CASE REPORT

Primary anaplastic lymphoma kinase-negative anaplastic large-cell lymphoma of the breast in a male patient

¹E S KO, MD, ²H SEOL, MD, ¹J H SHIN, MD and ¹E Y KO, MD

¹Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, and ²Department of Pathology, Korea Cancer Center Hospital, Seoul, Republic of Korea

ABSTRACT. Anaplastic large-cell lymphoma is an extremely rare lymphoma subtype. We describe the mammographic and ultrasonographic findings in a 51-year-old male patient who suffered from a palpable lump caused by this rare disease.

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Primary breast lymphoma (PBL) is uncommon, comprising <1% of all primary breast malignancies and about 2% of all extranodal non-Hodgkin's lymphomas [1, 2]. Given that the majority of PBLs are of B-cell origin, primary breast T-cell lymphoma is rare, comprising <10% of all primary breast non-Hodgkin's lymphomas [1–3]. Anaplastic large-cell lymphoma (ALCL) is a T-cell lymphoma typically seen in children and young adults, and accounts for 10–15% of all childhood lymphomas and <5% of adult non-Hodgkin's lymphomas [4].

Given that <1% of all malignant breast tumours occur in males [5], primary lymphoma of the breast in a male patient is extremely rare. We describe the mammographic and ultrasonographic findings of this rare anaplastic lymphoma kinase (ALK)-negative ALCL in the breast of a 51-year-old man.

Case report

A 51-year-old man presented with a 3-month history of a palpable mass in his left breast. On physical examination, a soft, mobile 2 cm mass was palpated on the upper outer quadrant of the left breast. The patient had no ipsilateral axillary lymphadenopathy. Mammography showed a 2.3 cm, ill-defined high-density mass in the left breast (Figure 1a). On ultrasonography, the mass measured 2 cm and was solid, almost entirely hyperechoic and of oval shape, and had a circumscribed margin in the palpable area (Figure 1b). The patient had no significant medical history. The radiological findings were assessed prospectively according to the American

College of Radiology Breast Imaging-Reporting and Data System (BI-RADS) [6] as Category 4a (low suspicion for malignancy). An excisional biopsy of the breast was performed. On microscopic examination, an atypical lymphoid nodule was identified (Figure 1c). The immunohistochemical profile was positive for cluster of differentiation-3 (CD3) and CD30 (Figure 1d) and negative for B-cell lymphoma-2 (Bcl-2), Bcl-6, CD10, CD20 and ALK (Figure 1e); these results confirmed the diagnosis of an ALK-negative ALCL of the breast.

The patient underwent further studies for metastatic disease, including CT of the thorax and abdomen and positron emission tomography/CT. There was no evidence of further disease. This established the diagnosis of a primary non-Hodgkin's lymphoma of the breast. He was referred for chemotherapy and treated with five cycles of cyclophosphamide, doxorubicin, vincristine and prednisone. In a follow-up period of 1 year, there was no evidence of disease recurrence.

Discussion

PBL remains a rare entity with an incidence that is difficult to assess because many published series include patients with extramammary lymphoma at the time of diagnosis. Reports of increasing incidence in the past few years may be accurate or may represent increasing awareness of the disease [7]. Nevertheless, most patients are women and the incidence of breast lymphoma in men is extremely low.

The criteria for the diagnosis of PBL are defined by Wiseman and Liao [8] and include an adequate pathological specimen, close proximity of mammary tissue and lymphomatous infiltrate with no prior diagnosis of extramammary lymphoma and no concurrent widespread lymphoma. Secondary breast lymphoma is a

Address correspondence to: Dr Eun Sook Ko, Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea. E-mail: mathilda0330@gmail.com

Figure 1. Anaplastic lymphoma kinase (ALK)-negative anaplastic large-cell lymphoma in a 51-year-old man. (a) Mediolateral oblique mammogram of the left breast shows a 2.3 cm, ill-defined high-density mass in the left breast. (b) Ultrasonography of the left breast shows a 2 cm, hyperechoic, parallel oval mass with circumscribed margin (arrows). (c) A photomicrograph of the specimen reveals an atypical lymphoid nodule composed mainly of medium to large lymphoid cells with one or more nucleoli. Hallmark cells showing horseshoe- or kidney-shaped nuclei are absent. (d) Immunohistochemical stain shows that the lymphoid cells are diffusely positive for cluster of differentiation-30. (e) Immunohistochemical stain shows that the lymphoid cells are negative for ALK.

systemic lymphoma that invades the breast tissue [9]. According to these criteria, the tumour in our patient was considered to be a primary lymphoma of the breast.

Most extranodal non-Hodgkin's lymphomas are of the B-cell phenotype [10] and are more common on the right side, with only rare cases showing the T-cell phenotype [11]. ALCL, as defined in the Revised European-American Classification of Lymphoid Neoplasms and World Health Organization Classification of Hematopoietic and Lymphoid Neoplasms, is a T-cell or null-cell lineage lymphoma that consistently expresses the activation marker CD30 [12, 13]. ALCL of the breast is rare; only a subset of these neoplasms has been further specified as systemic *vs* cutaneous with dissemination, or as ALK-positive *vs* ALK-negative. It is important to distinguish ALK-negative from ALK-positive ALCLs because the prognosis is quite different. Whereas the 5-year disease-free survival rate was found to be 71–100% in ALK-positive ALCL cases, it was found to be 15–45% in ALK-negative ALCL cases [14, 15].

The breast is one of the least commonly involved locations of ALCL [4, 16]. It seems that most ALCLs in

the breast have been reported as primary lymphomas [16]. It is interesting to note that most of the primary ALCLs have developed as a consequence of breast implants [9, 10, 16, 17]. The first case of ALCL in association with a saline-filled breast implant was reported by Keech and Creech [17]. According to an analysis by Li and Lee [18], among the 30 cases of primary breast ALCL reported in the English literature so far, 22 were associated with silicone-based implants. Li and Lee reported that most patients with primary breast ALCL associated with silicone implants presented with implant-related symptoms with or without a mass lesion, with seroma being the most common presentation. This unusual presentation indicates the importance of careful pathological examination of tissues removed for implant-related complications. In implant-associated primary breast ALCL, both sides are equally affected; by contrast, the reported predilection in other types of PBL is for involvement of the right breast [19].

It appears that silicone implants may play a role in the development of primary breast ALK-negative ALCLs. The underlying mechanism of this possible link is

unknown. Silicone has been shown to incite a chronic inflammatory response with production of auto-antibodies. Given that chronic inflammation has been associated with the development of malignant lymphoma (e.g. *Helicobacter pylori* infection in gastric extranodal marginal zone lymphoma and hepatitis C infection in marginal zone B-cell lymphoma), Li and Lee [18] postulated that chronic inflammatory stimulation is related to an increased risk of development of primary breast ALK-negative ALCL in silicone implant recipients.

To our knowledge, there have been only two cases of primary ALCL in a male patient. One involved a 19-year-old man whose ALK status was not available [20]. The other involved a 65-year-old man who was ALK-positive [3]. Therefore, we believe this is the first case of ALK-negative ALCL in an older man.

There has been no study about specific imaging findings for ALCL. We believe that findings are not specific and are similar to the general findings of breast lymphoma. According to a 2007 study by Yang et al [21], the most common mammographic feature of breast lymphoma was a mass, noted in 76% of tumours in their study. The majority of masses were solitary (72%), but there were multiple masses in 3%. The authors found diffuse, increased opacity (now termed "global asymmetry") in 16%. These results are similar to those of Liberman et al [22], who described a solitary mass in 69%, multiple masses in 9% and global asymmetry in 9% of tumours. In the study by Yang et al [21], masses were most frequently lobular (56%) or irregular (22%) in shape and most had indistinct margins (72%). Tumours were of equally high density (56%) and isodense (44%). Associated overlying skin and subcutaneous changes were present in 8%. Our patient had a solitary, ill-defined high-density mass.

Previous reviews [19, 22] described non-specific ultrasonographic features of breast lymphoma, including a large heterogeneously hypoechoic mass with indistinct margins and overlying skin and subcutaneous oedema, circumscribed hypoechoic masses or diffuse nodular infiltration of the breast. According to Yang et al [21], the most common ultrasonographic feature of breast lymphoma was a solitary hypervascular mass (64%) that was irregular in shape (45%) with indistinct margins (59%) or an echogenic boundary (27%). Lymphomas were hypoechoic (59%) or mixed hypo- and hyperechoic (23%) in echo pattern, with no posterior acoustic phenomena (64%). In our case, ultrasonography revealed an oval, circumscribed hyperechoic mass mimicking a benign tumour.

We report a very rare case of a primary ALK-negative ALCL in a male patient. Because the clinical and radiological findings are non-specific, a histological diagnosis should be obtained for a solid mass in a male patient by core biopsy or surgical excision, even if the imaging features appear benign, owing to the rare possibility of malignancy.

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