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Malignant Lymphomas

Primary non-Hodgkin's lymphoma of the breast: a report of 11 cases

The breast is a rare localization of primary non-Hodgkin's lymphoma. We review our 15 years' experience in 11 patients with primary breast lymphoma. Based on our experience and on literature data we support a management scheme with CHOP or CHOP-like combination chemotherapy followed by involved field radiotherapy.

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Primary breast lymphoma (PBL) is a rare disease and its prognosis and treatment have not been clearly defined. Relatively small cohorts of patients are reported in the literature.[1-4] A retrospective single Institution review was carried out on all lymphoma patients admitted to Cagliari Hematology Unit between January 1st, 1989 through December 31st, 2003 in order to select patients who had Ann-Arbor stage I-II E lymphoma of the breast.

Of 1293 consecutive cases of non-Hodgkin lymphoma, 11 cases (0.85%) fulfilling the Wiseman and Liao criteria for primary breast lymphoma were identified.[5]

The patients' characteristics are detailed in Table 1. The median age at presentation was 65 years (range 33-84 years). Stage was IE in 3 patients and IIE in 8, none presented with bilateral involvement. Histology revealed 8 cases of diffuse large B-cell lymphoma, one case of follicular grade 1 lymphoma and two cases of extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma). None presented with B symptoms. All patients were staged by total body computerized tomography and bone marrow biopsy. Gallium scanning was performed in 4 patients and lymphangiography in one.

Four patients had mastectomy and three a wide excision of the breast lesion (2 quadrantectomy and one tumorectomy); the other patients underwent diagnostic biopsy. Axillary dissection was performed in 2 patients.

Two patients (both with stage IE disease) were treated with surgery alone. The first (case 6) underwent a mastectomy for a clinical diagnosis of ductal carcinoma and, after the correct diagnosis, refused further treatment. The second patient (case 10) received no further treatment because of age and co-morbid conditions. Both patients are alive and free of disease 41 and 9 months, respectively, after diagnosis. Postoperative treatment of all but two patients included CHOP or CHOP-like chemotherapy. In the case with follicular lymphoma, the CHOP chemotherapy was combined with rituximab (CHOP-R). The other treatment schemes are given in Table 1.

Six patients received radiotherapy with the photon beam of a 6MV linear accelerator. The radiation dose delivered ranged from 36 Gy to 50 Gy directed to the breast alone (two cases), axilla alone (one case), breast and regional nodes (three cases). Conventional fractionation (1.8 - 2 Gy, five times a week) was used. All patients achieved a complete response by the end of the therapy. Ten patients are currently alive and free of disease with follow-up ranging from 9 to 123 months (median, 25 months).

Patient 4 was diagnosed as having stage IIE large B-cell PBL when she was 12 weeks pregnant. She refused pregnancy termination and therapy. Delivery was induced at the 35th week. Subsequently, after complete re-staging which confirmed PBL, she was treated with MACOP-B and 50 Gy radiotherapy to the involved field. She achieved a complete remission but systemic relapse occurred 4 months later and she subsequently died of progressive disease.

PBL is a rare, potentially curable, disease and has been considered a distinct clinicopathologic entity.[6]

The prognosis, as reported in the literature, varies as do the applied treatment modalities, which include surgery, radiotherapy and chemotherapy used alone or in combination. Mastectomy or wide excision, used in seven of our patients is no longer indicated and can be avoided.[7] Radiotherapy has been advocated by many authors as the first-line treatment for stage I disease;[8] the efficacy of this management in terms of local control was confirmed in our series since no patients treated with 36-50 Gy radiotherapy relapsed locally or in the regional nodes.

With a follow-up ranging from 9 to 130 months, ten out of eleven of our patients are alive and free of disease. Nine of them received anthracycline-based chemotherapy followed by radiotherapy in six.

Distant recurrence is reported to be a significant problem for patients with PBL with a high incidence of central nervous system relapses after CHOP or CHOP-like regimens in patients with aggressive lymphoma.[1,9] Our study shows that favorable results can be obtained in well-staged primary breast lymphoma using anthracycline-based chemotherapy combined with local-regional radiotherapy. On the basis of our experience and literature data we treat PBL with 3-6 cycles of the CHOP (or CHOP-like) scheme according to the IPI score (3 cycles with an IPI score of nil); rituximab is added in cases of CD20 positive lymphomas. Our good results without any central nervous system prophylaxis in patients without risk factors suggest that central nervous system prophylaxis is not necessary in all patients with primary breast lymphoma.

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Table 1. Patients' characteristics.

Case No.	Age/ sex	Ann Arbor	Site/size, cm	Path	IPI	Clinical informations	Surgery	Radiotherapy	Chemotherapy	Response	Follow-up
1	52/F	IIAE	L/4	MALT	0	palpable mass, axillary nodes	quadrantectomy + axillary dissection	no	CHOP× 7	CR	AW+84 mo.
2	68/F	IIAE	L/3	DLCL	1	palpable mass, axillary nodes	mastectomy	axilla and supraclavicular fossa 44 Gy/22 fr	ACOP-B	CR	AW+42 mo.
3	44/M	IIAE	L/2	DLCL	N/A	palpable mass, axillary nodes	tumorectomy	breast, axilla and supraclavicular fossa 36 Gy/22	ACOP-B	CR	AW+123 mo.
4	38/F	IIAE	L/12	DLCL	1	palpable mass, pregnant	biospy	breast, axilla, supraclavicular fossa 50 Gy/25 fr	MACOP-B	CR	relapse after 6 months. Dead at 20 months
5	33/F	IIAE	R/15	DLCL	2	palpable mass, axillary and supraclavicular nodes	biospy	breast, axilla, supraclavicular fossa 36 Gy/18 fr	MEGACEOP	CR	AW+66 mo.
6	76/F	IAE	L/4	DLCL	2	palpable mass	mastectomy	no	No	CR	AW + 41 mo.
7	66/F	IIAE	L/2	Follicular	1	palpable mass, axillary nodes	quadrantectomy + axillary lymphadenectomy	no	R-CHOP×6	CR	AW + 25 mo.
8	65/F	IIAE	L/8	DLCL	1	palpable mass,	mastectomy	no	CHOP×6	CR	AW + 19 mo.
9	33/F	IIAE	R/8	DLCL	1	palpable mass, axillary and supraclavicular nodes	biopsy	breast 46 Gy/ 23 fr	CHOP×6	CR	AW + 21 mo.
10	84/F	IAE	R/5	MALT	1	palpable mass	mastectomy	no	No	CR	AW + 9 mo.
11	72/F	IAE	L/3	DLCL	0	palpable mass	biopsy	breast 36 Gy/18 fr.	CHOP×6	CR	AW + 11 mo.

F: female; M: male; L: left; R: right; DLCL: diffuse large cell lymphoma; IPI: International Prognostic Index; N/A: data not available; AW: alive and well; fr: fraction size; CR: complete remission; CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone; ACOP-B: doxorubicin, cyclophosphamide, vincristine, prednisone, bleomycin; MACOP -B: methotrexate, doxorubicin, cyclophosphamide, vincristine, prednisone, bleomycin; MEGA-CEOP: cyclophosphamide, epidoxorubicin, vincristine, prednisone; R: rituximab.

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Maria Giuseppina Cabras, Maurizio Amichetti, Michele Nagliati,* Paola Orrù,* Angela Maria Mamusa, Emanuele Angelucci*

*Department of Haematology, Department of *Radiation Oncology "Armando Businco" Oncological Hospital, Cagliari, Italy*

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Correspondence: Emanuele Angelucci, MD, Unità Operativa Ematologia e Centro Trapianto Cellule Staminali Emopoietiche, Ospedale Oncologico Armando Businco, 09121 Cagliari, Italy. Phone: international +39. 070.6095312. Fax. international +39.070.6095312. E-mail: emnang@tin.it

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