FDA provides update on Breast Implant Associated-Squamous Cell Carcinoma (BIA-SCC)

Wednesday, March 8, 2023

On March 8, 2023, the Food and Drug Administration (FDA) released an update to its September 2022 safety communication (**https://www.fda.gov/medical-devices/safety-communications/update-reports-squamous-cell-carcinoma-scc-capsule-around-breast-implants-fda-safety-communication**) about squamous cell carcinoma (SCC) and various lymphomas in the capsule around breast implants. This document is now available to healthcare providers, patients and caregivers on the FDA Medical Device Safety webpage (**https://www.fda.gov/medical-devices/safety-communications/2023-safety-communications**).

The American Society of Plastic Surgeons (ASPS) and The Plastic Surgery Foundation (PSF) continue to communicate with the FDA regarding this emerging issue. Though data on Breast Implant-Associated Squamous Cell Carcinoma (BIA-SCC) is limited and evolving, the Society will continue to notify membership as new information becomes available to support increased clinical awareness and enhanced clinical decision-making. Additionally, ASPS/PSF expect to announce later this month how surgeons can report cases to The PSF's PROFILE registry.

In the updated communication, the agency also notes that it "continues to collect and evaluate all available information about SCC, lymphomas and any other cancers in the capsule around the breast implant. We are collaborating with other regulatory authorities, clinical and scientific experts, professional societies, manufacturers, and breast implant registries, to increase awareness of SCC in the capsule around the breast implant. In addition, the FDA is working with breast implant manufacturers to help ensure that patients receive and understand information about this emerging issue. The FDA continues our collaborative efforts with ASPS and The PSF to better characterize these cancers in people with breast implants."

BIA-SCC is a rare but potentially aggressive epithelial-based tumor that appears to be associated with breast implants and emanates from the breast implant capsule. At this time, ASPS/PSF is aware of so few reported cases of BIA-SCC (in its update, the FDA notes it is aware of 19 cases of SCC in the capsule around the breast implant from published literature) that it is not possible to determine what factors increase patient risk.

RELATED

- Beware of email scam requesting money transfer for ASPS
- Remembering a plastic surgeon and a friend to many
- 'Much more than a surgeon': Remembering David Genecov, MD, 1963-2022
- Vote now on proposed amendments to ASPS/PSF Bylaws, Code of Ethics
- Colleagues pay tribute to Howard Gordon, MD

Available information and recommendations are listed below, but the FDA did provide the following updated recommendations for healthcare providers in Wednesday's communication:

- Include information about SCC and various lymphomas in the capsule around the breast implant in your discussions with people who have or are considering breast implants.
- For patients who have been diagnosed with SCC or various lymphomas in the capsule around the breast implant, develop an individualized treatment plan in coordination with a multidisciplinary team of experts including surgical oncology, plastic surgery, breast surgery, radiology, oncology, and pathology.
- Report all cases of SCC, lymphomas, and any other cancers in the capsule around the breast implant to the FDA. Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with medical devices.
    - Please include the following information in the report, if known:
        - Clinical presentation and breast implant history
        - Imaging studies performed
        - Pathology of the capsule tissue
        - Treatment therapy
        - Outcomes

ASPS/PSF is committed to driving patient safety and informed decision-making through research and the ongoing and persistent surveillance of breast implants. Information for your patients may be found on the ASPS webpage (***Breast Implant Safety: What Patients Need to Know***).

Overview

The following overview is presented to help plastic surgeons recognize Breast Implant-Associated Squamous Cell Carcinoma (BIA-SCC) as a distinct disease entity and long-term complication of breast implants. In light of broad specialty-wide awareness concerning Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL), information regarding BIA-SCC is presented in a comparative format below. A reference list of all available published case reports is included at the end of this statement, and The PSF is finalizing a manuscript summarizing the current state of knowledge for *Plastic and Reconstructive Surgery.*

	BIA-SCC	**BIA-ALCL**
What is it?	Breast implant-associated squamous cell carcinoma (BIA-SCC) is a very rare but potentially aggressive, epithelial-based tumor that appears to emanate from the breast implant capsule. Pathology shows sheets of	Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is an uncommon and treatable type of T-cell lymphoma that can develop around breast implants. BIA-ALCL can exhibit highly invasive properties, including spread to lymph nodes, local tissues and distant sites.

	squamous cells lining the capsule in nests and bundles. BIA-SCC can exhibit highly invasive properties including spread to lymph nodes, local tissues and distant sites, such as muscle and bone. BIA-SCC is not a cancer of the breast tissue itself.	BIA-ALCL is not a cancer of the breast tissue itself.
Number of Known Cases	To the best of our knowledge, there are 19 cases reported in the literature.	ASPS recognizes approximately 411 both suspected and confirmed cases in the United States and nearly 1,400 cases worldwide as of March 2023.
Lifetime Risk	Unknown	Current lifetime risk of BIA-ALCL varies widely (e.g., estimates of 1:2,207-1:86,029 based upon variable risk with different manufacturer types of textured implants. More recently, cumulative risk over 20 years in breast reconstruction patients implanted with Biocell devices was estimated at 1:100 (Cordeiro et al, 2020).
Age at presentation	55.8 years (range 40-81)	55.3 years (range 28-84)
Average length since initial implantation	22.74 years (range 11-40 years)	10.32 years (range 0.08-41 years)
Implant Surface	In case reports, BIA-SCC has been reported in patients who have had smooth and/or textured implants.	No cases of BIA-ALCL have been confirmed in patients who have only had smooth implants in case series, case reports or registries. However, it is not possible to exclude the appearance of BIA-ALCL in association with smooth implants at this time. The FDA states that all confirmed cases worldwide either have a history of a textured device or an incomplete clinical history available for review.
Implant Type	BIA-SCC has been associated with both silicone and saline implants in aesthetic as well as reconstructive patients.	BIA-ALCL has been associated with both silicone and saline implants in aesthetic as well as reconstructive patients.
Presentation		
• Delayed seroma	Yes	Yes
• Unilateral swelling	Yes	Yes
• Pain, erythema	Yes	Yes

• Capsular contracture	Often	Sometimes
Extracapsular spread at presentation	80% at presentation	28% at presentation
Typical Pathology	Squamous cells in sheets with varying degrees of atypia and metaplasia and at least one focus of SCC.	Lymphoma with mass confined to single area on capsule.
Diagnostic Assessment	CK 5/6+; p63+; Flow cytometry + for squamous cells and keratin	CD30+; ALK-; Flow cytometry + for T-cells
Imaging	Ultrasound to evaluate for peri-prosthetic fluid +/- aspiration; MRI with and without contrast to evaluate capsule to rule out mass; PET-CT for extent of disease, if present.	Ultrasound to evaluate for peri-prosthetic fluid +/- aspiration; PET-CT is performed following a positive diagnosis. Mammograms are not helpful for evaluating lymphoma but are important for the evaluation of breast cancer.
Treatment	Official treatment recommendations will need to be based on emerging data. At present, it appears that explantation with complete (en bloc) capsulectomy will provide the best outcomes. Based on existing case reports, it appears that incomplete resection of BIA-SCC can result in early and/or aggressive recurrence.	In the majority of cases, explantation with complete (en bloc) capsulectomy is curative. Incomplete capsular resection has been associated with both recurrence and significantly lower survival. Rare patients will present with more advanced disease and may require radiotherapy and chemotherapy. Treatment approach should follow international guidelines established by the National Comprehensive Cancer Network (NCCN) for BIA-ALCL. Current treatment recommendation is for bilateral complete capsulectomy and implant removal, as a small number of women have had contralateral disease found incidentally.
Chemotherapy / Radiation Therapy	Patients treated within these cases did not appear to respond.	Responds to Brentuximab plus CT.
Mortality	43.8% at six months.	2.8% at one year.
Reporting	The FDA recommends that any suspected or confirmed cases of SCC, lymphomas, or any other cancers around the breast implant be reported to the FDA's Manufacturer and User Facility Device Experience (MAUDE) database and the device manufacturer. To submit a case to the MAUDE database, which	The FDA recommends that any suspected or confirmed cases of BIA-ALCL be reported to the PROFILE registry, the FDA's Manufacturer and User Facility Device Experience (MAUDE) database and the device manufacturer. To submit a case to the MAUDE database, which collects medical device reports (MDRs) of suspected device-associated deaths, serious injuries and malfunctions, visit **www.accessdata.fda.gov**.

	collects medical device reports (MDRs) of suspected device-associated deaths, serious injuries and malfunctions, visit **www.accessdata.fda.gov**. Pending IRB approval, The PSF will soon enable plastic surgeons to report confirmed or suspected breast implant-associated capsular pathologies, including BIA-SCC cases, to PROFILE (**ThePSF.org/PROFILE**)	To report a case to PROFILE, go to **ThePSF.org/PROFILE**.
Patient Counseling and Informed Consent	BIA-SCC should be discussed with any patient considering breast implants as part of the informed-consent process.	BIA-ALCL should continue to be discussed with any patient considering breast implants as part of the informed-consent process.

ASPS/PSF Recommendations

- Prior to implantation of any breast implant, plastic surgeons should provide patients with the manufacturer's patient labeling, the FDA-required patient decision checklist and any other educational material to best discuss the benefits and risks of breast implants.
- Preoperative workup is essential. All patients presenting with a late seroma should have fine needle aspiration (FNA) and cytology testing. Specimens should be sent for immunohistochemistry including CD30, ALK, CK 5/6, p63 and flow cytometry to look for T-cells, squamous cells and keratin.
- All patients presenting with a late seroma should undergo a breast ultrasound and MRI with and without contrast. If disease is confirmed, a PET-CT should be considered prior to surgical intervention. *A thorough preoperative work-up allows for potentially the most appropriately planned, single-stage surgery with the greatest chance of success for cure.*
- Consider the possibility of BIA-ALCL, BIA-SCC and other lymphomas when treating a patient with late onset, peri-implant changes. If you have a patient with suspected BIA-ALCL or BIA-SCC, refer them to experts familiar with the diagnosis and treatment of BIA-ALCL and BIA-SCC.
- At surgery, collect fresh seroma fluid, representative portions of the capsule, and specific pathology requests to rule out both BIA-ALCL and BIA-SCC.
    - Diagnostic evaluation should include cytological evaluation of seroma fluid or mass with Wright Giemsa stained smears and cell block immunohistochemistry/flow cytometry testing for cluster of differentiation (CD30) and Anaplastic Lymphoma Kinase (ALK) markers, as well as Cytokeratin 5/6 (CK 5/6) and p63.
        - Flow cytometry should include instructions to look for T cells, squamous cells, and keratin.

- All confirmed or suspected BIA-SCC data should be entered into the PROFILE Registry *(Data entry mechanism forthcoming)*.
- Data for all patients with seroma should be entered into the National Breast Implant Registry (NBIR).

ASPS/PSF is committed to patient safety, advancing quality of care and practicing medicine based upon the best available scientific evidence. We will continue to monitor and review all new information as it becomes available to keep the plastic surgery community informed. If you have any further Questions, please do not hesitate to contact Amy Hughes at **ahughes@plasticsurgery.org**.

References

Buchanan PJ, Chopra VK, Walker KL, Rudolph R, Greco RJ. Primary Squamous Cell Carcinoma Arising From a Breast Implant Capsule: A Case Report and Review of the Literature. Aesthet Surg J. 2018 Jun 13;38(7). doi: 10.1093/asj/sjy092. PMID: 29659713.

Cordeiro PG, Ghione P, Ni A, et al. Risk of breast implant associated anaplastic large cell lymphoma (BIA-ALCL) in a cohort of 3546 women prospectively followed long term after reconstruction with textured breast implants. *J Plast Reconstr Aesthet Surg.* 2020;73:841–846.

Goldberg MT, Llaneras J, Willson TD, Boyd JB, Venegas RJ, Dauphine C, Kalantari BN. Squamous Cell Carcinoma Arising in Breast Implant Capsules. Ann Plast Surg. 2021 Mar 1;86(3):268-272. doi: 10.1097/SAP.0000000000002524. PMID: 32804719.

Olsen DL, Keeney GL, Chen B, Visscher DW, Carter JM. Breast implant capsule-associated squamous cell carcinoma: a report of 2 cases. Hum Pathol. 2017 Sep;67:94-100. doi: 10.1016/j.humpath.2017.07.011. Epub 2017 Jul 22. PMID: 28739500.

Kitchen SB, Paletta CE, Shehadi SI, Bauer WC. Epithelialization of the lining of a breast implant capsule. Possible origins of squamous cell carcinoma associated with a breast implant capsule. Cancer. 1994 Mar 1;73(5):1449-52. doi: 10.1002/1097-0142(19940301)73:5<1449::aid-cncr2820730520>3.0.co;2-j. PMID: 8111712.

Liu Z, Liu, C, Chengglong, Z, Yu, Q, Zhang G, Wang X, Yu Z. Breast prosthetic implant-associated Squamous Cell Carcinoma: A case report and Literature Review. Research Square. 2021 Jan. doi.org/10.21203/rs.3.rs-141167/v1

Paletta C, Paletta FX Jr, Paletta FX Sr. Squamous cell carcinoma following breast augmentation. Ann Plast Surg. 1992 Nov;29(5):425-9; discussion 429-32. doi: 10.1097/00000637-199211000-00009. PMID: 1444131.

Satgunaseelan L, Cheung D, Reddy, J. Breast Implant-Associated Squamous Cell Carcinoma – A Rare Long Term Complication. Pathology. Volume 47, Supplement 1, S72-S73, JANUARY 01, 2015.

Alikhan MB, Nassar A, Mansoor I. Squamous metaplasia on the breast implant capsule. Int J Surg Pathol. 2010 Dec;18(6):570-4. doi: 10.1177/1066896908329587. Epub 2009 Jan 14. PMID: 19147510.

Soni SE, Laun JC, Beard AS, Kuykendall LV. "Breast Implant Capsule-Associated Squamous Cell Carcinoma During Pregnancy: A Mimicker of Breast Implant-Associated Anaplastic Large Cell Lymphoma". Plast Reconstr Surg. 2022 Aug 12. doi: 10.1097/PRS.0000000000009506. Epub ahead of print. PMID: 35960919.

Whaley RD, Aldrees R, Dougherty RE, Prieto Granada C, Badve SS, Al Diffalha S. Breast Implant Capsule-Associated Squamous Cell Carcinoma: Report of 2 Patients. Int J Surg Pathol. 2022 Mar 18:10668969221086940. doi: 10.1177/10668969221086940. Epub ahead of print. PMID: 35300538.

Zhou YM, Chaudhry HE, Shah A, Andrews J. Breast Squamous Cell Carcinoma Following Breast Augmentation. Cureus. 2018 Oct 3;10(10):e3405. doi: 10.7759/cureus.3405. PMID: 30533339; PMCID: PMC6278994.

Zomerlei TA, Samarghandi A, Terando AM. Primary Squamous Cell Carcinoma Arising from a Breast Implant Capsule. Plast Reconstr Surg Glob Open. 2016 Jan 7;3(12):e586. doi: 10.1097/GOX.0000000000000567. PMID: 26894011; PMCID: PMC4727695.