CASE REPORT

Unusual breast neoplasm: primary breast lymphoma

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SUMMARY

Primary breast lymphoma (PBL) is a rare clinical entity. The clinical and imaging findings in breast lymphoma can mimic those of breast carcinoma. As a result, the diagnosis of PBL relies on histological evaluation and confirmed by immunohistochemical staining. The treatment of choice of this rare disease is controversial. This case report highlights the diagnosis and management of a 48-year-old woman residing in Iran with PBL.

BACKGROUND

Malignant lymphoma is a neoplasm arising from lymph nodes or lymphoid tissue of other organs such as the intestinal tract. The incidence of non-Hodgkin's lymphoma (NHL) has been increasing in the last decades, and the increase occurred particularly for extranodal lymphomas. Breast lymphoma may be because of secondary involvement by disseminated lymphoma or may represent a primary lesion. Secondary breast involvement by lymphoma should be excluded before a diagnosis of primary breast lymphoma is made. Primary NHL of the breast is a rare disease, representing only 0.12–0.53% of all reported malignant breast tumours.[1] Ferguson[2] suggested that the rarity of primary breast lymphoma (PBL) is related to negligible amount of lymphoid tissue of the breast. Imaging studies are less helpful in the diagnosis of breast lymphomas compared with breast adenocarcinoma and its diagnosis relies on surgical or fine needle aspiration (FNA) biopsy.[3] The therapeutic management of this disease is controversial and is not fully established as yet. In this paper we present a case of PBL.

CASE PRESENTATION

A 48-year-old woman was referred to the surgical ward presenting with a palpable mass in her left breast discovered on breast self-examination. She reported initially discovering the mass approximately 5 months prior to presentation. She denied the presence of previous breast nodules, skin changes and nipple drainage or nipple retraction. The mass was reported to be approximately the size of 60×25 mm when initially discovered and had increased in size over the last several weeks. There was no history of breast trauma. The patient was G5, P4 and did not take exogenous hormones. There was no family history of breast cancer. Reviews of systems were otherwise unremarkable. Physical examination demonstrated symmetric breasts without evidence of breast skin changes or nipple retraction. There were no palpable masses in her right breast and an 80×50 mm mass in the lateral part of her left breast was palpated. The mass was mobile and non-tender to palpation. There were several small lymph nodes of left axillary fossa. Examination of other lymph node basins demonstrated no evidence of lymphadenopathy.

INVESTIGATIONS

Left breast ultrasound demonstrated changes compatible with fibrocystic disease and also a hypoechoic and non-homogeneous mass measuring 75×35 mm in the lateral part of that breast which contained microcalcification. These sonographic findings were highly suspicious for malignancy. There were also eight small lymph nodes with decreased central fat in the left axillary fossa (figure 1). An excisional biopsy was performed to

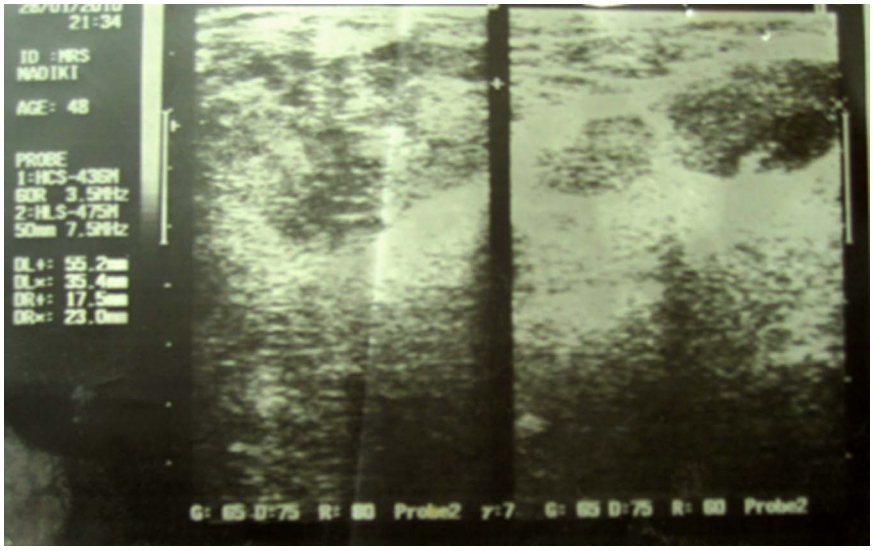

Figure 1 Ultrasound showing a hypoechoic and non-homogeneous mass.

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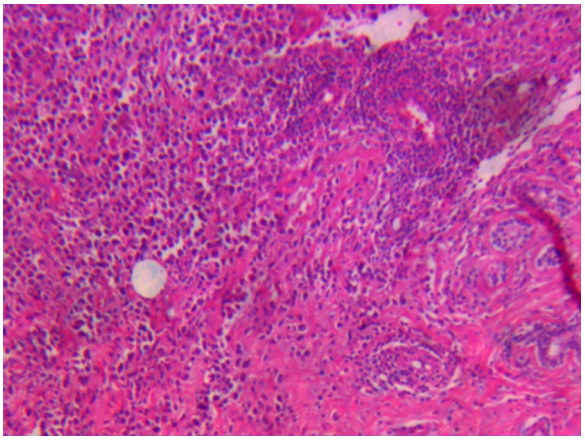

Figure 2 Section showing breast tissue with mononuclear large cell infiltrate with poorly defined cytoplasmic borders, large and prominent nucleoli (H&E ×10).

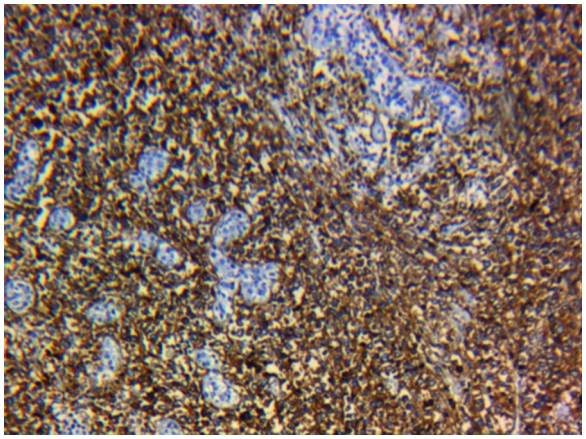

Figure 4 Neoplastic cells revealed positive staining for CD 20 (immunohistochemistry ×10).

confirm the detailed histological classification. Microscopic examination revealed mononuclear large cell infiltrate with poorly defined cytoplasmic borders, large, prominent nucleoli and frequent mitoses (figures 2 and 3). Immunohistochemical staining was positive for CD45 and CD 20. CD3 and pancytokeratin stains were negative (figures 4 and 5). Based on morphology and immunohistochemistry staining, the final diagnosis of diffuse large B-cell lymphoma was made. Investigations to rule out any other site of lymphoma proved it to be primary NHL of the breast.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses of breast lymphoma include pseudolymphoma, medullary carcinoma, amelanotic melanoma, lobular carcinoma and poorly differentiated ductal carcinoma.[4] Immunohistochemistry is helpful in differentiating primary breast lymphoma with others.

TREATMENT

The patient received R-CHOP ×8 (Rituximab (375 mg/m^2, D_1), cyclophosphamide (750 mg/m^2, D_1), doxorubicin (50 mg/m^2, D_1), vincristine (1.4 mg/m^2, D_1), prednisone (50 mg twice a day, D_1–D_5)). She also received intrathecal methotrexate (12.5 mg×4), radiotherapy (4500 cGY) to the breast and regional lymph nodes with 180 cGY daily fractions and brain prophylactic radiotherapy 2500 cGY) with 250 cGY daily fractions.

OUTCOME AND FOLLOW-UP

She is currently well at follow-up 15 months after presentation and without evidence of residual disease (figure 6).

DISCUSSION

PBL is a rare clinical entity representing less than 1% of all breast malignancies.[5] The original criteria for PBL suggested by Wiseman and Liao[6] are as follows:

1. The availability of adequate pathology material.
2. Both mammary tissue and lymphomatous infiltrate are present.
3. No widespread disease or preceding extramammary lymphoma.
4. Ipsilateral axillary node involvement is considered acceptable.

PBL mostly occurs in women. It has a bimodal age distribution with one peak in the middle of the fourth and another in the seventh decade of life.[7] Our patient was a 48-year-old women. Mention should be made that although breast adenocarcinoma occurs more frequently in the left breast, primary breast lymphoma occurs more frequently in the right,[8] it was not true about our patient. Bilateral synchronous breast lymphoma occurs in 10% of patients, and contra lateral metachronous disease occurs

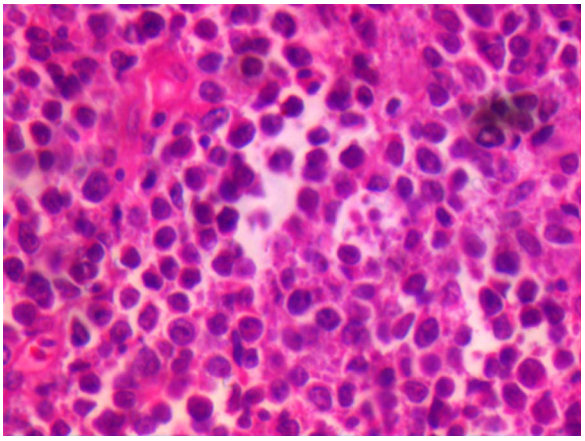

Figure 3 Section showing mononuclear large cell infiltrate with poorly defined cytoplasmic borders, large and prominent nucleoli (H&E ×40).

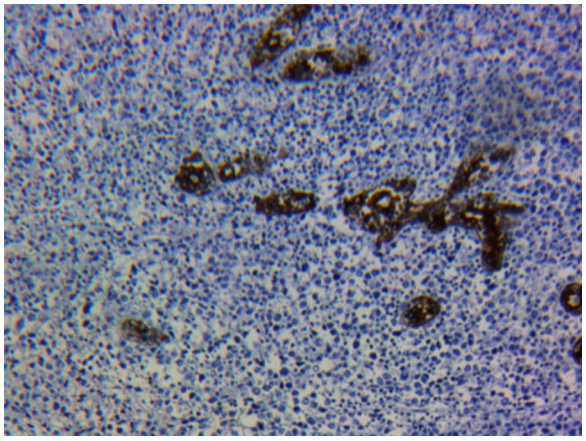

Figure 5 Neoplastic cells revealed negative staining for pancytokeratin (immunohistochemistry ×10).

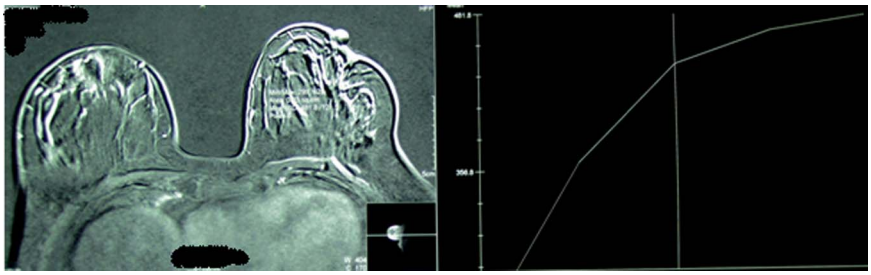

Figure 6 Dynamic contrast-enhanced MRI showing there was no evidence of residual disease.

in up to 15%.[9] The most common presenting symptom is a breast lump which closely mimics breast carcinoma.[10] Nearly one-quarter of masses are painful.[9] Skin fixation and cutaneous inflammatory change are reported and they simulate inflammatory carcinoma.[11] Skin involvement is more common in high-grade lymphoma.[10] Contrary to breast carcinoma, nipple retraction or discharge and skin retraction are not common.[10] In the current case, the patient presented with a firm breast mass. However, clinically it is impossible to differentiate between PBL and carcinoma and as a result the diagnosis is not made before histological examination.[1] It was true in our case. It has been shown that there are no pathognomonic radiological findings for the differential diagnosis between breast lymphoma and carcinoma.[12] In PBL, ultrasound examination reveals a hypoechoic lesion with well-defined borders that lack significant posterior enhancement; these findings are similar to those in this case.[13] In fact the principal role of ultrasound in the diagnosis of PBL is to confirm the presence of a solid mass.[10] Positron emission tomography (PET) is a valid functional imaging technique that provides several inherent advantages over conventional nuclear scintigraphy. This method is used for diagnosis and follow-up of patients with breast lymphoma. There are two major roles of functional scans such as PET in the evaluation of a patient with lymphoma.[14] These functional scans are complementary to anatomic imaging, and may improve staging at the time of diagnosis, particularly through the detection of otherwise occult disease. Unfortunately, this method is not available in Iran, but in these case investigations, to rule out any other site of lymphoma, proved it to be primary non-Hodgkin's lymphoma of the breast. Mention should be made that since the clinical presentation and imaging findings of breast lymphoma and carcinoma are similar, biopsy is the gold standard procedure to establish a diagnosis. FNA cytology is a useful procedure in the diagnosis of PBL. Although its sensitivity is 90%, it has its own limitations. Most authors recommend core needle biopsy as a confirmatory method. Histologically, PBL is predominately of B-cell origin and most commonly large cell type.[11] It was true in the current case. There has been no uniform approach to the treatment of breast lymphoma. Some believe that low-grade lymphoma may be treated with local excision and/or radiation therapy, whereas high-grade lymphoma should be treated with combination therapy with or without external beam radiotherapy.[15] Ablation surgery is not necessary for many of these patients. A study showed that mastectomy alone offered no benefit in the treatment of PBL, and treatment that included chemotherapy and/or radiation therapy provided good results with regard to both the survival and recurrence rates.[16] Thus it is suggested that, if technically feasible, a limited resection of the neoplasm is sufficient and that mastectomy does not change the outcome.[17] On the other hand, Jeanneret-Sozzi[18] reported that chemotherapy has only scant advantages in the local control, and none in terms of overall survival and disease free survival. However, more recently chemotherapy using various agents has been recognised as the preferred treatment. Radiation therapy alone is inadequate in controlling this disease.[19] Radiotherapy may be used as an adjuvant therapy or as a primary local therapy to increase local control.[18–20] Various doses of radiation to the breast, chest wall and regional lymph nodes had been used in previous studies. The range of total doses were between 1200 and 5500 cGY[18 21] and daily doses were between 180 and 300 cGY.[18] Most authors recommend that aggressive forms of PBL should have central nervous system (CNS) prophylaxis even in the early stages.[21] Ribrag *et al*[22] reported that malignant PBL was usually a diffuse pattern and metastasizes to CNS; therefore, the dynamic observation should be strictly followed during the course of treatment for PBL. Chemotherapy drugs given through intrathecal injection can improve the prognosis of patients with PBL [23] and may prevent CNS metastasis. Some scholars even think that the preventive treatment of CNS metastasis should be applied at the beginning of the treatment for all patients with PBL.[24]

Although there are some controversies about likelihood of CNS relapse in different studies from 3% to 50%,[18 21 25 26] we decided to use combination of intratechal metothrexate and cranial radiation therapy for prophylactic CNS management. Some believe that the prognosis in PBLs is related to the cell type and clinical stage, as in lymphomas located elsewhere[9 27] but others suggested that the natural history of primary breast lymphoma is somewhat different from that of the other extranodal NHL and it is related to its rapid progression and worse prognosis. In a case series study reported by Giardini[28] the total five-year survival rate was 43%.The International Prognostic Index predicts 5 year survival based on age, lactate dehydrogenase level, staging, extranodal disease and performance status.[27 29] In conclusion, breast lymphoma must be considered in the differential diagnosis of a breast lump. Diagnosis is dependent on adequate tissue sampling for histology examination and immunophenotyping. It is considered a non-surgical potentially curable disease.

Learning points

- Breast lymphoma must be considered in the differential diagnosis of a breast lump.
- It has been shown that there are no pathognomonic radiological findings for the differential diagnosis between breast lymphoma and carcinoma.
- Nevertheless, imaging is a useful method to monitor a patient's response to therapy.
- It is suggested that if technically feasible a limited resection of the neoplasm is sufficient and that mastectomy does not change the outcome.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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