Case Reports in Oncology

Case Rep Oncol 2020;13:1103–1108
DOI: 10.1159/000508494
Published online: September 18, 2020

Case Report

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

Chace Henning[a] James Wang[a] Regina Swift[a] Benjamin Eades[a]
Tanya M. Spektor[b] James R. Berenson[a, b]

[a]Institute for Myeloma & Bone Cancer Research, West Hollywood, CA, USA;
[b]Oncotherapeutics, West Hollywood, CA, USA

Keywords
Multiple myeloma · Silicone gel · Breast implants · Monoclonal gammopathy of undetermined significance · B-cell malignancies

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.

James R. Berenson
Institute for Myeloma & Bone Cancer Research
9201 W. Sunset Blvd., Suite 300
West Hollywood, CA 90069 (USA)
jberenson@imbcr.org

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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

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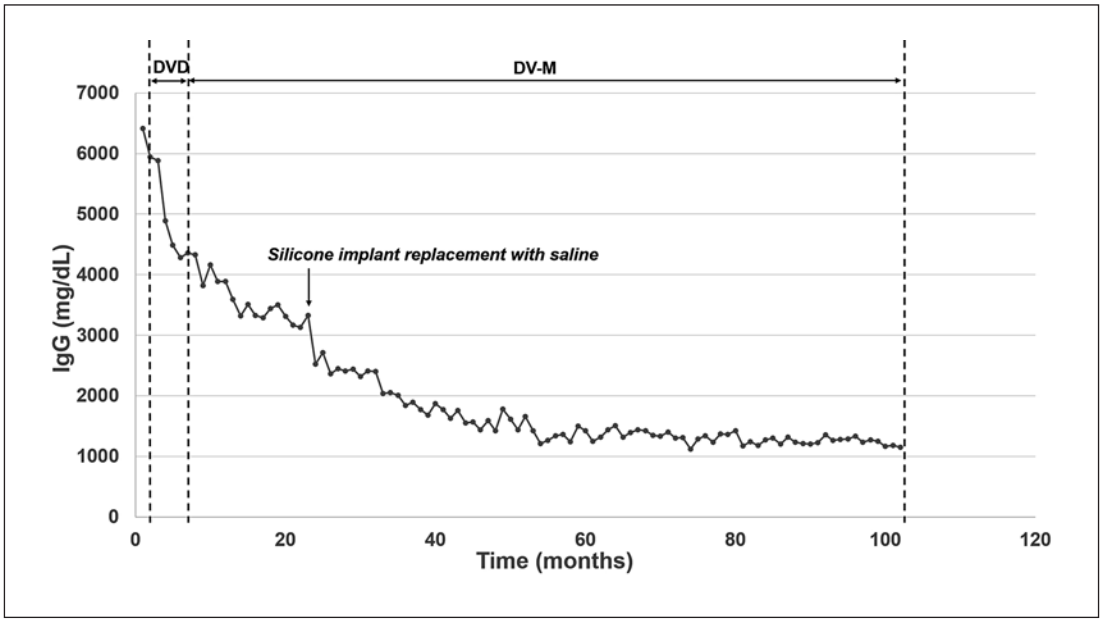

Fig. 1. The patient's multiple myeloma significantly improved after silicone-to-saline implant replacement, as demonstrated by the reduction in IgG levels.

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/m^2 IV, and pegylated liposomal doxorubicin 5.0 mg/m^2 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. In December 2011, she started maintenance therapy with dexamethasone 40 mg IV and bortezomib 1.3 mg/m^2 IV every other week, and methylprednisolone 20 mg orally every other day (DV-M) and ongoing monthly administration of zoledronic acid. In December 2012, her IgG and M-protein levels were 3,310 mg/dL and 2.14 g/dL, respectively (Table 1).

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

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Table 1. Summary of MM marker measurements

	Jan 2009	Oct 2010	Mar 2011	Dec 2011	Dec 2012[a]	Oct 2015	Mar 2020
Therapy	MGUS[b]	Initial MM diagnosis; DV	DVD	DV-M	DV-M	DV-M	DV-M
IgG, mg/dL	3,950	8,548	5,947	3,890	3,310	1,210	1,138
Serum M-protein, g/dL	–	–	4.07	2.81	2.14	0.83	0.53

MM, multiple myeloma; MGUS, monoclonal gammopathy of undetermined significance [a] Silicone implant replacement with saline. [b] Elevated IgG first observed.

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 Declaration 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.

Funding Sources

There are no funding sources and sponsor names to report.

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.

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