

## Rong-Hsin Yang<sup>1</sup>, Tse-Hao Lee<sup>2</sup>, Yum-Kung Chu<sup>2</sup>

<sup>1</sup>MacKay Memorial Hospital Taitung Branch, Taiwan

<sup>2</sup>Taipei Veterans General Hospital, Taiwan

# A rare metastasis to the vitreous from primary breast lymphoma

### Address for correspondence:

Yum-Kung Chu, M.D.  
 Department of Nuclear Medicine,  
 Taipei Veterans General Hospital  
 No. 201, Shipai Road Sec. 2,  
 Beitou District, Taipei, Taiwan 112  
 Phone: 886-2-28757301  
 Fax: 886-2-28715849  
 e-mail: ykchu@vghtpc.gov.tw

Oncology in Clinical Practice  
 2016, Vol. 12, No. 3, 108–111  
 Copyright © 2016 Via Medica  
 ISSN 2450–1654

### ABSTRACT

Primary breast lymphoma (PBL) is a rare neoplasm that appears exclusively in the breast at the time of diagnosis. Isolated lymphoma metastasis to the vitreous is exceedingly rare and may pose a great diagnostic challenge. Herein, we describe a case of a 75-year-old Taiwanese female with initial presentation of PBL of B-cell origin, which remitted after six cycles of CHOP chemotherapy. Two years after the achievement of a complete response, she was noted to develop a progressive blurring due to vitreous floaters in the left eye. Histopathological features of vitrectomy specimens and clinical implications were consistent with vitreous spread of B-cell lymphoma. This presentation aims to improve knowledge on these extranodal lymphomas and to avoid unnecessary delay in the treatment of patients presenting with similar scenarios.

**Key words:** breast lymphoma, diffuse large B-cell, PET/CT, vitreous metastasis

Oncol Clin Pract 2016; 12, 3: 108–111

## Introduction

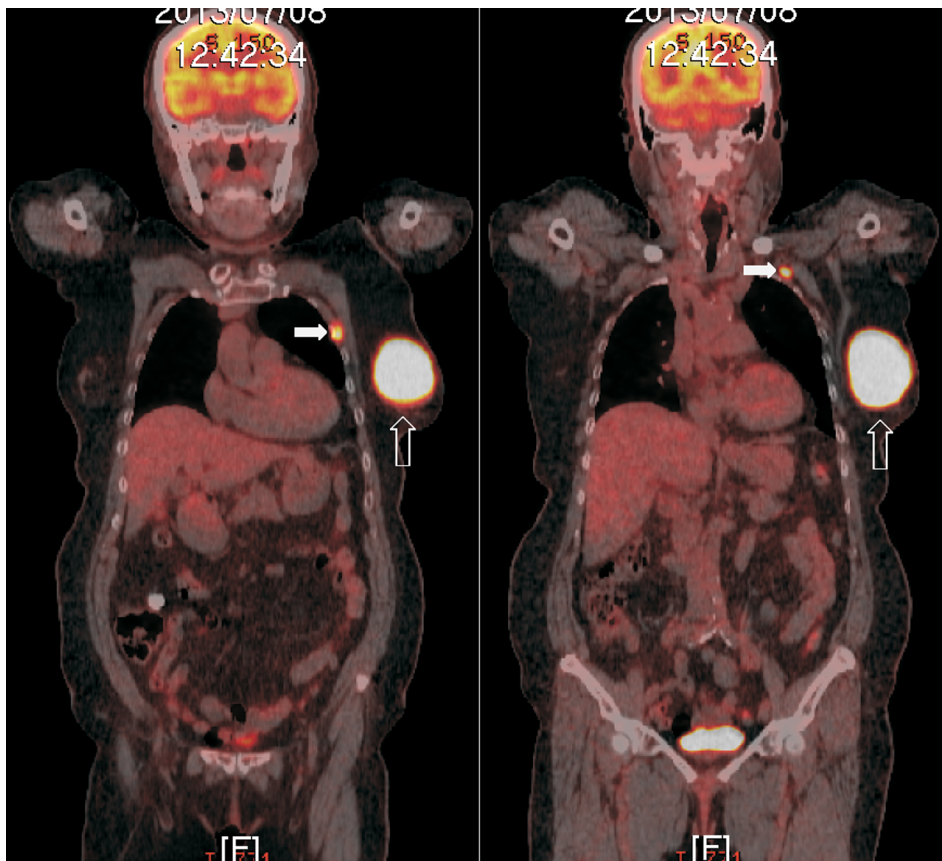
Primary breast lymphoma (PBL) is a rare neoplasm of the breast. By definition, the breast is the principal site of lymphomatous manifestation, in the absence of disseminated disease, other than ipsilateral axillary lymphadenopathy [1]. Intraocular metastasis of lymphoma, like other cancers spreading via the choroidal circulation, is often present in the uvea — in particular, the choroid [2, 3]. Isolated lymphoma metastasis to the vitreous, as shown in this presentation, is exceedingly rare. Most PBLs [4, 5] and intraocular lymphomas [2, 6] are non-Hodgkin's lymphomas, and the vast majority are of B-cell subtype. Reported cases of these two extranodal lymphomas are quite sparse in the literature. Consensus guidelines for their treatment have not been established.

## Case report

A 75-year-old Taiwanese female presented with a painless, growing lump in the left breast noted for one month. The patient reported no pain or systemic symptoms, such as fever or weight loss. She had a history of

essential hypertension and gastric ulcer. Her breast ultrasonography disclosed a hypoechoic ovoid mass measuring  $8.1 \times 5.0$  cm in the left breast, and several lymph nodes in the left axilla with the largest of 1.3 cm in size. An ultrasound-guided core needle biopsy of the breast mass was performed, and pathology revealed diffuse proliferation of atypical lymphoid cells with individual cell necrosis. The neoplastic cells were immunoreactive for CD20, CD10, BCL-2, and BCL-6, but non-reactive for CD3 staining. The features were compatible with diffuse large B-cell lymphoma (DLBCL), germinal centre type. Bone biopsy showed no evidence of infiltration.

Positron emission tomography (PET) with F-18 fluorodeoxyglucose (FDG) for staging revealed an  $8 \times 5$  cm hypermetabolic tumour in the left breast. A few interpectoral nodes extending to the left subclavicular area were also noted (Fig. 1). As defined by Wiseman and Liao [1], primary breast lymphoma (stage II, lymphoma limited to the breast and ipsilateral axillary nodes) was established. She was treated with six cycles of CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone) plus rituximab. The patient initially responded well to chemotherapy and had been free of disease for two years.



**Figure 1.** A case of primary breast lymphoma in a woman who presented with a painless, growing lump in the left breast. Coronal PET/CT slices revealed a hypermetabolic tumour of the left breast (hollow arrow). A few hot foci over the left upper chest corresponded with interpectoral lymph nodes (white arrows). The findings were consistent with an intramammary neoplasm and ipsilateral axillary lymphadenopathy

Two years after completion of therapy, the patient noticed progressive painless blurring and floaters in the left eye of uncertain duration. Best corrected visual acuity (BCVA) was 6/8 OD and 6/20 OS, and mild conjunctival congestion was observed in both eyes. Indirect ophthalmoscopy illustrated vitreous haze with 3+ cells OS, but was quiet OD. No corneal, retinal, or choroidal lesions were visible bilaterally. Intraocular pressure (IOP) of the left and right eyes was 15/15 mm Hg. Further metastatic survey was performed, but there was no evidence of intracranial or systemic involvement on CT scans of the head and the chest. Specimens from a diagnostic vitrectomy subsequently exhibited large atypical lymphocytes, necrotic lymphoid cells, and nuclear debris, with positive immunostaining for CD20 and negative for CD3. The findings were consistent with vitreous metastasis of B-cell lymphoma. The intraocular lesion was the only site at relapse. External beam radiotherapy to the involved eye was recommended. Nevertheless, the patient requested referral services at her nearest university hospital and was lost to follow-up.

## Discussion

Primary breast lymphoma (PBL) was first described by Wiseman and Liao in 1972. By definition the breast should be the first or major site of lymphomatous manifestation, in the absence of concurrent systemic lymphoma [1, 7]. It is a unique extranodal lymphoma sub-type, accounting for 0.4–0.5% of all breast malignancies [8]. The rarity of lymphoma in the breast may be attributed to the fact that the breast contains little lymphoid tissue [4].

Clinically, PBL lacks specific clinical and radiological features [7]. It is commonly described as painless rapid growth after first detection, as seen in our patient. Rapid breast growth is not typical for adenocarcinoma, as suggested by the possibility of lymphoma [9]. Most series documented that lymphomas tend to involve the right breast [1]. In a retrospective review of 36 breast lymphomas (22 primary and 14 secondary), however, Surov et al. observed that involvement of the left breast occurred more frequently in PBL than in secondary breast lymphoma [4]. Morphologically, there are no differences

between primary and secondary breast lymphoma. Lesions are mostly oval in shape with circumscribed margins, and appear hypoechoic sonographically [4]. The masses are characterised as hyperintense compared with surrounding breast parenchyma on T2-weighted images of magnetic resonance imaging (MRI) [10]. Breast tumours and metastatic foci accumulate F-18 FDG on PET [11, 12], as seen in our patient. However, there are no pathognomonic features for breast lymphoma on imaging, hence diagnosis can only be confirmed on histology. Fine needle aspiration cytology (FNAC) is the first choice to diagnose PBL.

Intraocular lymphoma is a rare form of malignancy, probably accounting for less than 0.01% of ophthalmic diseases [3, 13]. There are two distinct forms of intraocular lymphoma, namely 1) primary oculo-CNS lymphoma and 2) intraocular lymphoma metastasis [6]. Owing to the close relationship between the brain and the eye, 80% of patients with primary intraocular lymphoma develop CNS involvement [6]. In the site-specific classification, intraocular lymphoma has been divided into vitreoretinal and uveal forms. Primary oculo-CNS lymphoma classically manifests as vitritis. Intraocular metastasis of lymphoma, like other cancers spreading via the choroidal circulation, is often present in the uvea — in particular, the choroid [2, 3].

Malignant metastasis to the vitreous and not associated with choroidal involvement is exceedingly rare [14]. Interestingly, our cases of intraocular metastasis presented as vitritis, not choroidal infiltrates, masquerading the features of primary intraocular lymphoma. The mechanism of the isolated metastasis to the vitreous is unclear but may include extravasation of neoplastic cells through the retinal vessels [14], or direct seeding via the optic nerve [15]. With regard to the nonspecific nature of eye findings in intraocular lymphoma, diagnostic vitrectomy is the procedure of choice to discriminate the causes of uveitis. Immunohistochemistry is good at identifying markers for leukocytes (CD45), B-cells (CD20, CD79a, PAX-5), and T-cells (CD3, CD45RO).

Due to the rarity of PBL, optimal management of this specific entity is not yet realised [16]. Surgery should not be regarded as a therapeutic modality, and extensive procedure over lumpectomy has no role in the treatment of this rare entity [16]. Lymphomatous lesions are responsive to cytotoxic systemic chemotherapy. Many patients will not ultimately require surgical ablation. As in nodal forms of DLBCL, an anthracycline-based regimen is the mainstay of treatment, with R-CHOP being the most frequent regimen used. There is debate concerning the application of intrathecal chemoprophylaxis in preventing the dismal prognosis of CNS relapse. The growing number of reports show that universal prophylaxis is probably ineffective, and most patients would be overtreated [16]. Patients with stage I and II

PBL need not routinely receive CNS prophylaxis. However, those with high-grade disease, more than one extranodal localisation, and raised LDH may benefit from the addition of CNS prophylaxis [17]. Radiation therapy can also be of benefit when used in an adjuvant setting. Based on the common assumption that the eye is an immune privileged site, with strong blood-tissue barriers and altered immune response. Chemotherapy can treat systemic lymphomas, but intraocular penetration is poor and invalid. External beam radiotherapy has been the most common treatment for intraocular lymphoma. Local delivery of intravitreal methotrexate or rituximab was recently developed [18]. However, both irradiation and intravitreal chemotherapy might result in some complications. Consensus guidelines of intraocular lymphoma treatment need to be established.

## Conclusions

PBL is a rare disease and its management differs from other breast cancers. Metastasis to the vitreous and not associated with choroidal involvement is exceedingly rare, and the pathogenesis of spreading is still unclear. Herein, a clinical case of an isolated metastasis to the vitreous from primary breast lymphoma confirmed by diagnostic vitrectomy is described. The goal of this presentation is to raise awareness of these extranodal lymphomas and to avoid unnecessary delay in treatment.

## Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

## References

1. Wiseman C, Liao KT. Primary lymphoma of the breast. *Cancer* 1972; 29: 1705–1712. doi: 10.1002/1097-0142(197206)29:6<1705::AID-CNCR2820290640>3.0.CO;2-I.
2. Fredrick DR, Char DH, Ljung BM, Brinton DA. Solitary intraocular lymphoma as an initial presentation of widespread disease. *Arch Ophthalmol* 1989; 107: 395–397. doi:10.1001/archophth.1989.01070010405034.
3. Chan CC, Rubenstein JL, Coupland SE et al. Primary vitreoretinal lymphoma: a report from an international primary central nervous system lymphoma collaborative group symposium. *Oncologist* 2011; 16: 1589–1599. doi: 10.1634/theoncologist.2011-0210.
4. Surov A, Holzhausen HJ, Wienke A et al. Primary and secondary breast lymphoma: prevalence, clinical signs and radiological features. *Br J Radiol* 2012; 85: e195–e205. doi: 10.1259/bjr/78413721.
5. Domchek SM, Hecht JL, Fleming MD, Pinkus GS, Canellos GP. Lymphomas of the breast: primary and secondary involvement. *Cancer* 2002; 94: 6–13. doi: 10.1002/cncr.10163.
6. Peterson K, Gordon K, Heinemann M, Deangelis L. The clinical spectrum of ocular lymphoma. *Cancer* 1993; 72: 843–849. doi: 10.1002/1097-0142(19930801)72:3<843::AID-CNCR2820720333>3.0.
7. Mason HS, Johari V, March DE, Crisi GM. Primary breast lymphoma: radiologic and pathologic findings. *Breast J* 2005; 11: 495–496. doi: 10.1111/j.1075-122X.2005.00167.x.

8. Park YH, Kim SH, Choi SJ, Ryou BY, Kang YK, Lee SS. Primary malignant lymphoma of the breast: clinicopathological study of nine cases. *Leuk Lymphoma* 2004; 45: 327–330. doi: 10.1080/10428190310001597892.
9. Offodile RS, Arce V, Cross J, Reed J, Beech DJ. Primary breast lymphoma: A rare clinical entity. *World J Oncol* 2011; 2: 147–150. doi:10.4021/wjon319w.
10. Yang WT, Lane DL, Le-Petross HT, Abruzzo LV, Macapinlac HA. Breast lymphoma: imaging findings of 32 tumors in 27 patients. *Radiology* 2007; 245: 692–702. doi: http://dx.doi.org/10.1148/radiol.2452061726.
11. Cheson BD. Role of functional imaging in management of lymphoma. *J Clin Oncol* 2011; 29: 1844–1854. doi: 10.1200/JCO.2010.32.5225.
12. Santra A, Kumar R, Reddy R et al. FDG PET-CT in the management of primary breast lymphoma. *Clin Nucl Med* 2009; 34: 848–853. doi: 10.1097/RLU.0b013e3181becdfc.
13. Mochizuki M, Singh AD. Epidemiology and clinical features of intraocular lymphoma. *Ocul Immunol Inflamm* 2009; 17: 69–72. doi: 10.1080/09273940902957305.
14. Jaissle GB, Szurman P, Rohrbach JM, Gelissen F, Bartz-Schmidt KU. A case of cutaneous melanoma metastatic to the vitreous cavity: possible pathomechanism and review of the literature. *Graefes Arch Clin Exp Ophthalmol* 2007; 245: 733–740. doi: 10.1007/s00417-006-0469-1.
15. Gündüz K, Shields JA, Shields CL, Eagle RC Jr. Cutaneous melanoma metastatic to the vitreous cavity. *Ophthalmology* 1998; 105: 600–605. doi: 10.1016/S0161-6420(98)94011-8.
16. Aviv A, Tadmor T, Polliack A. Primary diffuse large B-cell lymphoma of the breast: looking at pathogenesis, clinical issues and therapeutic options. *Ann Oncol* 2013; 24: 2236–44. doi: 10.1093/annonc/mdt192.
17. McMillan A, Ardeshta KM, Cwynarski K, Lyttelton M, McKay P, Montoto S. Guideline on the prevention of secondary central nervous system lymphoma: British Committee for Standards in Haematology. *Br J Haematol* 2013; 163: 168–181. doi: 10.1111/bjh.12509.
18. Smith JR, Rosenbaum JT, Wilson DJ et al. Role of intravitreal methotrexate in the management of primary central nervous system lymphoma with ocular involvement. *Ophthalmology* 2002; 109: 1709–1716. doi: http://dx.doi.org/10.1016/S0161-6420(02)01125-9.