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A case report: B cell lymphomas associated with breast implants

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Abstract:
Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is predominantly a T-cell lymphoma, with rare cases of B-cell lymphoma reported. As of April 2020, 68 BIA-ALCL cases were confirmed in the UK and approximately 800 worldwide, with 33 related deaths. Textured implants are implicated as the primary risk factor, as no cases have been linked to exclusively smooth implants.

Background:
The majority of the reported cases of lymphomas associated with breast implants of T-cell type-with anaplastic large cell lymphoma (ALCL). 6 cases of B-cell lymphoma associated with breast implants have been reported worldwide. All cases presented with unilateral breast involvement. As of April 2020, there are 68 confirmed reports of BIA-ALCL in the UK and about 800 cases worldwide, with 33 deaths attributed to BIA-ALCL. Reports suggesting that textured implants are the causative factor, as there have been no reported cases of BIA-ALCL in patients with a breast implant history which includes a smooth textured implant.

Case Presentation:
An 83 -year-old female with a history of breast augmentation over 40 years with subsequent bilateral sub-pectoral implant exchange 8 years ago with Nagor silicone implants, right side 360cc, left side 240cc. Presented to the one stop breast clinic with bilateral diffuse breast pain more on the left breast for 5-month duration. She was clinically fit, non-smoker, on Ramipril for hypertension and Gabapentin for facial trigeminal neuralgia. She didn't t have any children. There was no family history of note.

On examination, a grade 4 capsular contracture on the left side with some waterfall deformity with breast tissue that has closed below the implant. There was some tenderness elicited on the inferior aspect of the left sided implant. There were no palpable masses within the breast tissue itself. There was no lymphadenopathy on both axillary regions. The contralateral right breast implant was soft with a grade 2 capsular contracture.

Bilateral mammography performed showing marked radial folding and capsular calcification particularly on the left side. Ultrasound scan revealed periprosthetic fluid within the radial folds of the implant suggesting no evidence of rupture, however more compatible with prior implant exchange. Ultrasound guided aspiration performed and sent for cytological analysis. Cytology revealed no malignancy, CD30 was negative. MRI both breasts has shown bilateral single lumen breast implants in place. The left implant appears contracted compared to the right and there was some free silicone seen within the left axilla.

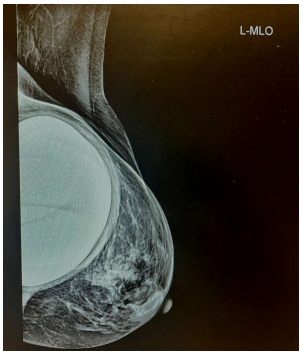

Fig (1). Mammogram of left breast mediolateral view

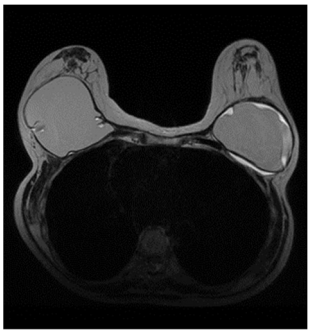

Fig (2). MRI breast showing calcifications on the left side

Multidisciplinary team meeting (MDT) recommended bilateral implant removal with partial capsulectomy which was performed and part of the capsules on both sides sent for histopathological assessment. Pathology revealed, left side capsule was associated with diffuse large B-cell lymphoma (DLBCL) and Epstein-Barr virus (EBV) positive.

Positron emission tomography (PET) scan for staging was requested and revealed a left 16mm low grade fluorodeoxyglucose (FDG) avid elongated lymph node. A second look axillary ultrasound scan demonstrated a snowstorm appearance in a low lying left axillary lymph node which was indicative of previous implant rupture and free silicone however, the visible lymph nodes within the left axilla appeared within normal limits and retain a normal morphology.

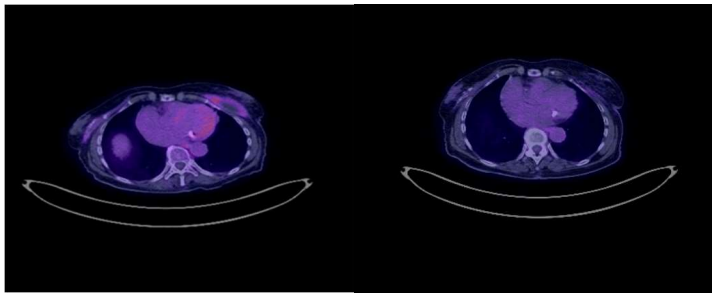

Fig. (3), (4) Preoperative and postoperative PET scan respectively

A left breast En-bloc total capsulectomy was done with careful dissection off the pectoralis muscle. Specimen was sent for histopathological assessment. Gross features revealed a fibrofatty grey and yellow piece of capsule tissue measuring 60x55x15mm and weighing 22g. The external surface was ragged. The inner surface was

ragged and tan plus yellow in color with calcified area. The capsule wall measures up to 8mm. The specimen was serially sliced. Representative sections were taken which confirmed a residual small focus of "Breast implant associated EBV positive and Diffuse Large B cell lymphoma". Additional immunohistochemistry disclosed that the atypical cells are positive for CD20 and CD79a and are negative for CD3, CD5 and ALK1. A background mixed population of B cells (CD20 and CD79a) and T cells (CD3 and CD5) was scattered elsewhere.

Patient was then referred for Heme-oncology review after proper staging (stage 1C, T3 N0 M0), who recommended adjuvant radiotherapy as the disease was localized and capsulectomy revealed clear margins. Being non-extensive disease, chemotherapy wasn't recommended. A referral to the Royal Marsden Hospital took place and a dose of 30 Gy in 15 fractions was advised. Radiotherapy was completed and a follow up PET scan was requested and revealed no evidence of metastasis with complete resolution of FDG avidity in left breast and axilla.

Fig. (5) Gross appearance of left En-bloc total capsulectomy

Discussion:

Anaplastic large cell lymphomas (ALCL) are a rare type of primary breast lymphoma. The association between breast implants and ALCL was first described in 1997. Breast implant associated (BIA)-ALCL arises from the inflammatory T cells predominately. Lymphoma cells were positive for CD20, CD5, BCL-2, CD21, CD23, IgD, IgM, with very low Ki-67 of 1%. Nevertheless, cases of ALCL associated with breast implants are rare but much more documented in the literature than B-cell lymphomas associated with breast implants, as in this patient.

In contrast with a case series by L.J. Medeiros et al. on 8 patients diagnosed with EBV+ large B-cell lymphoma with breast implant, there were few significant morpho-logic differences between Anaplastic t-cell lymphoma and EBV + large B cell lymphoma as well as oncologic outcome post removal of implant and total capsulectomy. Their case series suggested that the pathogenesis of EBV+ large B-cell lymphoma is uniquely related to textured breast implants and differs, at least in part, from cases of fibrin-associated large B-cell lymphoma which accounts for 90% of breast lymphoma in general. This conclusion is in line with the opinion of Rodriguez-Pinilla et al. who suggested the term breast- implant-associated EBV+ large B-cell lymphoma. The pathogenic mechanisms are not yet understood, but localized immunosuppression with high IL-10 levels as well as hypoxia have been postulated according to their study.

No standardized treatment plan apart from implant removal and total capsulectomy as per literature and guidelines. L.J. Medeiros et al. stated in their case series that only one patient with invasive lymphoma received 3 cycles of chemotherapy in the form of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), as well as intrathecal methotrexate. Similarly, Chen, Vivi W et al. presented a case report of bilateral

EBV+-large B cell lymphoma bilaterally who had previous history of Hodgkin's lymphoma and had to have adjuvant rituximab. In our report, we recommended radiotherapy because the patient had two-staged operations and was only diagnosed post her first surgery of explanation and partial capsulectomy.

On 18 November 2019 an Australian article provided the first statistical data showing the incidence of BIA-ALCL. The article provides an analysis of all cases of BIA-ALCL reported in Australia since 2007. The team found that the risk of BIA-ALCL for three implant brands, based on sales data and single implant exposure, was as follows: one in 2596 patients with Silimed PU implants; one in 3194 patients with Allergen Biocell implants; and one in 6024 patients with Nagor implants.

This latest data contrasts significantly with the risk incidence published by the Medicines and Healthcare products Regulatory Agency (MHRA), the UK regulator, which at the moment indicates that BIA-ALCL has an incidence rate of 1:24,000 cases. Importantly, that figure takes account of all implants in the UK and, in contrast to the Australian data, provides no breakdown by brand. The available evidence indicates that the risk of BIA-ALCL is significantly higher for some types of breast implants, than others.

In October 2019, the sale of all higher surface area/textured implants were suspended from the Australian market. The authors conclude that their data supports the growing consensus that '***implants with higher surface area and surface roughness confer significantly higher risk to patients'***. Identification of a relationship between breast cancer and silicone is still ongoing in the literature, with long-term clinical follow up required.

CONCLUSION

In summary, we presented a case of a patient with unilateral breast implant-associated EBV +, diffuse B-cell lymphoma with longstanding history of breast implants for augmentation. Literature confirmed that BIA – ALCL is rare and B cell lymphoma is even rarer, discussion of breast implant-associated lymphoma continues, it is our hope that researches establishing a clear link between breast implants and lymphomas in order to properly guide diagnosis, management and prognosis.

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