despite more than 91% of plastic surgeons being aware of BIA-ALCL, only 58% educate their patients about the condition, and 25% educate them only sometimes. Also, 30% of plastic surgeons had seen late seroma

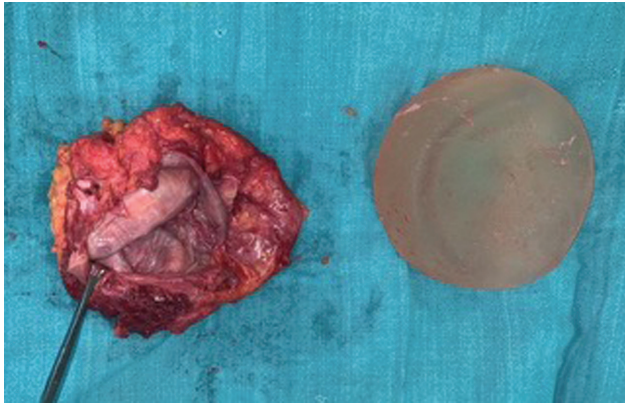
cases, but only two-thirds sent the fluid for cytology and pathology. No cases of BIA-ALCL were diagnosed by the respondents. Almost 46% of surgeons preferred smooth implants and 30% chose micro/nanotextured implants. However, 22% still preferred macro-textured implants.



**Fig. 5** Image showing intact implant capsule covered with latissimus dorsi muscle.



**Fig. 6** Image showing the areas of adhesion of the posterior part of the capsule with ribs. The site is marked with difficulty in dissection and there is a possibility of capsule rupture during this surgery step.



**Fig. 7** The image showing capsule with a smooth inner surface and no nodularity. The implant was intact.



**Fig. 8** The posterior surface of the macro-textured implant with adhered fibrous tissue.

## Discussion

There are still many unanswered questions regarding the diagnosis and management of BIA-ALCL. With the formal

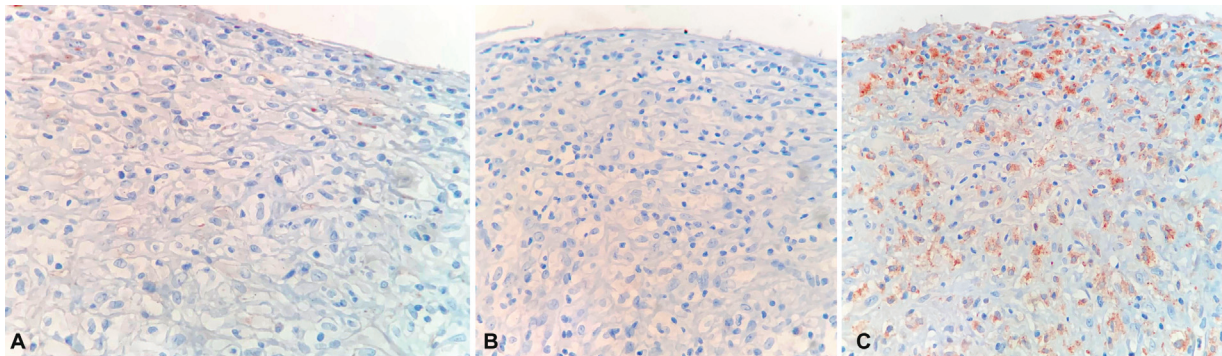
arrival of BIA-ALCL in India, it is paramount for the fraternity to heighten its awareness. Early recognition of this disease is associated with a good prognosis, less morbidity and a high 5-year survival rate.<sup>9</sup>

We have four important questions for our fraternity:

1. Is it not the time for us to discuss and start a formal 'Indian Breast Implant Registry'? No evidence-based research is possible without this database. In our view, this should be made a legal requirement for all breast implant surgeons.
2. There are no clear guidelines for managing peri-implant fluid spillage during capsulectomy. Does it require any adjuvant therapy? So far, none is suggested in the current guidelines, but no sizeable long-term study has addressed this question.
3. What is the role of the microbiome in the development of BIA-ALCL? Although many bacteria, such as *Ralstonia* spp. and *Staphylococcus* spp. have been isolated in many BIA-ALCL cases, no causal relationship has been established.<sup>10</sup>
4. Have surgeons discussed this entity with their local cytopathologists or another regional advanced center, as they are the key to clinching the diagnosis? Due to the rarity of this entity, their local laboratory may even be ill-equipped to do the detailed and advanced flow cytometry and immunohistochemistry, and a tie-up with a regional advanced cytopathology center may be necessary. A detailed cytopathological protocol, as already described above, must be put into place never to miss even a single case of BIA-ALCL.<sup>11</sup>
5. Does the patient's ethnicity play a role in the etiopathogenesis of BIA-ALCL? The genetic biomarkers of each patient may be done, which can predict the development of BIA-ALCL.

## Conclusion

With increasing incidence and recognition, the cases of BIA-ALCL will rise in India. Our national associations must formulate and implement an 'Indian Breast Implant Registry' to collect scientific data to provide accurate data and facilitate evidence-based research. All implant-associated seromas should be subjected to proper cytology and diagnostics.



**Fig. 9** Immunohistochemistry (IHC) of the capsule; A: The inflammatory cell infiltrate in the capsule wall is negative for CD30. B: The inflammatory cell infiltrate in the capsule wall is negative for ALK immunostains. C: IHC for CD68 demonstrates a fair number of histiocytes admixed with other inflammatory cells in the capsule wall.

There is an acute need for relevant National guidelines on implant handling at primary surgery and management of BIA-ALCL within a multidisciplinary forum.

#### Conflict of Interest

None declared.

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