LETTER TO THE EDITOR

WHO reclassification of breast lymphomas

M B Loughrey, P Windrum, M A Catherwood, H D Alexander, G M Markey, D T McManus, T C M Morris

J Clin Pathol 2004;57:1213–1214. doi: 10.1136/jcp.2004.018994

Fourteen cases of breast lymphoma, identified from hospital records between 1990 and 2004, were reclassified according to the World Health Organisation criteria. Primary cases occurred more frequently and all cases were of B cell origin, predominantly involving the right breast. Most primary cases were diffuse large B cell lymphomas, whereas secondary cases were heterogeneous in type and most had a poor prognosis.

Primary breast lymphoma accounts for approximately 2% of extranodal non-Hodgkin lymphoma (NHL).¹ NHL is the most common secondary tumour of the breast, with a reported incidence similar to primary breast NHL.¹ Breast lymphomas are usually of B cell lineage and are more commonly right sided.¹ Our present study reclassified previously diagnosed cases using World Health Organisation (WHO) criteria and compared the features of primary and secondary tumours.

METHODS/RESULTS

Fourteen cases were identified between 1990 and 2004 (13 women, one man; median age, 71 years; age range, 53–88). The immunohistochemical panel comprised antibodies to CD45, CD3, CD20, CD5, CD10, CD23, CD30, cyclin D1, and Ki-67. In 11 cases, DNA was extracted and the t(11;14) and t(14;18) translocations were looked for using a seminested polymerase chain reaction (PCR).^{2,3}

Nine cases met the criteria of Wiseman and Liao⁴ for primary breast lymphoma, and nine involved the right breast (table 1). All cases were of B cell lineage. Six of the primary cases were classified as diffuse large B cell lymphoma (DLBCL), one as follicular lymphoma (FCL), one as marginal zone lymphoma, and the remaining case was unclassified because of poor tissue preservation. Three of the nine patients died with active disease at a median time of 18 months (range, 5–83 months) after diagnosis. The fourth patient who relapsed has undergone peripheral blood stem cell transplantation. One patient had no evidence of further disease at 34 months; of the two patients diagnosed recently, one is undergoing treatment with fludarabine and cyclophosphamide and the other has not yet started treatment. In addition, two other patients died of unrelated disease at 13 and 30 months. Two of the four patients who relapsed developed central nervous system (CNS) involvement.

Of five patients with secondary disease, three presented with synchronous disease elsewhere (case 11, bone marrow involvement; case 13, generalised lymphadenopathy; and case 14, intranasal disease). The other two patients had known extramammary lymphoma presenting some months before breast involvement. The secondary lymphoma cases included one FCL, one mantle cell lymphoma (MCL), one DLBCL, and one small lymphocytic lymphoma. The remaining case was classified as B cell lymphoma, not otherwise

specified as a result of crush artefact in the core biopsy. In the patient with secondary FCL, the diagnosis of nodal FCL was made earlier on a cervical node biopsy. The patient with MCL presented with a breast mass and had synchronous bone marrow involvement. The t(11;14) translocation was confirmed by PCR.⁴ In all other cases tested, PCR for t(11;14) and t(14;18) was negative. The patient with small lymphocytic lymphoma presented with a breast mass but on examination had generalised lymphadenopathy. Four of the five patients with secondary breast lymphoma died with active disease (median survival, 12.5 months; range, 4–30). At 25 months follow up, the patient with MCL had evidence of residual bone marrow involvement after peripheral blood stem cell transplantation, but remains well at 51 months.

DISCUSSION

In keeping with previous series, the most common primary breast lymphoma was DLBCL.¹ Interestingly, three of the nine primary lymphomas showed lymphoepithelial lesions but did not show the characteristic polymorphous lymphoid population of mucosa associated lymphoid tissue lymphoma.⁵ All were classified as DLBCL. Two of the four cases of relapsed primary breast lymphoma had CNS involvement, suggesting that CNS prophylaxis should be considered along with systemic chemotherapy as primary treatment.

Survival was poor in most cases of secondary breast lymphoma, as expected given their advanced stage. Various therapeutic regimens were used but no definitive conclusions can be made on the best treatment options. Immunohistochemistry and molecular techniques may be necessary for the identification of WHO NHL subtypes, including MCL or FCL, which may involve the breast secondarily.

ACKNOWLEDGEMENTS

We would like to thank Mrs H Foster for her technical assistance with immunohistochemistry.

Authors' affiliations

M B Loughrey, D T McManus, Department of Pathology, Belfast City Hospital, Belfast BT9 7AB, Northern Ireland, UK

P Windrum, M A Catherwood, H D Alexander, G M Markey, T C M Morris, Department of Haematology, Belfast City Hospital

Correspondence to: Dr P Windrum, Department of Haematology, C Floor, Belfast City Hospital, Lisburn Rd, Belfast BT9 7AB, Northern Ireland, UK; philip@pwindrum.freeserve.co.uk

Accepted for publication 1 June 2004

Abbreviations: CNS, central nervous system; DLBCL, diffuse large B cell lymphoma; FCL, follicular lymphoma; MCL, mantle cell lymphoma; NHL, non-Hodgkin lymphoma; PCR, polymerase chain reaction; WHO, World Health Organisation

Table 1 Summary of patients with breast lymphoma

Patient	Age	1°/2°	Side	Size (cm)	Biopsy	WHO type	Treatment	Survival (months)	Remission status/ cause of death
1	75	1°	Right	2.5	E	DLBCL	E	13	UD
2	83	1°	Right	8	E	DLBCL*	E	5	NHL
3	61	1°	Right	5	E	DLBCL	E+CHOP	83	NHL
4	88	1°	Left	3	E	BCL NOS	E+P	30	UD
5	67†	1°	Right	6	C	DLBCL*	CHOP, It Mtx, CNS XRT	18	NHL
6	66	1°	Left	4	E	DLBCL	CHOP, XRT	34+	CR
7	62	1°	Right	3.5	E	DLBCL	E+CHOP, R+CHOP, APBSCT	36+	CR
8	71	1°	Right	2 1.5	E	FCL	E+FC	12+	CR
9	73	1°	Right	1.8	E	MZL	ND	ND	ND
10‡	59	2°	Right	1.5	E	FCL (III)	E, CI, CHOP APBSCT	30	NHL
11	53	2°	Right	4	C	MCL (IV)	CHOP, APBSCT	51+	MRD
12	75	2°	Left	5	C	DLBCL (IV)	R+P	12	NHL
13	86	2°	Right	1	E	SLL	None	13	NHL
14	78	2°	Left	6	C	BCL NOS (IV)	CVP	4	NHL

*CNS involvement at relapse; †male patient; ‡insufficient material for immunohaematology/genetics.

1°, primary; 2°, secondary; APBSCT, autologous peripheral blood stem cell transplant; BCL NOS, B cell lymphoma not otherwise specified; C, core; CHOP, cyclophosphamide/adriamycin/vincristine/prednisolone; CI, chlorambucil; CNS, central nervous system; CR, complete remission; CVP, cyclophosphamide/vincristine/prednisolone; DLBCL, diffuse large B cell lymphoma; E, excision; FC, fludarabine/cyclophosphamide; FCL, follicular cell lymphoma; It Mtx, intrathecal methotrexate; MCL, mantle cell lymphoma; MRD, minimal residual disease; MZL, marginal zone lymphoma; NHL, non-Hodgkin lymphoma; P, prednisolone; SLL, small lymphocytic lymphoma; WHO, World Health Organisation; XRT, radiotherapy.

REFERENCES

- 1 Topalovski M, Crisan D, Mattson JC. Lymphoma of the breast: a clinicopathologic study of primary and secondary cases. *Arch Pathol Lab Med* 1999;**123**:1208–18.
- 2 McCluggage WG, Catherwood MA, Alexander HD, et al. Immunohistochemical expression of CD10 and t(14;18) chromosomal translocation may be indicators of follicle centre cell origin in nodal diffuse large B-cell lymphoma. *Histopathology* 2002;**41**:414–20.
- 3 Windrum P, Morris TCM, Catherwood MA, et al. Mantle cell lymphoma presenting as a breast mass. *J Clin Pathol* 2001;**54**:88.
- 4 Wiseman C, Liao KT. Primary lymphoma of the breast. *Cancer* 1972;**29**:1705–12.
- 5 Mattia AR, Ferry JA, Harris NL. Breast lymphoma. A B-cell spectrum including the low grade B-cell lymphoma of mucosa associated lymphoid tissue. *Am J Surg Pathol* 1993;**17**:574–8.