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Primary breast lymphoma: case reports and review of the literature

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SUMMARY: Primary breast lymphoma: case reports and review of the literature.

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As the prevalence of breast cancer has increased over recent years many cases with unusual presentation are emerging. This review attempts to identify different types of primary malignancies that can affect the breast.

A five years review was undertaken at the Breast Unit of Azienda Ospedaliera "Santa Maria", Terni (Italy). All cases of breast malignancy admitted to the Breast Unit between 2001 and 2005 were reviewed: 750 patients were diagnosed with malignant breast disease. Primary breast lymphoma (was found only in two cases accounting for an incidence of 0,26%. The pre-operative diagnosis was infiltrating carcinoma in both cases and the patients were treated with surgery and systemic chemotherapy; currently they are disease-free.

RIASSUNTO: Linfoma primitivo della mammella: casi clinici e revisione della letteratura.

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Negli ultimi anni, con l'aumento della diagnosi di cancro della mammella, sono emersi numerosi casi di neoplasie primitive con aspetti istologici e manifestazioni cliniche inusuali.

Gli Autori analizzano la casistica di 5 anni dell'Unità di Senologia dell'Azienda Ospedaliera "Santa Maria" di Terni (Italia). Nel suddetto quinquennio sono stati diagnosticati e trattati 750 cancri della mammella; due di questi (0,26%) sono risultati linfomi primitivi della mammella. In entrambi i casi la diagnosi pre-operatoria è stata di carcinoma infiltrante; le pazienti sono state trattate con terapia chirurgica e chemioterapia sistemica. Al momento sono libere da malattia.

KEY WORDS: Breast cancer - Lymphoma - Diagnosis and treatment.
Cancro della mammella - Linfoma - Diagnosi e terapia.

Introduction

Breast cancer is world's most common malignancy among women (1). It is known that the incidence of breast cancer varies in different ethnic groups, higher figures having been reported in North America with lower incidence rate from Lower East and Middle East.

Primary Breast Lymphoma (PBL) is a rare neoplasm that doesn't show inter-racial differences in inci-

dence. In addition, its outcome remains unclear as compared to other lymphomas. The PBL incidence is 0.04% to 0.53% of all primary malignant tumors of the breast and 2.2% of extranodal lymphomas. Most breast lymphomas are diffuse B-cell type. The prognosis in breast PBLs is related to the cell type and clinical stage, as in lymphomas located elsewhere. Differentiation of PBL from other breast tumors is difficult preoperatively, especially by fine-needle aspiration biopsy (FNAB) in which it can resemble breast carcinoma.

We report two cases that were diagnosed as malignant on FNAB and as breast lymphoma on microscopic evaluation of the incisional biopsy specimens. Some Authors claim that PBL may not be rare but occasionally misdiagnosed as anaplastic carcinoma (2, 3).

A high index of clinical suspicion and modern imaging are the key for the correct diagnosis.

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Case reports

Case n. 1

A 75 years old woman presented with a mass in the upper lateral quadrant of the right breast in April 2003. The patient had no past or family history.

On admission, blood chemistry, including serum levels of tumor markers CEA and CA. 15-3, showed no abnormalities except anemia (Hb 8,7 g/dl). An ill-defined, firm and large tumor, measuring 6,8 x 7,3 cm, was recognized in the upper lateral quadrant of the breast; the tumor was fixed to the chest wall. Neither nipple-areola complex discharge nor ipsilateral axillary lymphadenopathy was detected.

An ultrasonography of the right breast revealed an hypoechoic and heterogeneous mass; results of a fine needle aspiration cytology (FNAC) of the mass revealed infiltrating carcinoma.

A right radical mastectomy was performed and the histology of the mass revealed diffuse large B-cell lymphoma according to REAL classification.

The patient received postoperatively six cycles of systemic chemotherapy with CHOP regimen (iv Cyclophosphamide 750 mg/m²; Doxorubicin 50 mg/m²; Vincristine 2 mg; and Prednisone 50 mg orally twice daily). Each cycle was three weeks apart.

The patient showed remarkable tolerance to treatment and presently is disease-free.

Case n. 2

A 49 years old woman came to our institution for a lump that was 2 cm in diameter and located in the upper lateral quadrant of the left breast. The patient had no past medical history or family history.

On admission the lesion was well circumscribed and firm, measuring 2,6 x 1,7 cm. Laboratory tests were normal. A mammogram revealed a tumor shadow without microcalcifications or spiculations; FNAC was positive for class II cells.

Lumpectomy and sentinel node biopsy were carried out and the tumor was diagnosed as malignant lymphoma (stage III E by Ann Arbor staging), extranodal marginal zone B-cell lymphoma (low grade B-cell lymphoma of MALT type) by REAL classification.

This case was classified as a low-intermediate risk disease and the patient underwent, after surgery, six cycles of CHOP regimen (Cyclophosphamide 670 mg/m² d.i.v day 1; ADM 45 mg/m² d.i.v day 1; and Prednisolone 50 mg orally days 1-5).

At the last control the patient was disease-free.

Discussion

Breast cancer is the most common malignancy among women in the world; hormonal, environmental and genetic factors have been shown to play an important role in the pathogenesis of breast malignancies. The incidence of breast cancer varies in the different ethnic groups, and has the higher rate in North America and Europe.

Breast lymphoma, either a manifestation of primary extranodal disease or secondary involvement by systemic disease, is a rare malignancy. Primary breast lymphoma (PBL) has a reported incidence ranging from 0.12% to 0.53% of all breast malignancies. Secondary breast lymphoma had reported incidence of

0.07%, i.e. 17% of all malignancies metastatic to the breast (4). Primary non-Hodgkin lymphoma of the breast should fulfill following criteria: adequate pathological evaluation, with both mammary and lymphomatous infiltrate in closed association and exclusion of either systemic lymphoma or previous extramammary lymphoma. Secondary lymphomas involving the breast are infrequent as well, however they represent the largest group of metastatic tumors to the breast (5-6). The relative frequency of primary versus secondary breast lymphomas is variably reported, therefore the prevalence of one type versus the other is yet unclear.

It is important to determine whether ML of the breast originated in the breast or elsewhere; some Authors, in fact, claim that PBL may be a not so rare disease, mistaken at times for an anaplastic carcinoma, as occurred indeed in one of our cases on the initial biopsy (7-9). Secondary breast involvement should also be considered when a breast mass appears or inflammatory changes occur in a patient previously diagnosed with lymphoma.

Metastasis to the breast is generally uncommon, with a reported incidence of 1,3 – 6,5% of all breast malignancies. Tumours commonly metastasizing to the breast are lymphoma, leukaemia and malignant melanoma.

Breast involvement by lymphoma usually manifests as a painless mass incidentally detected by self examination or clinical exams. The majority of cases are unilateral and B-cell histological lineage as in our cases.

The mammogram often shows a homogeneous faint tumor shadow without either microcalcification or spiculation. Ultrasonography reveals a coarse internal echo, a hypoechoic mass with irregular border and sometimes a lobulated mass representing a huge tumor (10). It is a common opinion that there are not typical imaging characteristics able to distinguish it from other breast masses or neoplasms. This mandates a needle biopsy or an excision biopsy in the primary clinical presentation.

In any case, it is very difficult to distinguish PBL from breast cancer at early stage; often PBL is misdiagnosed because neither excisional biopsy with frozen section nor FNAC is helpful in pathological differentiation (11, 12).

Therapeutic management of PBL is controversial and is not completely established as yet. Some authors report that localized lesions within the breast have a good prognosis by radical surgical intervention alone. However, many others report relapses 10 years after surgery without adjuvant therapy; on the other hand if the lymphoma is diagnosed to be of systemic origin, surgery plus chemotherapy is more effective (13-15).

Prognosis is variable and depends on histological grade and clinical stage. Reported outcomes for PBL in a series after 22,5 months of follow-up showed complete remission in 67% of patients, partial response in 28% and progression of disease in 5%. Bilateral diffuse disease has special predilection for pregnant and lactating women (16, 17).

As far as outcome is concerned, some authors state that PBL has a grim outlook, despite various treatment options, while others believe that prognosis is better than that of a patient with disseminated lymphoma or breast cancer, although survival has been deemed as inversely linked to tumour size (16, 17). Patients who re-

ceived chemotherapy and radiotherapy had a better survival and a lower relapse rate.

Conclusion

In conclusion, despite the increasing prevalence of breast cancer, PBL remains a rare event. A high index of clinical suspicion, supported by modern imaging, is the key in reaching the diagnosis. Currently, extensive histopathology review is ongoing for tissue obtained in the last decade to exclude the possibility of missed PBL cases.

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