

# Scleroderma-like syndrome in a woman with silicone breast implants – case report and critical review of the literature

Jakub Wroński, Krzysztof Bonek, Ewa Stanisławska-Biernat

Clinic and Polyclinic of Rheumatology, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland

## Abstract

Various silicon compounds have been reported to stimulate autoimmune reactions in the human body. Based on case reports, a possible causal association between silicone breast implants and systemic sclerosis has been suggested since the end of the 1970s. Although the relationship between systemic sclerosis and silicone breast implants has been intensely investigated, no clear evidence of such an association has ever been found in epidemiological studies. Instead, it is now proposed that silicone breast implants can induce nonspecific symptoms of inflammatory diseases, despite not fulfilling the diagnostic criteria for a specific autoimmune disease. This phenomenon was named autoimmune syndrome induced by adjuvants (ASIA syndrome). ASIA syndrome is worth considering in the differential diagnosis in rheumatology patients. In this paper, we present a case of the scleroderma-like syndrome in a 48-year-old woman with a broken silicone breast implant and a review of the current literature on this issue.

**Key words:** systemic sclerosis, autoimmune syndrome induced by adjuvants, silicone breast implants, siliconosis.

## Introduction

Systemic sclerosis (SSc) is a connective tissue autoimmune disease, characterized by damage of blood vessels and progressive fibrosis of the skin and internal organs. Though the etiology of SSc remains unknown, both genetics and environmental factors may play some role in the pathogenesis of SSc. One of the known environmental factors is silicon dioxide [1]. However, not only crystalline silica may trigger an autoimmune response. Different silicon compounds were also described to stimulate autoimmune reactions in the human body.

A possible causal association between silicone breast implants (SBI) and connective tissue disease (CTD) has been suggested since the 1960s, soon after the introduction of SBI [2]. The first case reports of SSc after augmentation mammoplasty emerged in 1979 [3]. Although the relationship between SSc and SBI was intensely investigated, no clear evidence of such an association was ever found [1, 4, 5]. It is now proposed instead that SBI may cause non-specific autoimmune symptoms

without meeting the diagnostic criteria of any specific autoimmune disease. This phenomenon was named siliconosis, a part of the autoimmune syndrome induced by adjuvants (ASIA syndrome) [6].

ASIA syndrome is worth considering in the differential diagnosis in rheumatology patients. In support for this opinion, we present a case of a scleroderma-like syndrome in a 48-year-old woman with a broken silicone breast implant.

## Case report

A 48-year-old woman presented with Raynaud's syndrome (Fig. 1) lasting for 3 years and chronic unproductive cough for 5 years. Additionally, she reported dyspnea and fatigue for over 1 year, and from about 2 months she complained of difficulty with swallowing and choking during meals. In laboratory tests performed on an out-patient basis antinuclear antibodies in a titer of 1 : 320 with anti-Scl-70 antibodies were found. Based on those

---

### Address for correspondence:

Jakub Wroński, Clinic and Polyclinic of Rheumatology, National Institute of Geriatrics, Rheumatology and Rehabilitation, 1 Spartańska St., 02-637 Warsaw, Poland, e-mail: [jakub-wronski@wp.pl](mailto:jakub-wronski@wp.pl)

Submitted: 6.11.2018; Accepted: 14.01.2019



**Fig. 1.** Puffy fingers with Raynaud's syndrome; photo taken by the patient on a cold day.

findings the patient was directed to our rheumatology department for further evaluation.

Investigation of her past medical history revealed augmentation mammoplasty 11 years before her first symptoms. On admission, physical examination did not reveal any abnormalities other than Raynaud's syndrome and puffy fingers.

In laboratory tests, we detected antinuclear antibodies in a titer of 1 : 640 in a homogeneously speckled and nucleolar staining pattern. The qualitative test panel for systemic sclerosis-associated antibodies showed anti-Scl-70 antibodies in a high titer (+++) and anti-RP155 antibodies in a low titer (+). No additional abnormalities in laboratory tests were found. Despite clinical symptoms of Raynaud's syndrome, nailfold capillaroscopy showed a normal capillary pattern. X-ray examination with barium contrast demonstrated no abnormalities in the upper gastrointestinal tract. Lung function testing showed no ventilation disorders – vital capacity was 102% of predicted value and diffusing capacity for carbon monoxide 92.5% of predicted value. Echocardiography demonstrated no evidence of pulmonary hypertension nor any other abnormalities. High resolution computed tomography of the thorax revealed no pulmonary fibrosis, but detected inhomogeneous density with spiral structure in the left breast implant, suggesting a broken implant capsule. The patient was aware of this problem, as 3 years earlier in ultrasound breast examination inhomogeneous echogenicity with streaks that may correspond to a broken implant was found, but due to economic reasons, she postponed reimplantation.

Based on all clinical findings we diagnosed scleroderma-like syndrome induced by SBI in the course of ASIA syndrome. We recommended removal of the breast implants, but at that time no pharmacotherapy directed

toward autoimmune disease was introduced. As early stages of SSc could not be excluded, the patient was referred for active surveillance in our outpatient clinic.

The patient removed both SBI after a few months. One year later the chronic cough and difficulty with swallowing have resolved, but dyspnea has persisted and Raynaud's syndrome has intensified. Meanwhile, the patient has been diagnosed with Hashimoto's thyroiditis. The titer of antinuclear antibodies has risen to 1 : 1280. Also, anti-citrullinated protein antibodies were detected (40 U/ml), as well as proteinuria (0.3 G/l) and persistent microscopic hematuria (up to 16 RBC/HPF). Due to disease progression, hydroxychloroquine therapy was initiated. The patient was also referred to a nephrologist.

## Discussion

The mechanism of autoimmunological reaction induced by SBI is still elusive. It has been proposed that in patients with SBI, foreign body reaction stimulates CD68+ macrophages and CD4+ T-cells to form a periprosthetic capsule around the SBI. In persons with a genetic predisposition, IL-6, TGF- $\beta$  and Th-17 cells may convert an acute reaction into a chronic reaction, which may trigger systemic disease [7]. Some studies suggest that vitamin D deficiency [8, 9] and pre-existing allergies [9] may be risk factors for the development of autoantibodies in patients with SBI. "Bleeding" of silicone outside the SBI capsule may further increase the risk of an autoimmunological reaction. The leakage of silicone from implants was reported in one study to increase the risk of self-reported CTD [10] and in another study increased development of antinuclear antibodies [11].

The postulated causal association between SBI and development of SSc was intensively studied in the 1990s, but at that time was not confirmed. All meta-analyses performed until 2000 showed no evidence of an association of SSc or any other CTD with SBI [4, 12–15]. However, the most recent meta-analysis by Rubio-Rivas et al., performed in 2017, showed increased risk of SSc in patients with SBI when case-control studies were taken into consideration (relative risk [RR]: 1.68, 95% confidence interval [CI]: 1.65–1.71), but no increased risk in cohort studies (RR: 2.13, 95% CI: 0.86–5.27) [1]. This discrepancy may result from the fact that for rare outcomes, such as SSc occurrence, case-control studies may better identify the risk than cohort studies.

Further important evidence regarding the safety of SBI comes from just published largest cohort study to date by Coroneos et al. [5]. Nearly 42,000 patients with SBI were analyzed and SIR of SSc was calculated to be 7.00 (95% CI: 5.12–9.34) [5]. The data come from post-approval studies conducted in the USA on behalf of the Food and Drug Administration. Unfortunately,

although original data covered nearly 100,000 people after mammoplasty, including over 83,000 people with SBI, due to low compliance, analysis of SSc occurrence was performed on a small proportion of the population. The data were also based on self-reporting, which may be a significant limitation. The RR of self-reported CTD after mammoplasty augmentation was found to be significantly increased in cohort studies by Brinton et al. (RR: 2.0, 95% CI: 1.5–2.8) [16] and Lee et al. (RR: 1.6, 95% CI: 1.28–2.0) [17], but the risk disappeared when medical records were taken into consideration.

Although the question whether SBI triggers SSc is still without a definitive answer, it was shown in previous studies that patients after augmentation mammoplasty may present different nonspecific autoimmune reactions and symptoms not fulfilling diagnostic criteria for the defined CTD. Several studies have reported an increased incidence of Raynaud's syndrome [16, 18], the presence of antinuclear antibodies [19, 20] and Scl-70 antibodies [21] after SBI mammoplasty. Other studies have reported significant increases in many nonspecific symptoms such as arthralgia, myalgia, chronic fatigue or impaired cognition [9, 22, 23].

In 2011, Shoenfeld and Agmon-Levin proposed that SBI may trigger an autoimmune reaction in genetically predisposed subjects leading to a collection of different unspecified symptoms. They called it siliconosis, and proposed it to be a part of the ASIA syndrome [6]. Colaris et al. [24] in their literature review found 18 cohort studies of SBI patients fulfilling proposed ASIA criteria.

Our patient did not fulfill the diagnostic criteria of SSc, but she met the criteria for recognizing the ASIA syndrome. We suggested removal of our patient's breast implants, as it was shown in the systematic literature review (23 studies, 622 patients included) that up to 75% of complaints related to SBI disappear after implants' explantation [25]. However, the study by Colaris et al. [24] showed that in 26% of patients the improvement after SBI removal was only temporary.

It may be partially due to psychological distress of women requesting removal of silicone breast implants [26]. In the literature review, only 16% of patients had improvement of symptoms when they were diagnosed with the defined autoimmune disease and did not receive additional immunosuppressive therapy. Removal of SBI also did not have an effect on autoantibodies [25]. That is what happened to our patient. Only part of the symptoms subsided and autoimmunization increased – ANA titers increased and the patient developed anti-citrullinated protein antibodies and was diagnosed with Hashimoto's thyroiditis. She remains under further rheumatological observation.

## Conclusions

Our case along with other cases and epidemiological studies shows that patients with SBI may present with various nonspecific symptoms and immunological abnormalities, which may cause the patient to be referred to the rheumatologist. Physicians should be aware of the fact that these cases may resemble different CTDs.

---

*The authors of this publication had no research support. The rights revenue was paid by Stowarzyszenie Zbiorowego Zarządzania Prawami Autorskimi Twórców Dzieł Naukowych i Technicznych KOPIPOL of Kielce from fees collected pursuant to Article 20 and Article 20<sup>1</sup> of the Copyright and Neighbouring Rights Act.*

*Wynagrodzenie autorskie sfinansowane zostało przez Stowarzyszenie Zbiorowego Zarządzania Prawami Autorskimi Twórców Dzieł Naukowych i Technicznych KOPIPOL z siedzibą w Kielcach z opłat uzyskanych na podstawie art. 20 oraz art. 20<sup>1</sup> ustawy o prawie autorskim i prawach pokrewnych.*

*The authors declare no conflict of interest.*

## References

1. Rubio-Rivas M, Moreno R, Corbella X. Occupational and environmental scleroderma. Systematic review and meta-analysis. *Clin Rheumatol* 2017; 36: 569-582.
2. Miyoshi K, Miyamura T, Kobayashi Y. Hyper-gammaglobulinemia by prolonged adjuvanticity in men. Disorders developed after augmentation mammoplasty. *Jap Med J* 1964; 2122: 9-14.
3. Kumagai Y, Abe C, Shiokawa Y. Scleroderma after cosmetic surgery: four cases of human adjuvant disease. *Arthritis Rheum* 1979; 22: 532-537.
4. Janowsky EC, Kupper LL, Hulka BS. Meta-Analyses of the Relation between Silicone Breast Implants and the Risk of Connective-Tissue Diseases. *N Engl J Med* 2000; 342: 781-790.
5. Corneos CJ, Selber JC, Offodile AC, et al. US FDA Breast Implant Postapproval Studies: Long-term Outcomes in 99,993 Patients. *Ann Surg* 2019; 269: 30-36.
6. Shoenfeld Y, Agmon-Levin N. "ASIA" – Autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun* 2011; 36: 4-8.
7. Bassetto F, Scarpa C, Vindigni V, Doria A. The periprosthetic capsule and connective tissue diseases: A piece in the puzzle of autoimmune/autoinflammatory syndrome induced by adjuvants. *Exp Biol Med* 2012; 237: 1117-1122.
8. Colaris MJL, van der Hulst RR, Tervaert JWC. Vitamin D deficiency as a risk factor for the development of autoantibodies in patients with ASIA and silicone breast implants: a cohort study and review of the literature. *Clin Rheumatol* 2017; 36: 981-993.
9. Cohen Tervaert JW. Autoinflammatory/autoimmunity syndrome induced by adjuvants (ASIA; Shoenfeld's syndrome): A new flame. *Autoimmun Rev* 2018; 17: 1259-1264.

10. Brown SL, Pennello G, Berg WA, et al. Silicone gel breast implant rupture, extracapsular silicone, and health status in a population of women. *J Rheumatol* 2001; 28: 996-1003.
11. Gaubitz M, Jackisch C, Domschke W, et al. Silicone breast implants: Correlation between implant ruptures, magnetic resonance spectroscopically estimated silicone presence in the liver, antibody status and clinical symptoms. *Rheumatology* 2002; 41: 129-135.
12. Perkins LL, Clark BD, Klein PJ, Cook RR. A meta-analysis of breast implants and connective tissue disease. *Ann Plast Surg* 1995; 35: 561-570.
13. Hochberg MC, Perlmutter DL. The association of augmentation mammoplasty with connective tissue disease, including systematic sclerosis (scleroderma): a meta-analysis. *Curr Top Microbiol Immunol* 1996; 210: 411-417.
14. Wong O. A Critical Assessment of the Relationship between Silicone Breast Implants and Connective Tissue Diseases. *Regul Toxicol Pharmacol* 1996; 23: 74-85.
15. Whorton D, Wong O. Scleroderma and silicone breast implants. *West J Med* 1997; 167: 159-165.
16. Brinton LA, Buckley LM, Dvorkina O, et al. Risk of connective tissue disorders among breast implant patients. *Am J Epidemiol* 2004; 160: 619-627.
17. Lee I-M, Cook NR, Shadick NA, et al. Prospective cohort study of breast implants and the risk of connective-tissue diseases. *Int J Epidemiol* 2011; 40: 230-238.
18. Contant CME, Swaak AJG, Obdeijn AIM, et al. A prospective study on silicone breast implants and the silicone-related symptom complex. *Clin Rheumatol* 2002; 21: 215-219.
19. Englert H, Joyner E, McGill N, et al. Women's health after plastic surgery. *Intern Med J* 2001; 31: 77-89.
20. Claman HN, Robertson AD. Antinuclear Antibodies and Breast Implants. *West J Med* 1994; 160: 225-228.
21. Bar-Meir E, Teuber SS, Lin HC, et al. Multiple autoantibodies in patients with silicone breast implants. *J Autoimmun* 1995; 8: 267-277.
22. Fryzek JP, Signorello LB, Hakelius L, et al. Self-reported symptoms among women after cosmetic breast implant and breast reduction surgery. *Plast Reconstr Surg* 2001; 107: 206-213.
23. Vermeulen RCW, Scholte HR. Rupture of silicone gel breast implants and symptoms of pain and fatigue. *J Rheumatol* 2003; 30: 2263-2267.
24. Colaris MJL, de Boer M, van der Hulst RR, Cohen Tervaert JW. Two hundreds cases of ASIA syndrome following silicone implants: a comparative study of 30 years and a review of current literature. *Immunol Res* 2017; 65: 120-128.
25. de Boer M, Colaris MJL, van der Hulst RR, Cohen Tervaert JW. Is explantation of silicone breast implants useful in patients with complaints? *Immunol Res* 2017; 65: 25-36.
26. Wells KE, Roberts C, Daniels SM, et al. Comparison of Psychological Symptoms of Women Requesting Removal of Breast Implants with Those of Breast Cancer Patients and Healthy Controls. *Plast Reconstr Surg* 1997; 99: 680-685.