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A Primary Breast Hodgkin Lymphoma: A Case Report

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Abstract

Primary breast Hodgkin lymphoma is an uncommon and rare type of breast malignancy with little clinical and imaging specificity. As in all forms of Hodgkin lymphoma (HL), the diagnosis of breast HL is difficult and can only be made if an immunohistochemical study is carried out to exclude other types of cancer and avoid unnecessary surgery. The role of positron emission tomography scanning (PET/CT) is important in assessing lesions and making treatment decisions. We present a unique case of primary breast Hodgkin lymphoma in a 49-year-old woman. The diagnosis is confirmed by histology. Immunohistochemistry on an axillary lymph node biopsy. A complete response was obtained after first-line chemotherapy: BEACOP-DAC (bleomycin-dacarbazine-cyclophosphamide-doxorubicin-etoposide-vincristine). Furthermore, the patient did not receive radiotherapy.

Keywords

Hodgkin Lymphoma, Breast Lymphoma, Immunochemistry, Chemotherapy

1. Introduction

Primary breast lymphoma (PBL) is a rare form accounting for less than 2.2% of extranodal lymphomas and less than 0.5% of breast malignancies [1]. PBL comprises only tumors in stage I (limited to the breast) and stage II (limited to the breast and axillary lymph nodes) and not tumors originating from nonbreast sites [2]. Primary breast Hodgkin lymphoma is a rare entity representing less than 0.5% of all malignant neoplasms of the breast and less than 2% of extranodal lymphomas [3]. There are several subtypes of Hodgkin's disease, the most common of which is nodular sclerosis. It tends to affect adolescents and young adults more commonly and usually presents with localized disease involving supraclavicular,

cervical and mediastinal regions [4]. Multinucleated giant Reed-Sternberg cells within the characteristic reactive cellular background are the stamp of authentication of classical HL [5]. Mixed cellularity HL is more commonly associated with an advanced stage of disease and high prevalence in the pediatric as well as older age groups [6]. The incidence of lymphocyte depletion HL appears lower, with many of the cases reclassified as non-HL [5]. Diagnostic criteria for primary lymphoma of the breast depend essentially on histology and PET/CT imaging: absence of concurrent extensive disease or preceding extramammary lymphoma, close association between breast tissue and lymphomatous infiltrate [7].

The treatment of Hodgkin lymphoma of the breast is based on immunotherapy, radiation therapy, chemotherapy with stem cell transplant, and surgery. The choice of treatment depends on the disease's progression, including early favorable and unfavorable classic HL, recurrent classic HL, and advanced HL [8]. Chemotherapy regimens are selected according to the patient's clinical state.

We report an interesting case of a middle-aged woman with a left axillary adenopathy with general signs and no skin lesions on the homolateral breast, whose biopsy and TEP/CT were in favour of primary HL of the breast.

2. Case Presentation

We present the case of a 49-year-old female with no notable pathological history, notably a regular menstrual cycle and no family history of neoplasia. She had a cervical adenopathy for a year, followed by the appearance of another in the left axilla, presenting with apyrexia, night sweats, and weight loss, without any associated infectious or haemorrhagic syndrome. Her clinical examination on admission revealed a preserved general condition, discoloured conjunctivae, and a left supraclavicular adenopathy that was hard on palpation and fixed in both the superficial and deep planes, with no signs of inflammation opposite. A left axillary adenopathy measuring 14 mm with the same characteristics as above. The skin examination showed a diffuse subcutaneous infiltration in the left breast. Her laboratory results showed anaemia with no detectable abnormalities in other blood lines. There was a polyclonal hypergammaglobulinaemia and a normal lactate dehydrogenase level. The rest of the biological exploration is as follows: Hb 10.3 g/dL, MCV 82 fL, MCHC 31 g/dL, WBC 8.1 × 10^3/μL, ANC 5.7 × 10^3/μL, and platelet count 388 × 10^3/μL. Viral tests were negative, including for hepatitis B, hepatitis C, and HIV. EBV PCR was not performed due to a lack of resources.

A mammary magnetic resonance imaging (MRI) showed several axillary and internal mammary adenopathies. Mastitis of the left breast with tumour nodules in the pectoralis major muscle associated with discrete micronodular infiltration of the pre-pectoral fat was classified as ACR4. The presence of lymph node formations in the internal quadrant of the right and left breast was classified as ACR4 (**Figure 1**).

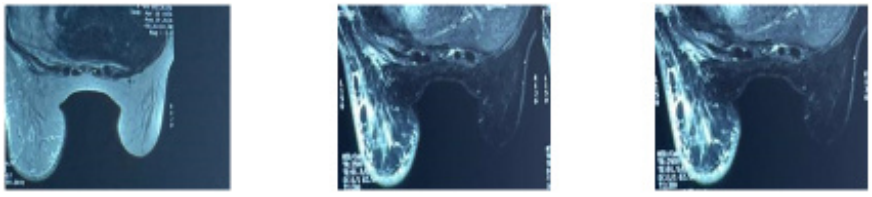

Figure 1. Image MRI showing axillary and internal mammary lymphadenopathy with discrete micronodular infiltration pre-pectoral fat classified ACR4.

The TEP/CT presents hypermetabolic adenopathy of the left axilla measuring 19 × 17 mm (SUVmax 11.7). Hypermetabolic infiltration of the left pectoral muscle (SUVmax 6.5) is associated with hypermetabolism on the left mammary skin, 12 mm (SUVmax 3.1), with a few bilateral glandular nodules (Figure 2).

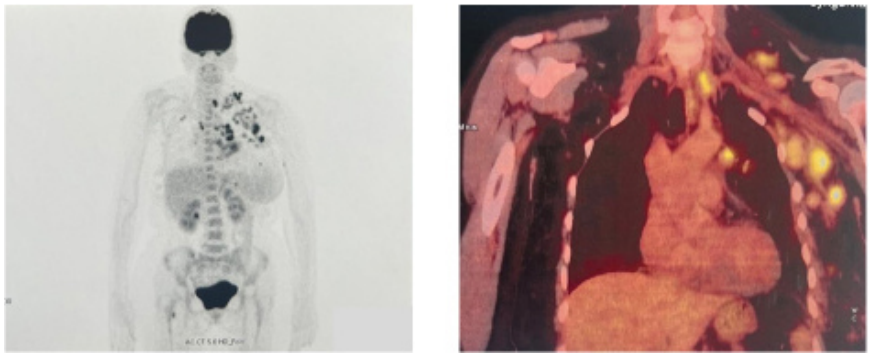

Figure 2. TEP/CT axial slide, hypermetabolism on the left pectoral muscle SUVmax 6.5, with hypermetabolism on the left mammary skin SUVmax 3.1, with a left axillary adenopathy SUVmax 11.7.

Histology shows a cell population made up of large, scattered elements with atypical, pleomorphic, budding nuclei with retracted cytoplasm, associated with a few Reed-Sternberg-type cells with bilobed, mirror-like nuclei. Immunohistochemistry reveals a characteristic phenotypic profile of CD30+, PAX5+, LMP−, and CD3+ tumour cells, revealing a reactive background composed of T lymphocytes. Diagnosis of Nodular Sclerosis Classical Hodgkin Lymphoma was obtained (Figure 3).

The patient is classified as Ann Arbor stage IIE: stage II with direct extension to an extranodal site. It is considered unfavorable form with two risk factors according to the EORTC (European Organization for Research and Treatment of Cancer) and two risk factors according to the GHSG (German Hodgkin's Lymphoma Study Group).

The patient received escalated chemotherapy represented by the BAECOP-DAC regimen (Bleomycin-Doxorubicin-Etoposide-Cyclophosphamide-Vincristine-Prednisone-Dacarbazine). Complete metabolic remission (CR) was achieved after two courses of treatment (Figure 4).

The patient continued four deescalated courses: ABVD (Adriamycine-Bleomycine-Vincristine-Dacarbazine), preserving her CR. She is currently ten months (M

+ 10) away from the end of treatment, with good clinical and biochemical evolution.

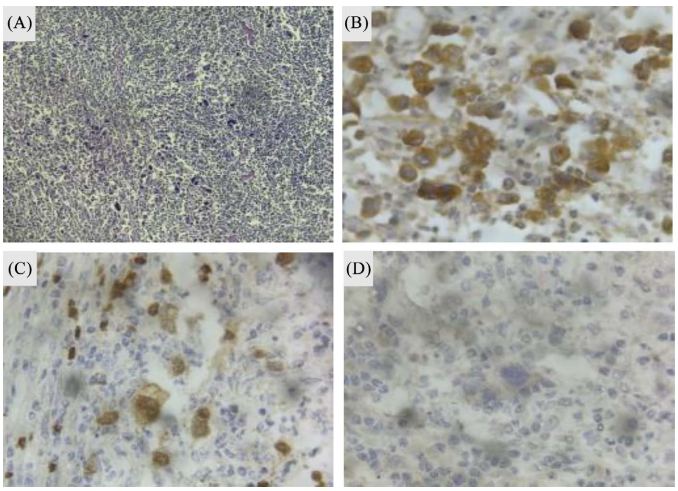

Figure 3. Cytology: (A) breast histology showing scattered Hodgkin and Reed-Sternberg cells admixed with eosinophils and lymphocytes (Hemacolor stain, 20X); (B) CD30 immunoreactive Reed-Sternberg and Hodgkin cells (40X), (C) PAX-immunoreactive Reed-Sternberg and Hodgkin cells (40X); (D) Latent membrane protein (LMP). Immunoreactive Reed–Sternberg and Hodgkin cells (40X).

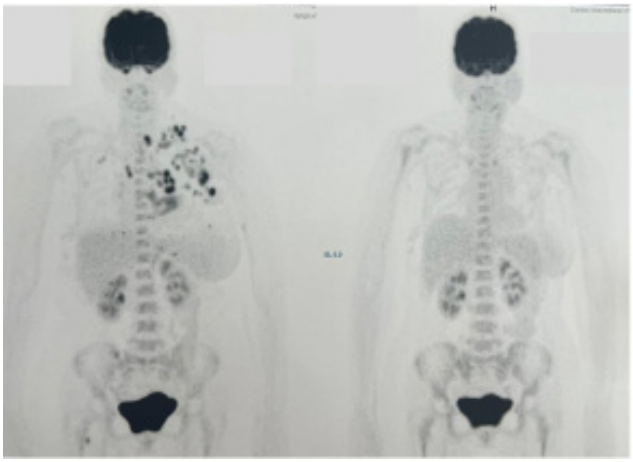

Figure 4. Comparative PET/CT images showing the achievement of complete metabolic remission.

3. Discussion

Primary breast Hodgkin lymphoma is a very rare entity: 1.7% - 2.2% of extranodal lymphomas and 0.5% of primary malignant tumors of the breast [9]. In the literature, 50% of breast lymphomas reported are B-cell lymphomas, and a minority of cases are mucosa-associated lymphoid tissue lymphoma (MALT), follicular lymphoma, or Burkitt lymphoma [10]. According to the first description by Wiseman in 1972, primary breast lymphoma must meet several criteria. These prerequisites include a suitable pathological specimen; mammary tissue and

lymphomatous infiltrate should be in close association, without any notion of a previous lymphoma site [11].

The pathophysiology of the PBHL is not always clear; it is probably linked to intra-mammary lymph nodes or even mucosa-associated lymphoid tissue (MALT) and lymphoid tissue adjacent to breast lobes and ducts [12]. Mammary infiltration is, in most cases, the consequence of direct extension from mediastinal or axillary nodes, a manifestation of systemic disease, or a part of regional disease with discontinuous axillary node involvement [7]. Also, some authors found an association between pregnancy and lymphoma; this finding suggests that hormonal disorders can lead to lymphoma proliferation [13].

A few cases of PBL have been reported in men; it almost occurs in females. The age of presentation is between 60 and 65 years [14]. PBHL may occur at a younger age, which was the case of our patient who is aged 49 years. A single painless and palpable mass is the most common manifestation of the clinical presentation (61% of cases), but it can be multiple in some cases [12]. Other cutaneous signs like local inflammatory signs and skin retraction are rarely seen. Axillary lymph nodes are reported in 14% - 50% of cases [14]. The diagnosis of PBL is based firstly on ultrasound and mammography [3]. In fact, the imaging findings are non-specific. Magnetic resonance imaging (MRI) shows an iso-intensity on T1 and hyperintensity on T2 with heterogeneous or homogeneous enhancement [15]. TEP-CT is useful in the staging, the evaluation of response to treatment, and follow-up of lymphoma patients [3]. As with all lymphomas, the diagnosis of PBHL is confirmed by histology: excisional biopsy, needle aspiration or core biopsy, reporting the Nodular Sclerosis Classical Hodgkin Lymphoma type often observed in this particular breast form [12] [16]. Presence of typical Reed–Sternberg cells is the diagnostic clue. The use of immunochemistry showed positivity of proteins CD30 and CD15, in conjunction with CD45 negativity, further reinforced the diagnosis [17]. The other tests carried out as part of the pre-therapy work-up are: blood count, metabolic panel, lactate dehydrogenase, liver and renal function tests, hepatitis B, and hepatitis C [18]. Risk stratification of HL is based on the Ann Arbor stage and is done according to the EORTC or GHSG scores [5]. Early stage disease with direct extension to an extra-nodal site is considered as an advanced stage. It is typically treated with combined chemotherapy, targeted therapy, immunotherapy, radiation therapy and autologous stem cell rescue [18]. The role of surgery has not yet been established. The most common choice is between ABVD and BEACOPP, which is more effective but incriminated because of its toxicity and should not be recommended for patients over 60 years of age. TEP/CT is essential to assess interim response and modulate treatment accordingly: For BEACOPP-treated patients, if the interim PET is negative (Deauville 1 - 3), patients can be de-escalated to ABVD × 4 with no consolidation by radiotherapy. If the interim PET is positive (Deauville 4 - 5) patients should complete a total of six cycles of BEACOPP [19]. Brentuximab Vedotin (anti-CD30), Pembrolizumab (anti-PD1) are proposed for relapse/refractory Hodgkin lymphoma in combination

with chemotherapy regimens or as monotherapy with promising results [5] [17].

4. Conclusion

The importance of this case report is to present PBHL as a rare subset of extranodal HL. It is an uncommon oncologic disorder in its clinical, histopathologic, and radiological presentations. Given the rarity of the disease, treatment recommendations are not yet well established.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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