Clinics in Oncology

Case Report
Published: 17 May, 2016

Primary Manifestation of Marginal Zone Lymphoma in the Breast

*Gloustianou G[1], Lakiotaki E[1], Riccioni O[1,2] and Lazaris AC[1]**

[1]Department of Pathology, School of Medicine, The National and Kapodistrian University of Athens, Greece

[2]School of Medicine, La Sapienza University of Rome, Italy

Abstract

Primary breast lymphoma is a rare disease. Marginal zone lymphoma is a kind of low grade mature B cell lymphoma that arises mostly in Mucosa-Associated Lymphoid Tissue, or, less commonly, in non-mucosal sites. Its primary manifestation in the breast, as we report in this article, is an exceedingly rare entity.

We report the case of a 50-year-old female, presented with the complaint of painless palpable mass in the right breast. Mammogram revealed a lesion suspicious of breast carcinoma. An open biopsy was performed and then, immunohistochemistry was carried out. The diagnosis of primary breast marginal zone lymphoma was achieved by a combination of clinical, morphological, cytogenetic and, above all, immunehistochemical findings.

Neoplasms can rarely arise in unusual sites, as the primary breast marginal zone lymphoma of our case report. This awareness is a prerequisite to achieve the correct diagnosis.

Background

Breast cancer is among the most common tumors in women, both in developing and in developed areas [1,2]. Lesions are usually of epithelial or stromal origin. Primary breast lymphoma is a rare disease [3,4]. It accounts for 0.04-0.5% of all breast malignancies, 0.38-0.7% of all lymphomas, and 1.7-2.2% of all extra nodal lymphomas [5,6]. In particular, Extra nodal Marginal Zone Lymphoma (ENMZL), which is a special category of mature B cell lymphomas, arises most frequently in mucosa-associated lymphoid tissue. Its primary manifestation in the breast is an exceedingly rare entity [7].

Case Report

We report the case of a 50-year-old female, presenting with the complaint of painless palpable mass in the right breast. Both her personal and familial medical history were unremarkable. Physical examination revealed a hard lump in the lower outer quadrant of the right breast, close to the axilla; left breast was normal. A lesion measuring 1,2cm was mammographic ally detected. She subsequently underwent an open biopsy and the lesion was totally resected.

The histology examination showed an atypical pattern, suspicious for a low-grade mature B-cell non-Hodgkin's lymphoma. A polymorphous population made of small-medium size, irregular cells with nuclear atypia were noticed. The majority of these cells showed dispersed chromatin, and inconspicuous nucleoli, resembling centrocytes.

Immunohistochemistry confirmed the predominance of B cells which were CD20+, CD45+, CD23+, CD5-, CD10-, Bcl6-, and CyclinD1-. This leaded to the diagnosis of MZL. Diffuse intense membranous positivity for CD20 (Figure 1) confirmed B lineage. Staining for CD43 presented faint membranous positivity in a small number of B cells, as opposed to the strong staining of T cells (Figure 2), while staining for CD5 was negative in all B cells. With regard to CD23, membranous and cytoplasmic positivity in B cells were revealed (Figure 3). These outcomes led us to a diagnosis of breast MZL, despite the positivity for CD23, which is a rare finding in this subtype of neoplasm.

The diagnosis was unlooked for a breast lump, since this is not a common location for the diagnosed lymphoma. Afterwards, a closer inspection of regional lymph nodes revealed their involvement.

Discussion

The WHO classification distinguished three subtypes of MZL: Nodal, Splenic, and Extranodal

OPEN ACCESS

Correspondence:
Andreas C. Lazaris, The National and Kapodistrian University of Athens, Greece;
E-mail: alazaris@med.uoa.gr

Received Date: *21 Apr 2016*
Accepted Date: *11 May 2016*
Published Date: *17 May 2016*

Citation:
Gloustianou G, Lakiotaki E, Riccioni O, Lazaris AC. Primary Manifestation of Marginal Zone Lymphoma in the Breast. Clin Oncol. 2016; 1: 1006.

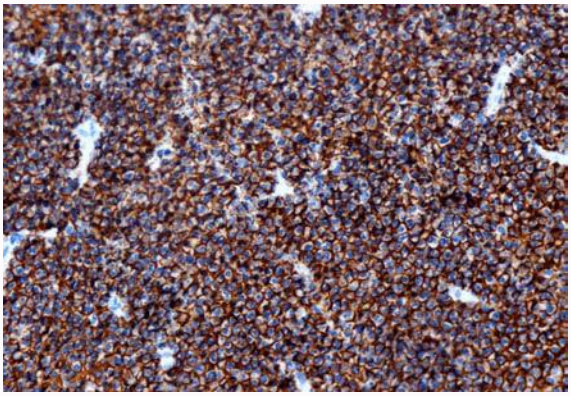

Figure 1: Diffuse intense membranous immunopositivity for CD20 indicating B lineage in a primary breast Marginal Zone Lymphoma. Immunohistochemistry for CD20, X100.

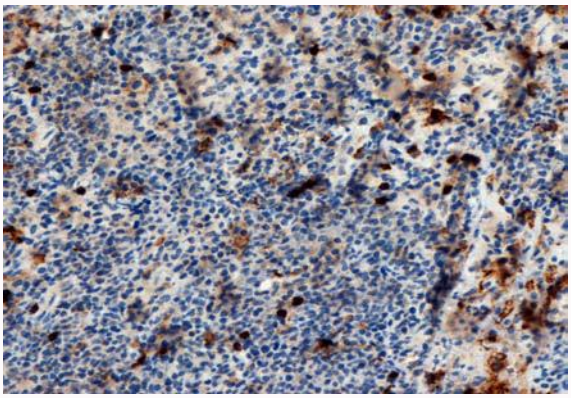

Figure 2: Primary breast Marginal Zone Lymphoma. Faint membranous CD43 positivity in a small number of B cells, as opposed to the strong staining of T cells. Immunohistochemistry for CD43, X100.

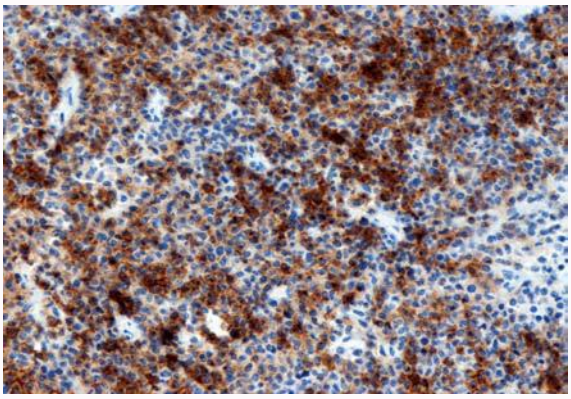

Figure 3: Primary breast Marginal Zone Lymphoma with B cell membranous and cytoplasmic positivity for CD23. Immunohistochemistry for CD23, X100.

MZL (NMZL, SMZL and ENMZL) [8]. The latter defines a kind of low grade mature B cell malignancies that arise mostly in the Mucosa-Associated Lymphoid Tissue (MALT), whose most common site of involvement is the gastrointestinal tract [7] or, less frequently, in non-mucosal sites. Primary MZL of the breast is not a common entity [7].

It is important to distinguish ENMZL from other MZLs, as well as from other subtypes of mature small B-cell lymphomas, since these subsets present different clinical behaviors, treatment and prognosis. In addition to NMZL, ENMZL and SMZL, small

Table 1: Immunophenotype in the differential diagnosis of small B cell lymphomas.

	MZL*	MCL†	CLL/SLL‡	LPL§	FL‖
CD20	+	+	+	+	+
CD5	-	+	+	-	-
CD10	-	-	-	-	+
CD23	-	-	+	-	+/-
CD43	+/-	+	+	+/-	-
Cyclin D1	-	+	-	-	-
Bcl2	+	+	+	+	+
Bcl6	-	-	-	-	+

*__Marginal Zone Lymphoma__. †Mantle Cell Lymphoma ‡Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. §Lymphoplasmacytic Lymphoma. || Follicular Lymphoma.

B cell category includes Mantle Cell Lymphoma (MCL), Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL), Lymphoplasmacytic Lymphoma (LPL), and Follicular Lymphoma (FL).

Even though these lymphomas share some basic features that make them join the same category, they are distinct entities with several biologic and clinical differences [9]. The combination of morphological and immune phenotypic evaluation can allow the correct diagnosis and classification of these subsets [10]. Immunohistochemistry plays a key role in the differential diagnosis: at present, with a panel of antibodies, most cases can be categorized (Table 1). CD20 (or other B cell markers, such as CD19, PAX-5, CD79a and CD79b) indicates B cell lineage, and is expressed on the great majority of mature B-cell lymphomas. Other markers are useful in differentiating a specific small B-cell lymphoid neoplasm from others, i.e. CD5 and CD23 co-expression distinguishes CLL/SLL, and positive nuclear staining of cyclin D1 is specific for MCL, as well as CD10 is for FL [11-13]. With regard to the distinguishing immunophenotypic pattern of MZL, CD20 shows a characteristic intense positivity, CD5 and CD10 are not expressed, CD23 is rarely positive (8%) and CD43 is variable (35%) [9,14,15]. Nowadays, also cytogenetics is a useful tool for the diagnosis of some lymphomas, according to the presence of a characteristic cytogenetic pattern in the specific disorder [16]. In some Neoplasms, consistent cytogenetic abnormalities have not been identified yet, while in others the identification of a specific pattern is of main importance in the diagnosis, as it is the 11;14 translocation for MCL [16]. With regard to MZLs, some recurrent chromosomal translocation have been described. The most characterized of them include t(11;18)(q21;q21), t(1;14)(p22;q32), and t(14;18)(q32;q21) [17-19]. Trisomy 3 and trisomy 18 have also been reported [18,19].

Despite the advantage in classification, sometimes it is not easy to make the definitive diagnosis ascribing a low grade lymphoma to a precise subtype [20]. In the past, MZL and the extranodal variant in particular were probably the most under-diagnosed mature B cell neoplasms [11]. Still today several issues regarding low grade lymphomas remain to be well-defined. The relative rarity of these neoplasms is not helpful and the primary breast manifestation of a lymphoma, especially MZL, is a rare entity [3-5,7].

Conclusion

With regard to breast tumors, not all lesions are of epithelial or stromal origin, although these are the most common tumor types; other kinds of neoplasms can occur on the breast, such as the ENMZL of our case report. Treatment and prognosis may change according to

the neoplasm subtype, thus it is important to make the most precise diagnosis as possible. The correct classification of different subsets depends on the integration of clinical, morphological, cytogenetic and, above all, immunohistochemical findings, as well as on the pathologist's awareness that neoplasms can rarely arise in unusual site. The rarity of some tumors requires the collaboration of clinicians and pathologists in defining stringent diagnostic criteria; it would be helpful for the pathologists to share their professional experiences.

We start with the report of a rare case. The idea of conducting epidemiological surveys to design diagnostic criteria and clinical features of rare neoplasms subtypes, is the challenge.

References

1. Bray F, McCarron P, Parkin DM. The changing global patterns of female breast cancer incidence and mortality. Breast Cancer Res. 2004; 6: 229-239
2. Parkin DM, Bray F, Ferlay J, Pisani P. Estimating the world cancer burden: Globocan 2000. Int J Cancer. 2001; 94: 153-156.
3. Martinelli G, Ryan G, Seymour JF, Nassi L, Steffanoni S, Alietti A, et al. Primary follicular and marginal-zone lymphoma of the breast: clinical features, prognostic factors and outcome: a study by the International Extranodal Lymphoma Study Group. Ann Oncol. 2009; 20: 1993-1999.
4. Raghavan D, Blanke C, Johnson DH, Moots PL, Reaman GH, Rose PG, et al. 4th ed. Textbook of Uncommon Cancer. Hoboken: John Wiley & Sons; 2012. p225-277.
5. Palazzo JP. Difficult Diagnoses in Breast Pathology. USA: Demos Medical Publishing; 2011; p196-242.
6. Rock K, Rangaswamy G, O'Sullivan S, Coffey J. An Unusual Case of Marginal Zone B-Cell Lymphoma Arising in the Breast - Its Diagnosis and the Role of Radiotherapy in its Management. Breast Care (Basel). 2011; 6: 391-393.
7. Kambouchner M, Godmer P, Guillevin L, Raphaël M, Droz D, Martin A. Low grade marginal zone B cell lymphoma of the breast associated with localised amyloidosis and corpora amylacea in a woman with long standing primary Sjögren's syndrome. J Clin Pathol. 2003; 56: 74-77.
8. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon: IARC; 2008.
9. His ED. Hematopathology: A Volume in the Series: Foundations in Diagnostic Pathology. 2nd ed. Elsevier; 2012. p203-384.
10. Jaffe ES, Banks PM, Nathwani B, Said J, Swerdlow SH. Recommendations for the reporting of lymphoid neoplasms: a report from the Association of Directors of Anatomic and Surgical Pathology. The Ad Hoc Committee on reporting of lymphoid neoplasms. Hum Pathol. 2002; 33: 1064-1068.
11. Rizzo K, Nassiri M. Diagnostic Workup of Small B Cell Lymphomas: A Laboratory Perspective. Lymphoma. 2012.
12. Kilo MB, Dorfman DM. The utility of flow cytometric immunophenotypic analysis in the distinction of small lymphocytic lymphoma/chronic lymphocytic leukemia from mantle cell lymphoma. Am J Clin Pathol. 1996; 105: 451-457.
13. Coelho Siqueira SA, Ferreira Alves VA, Beitler B, Otta MM, Nascimento Saldiva PH. Contribution of immunohistochemistry to small B-cell lymphoma classification. Appl Immunohistochem Mol Morphol. 2006; 14: 1-6.
14. Extra nodal marginal zone lymphoma of breast and stomach. University Pathologists. 2011.
15. Extranodal Marginal Zone B Cell Lymphoma. Differential Diagnosis, Stanford Medicine. 2006.
16. Campbell LJ. Cytogenetics of lymphomas. Pathology. 2005; 37: 493-507.
17. Armitage JO, Coiffier B, Dalla-Favera R, Harris NL. Non-Hodgkin Lymphomas. 2nd ed. Lippincott Williams & Wilkins; 2009; P232-251.
18. Dierlamm J, Wlodarska I, Michaux L, Stefanova M, Hinz K, Van Den Berghe H, et al. Genetic abnormalities in marginal zone B-cell lymphoma. Hematol Oncol. 2000; 18: 1-13.
19. Cuneo A, Castoldi GL. Marginal zone B-cell lymphoma. Atlas Genet Cytogenet Oncol Haematol. 2006; 10: 180-183.
20. Thieblemont C. Clinical presentation and management of marginal zone lymphomas. Hematology Am Soc Hematol Educ Program. 2005; 307-313.