ISSN: 2578-3335 (Print) 2578-3343 (Online)

Volume 4 | Issue 1 Article 10

2022

Breast Implant-Associated Anaplastic Large Cell Lymphoma: A Case Report

Jennie Tan
Kettering Medical Center, jengt27@gmail.com

Jamie Johnson-Eddy
Wright State University/Boonshoft School of Medicine, jjohnsoneddy@gmail.com

Wesley Tang
Kettering Medical Center, wctang24@gmail.com

Yanchun Li
Kettering Pathology Associates, yanchun.li@ketteringhealth.org

Breast Implant-Associated Anaplastic Large Cell Lymphoma: A Case Report

Breast Implant-Associated Anaplastic Large Cell Lymphoma: A Case Report.

Jennie Tan, DO[1]*, Jamie Johnson-Eddy, MD[2], Wesley Tang, DO[1] & Yanchun Li, MD[1]

[1]Kettering Medical Center, Kettering, Ohio

[2]Boonshoft School of Medicine, Wright State University

*Corresponding author: jennie.tan@ketteringhealth.org (Jennie Tan, DO)

ABSTRACT

This report aims to review a case of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) by comparing the patient's course with the current literature.

BIA-ALCL is a specific type of T-cell lymphoma that can develop after breast implantation, but has only recently been recognized within the last decade. Although overall rare, certain types of breast implants have increased association with developing subsequent lymphoma. This case occurred after mastectomy with breast reconstruction for unilateral invasive ductal carcinoma with a textured, saline Allergan breast implant. BIA-ALCL manifested and was symptomatic nine years after implantation.

Keywords: breast implant, ALCL, textured implant, lymphoma

BACKGROUND

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is rare, but as the number of reported cases grows, so has its global recognition. The first case of breast implant-associated anaplastic lymphoma was reported in 1997 by Keech and Creech with a McGhan (now Allergan) textured saline implant.[1] In 2011, after 34 published cases, the U.S. Food and Drug Administration (FDA) issued a safety communication to announce the possibility of an association between breast implants and developing anaplastic large cell lymphoma in the scar capsule adjacent to the implant.[2] In 2016, the World Health Organization officially recognized an association between breast implants and ALCL from approximately 258 reported cases.[3] In July of 2019, the FDA requested Class I recall of the Allergan Natrelle BIOCELL Textured Products.[4] Allergan subsequently announced a voluntary worldwide recall of their textured saline and silicone implants, as well as their tissue expanders. By October 2019, the American Society of Plastic

Surgeons confirmed 809 cases of BIA-ALCL worldwide.[5] The exact number of BIA-ALCL has been difficult to determine because of underreporting, lack of awareness, lack of worldwide breast implant sales data, and fear of litigation.[6,7] We will review a specific case of BIA-ALCL after Allergan textured saline implant breast reconstruction.

Case description

A 73-year-old Caucasian woman with a past medical history of papillary thyroid carcinoma and right breast cancer presented with chest pain. She had been diagnosed eight years prior with invasive ductal carcinoma of her right breast (ER/PR positive, HER2 negative). For treatment, she underwent a right simple mastectomy with reconstruction using a permanent Allergan textured, shaped saline implant. Based on her staging and pathology, no adjuvant therapy nor hormonal therapy was indicated. Her last screening mammogram had been two years ago of her left breast that showed scattered fibroglandular densities, interpreted as breast imaging reporting and data system – 1 (BI-RADS-1) normal.

At presentation, her chest pain was described as sharp and pleuritic, accompanied by chest congestion, wheezing, and a non-productive cough. Acute coronary syndrome and respiratory workup were negative, and she was discharged home with five days of prednisone therapy and a refill of her home albuterol inhaler. A month later, she returned with shortness of breath and swelling of her right breast, extending along her neck. Upon examination, she had fluctuance and a hard palpable rind consistent with a Baker Grade 3 capsular contracture around her saline implant. A computed tomography of her chest revealed a loculated fluid attenuation around her right breast implant without axillary or mediastinal lymphadenopathy Figure 1.

Two days later, she underwent ultrasound-guided aspiration of the fluid collection to remove 650 cc of straw-colored fluid. Initial flow cytometry analysis of the peri-implant fluid demonstrated 74% lymphocytes without immunophenotypic evidence of monotypic B-cell or aberrant T-cell population. After discussion with the patient, it was recommended that she undergo removal of the implant for suspected ALCL due to the abnormal presence of lymphocytes in her periprosthetic seroma.

Approximately one month later, she underwent surgical removal of her right breast implant with en bloc capsulectomy and drain placement. The fluid and capsule specimens were sent to a tertiary center for further analysis. Cytologic analysis revealed atypical cells with pleomorphic nuclei that stained positive for CD30, EMA, CD45, weakly CD3, and negative for AE1/3 and ALK (Figures 2, 3 and 4). These results were concerning for a lymphoproliferative process, specifically BIA-ALCL.

After drain removal, she had a PET-CT scan that revealed post-surgical inflammatory changes in the right chest wall without abnormal uptake elsewhere (Figures 5 and 6). TNM staging of BIA-ALCL was determined to be T2N0M0, confined to the effusion and capsule. She required no further treatment. She has denied further symptoms and has suffered no disease recurrence for two years.

DISCUSSION

BIA-ALCL is a unique type of non-Hodgkin's lymphoma. It is a T-cell lymphoma that develops in the scar capsule or fluid surrounding the breast implant consisting of large pleomorphic cells staining CD30 positive and ALK-1 negative. These lack anaplastic lymphoma kinase expression or genetic abnormalities involving systemic anaplastic lymphoma kinase at chromosome 2q23.[6] Because the lymphoma cells are initially contained inside the fibrous scar capsule that surrounds the breast implant, patients often present with breast pain, enlargement, asymmetry, mass, rash, and/or hardening of the breast caused by capsular contracture.[8,9] Most commonly, patients present with a late-onset, persistent seroma with breast pain and swelling at least 1 year after, but typically 9-10 years after placement of a textured breast implant.[7,9–11] One systematic review of BIA-ALCL in 2017 noted that 66% patients presented with an isolated late-onset seroma and 8% with an isolated new breast mass.[12]

When suspecting BIA-ALCL, National Comprehensive Cancer Network guidelines recommend imaging with ultrasound or MRI of the breast, which can reveal an effusion or seroma around the implant that can be sampled by fine needle aspiration.[7] If it presents as a mass, core needle biopsy or incisional biopsy should be obtained. The histopathological workup should include cytology, flow cytometry, and immunohistochemistry for CD30 and ALK markers. If pathology reveals strong CD30 positivity and EMA positivity, this should raise suspicion of BIA-ALCL, especially if ALK is negative.[8] ALCL can be detected with CD30, as it is a surface protein from the TNF receptor family not found in benign periprosthetic seromas.Per the 2016 World Health Organization classification of lymphoid neoplasms, diagnosis for BIA-ALCL is made by clinical correlation with immunohistochemical analysis of tumor cells expressing CD30+, ALK-, having large anaplastic morphology on cytology, and demonstrating a single T-cell clone.[3] TNM staging is classified as IA (35-70%, effusion only), IB (3-11%, confined to effusion or layer on luminal side of capsule), IC (8-13%, early capsule infiltration), IIA (8-25%, cell aggregates or sheets infiltrating the capsule), IIB (3-5%, lymphoma infiltrates beyond capsule), and III (3-9%, lymph node involvement) to stage IV (1-2%, metastasis).[7,13]

In 2017, the first U.S. retrospective review by Doren et al. attempted to determine the risk of developing BIA-ALCL and discovered that there seemed to be higher risk of developing primary breast ALCL with a textured implant than in the general population without such an implant.[6] Regarding the most recent estimation of total reports of BIA-ALCL worldwide, 481 of the 573 cases have occurred with the use of Allergan (formerly McGhan) textured implants and has resulted in 12 deaths.[4]

It is not currently known why there is an association between textured breast implants and ALCL, but there are several theories regarding pathogenesis. Chronic inflammation from the implant itself may be triggering the immune system, and over many years, may increase the risk of malignant

transformation.[14,15] Texturing the implant's surface can result in residual silicone particulate. This combined with a bacterial antigen may be promoting the activation and proliferation of T cells that are encouraged with a textured implant.[15,16] Activation of the JAK/STAT pathway may also suggest that investigation into possible genetic involvement may be needed. In a review of twenty-six BIA-ALCL samples, there was a high bacterial load with bacteria biofilm in both BIA-ALCL and nontumor capsule samples, but the microbiome of the BI-ALCL samples showed a greater proportion of Ralstonia species and less Staphylococcus species, suggesting an infectious contributing cause.[17]

Primary treatment is en bloc capsulectomy to remove the breast implant and the entire fibrous capsule as one piece, along with any suspicious masses or lymph nodes.[18] Bone marrow biopsy may be obtained if there is concern for local invasion or metastasis.[7] After surgical excision, the patient should be followed every 3-6 months for two years and consider CT or PET/CT every 6 months for surveillance of disease recurrence. If residual disease exists or if the lymphoma is advanced (stage IIB-IV), systemic therapy with Brentuximab vedotin, anthracycline-based systemic ALCL regimens, and/or radiation therapy should be discussed, based on results from the ECHELON-2 trial.11,19,20 ECHELON-2 compared brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone (A+CHP) therapy versus cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) therapy for the treatment of CD30-positive peripheral T-cell lymphomas and concluded that A+CHP therapy was superior to CHOP with improvement in overall survival.[19]BIA-ALCL is surgically curable with good prognosis and high survival rates when diagnosed in early stages.[6,11]

The case discussed here had the expected presentation and course of BIA-ALCL. She presented nine years after her unilateral mastectomy and breast reconstruction with an Allergan textured, saline implant. Her initial symptoms were chest pain and shortness of breath, followed by fullness and hardening of the capsule around her saline implant. Diagnosis was made by analysis of the periprosthetic fluid and tissue analysis after capsulectomy.

Efforts should be made to educate and inform those patients who have already received reconstruction with textured breast implants. With increased awareness, detecting additional cases will allow for further reviews to evaluate pathophysiology for future breast implant research. If a case is confirmed, it should be reported to the FDA through the Adverse Event Reporting program. BIA-ALCL should be treated by removing the fibrous capsule and implant using an en bloc oncologic resection method. The capsule should be further examined for confirmation of the diagnosis and staging to guide management.

REFERENCES

1. Keech J A, Creech B J. Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. *Plast Reconstr Surg.* 1997;100(2):554-555.
2. *FDA update on the safety of silicone gel-filled breast implants.* 2011.
3. Swerdlow S H, Campo E, Pileri S A. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood.* 2016;127(20):2375-2390.
4. *FDA takes action to protect patients from risk of certain textured breast implants; requests Allergan voluntarily recall certain breast implants and tissue expanders from market.* 2019.
5. *BIA-ALCL Physician Resources.* 2021.
6. Doren E L, Miranda R N, Selber J C. Epidemiology of Breast Implant-Associated Anaplastic Large Cell Lymphoma. *Plast Reconstr Surg.* 2017;139(5):1042-1050.
7. Clemens M W, Jacobsen E D, Horwitz S M. NCCN Consensus Guidelines on the Diagnosis and Treatment of Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL). *Aesthet Surg J.* 2019;39(Suppl_1):3-13.
8. Jones J L, Hanby A M, Wells C. 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(6):787-796.
9. Miranda R N, Aladily T N, Prince H M. Breast implant-associated anaplastic large-cell lymphoma: long-term follow-up of 60 patients. *J Clin Oncol.* 2014;32(2):114-120.
10. Brody G S, Deapen D, Taylor C R. Anaplastic large cell lymphoma occurring in women with breast implants: analysis of 173 cases. *Plast Reconstr Surg.* 2015;135(3):695-705.
11. Johnson L, O'donoghue J M, Mclean N. Breast implant associated anaplastic large cell lymphoma: The UK experience. Recommendations on its management and implications for informed consent. *Eur J Surg Oncol.* 2017;43(8):1393-1401.
12. Leberfinger A N, Behar B J, Williams N C. Breast Implant-Associated Anaplastic Large Cell Lymphoma: A Systematic Review. *JAMA Surg.* 2017;152(12):1161-1168.
13. Adrada B E, Miranda R N, Rauch G M. Breast implant-associated anaplastic large cell lymphoma: sensitivity, specificity, and findings of imaging studies in 44 patients. *Breast Cancer Res Treat.* 2014;147(1):1-14.

14. George E V, Pharm J, Houston C. Breast implant-associated ALK-negative anaplastic large cell lymphoma: a case report and discussion of possible pathogenesis. *Int J Clin Exp Pathol.* 2013;6(8):1631-1642.

15. Bizjak M, Selmi C, Praprotnik S. Silicone implants and lymphoma: The role of inflammation. *J Autoimmun.* 2015;65:64-73.

16. Laurent C, Haioun C, Brousset P, Gaulard P. New insights into breast implant-associated anaplastic large cell lymphoma. *Curr Opin Oncol.* 2018;30(5):292-300.

17. Hu H, Johani K, Almatroudi A. Bacterial Biofilm Infection Detected in Breast Implant-Associated Anaplastic Large-Cell Lymphoma. *Plast Reconstr Surg.* 2016;137(6):1659-1669.

18. Clemens M W, Medeiros L J, Butler C E. Complete Surgical Excision Is Essential for the Management of Patients With Breast Implant-Associated Anaplastic Large-Cell Lymphoma. *J Clin Oncol.* 2016;34(2):160-168.

19. Horwitz S, O'connor O A, Pro B. Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): a global, double-blind, randomised, phase 3 trial. *Lancet.* 2019;393:229-240.

20. Duvic M, Tetzlaff M T, Gangar P, Clos A L, Sui D, Talpur R. Results of a Phase II Trial of Brentuximab Vedotin for CD30+ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis. *J Clin Oncol.* 2015;33(32):3759-3765.

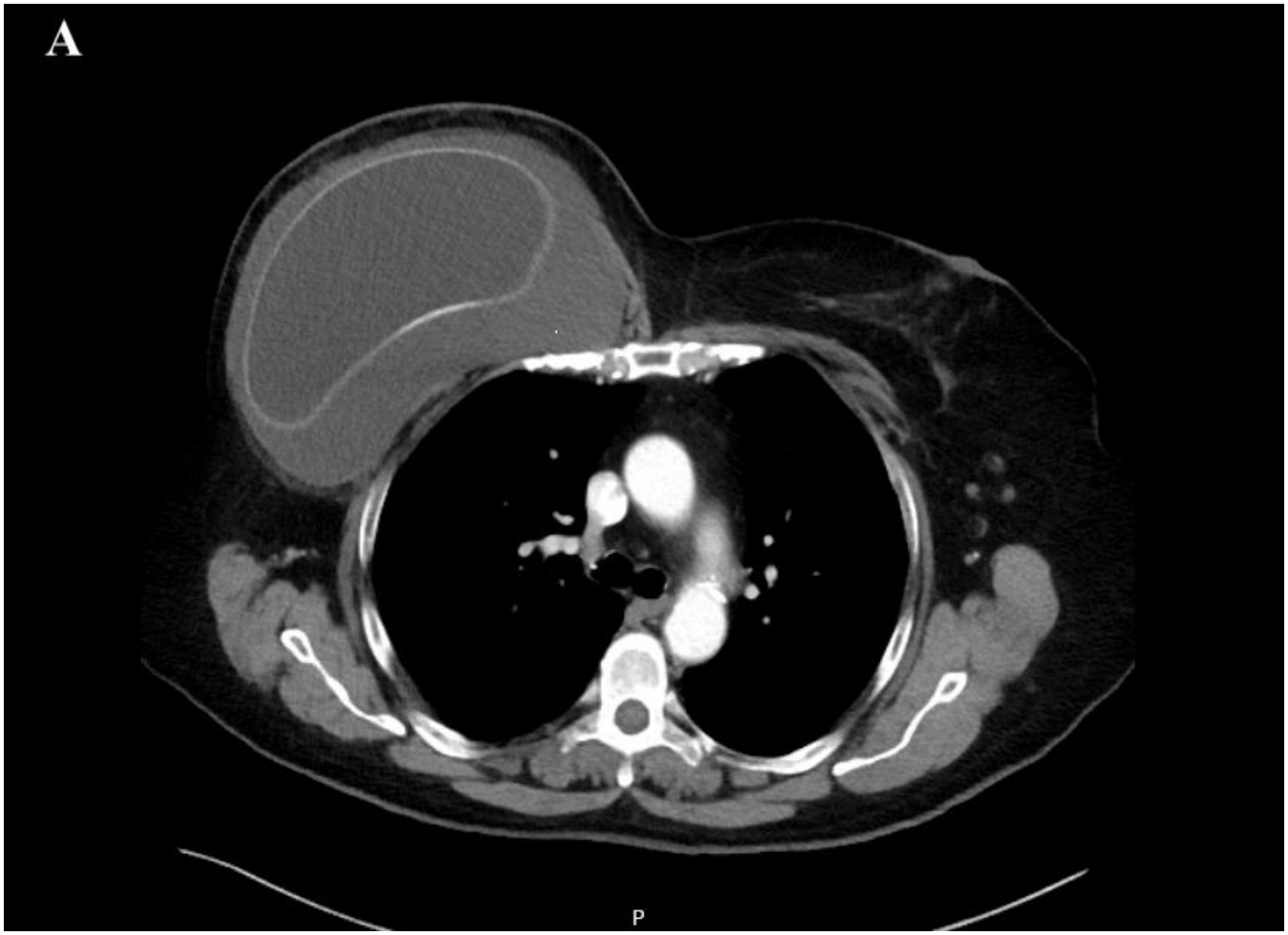

Figure 1 Computed tomography scan with peri-implant fluid.

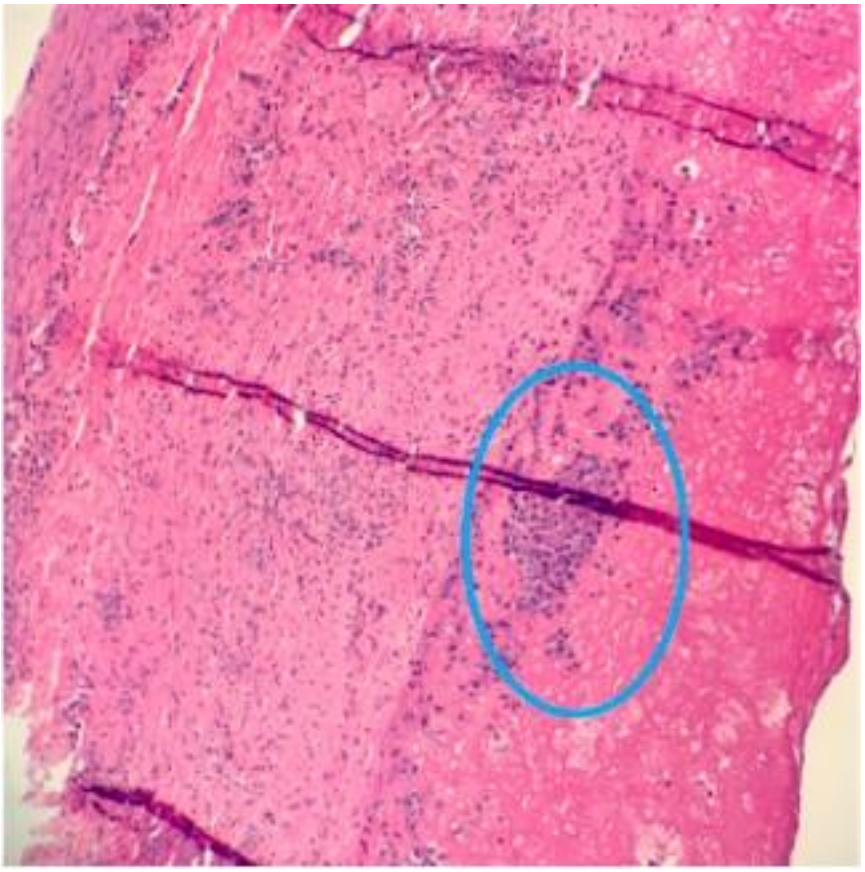

Figure 2 Right breast capsulectomy excision specimen. The tumor cells (circled) are not mass-forming. Abundant background fibrosis and inflammation (H&E 10x).

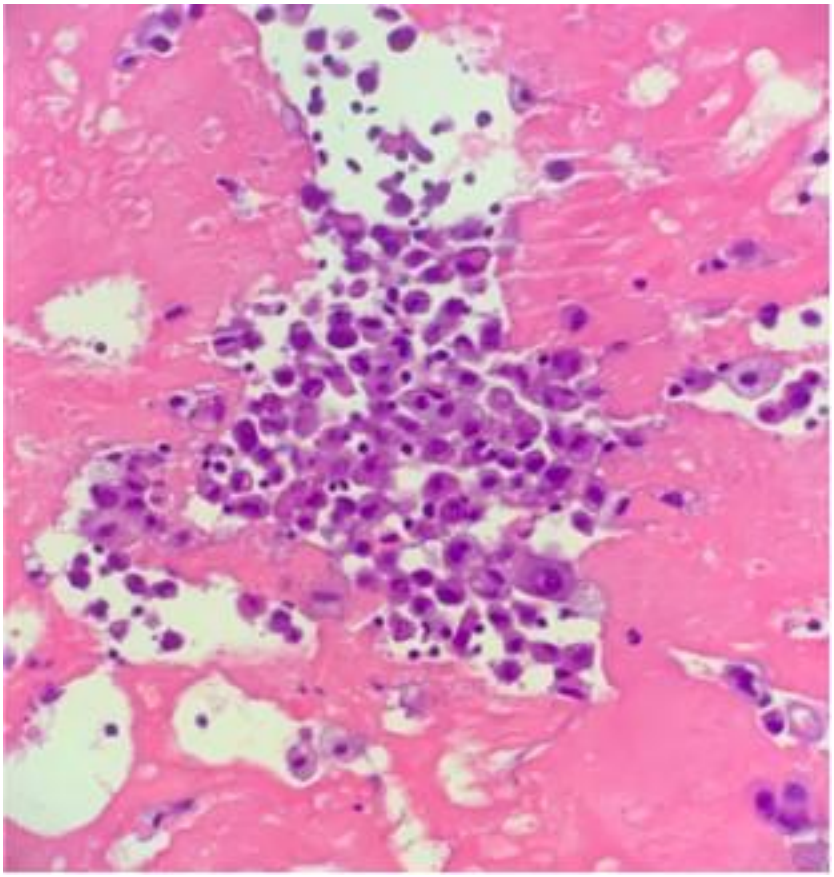

Figure 3 Atypical, pleomorphic cells (H&E 40x).

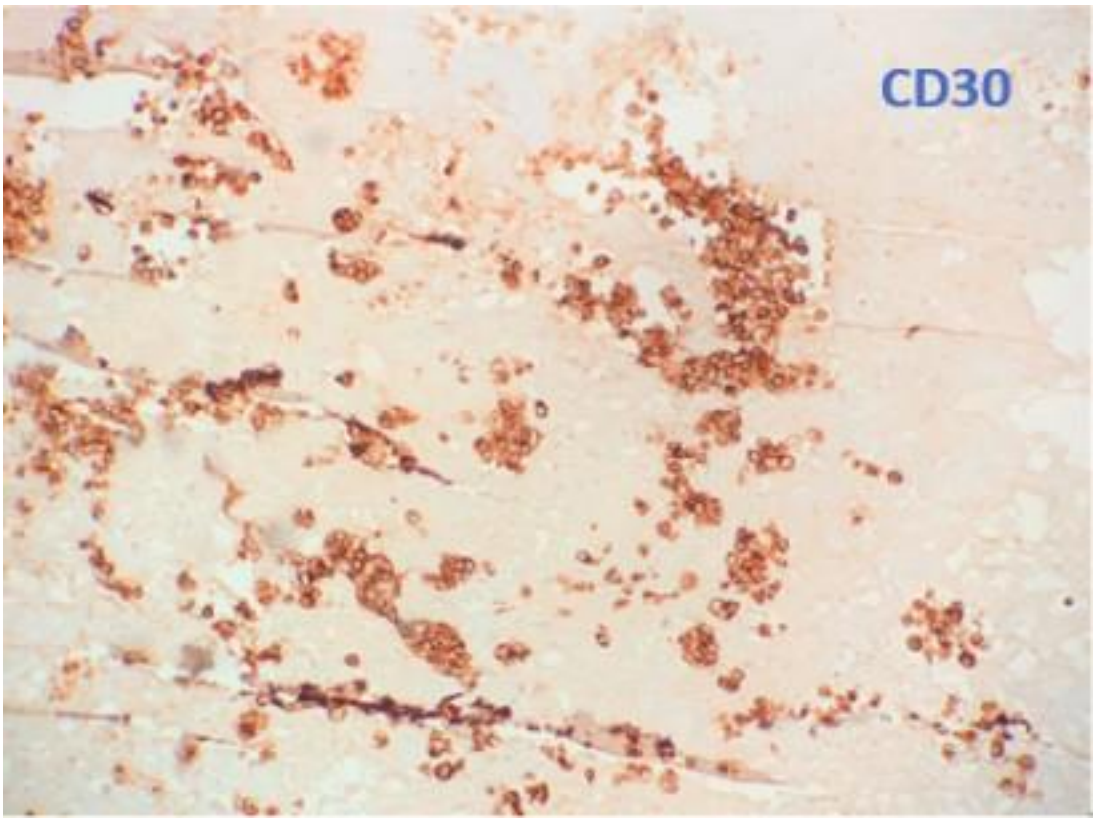

Figure 4 CD30 positive stain.

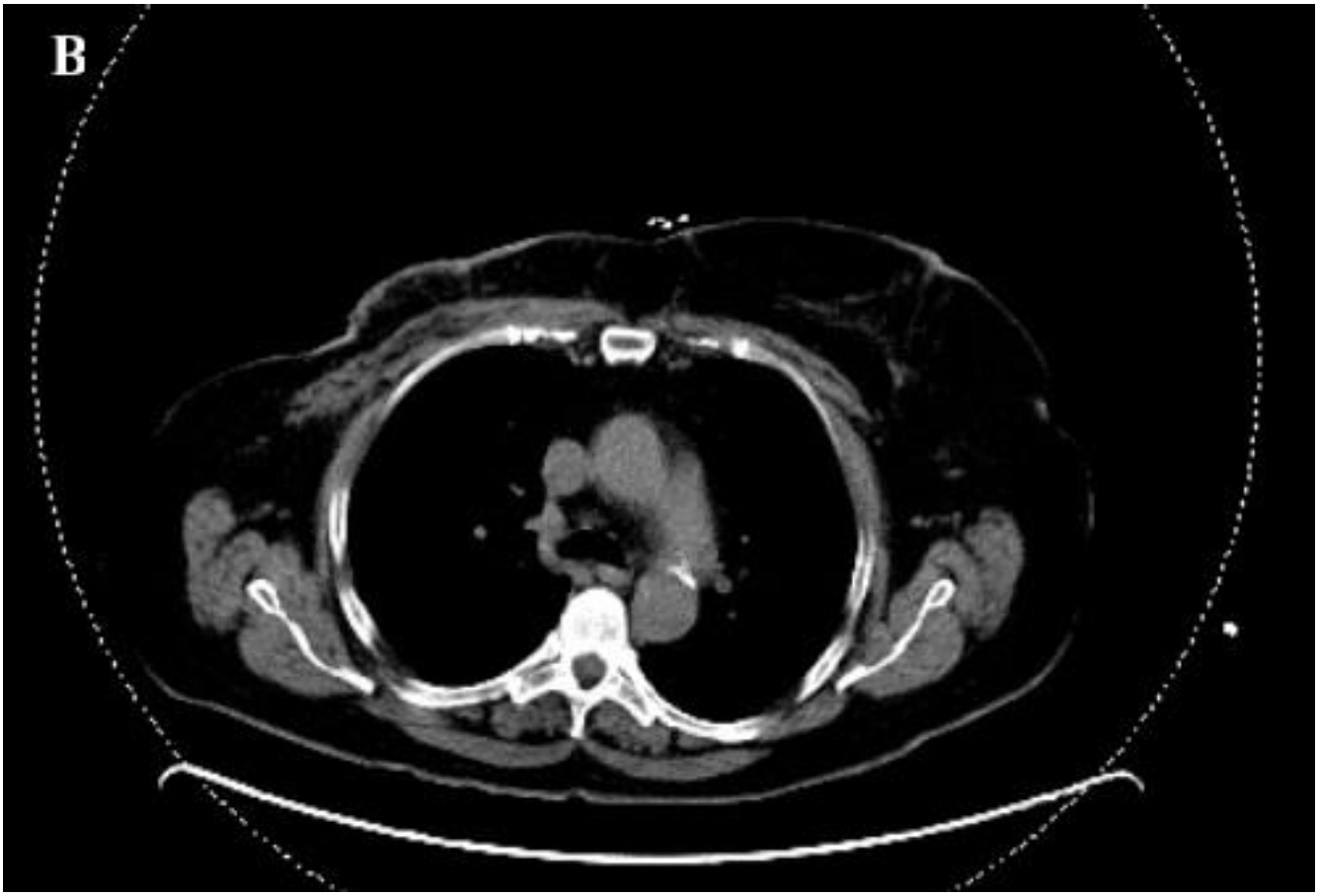

Figure 5 Computed tomography after en bloc capsulectomy in axial section.

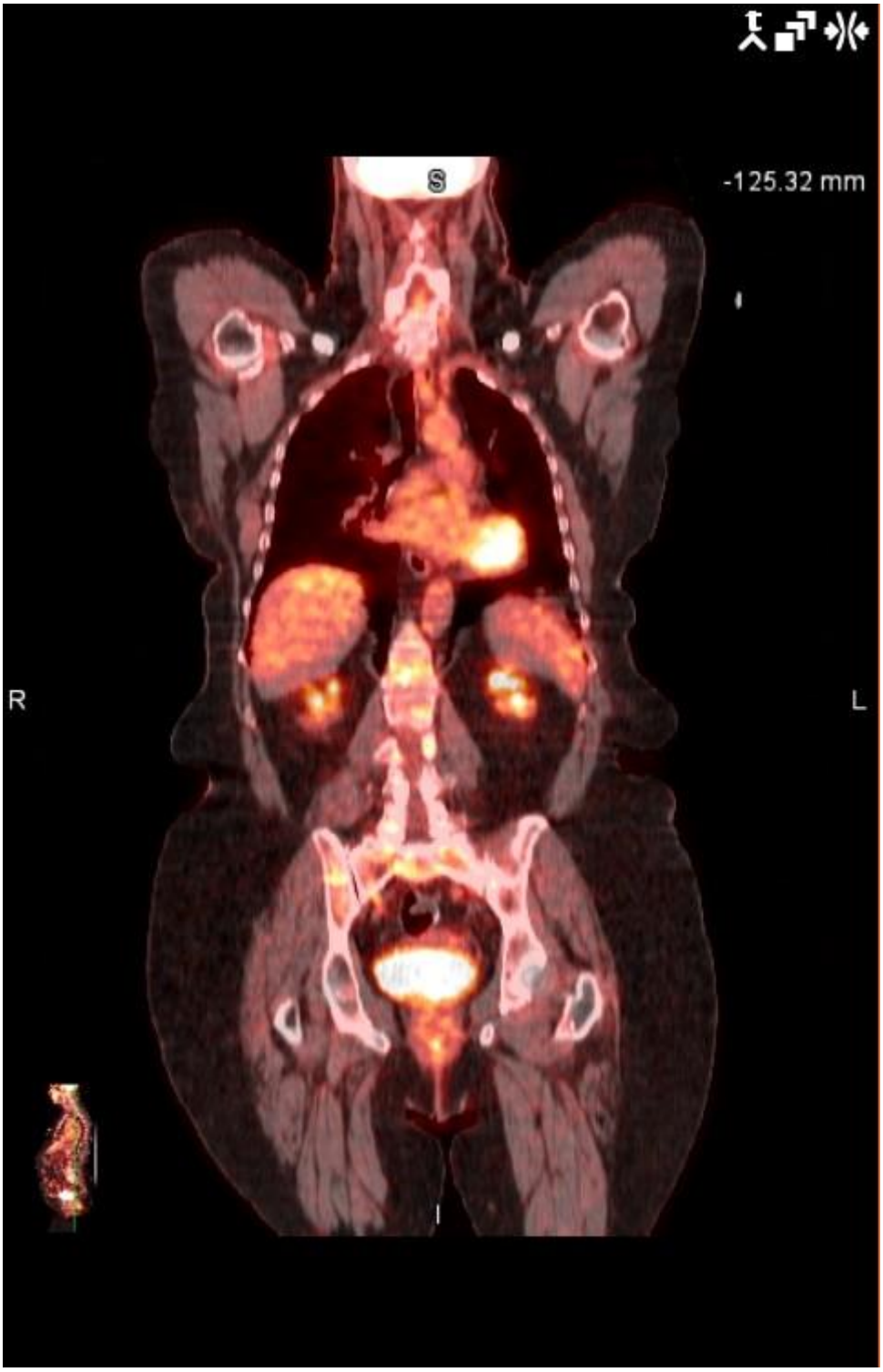

Figure 6 Positron emission tomography-computed tomography after en bloc capsulectomy in coronal section showing no metastatic disease.