ALLERGIC CONTACT DERMATITIS TO SYNTHETIC RUBBER FOLLOWING BREAST AUGMENTATION

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Allergic reactions associated with silicone injection and implant were examined in a 50-year-old woman with a granulomatous reaction following breast silicone-gel prosthesis rupture who developed a delayed hypersensitivity to rubber compounds.
Patch tests with SIDAPA, dental, and rubber series as well as open tests with latex, silicone and non silicone tubes, open application test with silicone gel, and skin prick test for aero and food-allergens were performed. Total and specific serum IgE measured by CAP-FEIA.
Skin tests revealed a delayed-type hypersensitivity to thioureas, thiuram mixture and platinum. Specific IgE to natural rubber latex were found.
Allergic contact dermatitis from thioureas, thiurams and platinum might be under-diagnosed, as they are not tested as part of the standard patch test series. Clinicians should consider this diagnosis in patients submitted to several cosmetic treatments.
Breast implant - Delayed type hypersensitivity - Platinum - Prosthesis rupture - Siliconoma, thiourea.

INTRODUCTION

Silicone materials have been widely used in medical applications for at least 30 years. Despite its broad use, the question whether silicone can mediate an immunological reaction remains speculative and unanswered (1). Most studies on its biocompatibility state that they are chemically stable compounds, which however are often capable of elicit several benign chronic inflammatory responses, sometimes resulting in tissue destruction. Usually these reactions are unpredictable and occasionally un-correctable (2-3). Until recently, about 150.000 women underwent breast augmentation annually in the United States, 80% for cosmetic purposes (4). There is little doubt about the beneficial psychological effects of breast implants, but there is increasing awareness of alleged adverse effects of implants containing silicone. The designation of medical-grade silicone refers to a pure and sterile preparation, with a constant viscosity of 360 centigrades, and it is said to be very safe when is used in a proper form. Silicone material used for medical devices, or polydimethylsiloxane, can be formulated in different ways resulting in materials of varying structures and properties, such as rubbers, gels, or oils (5). Mostly, silicone containing implants are used. These may be divided into four main types: silicone rubber envelopes filled with saline; silicone rubber envelopes filled with silicone gel; silicone rubber envelopes covered with a polyester polyurethane foam coating; and dual silicone rubber envelopes, the inner envelope containing silicone gel and the outer envelope filled with saline (6). Many variants exist, including differences in the outer envelope such as assorted surface textures and various chemical side groups bonded to the envelope. Silicone oils, gels, and rubbers are potentially bioactive agents that may induce host reactions, but there are many questions as to the exact biological activity of the different silicones and its long term significance (7), since silicone itself may be safe, but unknown allergens, used during the manufacture of silicone breast implants, may not. Thus, highly cohesive gel implants, characterized by an inner and an outer envelope, might be not as safe as is commonly believed in case of implant ruptures, irrespective of the cohesiveness of the silicone gel, and should be investigated thoroughly.

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CASE REPORT

A 50-year-old woman was referred for allergologic diagnostic tests following two intra-operative anaphylactic reactions. She had had cosmetic bilateral breast augmentation six years before using polyurethane-silicone-covered mammary prosthesis that had been followed by breast prosthesis rupture, capsular contracture and left nipple's retraction. She underwent additional surgery for prosthesis removal, replacement and several subcutaneous injections of liquid silicone oil, for cosmetic lip augmentation. Except for having hepatitis B virus infection, the patient had no history of additional diseases. For several years, after the operation, she had experienced episodes of local discomfort, change in nipple's sensation, breast pain, bruising, arthralgias, flu-like syndrome, weakness, malaise, cervical lymphadenopathy, followed by change in the shape and in the size of her breast and lips. On physical lip examination a diffuse swelling of the whole area injected was appreciated (Fig. 1) and were multiple subcutaneous nodules, 3 to 6 mm in size, along the vermillion border. There were palpable cervical lymphadenopathies, and breast examination revealed that the breast implant had a lump and a large tear, at the posterior wall of the shell, with intra-capsular leakage of silicone and left nipple's retraction (Fig. 2).

The patient was patch tested with SIDAPA, dental, and rubber hapten series and open tests with silicone, non-silicone and latex tube were performed. The test substances (FIRMA, Firenze, Italy; and Hermal-Trolab, Reinbeck, Germany) were applied onto the healthy skin of the back by Finn Chambers (Epitest OY, Tuusula, Finland) and read after 48 hours (8). Patch test responses were evaluated according to ICDRG guidelines, 1/2 to 3 hours after patch test removal (9). Repeated open application test with silicone gel was performed by applying 0.1 ml of silicone gel twice daily to the left antecubital area for 14 days without occlusion. Skin prick tests with commercial extracts (Alk-Abellò, Madrid, Spain) of inhalant and food allergens were performed as well. Total and specific serum IgE were measured by the UniCAP method (Phadia) according to manufacturer's instructions.

Our patch testing protocol showed strong skin reactivity to thiuram mix (+++). Skin prick tests for aero food-allergens were negative. As a consequence we tested additional substances, including rubber and dental series, which showed skin reactivity to diethylthiourea (+++) and to platinum chloride (++) (Fig. 3-4).

Figure 1: Shows a diffuse swelling of the whole lip area.

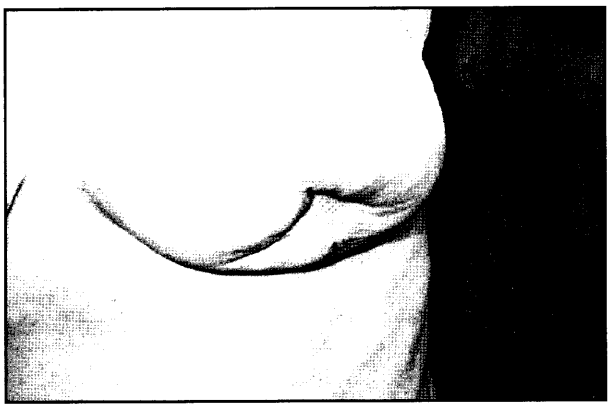

Figure 2: Shows an alterated breast profile and a left nipple's retraction.

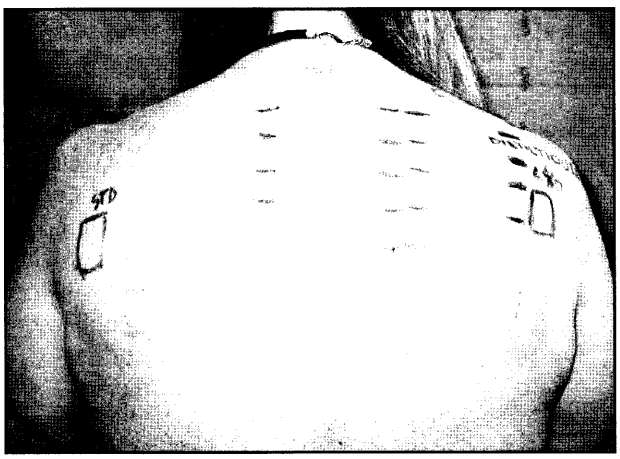

Figure 3: Rubber series showing skin reactivity to diethylthiourea (+++).

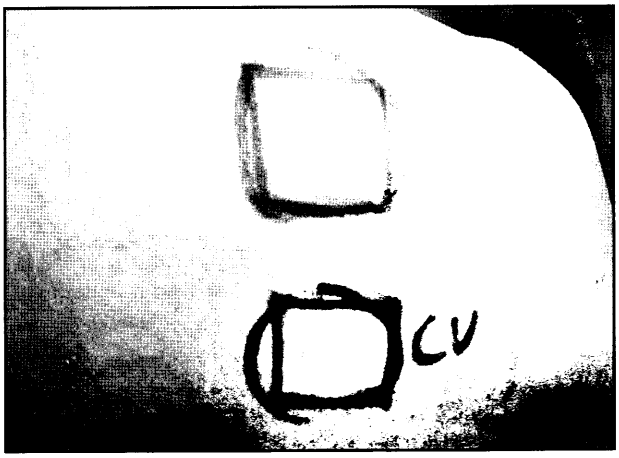

Figure 4: Platinum chloride skin reactivity (++) .

The open test with silicone tube, non silicone, and latex tube showed a slight reactivity to non-silicone tube. The repeated open application test with silicone gel was negative.

Biochemical and haematological investigations were within normal range, except for positive antinuclear antibodies (homogeneous pattern), a common finding in chronic hepatitis B positive patients. Total serum IgE levels were 1116 kU/L (n.v. 18-199) and specific IgE levels for latex, peach, peanuts and kiwi were 10.9, 1.62, 7.68, and 1.47 ARU/mL, respectively (n.v. <0.35).

Breast MRI was conducted with TIRM sequences on axial, coronal, sagittal planes.

Sagittal T2-WI depicted fine linear bands of the elastomer shell freely floating within the fibrous capsule consistent with intracapsular rupture. No silicone extension beyond the fibrous capsule was revealed.

X-ray mammography showed an extensive opacity 6 cm x 5 cm in diameter at the site where the silicone implant was positioned.

At ultrasound examination (US) the mass corresponded to the anechoic mass with thick septa.

Controlaterally another mild opacity of 6.5 x 5 cm, located within the place of previous breast prostesis was evident; at ultrasound examination this was consistent with fluid mass.

A breast biopsy showed a chronic inflammatory reaction (consisting of polymorphonuclear cells, some lymphocytes and foreign-body giant cells) and a more striking collection of lymphocytes, plasma cells and giant cells with ingested silicone.

The aesthetic problem was corrected and preventive measures were taken to avoid latex exposure.

DISCUSSION

In recent years, the demand for cosmetic procedures for soft tissue augmentation by implanting and injecting different substances has increased, due to their apparent harmlessness (7). However, these procedures can be associated with adverse reactions such as the formation of foreign body granulomas, a phenomenon that can be associated with most of the materials used. The frequency of asymptomatic rupture of silicone rubber envelopes has been estimated between 0.2% and 4%, and increases with the aging of the implant (10). Siliconomas, first described in 1964, have little or no consequence and are incidentally found after extra-capsular rupture of an implant and after injections with silicones (11). Significant risk factors for breast implant rupture identified so far include older implants, retroglandular implant location, implant contracture, local symptoms, certain implant types, and certain manufacturers. Yet, the cause of capsular contracture remains unknown (12). Formation of a granuloma is a common tissue response to the presence of a variety of foreign materials. Although most other complaints have been regarded as subjective or unrelated to exposure to silicone, the presence of a granuloma has been considered as a basis for claims of local complication or even as a mechanism suggesting hypothetical systemic disease. The low grade chronic inflammation around a silicone gel implant (during capsule formation around the prosthesis that continues until the implant is in place) may lead to a chronic illness that cannot be eradicated by the immune system. Most silicones are non-toxic and non-immunogenic, but differences in composition, as well as in chemical and biologic characteristics between medical implants may exist.

All medical devices are associated with the risk of both early and late complications. Adverse events that last longer than two weeks can be attributable to technical shortcomings (e.g., too superficial implantation of a long-lasting filler substance may have altered its bioreactivity). Late adverse events also include immunologic phenomena such as late-onset allergy and non-allergic foreign body granuloma (13).

An immune response would be expected in a recipient with a predisposition and/or pre-existing immune disorder, or if silicone implants become contaminated with sensitizers such as rubber or metal compounds during manufacture. Hence, it is impossible to demonstrate that an implant is completely immunologically safe (14).

The repeated exposure to silicone implants, or to silicone gel following rupture of the outer envelope, may induce delayed hypersensitivity (15). Although several mechanisms have been proposed to explain this reaction, the one that best fits the current evidence is that silicone-containing microparticles would behave as hapten-like substances absorbing tissue or plasma proteins to form an antigenic complex. In this view silicone gel implants would elicit an antigen-specific immune response rather than a non specific foreign body reaction (16).

Our patient developed a late-onset foreign body granuloma following both rupture of a polyurethane-covered mammary prosthesis and several subcutaneous injections of liquid silicone oil for cosmetic lip augmentation. Two years later she developed a granulomatous reaction and two anaphylactic intra-operative reactions, possibly due to latex allergy. Our investigations showed allergy to thioureas, tiurams and platinum chloride. These substances may be used during implant manufacturing. Accelerators such as thioureas (CH_4N_2S) (17) are used as catalysts to speed up the prosthesis envelop development. Thioureas include DETU diphenylthiourea, ethylene

thiourea and DBTU which has the highest sensitizing potential (18). Thiourea allergy is relatively uncommon and an allergic patch test reaction was observed in only 1.2% of all patients (19). Thiurams are chemicals used as accelerators in the production of both natural rubber latex and synthetic rubber (20). Platinum is used as a catalyst in the manufacture of silicone breast implants (21). Platinum may behave as a potent sensitizer under certain circumstances. Although these compounds' potential immune reactivity remains speculative and controversial, they all behave as foreign bodies and elicit a host response that tries to remove them (16).

Delayed-type hypersensitivity responses to various types of silicone implants may occur in a subset of patients (22). Due to the ubiquitous nature of medical silicone devices, some patients might have already developed hypersensitivity during previous exposures, although non-specific augmentation of the immune response may also occur in previously non-sensitized hosts (16).

Inflammatory reactions may also develop many years after injection in the absence of any predictive factor. It has been suggested that infections may play a role in granulomatous reactions as the possible trigger of a cross-reaction. Our patient had a viral infection before the development of the granulomatous reaction.

We encourage clinicians to consider delayed type hypersensitivity reactions in patients who are exposed to several cosmetic procedures (16). Complications may occur, even after years, as a result of anatomic location technique deficiencies, type of defect treated, identifiable host factors, infectious processes, allergies, and intrinsic characteristics of any implant. They can also occur in the absence of any identifiable host factors and flawless technique (23). Probably the cases reported in the literature underestimate the real incidence of these complications and, in the future, more cases will be diagnosed. Patch testing can predict possible adverse reactions to rubber, and may be particularly useful in patients who have undergone many cosmetic procedures or have experienced implants rupture. There is a need to go on studying the kinetics and nature of these responses both *in vivo* and *in vitro*.

Acknowledgments: *We would like to thank Merck Allergy S.p.A. for its support.*

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