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Breast Implant-Associated Anaplastic Large-Cell Lymphoma: A Case Report

Meme İmplantı ile İlişkili Anaplastik Büyük Hücreli Lenfoma: Olgu Sunumu

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To the Editor,

Breast implant-associated anaplastic large-cell lymphoma (BIA-ALCL) is a rare type of peripheral T-cell lymphoma, also recognized as a specific disease in the 2016 revision of the World Health Organization classification of tumors of the hematopoietic and lymphoid tissues [1]. Although BIA-ALCL has an indolent course, infiltrative forms may be life-threatening and 9 deaths have been reported [2]. The annual incidence is estimated as 0.1 to 0.3 per 100,000 women with implants [3]. The median age is 53, with the disease being detected after a median of 8 years following implantation [4]. Herein, we report a rare case of BIA-ALCL, the first from Turkey.

A 40-year-old Caucasian female presented to our clinic with right-sided breast swelling and asymmetry. Five years ago, she was diagnosed with left-sided invasive ductal carcinoma. She received neoadjuvant chemotherapy, followed by mastectomy and axillary lymph node dissection of the left side and nipple-sparing mastectomy of the right side. Macro-textured anatomical silicone gel implants and fat grafting were applied, followed by adjuvant chemotherapy. Five years later, breast ultrasound and MRI revealed effusion in the fibrous capsule surrounding the breast implant (Figures 1A and 1B). Initial evaluation of the effusion was benign and the implant was replaced by another one

after partial capsulectomy. However, the seroma recurred. In the third sampling, the immunochemical analysis revealed typically large and pleomorphic CD30-positive so-called hallmark cells (Figures 1C and 1D). She was diagnosed with BIA-ALCL. The Ann Arbor stage was IE and the TNM stage was IA. Complete excision of the breast implant and capsule was performed and no capsule invasion was reported upon pathological evaluation. Neither further surgery nor chemotherapy was applied. She has remained in remission to date, at the 18th month after the surgery.

Although it is a very rare entity, detection and diagnosis of BIA-ALCL is an emerging topic. BIA-ALCL is surgically treated and it has an indolent course, with the risk of death being 0.4 micromorts per patient [5]. Most cases are unilateral; however, rare bilateral cases have been reported. Patients mainly present with malignant effusions associated with the fibrous capsule surrounding the implants [6]. Lack of ALK expression and strong membranous expression of CD30 constitute the main immunochemical profile. The largest series published in the literature are summarized in Table 1.

The pathogenesis of BI-ALCL is still unclear. Textured implants are likely to induce a marked local T-cell immune response compared to smooth implants. Textured implants are known

to shed silicone particulate. Macrophages digesting silicone particulate form foamy cells and release cytokines, eliciting T-cell chemotaxis and replication. These findings help us to hypothesize that BI-ALCL originates from aberrant reactive T-cell populations [7]. The main treatment is surgical removal of the implant and total capsulectomy with complete excision of any associated mass until reaching negative margins on final pathologic evaluation, defined as complete surgical excision. Removal of the contralateral breast implant is controversial, as bilateral capsule involvement was reported in the literature [6,8]. Although there is no randomized controlled trial managing patients with incomplete capsulectomy, with residual disease and with stage II-IV disease, the postulated approach is chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) [6]. CHOP plus etoposide and brentuximab vedotin are alternatives for ALCL treatment [7].

Our patient's diagnosis was based on CD30 positivity and the presence of large pleomorphic cells. Immunohistochemical staining for ALK was not performed and this is a limitation of our report. Immunohistochemical evaluation of the expressions of CD2, CD3, CD4, CD5, CD7, CD8, CD30, and ALK is necessary and constitutes a widely accepted strategy to evaluate seroma samples.
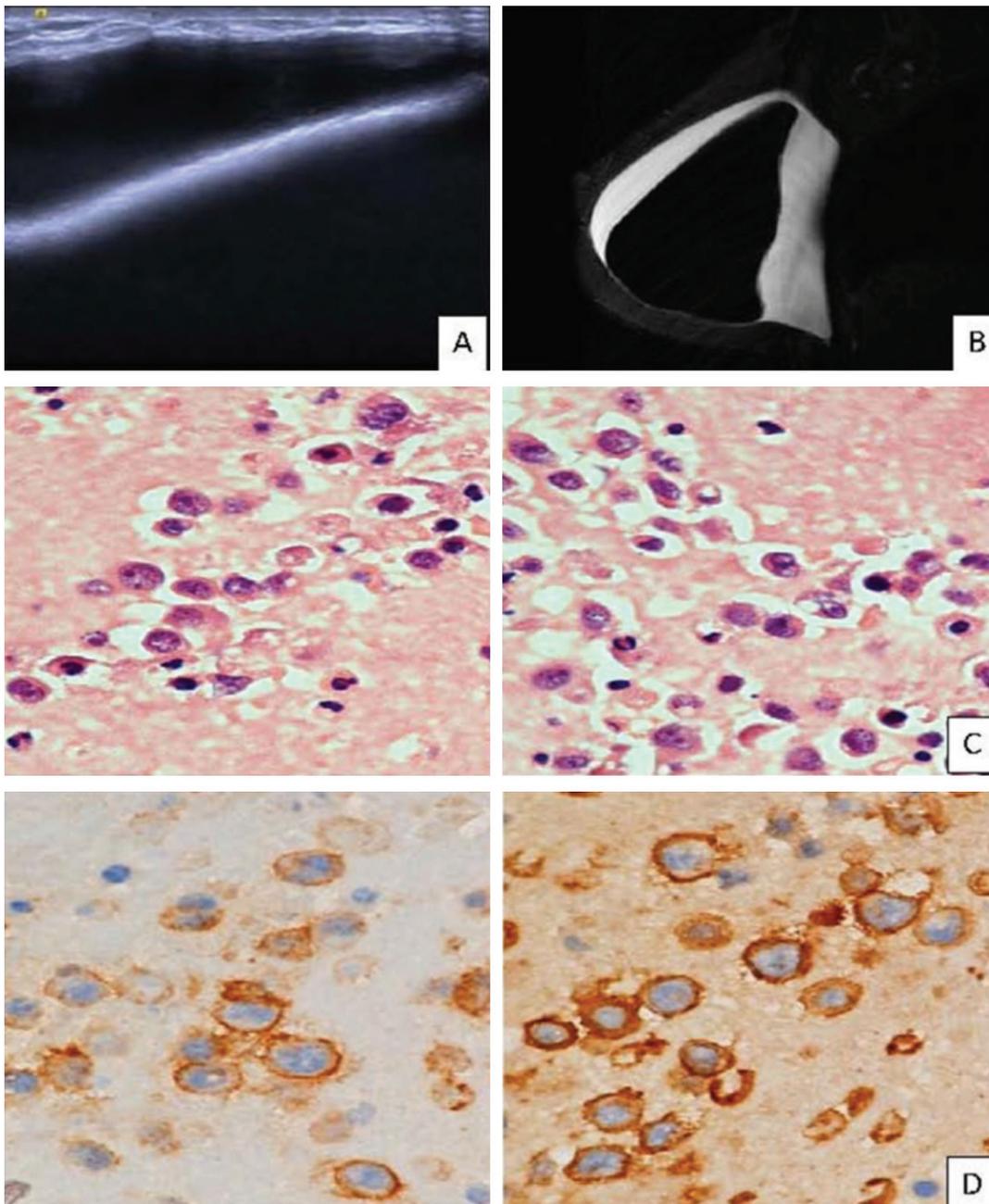

Figure 1. A&B: Ultrasound (A) and magnetic resonance imaging (B) of the capsule of the implant and the seroma at breast. C: Hematoxylin eosin staining, large cells, pleomorphic cells with abundant cytoplasm. D: CD30 (+) lymphocytes.

Table 1. Summary of large series of breast implant–associated anaplastic large-cell lymphoma cases.

Study	n	Age	Interval from implant to diagnosis	Implant characteristics	Treatment and outcome
Doren et al. [9]	100	Mean 53.2±12.3 years	Mean 10.7±4.6 years	Textured (n=51) Smooth (n=0) Unknown (n=49)	No data available.
Loch-Wilkinson et al. [10]	55	Median 47.1 years	Median 7.46 years	Biocell (n=44) Polyurethane (n=15) Salt loss (n=5) Siltex (n=5) Poly Implant Prothèse (n=2) Smooth (n=4)	All patients underwent total capsulectomy and removal of implants on both the diseased and non-diseased sides. Twelve patients had evidence of tumor infiltrating the capsule. Nine patients had adjuvant chemoradiotherapy, 1 patient had adjuvant chemotherapy; 5 of them had local recurrence. Two had positive tumor margins in histopathology. Three patients survived and remained disease-free. One patient received neoadjuvant chemotherapy. One patient had autologous bone marrow transplant. Overall, 1 patient who presented with seroma and 3 patients who presented with mass and/or metastatic disease died.
de Boer at al. [11]	32	Median 59 years	Median 13 years	Macro-textured (n=23) Micro-textured (n=5) Unknown (n=4)	Surgery only (n=11). Neoadjuvant chemotherapy (n=2). Neoadjuvant chemoradiotherapy (n=1). Adjuvant radiotherapy (n=2). Adjuvant chemotherapy (n=9). Adjuvant chemoradiotherapy (n=6). Chemotherapy only (n=1). Autologous stem cell transplantation performed for 5 patients. Twenty-nine patients were in complete remission after first-line (n=23) or second-line (n=6) treatment. Two patients died of disseminated disease after second-line treatment.
Campanale et al. [12]	22	Mean 49.6 years	Mean 7.8 years	Textured surface and silicone filler device (n=21) Textured surface and a double lumen saline/silicone filler device (n=1)	Implant removal with total capsulectomy only (n=14). Adjuvant chemotherapy and autologous stem cell transplantation (n=2). Adjuvant chemotherapy + anti-CD30 (n=1). Adjuvant chemotherapy (n=3). Adjuvant chemoradiotherapy (n=1). Mastectomy and chemotherapy (n=1). Nineteen patients are apparently free of disease, 1 patient died, and 2 are still undergoing chemotherapy.

As the number of breast implant surgeries is rising continuously, the diagnosis of BIA-ALCL is increasing. Patients undergoing breast implantation should be informed of the risk of lymphoma development. Recurring effusions around the capsule may reveal the suspicion of BIA-ALCL. Patients should be treated with surgery-based treatments. Randomized controlled studies are needed to determine standard chemotherapy protocols.

Keywords: Breast implants, Lymphoma, Large-cell, Anaplastic, Seroma

Anahtar Sözcükler: Meme implantı, Lenfoma, Büyük hücreli, Anaplastik, Seroma

Conflict of Interest: The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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A Rare Cause of Cyanosis Since Birth: Hb M-Iwate

Doğumdan İtibaren Mevcut Olan Siyanozun Nadir Bir Nedeni: Hb M-Iwate

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To the Editor,

Cyanosis in an apparently healthy newborn baby may be caused by hemoglobin (Hb) variants associated with the formation of methemoglobin. Such Hb variants are collectively known as M Hbs [1]. Hb M-Iwate [alpha2 87(F8) His>Tyr, HBA2:c.262C>T] is one of the Hb variants associated with methemoglobinemia [2].

Many Hb variants have been reported so far from Turkey [3,4,5]. We report herein a newborn baby from Bursa, Turkey, with methemoglobinemia and (pseudo) cyanosis having Hb M-Iwate as the underlying cause. To our knowledge, this is only the second report of Hb M-Iwate from Turkey, and more than four decades have passed since its first observation in Turkey in a 21-year-old male by Ozsoylu [6]. In addition, our case represents the first case of Hb M-Iwate from Turkey identified through genetic analysis of the α-globin chain gene (*HBA*).

The boy, born at term to a 32-year-old mother, was noted to be cyanotic immediately after birth. He had findings of dyspnea and he received oxygen by hood.

In the family history, the mother had history of cyanosis, particularly in the peroral area, and was otherwise healthy. In addition, the maternal grandfather and his mother, who had migrated from Thessaloniki (Greece), also had a history of cyanosis.

The oxygen saturation (SpO_2) of the baby, measured by pulse oximeter, was between 50% and 60%. Administration of oxygen did not result in an increase of the measured SpO_2. In venous blood gas analysis, pH was 7.43, pCO_2 was 34.6 mmHg, pO_2 was 45.3 mmHg, and the p_{50} value was 39.2 mmHg (normal range: 22.6-29.4 mmHg). Methemoglobin relative concentration was 13.5% (normal: <1.5%). Complete blood