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## Marginal zone lymphoma with central nervous system spread – A case report

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### Abstract

Parenchymal central nervous system (CNS) presentation or spread of marginal zone lymphoma (MZL) is a rare event. We report a case of 55-year old patient who presented initially with a MZL of the right breast with widespread lymphadenopathy that responded well to immune-chemotherapy, who subsequently relapsed approximately 18 months later with a solitary CNS parenchymal lesion. We review the literature of both breast and CNS presentation of lymphomas.

### 1. Introduction

Marginal zone lymphoma (MZL) is an indolent lymphoma of B-lymphocytes normally found in the marginal zone of the secondary lymphoid follicles in the spleen and lymph nodes. It accounts for approximately 12% of B cell non-Hodgkin lymphomas (1), and encompasses three basic types sharing some common phenotypic and genetic characteristics; 1) extranodal or mucosa-associated lymphoid tissue (MALT) occurring outside the lymph nodes; 2) nodal, occurring within the lymph nodes; 3) splenic, occurring mostly in the spleen and blood. Skin-associated lymphoid-tissue-related B-cell lymphoma (SALT) is also considered a form of MALT lymphoma (1).

Although the extranodal variety (EMZL) is the most common entity, accounting for approximately 70% of all MZLs, involvement of the central nervous system is rare. We report here a patient with EMZL who was in complete remission following aggressive chemotherapy, only to relapse solely within the CNS 18 months later.

### 2. Case Report

The patient, a 55 year old female of Indian ethnicity, presented with a swollen, painful right breast and painless axillary lymph nodes for six weeks. Tru-cut<sup>(R)</sup> biopsy of the right breast revealed breast tissue infiltrated by neoplastic lymphoid cells, which had irregular vesicular nuclei with inconspicuous nucleoli. Immunohistochemical stains were positive for CD20 and DCL2 and negative for CD3, CD5, cyclin D1, CD15, CD23, CD10 and CD43, consistent with marginal zone B cell lymphoma. On computerized tomography (CT) scan, there was a large homogenous enhancing soft tissue mass noted in the right breast which measured 13.7 x 6.9 x 13cm. Another large well-defined soft tissue mass was noted at anterior aspect of the right chest wall, which infiltrated the thoracic cavity, compressing the right upper lobe and displacing

mediastinal structures. Multiple right axillary nodes noted, the largest 4.6 x 3.7cm, multiple right pleural nodules, largest 5.4 x 1.7cm and a large right pleural effusion. There were also enlarged mediastinal nodes noted in the right paratracheal area measuring 1.9 x 1.4 cm, enlarged right hilar node measuring 2.7 x 2.3cm, enlarged right supraclavicular node measuring 4.8 x 3.2cm. She was symptomatic having lost more than 10% of body mass during the past six months

She was staged as IVB (extranodal, symptomatic) and received six cycles of tri-weekly rituximab (375mg/m<sup>2</sup>), cyclophosphamide (600 mg/m<sup>2</sup>) vincristine (2.0 mg total dose), prednisone (60 mg/m<sup>2</sup>) (R-COP). She lost substantial weight during therapy. Positron Emission Tomography (PET scan) after completion of the therapy showed no evidence of FDG acid active lymphomatous disease and she was judged to be in complete remission. She subsequently regained her weight over time.

Approximately 18 months following the therapy, she developed sudden onset right sided weakness causing her to fall while showering. There was no accompanying headache, nausea, visual disturbance, seizure, etc. She was seen to have right upper and lower limb weakness. No peripheral adenopathy was appreciated on examination, but a non contrast and contrast CT scan revealed a large, hyperdense, left temporal mass, 3.2 x 3.5 cm, with perilesional edema, mild midline shift and mild compression of the left ventricle (Figure 1). Complete blood count, electrolytes, liver function tests, lactic dehydrogenase, renal function tests, coagulation studies, sedimentation rate, C reactive protein, bone marrow aspiration/biopsy were all normal and CT scans of neck, chest, abdomen and pelvis showed no evidence of recurrent lymphoma. A biopsy of the cerebral lesion revealed infiltrating neoplastic lymphoid cells, predominantly showing small to medium size in an angiocentric pattern with slightly basophilic nuclei, scanty cytoplasm and monocytic appearance; numerous apoptosis with glial tissue seen. The neoplastic lymphoid cells were positive for CD20, CD79a, and CD 43, and negative for CD3, CD5, CD10, CD21, CD23, and cyclin D1, consistent with non-Hodgkin marginal zone lymphoma.



**Figure 1.** CT scan showing right temporal lesion with MZL lesion.

The patient was treated with a high dose methotrexate and leucovorin rescue containing protocol (Appendix 1) with response and received two full courses of this regimen. Post-chemotherapy, the muscle power in her right upper and lower extremity improved. Follow-up CT scan of brain, neck, thorax, abdomen and pelvis showed a resolved left parietal lesion, and no peripheral lymphadenopathy. She has done well until the present time.

### 3. Discussion

Cerebral involvement of marginal zone lymphoma (C-MZL) is generally a rare disorder with primary C-MZL accounting for only 0.1% to 1% of all non-Hodgkin's lymphoma (2, 3). Prognosis is usually very poor when patients with non-Hodgkin lymphoma develop CNS involvement during or after first-line treatment (4-9). Most cases of C-MZL have been of dural involvement (10-18), with very few in the literature actually involving the brain parenchyma. Some presented as primary CNS disease without involvement elsewhere and only very few secondary to MZL, an otherwise indolent form of lymphoma. Interestingly, a majority of the reported cases have been female (11-17).

Our case actually presented initially similar to an aggressive breast cancer case. One of the reported cases presented in like fashion, but apparently had an inflammatory breast cancer and later presented with MZL in the brain, but of a dural spread unlike our patient who had parenchymal involvement (18).

Breast lymphoma is a rare disease, either as primary or secondary, representing 0.04%-0.5% of malignant breast tumours (19). The most frequent histopathologic types being diffuse large B-cell lymphoma which accounts for up to 50% of all primary breast lymphoma (PBL), follicular lymphoma 15%, MALT lymphoma 12.2% and Burkitt's lymphoma 10.3%. Other rare types are other forms of MZL, small lymphocytic lymphoma and anaplastic large cell lymphoma (20). However, secondary involvement beyond the breast in patients with diffuse disease is more common (21). One case was reported of an asymptomatic low grade MZL of breast associated with lobular ductal amyloidosis in a patient with long standing primary Sjögren's syndrome (32).

The majority of breast lymphomas present as a unilateral painless breast mass in older women (average age at diagnosis 55 to 60), almost always of B cell type (22,23). For unknown reasons, the right breast is involved more often than the left. Ipsilateral axillary lymphadenopathy is present in 30 to 40 percent of cases (24,25,26). A less common but distinctive presentation is that of a young woman of childbearing age who presents during or immediately after pregnancy (24,27). Disease is often bilateral and may clinically mimics inflammatory breast cancer (27,29). Most of these women have highly aggressive lymphoma, often Burkitt's lymphoma. In a patient presenting with a rapidly growing breast tumour,

lymphoma should be considered before any surgical intervention is performed (28). Early diagnosis and treatment is crucial considering its aggressive nature.

Survival rates reported in PBL varied widely. Some authors have reported 5 year survival rates up to 80% and 50% in stages I and II, respectively (33). Others have reported PBL to have a poor prognosis irrespective of treatment with median survival time as low as 12 months (34,35). The underlying prognosis of the lymphoma rather than its breast location is probably the determining prognostic factor. Local control is excellent with radiotherapy or combined modality treatment. However, systemic relapses including CNS still commonly occur (36, 37). Our patient had undergone six cycles of R-COP regime, achieved complete peripheral remission and then presented with sudden onset right sided body weakness, which proved to be relapsed non-Hodgkin MZL. The large size of the CNS lesion at diagnosis, and the fact that this was a slow growing lesion, most likely indicate the lesion had been present for most of the 18 months; that it took for the lesion to become manifest.

In a study conducted among 2514 patients with non-Hodgkin lymphoma (NHL), the incidence of CNS relapse in patients with low grade NHL was 2.8%, while high grade NHL was 4.3%, and lymphoblastic or Burkitt's lymphoma was 24.4% at 5 years (38). Why some lymphoma spread to brain is not clear but it is postulated that lymphoma cells circulate in the vasculature of the CNS, and due to blood-brain barrier, escape the effects of peripheral chemotherapy to finally present as CNS disease. The time lapse in our case, the slow growth of MZL and the sizeable lesion in the CNS would be consistent with this hypothesis.

This is a case of a rare secondary CNS presentation of MZL and clinicians should be aware of this potential complication when assessing neurologic disease in patients who have had a previous diagnosis of lymphoma. Misdiagnoses are common with the initial presumption being meningioma if dural spread (11-15), and of astrocytoma if parenchymal spread. Being rare, there is no standardised therapy for CNS MZL with chemotherapy (11), surgery (12,16), radiation therapy (11,14) or combinations (11), all having been used with success.

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## Appendix 1: relapse protocol used

### Block A

Drug	Dosage & Route	Day
MTX	1,500mg/m <sup>2</sup> IVI in 1 L D5% over 24H	D1
MTX	10mg/m <sup>2</sup> (max 15mg) IT	D1 & 5

Drug	Dosage & Route	Day
ARAC	40mg IT	D1 & 5
DEXA	4mg IT	D1 & 5
Vincristine	2mg IVB	D1
Cyclophosphamide	200mg/m <sup>2</sup> IV slow bolus	D1-5
Doxorubicin	25mg/m <sup>2</sup> IVI in 100ml NS over 30 min	D4 & 5
DEXA	10mg/m <sup>2</sup> IV/PO	D1-5
Folinic Acid rescue	30mg/m <sup>2</sup> IV at 42 and 48H from start of MTX	D3
Folinic Acid rescue	15mg/m <sup>2</sup> IV at 54, 60, 66 & 72 H from start of MTX	D4

### Block B

Drug	Dosage & Route	Day
MTX	1,500mg/m <sup>2</sup> IVI in 1 L D5% over 24H	D1
MTX	10mg/m <sup>2</sup> (max 15mg) IT	D1 & 5
ARAC	40mg IT	D1 & 5
DEXA	4mg IT	D1 & 5
Vincristine	2mg IVB	D1
Ifosfamide	800mg/m <sup>2</sup> IVI in 500ml NS over 1 H	D1-5
Mesna	200mg/m <sup>2</sup> IV at 0, 4 and 8 H from ifosfamide	D1-5
ARAC	150mg/m <sup>2</sup> IVI IN 500ml NS over 1H BD	D4 & 5
VP16	100mg/m <sup>2</sup> IVI in 500ml NS over 3H	D4 & 5
DEXA	10mg/m <sup>2</sup> IV/PO	D1-5
Folinic Acid rescue	30mg/m <sup>2</sup> IV at 42 and 48H from start of MTX	D3
Folinic Acid rescue	15mg/m <sup>2</sup> IV at 54, 60, 66 & 72 H from start of MTX	D4

## References

- [1] Marginal Zone Lymphoma. Lymphoma Research Foundation (20). Retrieved from: <http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6554677>
- [2] Murphy JK, O'Brien CJ, Ironside JW. Morphologic and immunophenotypic characterization of primary brain lymphomas using paraffin-embedded tissue. *Histopathology* 1989;15:449-60.
- [3] O'Neill BP, Illig JJ: Primary central nervous system lymphoma. *Mayo Clinic Proc* 1989;64:1005-1020.
- [4] Herman TS, Hammond N, Jones SE et al. Involvement of the central nervous system by non-Hodgkin's lymphoma. The Southern Oncology Group Experience. *Cancer* 1979;43:390-7.
- [5] Levitt LJ, Dawson DM, Rosenthal DS, et al. CNS involvement in the non-Hodgkin's lymphomas. *Cancer* 1980; 45: 545-52.
- [6] Mackintosh, FR, Colby TV, Podolsky WJ et al. Central nervous system involvement in non-Hodgkin's lymphoma: an analysis of 105 cases. *Cancer* 1982; 49: 586-95.
- [7] Recht L, Straus DJ, Cirrincione C et al. Central nervous system metastases from non-Hodgkin's lymphoma: treatment and prophylaxis. *Am J Med* 1988; 84: 425-35.

- [8] Bashir RM, Bierman PJ, Vose JM et al. Central nervous system involvement in patients with diffuse aggressive non-Hodgkin's lymphoma. *Am J ClinOncol* 1991;14:478-82
- [9] Hollender A, Kvaloy S, Lote K et al. Prognostic factors in 140 adult patients with non-Hodgkin's lymphoma with systemic central nervous system (CNS) involvement: a single center analysis. *Eur J Cancer* 2000; 36: 1762-8.
- [10] Bayraktar S, Stefanovic A, Montague N, et al. Central nervous system manifestations of marginal zone B-cell lymphoma. *Ann Hematol.* 2010; 10: 1003-9
- [11] Kumar S, Kumar D, Kaldjian EP, et al. Primary low grade B-cell lymphoma of the dura: A mucosa associated lymphoid tissue-type lymphoma. *Am J SurgPathol* 1997;21:81-7
- [12] Kambham N, Chang Y, Matsushima AY: Primary low-grade B cell lymphoma of mucosa-associated lymphoid tissue (MALT) arising in dura. *Clin Neuropath* 1998;17:311-17
- [13] Rottnek M, Strauchen J, Moore F, et al. Primary dural mucosa-associated lymphoid tissue-type lymphoma: Case report and review of literature. *J Neurooncol* 2004;68:19-23.
- [14] Goetz P, Lafuente J, Revesz T, et al: Primary low-grade B-cell lymphoma of mucoas-associated lymphoid tissue of dura mimicking the presentation of an acute subdural hematoma. Case report and review of the literature. *J Neurosurg* 2002;96:611-14.
- [15] Sanjeevi A, Krishnan J, Bailey PR, et al. Extranodal marginal zone B-cell lymphoma of the MALT type involving the cavernous sinus. *Leuk Lymphoma* 2001;42:1133-7.
- [16] Itoh T, Shimizu M, Kitami K, et al. Primary extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue type in CNS. *Neuropathology* 2001;21:174-80.
- [17] Altundag MK, Ozisik Y, Yalcin S, et al. Primary low grade B-cell lymphoma of the dura in an immunocompetent patient. *J ExpClin Cancer Res* 2000;19:249-51.
- [18] Ancheta RG, Lewin H, Said J, et al. Primary dural marginal zone lymphoma in a woman with inflammatory breast cancer. *J ClinOnc.* 2008; 26: 326-8.
- [19] Ghasem J, Shaghayegh K et al: Bilateral breast swelling in a 23-year old women with Burkitt lymphoma. *Journal of Research in Medical Sciences* 2012; 17(11): 1188-1191.
- [20] Hugh JC, Jackson FI, Hanson J et al. Primary breast lymphoma. An immunohistologic study of 20 new cases. *Cancer* 1990;66:2602-11
- [21] Joks M, mysliwiec K, Lewandowski K. Primary breast lymphoma: A review of the literature and report of three cases. *Arch Med Sci.* 2011;7:27-33.
- [22] Liberman L, Giess CS, Dershaw DD. Et al. Non-Hodgkin lymphoma of the breast: Imaging characteristics and correlation with histopathologic findings. *Radiology.* 1994;192: 157-60.
- [23] Darnell A, Gallardo X, Sentis M, et al. Primary lymphoma of the breast: MR imaging features. A case report. *MagnReson Imaging.* 1999;17:479-82
- [24] Barista I, Baltali E, Tekuzman G, et al. Primary breast lymphomas: A retrospective analysis of twelve cases. *ActaOnco.* 2000;39:135-9.
- [25] Brogi E, Harris NL. Lymphomas of the breast: Pathology and clinical behaviour. *Sem in Oncol.* 1999;26:357-64
- [26] Domcchek SM, Hecht JL, Fleming MD, et a. Lymphomas of the breast: Primary and secondary involvement. *Cancer.* 2002;94:6-13.
- [27] Schouten JT, Weese JL, Carbone PP. Lymphoma of the breast. *Ann Surg.* 1981;194:749-53.
- [28] Wiseman C, Liao KT. Primary lymphoma of the breast. *Cancer* 1972;29:1705-12
- [29] Hugh JC, Jackson FI, Hanson J, et al. Primary breast lymphoma. An immunohistologic study of 20 new cases. *Cancer.* 1990;66:2602-11
- [30] Giardini R, Piccolo C, Rilke F. Primary non-Hodgkin's lymphomas of the female breast. *Cancer.* 1992;69:725-35
- [31] Sabate JM, Gomez, A, Torrubia S, et al. Lymphoma of the breast: Clinical and radiologic features with pathologic correlation in 28 patients. *Breast J.* 2002;8:294-304.
- [32] Kambouchner, M, Godmer P, Guillevin L, et al. Low grade marginal zone B cell lymphoma of the breast associated with localised amyloidosis and cororaamyloacea in a woman with long standing primary Sjogren's syndrome. *J ClinPathol.* 2003; 56:74-7.
- [33] Soyupak SK, Sire D et al. Secondary involvement of breast with non-Hodgkin's lymphoma in apaediatric patient presenting as bilateral masses. *EurRadiol.* 2000;10:519-20
- [34] Brustein S, Filippa DA et al. Malignant lymphoma of the breast. A study pf 53 patients. *Ann Surg.* 1987;205:144-50.
- [35] Ha CS, Dubey P et al. Localized primary non-Hodgkin lymphoma of the breast. *Am J ClinOncol.* 1998;21:376-80.
- [36] Telesinghe PU, Anthony PP. Primary lymphoma of the breast. *Histopathology.* 1985;9:297-307.
- [37] Ryan GF, Roos DR et al. Primary non-Hodgkin;s lymphoma of the breast: Retrospective analysis of prognosis and patterns of failure in two Australian centres. *Clin Lymphoma Myeloma.* 2006;6:337-41.
- [38] Hollender A, Kvaloy S, Lote K et al. CNS involvement following diagnosis of non\_Hodgkin's lymphoma: risk model. *Annals of Oncology.* 2002;13:1099-11