EXTRANODAL DIFFUSE LARGE B CELL LYMPHOMA WITH ADDITIONAL SPREAD TO THE BREAST: A CASE REPORT

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Abstract

Introduction. Non-Hodgkin Lymphoma (NHL) is a heterogeneous group of lymphoid malignancies with significant clinical, morphological, and genetic diversity. The most common subtype, Diffuse Large B-Cell Lymphoma (DLBCL), typically involves lymph nodes, spleen, or bone marrow, but can also present at extranodal sites. Extranodal involvement occurs in about 30% of cases, with the skin being a frequent site. Breast involvement, however, is rare.

Objectives. To describe the clinical case of a patient with primary cutaneous DLBCL and concurrent breast involvement, emphasizing the importance of detailed clinical examination and timely treatment.

Materials and Methods. A detailed clinical examination revealed a primary skin lesion on the thigh and a mass in the breast in a patient presenting to the QSUT Consultation Center. The patient underwent biopsy and imaging, and was treated with six cycles of the R-CHOP chemotherapy regimen. Hospital records were used to track the progression of the disease and treatment response.

Results. After completing the R-CHOP regimen, both the thigh and breast lesions completely regressed. Follow-up imaging and clinical evaluation confirmed complete remission, and the patient has remained in remission for two years.

Conclusions. This case highlights the clinical diversity of DLBCL and underscores the critical role of a comprehensive clinical examination in detecting extranodal involvement. The patient's complete remission following R-CHOP therapy further demonstrates the efficacy of this regimen in managing extranodal lymphoma.

Keywords. Non-Hodgkin Lymphoma, DLBCL, extranodal involvement, breast lymphoma, clinical examination.

LIMFOMA ME QELIZA B TË MËDHA DIFUZE EKSTRANODALE ME PËRHAPJE EDHE NË MAME: RAST KLINIK

Abstrakt

Hyrje. Limfoma Jo-Hodgkin (NHL) është një grup heterogjen i neoplazive limfoide me diversitet të rëndësishëm klinik, morfologjik dhe gjenetik. Nëntipi më i zakonshëm, Limfoma Difuze me Qeliza të Mëdha B (DLBCL), zakonisht përfshin nyjet limfatike, shpretkën ose palcën e kockave, por mund të paraqitet edhe në vende ekstranodale. Përfshirja ekstranodale ndodh në rreth 30% të rasteve, ku lëkura është një vend i shpeshtë. Megjithatë, përfshirja e gjirit është e rrallë.

Qëllimi. Të përshkruhet rasti klinik i një pacienti me DLBCL primare të lëkurës dhe përfshirje të njëkohshme të gjirit, duke theksuar rëndësinë e ekzaminimit të detajuar klinik dhe trajtimit në kohë.

Materiale dhe Metoda. Një ekzaminim i detajuar klinik zbuloi një lezion primar të lëkurës në kofshë dhe një masë në gji te një paciente që u paraqit në Qendrën e Konsultave QSUT. Pacientja iu nënshtrua biopsisë dhe ekzaminimeve imazherike dhe u trajtua me gjashtë cikle të regjimit të kimioterapisë R-CHOP. Regjistrat spitalorë u përdorën për të ndjekur progresionin e sëmundjes

dhe përgjigjen ndaj trajtimit.
Rezultatet. Pas përfundimit të regjimit R-CHOP, lezionet në kofshë dhe gji regreduan plotësisht. Imazheria dhe vlerësimi klinik gjatë ndjekjes konfirmuan remision të plotë, dhe pacientja ka qendruar në remision për dy vjet.
Përfundime. Ky rast nënvizon diversitetin klinik të DLBCL-së dhe thekson rolin thelbësor të një ekzaminimi të plotë klinik në zbulimin e përfshirjes ekstranodale. Remisioni i plotë i pacientes pas terapisë R-CHOP gjithashtu demonstron efikasitetin e këtij regjimi në menaxhimin e limfomës ekstranodale.

Fjalë kyçe: Limfoma Jo-Hodgkin, DLBCL, përfshirje ekstranodale, limfoma e gjirit, ekzaminim klinik

Introduction

Non-Hodgkin's Lymphoma (NHL) comprises a diverse group of lymphoproliferative disorders, characterized by significant clinical, morphological, histological, biological, genetic, and molecular variability (1). The annual incidence of NHL ranges from 14 to 19 cases per 100,000 individuals (2). NHL is generally categorized into B-cell and T-cell types, with approximately 90% of cases being of B-cell origin, which includes various subtypes, among which Diffuse Large B-Cell Lymphoma (DLBCL) is the most prevalent.

DLBCL is an aggressive lymphoma characterized by rapidly enlarging tumors, typically found in lymph nodes, spleen, liver, or bone marrow. It accounts for 20-50% of malignant NHL cases in adults (3) and has an annual incidence of 3-4 cases per 100,000 people (2). While DLBCL is commonly associated with nodal involvement, it can also arise in extra - nodal locations, with approximately 30% of cases exhibiting extra - nodal presentation. The gastrointestinal tract is the most common extra - nodal site, followed by the skin. At diagnosis, skin involvement may present as plaques, papules, nodules, or ulcers. Other extra - nodal sites may include the central nervous system (CNS), bone, thyroid, reproductive organs, and breast (4-7).

This article reports the case of a patient diagnosed with extra - nodal DLBCL, with initial presentation in the skin of the thigh and additional involvement of the breast. The patient was diagnosed with hematological malignancy for the first time and received treatment accordingly. Clinical data and imaging findings were obtained from hospitalization records in the Hematology clinic.

Clinical Presentation

A 48-year-old patient, V.K., presented to the Hematology Consultation Center at QSUT in June 2022 for initiation of treatment for lymphoma. The patient exhibited a large lesion on the right thigh extending into the inguinal region, accompanied by significant edema in the right leg. The disease had first manifested five years earlier as a localized skin lesion on the right thigh, progressively enlarging over the following year (Fig.1 a,b). Approximately three to four months before seeking consultation, the lesions expanded rapidly, and the patient developed severe lower-extremity edema.

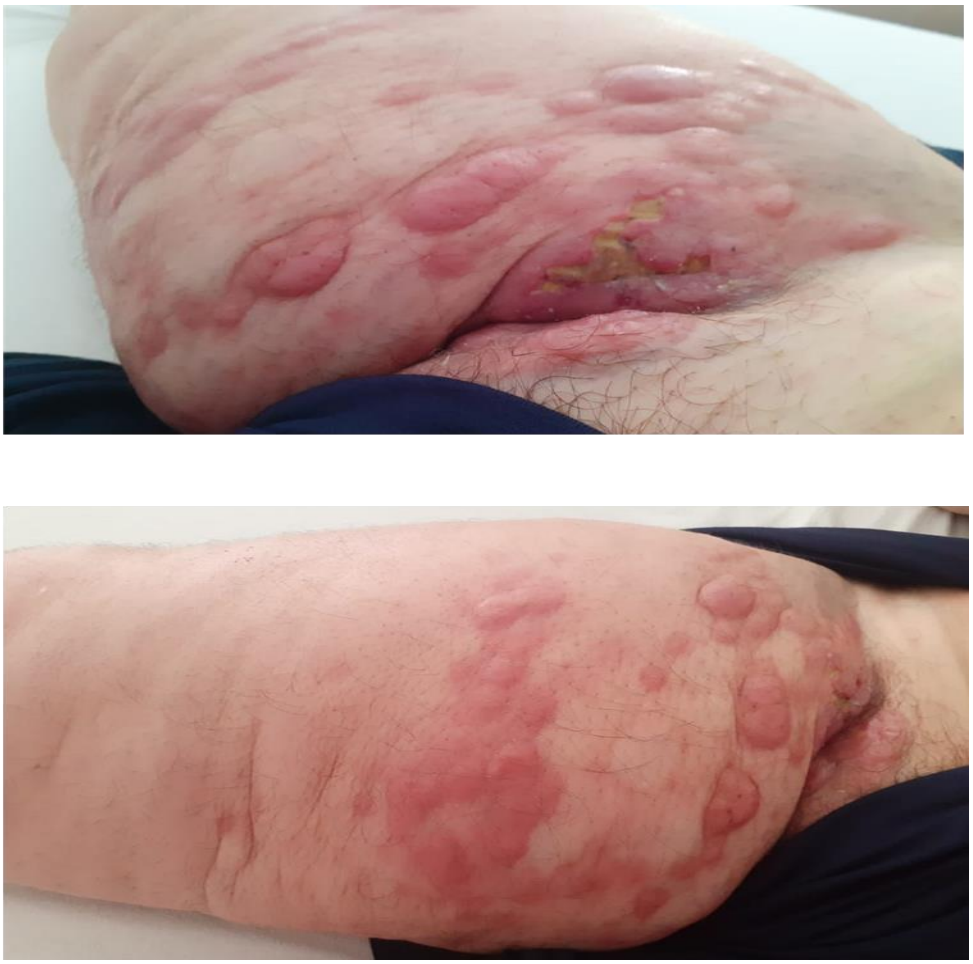
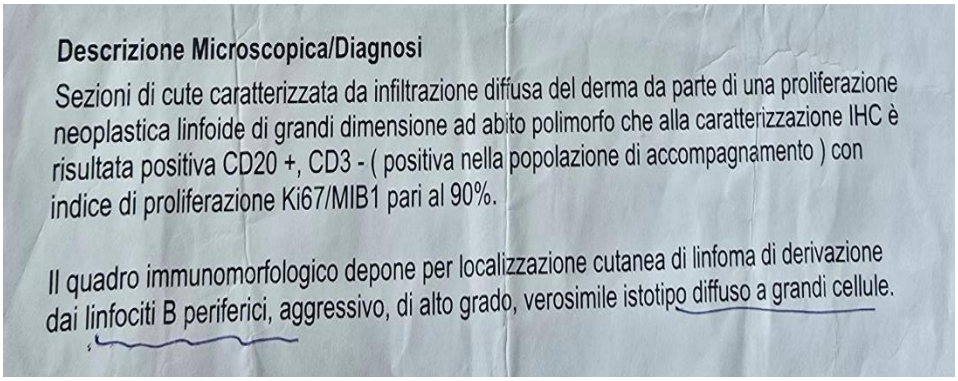


Figure 1 (a, b). Thigh lesions at the onset of treatment (June 2022). The images depict papulomatous, nodular, and ulcerative lesions on the skin, along with pronounced edema in the right leg.

The patient initially sought medical attention in her district of Durrës, where imaging studies were conducted. Subsequently, she visited a private hospital in Tirana, where a biopsy of the skin lesion on the right thigh was performed. The biopsy confirmed the diagnosis of Non-Hodgkin's Lymphoma (NHL), specifically Diffuse Large B-Cell Lymphoma (DLBCL). Following this, the patient was referred to the Hematology Consultation Center at QSUT to begin specific treatment.
Diagnostic Findings. On physical examination, no significant peripheral lymphadenopathy was observed, except for small inflammatory lymph nodes on MRI. Imaging studies revealed no thoraco-abdominal lymphadenopathy. The skin biopsy revealed diffuse infiltration of the dermis by a large lymphoid neoplastic proliferation with polymorphic characteristics. Immunohistochemistry (IHC) findings were CD20 positive, CD3 negative, and a Ki-67 proliferation index of 90%, confirming the diagnosis of DLBCL (Fig. 2).



Descrizione Microscopica/Diagnosi

Sezioni di cute caratterizzata da infiltrazione diffusa del derma da parte di una proliferazione neoplastica linfoide di grandi dimensione ad abito polimorfo che alla caratterizzazione IHC è risultata positiva CD20 +, CD3 - (positiva nella popolazione di accompagnamento) con indice di proliferazione Ki67/MIB1 pari al 90%.

Il quadro immunomorfologico depone per localizzazione cutanea di linfoma di derivazione dai linfociti B periferici, aggressivo, di alto grado, verosimile istotipo diffuso a grandi cellule.

Figure 2. Biopsy result of thigh lesions. The skin section shows diffuse infiltration of the dermis by a large lymphoid neoplastic proliferation with polymorphic characteristics. Immunohistochemistry (IHC) reveals CD20 positivity, CD3 negativity, and a Ki67 proliferation index of 90%. **Conclusion**: Malignant Non-Hodgkin Lymphoma, Diffuse Large B-Cell Lymphoma (DLBCL).

During the treatment process, a detailed physical examination identified a palpable mass in the left breast. Ultrasound examination categorized the mass as BI-RADS 5, indicating a high likelihood of malignancy. A biopsy of the breast mass revealed tissue fragments with extensive necrotic lesions and areas of infiltration by atypical basophilic cells (Fig.3). Immunohistochemical analysis demonstrated no nuclear staining for estrogen receptor (ER), slight nuclear staining in 30% of cells for progesterone receptor (PGR), and positivity for CD45 and CD20, confirming the diagnosis of NHL, consistent with DLBCL (Fig. 4 a,b)

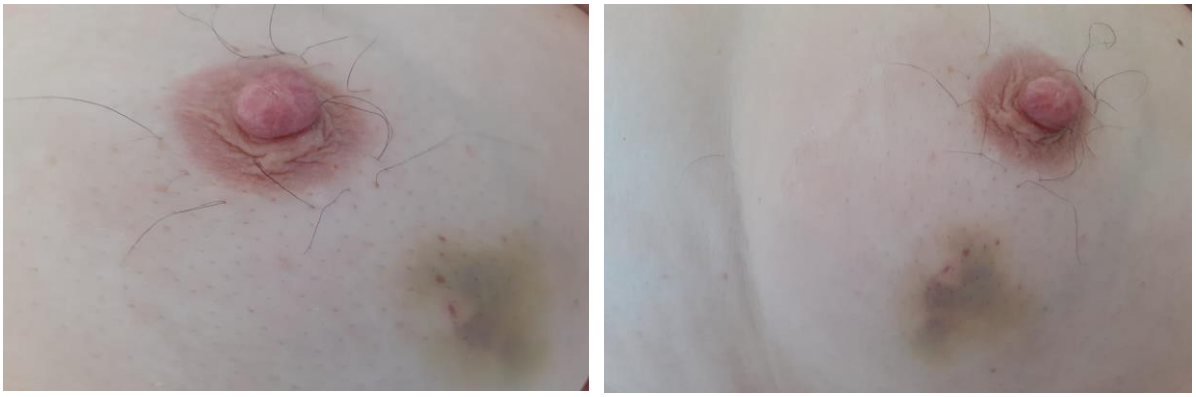
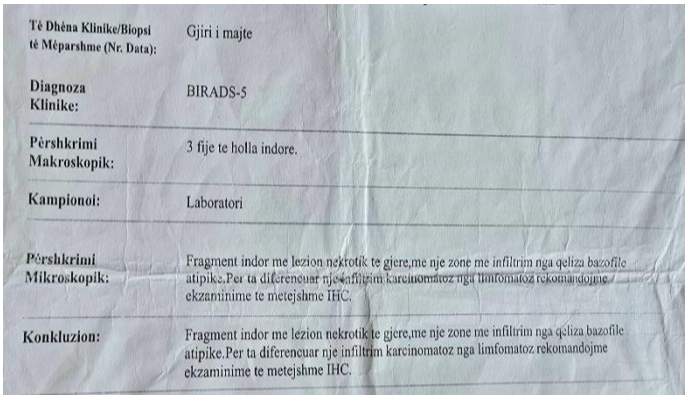


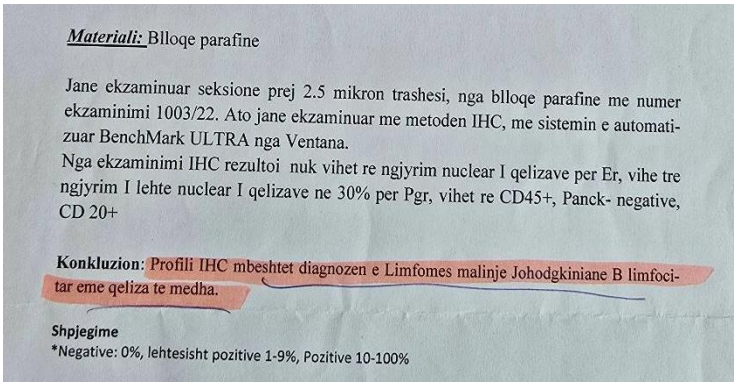
Figure 3. The mass in the left breast, following biopsy. The image shows the scar from the aspiration procedure.



Të Dhëna Klinike/Biopsi të Mëparshme (Nr. Data):	Gjiri i majte
Diagnoza Klinike:	BIRADS-5
Përshkrimi Makroskopik:	3 fije te holla indore.
Kampionoi:	Laboratori
Përshkrimi Mikroskopik:	Fragment indor me lezion nekrotik te gjere,me nje zone me infiltrim nga qeliza bazofile atipike.Per ta diferencuar nje infiltrim karcinomatoz nga limfomatoz rekomandojme ekzaminime te metejshme IHC.
Konkluzion:	Fragment indor me lezion nekrotik te gjere,me nje zone me infiltrim nga qeliza bazofile atipike.Per ta diferencuar nje infiltrim karcinomatoz nga limfomatoz rekomandojme ekzaminime te metejshme IHC.

Figure 4 a. Breast Biopsy Result: Tissue fragment showing extensive necrotic lesions, along with

an area of infiltration by atypical basophilic cells. Immunohistochemistry (IHC) examinations are recommended to differentiate between carcinomatous and lymphomatous infiltration.



Materiali: Blloqe parafine

Jane ekzaminuar seksione prej 2.5 mikron trashesi, nga blloqe parafine me numer ekzaminimi 1003/22. Ato jane ekzaminuar me metoden IHC, me sistemin e automatizuar BenchMark ULTRA nga Ventana.
Nga ekzaminimi IHC rezultoi nuk vihet re ngjyrim nuclear I qelizave per Er, vihe tre ngjyrim I lehte nuclear I qelizave ne 30% per Pgr, vihet re CD45+, Panck- negative, CD 20+

Konkluzion: Profili IHC mbeshtet diagnozen e Limfomes malinje Johodgkiniane B limfocitar eme qeliza te medha.

Shpjegime
*Negative: 0%, lehtesisht pozitive 1-9%, Pozitive 10-100%

Figure 4 b. Immunohistochemistry Result of the Breast Mass: Immunohistochemistry findings: No nuclear staining of cells for estrogen receptor (ER), slight nuclear staining observed in 30% of cells for progesterone receptor (PGR). CD45 positive, PanCK negative, and CD20 positive.

Conclusion: Non-Hodgkin Lymphoma (NHL), Diffuse Large B-Cell

Lymphoma (DLBCL).

Treatment. The patient began treatment with the R-CHOP protocol, which includes Rituximab, Cyclophosphamide, Vincristine, Doxorubicin, and Prednisolone. After the initial two cycles of treatment, there was a pronounced regression of the thigh lesions, with most of the lesions disappearing (Fig. 5a). By the fourth cycle, only scars remained (Fig. 6b). Upon completing six cycles of treatment, the lesions in both the thigh and breast had completely resolved.

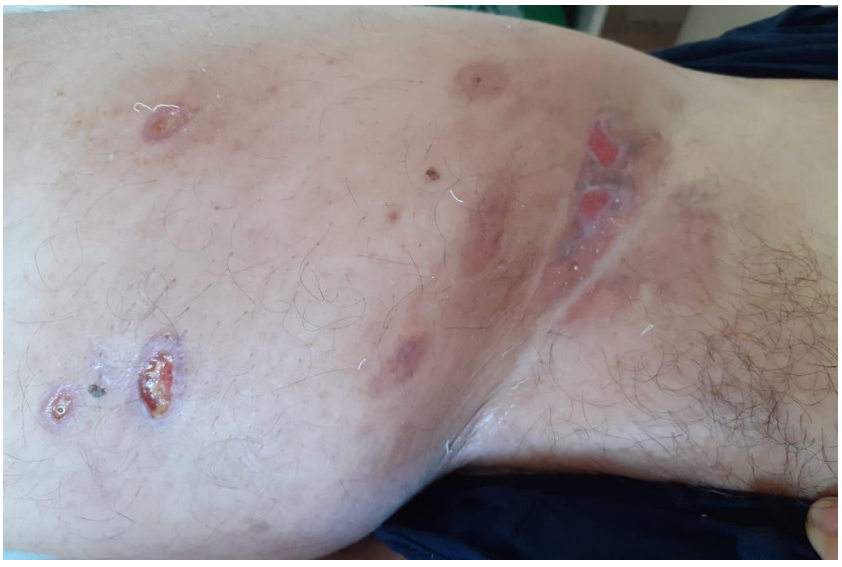


Figure 5 a. Thigh Lesions After Two Cycles of Treatment (July 2022):
Significant regression observed, with the disappearance of most of the lesions.

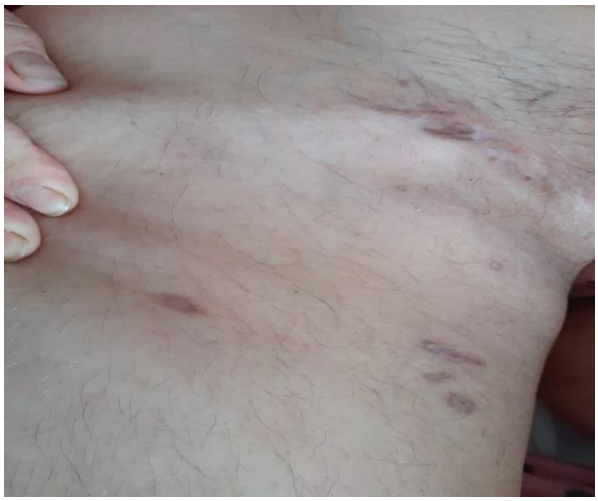
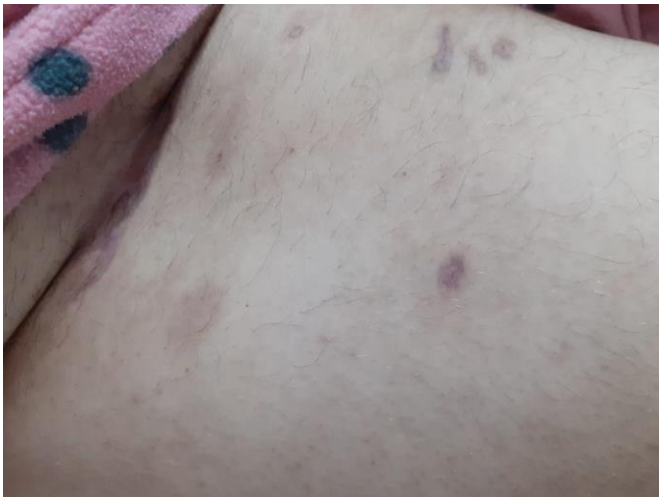



Figure 6 a,b. Lesions after 4 treatment cycles (September 2022). Only scars remain

Outcome. Currently, the patient remains in complete remission, with no recurrence of lesions for over two years. The patient's psychological well-being was also addressed during the treatment process, given her history of depressive disorder. She continues follow-up evaluations to monitor her long-term remission status.

Discussion

Diffuse Large B-Cell Lymphoma (DLBCL) is the most common subtype of Non-Hodgkin's Lymphoma (NHL), representing an aggressive malignancy with diverse clinical presentations. While nodal involvement remains the predominant site of disease, approximately 30% of DLBCL cases exhibit extranodal manifestations. Extranodal DLBCL can affect nearly any organ, with the gastrointestinal tract being the most frequent site, followed by other less common locations such as the skin, central nervous system, bone, and breast (2, 4-7). The case presented here highlights the significance of extranodal DLBCL involving the skin and breast, illustrating the diagnostic and therapeutic challenges associated with such presentations.

The patient's initial presentation with a large, ulcerated lesion on the thigh, along with extensive edema, underscores the variability in lymphoma manifestations. Skin involvement in lymphoma is uncommon but not rare, typically presenting as papules, nodules, or ulcers, and often mimicking other dermatologic or oncologic conditions (4). In this case, the delayed progression from localized skin lesions to more extensive involvement of the thigh over five years exemplifies the often insidious nature of the disease.

Of particular note is the involvement of the breast in this case, which is a rare extranodal site for DLBCL. Breast lymphoma accounts for less than 1% of all breast malignancies and is most frequently associated with NHL. The presence of a palpable breast mass, confirmed to be DLBCL via biopsy and immunohistochemistry, reinforces the need for thorough and systematic clinical examinations, especially in patients with known or suspected lymphoproliferative disorders (6).

Histopathological and immunohistochemical evaluations were pivotal in establishing the diagnosis. CD20 positivity and a high Ki-67 proliferation index supported the classification of this malignancy as DLBCL, distinguishing it from other lymphoid or carcinomatous infiltrations. The biopsy results from both the thigh and breast were concordant, affirming the diagnosis of extranodal DLBCL with multifocal involvement (5).

The successful response to R-CHOP therapy, with complete remission achieved after six cycles, highlights the efficacy of this standard treatment protocol. R-CHOP remains the cornerstone for managing DLBCL, offering a high likelihood of durable remission even in advanced or extranodal cases. The pronounced regression of lesions after the initial cycles and the absence of residual disease after treatment underscore the importance of timely and appropriate therapeutic interventions (3).

This case also underscores the psychological impact of a lymphoma diagnosis and the critical role of mental health support during treatment. The patient's history of depressive disorder necessitated a multidisciplinary approach, integrating psychological support with oncologic care. Addressing the emotional and psychological well-being of patients is integral to achieving holistic and effective treatment outcomes.

Conclusion

This case highlights the diagnostic challenges posed by extranodal DLBCL and emphasizes the value of a comprehensive clinical examination, systematic diagnostic workup, and multidisciplinary care. The rare presentation of DLBCL involving both the skin and breast serves as a reminder of the disease's diverse manifestations and underscores the importance of individualized patient management.

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