VIA MEDICA

CASE REPORT

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Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)

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ABSTRACT

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) has recently been recognised, and so far approximately 200 cases have been described worldwide. From a histopathological and molecular perspective, it does not differ from classical breast anaplastic large cell lymphoma without ALK kinase expression. However, it has a different clinical course and prognosis, with a five-year survival rate about 92% as compared to 20–50% in patients with the classic form. A 60-year-old female patient had undergone bilateral mastectomy at the age of 45 years due to fibrocystic mastopathy and frequent breast cancer in her family history. Her implants were changed twice due to rupture. In 2018 the patient noticed a growing swelling of the right breast and fluid accumulation in the implant pouch; in September 2018 both implants were removed together, with the pouch also thoroughly removed during the procedure, and other PolyTech implants were inserted. Histological examination revealed the following: breast implant-associated anaplastic large cell lymphoma, immunophenotype: CD30+, ALK–, CD68, PGM–, CKAE1/AE3–, Ki 67 in 90% of cell nuclei. The patient was in very good general condition and without abnormalities in haematological tests. In PET-CT with 18F-FDG (13/12/2018), areas of slightly increased 18F-FDG activity were found in the vicinity of the implants on the right side (SUV max = 1.9) and on the left side (SUV max = 2.3), in addition to left axillary lymph node 12 × 7 × 8 mm (SUV max = 2.0). The patient did not decide to go ahead with the proposed removal of the implants, and a suspicious node was taken for examination — no cancer architecture was found. A control PET-CT test was performed after four months, the result of which was comparable to the previous one. The patient is under observation.

Key words: anaplastic breast lymphoma, breast implant, textured implant

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Introduction

Due to the constantly increasing number of breast reconstructions after mastectomy for breast cancer or other reasons, more and more is being said about the complications of such a procedure. At this point, breast implant-associated anaplastic large cell lymphoma should be remembered. The number of women in whom this malignancy could develop is small. Nevertheless, due to the lack of the possibility to identify women at highest risk, it should be considered as a potential danger for all women with implants. In the US breast anaplastic large cell lymphoma (ALCL) develops in about three out of 100 million women without implants. According to FDA representatives, as many as 60 cases of ALCL have been identified among women with implants, with their global population estimated at 5–10 million [1].

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) was described only recently. The first patient with BIA-ALCA was described in the US in 1997 [2]. In 2011, the US Food and Drug Administration officially issued a warning that breast implants increase the risk of developing ALCL [3]. To date, around 200 cases have been described worldwide [1]. BIA-ALCL belongs to the group of non-Hodgkin's lymphomas (NHLs), which account for only 0.01–0.5% of all malignant breast cancers [5]. Primary NHL of the breast includes primarily B-cell lymphomas, such as diffuse large B-cell lymphoma (DLBCL) or extra-nodal marginal zone lymphoma (MZL) [6]. T-cell lymphomas,

which include BIA ALCL, represent only about 10% of primary NHL of the breast, and ALCL alone accounts for about 3% of all NHL of the breast [7].

From a histopathological and molecular perspective, it does not differ from classical breast anaplastic large cell lymphoma without ALK kinase expression. However, it has a different clinical course and prognosis, with a five-year survival rate of about 92% as compared to 20–50% in patients with the classic form [8].

The disease is not associated with implants from a particular manufacturer or the type of implant filling: silicone or saline. BIA ALCL only accompanies implants with a textured surface. This could be related to a more intense productive as well as inflammatory reaction than with implants with a smooth surface, but the aetiopathogenesis of the disease has not yet been clarified [9]. It is also possible that the cause of the inflammatory reaction and clonal T lymphocyte expansion is the silicone itself or other substances used in the production of the outer shell of the breast implant, e.g. diaminotoluene [7]. Recently, it has been postulated that textured implants act only a passive potentiating factor, and the real aetiological factor of BIA ALCL is the bacterial biofilm around the implant. This biofilm is not detectable by traditional microbiological culture. Texturing of implant surface increases the area on which a biofilm layer can form, which is responsible for the T lymphocyte activation and productive reactions, e.g. capsular contracture [1, 10].

The incidence does not seem to depend on the time elapsed since the implant placement — in the analysed cases it ranged from four months up to 25 years (median 9.3 years) [11] and the average age of patients at the time of diagnosis was about 50 years [12]. The risk of generalised dissemination probably does not depend on the time interval between the onset of symptoms and treatment introduction; in the collected cases this time ranged from a month to two years [11]. Over 80% of patients were diagnosed in stage I according to Ann Arbor classification [1, 13]. The main reason for patients reporting to a physician was breast swelling, with moderate discomfort, without obvious pain. The cause of the symptoms is the formation of a seroma — accumulation of serous exudate under the fibrous capsule of the implant [9]. The volume of seroma varied between 200 and 1000 mL [1, 8, 14]. Occasionally (nine cases) the originally detected lesion was a nodule within the implant's fibrous capsule, which was always accompanied by exudate. In a few cases (six patients), the primary lymphoma tumour was accidentally detected during revision of an implant pouch [1]. The diameter of the nodules ranged from 4 mm to 10 cm (mean 4.4 cm) [1]. In individual cases, BIA ALCL manifested as breast ulceration (three cases) or local lymphadenopathy (three cases), which further led to the detection of a primary lesion in the implant's fibrous capsule [11]. During further diagnostics, the tumour cells were found simultaneously in the serous exudate and the implant's fibrous capsule, resulting in the cultures being negative in all cases.

The clinical stage of the disease in the documented cases varies greatly — from only single lymphoma cells in the aspirate of serous exudate without any tissue involvement in five patients to the rapid progression of disseminated, refractory disease, being fatal in 9 out of 10 described patients [15]. In most cases the lesions did not exceed the implant's fibrous capsule, ad in eight patients local metastases to axillary and mediastinal lymph nodes occurred [11]. One patient had central facial palsy in the course of lymphoma infiltration of the central nervous system [1]. General symptoms specific to lymphomas such as night sweats, fatigue, and weight loss occurred only in five patients [11]. Some speculations were raised about the relationship between aggressive disease course and manifestation of a primary lesion in the form of a nodule [1]. They were not unequivocally confirmed; in Brody's study only in four out of nine patients who died was the primary lesion a palpable breast mass [11], while in Laurent's publication, the presence of a palpable nodule was associated with a two-year survival rate of 52.5% *vs.* 100% in the group of patients with seroma as the only clinical manifestation [1].

The clinical picture is characteristic. With this in mind, BIA ALCL should be excluded mainly in patients with silicone breast implants, who report to the physician for breast swelling/late seroma (more than one year after implant placement) with no signs of infection or inflammatory exudate despite resolution of inflammation symptoms. Patients with capsular contracture or palpable masses within the implant's fibrous capsule also require increased vigilance [1]. There are no clearly established diagnostics. The material, without fixation, should be sent to a histopathological laboratory, where the diagnosis can be made mainly on the basis of immunohistochemical tests — the presence of CD30 marker and lack of ALK kinase expression are decisive [1]. To exclude lymphoma dissemination, computed tomography of the chest, abdomen, and pelvis is recommended. In high-risk cases, PET-CT with glucose should be performed [1].

Consensus on treatment has also not been reached yet. The disease is most often confined to the implant's fibrous capsule, and in such cases it seems sufficient to remove the implants along with the fibrous capsules and close follow-up [13]. Monitoring should be carried out every six months for five years by performing a breast ultrasound at least every two years [1]. Sentinel node biopsy is not recommended because the implant capsule is drained through several groups of regional lymph

nodes without a constant lymph flow pattern; however, axillary lymph nodes are most often involved in cases of dissemination to regional lymph nodes [16]. In the more advanced stages, complementary chemo- and radiotherapy, and even bone marrow transplantation, could be considered. The most commonly used chemotherapy protocol includes cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), but radical surgical resection remains crucial [16].

Case report

A 60-year-old female patient had undergone bilateral mastectomy at the age of 45 years due to fibrocystic mastopathy and frequent breast cancers in her family history. Implants were changed twice due to rupture. In 2004, textured implants were inserted in these places. Due to rupture of the left prosthesis in 2007, both were replaced with new ones. In 2018 the patient reported to the operating surgeon due to growing swelling of the right breast and fluid accumulation in the implant pouch. In September 2018 both implants were removed, together with the pouch, and other PolyTech implants were inserted, in which the micro-polyurethane surface minimises the risk of capsular contracture.

Histological examination: breast implant associated anaplastic large cell lymphoma, immunophenotype: CD30+, ALK–, CD68, PGM–, CKAE1/AE3–, Ki 67 in 90% of cell nuclei.

The patient, in very good general condition, has undergone haematological examination, including bone marrow trepanobiopsy and no abnormalities were found. In PET-CT with 18F-FDG (13/12/2018), areas of slightly increased 18F-FDG activity were found in the vicinity of the implants on the right side (SUV max = 1.9) and on the left side (SUV max = 2.3), in addition left axillary lymph node 12 × 7 × 8 mm (SUV max = 2.0).

In this case, implant removal is recommended as a treatment method.

However, the patient did not agree to such a solution, so only the lymph nodes suspected in PET-CT were taken for histological examination; five reactive lymph nodes were prepared with features of fat loss, sinus histiocytosis, and single polynuclear cells of "around the foreign body" type. There are no explicit features of atypical hyperplasia. Immunohistochemical reactions: CD20 (+++) in lymphatic follicle, blcl2 (+) in mantle cells, and Ki 67 (+) 70% in secondary lymphatic follicle. The microscopic image and immunohistochemical profile do not allow the diagnosis of lymphoma.

A control PET-CT test was performed after four months, the result of which was comparable to the previous one. The patient is under observation.

Discussion

Considering the increasing use of breast implants in women treated for breast cancer, and for other reasons, the risk of anaplastic large cell lymphoma associated with such implants should be highlighted. This should not limit the use of this type of surgery, but it certainly requires that the patient be informed about the possibility of such a complication, and informed consent should be obtained for this type of surgery.

BIA ALCL is rare, and accurate assessment of the scale of the problem and epidemiological surveillance is difficult due to low awareness of this issue among physicians.

Because the current incidence is probably underestimated, a uniform international reporting system should be developed.

Physicians monitoring patients after breast implants should be reminded to maintain high oncological alertness in case of late seroma or productive lesions around the breast implant. Treatment should be carried out by multispecialist teams, including haematologists.

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