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MASSIVE INFLAMMATORY REACTION FOLLOWING THE REMOVAL OF A RUPTURED SILICONE IMPLANT MASKING THE INVASIVE BREAST CANCER – CASE REPORT AND LITERATURE REVIEW

PIOTR NOWACZYK[1], ALEKSANDRA BUDNICKA[2], MATEUSZ WICHTOWSKI[1], PAWEŁ KURZAWA[3], DAWID MURAWA[1,4]

1st Department of Surgical Oncology and General Surgery, Wielkopolska Cancer Center in Poznań[1]
Ordynator: prof. zw., dr hab. *P. Murawa*
Student Research Group at the 1st Department of Surgical Oncology and General Surgery, Wielkopolska Cancer Center in Poznań[2]
Opiekun: dr n. med. *P. Nowaczyk*
Department of Clinical Pathomorphology, Medical University in Poznań[3]
Kierownik: prof. dr hab. *P. Majewski*
Regional Specialist Hospital in Wrocław, Research and Development Cente[4]
Kierownik: prof. dr hab. *W. Witkiewicz*

This paper presents a case of a patient with invasive ductal breast cancer following breast augmentation. Following breast implants rupture in March 2013 the breast implants have been removed – histopathological examination revealed leaked silicone with inflammatory infiltration, without evidence of cancerous lesions. Diagnostic imaging revealed multiple encapsulated silicone particles and clusters of post-inflammatory macrocalcifications in both breasts. In January 2014 the patient presented with symptoms of massive inflammation of the left breast. Following surgical consultation the patient had undergone radical left-sided mastectomy with lymphadenectomy. Postoperative histopathological examination revealed a multifocal advanced invasive ductal cancer G3 pT3pN3a (vascular invasion, metastases in 11 of 12 examined axillary lymph nodes). Following surgery the patient was qualified for further treatment – chemotherapy, radiotherapy, hormone therapy. The discussion includes a review of literature on the risk evaluation of co-occurrence of breast cancers in women with silicone breast implants and presents diagnostic challenges of breast cancer in this patient group.
Key words: breast augmentation, breast implants, breast implant rupture, silicone granuloma, breast cancer

In breast surgery implants are used predominantly in cosmetic surgery (80% of cases), in patients following mastectomy and to repair congenital and acquired breast deformations (1, 2). Approximately 2-3 mln women have undergone breast augmentation procedure to enhance breast contour and appearance with various types of implants in the US since 1962 (statistical data for Poland are not available) (1, 2).

Breast implants can be classified into several groups based on various criteria, i.e. substance used to fill the implant shell, surface, shape, profile and size. The surface of the implant may be smooth or textured (coarse). The implants may be round or have an anatomical teardrop shape. Currently in Europe and the US three types of breast implants are used: implants filled with saltwater solution (saline), implants filled with cohesive silicone gel (silicone), implants filled with saltwater and cohesive silicone gel. Silicone implants were the first implants available (since 1962 – Cronin and Gerow) and are most commonly used today. They are available as single lumen implants with a silicone shell filled with silicone gel or a double lumen implants – the inner silicone shell filled with saline and the outer

shell filled with coherent silicone gel. Breast implants are manufactured with silicone gel of various degree of cohesiveness. First generation breast implants were available with a thin shell filled with polymerized silicone gel of very fluid consistency, which easily migrated through the implant shell thus resulting in shrinkage of the implant capsule and breast contour deformation. The currently used implants are filled with cohesive silicone gel and comprise a leak-proof multilayer shell, which minimizes the risk of silicone gel leakage and the related consequences.

Radiological diagnosis of breasts with breast implants is difficult, thus affecting interpretation of results and detectability of breast cancer. The patient should inform the radiologist on the type of the breast implant before the procedure, because each type of implant produces a different radiological image. Breast implants may obscure breast tissue in mammograms, thus sometimes requiring additional, special projections (targeted, enlarged imaging) or application of other diagnostic techniques (USG, MRI) (3, 4). Ultrasonography also does not allow for a detailed evaluation of the prosthesis and its shell and implant rupture often results in non-diagnostic image quality. MRI imaging is currently the most sensitive diagnostic technique in breast assessment in women with breast implants (5, 6). Unfortunately this method is the most expensive and still poorly available.

Breast implant rupture is one of the most common complications of the breast augmentation procedure. Available clinical trial data provide ambiguous evidence regarding a causal relationship between silicone implants and breast cancer or other known conditions. However, there have been reports in literature of breast cancers in women following implant shell rupture and leakage of the silicone gel into surrounding tissues (3, 5, 6).

This paper presented a case of a patient with invasive ductal breast cancer following breast augmentation with silicone implants, who experienced an implant rupture. The reported case also demonstrates diagnostic challenges of breast cancer in women with breast implants.

CASE REPORT

A 69-year-old patient admitted on February 6, 2014 to the operative unit of one of the non-public hospital in Poznań with a diagnosis of a massive inflammation of the left breast. History of breast augmentation in 1982 with silicone gel-filled implants inserted below the pectoralis major muscle. In March 2013 the implants were removed due to rupture of the implant shell (no history of injury). Infiltrated inflammatory tissue was collected during surgery for histopathological examination. Diffused microvesicular mass with giant cell granulomatous foreign body reaction were found in the fatty tissue and in the fibrous capsule (fig. 1). Additional immunohistochemical examinations for broad-spectrum cytokeratins excluded the presence of cancer cells and only "stained" the cytoplasm of multinucleated cells (fig. 2). Reaction was more intense in the left breast – larger silicone leakage

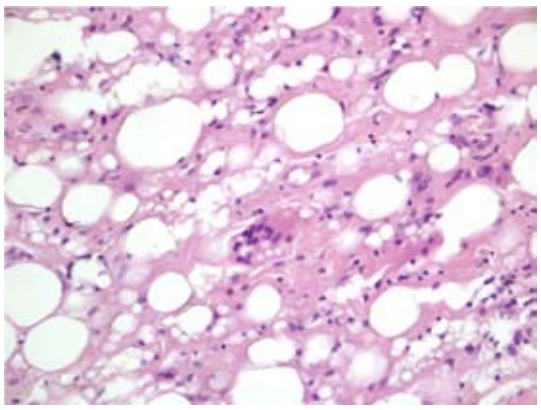

Fig. 1. Fatty tissue fragment with diffuse silicone deposits, H&E stain, magn. 400x

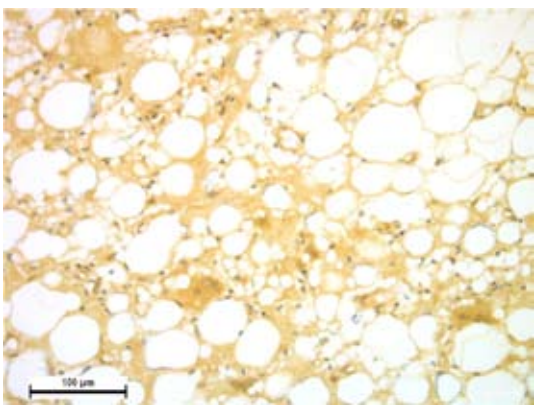

Fig. 2. Negative reaction with broad spectrum cytokeratin antibody CK AE1/AE3, magn. 200x

(thicker capsule and surrounding stronger reaction in the fatty tissue up to 1.2 cm). Cancerous lesions have not been identified at that time.

Diagnostic mammography and ultrasonography in October 2013 revealed multiple encapsulated silicone particles and clusters of post-inflammatory macrocalcifications in both breasts. Largest lesions in mammography imaging of the left breast: in the tail of Spence, well-saturated polycyclic lesion 4.5 x 3 cm (in ultrasonography heterogenous, solid-cystic, diffused, involving the upper quadrant and retroareolar area with skin thickening), on the border of the left axillary fossa well-separated, strongly saturated lesion 2 x 1.3 cm (in ultrasonography calcified lymph node 1.8 cm long), in the projection of lower quadrant of the left breast architectural disorder 2 x 3 cm and cluster of macrocalcification with a 0.8 cm diameter (no counterpart in ultrasonography). Radiologically both in MMR and USG the lesions have been described as inflammatory lesions accompanied by encapsulated silicone particles.

Based on the above mentioned findings and clinically progressive inflammation of the left breast in the following months, the patient was referred to a surgical oncologist for further diagnostics and treatment.

Upon admission inflammatory reaction in the left breast was found with skin thickening and Peau de Orange (fig. 3). Increased structural coherence of the entire breast tissue was palpable. Following surgical consultation the patient has given consent to radical left-sided mastectomy. During surgery a characteristic

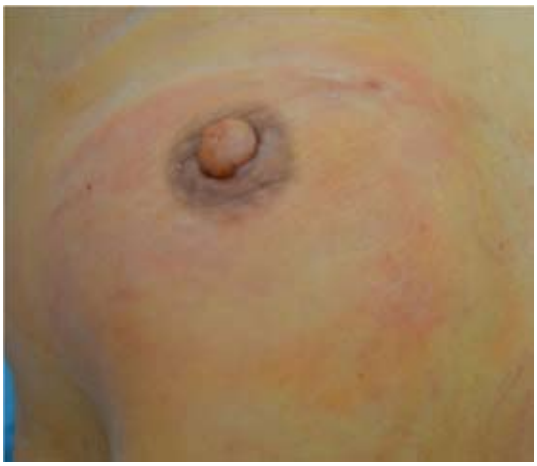

Fig. 3. Peau de Orange visible following disinfection of the surgical field

leakage of a silicone-like fluid from the breast tissues was observed. Similarly a segmental infiltration of the pectoralis major muscle with silicone was observed – the fragment was removed en bloc with the breast gland (fig. 4 and 5). Axillary lymph nodes were lesioned, significantly increased and filled with silicone (fig. 6). Postoperative histopathological examination revealed a multifocal invasive ductal cancer G3 with metastases to 11 of 12 removed lymph nodes (pathological progression pT3, pN3a). In tissue histology severe resorptive lesions related to foreign body (silicone) reaction were observed besides the tumour. Evaluation of receptor status of cancer revealed: estrogen receptors (+), progesterone receptors (+), HER2 receptors (-).

The patient was discharged home on February 9, 2014 in good overall condition. Following

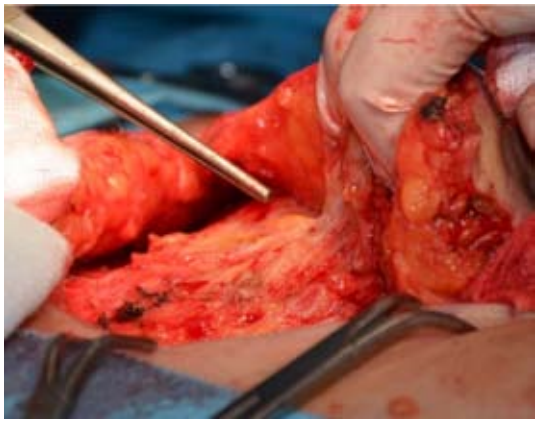

Fig. 4. Inflammatory/malignant infiltration of the pectoralis major muscle

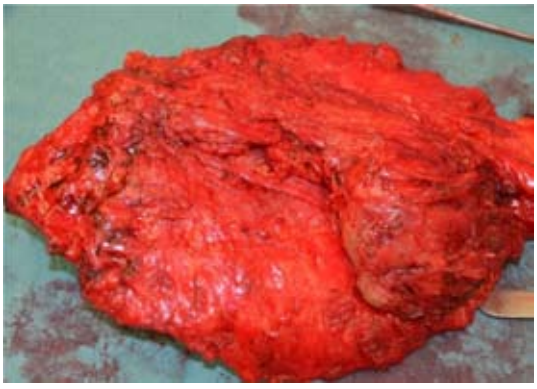

Fig. 5. Mastectomy specimen, the pectoralis major muscle surface, multiple silicone deposits are visible

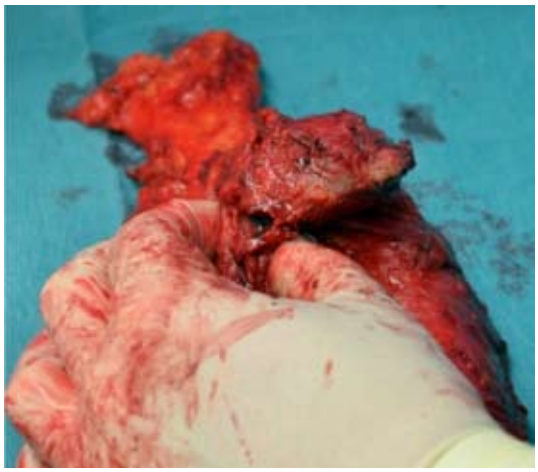

Fig. 6. Pathological lymph nodes filled with silicone

the histopathological results the patient was referred to a chemotherapist and radiotherapist for consultation and qualification for supplementary therapy as per current standards.

DISCUSSION

Silicones (alkyl- and aryl polysiloxanes) are macromolecular organosilicon compounds with a siloxane backbone made up of silicon and oxygen atoms to which various organic radicals are bound. They occur in liquid, gel or solid form. Silicones are widely used in medicine for the manufacturing of multiple medical devices, such as drains, probes, catheters, intraocular lens and tissue expanders. There have been many clinical trials which demonstrated the safety of silicone implants. In 1999 the Institute of Medicine (IOM), founded under the congressional charter, published a report which unequivocally states that women with breast implants are not at higher risk of cancer, immune diseases or neurological complications compared to the overall female population (7).

Implant-related complications can be divided into: early (directly related to surgery) and late (develop within several weeks, months or years after surgery). The most commonly reported early complications are: haematoma, seroma, breast swelling and skin thickening, infection, loss of nipple sensitivity. Late complications include: capsular contracture (induration and retraction of the fibrous capsule), implant herniation, extra- and intracapsular implant rupture, fat necrosis and breast tissue atrophy. According to FDA, breast implants must be removed due to various reasons within 10 years in approx. 20% of patients following breast augmentation and approx. 50% of patients following breast reconstruction in the US, however in 80% of patients the breast implant is reinserted (8). The breast implant rupture rate before fifth generation breast implants (filled with high strength cohesive silicone gel) became available was over 10% (9). Breast implants may rupture for a variety of reasons. The most common cause of breast implant rupture is injury or excessive force applied to the chest, capsular contraction, mammography or the shell fatigue. In the case of silicone implant ruptures the breasts are not reduced in size, and the rupture may be clinically asymptomatic. In patients with silicone breast implants for screening of asymptomatic implant shell ruptures the FDA recommends a follow-up MR within 3 years following implantation and every 2 years thereafter (8). In the case of an extracapsular rupture of the silicone implant (rupture of the implant shell and the fibrous capsule) the implant must be surgically removed. In the case of intracapsular implant rupture (rupture of the implant shell and undamaged fibrous capsule) the implant removal is usually not necessary, due to minimal risk of silicon leakage into surrounding tissues. Extracapsular implant rupture is always accompanied by intracapsular rupture. In the case of rupture of the outer shell the gel usually remains close to the implant or rarely small amounts of silicone may migrate into surrounding body tissues, such as abdominal integument, axilla, dorsal region, intermuscular space and through lymphatic vessels to the regional lymph nodes (9). The presence of silicone in the lymph nodes may mask the presence of cancer cells. There have been reports in literature of co-presence of silicone granulomas and breast cancer metastases in the same lymph nodes (10).

The overall biological response to silicone (liquid form) comprises of conventional body responses to foreign body (7). Silicone particles induce acute and chronic inflammatory resorptive granuloma-type reaction with fibrosis (known as “siliconoma”), resulting in breast deformation and induration.

Eventually the relationship between the use of silicone implants and breast cancer in women has not been demonstrated (11). In an analysis in a group of 11,676 women in Cana-

da with breast implants for an average period of 10.2 years and entered in the Alberta Cancer Registry Berkel et al have observed that breast cancer developed in 41 women (0.35%), which was a lower percentage than epidemiological estimates in the female population in the same region, without breast implants. The average time from breast augmentation surgery to diagnosis of breast cancer was 7.5 years (12). Similar results have been observed in Los Angeles by Deapen, who analyzed a group of 3182 women with breast implants. In this group only 31 (0.97%) women developed breast cancer within 14.4 years, whereas 49.2 breast cancer cases were observed in the female population without breast implants. Follow-up of patients in this study demonstrated that the risk of breast cancer remains at a low level of 0.63 – 0.69% (13). Data from European studies support the observations of American physicians. McLaughlin has concluded that in a group of 3473 women in Sweden who have undergone breast implant augmentation, on average only 18 (0.51%) women developed cancer within 10.3 years after surgery, whereas 25 cancer cases were identified in the population without breast implants (14).

Furthermore Deapen, Brinton and Dreyfuss suggest a protective effect of breast implants against breast cancer (15). Two theories have been offered to explain the potential underlying mechanisms. Firstly, the presence of breast implants activates the immune cells in response to a foreign body, thus contributing to an earlier identification and destruction of cancer cells. Secondly, the compression of implants on the breast tissue reduces the local blood flow and contributes to a slowing-down of cellular processes (including malignant transformation).

Another problem is the breast implant rupture and leakage of silicone to surrounding tissues (previous generation implants). The opinion on potential breast cancer development in such cases is based on case reports which do not however provide a strong evidence of a causal relationship (16, 17, 18). Further evidence of a relationship between breast cancer and silicone is derived from case reports of female patients following liquid silicone injections (currently withdrawn from the market) (5). Increased incidence of breast cancer has not been demonstrated in patients with PIP breast implants, despite significantly higher extra- and intracapsular implant rupture rates in these implants (6, 19). The majority of studies emphasize the fact, that despite reduced mammography sensitivity, women with breast cancer following breast augmentation are diagnosed at a comparable stage of disease and have a similar prognosis to patients without history of cosmetic surgery. Implants interfere with radiologic examination, but through compression, atrophy and reduced glandular tissue thickness they enhance the detection of palpable lesions (20, 21). A large analysis of over 40,000 female patients in Canada compared a group of patients following breast augmentation to a group of women with history of other cosmetic surgery. Women with breast implants had a statistically significant higher incidence rate of advanced breast cancer. However this did not in any significant way impact the distribution of cancers by age, tumor size, histological type, the period during which the patient was diagnosed nor duration of follow-up. No differences were also observed in terms of prognosis or disease related survival (22). A meta-analysis of 28,000 breast cancer cases demonstrated that breast augmentation has a significant adverse effect on survival and early diagnostics in women with known breast cancer. However this conclusion is not entirely appropriate, because the survival analysis failed to demonstrate survival specific for breast cancer, and was based only on overall survival (23).

On the other hand data regarding implant ruptures, silicon leakage and relationship between implant rupture and breast cancer are derived mostly from case reports. Due to incidental nature of co-existence of implant rupture and breast cancer comprehensive studies on this subject have not been carried out. In these cases a diagnostic challenge should be emphasized caused by deposits of leaked silicone in the glandular tissue and in the tissue of the lymphatic system. Inflammatory reaction surrounding the foreign body may often mask the cancer and requires also a differentiation with inflammatory breast cancer (24). Clinical picture in implant rupture may be so ambiguous that patients are diagnosed for breast cancer not only with mammography with ultrasonography and breast magnetic resonance, but also CT and PET imaging. The arising doubts result in qualification of patients not only to fine-needle aspiration or

core-needle biopsy but often also open breast or lymph nodes biopsy or even mastectomy (10, 17, 25). A similar qualification to surgery took place in the above mentioned case. In the case of implant rupture and migration of silicone to axillary lymph nodes or sub- or supraclavicular lymph nodes patients are often diagnosed with painful shoulder syndrome (24). Depending on the clinical situation, effective biopsy of the sentinel lymph node is possible, also in lymph nodes with silicone deposits (26).

In conclusion diagnostic challenges should be emphasized arising from silicon implant rupture associated with accumulation of silicone in breast tissue and axillary lymph nodes. Intensified inflammatory reaction resulting from this clinical condition always requires a differential diagnosis with breast cancer, and if significant diagnostic doubts arise from radiological examinations or biopsy, surgery including mastectomy seems to be justified.

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Adress correspondence: 61-866 Poznań, ul. Garbary 15
e-mail: piotr_nowaczyk@o2.pl