

Original Research Article**Primary breast lymphoma : study of 9 cases****Abstract:****Introduction:**

Non-Hodgkin's primary lymphoma of the breast is a rare entity. These tumors represent 0.04 to 0.52% of malignant breast pathology, 2.2% of extranodal lymphoma and 0.4% of all non-Hodgkin lymphoma. Clinical and radiological aspects show no special characteristics. The diagnosis is defined is based on the presence of a lymphomatous proliferation strongly associated to the breast tissue and the diagnosis of an extra-mammary lymphoma must be removed except the presence of ipsilateral axillary lymphadenopathy.

Patients and methods:

This is a retrospective study of 9 patients treated for Non-Hodgkin's primary lymphoma of the breast. They were collected over a period of 14 years (2000-2013). They interested 1 case of follicular lymphoma, 1 case of large T-cell lymphoma and 7 cases of large B-cell lymphoma.

The average age was 50 years, ranging from 30 to 76 years. The sex ratio was 0.11 (1 man/ 8 women). The average consultation time was 3 months (5 days -8 months). The median follow-up was 43 months (4-192). Six patients were older than 60 years; one had disseminated disease and was classified as stage III Ann Arbor. Concerning the histology, all the tumors were architecturally diffuse. The overall survival was 100 % at one year 75% at 3 years. Seven patients achieved a complete remission after initial treatment; one had relapsed after 2 months. Among the 7 cases of large B cell lymphoma, two cases result from follicular lymphoma's transformation. The average processing time was 17 months.

Conclusion:

The primary breast lymphoma is often diagnosed late. Treatment should be rapidly implemented. Indeed, the 5-year survival of stage I of the Ann Arbor classification is better than for stage II.

Keywords: breast, non hdgkinien lymphoma, histology, immunohistochemistry

Introduction:

Primary breast lymphoma (PBL) is defined as the affection of one or both breasts. Lymphomatous proliferation should be strongly associated to the breast tissue and the diagnosis of an extra-mammary lymphoma must be removed except the presence of ipsilateral axillary lymphadenopathy.

Wiseman and Liao first defined PBL according to four criteria [1]: the close anatomic proximity of mammary and lymphomatous tissue, absence of a previous diagnosis of an extra-mammary lymphoma, lack of evidence of a disseminated disease (except for the ipsilateral axillary nodal involvement) and an adequate quality of the histopathological specimen. These criteria are still widely accepted.

PBL represents only 0.04 to 0.52% of breast malignancies, 2.2% of extranodal lymphomas and 0.4% all non-Hodgkin's lymphoma [2, 3]. We propose in this work to study the clinical, radiological, histological, immunohistochemical, treatment and results of non-Hodgkin primary lymphoma of the breast.

Patients and methods:

This is a retrospective study of 9 patients treated for Non-Hodgkin's primary lymphoma of the breast. They were collected over a period of 14 years (2000-2013).

Data on patient characteristics, the management procedures and evolution were collected from medical records and information sheets. This study concerns patients with a pathologic diagnosis of breast lymphoma. An extra -mammary location has been eliminated in all cases.

Results:

The average age of patients was 50 years, ranging between 30 to 76 years. The population analyzed showed a female predominance. Indeed, 8 patients were female while only one patient was male (sex ratio: 0.14). In our study, three patients had breast pathology history, one a history of an in situ ductal carcinoma and two patients a history of breast primitive follicular lymphoma who have become diffuse large cell lymphoma B after 2 years and 10 months of evolution. One patient had a family history of infiltrating ductal carcinoma reported in a paternal aunt and a cousin. Three patients were already postmenopausal for 10, 15 and 21 years, while 5 patients were still in childbearing age. One of our patients was under

hormonal contraception for seven years. One of our patients, aged 30 years old, was pregnant for five months at the moment of breast lymphoma diagnosis.

The PBL discovery circumstances were mammary masses, increasing the volume of the breast and skin inflammatory signs. This pathology has interested the right side in 3 patients and left side in 5 patients. It was bilateral, at diagnosis, in only one patient. The most frequent location was the left upper outer quadrant in 5 patients, and the super-outer quadrant right in one case.

The average clinical size was 6.4 cm, up to a maximum of 15 cm. It was more than 5 cm in 3 patients. The ipsilateral axillary lymph nodes were palpated in 5 patients. In a patient with left axillary lymph nodes, clinical examination revealed a supraclavicular lymphadenopathy. The histological exam concluded to a reactional node in all cases.

A mammography was performed in 6 patients, always associated with ultrasound. The average tumor size in the mammography was 40.5 mm, ranging from 10 to 70 mm. Mammographic aspects that were observed: a poorly circumscribed opacity with indefinite and irregular contours or spiculated dense center, a dense heterogeneous and irregular mass and retraction and thickening of superficial skin plans.

Observed ultrasound aspects were: a hypoechoic irregular mass, a multilobulated mass or a rounded supra areolar opacity, heterogeneous hypoechoic, surrounded by a hyperechoic halo interrupting the glandular architecture and hypervascular on color Doppler. MRI was performed in only two patients and showed a spiculated lesion with polycyclic limits. This lesion is hypo signal T1, iso signal T2 and hyper signal FS. The scan of the male patient showed contiguous right axillary lymph nodes of 2 to 4 cm in diameter, a large multilobed right parieto-axillary mass of 11 cm and a multinodular splenomegaly.

In our study 8 patients had localized stages (I + II) at diagnosis and 1 patient with a disseminated stage (stage III).

Studied PBL involve 7 cases of large B-cell lymphoma, a case of follicular lymphoma and a case of large T-cell lymphoma (fig 1, fig 2). Immunohistochemical study allowed us to confirm the diagnosis of non hodgkin's lymphoma and eliminate other diagnoses. We used a large pannel of antibody: B marker (CD20), T marker (CD3), CD30, CD45, CD15, vimentin, CD10. In 7 cases, the I.H.C study showed a diffuse and intense labeling with anti-CD20 (Figure 3). In one case the tumor cells had diffusely expressed anti CD3. In one case, we found a diffuse expression of anti CD 20 and CD 10. Five patients had only chemotherapy

treatment; four had chemotherapy with radiotherapy. One patient had received radiotherapy alone. The surgery was performed in 7 cases. 5 had a lumpectomy with axillary dissection while 2 had a surgery type Patey. Sixty six per cent of operated patients underwent neoadjuvant chemotherapy. Progression free survival was 43% at 3 years and 24% at 5 years. The median follow-up of our patients was 41 months with extremes ranging from 1 to 159 months. Overall survival was 60% at 3 years and 42% at 5 years.

Discussion :

PBL occurs specially in women whose median age is between the fifth and sixth decade [4,5]. Man is indeed exceptionally touched. Only a few cases have been published [6]. Results of this study showed that 8 of 9 patients were female with one male case.

PBL is also a tumor of elderly women [2, 3]. However, some authors have shown that a median of 28 years was found in 15% of cases in pregnant women or during breast-feeding [7]. In our study, a patient with diffuse large B cell lymphoma was 30-year-old and was pregnant at the fifth month.

The association lymphoma and pregnancy is increasingly described and some authors have found that it is more important than pregnancy- carcinoma association. Thus, we can conclude that hormonal disturbances likely play a role of inducing proliferation lymphoma [7].

The affection is often unilateral. In 18% of cases, it is bilateral; it can be simultaneous (12%) or sequential (6%) [8,9]. The mode of revelation is almost always a breast tumor with an inflammatory mastitis [2]. The axillary lymph nodes are found in 20-40% of cases [10].

The primitive character of breast lymphoma is based on clinical investigation. Indeed, we should eliminate secondary breast's invasion during the natural evolution of non hodgkin lymphoma [11].

The radiologic imaging' aspects are nonspecific. Mammogram often shows a well limited mass with homogeneous density and benign appearance, evoking a cyst, a fibroadenoma or phyllodes tumor. Less frequently, it is a mastitis appearance with diffuse increase breast density or an ill-defined or spiculated contours mass [12].

Rarely, a suspicious aspect of malignancy is observed, but there is never stellar opacity or microcalcifications [10].

Ultrasound presentation is not specific, usually as a hypoechoic and homogenous mass, with

regular contours. Rarely a mastitis appearance is seen on ultrasound. The discrepancy between alarming clinical presentation and reassuring mammography may suggest the diagnosis [10].

The standard histological examination left little doubt in case of medullary and anaplastic carcinoma whereas lymphoma's diagnosis is often difficult [13, 14]. As he let it probably would be lifted by a histological and immunohistochemical study on paraffin sections [15].

The most frequently observed type in the literature is the diffuse large B-cell lymphoma (45% to 80%), especially in localised forms while follicular lymphoma appears more common in disseminated forms. All histological types have been described. Lymphoma of the MALT type marginal zone are common (0-44%) and Burkitt's lymphoma often associated with bilateral involvement. [16] In our work no cases of Burkitt's lymphoma has been described this can be related to a particular geographical distribution of this type of lymphoma [13, 14].

The management strategies for PBL vary broadly, from surgical intervention to combination chemotherapy and radiotherapy. However, there is no up to date standard guideline for PBL treatment. Mastectomy for PBL is not well-supported because it shows neither improved survival nor reduced risk of recurrence. Several studies have recommended that surgery should be offered for diagnosis only and that minimally invasive surgery is the preferable option because extensive surgery may carry a high risk of morbidity. Also, axillary dissection adds no therapeutic advantage [17].

At present, early stages of PBL can be successfully treated with combination therapy, in which CHOP regimen is the most common chemotherapeutic agent. Several investigators have recommended a treatment regimen involving combination chemotherapy with or without radiation therapy [17].

The prognosis of diffuse large B-cell lymphoma is poor. Among 215 cases whose outcome was known, Prevot [18] notes that more than half of the patients died within a period ranging from 4 days to 178 months after diagnosis. Baltali estimated survival rate at 5-year 30 to 50%. [19] Histological type and clinical stage of the disease are the two main prognostic factors. Indeed, the risk of death is nearly double if PBL stage II versus stage I [20].

Conclusion :

Primary lymphoma is a very rare pathology. If symptoms not yielding to treatment, histological sampling is imperative. Treatment should be quickly implemented. Indeed, the five-year survival for stage I of the classification of Ann Arbor is better than for stage II.

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Legends:

Fig 1: Diffuse lymphoma proliferation with nodular enhancement

Fig 2: large tumor cells with nuclei containing prominent nucleoli

Fig 3: The tumor cells expressing intensively and diffusely the anti CD20 anti body

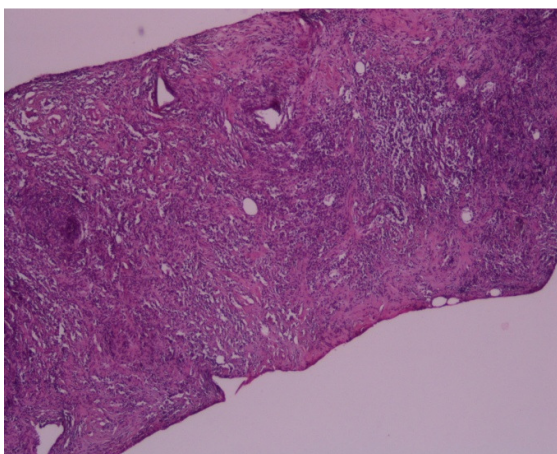


Figure1.

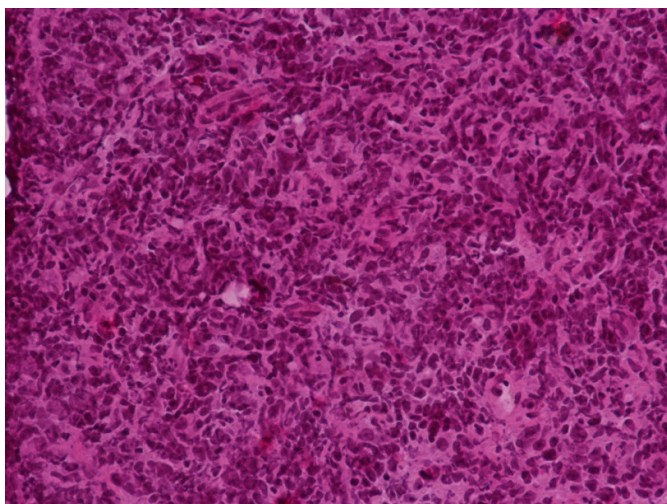


Figure2.

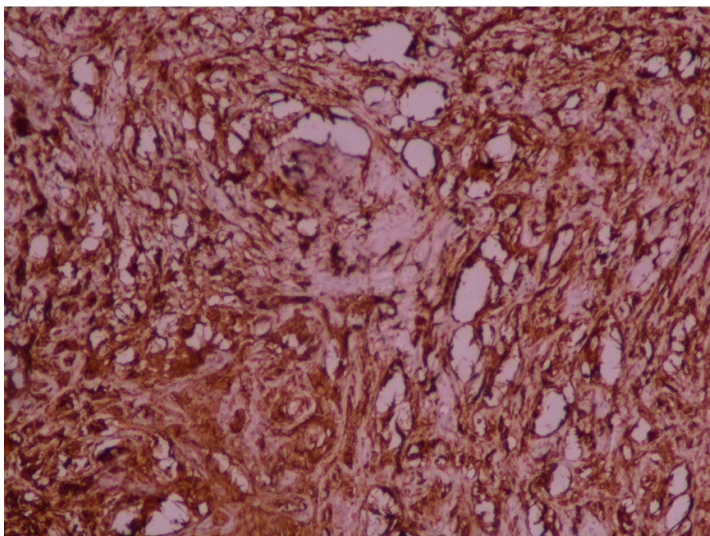


Figure 3.