REVIEW

PRIMARY BREAST LYMPHOMA – A RARE DISEASE

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ABSTRACT

Primary breast lymphoma (PBL) is breast lymphoma that develops only in the breast without lymphoma disease in any other area of the body. PML constitutes less than 0.5% of all breast cancers. Treatment options are not clear because primary breast lymphomas are rare. The aim of this review is to raise awareness about PBL disease, to give information about its symptoms, choice of diagnosis and treatment methods.

KEYWORDS: *primary breast lymphoma, surgical therapy, chemotherapy, radiotherapy*

INTRODUCTION

Lymphoma is a disease characterized by excessive multiplication of lymphocytes. Primary breast lymphoma (PBL) is the breast lymphoma that develops only in the breast without lymphoma disease in any other area of the body. If the breast is involved in addition to the common systemic lymphomatous involvement, it is considered as "secondary" [1, 2]. PBL constitutes less than 0.5% of all malignant neoplasms of the breast [3, 4]. It was described for the first time in 1959 by Dobrotina et al. [5, 6]. In 1972, pathological criteria for the diagnosis of PBL was described by Wiseman and Liao [7]. PBL originates from stromal lymphocytes located in breast tissue [1, 7, 8]. PBL is generally a type of "Non-Hodgkin" lymphoma, mostly B cell lymphoma [1, 9, 10]. The patients with PBL carry the increased risk of systemic lymphoma [2]. No specific risk factors have been identified for the lymphoma of breast, but older individuals commonly have a higher risk.

The aim of this review is to raise awareness about PBL disease, to give information about its symptoms, choice of diagnosis and treatment methods.

MATERIALS AND METHOD

An extensive literature search was conducted on PubMed and Google Scholar with the keywords, primary breast lymphoma, surgery, chemotherapy, radiotherapy. Inclusion criteria were studies from 1959 to present (2020), human studies, original research, case reports and reviews whereas exclusion criteria were studies published before 1959, animal studies, presentations.

DISCUSSION

PBL is a rare disease. Primary breast lymphomas are mostly of the B-cell lineage, and the most common subtype is diffuse, large cell lymphoma. If it arises in the breast without any evidence of systemic lymphoma disease, it is

named PBL. It occurs almost exclusively in women, and this situation is explained by estrogen-related mechanism [11-13]. It is often seen in the right-side breast but can also be seen in the other breast. In the physical examination and diagnostic tests, it is very important to evaluate both breasts [12-14]. A large part of the patients presents with a painless breast mass on hand [7].

PBL diagnosis might be very difficult with only imaging. Imaging methods are ultrasonography, mammography MRI and PET (Positron Emission Tomography) [1, 15]. They are generally seen as a homogeneous, smooth surface, oval or lobule, hypoechoic mass in the USG [7, 16]. Differentiating the mammographic findings from other breast tumors is difficult [7, 17]. In mammography, it is often seen as a smooth surface, round or slightly lobulated mass without calcification. In some cases, edema and thickening may be observed in the skin [2]. In addition, MRI and PET have a place in diagnosis [2, 16, 17]. There is no difference between primary and secondary lymphoma in the MRI imaging [2,18]. PET-CT scans are used to determine how far the lymphoma has spread, by checking the size and metabolic rate of lymph nodes throughout the body [2, 16, 17]. Breast lymphoma can be bilateral so the other breast must also be carefully evaluated.

Immunohistochemical biomarkers, and pathologic examination as fine needle aspiration (FNA), true cut biopsy, excisional biopsy and postsurgical procedures is very important to diagnosis. Based on the histopathological findings, breast tumors can be categorized as large cell B-cell lymphomas. Histological view of breast lymphoma is similar to other types of lymphomas. Although the majority is non-Hodgkin lymphoma, Hodgkin lymphoma can also be observed histologically [2-5]. It might be difficult to differentiate the poorly differentiated breast carcinoma from pseudolymphoma.

There is no consensus on PBL treatment [4]. The main reasons for this are being a rare disease, not enough follow-up in a single center, and the studies are often limited to case reports or case series. Multiple treatment strategies involving surgery, radiation, and chemotherapy (alone or in various combinations and sequences) have been reported for the treatment of PBL. However, treatment options are not clear. But chemotherapy, radiotherapy and targeted treatment methods are among the options [19]. Surgery may be the best treatment for some breast lymphomas. Although some may not need surgery at all. Earlier cases were treated by surgery but nowadays, studies showed that only mastectomy carries no benefit over the treatment of PBL. It is also important to note that surgery is infrequently used as a treatment modality for the lymphoma of breast [4, 20-22]. But mastectomy seemed to provide better local control [5]. Luo et al. [19] reported that if PBL patients were treated initially by mastectomy, supplementary radiotherapy, chemotherapy, and immunotherapy should be administered promptly following surgery. There are studies showing that adding radiotherapy to chemotherapy increases the success of treatment and the use of chemotherapy combined with radiotherapy could reduce local recurrence [10,12,18,23]. In a study in which 46 patients were evaluated retrospectively, the positive effect of chemotherapy treatment on overall survival (OS) and progression-free survival (PFS) was reported. In the same study, it was mentioned that radiotherapy treatment is effective in local disease control, but it does not have any effect over OS and PFS [19]. Radkani et al. [5] suggested that combination therapy (i.e., using various modalities) produces the most favorable results and that there is a definite role for the surgical excision and local radiation for better local control. At the end of day, treatment of breast lymphoma remains somewhat controversial, but treatment regimen consisting of combination chemotherapy with or without concurrent radiotherapy can help to survive. Primary breast lymphoma treatment protocol has not been revealed yet. A multidisciplinary approach is important when facing a patient with PBL. We think that evaluation in a tumor board with general surgeon, plastic surgeon, radiologist, nuclear medicine, pathologist and hematologist is important in determining the most appropriate treatment for the patient.

CONCLUSION

As a result, because of being a very rare disease, PBL might be confused with other

breast cancers in differential diagnosis. The combination treatment which evaluation with a tumor board is necessary. Therefore, PBL should be kept in mind in painless breast masses. We believe that larger randomize clinical studies and follow-up data results are needed to establish a treatment protocol in Primary Breast Lymphoma.

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