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Case report

Primary breast non-Hodgkin lymphoma. A report of an unusual case

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Abstract

Although lymphomas are generally considered as tumors of lymph nodes about 25-40% arise at extranodal sites. We report a case of a 60 years old female who developed a right breast B-diffuse large cell non-Hodgkin lymphoma in 2005 treated by chemo/radio-therapy which relapsed at the same breast in 2007 and at the other breast in 2010. The patient underwent both radiologic and nuclear medicine studies.

Key words: primary breast non-Hodgkin lymphoma, PET/CT, mammography

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Introduction

Hematopoietic malignancies can be encountered in the breast and can occasionally mimic primary breast cancers. Although lymphomas are generally considered as tumors of lymph nodes about 25–40% arise at extranodal sites [1, 2] and it's important to distinguish them from secondary extranodal involvement by disseminated nodal disease. Despite there isn't a precise and agreed definition, extranodal lymphomas are considered all lymphomas confined to a solitary extranodal site (and possibly its contiguous lymph nodes) or, at least and less strictly, a lymphoma which presents the main bulk of diseases at an extranodal site [2, 3]. Wiseman and Liao [4] have proposed that the diagnosis of primary breast non-Hodgkin lymphoma (PBNHL) must satisfy three criteria: 1) adequate pathologic evaluation, 2) both mammary tissue and lymphomatous infiltrate in close association, and 3) exclusion of either systemic lymphoma or previous extramammary lymphoma. PBNHL are mainly diffuse large B-cell non-Hodgkin lymphoma (B-DLC-NHL) and are very rare, accounting for 2.2% of all extranodal lymphomas [1] and for 0.04% to 0.5% of malignant breast neoplasms [4–7]. The most common symptom of primary breast lymphoma is a palpable lump but it may also present as breast enlargement [8]. The natural history of primary breast NHL is different from that of extra nodal NHL at other sites, because of its rapid progression and worse prognosis [9]; Giardini et al. have reported a total five-year survival rate of 43% [10].

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Case report

We report a case of a 60 year old female who developed a right breast B-diffuse large cell non-Hodgkin lymphoma (B-DLC-NHL) in 2005. A 67Gallium-citrate (67Ga-citrate) scintigraphy was performed before and after chemo/radio-therapy documenting complete response and disappearance of the pathologic uptakes (Figure 1). 67Ga-citrate scintigraphy was performed injecting intravenously an activity of 185MBq, acquiring total body planar images (anterior and posterior view) and tomographic studies of the thorax 3 days after injection on a dual headed Adac-Vertex Philips gamma camera (Philips Healthcare, Andover, MA, USA; medium energy collimator; speed 11cm/min; butterworth filter). In 2007 a 18fluorodeoxyglucose-positron emission tomography/computed tomography (F18-FDG-PET/CT) revealed right breast relapse of the NHL (Figure 1). F18-FDG-PET/CT was performed in the fasting state for at least 6 hours and the glucose level lower than 150mg/dl. An FDG dose of 5.5 mega-Becquerel (MBq)/Kg was administered intravenously and a 2D mode ordered-subset-expectation-maximization (OS-EM) imaging was acquired 60 minutes after injection on a Discovery ST PET/CT tomograph (General Electric Company - GE® - Milwaukee, WI, USA) with standard CT parameters (80 mA, 120 Kv without contrast; 4 minutes per bed-PET-step of 15cm). The reconstruction was performed in a 128 × 128 matrix and 60 cm field of view. PET images were analyzed visually and semi-quantitatively by measuring the maxi-

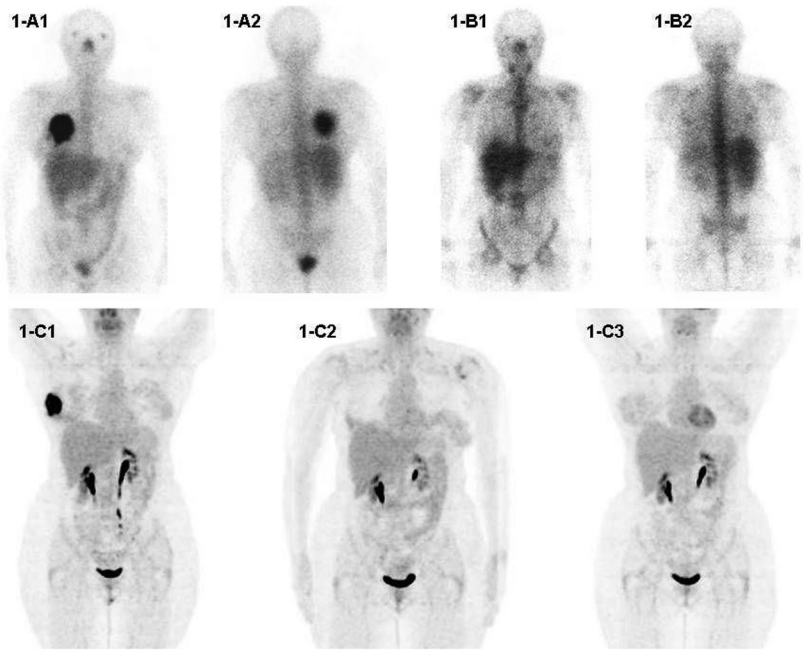

Figure 1. 67Ga-citrate anterior (1-A1) and posterior view (1-A2) of the total body planar images performed in 2005, revealing high pathologic uptake at right breast; anterior (1-B1) and posterior (1-B2) 67Ga-citrate images after chemotherapy revealing no pathologic uptake; anterior maximum intensity projection view of F18-FDG-PET/CT (1-C1) at first omolateral relapse in 2007; anterior maximum intensity projection view of F18-FDG-PET/CT performed in 2008 (1-C2) after chemotherapy and in 2009 during follow-up (1-C3) confirming the absence of pathologic uptakes

mum standardized uptake value (SUVmax). SUV was expressed as SUVbody weight (SUVbw – g/ml) and automatically calculated by the software (Volumetrix for PET/CT; Xeleris™ Functional imaging workstation; GE®). The patient underwent chemotherapy and right mastectomy. In 2008 and 2009 F18-FDG-PET/CT studies were negative (Figure 1). In 2010 was demonstrated a disease relapse at left breast; in particular, mammography revealed parenchymal areas without the fibro-adipose changes characterizing the remnant surrounding tissue (Figure 2). Mammography was acquired on Senographe Essential digital acquisition system (General Electric Company-GE®-Milwaukee, WI, USA; 31kV, 149mAs, Rh/Rh, Grid, AOP/STD 9, clan 79mm; WW:900, WL:2683, Zoom:0.69 ROT, Inc: Ø°-45°, AGD:2.07mGy, ESE:17.05mGy). Breast ultrasonography was acquired on a LOGIQ S6 (General Electric Company-GE®-Milwaukee, WI, USA; 11 Mhz probe) and revealed 3 large hypo-isoechoic nodules and no involvement of omolateral axillary lymph nodes (Figure 2). F18-FDG-PET/CT documented 6 pathologic uptakes at left breast (Figure 2). A breast biopsy confirmed the relapse of B-DLC-NHL and the patient started chemotherapy at the end of which, in 2011, a new F18-FDG-PET/CT showed complete disappearance of the pathologic uptakes (Figure 2). A written consensus was obtained by the patient before each study.

Discussion

Primary lymphomas of the breast are uncommon [1, 11] and, although rare, bilateral breast involvement has also been reported [12]. The old history of breast B-DLC-NHL relapsed twice after therapy, firstly at the same breast and subsequently at the other, makes this case of unique interest also because of the concurrent use of radiologic and nuclear medicine imaging. Despite the radiologic features are non-specific and the diagnosis cannot be made on the basis of imaging only, it's very relevant in establishing disease extent, possible involvement of other sites and therapy planning. Therapeutic procedures mainly rely on chemotherapy and radiotherapy [8, 13, 14] while surgery has had a progressive decline [15–17]. PBNHL doesn't show specific mammographic features; most commonly it has been reported as well-circumscribed lesion without calcifications or desmoplastic reaction, but also as lesion with sharp or minimally irregular margins, and less commonly as diffuse increased parenchymal density with skin thickening or as miliary densities [8, 13, 18–20]. Bilateral miliary densities on mammography have been reported in secondary involvement of the breast by NHL [20]. At ultrasonography examination breast lymphomas are generally described as masses that could be well or poorly defined, with an hypo- or hyperechoic aspect and showing both a focal and diffuse parenchymal involvement [21, 22]. In a recent study Li et al. have retrospectively reviewed 11 patients with PBNHL showing that the echo pattern of the mass was hypoechoic in 10 lesions, hyperechoic in 1 and complex echoic in 2; moreover no mass had speculated margins or calcifications and ipsilateral axillary lymph node involvements were noted in 6 patients [23]. Despite literature is poor and few data concerning radiological features of PBNHL are available in particular for magnetic resonance (MR), it seems to be relevant mainly in establishing the extent of disease, in the assessment of therapy response and in the diagnosis of recurrence. Rizzo et al. [13] evaluated 7 patients with PBNHL by MR suggesting that the occurrence of PBNHL should be considered in the presence of large enhancing lesions of the breast, especially if associated with skin thickening. They have found a mass-like enhancement with round shape, smooth margins, homogeneous enhancement

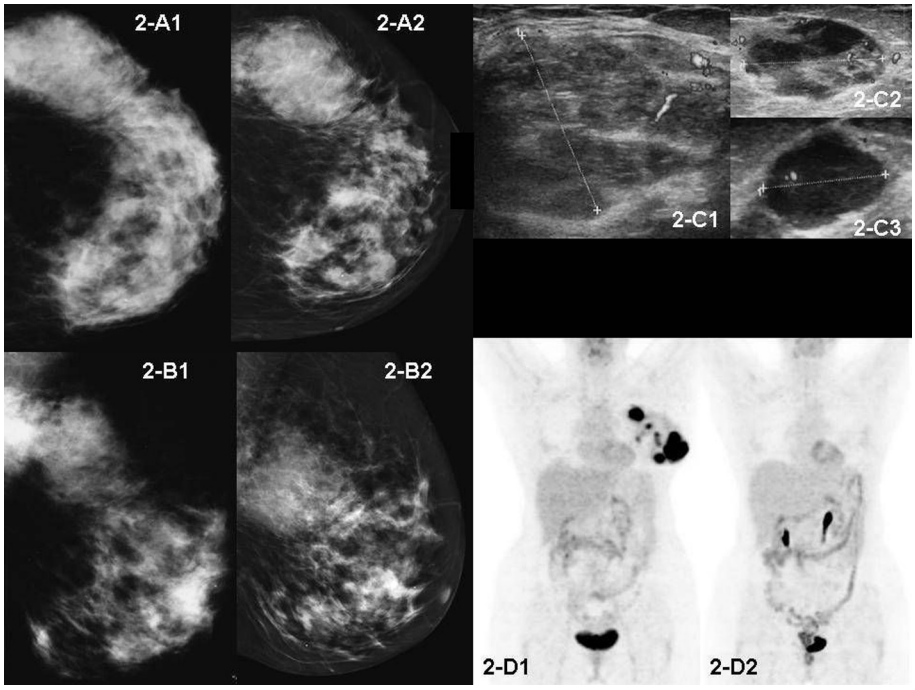

Figure 2. Cranio-caudal projection (2-A1) and oblique projection at 45° (2-B1) of mammography performed in 2007 and the same views of the study acquired in 2010 at second relapse (2-A2;2-B2); images of the three hypo-isoechoic lesions identified in 2010 at second relapse (2-C1;2-C2; 2-C3); anterior maximum intensity projection view of F18-FDG-PET/CT performed in 2010 at second contralateral relapse revealing pathologic uptakes at left breast (2-D1); anterior maximum intensity projection view of F18-FDG-PET/CT performed in 2011 after chemotherapy (2-D2) revealing no pathologic uptake

pattern, peak enhancement value of 90% and kinetics with slow rise and delayed plateau. Demirkazik et al. and Mussurakis et al. described multiple well- or ill-defined nonspiculated hypointense masses on T1 weighted images [19, 22]. Darnell et al. described a single, large, well-circumscribed mass, isointense relative to parenchyma on T1 images, associated with enhancing skin thickening [9]. A possible important role of MR seems to be its ability to evaluate multicentricity and multifocality of lesions as demonstrated by Kiresi et al. [24]; moreover, Espinosa et al. showed that MR could be more accurate than mammography and ultrasonography in detecting and staging multifocal breast lymphoma and it's very useful in the therapy response evaluation [25]. Although in the past 67Ga-citrate scintigraphy was an important tool for the evaluation of lymphomas, nowadays its role is very limited and it's not recommendable for dosimetric concerns and diagnostic accuracy; despite this, in a recent study by Takemura et al, published in 2009, a PBNHL was studied with this tracer [26].

F18-FDG-PET/CT role in the management of high-grade NHL and Hodgkin Disease is well established and many data are available in literature about its usefulness in evaluating extranodal lymphomas (bone, nasal region, pituitary, testis, ocular region, thyroid, adrenal) [27–33]. There are few reports on the role of F18-FDG-PET/CT for the management of PBNHL [34–38]. Most studies are case reports with few exceptions [38, 39] and in all cases is reported high FDG uptake. Yang et al. [38] studied with F18-FDG-PET/CT 13 tumors in 10 patients (three had bilateral tumors) and 12 (92%) tumors showed diffuse and intense hypermetabolic activity. All 10 patients underwent follow-up to evaluate response to chemotherapy and all 12 initially positive tumors showed complete resolution of hypermetabolism. In a recent study by Santra et al. [39] were evaluated 18 patients affected by breast lymphoma (16 unilateral and 2 bilateral); the indication was staging in 12 patients, evaluation of treatment response in 12 and restaging in 3. F18-FDG-PET/CT demonstrated high uptake in the masses despite non distinguishable from uptake of primary breast cancer or any other glucose avid tumor; F18-FDG-PET/CT was useful for staging, therapy response evaluation and restaging like in high-grade nodal and extranodal NHL.

To summarize, mammography and ultrasonography despite not specific have a primary role in the diagnosis while MR seems to be relevant in establishing the extent of disease, therapy response assessment, diagnosis of recurrence and multifocal lesion. Our case confirms the possible usefulness of F18-FDG-PET/CT in the management of PBNHL both in terms of staging, treatment response assessment and restaging, like in high-grade nodal and extranodal NHL.

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