A Retrospective Review of Patients Undergoing Total Capsulectomy and Removal of Breast Implants for Breast Implant Illness

Abstract:

Background: Breast implant illness (BII) is novel description that patients have coined to describe a syndrome which they ascribe to an immune reaction to their breast implants. The awareness of this entity is increasingly fueled by social media and has recently become a frequent topic at professional conferences. BII symptoms have been described to affect nearly all organ systems, and recommendations regarding how to approach treatment of this patient population has been variable and limited. Though the concept of implants as an underlying cause for a systemic illness has long been controversial, the epidemiology, treatment, and outcomes of patients who seek explanation for BII has largely been unreported. We present a retrospective review of 248 patients who presented with BII symptoms and underwent bilateral implant removal and total capsulectomy by the same surgeon.

Objectives: We sought to define the most common presenting symptoms, implant characteristics, and outcomes associated with patients who undergo implant removal and total capsulectomy for BII.

Methods: We retrospectively reviewed all women age 18 and older who presented to the senior author with systemic symptoms they attributed to their implants and underwent breast implant removal with capsulectomy from August 2016- February 2020. Intraoperative cultures were routinely obtained, and capsules were submitted to pathology. We reviewed medical history, pattern of symptoms, indication for implant placement, physical exam, laboratory findings, culture results and final pathology on the submitted capsules. Postoperative notes were reviewed for patient-reported symptom improvement and satisfaction with procedure. Chi-square and logistic regression analysis were performed to evaluate association between implant type (textured vs smooth), implant composition (saline vs silicone) and findings of inflammation on capsule pathology.

Results: 248 patients were included. The most commonly reported symptoms included generalized pain, fatigue, cognitive "fogginess", migraines, headaches, anxiety, arthritis, and vision changes. 98 (40.2%) of patients had silicone implants, 146 (59.8%) had saline implants, 207 (84.8%) patients had smooth implant, and 37 (15.2%) had textured implants. The number of complaints did not vary significantly between types of implants. 23% of capsules submitted to pathology demonstrated acute or chronic inflammation, which was significantly associated with silicone compared to saline implants ($p<0.01$) and textured compared to smooth implants ($p<0.02$). On logistic regression analysis, capsular inflammation was independently associated with silicone compared to saline (OR=2.18 [1.16-4.11], p=0.016 for right implant, OR=2.35 [1.08-5.12], p=0.03 for left implant) and textured compared to smooth implants (OR=2.18 [1.16-4.11], p=0.016 for right implant, and OR=2.25 [1.17-4.31], p=0.01 for left implant). Post-operative visit notes addressed specific symptoms in 46 patients, and of these, 44 (95.7%) reported a decrease in the number of symptoms after surgery. Six major complications occurred

which included one pneumothorax, three hematomas requiring evacuation, and two DVTs. Overall, 92 % of patients were pleased with the results of the surgery.

Conclusions: Though our study was limited by its retrospective nature, patient recall bias, and the inability to assess changes in specific symptoms after surgery, we found that evidence of capsular inflammation was common among patients presenting with complaints ascribed to breast implant illness syndrome, and was significantly associated with certain implant types, namely those consisting of a silicone fill and having a textured shell. The majority of patients who underwent implant removal and total capsulectomy were highly satisfied with the outcome of the procedure and expressed improvement in their preoperative symptoms. Thus, we believe that total capsulectomy and implant removal in patients with suspected BII can be safely performed and with a low complication rate and satisfactory outcome.

Introduction:

Breast implant illness (BII) is a novel syndrome involving a constellation of symptoms, potentially driven by a poorly characterized immune response to breast implants.[1,2] The name of this disease process has been coined by women who believe they have become ill from their implants rather than a medical professional society. Awareness of BII is fueled by the power of social media, with one online support group reportedly reaching nearly 110,000 members.[3,4] BII symptoms are frequently non-specific, vary widely, and can affect all organ systems, characteristics which have been noted to overlap with many somatization disorders.[5-7] Despite growing concern among the general public regarding BII, breast augmentation is on the rise, with nearly 330,000 procedures performed in 2018 (a 15% increase from 2014), and national data has revealed trends favoring implant-based breast reconstruction.[8,9] The leading societies in our field have hosted several panels to discuss BII, and continue to offer forums to facilitate dialogue between patients, their advocates, and surgeons.[10-12]

There is a paucity of knowledge about BII, and many of the studies regarding breast implants and systemic disease have occurred in nonsurgical fields with controversial conclusions.[2,6,13-18] We sought to better characterize the population of patients that self-identify as having BII by evaluating outcomes in a group of patients who presented to a single surgeon with BII symptoms and underwent bilateral implant removal and total capsulectomy.

Methods:

This study was conducted after receiving approval from the hospital institutional review board at Abington-Jefferson Health. We retrospectively reviewed the medical records of all women aged 18 and older who presented to the senior author from 2016-2019 with systemic symptoms that patients ascribed to their breast implants and who subsequently went on to undergo total capsulectomy and implant removal.

Data obtained from the chart review included demographics, indication for initial placement of implants (reconstruction versus cosmetic), medical history, symptoms both before and after breast implant removal, and follow-up. Any labs obtained by the senior author or stated in the chart were reviewed. Preoperative physical exam findings were noted as well. Patient characteristics are summarized in **Table 1**. Operative findings at the time of surgery, simultaneous procedures, and pathology results were reviewed. The first four post-operative visit

notes were reviewed to determine each patient's level of satisfaction with the results of the procedure.

Results:

The study population consisted of 248 patients who underwent bilateral implant removal and bilateral total capsulectomies with the senior author from August 2016 to February 2020. The majority (93%) had implants placed for cosmetic purposes. The average patient age was 44 years (Range: 22-72 years) and average BMI was 24. Most patients (92%) were nonsmokers. On physical exam, 130 patients (55%) exhibited Baker II and 95 patients (39%) exhibited Baked III/IV capsular contracture at initial presentation. Patient characteristics upon presentation are summarized in Table 1.

The most common symptoms mentioned at time of initial evaluation included generalized pain, fatigue, cognitive "fogginess," migraines, headaches, anxiety, arthritis, vision changes, dyspnea, hair loss, weight gain, back pain, thyroid disease, rashes, back pain, generalized gastrointestinal issues, and depression. The number of complaints did not vary significantly between types of implants. Symptoms are summarized in **Table 2**.

Simultaneous procedures at time of implant removal and total capsulectomy included mastopexy (53, 21%), scar revision (12, 4.9%), breast reconstruction (5, 2.0%), abdominoplasty (1, 0.4%), implant replacement (1, 0.4%). Six major complications occurred which consisted of one pneumothorax that required hospital admission for observation, three breast hematomas that required evacuation in the OR, and two DVTs. Minor complications consisted of several delayed seromas which were treated by aspiration and several suture infections in patients who received simultaneous mastopexies which were treated with antibiotics.

Ninety-eight patients (40.2%) had silicone implants, 146 (59.8%) had saline implants. 71 (39%) of the implants removed were Mentor saline. The remaining implants were Allergan silicone (38, 21%), Allergan saline (34, 19%), Mentor silicone (32, 18%), and Sientra silicone (6, 3%). Two-hundred and seven patients (85%) had smooth implants, while 37 patients (15%) had textured implants. Implant characteristics are summarized in **Figure 1**.

All capsules were sent to permanent pathology, and 111 (23%) of the capsules were found to have evidence of acute or chronic inflammation, which was defined as calcification or microcalcification, histiocytic reaction or an abundance of histiocytes/macrophages/giant cells, presence of sclerosis, lymphoid/lymphocytic infiltration, or the term "inflammation" contained in the final pathology report. One capsule did have atypical lymphocytic infiltration but was CD30 negative. Bacterial colonization was noted in culture results in 8 (3.28%) of right breast pockets, and 9 (3.69%) of left breast pockets.

Statistical analysis was performed using SAS® 9.4 (SAS Institute, Cary, NC). Chi-squared analysis was utilized for independent variables. Comparing silicone to saline implants, evidence of capsule inflammation was significantly more common in capsules associated with silicone implants compared to those associated with saline implants (right silicone 31.3% versus right saline 16.4%, $p=0.007$; left silicone 29.9% versus left saline 15.1%, $p=0.005$). Comparing textured to nontextured implants, inflammation was significantly more common in capsules associated with textured implants compared to those associated with nontextured implants (right textured 38.9% versus right smooth 19.9%, $p=0.01$; left textured 37.8% versus left smooth 18.5%, $p=0.008$). Rates of inflammation are presented in **Figure 2**.

Logistic regression modeling was performed. Regarding texturing, after controlling for implant fill (silicone versus saline), the odds ratio for inflammation is 2.26 (95%CI 1.04 - 4.90; p=0.040) for right textured compared to smooth and 2.35 (95%CI 1.08 - 5.12; p=0.031) for left textured compared to smooth. For implant fill, after controlling for texturing, the odds of inflammation are 2.18 (95%CI 1.16 - 4.11; p=0.016) for right silicone implants as compared with saline and 2.25 (95%CI 1.17 - 4.31; p=0.015) for left silicone implants as compared with saline. Logistic regression modeling revealed that textured and silicone characteristics independently increased inflammation when present together to approximately 51% but had an additive rather than synergistic effect on increasing inflammation.

The average number of follow-up visits was 3.9±2.1, with a mean follow-up of 1.8 to 6 months. Post-operative visit notes addressed specific symptoms in 46 patients, and of these, 44 (96%) reported a decrease in the number of symptoms after surgery. Overall, 92% of patients were pleased with the results of the surgery and had no or only minor complaints.

Discussion:

The association of breast implants with autoimmune or systemic symptoms is an ongoing, heavily debated controversy. Despite early reports of patients with silicone implants developing an immunoadjuvant disease[19-21], large retrospective studies comparing incidence of connective tissue diseases in women with silicone implants found no association, a finding confirmed by a special committee of the Institute of Medicine in 1999 which resulted in lifting of the FDA moratorium on silicone implants in 2004.[22-26] This has by no means put an end to the controversy however, as a large number of women with a prominent social media presence are seeking implant removal with total capsulectomy in recent years for a constellation of systemic symptoms that these patients refer to as breast implant illness. A recent review by Magnussen et al suggests that efforts at scientific investigation of an underlying pathology for these symptoms have unfortunately been hampered by misrepresentation in the media and an excessive focus on litigation.[2] The pathogenesis of an immunoadjuvant disease process associated with breast implants has been hotly contested in the literature, with several rheumatological studies suggesting a direct effect of silicone in potentiating an autoimmune response[13,20,27,28], while others argue that the constellation of somatic symptoms ascribed to implants may be the result of disrupted pain processing pathways leading to psychological distress in a manner similar to disorders like fibromyalgia.[5,29] We sought to study the demographics, symptoms, and outcomes of patients who have presented to the senior author for implant removal and self-identified as having BII.

In our cohort of patients, we found several interesting characteristics among the majority of women who underwent explanation with favorable results. Preoperatively, the most common presenting symptoms were non-specific somatic complaints such as generalized pain (163 patients, 67%) and fatigue (133 patients, 55%). We found that in 46 patients who had postoperative follow-up addressing specific symptoms, 44 patients (96%) reported improvement. A review by De Boer et al of 23 case series and reports from 1960-2016 evaluating outcomes of implant explantation in patients with silicone implants overwhelmingly found that 75% of

patients appeared to improve symptomatically, although this could not be linked to any specific change in autoantibody, inflammatory, or other serum markers.[29] Importantly, symptomatic improvement was predominantly observed in patients who had systemic complaints that did not meet criteria for a known autoimmune disease, whereas patients with diagnosed conditions such as rheumatoid arthritis or systemic lupus erythematosus demonstrated little to no improvement with explantation. A higher number of musculoskeletal complaints was shown to correlate with higher likelihood of improvement in a study by Rohrich et al of 38 patients with silicone implants undergoing explantation.[30] In contrast, two prior studies of explantation have failed to show any significant improvement in patients who underwent explantation for systemic symptoms.[31,32] Slavin et al studied 46 women who presented for implant removal, eight of whom complained of systemic symptoms, and found that although there was an initial period of improvement of symptoms, only one of the eight had sustained improvement after 2.5 year follow up.[31] The study was limited by the relatively small number of patients with symptoms that fit the pattern of BII, with the majority of patients requesting explantation either from fear of harmful consequences or aesthetic reasons. 74% of the patients from this study did undergo a capsulectomy with implant removal, and the authors found an overall low complication rate (4.3% wound infection), with the majority of patients satisfied with the result of the combined procedure. Godfrey et al studied the effect of explantation in 37 women who underwent explantation followed by reconstruction with transversus abdominis or latissimus dorsi flaps.[32] Importantly, only 10 patients had isolated systemic symptoms such as fatigue, myalgias, arthralgia, paresthesia, or sicca symptoms, whereas the others reported a combination of local/systemic symptoms or anxiety about the implants as the primary motivation for explantation. An initial improvement in 89.2% of the patients was followed by relapse, with only 32.4% demonstrating improvement in their systemic symptoms at six month follow up. Our patient cohort differed from this earlier study, as we aimed to study specifically the effect of explantation in patients who self-identified as having BII and were predominantly limited by their systemic symptoms. In the majority of previous explantation studies of patients who attribute systemic symptoms to their implants, definite conclusions have been limited by a small number of patients, the subjective nature of symptoms, difficulty in distinguishing patients limited by predominantly local symptoms from those with systematic complaints or anxiety about their implants, referral bias, short period of follow-up, or explantation for old generation implants that had a high rate of rupture or leakage. [30,32-37] Additionally, these studies focused on patients with silicone implants in light of the FDA moratorium, although one large retrospective controlled study evaluating the incidence of systemic complaints attributed to breast implants has found no increased risk with reported symptoms in patients with silicone as opposed to saline implants.[38]

In evaluating the histopathology of capsules removed from our patient cohort, we significantly found that both textured shell and silicone implants were independently associated with acute or chronic inflammation for textured compared to smooth implants, and for silicone compared to saline implants. Previous reports evaluating inflammation associated with silicone implants have found that silicone which enters the periprothestic space can induce chronic

inflammation by uptake into macrophages, subsequently triggering cytokine production and fibroblast activity.[39] The phenomenon of "silicone bleed" has been described, wherein small amounts of silicone are found in the capsule outside an otherwise intact implant shell.[40,41] In a study of 86 biopsies from 55 patients with intact silicone implants from 1982-1986, Thomsen et al found a positive correlation between the presence of inflammatory cells and median concentration of silicone contained within the capsule. Additionally, his group observed lymphocytes and macrophages containing droplets of non-refractile material on cross section of the biopsy specimen, suggesting silicone uptake and that an independent inflammatory process was occurring aside from foreign body reaction to the silicone prosthesis.[42] A histological study by Peters et al examining 404 implant capsules from 1981-1996 noted that calcification appeared to be associated with implant shell thickness, duration after placement, and integrity of the shell. With regard the implant thickness, Peters et al had observed that first-generation implants placed between 1963-1972, which had a thick capsule and dacron patches along the posterior surface, showed a nearly ubiquitous level of heavy calcification. The same study interestingly found that while silicone implants were associated with several forms of calcification such as aggregate crystallization and true bone formation, saline implants were only found to have calcium adherent to the elastomer shell. In the background of these findings, it is reasonable to suppose that capsular calcification is a response to an amplified inflammatory response associated with silicone as compared to saline implants. As silicone particles from both the filler of the implant and the elastomer shell appear to stimulate calcification, we speculate that textured implants may be associated with more inflammation due to a thicker shell or increased degree of surface area exposed to the host tissue, contributing to a higher immune response. In another study, Peters et al evaluated the implants and capsules of 100 women who underwent explantation of silicone implants between 1992-1995, 83 of whom had systemic symptoms without documented rheumatic or autoimmune disease.[35] They found that 42% of the capsules were colonized with bacteria and 25% were heavily calcified suggesting chronic inflammation. Similar to our study, they observed a high incidence of capsular contracture (61% Grade III/IV) among their population. Although we observed a similar rate of inflammatory capsular changes in nearly a quarter of our cohort, relatively few patients had any bacterial colonization based on our culture results (17 pockets, 3.5%). Our findings of a high rate of acute or chronic inflammatory changes and relatively low bacterial colonization based on culture data suggest that the source of inflammation in patients with BII is the implant itself, rather than a subclinical infection which is thought to be an inciting process for capsular contracture.[43] For this reason, we feel that performing a capsulectomy in patients who are requesting explantation for symptoms of BII is warranted when it can safely be performed. Though no conclusive evidence is available, a prior small retrospective controlled study by Kappel et al found a more pronounced improvement in systemic symptoms particularly with respect to arthralgia when capsulectomy was added to the explantation procedure.[44]

Our study is limited by its retrospective nature and lack of standard documentation, without which we were unable to evaluate changes in specific symptoms after explantation or correlate capsular findings on pathology with symptom severity preoperatively. Like prior

studies of explantation as a treatment for patients presenting with systemic symptoms, our study is additionally limited by the subjective bias of defining BII symptoms, lack of a control group, and selection bias as patients were predominantly self-referred to our office for explantation. Follow-up duration was also a mean of 6 months, which limits our ability to predict long-term symptom resolution or recurrence. Furthermore, we have few objective markers of systemic disease to remark on the prevalence of elevated inflammatory markers in BII. Nonetheless, we found that evidence of acute on chronic inflammation was commonly found on pathologic examination of the excised capsules and was significantly more common with silicone as well as textured implants. This interesting finding potentially suggests an association between a specific implant composition and development of symptoms described as BII. We also found that the majority of patients expressed satisfaction both with the implant removal procedure and a subjective improvement in their overall health during the follow-up period, suggesting that implant removal with capsulectomy is potentially an effective treatment for patients that choose to undergo the procedure. Building on the results of our retrospective study, we are currently conducting a prospective study focusing on standardized comparison of preoperative symptoms and postoperative improvement in order to determine which patients would most likely benefit from implant removal and capsulectomies.

Conclusions:

Our data support that there is an innate inflammatory response associated with implants in select patients, a response which is more common in silicone and textured implants. This response may be associated with symptoms of breast implant illness. More research is necessary to further elucidate the underlying process fueling BII, and how patients respond to implant removal and capsulectomy. We believe that total capsulectomy and implant removal in patients with suspected BII can be safely performed and with high patient satisfaction.

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