Sarcoidosis Masquerading as Breast Implant-Associated Anaplastic Large Cell Lymphoma – The Importance of Definitive Pathology to Guide Therapy

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ABSTRACT

Introduction: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare critical outcome of breast implantation that typically presents 8 to 10 years after textured-implant placement with periprosthetic seroma. Treatment consists of implant removal and capsulectomy, which is typically curative. But in rare case, malignant infiltration through the capsule results in disseminated disease, necessitating aggressive treatment with systemic chemotherapy. Sarcoidosis, a chronic systemic granulomatous disease characterized by noncaseating granulomas, is another rare cause of periprosthetic seroma.

Case Presentation: A 61-year-old female with a history of invasive ductal carcinoma of the breast status post textured implant-based reconstruction presented with late periprosthetic seroma and overlying rash. Cytology of seroma aspirate was suggestive of BIA-ALCL, and positron emission tomography-computed tomography was concerning for invasive disease. Surgical specimen pathology of the implant-capsule complex and skin punch biopsy of the overlying rash revealed only granulomatous inflammation. The patient was diagnosed with sarcoidosis and spared systemic chemotherapy treatment for disseminated BIA-ALCL.

Conclusions: BIA-ALCL should be ruled out in all cases of late periprosthetic seroma. Definitive surgical pathology is necessary to prevent misdiagnosis and inappropriate treatment of masquerading entities, such as sarcoidosis.

INTRODUCTION

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is a rare critical outcome of breast implantation. Defined as a subtype of T-cell lymphoma with monoclonal expansion of CD30-positive cells, BIA-ALCL typically presents 8 to 10 years after textured-implant placement with periprosthetic seroma.[1] Treatment consists of implant removal and capsulectomy which is typically curative. However, in rare cases, there may be malignant infiltration through the capsule resulting in disseminated disease. In these cases, the two-year survival rate is 52.5%, necessitating aggressive treatment with systemic chemotherapy.[2]

Another rare cause of late periprosthetic seroma is sarcoidosis, a chronic systemic granulomatous disease characterized by noncaseating granulomas.[3] Sarcoidosis demonstrates a wide range of presentations, but breast involvement is reported in less than 1% of cases.[4] Diagnosing sarcoidosis can be difficult as it is a disease of exclusion. To differentiate between BIA-ALCL and sarcoidosis of the breast, flow cytometry, immunohistochemistry, and surgical pathology must be evaluated.[3]

CASE PRESENTATION

A 61-year-old female with past medical history of invasive ductal carcinoma of the left breast status post textured implant reconstruction 7 years prior presented to plastic surgery clinic for evaluation of acute onset swelling of her left breast. She was afebrile, with marked left breast swelling and a linear rash overlying her surgical scar consisting of light brown, nonblanching, shiny, fibrous papules.

Ultrasound-guided aspiration of the periprosthetic seroma yielded 200 cc of transparent, yellow fluid sent for cytology, immunohistochemistry, and culture. Microbiology culture was negative. Effusion fluid was processed using standard cytospin and cell block preparations. The formalin fixed paraffin imbedded block was used for immunohistochemical stains. Microscopic examination revealed an admixture of small lymphocytes and large, atypi-

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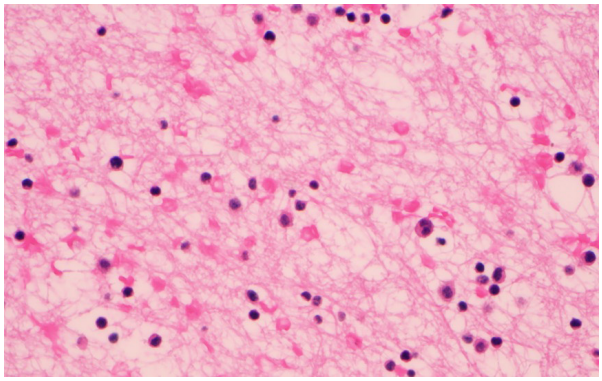
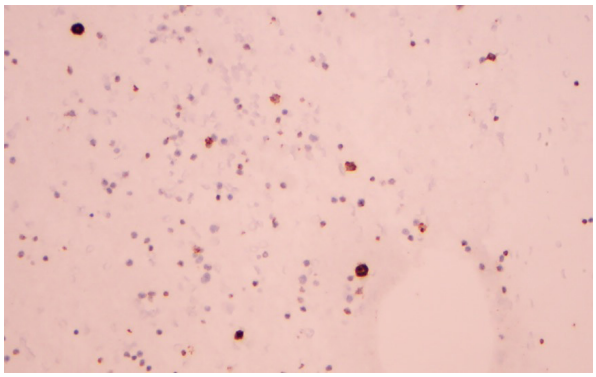
Figure 1. Cell Block Preparation From the Breast Fluid Aspiration at 40X Objective (400X magnification)



Scattered large, atypical cells are present.

Figure 2. CD30 Immunohistochemical Stain of Breast Fluid Aspirate at 20X Objective (200X magnification)

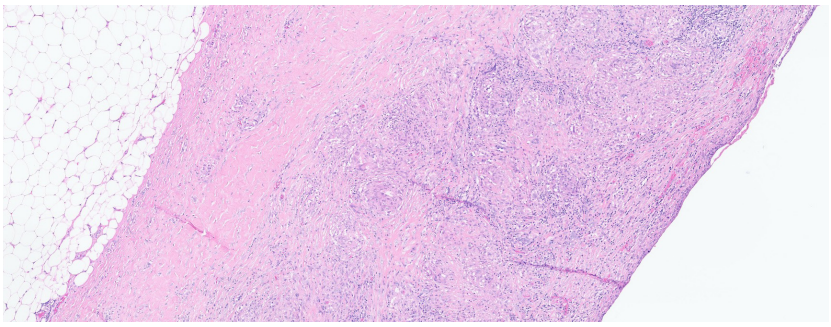


Large cells are strongly positive for CD30.

cal lymphocytes with pleomorphic nuclei and background histiocytes (Figure 1). By immunohistochemistry, the large, atypical cells were positive for CD3, CD4, CD30, CD43, and CD45, but negative for CD20, ALK, and EMA (Figure 2). This cytology pattern was suspicious, but not confirmatory, for BIA-ALCL.

Positron emission tomography-computed tomography (PET-CT) for baseline staging of presumed BIA-ALCL demonstrated hypermetabolic activity around the left breast implant with uncertain chest wall involvement and multiple hypermetabolic lymph nodes within the mediastinum, bilateral hilar, and internal mammary chain, suspicious for advanced disease.

Figure 3. Breast Capsule Excision at 10X Objective (100X magnification)



Fibrous tissue from the breast capsule contains diffuse non-caseating granulomatous inflammation.

Biopsies of mediastinal, hilar, and internal mammary lymph nodes all demonstrated noncaseating granulomas without evident lymphoproliferative disease. Punch biopsy of the breast rash also revealed noncaseating granulomas.

Bilateral surgical implant removal and capsulectomy were performed, and specimens were sent for postoperative pathology. The capsulectomy specimen was assessed using standard grossing procedures, with any suspicious areas of thickening submitted as formalin fixed paraffin embedded tissue that was utilized for immunohistochemical stains. Pathology showed florid granulomatous inflammation with no evidence of lymphomatous involvement in either specimen (Figure 3). These results were sufficient for the exclusion of BIA-ALCL and diagnosis of sarcoidosis.

DISCUSSION

Late seromas occur greater than 1 year after implant placement and may be caused by BIA-ALCL, which must be ruled out due to the mortality risk associated with disseminated disease. The most sensitive diagnostic test for BIA-ALCL is cytopathological evaluation with a CD30-positive, ALK-negative phenotype.[5] In most etiologies of seromas, the majority of cells are CD30-negative with possible rare reactive CD30-positive immunoblasts. In comparison, BIA-ALCL is characterized by numerous CD30-positive T cells. Current guidelines for the evaluation of suspected BIA-ALCL are outlined by the National Comprehensive Cancer Network.[6]

Previously, a suggestive cytopathologic phenotype was considered diagnostic of BIA-ALCL.[7] Surgical excision of the implant and capsule was completed with curative intent, and pathology was sent primarily to evaluate for invasive disease.

This case demonstrates the diagnostic importance of surgical pathology in all cases of suspected BIA-ALCL. Sarcoidosis is an entity also known to be associated with silicone breast implants and can contain reactive CD30-positive cells. It should, therefore, be included as a differential diagnosis for late seroma with CD30-postive aspirate suggestive of BIA-ALCL.[8]

In this case, surgical pathology revealed noncaseating granulomas consistent with sarcoidosis rather than lymphomatous deposits expected in BIA-ALCL. Correct diagnosis is imperative

due to disparate treatments. Treatment for sarcoidosis ranges from immunosuppressive therapy to observation, whereas treatment of advanced BIA-ALCL requires chemotherapy.

The similar clinical presentation between BIA-ALCL and sarcoidosis with breast involvement should be highlighted as there is growing evidence that breast implants may be associated with an increased risk for sarcoidosis.[9] Waiting for specimen pathology prior to initiation of treatment saved this patient from unnecessary, potentially harmful chemotherapy, as well as the deleterious impact of a second cancer diagnosis. Furthermore, implant removal and specimen pathology are necessary to adequately evaluate the etiology of a late seroma to guide proper treatment.

CONCLUSIONS

Our case demonstrates an atypical presentation of sarcoidosis of the breast initially thought to be BIA-ALCL in a woman with a late periprosthetic seroma status post textured implant-based reconstruction. In cases of late seroma, sarcoidosis must be considered as a differential diagnosis, and proper diagnostic pathways must be followed to confidently rule out BIA-ALCL. First, seroma aspirate should be sent for cytology to evaluate for CD30 positivity. However, CD30 positivity alone is insufficient for diagnosis of BIA-ALCL. Other entities, such as sarcoidosis, have also been known to cause CD30-positive seromas. If seroma aspirate is CD30 positive, surgical pathology of the implant and capsule is necessary to correctly elucidate an etiology. Misdiagnoses can greatly impact therapeutic management, success of treatment, and the psychological well-being of patients.

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REFERENCES

1. Nava MB, Adams WP, Botti G, et al. MBN 2016 Aesthetic Breast Meeting BIA-ALCL consensus conference report. *Plast Reconstr Surg*. 2018;141(1):40-48. doi:10.1097/PRS.0000000000003933

2. Laurent C, Delas A, Gaulard P, et al. Breast implant-associated anaplastic large cell lymphoma: two distinct clinicopathological variants with different outcomes. *Ann Oncol.* 2016;27(2):306-314. doi:10.1093/annonc/mdv575

3. Ibarra G, Vallejo A, Rivera A, Fernandez-Ibarburu B, Garcia-Ruano A. Sarcoidosis presenting as late seroma mimicking breast implant-associated anaplastic large cell lymphoma. *Ann Plast Surg*. 2021;87(4):415-420. doi:10.1097/SAP.0000000000002684

4. Panzacchi R, Gallo C, Fois F, et al. Primary sarcoidosis of the breast: case description and review of the literature. *Pathologica*. 2010;102(3):104-107.

5. Quesada AE, Medeiros LJ, Clemens MW, Ferrufino-Schmidt MC, Pina-Oviedo S, Miranda RN. Breast implant-associated anaplastic large cell lymphoma: a review. *Mod Pathol.* 2019;32(2):166-188. doi:10.1038/S41379-018-0134-3

6. Clemens MW, Jacobsen ED, Horwitz SM. 2019 NCCN consensus guidelines on the diagnosis and treatment of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). *Aesthet Surg J.* 2019;39(Supplement_1):S3-S13. doi:10.1093/asj/sjy331

7. Di Napoli A, Pepe G, Giarnieri E, et al. Cytological diagnostic features of late breast implant seromas: From reactive to anaplastic large cell lymphoma. *PLoS One.* 2017;12(7):e0181097. doi:10.1371/journal.pone.0181097

8. Nicod LP, Isler P. Alveolar macrophages in sarcoidosis coexpress high levels of CD86 (B7.2), CD40, and CD30L. *Am J Respir Cell Mol Bio*l. 1997;17(1):91-96. doi:10.1165/ajrcmb.17.1.2781

9. Watad A, Rosenberg V, Tiosano S, et al. Silicone breast implants and the risk of autoimmune/rheumatic disorders: a real-world analysis. *Int J Epidemiol.* 2018;47(6):1846-1854. doi:10.1093/ije/dyy217

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