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CLINICAL RESEARCH

Amelioration of Systemic Disease after Removal of Silicone Gel-filled Breast Implants

ARTHUR E. BRAWER MD

Department of Medicine, Division of Rheumatology, Monmouth Medical Center, Third and Pavilion Avenues, Long Branch, New Jersey 07740, USA

Abstract

Purpose: *To examine the post explantation clinical course in symptomatic recipients of silicone gel-filled breast implants.*

Design: *Solo private practice-based evaluation.*

Materials and Methods: *156 patients who developed a systemic illness following insertion of silicone gel-filled breast implants underwent removal of these devices. Mean implantation time was 12 years, and subsequent follow-up averaged 2.5 years.*

Results: *76/156 (49%) of patients noted amelioration of their disease starting an average 9 months after gel device removal. Longer durations of implantation were related to less clinical improvement, the latter declining from 67% of those with final surgery after 7.5 years to 31% at 14.5 years. Improvement was unaffected by prior rupture or multiple surgeries, and could not be predicted by age, unilateral implant, or subsets of clinical features. In 112/156 patients who opted for final gel device removal without saline exchange, 10% of all improved patients experienced paradoxical and simultaneous disease progression with the appearance of new symptoms and signs. This phenomenon was unaffected by prior rupture, multiple surgeries or prolonged implantation time, but had a risk nearly five times as great in any of the 44/156 patients who improved after gel for saline exchange. Transverse rectus abdominis myocutaneous (TRAM) flap surgery performed after final gel device removal was associated with a 50% incidence of panniculitis in the breast areas and/or abdominal site. Self-worth issues, usually via support groups, often needed to be addressed simultaneously with ongoing medical evaluation in order to effect explantation efforts in some seriously ill patients.*

Conclusions: *In this cohort of symptomatic breast implant recipients, disease amelioration following explantation provides additional supportive evidence for the existence of a novel illness triggered by silicone gel-filled devices. The demonstrated improvement of systemic phenomena following implant removal was more likely to occur if these devices were in place for less than 12 years. Saline implants appeared capable of perpetuating systemic disease progression following an initial gel-induced disorder.*

Keywords: silicone; breast implants.

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INTRODUCTION

The removal of silicone gel-filled breast implants in symptomatic recipients exhibiting a variety of systemic phenomena has been followed by clinical and laboratory improvement in some patients [1–11]. This is one of many observations supporting the implication that these devices are associated with the development of a novel illness. In general, post-explantation clinical data have lacked a comprehensive analysis of the influence and effects of prior gel exposure time, disease severity, age, multiple prior exchange surgeries, unilateral implant, subsets of clinical features, saline implant replacement, transverse rectus abdominis myocutaneous (TRAM) flap surgery or prior gel implant rupture. This report attempts to address some of these issues.

MATERIALS AND METHODS

One hundred and fifty-six female patients who developed a systemic illness beginning an average 2.5 years after insertion of silicone gel-filled breast implants underwent removal of these devices. The women are part of a larger cohort of 300 patients whose clinical features have previously been described [12,13]. Systemic manifestations, disease severity, chronological evolution, age, manufacturing diversity and ruptured devices were comparable in the two groups as ascertained by a single rheumatologist who interviewed and examined each patient directly. Mean gel implantation time was 12 years. Subsequent follow-up after removal averaged 2.5 years and was arranged by either re-examination or telephone contact.

The cohort was divided into five groups as noted in Table 1. Forty-four patients opted for implant exchange whereby the removal of their gel devices was followed immediately by saline implant replacement.

Improvement of the systemic illness was defined as a lessening of the frequency and/or severity of at least 50% of the total number of symptoms and signs manifested by a single patient. This did not require the complete resolution of any one item, and could coexist with any of the following scenarios (either singly or in combination):

(1) no changes in the remaining symptoms and signs;
(2) worsening of some or all of the remaining symptoms and signs;
(3) the appearance of new symptoms or signs.

Similar variabilities in the illness were recorded for the unimproved patients, in whom observations may or may not have revealed the simultaneous amelioration of a minority of their clinical features.

RESULTS

Group 1

Of the 27 patients who underwent removal of their original non-ruptured implants, the final

TABLE 1. Breast implant status of 156 patients who underwent final silicone gel-filled device removal

Group	Explantation categories	n (%)
1	Original non-ruptured gel	27/156 (17%)
2	Original ruptured gel	48/156 (31%)
3	Multiple gel sets, no ruptures	8/156 (5%)
4	Multiple gel sets, at least 1 rupture	29/156 (19%)
5	Gel exchange for saline	44/156 (28%)

surgery was performed an average of 7.5 years after implantation (span: 11 months to 18 years). Eighteen patients (67%) improved over an average follow-up time of 34 months. The onset of improvement began an average 9 months after explantation, with the earliest amelioration noted at 2 months. Two of the improved patients (11%) developed new systemic symptoms and signs despite their overall improvement. The 9 unimproved patients were followed up an average 37 months after explantation, with 1 (11%) manifesting new symptoms and signs.

Group 2

Ruptured original implants were removed in 48 patients. The average time to rupture was 8.3 years (span: 2–21 years), and the average elapsed time from implantation to final surgical removal was 12.83 years (span: 4–25 years). The longest interval from rupture to final surgery was 13 years. Improvement began an average 9 months following final surgery in 21 patients (44%), with the earliest amelioration noted at 2 months. Two of the 21 (10%) developed new symptoms and signs. Of the 27 unimproved patients, 8 (30%) developed new systemic features. Follow-up time averaged 26 months for each subdivision.

The most striking finding in this category was that rupture, by itself, did not determine whether or not improvement occurred after explantation. A subgroup was analyzed where the total implantation time for each patient was 10 years or less (average 7.5 years; average time to rupture 6.25 years). Sixty-three percent of patients in this subgroup improved, which is comparable to the improvement rate of 67% in Group 1. Thus, the duration of gel device exposure (but not rupture) appeared to determine whether or not improvement occurred following explantation. Further analysis of this same subgroup revealed that one-third of the unimproved patients developed new symptoms and signs. Thus, rupture (but not gel device exposure time) appeared to determine the threefold risk of disease progression in unimproved patients following explantation. Surprisingly, neither rupture nor gel device exposure time influenced the percentage of improved patients who developed new symptoms and signs, which remained constant at 10%.

The following case history is illustrative:

A 33-year-old white female, previously in excellent health, underwent bilateral cosmetic breast augmentation with the insertion of silicone gel-filled breast implants. Postoperative breast numbness and capsular contracture were followed 2 years later by the development of headaches, neck pain, and depression. Within three additional years she complained of abdominal cramps, loose stools, sinusitis, menstrual irregularities, fatigue, pain and swelling in multiple small and large joints and two hours of morning stiffness. Lateral implant displacement occurred in the right breast accompanied by bilateral bogginess, heaviness, sagging, and micronodularity. Over the next 9 years (up to the age of 47) she developed skin dryness, forearm numbness, seizures, wheezing, palpitations, multiple dental cavities, carpal tunnel syndrome, intermittent blurry vision, tinnitus, dysphagia, dry eyes and dry mouth, diffuse myalgias, a thirty-pound weight gain, oral ulcerations, intermittent periorbital edema, fevers, eyelid twitching, chills, dizziness, cognitive dysfunction, rib pains, nail cracking and splitting, skin rashes, itching, bilateral greenish-black breast discharge and night sweats, none of which was alleviated by the institution of estrogen replacement. Multiple laboratory tests including chemistries, thyroid function, complete blood count (CBC) sedimentation rate, anti-nuclear antibody, etc. were normal or negative, and a computed tomography scan of the brain was normal. Bilateral ruptured implants were removed, without replacement. Three months after explantation, at the age of 48 (and extending over the next 24 months), she began to notice gradual improvement (but by no means resolution) of her polyarthritis, morning stiffness, palpitations, night sweats, chills, dizziness, weight gain, depression, loose stools, abdominal cramps, dysphagia, fevers, sinusitis, eyelid twitching, periorbital edema, rib pains, tinnitus, forearm numbness, wheezing, headaches, mouth sores and neck pain. Current physical examination at age 50 reveals anterior chest

wall telangiectasias, vitiligo and freckling; a positive Phalen's sign; a Schirmer test exhibiting 0 mm of tear formation; parotid swelling; and palmar erythema.

Group 3

This category includes 8 patients who have undergone insertion and/or exchange of multiple sets of silicone gel-filled breast implants, with no documented ruptures, followed by final gel device removal. Total implantation time averaged 8.75 years (span: 3–17 years; longest single set = 9 years). The entire group had an average 28-month follow-up, but the number of patients was too small for comparable analysis.

Group 4

Twenty-nine patients had multiple sets of silicone gel-filled breast implants inserted and/or exchanged, with at least one documented rupture. The time from initial implantation to final surgery averaged 14.5 years (span: 3–22 years), and the average time to rupture was 6.67 years (span: 2 months to 16 years). Nine patients (31%) experienced improvement beginning an average 10 months after final explantation, with the earliest improvement noted at 4 months. One of these patients (11%) developed new symptoms and signs. Of the 20 unimproved patients, 5 (25%) developed new phenomena. Follow-up averaged 28 months for both subdivisions.

Within this explantation category a subgroup was analyzed, where the total implantation time for each patient was 16 years or less (average 13 years). Forty percent of this subgroup experienced improvement, which is comparable to 44% in Group 2. This reinforces the observation (in this series of patients) that the length of time of gel device exposure (but not rupture) determined whether or not improvement occurred following explantation.

The following case history is illustrative:

A 27-year-old white female with postpartum breast atrophy underwent bilateral insertion of silicone gel-filled implants. Postoperative breast itching and capsular contracture were followed one year later by recurrent urinary tract infections, leg edema and a skin rash on the trunk, at which time implant exchange was performed using another set of silicone gel-filled devices. Recurrent capsular contracture was accompanied at age 32 by hair loss, fatigue, nausea, weight loss, anterior chest pain and myalgias. At age 35 an excised breast nodule revealed silicone granuloma, and mammography was positive for bilateral rupture. At age 43, having developed livedo reticularis, polyarthritis, dry eyes and dry mouth, one hour of morning stiffness, periorbital edema, headaches and leg varicosities, she underwent bilateral implant exchange for a third set of silicone gel-filled breast implants. At the time of surgery it was noted that there was "gel all over the place." Capsular contracture recurred, and one year later diffuse skin freckling developed along with cognitive dysfunction and extremity dysesthesias. Bilateral implant exchange for a fourth set of silicone gel-filled breast implants revealed that the third set had already ruptured. Two years later, at age 46, she was noted to have diffuse telangiectasias on the anterior chest wall, splotchy hyperpigmentation on the face and trunk, and a Schirmer test of 0 mm. At the age of 48 her fourth set of implants was removed without replacement (one was noted to be ruptured). Over the next 4 months she developed chills, dyspnea on exertion, muscle weakness (with only a marginal elevation of creatinine phosphokinase), V-neck erythema and dizziness. Evaluation 24 months after her final explantation revealed no improvement in any of her systemic phenomena.

Group 5

The psychological and social issues confronted by these women prior to explantation were considerable. Despite deteriorating health coupled with participation in support groups, the

overriding issue was the vision of post-explantation physical deformity. This prompted the 44 women in this category to undergo immediate replacement with saline implants at the time of their final gel implant(s) removal. Total gel device exposure time prior to saline exchange averaged 10.5 years (span: 2–25 years). Ten months after the exchange, 26 patients (59%) experienced improvement of their systemic illness. Ruptures (35/44) of one or more prior set(s) of gel implants were equally divided between improved and unimproved groups (81 and 78% respectively). Subsequent saline implantation time (i.e. follow-up) averaged 2.5 years for each subgroup (span: 8 months to 7.25 years).

The most striking finding in the saline exchange group was the marked incidence of new symptoms and signs, which occurred in 12 of the 26 patients (46%) who had already exhibited improvement of their prior gel-related illness. Since both rupture and gel device exposure time had no influence on the appearance of new phenomena in all improved groups of patients in any other explantation category, the difference noted (46 versus 10%) appeared to be related to the saline implants. Of the 18 unimproved saline exchange patients, 13 (72%) developed new clinical features. Since rupture (but not gel device exposure time) influenced the occurrence of new phenomena in unimproved patients after explantation, the difference noted (72 versus 30%) appeared to be related to the saline implants. Fifty-two percent (13/25) of those with new clinical features exhibited a brand new skin rash of one type or another. This is in stark contrast to Groups 1 through 4, where the post explantation development of new symptoms and signs was totally random. Elapsed time to the development of new phenomena averaged 10 months (span: 2–24 months), and was comparable in all five explantation categories. This pattern was invariably much slower than the previously reported time sequence of disease evolution occurring while gel-filled implants were still in place [12].

The following case history is illustrative:

A 20-year-old white female underwent bilateral cosmetic breast augmentation with the insertion of silicone gel-filled implants. Postoperative breast numbness and itching were followed 3 months later by fatigue, right axillary lymphadenopathy and bilateral capsular contracture. By age 23 years puckering, dimpling, nodularity and increased itching were noted in the right breast, accompanied by dry skin, confusion, depression, nausea, epigastric pain, abdominal bloating, arm tremors, dry eyes, myalgias, and allergies to milk and wheat. Over the next 7 years slow shrinkage of the breasts occurred (from a size 36C bra to 36A), during which time the patient developed pain and swelling in multiple small and large joints, hoarseness, night sweats, dizziness, metallic taste, two hours of morning stiffness, anterior chest pain, hair loss, tinnitus, photosensitivity, neck lymphadenopathy, palpitations and a 29 lb weight gain. At age 30 bilateral ruptured implants were removed, followed by the immediate insertion of saline breast implants. Over the next two years she noted menstrual irregularities, poor wound healing and periorbital edema. One year later she began to notice gradual slow improvement (but by no means resolution) of her chest pain, polyarthritis, photosensitivity, palpitations, tinnitus, neck lymphadenopathy, night sweats, dizziness, hoarseness, metallic taste, hair loss, myalgias, nausea, tremors, epigastric pain and abdominal bloating. By age 36 she had developed headaches, sore throats, dysphagia, dysesthesias in her hands and a papular erythematous rash on the extremities (unrelated to sun exposure). One year later a Schirmer test was 8 mm, and an ANA positive 1:160 in a speckled pattern. All other lab tests (CBC, chemistries, thyroid function, multiple other serologies, etc.) were normal or negative.

Additional Observations

Table 2 summarizes the improvement data for the four explantation categories that were fully analyzed. Graphic illustration of the results is shown in Fig. 1. As the length of time of gel implantation increased, the percentage of improved patients decreased. Overall, 76/156 patients (49%) noted amelioration of their systemic illness starting an average 9

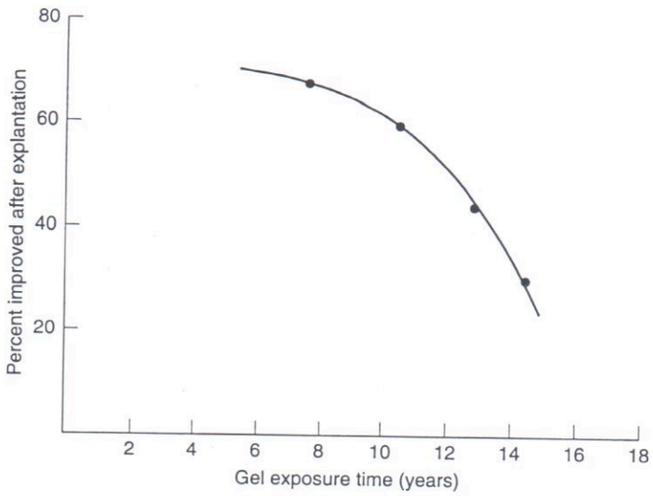

FIG. 1. The explantation improvement curve. The chance of realizing amelioration of systemic symptoms and signs following final implant(s) removal was inversely related to the length of prior gel exposure (i.e. total implantation) time.

months after final gel device removal. Improvement of disease phenomena (skin rash, fatigue, etc.) was totally random with no specific pattern detected. Within any single explantation category, the average gel device implantation time was similar for both improved and unimproved cohorts. Multiple other variables were also analyzed, including time to rupture (when applicable), age, disease severity, subsets of clinical features, unilateral versus bilateral implants and manufacturing diversity. Within any single explantation category no differences were demonstrated between improved and unimproved cohorts, and these same factors did not allow prediction or selection of specific individual patients who would subsequently improve and/or develop new symptoms and signs.

Ten patients underwent TRAM flap surgery after final gel device removal (average implantation time = 10 years). Five (50%) developed panniculitis (subcutaneous fat necrosis) in the breast areas and/or abdominal site, which is 5 times the expected incidence in non-symptomatic individuals without silicone exposure who have undergone similar surgery. No predisposing factors could be identified, such as malignancy, unilateral implant, prior rupture or multiple implant exchanges.

TABLE 2. Percentage of patients experiencing improvement of their symptoms and signs after final gel implant(s) removal

Group	Gel exposure (*years*)	Percent improvement
1	7.5	67
5	10.5	59
2	12.83	44
4	14.5	31

DISCUSSION

This report of 156 symptomatic breast implant recipients who underwent explantation revealed a declining occurrence of systemic improvement with increasing duration of gel device insertion. The best chance for disease amelioration was noted when implants were removed on average no later than 7.5 years after insertion. Shorter implantation time of less than 5 years did not yield better results. These observations are complementary to prior findings in the entire cohort of 300 patients in whom increasing severity of systemic illness was directly related to the length of time of gel device exposure [12]. Taken together, the sicker that patients became from their silicone-induced illness, the less likely they were to improve after removal of these devices.

Improvement began an average 9 months after implant removal, was unaffected by prior rupture or multiple surgeries, and could not be predicted by age, unilateral implant or subsets of clinical features. In patients without saline exchange, improvement was accompanied by a 10% occurrence of paradoxical and simultaneous disease progression characterized by the appearance of new symptoms and signs. This implies that residual mechanisms of silicone-induced disease causation continued to be operative despite a natural attempt by the body to heal itself following bulk device removal. This phenomenon was unaffected by prior rupture, multiple surgeries or prolonged implantation time, but had a risk nearly five times as great in any of those who improved after gel for saline exchange. Since the elastomer, or envelope, of a saline implant is similar to the envelope of a gel implant (i.e. both are solid silicone), in some patients already sensitized with a gel-induced illness further exposure to analagous devices proved to be deleterious. This risk increased seven fold in any of those who were unimproved after gel for saline exchange. The significance of rupture (in the absence of saline exchange) was confined to a three-fold risk of disease progression in unimproved patients.

Except for nonsteroidal anti-inflammatory drugs and/or analgesics, the essential cornerstone of managing systemic illness was the surgical removal of the silicone gel-filled breast implants. Verification of the results in Fig. 1. will require analysis of other groups of symptomatic implant recipients. In addition, the 12 years of gel-induced disease development will ultimately need to be balanced by a comparable observation period after explantation to help determine whether silicone-induced disease can persist indefinitely. If these results are sustained, it does not bode well for the remaining 144 patients (from the original cohort of 300) in whom silicone gel-filled devices remain implanted over an average 14 1/3 years (longest 27 years). Of these 144 patients, 79 (55%) presently have a ruptured implant in place, and when placed on the curve in Fig. 1 can be expected to have less and less chance of improvement (and a corresponding increased risk of disease progression) despite future anticipated explantation. In many of these patients, a lack of adequate health insurance coverage is one of many factors adding to the delay in surgical removal.

Improvement data in this report were not evaluated or adjusted for time to disease onset, as the numbers of patients were too small to permit such an analysis. Instead, the average disease onset of 2.5 years after implant insertion was utilized. It may well be subsequently shown that the explantation improvement curve noted in Fig. 1 shifts to the right for a later disease onset. As an example, a patient with 15 years' total implantation time, whose silicone-induced illness did not begin until 10 years from the time of original insertion, might be expected to have a 67% chance of improvement (based on five years of systemic disease activity) instead of a less than 30% chance of amelioration (based on total implantation time). For this latter premise to be proven correct, it would mean that increasing latency of systemic disease onset has a favorable effect on the chance of improvement following explantation. Superimposed on this are potential treatment variables, such as dietary inclusions or exclusions, exercise, metabolic supplements and alterations, pharmacologic regimens, or other innovative interventions. Any treatment

modalities claiming long-term success for disease amelioration must be measured against the natural course of the illness.

In summary, the findings in this cohort of symptomatic breast implant recipients provide supportive evidence for the existence of a novel systemic illness triggered by silicone gel-filled devices. As the duration of gel device exposure increased, the chance of clinical improvement following explantation decreased. These results are directly complementary to previously reported disease development data [12] and strengthen the recommendation that advice given to symptomatic patients for implant removal should be based primarily on the total duration of implantation and not on whether implants are thought to have ruptured. The risk of gel for saline exchange is in need of further assessment as this was capable of perpetuating systemic disease progression in patients already demonstrating established silicone gel toxicity.

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