Gac Méd Caracas 2026;134(1):264-269
DOI: 10.47307/GMC.2026.134.1.21

Unlocking the Treatment Challenges of Diffuse Large B-Cell Lymphoma in the Third Trimester of Pregnancy: A Case Report

Superando los desafíos del tratamiento del linfoma difuso de células B grandes en el tercer trimestre del embarazo: Informe de un caso

Tita Agrippina Indira Hapsari[1ac], Merlyna Savitri[2bc*], Muhammad Noor Diansyah[3bc], Pradana Zaky Romadhon[4bc], Putu Niken Ayu Amrita[5bc], Ami Ashariati[6bc], Siprianus Ugroseno Yudho Bintoro[7bc]

SUMMARY

A 24-year-old woman in her third trimester of pregnancy presented with a progressively enlarging mass in the posterior thigh. Histopathological examination from an incisional biopsy, followed by immunohistochemistry, demonstrated diffuse large B-cell lymphoma, germinal center B-cell subtype. Staging MRI at 30 weeks' gestation revealed extensive disease involving the popliteal fossa, inguinal nodes, parailiacal nodes, and bone marrow replacement of the femur, consistent with stage IIB disease. Following multidisciplinary discussion, chemotherapy with R-CHOP was initiated at 30 weeks and was well tolerated. At 36–37 weeks, she developed premature rupture of membranes and delivered a healthy late-preterm infant vaginally. Chemotherapy was resumed postpartum with continuation of R-CHOP until the 6th cycle. MRI provided safe and effective disease staging. At the same time, timely biopsy and immunophenotyping were crucial for accurate diagnosis. Administration of chemotherapy during the third trimester was feasible and allowed maternal treatment without compromising neonatal

DOI: https://doi.org/10.47307/GMC.2026.134.1.21

ORCID: 0009-0004-5399-1562[1]
ORCID: 0000-0003-1923-0984[2]
ORCID: 0000-0002-5949-432X[3]
ORCID: 0000-0001-9306-5425[4]
ORCID: 0000-0003-4837-1786[5]
ORCID: 0000-0003-0508-4496[6]
ORCID: 0000-0003-1360-5298[7]

[a]Department of Internal Medicine, Dr. Soetomo General/Academic Hospital.
[b]Division of Hematology and Clinical Oncology, Department of Internal Medicine, Dr. Soetomo General/Academic Hospital.
[c]Faculty of Medicine, Universitas Airlangga, Surabaya.

*Corresponding author: Merlyna Savitri, MD.
Division of Hematology and Clinical Oncology, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya
E-mail: merlyna.savitri@gmail.com

Recibido: 10 de noviembre 2025
Aceptado: 5 de enero 2026

outcome. This report underscores the importance of multidisciplinary coordination, supportive care, and reproductive counseling in the management of aggressive lymphoma during pregnancy.

Keywords: *Case report, B-cell lymphoma, non-Hodgkin lymphoma, third trimester, pregnancy.*

RESUMEN

Una mujer de 24 años, en su tercer trimestre de embarazo, presentó una masa de crecimiento progresivo en la cara posterior del muslo. El examen histopatológico de la biopsia incisional, seguido de inmunohistoquímica, demostró un linfoma difuso de células B grandes, del subtipo de células B del centro germinal. La resonancia magnética de estadificación a las 30 semanas de gestación reveló una enfermedad extensa que afectaba la fosa poplítea, los ganglios inguinales y parailíacos, así como el reemplazo de la médula ósea del fémur, compatible con un linfoma en estadio IIB. Tras una discusión multidisciplinaria, se inició quimioterapia con R-CHOP a las 30 semanas, la cual fue bien tolerada. Entre las 36 y 37 semanas, presentó rotura prematura de membranas y dio a luz por vía vaginal a un bebé sano, prematuro tardío. Se reanudó la quimioterapia en el posparto y se continuó con R-CHOP hasta completar seis ciclos. Este caso pone de manifiesto las dificultades en el diagnóstico de linfoma durante el embarazo, ya que los síntomas pueden simular cambios fisiológicos, así como los dilemas terapéuticos que implican equilibrar el control de la enfermedad materna con la seguridad fetal. La resonancia magnética proporcionó una estadificación segura y eficaz de la enfermedad, mientras que la biopsia oportuna y la inmunofenotipificación resultaron cruciales para un diagnóstico preciso. La administración de quimioterapia durante el tercer trimestre fue factible y permitió el tratamiento materno sin comprometer el resultado neonatal. Este informe subraya la importancia de la coordinación multidisciplinaria, la atención de apoyo y el asesoramiento reproductivo en el manejo del linfoma agresivo durante el embarazo.

Palabras clave: *Informe de caso, linfoma de células B, linfoma no Hodgkin, tercer trimestre, embarazo.*

INTRODUCTION

Non-Hodgkin lymphoma (NHL) accounts for approximately 6 % of all newly diagnosed cancers, with more than 509,000 cases reported in 2018. Among its subtypes, diffuse large B-cell lymphoma (DLBCL) is the most common, comprising 30–50 % of cases (1). Compared to Hodgkin lymphoma, NHL is less frequently diagnosed during pregnancy, with an incidence of 5.39 versus 8.06 per 100 000 live births. Recent population-based studies have demonstrated an increase in pregnancy-associated NHL, from 4.44 to 7.17 per 100 000 live births over nine years, possibly reflecting the trend of delayed childbearing and the rising incidence of NHL with advancing maternal age (2).

Malignancy in pregnancy presents a unique challenge, requiring a careful balance between ensuring optimal maternal outcomes and minimizing fetal risks. With the rising incidence of lymphoma in younger women, the number of pregnancy-associated lymphoma cases is expected to increase, despite declining fertility rates (1). Management of lymphoma during pregnancy remains difficult, as it must consider fetal safety, appropriate timing of therapy initiation, selection and dosing of chemotherapeutic agents, and potential adverse effects. Treatment decisions are primarily influenced by disease aggressiveness and gestational age, and therefore require a multidisciplinary approach. Due to limited safety data regarding chemotherapeutic use in NHL during pregnancy, therapeutic regimens often need to be individualized (1).

Here, we report a case of NHL diagnosed in the third trimester of pregnancy and review the literature on therapeutic approaches to managing NHL during pregnancy.

CASE

A 24-year-old woman in her third trimester of pregnancy presented with a progressively enlarging mass in the posterior aspect of her left thigh, above the popliteal fossa (Figure 1A). The swelling had appeared in the second trimester and gradually increased in size. Initial ultrasound of the thigh suggested a lipoma, but fine-needle aspiration biopsy confirmed NHL. She was referred to our tertiary center for further evaluation.

Staging investigations included chest radiography, which showed no pulmonary or metastasis, and a non-contrast magnetic

resonance imaging (MRI) of the extremity and pelvis at approximately 30 weeks' gestation, which revealed a significant soft tissue mass in the left popliteal fossa (13.8 × 10.1 × 16.9 cm), an inguinal mass (7.9 × 5.3 × 7.0 cm) (Figure 2A-B), and a parailiacal lesion (5.0 × 7.3 cm). Multiple malignant lymphadenopathies were present in the parailiacal, inguinal, and femoral regions, with bone marrow replacement of the left femur. An incisional biopsy performed in the late second trimester confirmed NHL of diffuse large B-cell type (Figure 2C-D). Immunohistochemistry demonstrated positivity for cluster of differentiation (CD)-20, CD10, and B-cell lymphoma gene (BCL)-6, with negativity for cell cycle regulator protein (Cyclin D1) and terminal deoxynucleotidyl transferase (TdT), and partial positivity for multiple myeloma oncogene 1 (MUM1) (Figure 2E-K), consistent with DLBCL, germinal center B-cell (GCB) subtype.

Her past medical history included open reduction and internal fixation for a left femoral fracture in 2020 and laparotomy for ruptured ectopic pregnancy in 2022. She had no history of diabetes mellitus, hypertension, asthma, or allergies. The patient is a housewife and has no family history of similar symptoms, malignancy, or genetic disorders.

On admission at around approximately 30 weeks' gestation, she reported progressive swelling of the left leg, pain at the biopsy site VAS score 8-9, difficulty ambulating, intermittent fever over three months, and exertional dyspnea. She denied vaginal fluid leakage and reported normal fetal movement.

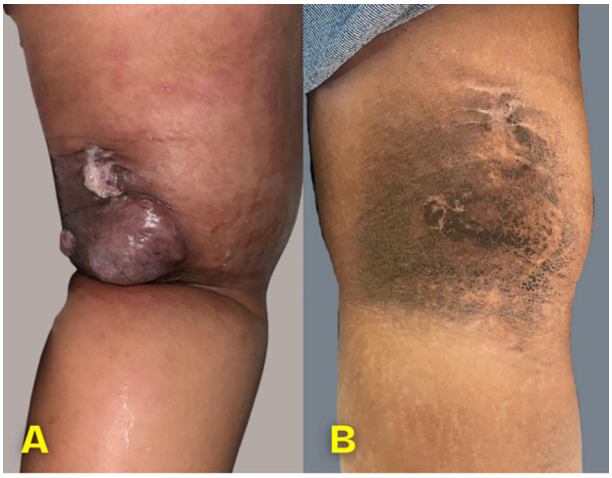

Figure 1. Clinical picture of the palpable mass on the posterior left thigh, above the popliteal fossa. A) on the day of admission; B) after completion of the 6th cycle of chemotherapy.

Examination revealed tachycardia (110 bpm), but otherwise stable vital signs. A large posterior thigh mass with serous discharge from the biopsy site was noted, without purulence. Cardiopulmonary and abdominal examinations were unremarkable, and fetal heart activity was reassuring. Laboratory evaluation demonstrated microcytic hypochromic anemia (Hb 8.7 g/dL), elevated lactate dehydrogenase (802 U/L), and hypoalbuminemia (3.2 g/dL). Serologic testing for hepatitis B, hepatitis C, human immunodeficiency virus, and syphilis was negative. Fetal ultrasound at 29-30 weeks confirmed normal intrauterine growth with an estimated fetal weight of 1,389 g.

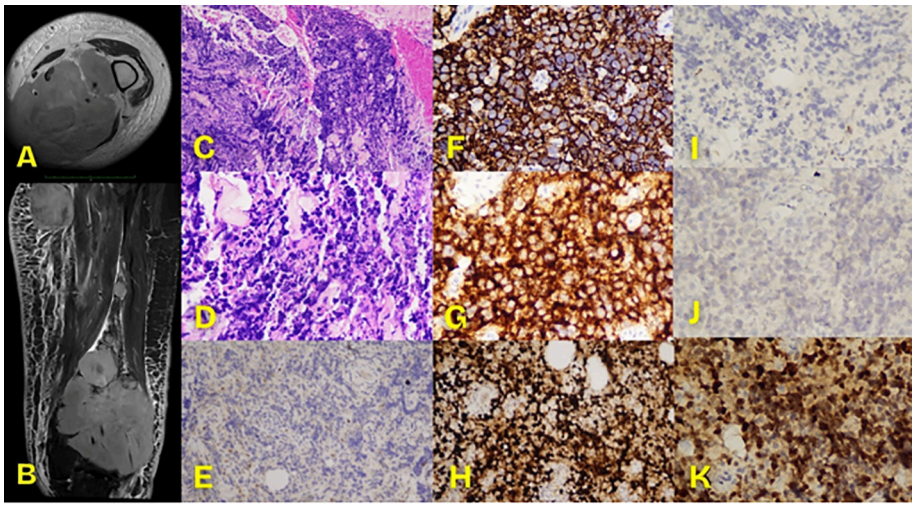

Figure 2. Radiological and histopathological examination. A-B) MRI demonstrating large soft tissue mass in the left popliteal fossa and the left inguinal region; C-D) Hematoxylin–eosin–stained sections from incisional biopsy showing diffuse infiltration by atypical lymphoid cells, consistent with non-Hodgkin lymphoma; E-K) Immunohistochemistry: E) CD30 negative, F) CD20 positive, G) CD10 positive, H) BCL6 positive, I) Cyclin D1 negative, J) TdT negative, and K) MUM 1 partial positivity.

The patient was diagnosed with high-grade DLBCL, GCB subtype, stage IIBE, complicated by anemia and obesity. Supportive management included blood transfusions, high-protein diet, analgesics, and antenatal corticosteroids for fetal lung maturation.

Following multidisciplinary discussion, chemotherapy was initiated at 30 weeks' gestation with the R-CHOP regimen: rituximab (375 mg/m^2), cyclophosphamide (750 mg/m^2), doxorubicin (50 mg/m^2), vincristine (1.4 mg/m^2, capped at 2 mg), and prednisone (100 mg daily for 5 days). She tolerated the first cycle well and was discharged with a plan for six 21-day cycles.

Before the cycle 3 of chemotherapy, she presented with premature rupture of membranes at 36-37 weeks of gestation. Therefore, chemotherapy was withheld, and induction of labor was undertaken, giving birth to a live male infant weighing 2,700 g with Apgar scores of 6 and 8 at 1 and 5 minutes, respectively. Postpartum recovery was uncomplicated, aside from mild perineal pain. The patient was discharged in stable condition and was scheduled to resume the third cycle of R-CHOP two weeks postpartum. She subsequently completed six cycles of chemotherapy without notable adverse effects and remained in good clinical condition (Figure 1B).

DISCUSSION

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of NHL, accounting for 30 %-40 % of cases worldwide, with the highest incidence reported in the United States and Western Europe. It predominantly affects older adults, with a median age at diagnosis of approximately 66 years, although some regions, such as South Asia, report earlier onset. The age-adjusted incidence is approximately 5.5-5.6 per 100 000 persons annually, with a five-year relative survival rate of roughly 65 %, which decreases significantly among patients aged 65 years and older (3). DLBCL represents a biologically heterogeneous disease characterized by clonal proliferation of germinal center or post–germinal center B cells with aggressive clinical behavior. The diagnosis requires histopathologic confirmation by lymph node or extranodal mass biopsy, typically demonstrating effacement of normal architecture and expression of pan–B–cell antigens such as CD20 and CD79a (3).

Immunohistochemistry (IHC) plays a critical role in establishing the diagnosis, subtyping, and guiding therapy for DLBCL. CD20 is a pan–B–cell marker that is almost universally expressed in DLBCL, not only confirming B-cell lineage but also providing a therapeutic target for anti-CD20 monoclonal antibodies such as rituximab. The combination of CD10, BCL6, and MUM1 is used to classify tumors into germinal center B-cell (GCB) activated B-cell (ABC) subtypes. CD10 and BCL6 positivity typically indicate the GCB subtype, which has a relatively favorable prognosis and a better response to R-CHOP chemotherapy. In contrast, MUM1 positivity is more consistent with the ABC subtype, which is often associated with poorer outcomes and a need for targeted therapy. Cyclin D1 negativity helps exclude mantle cell lymphoma, which otherwise can mimic DLBCL but typically demonstrates Cyclin D1 overexpression (4).

Our patient represents an unusual presentation of high-grade DLBCL, GCB subtype, diagnosed during late pregnancy (gestational age 30-31 weeks). While DLBCL is the most common NHL subtype, it is rare in young women and even rarer during pregnancy. The diagnosis in this case was confirmed by an incisional biopsy and immunophenotyping, which showed CD20+, CD10+, BCL6+, MUM1+, and cyclin D1, consistent with DLBCL-GCB.

The clinical diagnosis of lymphoma in pregnancy poses unique challenges, as symptoms such as anemia, leukocytosis, fatigue, and dyspnea may mimic common physiologic changes of pregnancy. Imaging studies are essential for staging and treatment planning, but ionizing radiation poses fetal risks. In this context, MRI is the preferred imaging modality since it avoids ionizing radiation and provides high-resolution imaging of nodal and extranodal disease (5). In our patient, MRI revealed extensive disease involving the popliteal fossa, inguinal lymph nodes, parailiacal lymph nodes, and bone marrow replacement of the left femur, consistent with Lugano stage IIBE disease.

Therapeutically, NHL in pregnancy is stratified as indolent, aggressive, or highly aggressive. DLBCL falls into the aggressive category, necessitating prompt chemotherapy initiation (6). R-CHOP remains the standard of care for DLBCL and is generally considered safe during the second and third trimesters of pregnancy. Although congenital malformations are not typically associated with chemotherapy in later gestation, risks of preterm birth, intrauterine growth restriction, and low birth weight are increased. Several case reports and case series support favorable maternal and fetal outcomes following R-CHOP during pregnancy, though preterm delivery remains common (5,7). In this case, initiation of R-CHOP in the third trimester balanced maternal disease control with minimization of fetal risk.

An additional consideration is cardiotoxicity, particularly from anthracyclines and alkylating agents included in R-CHOP. Patients with NHL have an approximately twofold increased risk of cardiovascular disease compared to the general population, largely due to chemotherapy-related cardiac dysfunction. A systematic review involving more than 21 000 patients found that 2.35 % developed severe cardiovascular toxicity and 4.62 % developed heart failure following treatment with CHOP or R-CHOP (8). Our patient had stable baseline cardiac function, allowing chemotherapy to proceed safely; however, longitudinal cardiac monitoring remains critical.

The rarity of lymphoma during pregnancy further underscores the importance of this case. NHL is significantly less common than Hodgkin lymphoma in pregnancy, but the incidence has been rising in parallel with increasing maternal age, with a reported rate of 7.17 per 100 000 births. Notably, NHL in pregnancy is often diagnosed at advanced stages, necessitating urgent therapy. In the most significant available cohort, Maggen et al. studied 80 pregnant patients with NHL, including 57 with DLBCL, and found that 68 % required chemotherapy during pregnancy. While stillbirth was rare (1.3 %), high rates of small-for-gestational-age infants (39%) and preterm births (52 %) were reported, with nearly half of the preterm deliveries being medically induced to accommodate maternal oncologic treatment (2). In our case, the fetus demonstrated appropriate growth, and delivery occurred at late preterm gestation, resulting in a healthy infant.

Finally, reproductive counseling is a critical yet often overlooked component of care in young women with lymphoma. Chemotherapy carries risks to fertility and subsequent pregnancies,

while ongoing cancer therapy poses substantial maternal and fetal risks if conception occurs inadvertently. Non-hormonal contraceptives, such as intrauterine devices, are preferred in patients with malignancy due to the increased risk of venous thromboembolism associated with estrogen-containing methods. Our patient agreed to immediate implantation of a copper intrauterine device postpartum.

In summary, this case illustrates the therapeutic challenges of managing high-grade DLBCL during pregnancy. It underscores the importance of timely biopsy, multidisciplinary coordination, careful balancing of maternal and fetal risks, and the critical role of supportive care, including cardiac monitoring, nutritional optimization, and reproductive counseling. The successful maternal and neonatal outcomes in this case highlight that with careful planning, standard-of-care chemotherapy can be safely administered during late pregnancy. However, the lack of advanced in molecular testing, the limited imaging options available during pregnancy, and the limited long-term follow-up limit its generalisability.

Acknowledgements. None.

Conflict of interest. All authors declared no conflict of interest.

Funding. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

The author's contribution. TAIH. conception and design, collected the data, manuscript writing; MS, data analysis, manuscript writing and reviewing, MND, manuscript review; PZR, manuscript review, PNAA, manuscript review; AA, supervision; SUY, supervision

REFERENCE

1. Pirosa MC, Peccatori FA. Lymphomas in pregnancy. Hematol Oncol. 2023;41(S1):70-74.
2. Maggen C, Dierickx D, Cardonick E, Mhallem Gziri M, Cabrera-Garcia A, Shmakov RG, et al. Maternal and neonatal outcomes in 80 patients diagnosed with non-Hodgkin lymphoma during pregnancy: Results from the International Network of Cancer, Infertility and Pregnancy. Br J Haematol. 2021;193(1):52-62.
3 Berhan A, Almaw A, Damtie S, Solomon Y. Diffuse large B cell lymphoma (DLBCL): epidemiology, pathophysiology, risk stratification, advancement in diagnostic approaches, and prospects: narrative review. Discover Oncology. 2025;16(1):184.
4. Cho J. Basic immunohistochemistry for lymphoma diagnosis. Blood Res. 2022;57(Suppl 1):S55-61.
5. Zayac AS, Egini O, Palmisiano ND, Evens AM. Lymphoma and leukemia occur during pregnancy. Semin Perinatol. 2025;49(2):152041.
6. Shah MR, Brandt JS, David KA, Evens AM. Lymphoma Occurring During Pregnancy: Current Diagnostic and Therapeutic Approaches. Current Oncology Reports. 2020;22(11):113.
7. Lee EJ, Ahn KH, Hong SC, Lee EH, Park Y, Kim BS. Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) chemotherapy for diffuse large B-cell lymphoma in pregnancy may be associated with preterm birth. Obstet Gynecol Sci. 2014;57(6):526.
8. Linschoten M, Kamphuis JAM, van Rhenen A, Bosman LP, Cramer MJ, Doevendans PA, et al. Cardiovascular adverse events in patients with non-Hodgkin lymphoma treated with first-line cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or CHOP with rituximab (R-CHOP): A systematic review and meta-analysis. Lancet Haematol. 2020;7(4):e295-308.