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Destructive Breast Relapse of Diffuse Large B-cell Lymphoma After Complete Remission: Surgical and Reconstructive Management

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Abstract

Breast involvement in diffuse large B-cell lymphoma (DLBCL) is rare, and breast relapse after complete remission is particularly uncommon. DLBCL is treated primarily with systemic immunochemotherapy, but surgery may be indicated for severe local complications.

We report a woman diagnosed with DLBCL at the age of 41 years who developed a breast relapse seven years after a second complete metabolic response. She presented with a massive ulcerated, necrotic, and bleeding lesion involving over 50% of the left breast and the nipple-areolar complex. Histopathological examination confirmed recurrent DLBCL, and positron emission tomography/computed tomography (PET/CT) showed nodal involvement without confirmed distant disease. Given the extent of tissue destruction, bleeding, and risk of secondary infection, multidisciplinary consultation recommended mastectomy with axillary lymph node dissection and immediate reconstruction with a pedicled latissimus dorsi flap. The flap survived completely, and the only complication was a small donor-site seroma that resolved with conservative management. Six cycles of R-DHAP (rituximab, dexamethasone, cytarabine, and cisplatin) were started one month after surgery without radiotherapy. At one year of follow-up, the flap was viable, and the patient was doing well.

This case illustrates that radical surgery with immediate reconstruction may be considered as a complement to systemic therapy in selected patients with breast DLBCL when severe local complications require surgical intervention.

Categories: Plastic Surgery, Pathology, Oncology
Keywords: breast lymphoma, breast reconstruction, breast relapse, diffuse large b-cell lymphoma, latissimus dorsi flap, mastectomy

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, accounting for approximately 30%-40% of cases worldwide [1]. Extranodal involvement is observed in a substantial proportion of patients, with the gastrointestinal tract, bone, and central nervous system among the commonly affected sites [1]. Breast involvement is rare and may occur as either primary breast lymphoma or secondary breast involvement in the setting of systemic lymphoma. Breast DLBCL is classified as primary when it arises within the breast without evidence of lymphoma elsewhere, and as secondary when it reflects systemic disease, relapse, or dissemination from a previously diagnosed lymphoma [2].

Breast relapse after complete remission is particularly uncommon and may pose a diagnostic challenge, as its clinical and radiological features can overlap with those of primary breast carcinoma, including inflammatory breast cancer [2]. Histopathological examination, complemented by immunohistochemistry, is essential to establish the diagnosis and confirm the B-cell origin of the lymphoma.

Because DLBCL is a systemic hematologic malignancy, treatment is primarily based on systemic immunochemotherapy, with rituximab-containing regimens forming a cornerstone of therapy [1,3,4]. Surgery generally has a limited role and is mainly performed for diagnostic purposes or for selected local complications [3,4]. Extensive resection is not routinely recommended but may be considered in exceptional circumstances, such as locally destructive disease with ulceration, bleeding, or infection that cannot be controlled by nonsurgical treatment.

In this report, we present a case of breast relapse of DLBCL with nodal involvement, occurring seven years after a second complete metabolic remission and presenting as an extensive ulcerated and necrotic lesion. The patient underwent mastectomy with axillary lymph node dissection, followed by immediate reconstruction with a pedicled latissimus dorsi flap, and remained well at one year of follow-up. This case

illustrates an exceptional indication for surgery in breast lymphoma and highlights the role of immediate autologous reconstruction in the multidisciplinary management of advanced, locally destructive disease.

Case Presentation

A woman, aged 41 years at the time, was diagnosed with Ann Arbor stage II DLBCL in 2013. She achieved a complete metabolic response (hereafter, complete remission) after six cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), confirmed by positron emission tomography/computed tomography (PET/CT) according to the Lugano classification [5]. She remained under regular surveillance, with clinical evaluations every three to six months during the first two years and annually thereafter.

In 2016, she had an isolated nodal relapse, treated with salvage rituximab, ifosfamide, carboplatin, and etoposide (R-ICE) chemotherapy, resulting in a second complete metabolic response.

Seven years later, in 2023, at the age of 51, she presented with a progressively enlarging, painful mass of the left breast. Over several months, the lesion evolved into a large exophytic tumor with ulceration, spontaneous bleeding, malodorous necrosis, and significant local discomfort (Figure *1*).

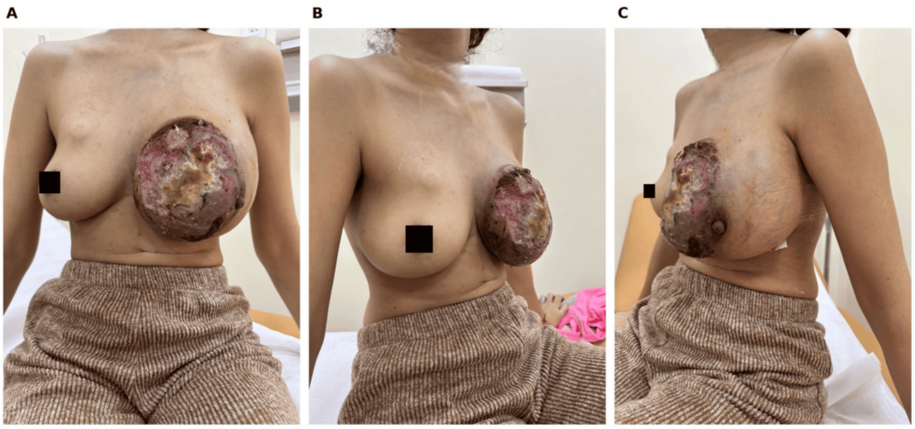


FIGURE 1: Preoperative clinical presentation of recurrent diffuse large B-cell lymphoma of the left breast.

Clinical photographs showing the extensive ulcerated, necrotic, and hemorrhagic lesion involving the left breast and nipple-areolar complex: (A) frontal view; (B) oblique view; (C) lateral view.

Clinical examination revealed a destructive lesion involving more than 50% of the breast surface and extending to all quadrants except the upper outer quadrant. The nipple-areolar complex was completely infiltrated, with disease extending from the parasternal region to the inframammary fold. A mobile, ipsilateral axillary lymph node of approximately 2.5 × 2 cm was also palpable (Table *1*).

Year	Event
2013	Ann Arbor stage II DLBCL diagnosed
	Six cycles of R-CHOP → complete remission
2016	Isolated nodal relapse
	Salvage R-ICE chemotherapy → second complete remission
2023	Destructive breast relapse
	Mastectomy with axillary lymph node dissection and immediate pedicled latissimus dorsi flap reconstruction
	R-DHAP, six cycles, started one month after surgery
2024	One-year follow-up: viable flap, patient doing well

TABLE 1: Clinical timeline of the patient's disease course.

DLBCL, diffuse large B-cell lymphoma; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; R-ICE, rituximab, ifosfamide, carboplatin, etoposide; R-DHAP, rituximab, dexamethasone, cytarabine, cisplatin

Fluorine-18 fluorodeoxyglucose (18F-FDG) PET/CT showed hypermetabolic uptake in the left breast/chest-wall region (SUVmax 6.62), the left internal mammary chain, and bilateral axillary lymph nodes, consistent with metabolically active nodal disease (Figure *2*). Additional hypermetabolic osseous foci were considered indeterminate in the absence of confirmatory imaging or histopathological correlation.

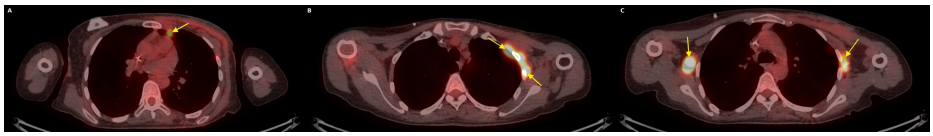


FIGURE 2: 18F-FDG PET/CT demonstrating hypermetabolic left breast and regional lymph node involvement in recurrent diffuse large B-cell lymphoma.

Yellow arrows indicate the hypermetabolic foci in each panel. (A) Axial fused PET/CT demonstrating hypermetabolic uptake in the left breast region (arrow; SUVmax 6.62). (B) Axial fused PET/CT demonstrating two hypermetabolic foci in the left internal mammary chain (arrows; SUVmax 8.36 and 14.12). (C) Axial fused PET/CT demonstrating bilateral hypermetabolic axillary lymph nodes (arrows; SUVmax 28.52 on the right and 26.92 on the left).

18F-FDG, fluorine-18 fluorodeoxyglucose; PET/CT, positron emission tomography/computed tomography

Ultrasound-guided core needle biopsy was subsequently performed. Histopathological examination demonstrated diffuse sheets of large atypical lymphoid cells with vesicular nuclei, prominent nucleoli, and numerous mitotic figures (Figure *3*). Immunohistochemical analysis showed diffuse positivity for CD20, CD45, CD79a, and PAX5, with a markedly elevated Ki-67 proliferation index of approximately 80%, supporting the diagnosis of recurrent DLBCL (Figure *4*).

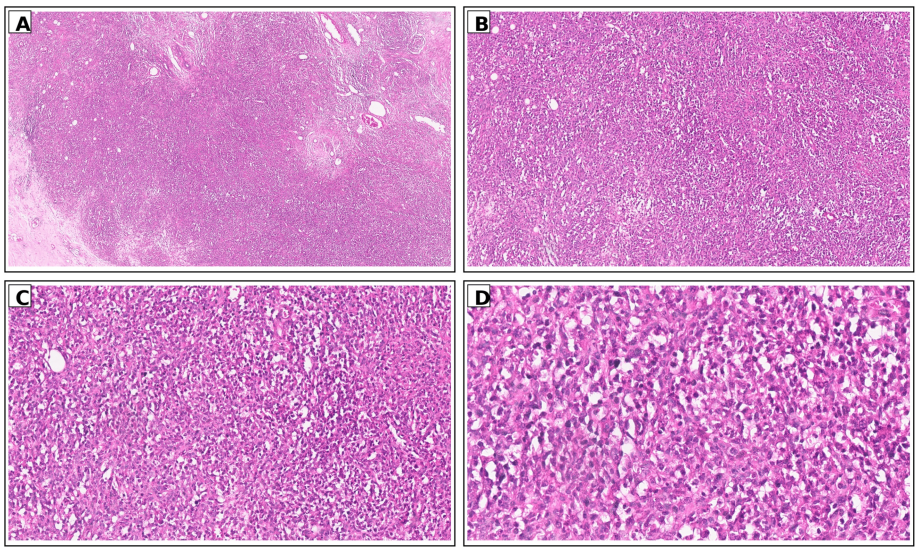


FIGURE 3: Histopathological findings of recurrent diffuse large B-cell lymphoma.

Hematoxylin and eosin (H&E)-stained sections showing diffuse infiltration by large atypical lymphoid cells at progressively higher magnifications: (A) H&E, ×4; (B) H&E, ×10; (C) H&E, ×20; and (D) H&E, ×40.

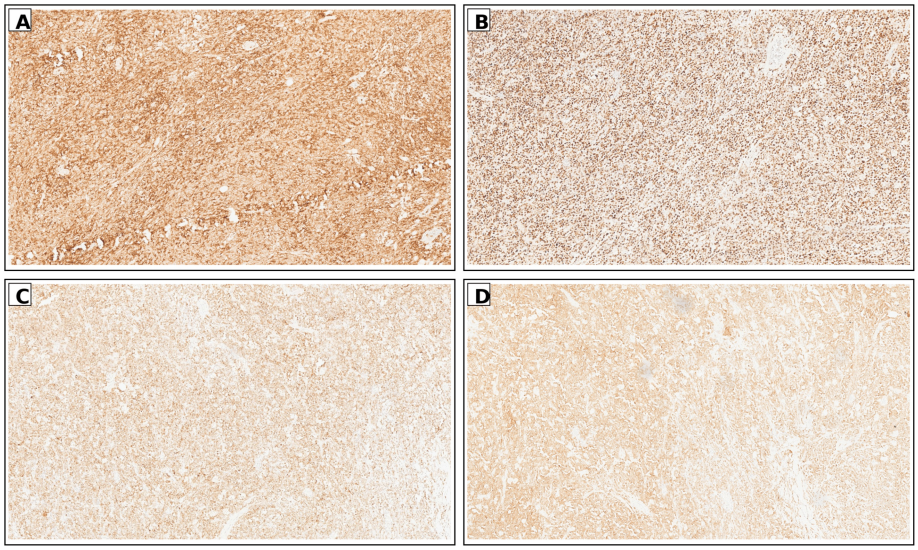


FIGURE 4: Immunohistochemical characterization of recurrent diffuse large B-cell lymphoma.

(A) Diffuse positive staining for leukocyte common antigen (LCA/CD45). (B) Ki-67 proliferation index estimated at approximately 80%. (C) Diffuse positive staining for CD79a. (D) Diffuse positive staining for PAX5. All panels show immunohistochemical staining at ×10 magnification.

Review of the available histopathological reports from 2013 to 2016 confirmed previous diagnoses of DLBCL, with documented CD20 positivity. However, direct histopathological comparison with the current breast specimen was not possible because the original slides from the previous episodes were unavailable for review.

Staging with PET/CT and laboratory investigations (complete blood count, serum lactate dehydrogenase, and renal and liver function tests) showed nodal involvement without definitive evidence of distant disease.

Following multidisciplinary discussion involving hematologists, breast surgeons, plastic surgeons, radiologists, and pathologists, surgery was recommended because of extensive local tissue destruction,

persistent ulceration, recurrent bleeding, malodorous necrosis, and a high risk of secondary infection. The objectives were local disease control, improved quality of life, and facilitation of subsequent systemic therapy.

A left mastectomy with complete excision of all necrotic and ulcerated tissue was performed, together with axillary lymph node dissection and partial resection of the pectoralis major muscle because of deep tumor infiltration. The defect was immediately reconstructed with a pedicled latissimus dorsi musculocutaneous flap based on the thoracodorsal vessels. A 16 × 9 cm skin paddle provided tension-free coverage of the chest wall defect. The donor site was closed primarily without tension, and closed-suction drains were placed at the donor and recipient sites (Figure *5*).

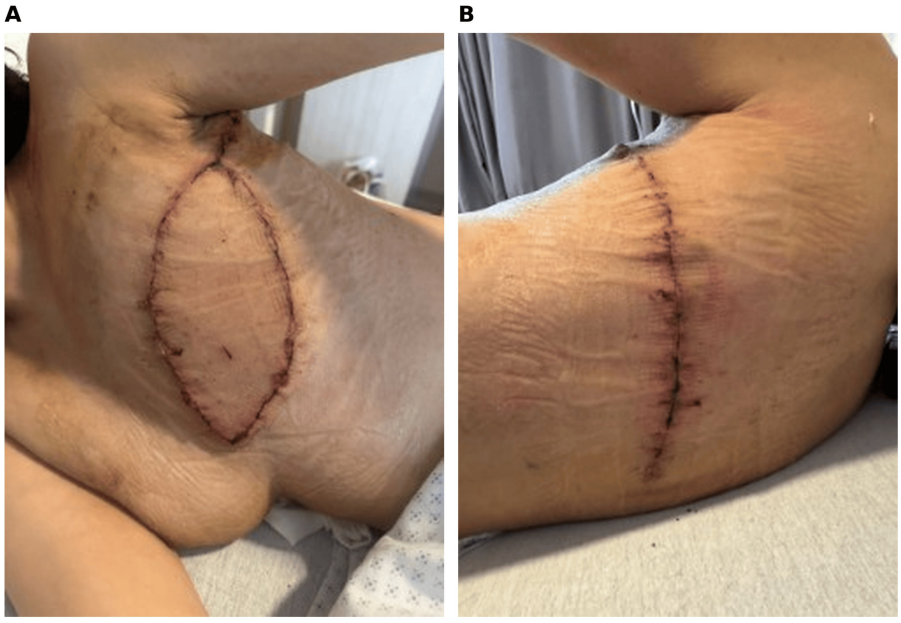


FIGURE 5: Postoperative outcome following breast reconstruction with a latissimus dorsi flap.

Postoperative assessment demonstrating flap viability, satisfactory wound healing, and durable chest wall coverage. (A) Anterior view of the reconstructed breast demonstrating a viable latissimus dorsi flap. (B) Lateral view showing the healed donor-site incision.

Histopathological examination of the mastectomy specimen revealed extensive infiltration of the mammary and muscular tissues by a malignant undifferentiated proliferation with lymphomatous features, consistent with the previously established diagnosis of DLBCL. Five gross lesions were identified within the specimen, measuring 5 × 4.5 × 12 cm, 4.5 × 2.2 × 12 cm, 7 × 6.5 × 12 cm, 2.3 × 1.2 × 2.5 cm, and 1.5 × 1.1 × 1.5 cm, respectively. The nipple was extensively infiltrated, although the epidermis was spared, and no features of Paget disease were identified. Microscopic examination confirmed infiltration of the striated muscle, with perineural invasion and no vascular tumor emboli. The deep margin was involved by tumor.

Regarding surgical margins, the lateral margins were free of tumor, while the superior margin was close, measuring less than 1 mm. The deep margin was involved by tumor. Axillary lymph node dissection yielded eight lymph nodes, five of which were involved by the same lymphomatous process; the remaining three showed reactive follicular hyperplasia and sinus histiocytosis.

Recovery was favorable. The flap remained fully viable, with no partial or total necrosis, wound dehiscence, or surgical-site infection. The only complication was a small donor-site seroma, which resolved completely within 15 days with conservative management.

One month after surgery, the patient received six cycles of systemic immunochemotherapy with rituximab, dexamethasone, high-dose cytarabine, and cisplatin (R-DHAP). No radiotherapy was administered. Follow-up PET/CT performed after completion of chemotherapy demonstrated persistent osseous lesions, which remained indeterminate. At one year of follow-up, the flap remained viable, and the patient was clinically doing well, with a satisfactory reconstructive outcome. However, the reconstructive outcome should not be interpreted as evidence of complete lymphoma remission. This case report was written in accordance with the CARE (CAse REport) guidelines [6].

Discussion

Breast involvement by DLBCL is uncommon, and breast relapse after complete remission is a rare presentation [1,2]. Although breast DLBCL may resemble primary breast carcinoma, its management differs substantially: systemic immunochemotherapy, rather than definitive surgical resection, remains the cornerstone of treatment, as recommended by current NCCN and ESMO guidelines [1,3,4].

Clinically and radiologically, breast DLBCL may mimic inflammatory breast carcinoma or breast abscess, and its presentation and imaging findings are variable and nonspecific. Features such as hypoechoic lesions on ultrasonography may raise suspicion for lymphoma but are insufficient to establish the diagnosis, which requires histopathological and immunohistochemical confirmation [2].

The mechanisms underlying delayed breast relapse remain incompletely understood. In our patient, relapse occurred seven years after the second complete remission, highlighting the possibility of late relapse and the importance of continued clinical surveillance in patients with a history of DLBCL.

Evidence on the role of surgery comes mainly from primary breast lymphoma, where mastectomy has not shown a clear survival advantage over less extensive approaches (Table *2*). Liu et al. analyzed prognostic factors and survival in a pooled series of 93 cases [7], and Jennings et al. found no survival or recurrence benefit from mastectomy [8]. Avilés et al. evaluated therapeutic approaches in a controlled clinical trial [9]. Hosein et al. described treatment patterns and outcomes in the rituximab era [10], and Ryan et al. reported no benefit from mastectomy compared with biopsy or lumpectomy [11]. These findings support a limited routine role for extensive breast surgery. However, because these studies predominantly concern primary breast lymphoma, their findings should be extrapolated cautiously to secondary breast involvement.

Study	Population/study design	Main finding relevant to the present case
Liu et al. (2005) [7]	Primary breast lymphoma; pooled analysis of 93 cases	Evaluated prognostic factors, treatment strategies, and survival
Jennings et al. (2007) [8]	Primary breast lymphoma; pooled analysis of published cases	No demonstrated survival or recurrence benefit from mastectomy
Avilés et al. (2005) [9]	Primary breast lymphoma; controlled clinical trial	Evaluated outcomes associated with different therapeutic approaches
Hosein et al. (2014) [10]	Primary breast DLBCL; multicenter retrospective study in the rituximab era	Described treatment patterns, survival outcomes, and relapse characteristics
Ryan et al. (2008) [11]	Primary breast DLBCL; international retrospective study	No demonstrated benefit from mastectomy compared with biopsy or lumpectomy
Present case	Secondary destructive breast relapse after complete remission	Mastectomy with axillary lymph node dissection and immediate pedicled latissimus dorsi flap reconstruction for severe local complications, followed by R-DHAP; flap viable and patient doing well at one year

TABLE 2: Selected studies on primary breast lymphoma and comparison with the present case.

DLBCL, diffuse large B-cell lymphoma; R-DHAP, rituximab, dexamethasone, cytarabine, cisplatin

Nevertheless, surgery may be considered in exceptional circumstances when severe local complications cannot be controlled by nonsurgical treatment alone. In our patient, extensive tissue destruction, ulceration, recurrent bleeding, and necrotic tissue prompted mastectomy with axillary lymph node dissection as a salvage procedure. Systemic therapy alone was not expected to control the ongoing bleeding, malodorous necrosis, and risk of secondary infection, nor to allow wound healing. Because PET/CT showed nodal involvement (Figure *2*), surgery was not intended to treat the disease systemically but to control the destructive local disease, remove severely compromised tissue, and create favorable conditions for wound healing and subsequent systemic therapy.

Following mastectomy, reconstruction was a critical part of treatment rather than a purely aesthetic procedure. Its main objective was to restore chest wall integrity with durable, well-vascularized tissue, promote wound healing, and reduce the risk of further local complications [12]. Autologous options include

pedicled perforator flaps [13], but a pedicled latissimus dorsi flap was considered most appropriate in our patient because of its reliable thoracodorsal pedicle, broad arc of rotation, and ability to provide vascularized muscle and skin to cover extensive chest wall defects without microsurgical anastomosis [14,15]. Implant-based reconstruction was avoided because extensive ulceration, tissue necrosis, and chronic inflammation raised concerns about wound contamination, infection, and implant-related complications. Free flap reconstruction was considered unnecessary because a suitable regional pedicled flap was available, and skin grafting alone would not have met the soft-tissue coverage requirements. The latissimus dorsi flap therefore offered the best balance between reliability, technical feasibility, and durable coverage [14,15].

The postoperative outcome supports this strategy. The flap survived completely, without necrosis, wound dehiscence, or surgical-site infection. The only complication was a small donor-site seroma, which resolved with conservative management. Donor-site seroma is a recognized complication of latissimus dorsi harvest, and donor-site morbidity should be weighed when choosing this flap [12,14]. Systemic immunochemotherapy (six cycles of R-DHAP) was started one month after surgery, and no radiotherapy was administered. At one year, the flap remained viable and the patient was doing well. Despite the favorable clinical and reconstructive outcome, follow-up PET/CT demonstrated persistent indeterminate osseous lesions after systemic treatment. Therefore, complete metabolic response could not be established based on the available imaging findings. This distinction is important, as successful reconstruction and satisfactory wound healing do not necessarily reflect oncological remission. This shows that complex reconstruction can be coordinated with subsequent systemic treatment in selected patients when healing allows timely initiation. As this is a single case, no general conclusions can be drawn about the effect of immediate reconstruction on treatment delays in breast lymphoma. The reconstruction should be regarded as complementary to, not a substitute for, systemic lymphoma-directed treatment [1,3,4].

As shown in Table *2*, most published studies address primary breast lymphoma, with systemic therapy as the principal component of management [7-11]. Our patient instead presented with destructive secondary breast involvement after previous complete remission, requiring mastectomy with axillary lymph node dissection for severe local complications, followed by immediate autologous reconstruction. The available literature offers little evidence on reconstructive management in this setting.

Strengths of this report include its description of an uncommon presentation with detailed clinical, radiological, and histopathological findings, the multidisciplinary decision-making, and a one-year follow-up documenting flap viability and the initiation of systemic therapy after immediate reconstruction. Its limitations are those of a single case: the findings cannot be generalized, and a one-year follow-up with no comparative data does not allow conclusions about the long-term oncological impact of surgery or the effect of immediate reconstruction on the timing of systemic treatment. Nevertheless, the case illustrates a potential approach for carefully selected patients with advanced, locally destructive disease.

Conclusions

This case illustrates an exceptional indication for extensive surgery and immediate autologous reconstruction in the management of locally destructive breast DLBCL relapse. Although the surgical and reconstructive outcomes were favorable at one year, these findings should not be interpreted as evidence of lymphoma remission or disease control. Treatment decisions in such complex cases should be individualized and guided by multidisciplinary collaboration. Further follow-up is necessary to assess long-term oncological outcomes. The rarity of this presentation and the limitations inherent to a single case report preclude broader conclusions regarding treatment efficacy.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Maria Kharbouch, Hamza Tazi, Rita Ait Benhamou, Hind Souiheb, Mounia El Omari

Acquisition, analysis, or interpretation of data: Maria Kharbouch, Hamza Tazi, Rita Ait Benhamou, Hind Souiheb, Mounia El Omari

Drafting of the manuscript: Maria Kharbouch, Hamza Tazi, Rita Ait Benhamou, Hind Souiheb, Mounia El Omari

Critical review of the manuscript for important intellectual content: Maria Kharbouch, Hamza Tazi, Rita Ait Benhamou, Hind Souiheb, Mounia El Omari

Supervision: Mounia El Omari

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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