CASE REPORT

Bilateral Primary Breast Lymphoma in A Teenage Girl with Multi-Organ Involvement

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Received: 16 Oct. 2012; Received in revised form: 27 Jan. 2013; Accepted: 15 Feb. 2013

Abstract- We present 16 years old girl with primary breast lymphoma involving the both breasts simultaneously and co-incidence of central nervous system (CNS) involvement which originated from the breast, in addition to evidence of lymphoma in multi-organ such as skin, mediastinum and some abdominal viscera. Bilaterality has been observed in some series, but reports are few and series are often very small. Radiologic features may be indistinguishable from those of the other breast malignancies, but it can be concluded that primary involvement of the breast with lymphoma should be considered when breast mass or inflammatory changes occur in a patient without any previously diagnosed lymphoma. The clinical behavior, imaging and therapeutic procedures are discussed. The findings of this report may have clinical impact on oncologists or that may alter the disease concept of bilateral breast lymphoma.

Acta Medica Iranica, 2013; 51(8): 572-576.

Keywords: Breast; Central nervous system; Primary lymphoma; Radiology

Introduction

Non-Hodgkin's lymphoma (NHL) involving the breast, either as a primary site or as a site of recurrence from lymphoma previously diagnosed elsewhere, is rare. Several series have reported varying incidences of primary and secondary cases (1-4). Primary breast lymphoma (PBL) is very rare and only accounts for 0.04-0.5% of primary breast cancer and 1.7% to 2.2% of extra-nodal lymphoma in most countries (1,2). Most of which belong to the category of diffuse large B cell lymphoma. Secondary cases are equally rare, but few studies have addressed this issue (1,4). Bilateral primary breast lymphoma typically affects younger women and is mostly associated with Burkitt lymphoma. Unilateral primary breast lymphoma manifests clinically similar to breast carcinoma, affecting older women, and typically has B-cell histologic features. Secondary breast lymphomatous involvement in a patient with diffuse NHL is more common (5).

In the present report, we describe a distinctive appearance of PBL involving the bilateral breasts in a teenage girl with the consequence of the involvement of multi-organ such as the central nervous system (CNS), skin, mediastinum and some abdominal viscera. The clinical behavior, imaging and therapeutic procedures are also discussed.

Case Report

A 16 years old girl with a history of one month's duration of dry cough, dyspnea, spinal column pain, hardness and pain of breasts was admitted to infections department with the primary diagnosis of mastitis. She did not mention any weight loss. In the primary evaluation cervical and bilateral axillary lymphadenopathy was also noted. The primary chest computed tomographic (CT) scan with IV contrast revealed bilateral pleural effusion and anterior mediastinal mass (80×60 mm) in addition to bilateral infiltrative nodular masses in the breast with infiltration of subcutaneous space around the nipples (Figure 1A). Abdominal CT showed Ascites, hepatosplenomegaly, enlarged kidney and striated nephrogram (Figure 1B).

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Para-aortic lymphadenopathy and multiple subcutaneous soft tissue masses through the abdominal wall (Figure 1C) were also detected. In the pelvic CT scan, soft tissue masses encased both ovaries which could not be differentiated from each other (Figure 1D). In the pelvic ultrasonography, two hypo-echoic masses in the Right and left adnexa were seen, which were undistinguishable from the ovaries. Mild fluid was also detected in the pelvic.

The Breast fine needle biopsy (FNB) revealed the NHL, and the patient went through chemotherapy. She also complained of blurred vision. After 6 months of the routine therapeutic procedures, her vision improved to near normal level, but recurred subsequently.

Three months later, patient had a complaint of vision of the right eye and blindness of the left one. After funduscopic examination, bilateral optical disk edema and hemorrhage in the left eye were detected. The CSF cytology exam revealed no malignant cells. Only 240/mm^3 WBCs were detected as well as lymphocyte-predominance, but no malignancies were found. Patient underwent five episodes of intrathecal (IT) administration of methotrexate (MTX) (15 mg) and hydrocortisone (50 mg) in the hospital. Patient had numbness of left 5th cranial nerve distribution and palsy of left 7th cranial nerve distribution. After IT chemotherapy, right eye vision returned to normal, but the left eye remained blind.

In the primary brain MRI, hyper-signal areas were noted in chiasma and both optic nerves sheet (Figure 2A). 3th cranial nerves as well as midbrain pial enhancement were also seen (Figure 2A). The result of bone marrow biopsy revealed normocellular marrow with erythroid hyperplasia and left-shifted myeloid maturation. No bone marrow involvements were detected.

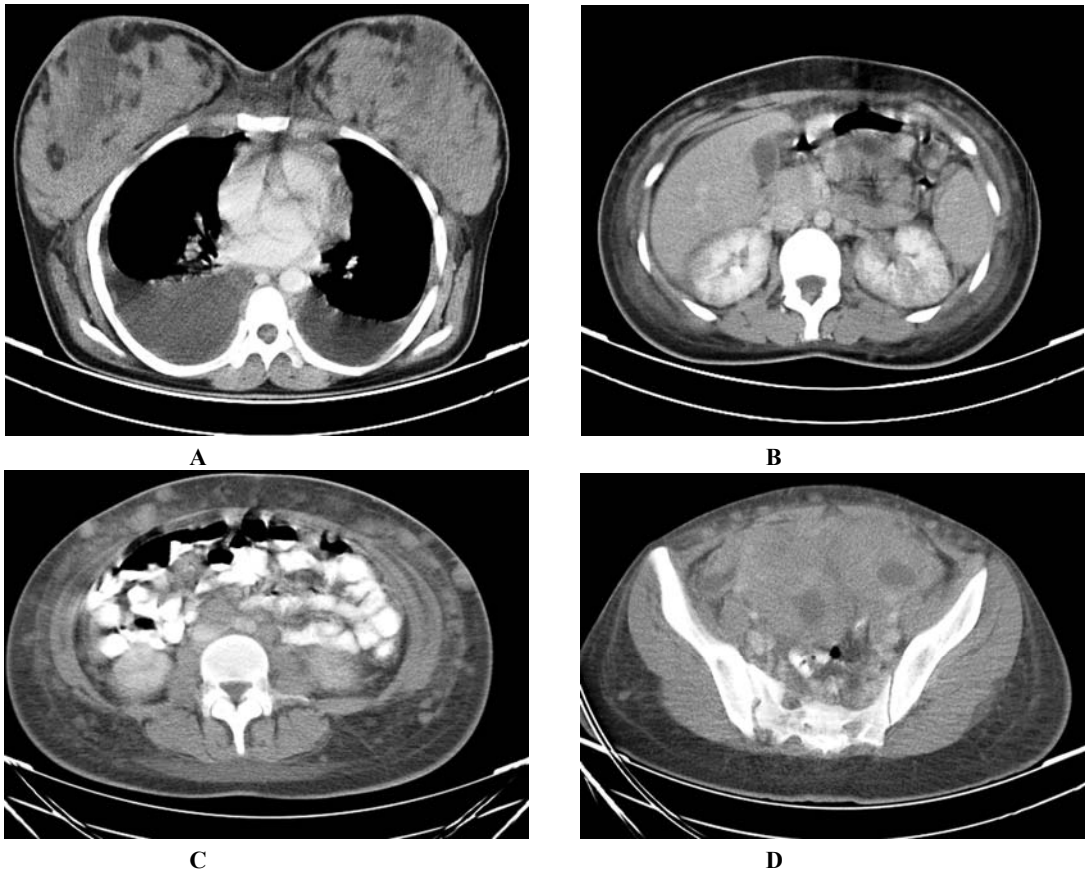

Figure 1. Image studies during the diagnostic work-up. A chest computed tomographic (CT) scan shows bilateral pleural effusion and anterior mediastinal mass (80×60 mm) in addition to bilateral infiltrative nodular masses in the breast with infiltration of subcutaneous space around the nipples (A); Abdominal CT showed enlarged kidney and striated nephrogram (B); para-aortic lymphadenopathy and multiple subcutaneous soft tissue masses through the abdominal wall (C); A pelvic CT scan revealed soft tissue masses encased both ovaries which could not be differentiated from each other (D).

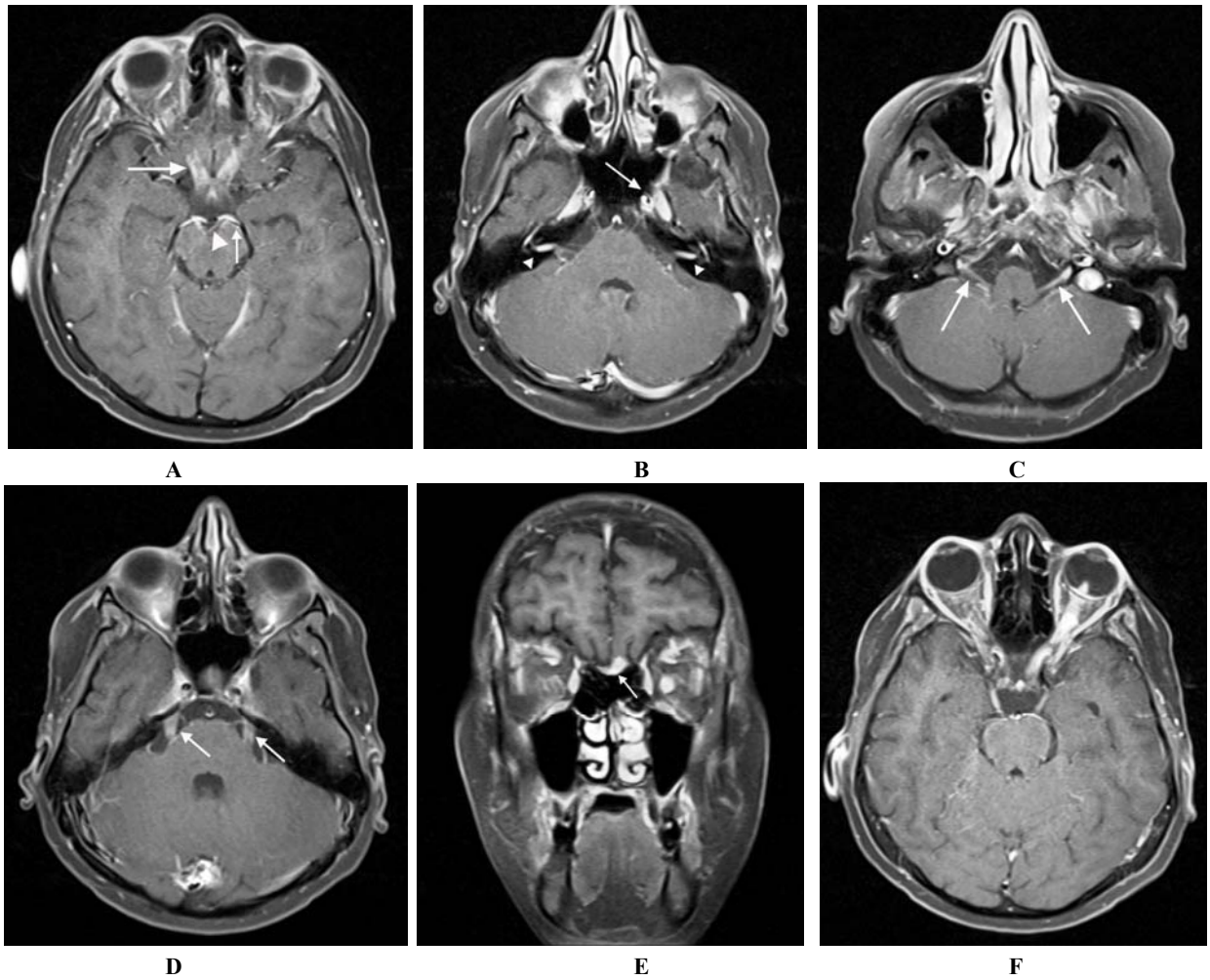

Figure 2. Cranial MR imaging during diagnostic and therapeutic work-up. Axial post contrast brain MRI shows enhancement of chiasma and both optic nerves sheet (large arrow), 3th cranial nerve (arrow head) and midbrain pial enhancement (small arrow) (A); bilateral 7&8th cranial nerves (arrow heads) and Mechel's cave enhancement (arrow) (B); 9th,10th,11th,12th cranial nerves complex enhancement (arrows) (C); both 5th cranial nerves enhancement (arrows) (D); coronal MRI of frontal lobe shows bilateral 1st cranial nerves which is more prominent in the left side (arrow) (E); axial post contrast image demonstrate left optical nerve sheet enhancement in its entire course (tram-tract like) and retinal tumor enhancement (F).

In the subsequent brain and skull base high resolution MRI, all of the cranial nerves including, I, II, V, VII, VIII, IX, X and XI were enhanced after IV contrast administration (Figures 2B, 2C and 2D). Bilateral auditory canal meningeal enhancement was another finding of brain post contrast MRI (Figure 2B). Enhancement along the both first cranial nerves in the frontal grove was also noted (Figure 2E). The enhancement of the left optical nerve sheet in its entire course (tram-track like) and retinal tumor enhancement were also revealed (Figure 2F). There was also some enhancement of the leptomeningeal which was noted especially in the posterior fossa along the cerebellar surface and the interpeduncular and ambient cisterns. Despite all efforts to save her, she died from severe cranial involvement after 17 months of diagnosis and judicious therapy.

Discussion

Lymphoma of the breast is a rare diagnosis (6). Literature reviews of PBL have indicated that there are two distinct clinicopathological subtypes: the unilateral subtype that shows indolence to aggressive histology and mimics breast carcinoma in age distribution, and the bilateral subtype affecting pregnant or lactating women. The latter group is further characterized by widespread dissemination with prominent ovarian and central

nervous system involvement, and characteristic histological findings identical to those of Burkitt lymphoma have been reported in African women (7).

Bilaterality has been observed in some series, but reports are few and series are often very small. Au *et al*. also reported a high incidence of CNS involvement of breast lymphoma among Hong Kong Chinese (3/14) with poor prognosis (8). The median age of the presentation was 51 years. Three patients had bilateral disease and five had disseminated disease. Jeon *et al*. divided primary breast lymphoma into a unilateral type that occurred in older women and a bilateral type that affected younger women. All patients were women; they ranged in age from 31 to 80 years (mean, 57.6 years) (9).

In an additional study, Ribrag *et al.,* reported a high incidence of CNS involvement of malignant lymphoma originating from the breast. Four out of 20 patients (20%) treated with chemotherapy [CHOP (cyclophosphamide, hydroxydoxorubicin, vincristine, prednisone) or CHOP like regimen], with or without radiotherapy, showed CNS relapse (10). Median age of the patients was 50 years (range 22-76 years). In the experiments of Yamazaki *et al*., the clinical records of 921 patients with breast tumors, treated from 1990 to 2002 were retrospectively reviewed. Eight patients were found to have malignant lymphomas during this period. Of these, four patients ranging from 46 to 80 years of age had CNS involvement, one with Burkitt type and three with diffuse large B-cell lymphoma. Four patients without CNS involvement were alive without tumor, whereas three of the four patients with CNS involvement died of the disease (3). Bilateral breast localization at diagnosis seems to differ from contralateral relapse because it is usually observed during pregnancy, in PBL of Burkitt's or Burkitt like histology (9). Our data, for some reason, does not concur with their observations. We experienced here a case of lymphoma, in 16 years old teenager girl, with rapidly progressing disease resulting in early death, even though the patient was very young and had not yet lactated or been pregnant. These characteristics made this case, somehow, distinct from those reported previously on this issue.

Rarely, bilateral inflammatory carcinoma of the breast may present florid features of inflammation. Burkitt lymphoma involving the breast, especially in lactating women, can also manifest itself as a rapidly enlarging mass with features of inflammation (1). From the clinical point of view, while the presentation of breast lymphoma is often similar to that of breast carcinoma (including the occurrence of “inflammatory” features), this issue is usually readily resolved by histological examination (6). It is rare for NHL to be presented with features suggestive of inflammatory or infectious breast disease (1). This clinical similarity (inflammatory process) was presented as mastitis of both breasts in first admission to hospital in this case, with both axillary lymphadenopathy, but FNB differentiated these two distinct phenomena. It is reasonable to make a diagnosis of mastitis in a patient with fever of short duration coupled with pain, swelling, and erythema of the breast. Axillary lymphadenopathy may be mistakenly thought to be due to infection rather than the primary disease. In such cases, medical history and associated clinical findings should also be considered as they are of paramount importance.

The radiologic features of breast lymphoma are nonspecific, and the diagnosis cannot be made solely on the basis of radiological findings. Radiologic features may be indistinguishable from those of the other breast malignancies (11). The value of magnetic resonance (MR) imaging for the evaluation of breast lymphomas is not yet firmly established, but strong and rapid enhancement of breast lymphomas has been observed on T1-weighted MR images obtained after the administration of contrast material (12,13). Currently, combined positron emission tomography (PET) - CT is generally performed for the initial staging of lymphoma and to evaluate any recurrence of the disease (14).

If the distinction between primary and secondary breast lymphomas and the related concept that primary breast lymphomas represent a specific instance of Mucosa-associated lymphoid tissue (MALT) cell malignancy are to have any validity, they must be based on specific pathological, immunohistological or biological (including prognosis and response to treatment) features. In this regard, however, there were no specific pathological features that distinguished breast lymphomas from lymphomas arising at other sites, or indeed that distinguished between patients with lymphomatous involvement confined to the breast, and those with more widespread involvement. In both the patients with localized lymphomas and those with breast involvement as part of disseminated lymphoma, the predominant histological subtype was diffuse large cell (type G, Working Formulation) (6).

The age and stage of NHL at diagnosis were significant prognostic factors in predicting the survival time, and not the location and size of the tumor at initial presentation, histopathologic type, terminal leukemic manifestation, and treatment modality (9).

According to author's knowledge, some features made our case different from those reported previously. These features included: Bilaterality of primary breast involvement by lymphoma, co-incidence of CNS involvement, evidence of lymphoma in multi-organ like skin, mediastinum and some abdominal viscera, and the patient's age at the time of presentation.

As a result of the findings in this study, it can be concluded that primary lymphomatous involvement of the breast should be considered when breast mass or inflammatory changes occur in a patient without any previously diagnosed lymphoma.

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