

Idiosyncratic Allergic Reaction: A Rare Complication of Augmentation Mammoplasty

Robert X. Murphy, Jr.

70.1 Introduction

The year 1992 was a landmark year in the history of medical implantable biomaterials in the United States. It was in that year that the U.S. Food and Drug Administration (FDA) placed a moratorium on silicone gel breast prostheses because of questions concerning their safety [1, 2]. These concerns would result in 15 years of unprecedented controversy, a national class-action lawsuit, and ultimately, the financial ruin of one of the leading U.S. manufacturing companies of its day.

To that point in time, silicone enjoyed great success in the medical community. Silicone is the second most abundant element on Earth. Silicone, in combination with oxygen, makes up 75% of the earth's crust. Although the ratio of silicone to carbon is about 250:1 in the earth's crust, it is approximately 1:5,000 in mammals [3]. In both free injectable and device form, silicone was used widely throughout the world. As an implantable biomaterial, silicone was considered a privileged inert substance, the complications of which were heretofore considered limited and acceptable. After all, silicone gel breast prostheses had been used in the United States since 1962 [4]. It was later estimated that the total number of U.S. women with silicone breast implants in 1989 was 815,700, for a prevalence rate of eight per 1,000 women, and by 1992 the estimated prevalence of breast implants had risen to approximately 11–12 per 1000 women [5]. During that 30-year period, the major post-implantation concerns of the surgical community had been capsular contracture, implant failure, and interference with mammography [6–10].

However, by 1991 enough pressure was brought to bear on the FDA by legal, women's rights, and media communities that silicone gel implants were withdrawn from the cosmetic, but not reconstructive, market. The literature was replete with reports of women with conditions ranging from fatigue and myalgias, to systemic autoimmune diseases, to even brain cancer [11–20], which they attributed to their silicone gel implants.

Studies addressing women's satisfaction at the time of this controversy were few. One survey conducted in

1992 queried 174 women who had undergone reconstruction after mastectomy and found that 34% would be “completely unlikely” to have silicone implants again [21]. In that same year, the Surveillance Program of the National Cancer Institute collaborated with the Postmarket Product Management of the FDA to survey women who had reported local or systemic issues after breast implant surgery to the Problem Repository Program of the FDA. Coon and her associates [22] later conducted telephone interviews with a cohort of these women who reported self-perceived problems with their implants as part of this program. They found that a full 99% of these women had heard of problems with silicone gel prostheses, with the main source of their information being television, newspapers, and magazines, but not the physicians, manufacturers, or the FDA [23–25]. Sixty-five percent of those surveyed reported being dissatisfied with their implants. In this report, some of the dissatisfactions in this self-selected cohort of patients were fear, anger, and perceived disability [22].

What is most interesting, however, is that despite the involvement of patients, the plaintiff's bar, the government, and physicians, the issue of simple allergy never arose. Arguably the most ubiquitous reactive response of the human being to all manner of agents—be they airborne, contact, ingested, or injected—allergic reaction was never raised as a significant issue. A single paper cited self-limited acute urticarial reactions to textured breast implants, but it failed to characterize these as true allergic reactions [6].

70.2 Case Reports

In 1995, Kirwan [26], in a letter to the editor in *Plastic and Reconstructive Surgery*, reported his experience with two cases of apparent allergy to silicone breast implants. In one scenario, a 45-year-old woman, who had had augmentation mammoplasty 10 years prior and a first-stage reconstruction of a scar contracture with tissue expander placed 2 months previously, developed a cervical rash. The rash persisted after the expander was

removed. The breast implants were exchanged with new gel implants because of rupture of the prostheses several months later. However, the rash did not resolve until the breast implants were removed and the patient underwent bilateral reconstruction using transverse rectus abdominis myocutaneous (TRAM) flaps. The second patient experienced a much stormier course. Five months after silicone gel implant mammoplasty, she developed a rapidly evolving rash of her breasts and axillae. The right implant was removed due to rupture and replaced. The rashes continued, ultimately resulting in angioneurotic edema and anaphylactic shock. Both implants were removed, with complete resolution of the patient's symptoms. Notably, a rash recurred several months later after placement of a silicone Port-a-Cath, requiring removal of that device.

One year later, with my colleagues, I reported a case of an allergic reaction to saline implants with textured shells [27]. Five months after undergoing a one-stage bilateral breast reconstruction using Siltex Becker tissue expander mammary prostheses (Mentor, Santa Barbara, CA, USA), the patient began complaining about a painful, pruritus rash of the scalp, chest, and arms, which did not respond to topical or oral steroids. Examination revealed erythematous papules and pustules on her chest and arms. Cultures did not document any pathologic bacteria. These lesions gradually spread to her neck, chin, and cheeks. A biopsy of these lesions documented perivascular lymphohistiocytic infiltrate consistent with a drug reaction, photodrug reaction, or polymorphous light eruption. In order to document a potential allergic etiology of this condition, representative materials were obtained from the Mentor Corporation. Patch testing was performed using the injection port, as well as the inner and outer aspects of the implant. The patient noted an itching and burning sensation within 15 min. Urticarial plaques developed exclusively under the textured shell patch without any reaction noted at the port or smooth surface of the implant test sites after 30 min. Reluctantly, the patient underwent removal of the textured-shell prostheses and, at her insistence, replacement with smooth-shell saline implants. Her symptoms resolved almost immediately. It was hypothesized that the process of vulcanization of the textured implant shell may have been responsible for her allergic reaction, since textured devices are cured at a higher temperature than smooth wall implants to texture the silicone (Mentor Corporation, personal communication, 1994).

A report of the Implant Awareness Society, published in the *Israel Journal of Occupational Health* in 1999 [28], studied eight breast implant patients who were referred for occupational medicine assessment in 1993 because

of respiratory symptoms, rhinorrhea, and pruritus. Although the focus of this study was respiratory and pulmonary symptomatology, patients had some measure of urticaria, characterized as being intermittent to "intolerable pruritus," and rashes. However, in only one case was it documented that the rash and breast pain resolved when the implants were removed.

70.3 Discussion

For the last 25 years, innumerable reports have appeared in the literature either positing or refuting a causative role for silicone breast prostheses in the evolution of a myriad of medical conditions. The questionable uniqueness of silicone breast implants in this phenomenon has always been an issue because silicone polymers are widely used in other implantable biomedical devices, such as shunts, pacemakers, artificial valves, penile implants, chin implants, nasal struts, finger and toe joints, tendon replacement devices, tissue expanders, ear pinna, pectoral and calf muscle implants, intraocular lenses, scleral bands, ophthalmic bands, silicone sheeting for replacement of inguinal and other hernias and dura mater of the brain, antireflux devices, bariatric devices, facial implants, and breast implants [29].

An exhaustive review of the literature failed to reveal any study that was able to definitively link silicone breast prostheses with connective tissue disease [17, 19, 30–44], neurologic disease [36, 45], perinatal problems [46, 47], congenital deformities, lactation of silicone in breast milk [43, 48], breast cancer [49–51], brain cancer [52], or other health issues [33, 53, 54]. The body of scientific literature led the Institute of Medicine to release its landmark 440-page report in 2000, the report summary of which stated that "a review of 17 epidemiological reports of connective tissue disease in women with breast implants was remarkable for the consistency in finding no elevated relative risk or odds ratio for an association of implants with disease" [55].

Other studies have examined the durability of silicone prostheses and the potential role of extracapsular or free silicone as an etiologic agent of disease. Marotta et al. [56] conducted a large cohort meta-analysis of failure data for silicone gel prostheses based on literature reports while also investigating shell and gel properties from explanted silicone gel breast implants. They postulated that implant failure would occur in a time-dependent manner. Brandon et al. [57] noted silicone implants that were intact for 32 years and suggested that shell degradation was not a primary mechanism for implant failure. Assuming this to be true, one would

expect a subpopulation of those women with silicone gel prostheses to have free silicone either within or outside the breast capsule. Although a high incidence of self-reported fibromyalgia was noted [19, 20], no conclusive evidence was found to support the hypothesis that silicone contributed in any way to any disease state [35, 36, 58–61].

Of course, if true allergic reactions to silicone breast implants were a significant issue, one would expect that one's immune system and the classic antigen–antibody reaction would play a significant role. Studies from around the world have investigated this phenomenon without defining a cause-and-effect relationship.

Studies in Denmark examined two different facets of the antibody issue and its potential role in the silicone breast implant controversy. First, the Danes developed a new assay to evaluate antipolymer antibody (APA) levels in women with silicone breast implants [62]. Their study concluded that women with silicone breast implants did not have higher levels of APAs than women without silicone breast implants. They used this assay to compare silicate antibody levels in women with and without silicone breast implants and to correlate this information with those who carried the diagnosis of “muscular rheumatism.” The authors determined that there was absolutely no correlation between silicate antibody levels and symptom severity scores [62].

The British literature contains a report based on four matched cohorts of 20 women each: those with silicone breast implants, those without silicone breast implants, those with documented seropositive autoimmune disease, and anonymous controls. These authors were not able to demonstrate a significant difference in antibody levels between silicone breast implant patients and women without silicone breast implants, but they did document a statistically significant difference in levels of patients with silicone breast implants and those without silicone breast implants but with autoimmune disease [63].

Numerous studies on this topic also appeared in the U.S. literature. Holmich and colleagues [59] identified a random population of 271 patients with silicone breast implants and obtained baseline magnetic resonance imaging (MRI) scans. Two years later, a cohort of these women who had not undergone explantation of their silicone breast implants were again evaluated by MRI. This identified a subset of 64 women who had untreated, confirmed ruptures of their silicone breast implants. Among other variables, comparisons were made for differences in serum values of antinuclear antibodies, rheumatoid factor, and cardiolipin antibodies immunoglobulin G and immunoglobulin M. Interestingly, there was no increase in levels of autoantibodies during the

study period in either of the groups of those with intact or ruptured implants [60].

Finally, in a study appearing in the *Journal of Rheumatology* [64], serological testing was performed on 298 women with silicone breast implants, 298 women without silicone breast implants, and 52 diabetic patients who had presumed silicone exposure due to needles. In 14 of 16 serologic tests, there was no statistically significant difference among the three groups. A difference was detected between implanted patients and those without silicone breast implants, with small decreased levels of C₃ and C₄ in those patients with silicone breast implants. These results seemed to indicate that there was little evidence of immune system activation in breast implant patients.

70.4 Conclusion

The human immune system is a very highly refined mechanism of defense. Although charged with mounting an antibody response to any unrecognized antigen threat, it must also possess enough checks and balances to not cause unwarranted host-versus-host reactions. Silicone exists naturally in all mammals. An exhaustive search of the literature seems to indicate that silicone, as it exists in the current forms of implantable biomedical devices including breast implants, is an immunologically privileged and inert material. It remains incumbent for the medical practitioner, however, to consider an idiosyncratic reaction as a diagnosis of exclusion in a differential diagnosis for an individual with a history of a bioimplantable device and an unusual allergic response beginning after device implantation. Appropriate confirmatory evaluation, including patch testing, is recommended. If this diagnosis is supported, explantation of the device is curative.

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