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Authors: Krystian Czernikiewicz, Łukasz Mazurkiewicz, Maria Joks, Andrzej Balcerzak, Monika Joks, Joanna Rupa-Matysek

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Breast implant-associated anaplastic large cell lymphoma as a late complication of breast implant placement: a report of three Polish cases

Krystian Czernikiewicz[1*], Łukasz Mazurkiewicz[1*], Maria Joks[1], Andrzej Balcerzak[1], Monika Joks[1], Joanna Rupa-Matysek[1]

1 Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Poznań, Poland

Correspondence to: Joanna Rupa-Matysek, MD, PhD., Department of Hematology and Bone Marrow Transplantation, Poznan University of Medical Sciences, Szamarzewskiego Street 84, Poznan 60-569, Poland, tel.: 61-854 9383, rupa.matysek@gmail.com

* These authors equally contributed to this manuscript

We present the cases of 3 women who developed breast implant-associated anaplastic large cell lymphoma (BIA–ALCL) following breast augmentation (2 patients) or implant reconstruction surgery. The time between the implant surgery and the occurrence of symptoms was 4–7 years (58–84 months; median = 84 months, mean = 75.33). All patients complained of breast edema. No other symptoms were present, no infection signs were observed. Ultrasound revealed seroma in all three patients and reactive axillary lymph nodes and singular lymph node with decreased echogenicity in one patient. Primary PET-CT scans showed infiltrations exclusively in the breasts, no other organs were involved (Figure 1, A-D).

Pathological assessment of resected material combined with CD30 positivity and ALK1 negativity found in immunohistochemistry confirmed the diagnosis of BIA-ALCL.

Both implants were removed in all patients. In the 2-year follow-up two women remain in complete response after implant removal and one developed a relapse of BIA-ALCL in lymph nodes on both sides of the diaphragm (Figure 1, E-H; Figure S1 I-J). She received six cycles of CHOEP chemotherapy and achieved complete metabolic response. All the women are under the care of the Hematology Clinic and remain in general good condition. Detailed characteristics are presented in Supplementary material, Table S1.

Breast implants, as well as other methods, are used for breast reconstruction following mastectomy and for breast augmentation. Breast implant insertion is a common and developing procedure, with high demand worldwide [1]. BIA-ALCL is an uncommon outcome of breast-implant surgery using textured devices with estimated overall prevalence of 1:13,745 for 28 European countries [2].

BIA-ALCL is a rare primary non-Hodgkin T-cell lymphoma distinguishing itself by CD30 positivity among anaplastic lymphoma kinase (ALK) negative ALCLs [3]. However, ALCLs might be ALK positive as well [4]. Theories on etiopathogenesis include a complex immune stimulation on the surface of a textured implant, as well as chronic inflammation leading to lymphoproliferation and lymphomagenesis. The innate and adaptive immunity factors – like IL-4 and IL-13 play a role. Further IL-1 secretion and production of interleukins, leads to the formation of a specific microenvironment. JAK/STAT signaling pathway may be involved. BIA-ALCL is distinguished by the triple-negativity in the context of ALK, DUSP22 and TP63 [2,5].

Persistent seroma (a localized accumulation of clear fluid that may cause swelling and discomfort) is the most common clinical presentation [4]. The findings are seen over one-year post-operation, with an average of 7-10 years. Other symptoms include erythema or skin ulceration, swelling or asymmetry [1]. The diagnosis must be set by performing ultrasound

imaging, followed by fine-needle fluid aspiration, which enables cytology, immunohistochemistry, and flow cytometry or core biopsy [2,3].

Ultrasound is a primary tool useful in breast imaging and BIA-ALCL diagnostic process. PET-CT is recommended to assess stage of disease and surgical planning. Surgical treatment with en-bloc excision including healthy tissue margins is recommended in localized disease. Prophylactic contralateral implant removal should be considered [2,3]. In advanced stages, lymphadenectomy is needed [5]. Adjuvant treatment concerning patients with positive residual disease is not set yet, however positive impact of systemic ALCL treatment regimens or brentuximab vedotin (BV) is observed [2,3,5].

The lowest relapse risk of BIA-ALCL is acquired by complete surgical excision, provided the disease is limited to the capsule which directly reflects on good/excellent prognosis up to 93% in 2-year follow-up due to its indolent clinical features [1,5].

In conclusion, the problem of BIA-ALCL is underestimated. It is necessary to increase awareness both among patients and primary care physicians, gynecologists, and radiologists on possibility of BIA-ALCL. The need for further research is especially high in methods of early detection, prevention, and treatment.

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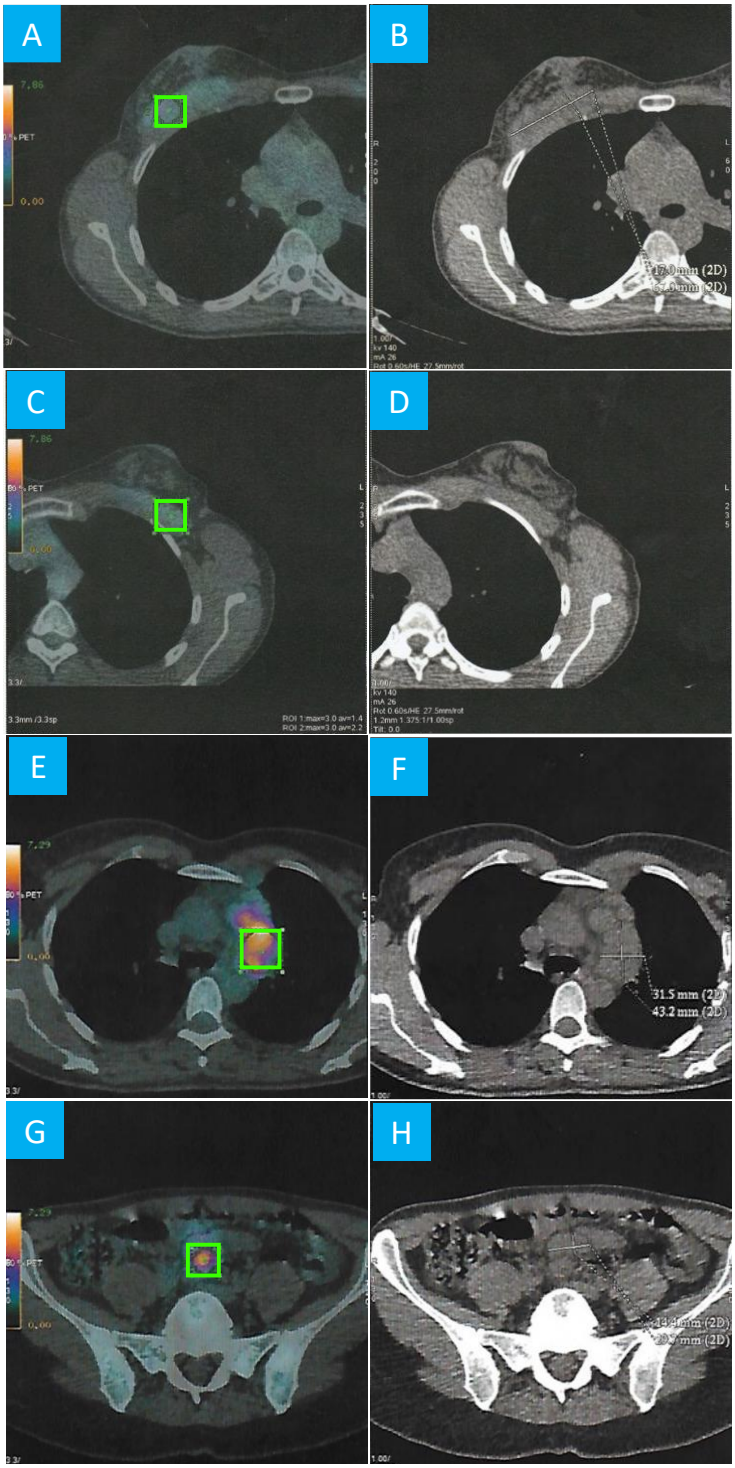

Figure 1 A, C, E, G (left column): combined PET-CT scans with metabolically active foci (marked green). B, D, F, H (right column): CT scans of lymphoma infiltrated nodules. A–B – Patient 2 PET-CT scan. At the border of the right glandular tissue of the breast and pectoral muscles visible lymphoma infiltrations 67.0 x 17.0 mm (SUVmax = 3.0). C–D Left pectoral

muscles with increased metabolic activity (SUVmax = 2.3) – possible lymphoma infiltrations or reactive changes. E–H – Patient 1 PET-CT scan performed in June 2021. Metabolically active lymphoma infiltrations in lymph nodes on both sides of the diaphragm confirming relapse of BIA-ALCL. E–F – Metabolically active lymph nodes in the pre- and para-aortic regions, with the largest measuring 43.2 x 31.5 mm. G–H – Metabolically active mesenteric lymph nodes located anteriorly to the common iliac vessels measuring 14.4 x 29.7mm (SUVmax = 6.9). Combination of a PET-CT scan with a biopsy of the supraclavicular lymph node, was the basis for implementing CHOEP chemotherapy.

Short title: BIA-ALCL as a late complication of breast implants: 3 Polish cases