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Silicone breast protheses and rheumatic symptoms: a retrospective follow up study

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Abstract

***Objectives*—To determine whether women with silicone breast protheses have more rheumatic complaints than controls.**

***Methods*—The study included 287 women who had silicone breast protheses implanted between 1978–90. For every patient a female control of the same age was selected who had had an aesthetic operation in the same year. A questionnaire was sent to this retrospective cohort of women with silicone breast protheses and controls.**

***Results*—Questionnaires were returned by 235 cases (82%) and 210 controls (73%). Patients reported more symptoms arising after surgery than controls (0·6 v 0·3 complaints per subject, $p < 0·001$). The average interval between surgery and onset of complaints was 5·1 years for patients and 5·9 for controls. Complaints presented by patients were: painful joints ($p < 0·005$), burning eyes ($p < 0·01$), and skin abnormalities ($p < 0·005$). Differences in the use of antirheumatic drugs or medical consultations related to rheumatic symptoms did not reach statistical significance. Further information obtained from the patients and controls reporting rheumatic symptoms did not reveal the presence of a specific syndrome in connection with silicone materials.**

***Conclusion*—Women with silicone breast protheses report more rheumatic complaints after silicone implantation than controls, but there is no evidence of increased prevalence of common rheumatic diseases.**

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In plastic surgery, silicone breast protheses are used for mammahypotrofy and mammaasymmetry correction, and for reconstruction after mastectomy. At present in the USA more than 1 000 000 women have silicone breast protheses. In 1992, the Food and Drug Administration announced that breast implants filled with silicone gel would only be available through controlled clinical studies.[1] Although this decision was based primarily on the manufacturers' refusal to prove the safety of these devices, and not on perceived risks of silicone materials, it caused anxiety among women with silicone breast protheses and led to considerable controversy.

Silicone has generally been regarded as a biologically inert material. However, there is silicone seepage through intact membranes and phagocytic cells tend to embed themselves within the envelope, possibly caused by an immune-mediated phagocytic process. Localised giant cells and foreign body granulomas were found surrounding the implants; also, axillary lymphadenopathy has been reported.[2 3] These manifestations are relatively harmless from a clinical point of view.

Of concern are reports of more than 100 cases with connective tissue diseases occurring after silicone implantation. Scleroderma, systemic lupus erythematosus, mixed connective tissue disease, rheumatoid arthritis (RA), Reiter's syndrome, Sjögren's syndrome, and Hashimoto's thyroiditis have been reported.[4–10] Rheumatic manifestations followed injection with silicone fluid of unknown purity, paraffin, and petroleum jelly,[4 5] and also occurred after implantation of silicone gel protheses or saline-filled implants.[6–10] In some reported cases a causal link between silicone and rheumatic symptoms was suggested by clinical improvement and partial normalisation of laboratory values after removal of the silicone materials. There are no obvious clues to the pathogenesis of silicone-induced disease. Based on animal models of adjuvant arthritis and on experimental immunological principles of adjuvant stimulation of the immune system, the term 'human adjuvant disease' was introduced for silicone-induced polyarthritis. Recently, the idea of an autoimmune process was supported by demonstration of antinuclear antibodies (ANAs) in association with silicone breast augmentation,[11–13] but controlled studies are scarce. In a single case-control study no association of RA and previous silicone implantation was found.[14]

So far, case reports and uncontrolled studies have raised more questions than they have answered. There is a continuing debate about the possible cause and effect relationship between silicone materials and connective tissue disease. Little is known about the frequency of such adverse reactions, and about the interval between implantation and the occurrence of symptoms. The first aim of the present study was to compare the frequency of rheumatic symptoms in women with silicone breast protheses and controls. A second aim was to assess the length of the interval between implantation and such symptoms and to verify the presence of well-known rheumatic diseases in patients and controls.

Patients and methods

The study was carried out among patients of the Department of Plastic Surgery, Free University Hospital, Amsterdam. All the women who had silicone breast augmentation between January 1978 and December 1990 were selected. For every patient an age matched female control was selected, who had had an operation, not involving the use of silicone, in the same year at the same department. An introductory letter was sent to the general practitioners of patients and controls. They were asked to state any objections to the participation of their patients, and to check their addresses. This procedure was requested by the Ethical Committee, who approved the study.

Subsequently, in June 1992 a questionnaire was sent to patients and controls, together with a covering letter and a stamped return envelope. Non-responders were sent one reminder. In the questionnaire we asked about the following symptoms: painful joints for at least three months, swelling of joints for at least one week, regularly burning eyes, ulcers in the mouth for three or more consecutive weeks, Raynaud's phenomenon, pleuritis, proteinuria or kidney disease, skin abnormalities worsening by exposure to sunlight, and low blood cell or platelet count.[15] For every complaint, the year of onset was asked. In addition, the questionnaire inquired about the use of antirheumatic drugs and medical consultations for rheumatic problems.

Statistical analysis was performed using the statistical software package SPSS-PC + 4·0. A Chi squared test with Yates' continuity correction was used to compare the incidence of each individual complaint between patients and controls. Student's *t* test was used to compare the total number of complaints per subject between cases and controls.

Results

A total of 374 cases and an equal number of controls met the inclusion criteria. All cases received silicone-gel filled, non polyurethane-coated breast protheses. Reasons for exclusion were: 15 cases (of whom 12 unilateral silicone implantation) and six controls had died since the operation; 64 cases and 77 controls were lost to follow up; for eight cases and four controls the family practitioner advised not to send the questionnaire. Thus questionnaires were mailed to 287 cases and 287 controls.

Of the 574 mailed questionnaires, 445 (78%) were returned, of which 235 (82%) were from patients and 210 (73%) from controls. Responders and non-responders did not show a significant difference for age, operation-type and year of operation. In the patient group, 70 women had unilateral and 161 bilateral silicone implantation, whereas the exact type of surgery was not reported in four women. About 80% of women undergoing unilateral implantation had previous mastectomy for breast cancer. Controls had the following surgery: fat reduction (95), uni- or bilateral breast reduction (105), and various other procedures (10). The mean age of cases and controls was 43 years for each group (range 19–73 years in patients and 19–84 in controls). Average follow up duration was 6·5 (2–14) years in patients and controls.

The answers are summarised in the table. Patients and controls reported equal numbers of problems with onset before the year in which surgery had taken place. Eighty eight (37%) cases and 44 (21%) controls ($p < 0·001$) presented with at least one complaint with onset after surgery. Symptoms arising after surgery were reported twice as often by patients (0·6 v 0·3 symptoms respectively per subject, $p < 0·001$). The average interval between surgery and reported onset of symptoms was 5·1 years for patients and 5·9 years for controls. There was no difference between the number of complaints presented by cases with unilateral and those with bilateral breast augmentation (0·7 and 0·6 symptoms respectively per subject). Individual complaints reported more frequently by cases than by controls were: painful joints, burning eyes, and skin abnormalities. These differences reach statistical significance, even when it is assumed that all non-responders had no symptoms. However, medical consultations with respect to the reported problems were minimally different between cases and controls. Ten patients and 10 controls reported current use of a non-steroidal anti-inflammatory drug.

On the basis of the questionnaires a rheumatologist (HJBM) made an assessment of the likelihood of a rheumatic disease for each patient and each control. In 220 (94%) patients and 193 (92%) controls the information provided on the questionnaires made the presence of a serious rheumatic condition highly unlikely. For the other 15 cases and 17 controls, an effort was made to obtain additional information by telephone interviews with patients, letters from general practitioners, and specialist discharge letters. Probable inflammatory disease with onset at least one year after plastic surgery had been diagnosed in four patients (unclassified lung disease; elevated ESR of unknown cause;

Number of symptoms, medication and medical consultations in patients and controls

Characteristic	*Controls (n = 210)*	*Patients (n = 235)*	*Odds ratio*	*95% Confidence interval*
Average number of symptoms arising:				
Before surgery	0·5	0·4		
After surgery	0·3	0·6*		
Subjects with at least one symptom arising after surgery	44 (21·0)	88 (37·4)	2·26	1·48 to 3·45**
Individual symptoms arising after surgery:				
Painful joints for at least three months	18 (8·6)	46 (19·6)	2·60	1·45 to 4·64**
Swelling of joints for at least one week	10 (4·8)	14 (6·0)	1·27	0·55 to 2·92
Regularly burning eyes	15 (7·1)	37 (15·7)	2·43	1·29 to 4·57**
Mouth ulcers for at least three weeks	2 (1·0)	4 (1·7)	1·80	0·33 to 9·93
Raynaud's phenomenon	7 (3·3)	12 (5·1)	1·56	0·60 to 4·04
Pleuritis	5 (2·4)	4 (1·7)	0·71	0·18 to 2·68
Proteinuria or kidney disease	4 (1·9)	8 (3·4)	1·81	0·54 to 6·11
Skin abnormalities worsening by sun exposure	4 (1·9)	20 (8·9)	5·05	1·71 to 14·97**
Low blood cell or platelet counts	1 (0·5)	2 (0·9)	1·79	0·16 to 19·93
Use of anti-rheumatic drugs	27 (12·9)	46 (19·6)	1·65	0·98 to 2·77
Medical consultations regarding rheumatic symptoms:	61 (29·0)	85 (36·5)	1·38	0·93 to 2·06
Family practitioner	47 (22·4)	66 (28·1)	1·35	0·88 to 2·09
Rheumatologist	9 (4·3)	5 (2·1)	0·49	0·16 to 1·47
Physician	9 (4·3)	14 (6·0)	1·41	0·60 to 3·34
Other	23 (11·0)	33 (14·0)	1·33	0°75 to 2·34

*Significant difference, $p < 0·001$
**Significant discrimination

palindromic rheumatism with RNP antibodies; rheumatoid factor (RF) negative rheumatoid arthritis) and in two controls (mild RF positive RA; possible Sjögren's disease, with absence of antinuclear antibodies). In the other 11 cases and 15 controls the presence of a rheumatic syndrome related to silicone implantation was rated 'remotely possible'. Additional information (available for eight patients and nine controls) revealed clinical diagnoses like arthralgia, fibromyalgia, and osteoarthritis, that were evenly distributed over patients and controls.

Discussion

Women with silicone breast protheses reported more rheumatic complaints arising after the index-year of surgery than controls. It is notable that differences are seen primarily for subjective problems: joint pain, dry eyes, and skin abnormalities. For findings that can be regarded as more objective indicators of the presence of inflammatory rheumatic diseases such as joint swelling, use of antirheumatic drugs, or consultation with a family practitioner or a specialist, there were no significant differences. The further analysis of data regarding patients' reported rheumatic symptoms also failed to reveal an increased prevalence of specific rheumatic diseases among women with implanted silicone materials. Scleroderma was most prominent among the diseases associated with silicone materials, but a very large study population will be required to observe an increased risk.[9]

The higher numbers of arthralgia, burning eyes, and skin abnormalities may be seen as an argument for their induction by silicone. However, women reporting these symptoms were aware of the hypothesis under study. Due to publicity in journals and papers it was not possible to avoid this bias. We can not exclude the possibility that increased awareness or anxiety contributed to the observed differences. On the other hand, the response in the control group was adequate and controls reported an equal number of symptoms with onset before the operation.

Another possible source of bias is the inclusion of women requiring silicone implantation after mastectomy for breast carcinoma. The higher number of deaths in the patient group is probably related to mastectomy for breast cancer before silicone implantation. Additional treatment, for example, chemotherapy or radiotherapy, may have contributed to symptoms in the patient group. It is worth noting that cases with unilateral (mostly related to breast cancer) and bilateral breast augmentation (mostly for aesthetic reasons) reported equal numbers of complaints. This argues against significant bias due to inclusion of patients with breast cancer. On the basis of these data we conclude that common and clinically manifest rheumatic diseases do not occur more frequently among women with silicone breast protheses. However, they report more arthralgia, burning eyes, and skin abnormalities that are made worse by sun exposure. This finding, and observations by others, of an association with antinuclear antibodies indicate a possible association with a Sjögren's- or Lupus like syndrome, which deserves further study.

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