Removal of a Silicone Gel Breast Implant in a Multiple Myeloma Patient Improved Disease Status: A Case Report

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Abstract
A 52-year-old African-American woman with a prior history of monoclonal gammopathy of undetermined significance (MGUS) developed infiltrating ductal carcinoma of the left breast. Following a mastectomy, she underwent reconstruction with a silicone gel breast implant. Three years later, her MGUS had progressed to active multiple myeloma (MM). She had a minimal response after two different regimens of bortezomib-based treatments and monthly zoledronic acid, and was placed on maintenance therapy with bortezomib, intravenous dexamethasone, and oral methylprednisolone, as well as ongoing monthly zoledronic acid. After 1 year of this maintenance therapy, during which her myeloma markers remained unchanged, she had her silicone implant replaced with saline. Despite no change in her myeloma treatment, her laboratory values began to steadily improve following removal of the silicone implant. Her M-protein decreased from 2.14 to 0.83 g/dL and her IgG levels from 3,330 to 1,210 mg/dL following replacement of her silicone implant with saline. To our knowledge, this is the first report in which removal of silicone implants improved the clinical status of a patient with MM following a year of maintenance therapy during which the patient’s myeloma laboratory values remained unchanged. Further studies are warranted to determine if silicone breast implant removal can, in fact, improve MM patients’ disease status.

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Introduction

Silicone gel breast implants (SGBIs) have been linked to many illnesses, including a variety of different cancers. Patients with these implants have been reported to have a higher risk of developing stomach cancer, brain cancer, and leukemia that could not be explained by lifestyle factors alone [1]. The exact prevalence of breast implantation in the USA is unknown, but the American Society of Plastic Surgeons in 2012 estimated the incidence of implantation at nearly 400,000 women [2]. Silicone implants specifically have been associated with many adverse events, especially when they rupture. The frequency of silicone implant rupture is estimated to be in three out of every 4 patients with a mean implant rupture age of 10.8 years [3]. In addition to the frequency of implant rupture, breast implants have been associated with capsular contractures and seromas [3–5].

As a result of these risks, the Food and Drug Administration (FDA) declared a moratorium on silicone breast implant use in 1992 [6–8]. However, there has been conflicting and inconclusive evidence calling into question the association of silicone implants with these conditions, particularly a study from the Institute of Medicine in 1999 that stated there was no evidence that implants caused any significant clinical conditions [7, 8]. As a result, in 2006, the FDA lifted the ban, but required the two companies that produced the implants, Allergan and Mentor Corp, to do post-approval studies for 10 years after the resumption of use of SGBIs [8]. In 2019, the largest study of breast implant outcomes was conducted in accordance with the US FDA large post-approval studies (LPAS). The LPAS included 99,993 patients where 56% of the implants were silicone for primary augmentation. The results of the study indicated that silicone implants were associated with an increased risk of certain rare harms including, but not limited to, connective tissue/autoimmune disease and cancer, yet such associations required further analysis with patient-level data. However, despite the number of breast implants followed up in these LPAS, the database had not been thoroughly analyzed or reported throughout the 10-year follow-up [9]. Therefore, research regarding the safety of silicone breast implants is ongoing.

In recent years, a number of studies have been published providing evidence regarding the potential link between SGBIs and multiple myeloma (MM) or its precursor disorder, monoclonal gammopathy of undetermined significance (MGUS) [10]. Notably, an animal model study conducted in 1994 determined that plasmacytomas can be induced at a high frequency in susceptible strains of mice following the intraperitoneal injection of silicone gels [11]. The gels tested in this study resembled the complex mixture of the different siloxanes found in mammary implants. Further studies will be necessary to fully assess which components of these gels are the active materials.

Here, we report the case of a female who rapidly developed MM from MGUS roughly 3 years after placement of an SGBI post-mastectomy for breast cancer. Following treatment with a combination of dexamethasone, bortezomib, and pegylated liposomal doxorubicin, the patient was treated with maintenance therapy for a year with bortezomib and steroids without significant change in her myeloma tumor markers. Upon replacement of her silicone gel implant with saline, both her IgG and M-protein levels markedly decreased, and these markers continue to steadily improve over time (Fig. 1).

Case Description

A 52-year-old African-American female with no family history of cancer presented with an elevated globulin level. Further workup revealed an IgG level of 2,214 mg/dL, with normal IgA and IgM levels. A bone marrow biopsy obtained at that time showed 5–8% plasma cells
with the absence of lytic lesions, anemia, hypercalcemia, or renal dysfunction. As a result, she was diagnosed with IgG kappa MGUS. In 2006, she underwent a mastectomy for an infiltrating ductal carcinoma of the left breast that was both ER and PR positive. She then underwent unilateral breast reconstruction with a silicone breast implant, and received adjuvant tamoxifen postoperatively.

In January 2009, the patient was found to have a rise in her IgG level to 3,950 mg/dL along with free kappa light chains and IgG kappa proteins in her urine. A bone marrow biopsy conducted in October 2010 showed 50% plasma cell infiltration, and she was diagnosed with International Staging System Stage 1 MM. Her IgG level continued to rise to 8,548 mg/dL. She was started on a combination of bortezomib, 2.6 mg IV administered on days 1, 4, 8, and 11, and dexamethasone, 40 mg orally administered on days 2, 5, 9, and 12 of a 21-day cycle (DV), with monthly zoledronic acid. After 5.5 cycles of treatment, her IgG level and M-protein had decreased to 5,947 mg/dL and 4.07 g/dL, respectively. However, due to significant side effects including peripheral neuropathy, lethargy, constipation, and diarrhea, this regimen was discontinued in March 2011.

A month later, she started a combination of dexamethasone 40 mg IV, bortezomib at a dose that was reduced to 1.0 mg/m² IV, and pegylated liposomal doxorubicin 5.0 mg/m² IV (DVD), all three drugs being administered on days 1, 4, 8, and 11 of a 28-day cycle along with monthly zoledronic acid. After 8 cycles of this therapy, her IgG and M-protein levels had decreased to 3,890 mg/dL and 2.81 g/dL, respectively. However, due to significant side effects including peripheral neuropathy, lethargy, constipation, and diarrhea, this regimen was discontinued in March 2012.

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In the same month, a year after starting her maintenance therapy, the patient underwent the removal of her SGBI and replacement with a saline alternative. Following this procedure, her IgG rapidly decreased to 2,520 mg/dL within 1 month (Fig. 1). More recently, her IgG and

![Fig. 1. The patient’s multiple myeloma significantly improved after silicone-to-saline implant replacement, as demonstrated by the reduction in IgG levels.](image)
M-protein levels have continued to decrease, reaching their lowest levels in March 2020 at 1,138 mg/dL and 0.53 g/dL, respectively (Table 1).

**Discussion**

The association with SGBIs may not be as clear for some disease processes, but the link is strong for several malignancies; specifically, breast implant-associated anaplastic large cell lymphoma, a rare aggressive B-cell malignancy which normally does not occur in or near breast tissue, but occurs in tissue contiguous to SGBIs [12, 13]. There is a wide range of severity of disease among affected patients, but, notably, most patients have experienced an excellent prognosis and removal of the implants has led to responses in many patients. In addition to implant removal, a smaller subset of breast implant-associated anaplastic large cell lymphoma patients who had presented with a tumor mass associated with the fibrous capsule were more likely to require a more aggressive therapeutic approach [13].

Furthermore, the 1994 study which demonstrated that the induction of plasmacytomas in genetically variant mice via silicone introduction highlights the presumable impact silicone implants may have on generating such rare malignancies [11]. The silicone materials that persisted in the peritoneal cavity of the mice had induced chronic inflammation for long periods before the plasmacytomas had developed. Due to the widespread use of silicone gels in medicine, further studies are required to better understand the capacity to, and what specific types of silicone gels do, induce both plasmacytomas in mice and other hematologic malignancies.

There are several known risk factors for MM, including age, race, gender, excess body weight, family history of MM, and MGUS [14, 15]. MM specifically has also been previously linked to silicone gel breast implantation [10]. In a case report regarding 3 patients, MM did not develop until more than 12 years after implant placement, which is consistent with the aforementioned mean implant rupture time [3]. Our study follows the first known documented case of significant improvement in MM occurring after a year of maintenance therapy during which the patient’s myeloma markers remained unchanged, which would also indicate that SGBIs may play a direct, but reversible, role in MM development.

**Conclusion**

We reported on a case of MM that showed dramatic improvement in the patient’s myeloma tumor markers following replacement of the SGBI with saline. Given the drastic nature of the change in MM disease status after removal of the silicone breast implant, especially occurring...
during the second year of maintenance therapy, and the evidence from other studies that
silicone does induce hematologic malignancies, further large-scale studies should be
conducted to determine if silicone breast implant removal in MM patients can improve
patients’ clinical status. Studies in other affected fields such as rheumatology potentially
could also show the same type of improvement in disease status with silicone implant removal
and, if true, would be important in improving the outcomes of women with MM who have
SGBIs.

Statement of Ethics

Informed consent was obtained from the patient in accordance with the ethical standards
of the institutional and/or national research committee and with the 1964 Helsinki Decla-
ration and its later amendments or comparable ethical standards. The subject had given
written informed consent to publish her case. The patient has also reviewed and approved
this manuscript for publication.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

J.R.B. designed the study. J.R.B., R.S., B.E., J.W., and C.H. collected the data. J.R.B., J.W., and
C.H. analyzed the data. J.R.B., J.W., C.H., and T.M.S. interpreted the results. J.R.B., C.H., J.W., and
T.M.S. wrote the manuscript. J.R.B. and T.M.S. reviewed the manuscript. All authors have
approved the manuscript and its submission to the journal.

References

1 Brinton LA, Lubin JH, Burich MC, Colton T, Brown SL, Hoover RN. Cancer risk at sites other than the breast
following augmentation mammoplasty. Ann Epidemiol. 2001;11(4):248–56.
2 American Society of Plastic Surgeons (ASPS), 2012 full report [Internet]. American Society of Plastic SURGEONS
(ASPS) [cited 2015 Dec 15]. http://www.plasticsurgery.org.
3 Brown, SL, Middleton MS, Berg WA, Soo MS, Pennello G. Prevalence of rupture of silicone gel breast implants
revealed on MR imaging in a population of women in Birmingham, Alabama. AJR An J Roentgenol. 2000;
175(4):1057–64.
4 Hedén P, Bronz G, Elberg JJ, Deraemaeker R, Murphy DK, Slipton A, et al. Long-term safety and effectiveness
of Style 410 highly cohesive silicone breast implants. Aesthetic Plast Surg. 2009;33(3):430–8.
5 Maxwell GP, Van Natta BW, Bengtson BP, Murphy DK. Ten-year results from the Natrelle 410 anatomical form-
stable silicone breast implant core study. Aesthet Surg J. 2015;35(2):145–55.
6 Sims S, Lundberg GD. Maybe now is the time to lift the ban on silicone breast implants, MedGenMed. 2001;
3(2):17.
7 Lipworth L, Holmich LR, McLaughlin JK. Silicone breast implants and connective tissue disease: no association.
Semin Immunopathol. 2011;33(3):287–94.
8 Tanne JH. FDA approves silicone breast implants 14 years after their withdrawal. BMJ. 2006;333(7579):1139.
9 Coroneos CJ, Selber JC, Offodile AC 2nd, Butler CE, Clemens MW. US FDA Breast Implant Postapproval Studies: long-term outcomes in 99,993 patients. *Ann Surg*. 2019;269(1):30–6.
10 Silverman S, Vescio R, Silver D, Rennier S, Weiner S, Berenson J. Silicone gel implants and monoclonal gammopathies: three cases of multiple myeloma and the prevalence of multiple myeloma and monoclonal gammopathy of undetermined significance. *Curr Top Microbiol Immunol*. 1996;210:367–74.
11 Potter M, Morrison S, Wiener F, Zhang XK, Miller FW. Induction of plasmacytomas with silicone gel in genetically susceptible strains of mice. *J Natl Cancer Inst*. 1994;86(14):1058–65.
12 Story SK, Schowalter MK, Geskin LJ. Breast implant-associated ALCL: a unique entity in the spectrum of CD30+ lymphoproliferative disorders. *Oncologist*. 2013;18(3):301–7.
13 Miranda RN, Aladily TN, Prince HM, Kanagal-Shamanna R, de Jong D, Fayad LE, et al. Breast implant-associated anaplastic large-cell lymphoma: long-term follow-up of 60 patients. *J Clin Oncol*. 2013;32(2):114–20.
14 Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. *Eur J Cancer*. 2011;47(11):1606–15.
15 Multiple Myeloma Research Foundation. Risk factors for multiple myeloma [Internet] [cited 2015 Dec 15]. Available from: http://www.themmrf.org/multiple-myeloma/multiple-myeloma-causes/myeloma-risk-factors.