



Palatine Tonsil Diffuse Large B-Cell Lymphoma and Pregnancy: Case Report

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Abstract

Diffuse large B-cell lymphoma is the most common and aggressive subtype of B-cell non-Hodgkin lymphoma, and its occurrence during pregnancy or the postpartum period is rare. Management in this setting is challenging, due to risks to the mother and infant. We herein report the case of a 37-year-old woman diagnosed with diffuse large B-cell lymphoma of the palatine tonsil during the first postpartum week following a twin pregnancy. The disease was staged as IIBE, with nodal and extranodal involvement. Treatment consisted of six cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, combined with prophylactic intrathecal methotrexate, cytarabine, and dexamethasone. Chemotherapy required early cessation of breastfeeding to ensure maternal safety and prevent neonatal exposure to cytotoxic agents. A complete metabolic response was confirmed by ¹⁸F-fluorodeoxyglucose positron-emission tomography. At 60 months of follow-up, the patient remains disease-free. This case highlights the therapeutic challenges of managing aggressive lymphomas in the postpartum setting.

Keywords

- ▶ diffuse large B-cell lymphoma
- ▶ postpartum
- ▶ palatine tonsil
- ▶ chemotherapy
- ▶ breastfeeding

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common and aggressive subtype of B-cell non-Hodgkin lymphoma (NHL), encompassing a heterogeneous group of malignancies with distinct clinical, morphological, and genetic features.^{1–4} It accounts for 30 to 40% of NHL cases in developed countries,⁴ it occurs predominantly in men aged ≥ 60 years,^{5,6} and it is rare during pregnancy.^{7,8} Highly invasive, DLBCL produces bulky nodal and extranodal masses, involving multiple organs.^{9,10} The reported risk factors include genetic alterations, autoimmune disorders, viral and bacterial infections, lifestyle, and environmental or occupational exposures.^{6,11,12}

Despite its aggressive nature, DLBCL is often curable in the early stages, and it shows a favorable response to standard immunochemotherapy with rituximab, cyclophosphamide,

doxorubicin, vincristine, and prednisone (R-CHOP) administered in 21-day cycles.¹³ Approximately 60% of the patients achieve long-term remission, whereas 30 to 40% are refractory cases or cases of relapse, requiring alternative therapeutic approaches.^{14,15}

Management during pregnancy and the postpartum period presents additional challenges due to risks for the mother and infant. Chemotherapy during lactation is generally contraindicated, as agents such as cyclophosphamide, cisplatin, methotrexate, and doxorubicin are excreted in breast milk and may cause severe neonatal adverse effects, including neutropenia.^{16,17}

We herein report a rare case of DLBCL of the palatine tonsil (PT) diagnosed on the seventh postpartum day in a patient with a twin delivery. We describe the staging process using

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immunohistochemical and molecular techniques, as well as the personalized immunochemotherapy regimen employed.

The present study was approved by the institutional Ethics in Research Committee (under CAAE: 88511825.7.0000.5475).

Case Description

A 37-year-old Caucasian woman delivered twins by cesarean section at 35 weeks. She was lactating when she was referred in August 2020 to NAIC – Instituto do Câncer, located in the municipality of Bauru, state of São Paulo, Brazil, with a diagnosis of high-grade PT lymphoma established by incisional biopsy on the seventh postpartum day.

On the initial onco-hematology evaluation, the patient reported a 2-month history of right PT enlargement and night sweats, with no fever, weight loss, or significant personal or family history. The physical examination revealed a right PT mass, without palpable peripheral lymphadenopathy. Her general condition was good, with a score of 0 on the Eastern Cooperative Oncology Group (ECOG) Scale of Performance Status (PS).

The baseline workup included complete laboratory tests (including viral serologies relevant to lymphoma), transthoracic echocardiogram (TTE), bone-marrow biopsy with immunohistochemistry (IHC), cerebrospinal fluid (CSF) immunophenotyping, repeat PT biopsy review, and staging ^{18}F -fluorodeoxyglucose positron-emission tomography/computed tomography (^{18}F -FDG PET/CT). The laboratory tests and TTE were within normal limits.

The initial IHC of the PT biopsy suggested an unclassified B-cell lymphoma with intermediate features between DLBCL and Burkitt lymphoma (BL). Additional IHC and molecular studies were performed, confirming a diagnosis of DLBCL of the germinal center B-cell (GCB) subtype, with expression of *BCL6* and *MYC*. The positivity for Ki-67 was of 100%, and the tumor cells were also positive for CD20, CD10, *BCL6*, and *MYC*. Fluorescence in situ hybridization (FISH) revealed no *MYC* gene rearrangement (locus 8q24), but it was positive for *BCL2* (locus 18q21) and *BCL6* (locus 3q27) rearrangements.

Staging PET/CT demonstrated marked enlargement and hypermetabolism of the right PT (maximum standardized uptake value [SUVmax]: 25.5), with additional uptake in bilateral level-IIa and right level-III cervical lymph nodes (largest: 1.4×1.0 cm; SUVmax: 4.7). The final diagnosis was stage-IIIE DLBCL, CD20-positive, of the GCB immunophenotype, FISH negative for *MYC* rearrangement, but positive for *BCL2* and *BCL6* rearrangements.

Treatment was initiated 17 days after the initial biopsy result, consisting of 6 cycles of R-CHOP administered every 21 days, combined with intrathecal prophylactic chemotherapy (methotrexate, cytarabine, dexamethasone). Breastfeeding was discontinued prior to treatment. All cycles were completed without complications, with only mild headache reported as an adverse effect.

After 3 cycles, interim PET/CT (iPET/CT) showed asymmetry PT uptake (right SUVmax: 4.5; left: 8.6) and minimal uptake in a left level-IIa cervical lymph node (size: 1.3×0.5 cm; SUVmax: 2.4). According to the Deauville and

SUVmax criteria, the patient achieved complete response (CR). Subsequent treatment cycles proceeded uneventfully. End-of-treatment PET/CT confirmed CR. The patient has remained disease-free during 60 months of follow-up.

Discussion

During pregnancy and the postpartum period, NHL is rare.^{18,19} We herein report a case of stage-IIIE DLBCL of the GCB subtype, diagnosed during the first postpartum week and located in the PT, an uncommon extranodal site.^{19–21} The literature⁸ suggests that lymphomas progress more rapidly after delivery, which highlights the importance of rapid diagnosis and timely initiation of therapy. In the patient herein reported, aggressive disease biology (Ki-67 = 100%) created an immediate risk of airway obstruction, making expedited staging and treatment initiation essential.

Diagnostic accuracy was achieved through the integration of IHC, FISH, and molecular profiling. While IHC raised concern for double-hit lymphoma due to *BCL6* and *MYC* expression, FISH excluded *MYC* rearrangement and confirmed *BCL2/BCL6* rearrangements only. This careful diagnostic pathway enabled a precise classification as DLBCL of the GCB subtype and informed the decision to administer R-CHOP chemotherapy rather than more intensive regimens.

A critical aspect of this case was the patient's postpartum and lactation status. Rituximab and most cytotoxic chemotherapy agents are known to be excreted in breast milk, posing significant risks to infants, including immunosuppression, cytopenia, and potential long-term toxicity.^{1,2,16,17} In accordance with international guidelines,¹⁶ breastfeeding was discontinued prior to the initiation of therapy to ensure neonatal safety. Chemotherapy during lactation is generally contraindicated, as agents such as cyclophosphamide, cisplatin, methotrexate, and doxorubicin have been detected in breast milk and are associated with severe adverse outcomes in infants, particularly neutropenia.^{22–24} Therefore, most sources²¹ recommend avoiding breastfeeding during maternal antineoplastic therapy. Although some studies have suggested that breastfeeding may be feasible during intermittent chemotherapy if an appropriate abstinence period is observed, this remains controversial. Early recommendations proposed an abstinence interval of 6 to 10 days,²³ but more recent pharmacokinetic modeling under worst-case scenarios²⁴ suggests that a minimum of 6 days may be sufficient to minimize systemic and gastrointestinal toxicity after the colostrum phase. For mothers who wish to preserve lactation, milk expression can be performed throughout treatment; however, the expressed milk must be discarded. Breastfeeding can only be safely resumed after the complete clearance of cytotoxic agents from the maternal body, a process that generally requires 60 to 90 days following the last chemotherapy cycle, depending on the pharmacokinetics of the drugs used.²⁴ These considerations highlight the importance of multidisciplinary counseling in postpartum oncology care, ensuring effective cancer management and neonatal safety.

A major concern during the postpartum period, when the immune system faces profound challenges, is the risk of

central nervous system (CNS) relapse following the R-CHOP treatment. This risk is particularly relevant due to the anatomical proximity and the nature of lymphoid tissue in the Waldeyer's ring, where the PTs are located, an anatomical site considered to be at high risk for CNS involvement.^{25–28} Although CNS relapse is relatively uncommon, with reported incidence rates ranging from 5 to 25% depending on specific risk factors, it is almost invariably fatal. Among patients with extranodal disease, the incidence is reported to be between 2 and 10%.^{29,30} Central nervous system relapse is a devastating complication that most often occurs within the first year after R-CHOP therapy in patients with DLBCL, with survival typically limited to 2 to 6 months.³¹ These poor outcomes have prompted substantial efforts to develop strategies to prevent this complication.

In the case herein reported, although the patient was considered low-risk according to the Ann Arbor staging system and had a score of 0 on the CNS International Prognostic Index (CNS-IPI) for DLBCL, the decision was made to administer prophylactic intrathecal (IT) chemotherapy during the postpartum phase. This approach aimed to minimize the likelihood of lymphoma infiltration into the CNS, given the unique immunological context of the puerperium.³² The prophylactic regimen consisted of methotrexate (MTX), cytarabine, and dexamethasone administered via the IT route. This route of administration ensures direct drug delivery into the cerebrospinal fluid (CSF), thereby maintaining therapeutic concentrations.³³ Cytarabine plays a critical role by sustaining elevated drug levels in the CSF for periods exceeding 14 days.³³ Although MTX is well known for its potential toxicity, the adverse effects in the present case were minimal, with only grade-1 headache reported according to the Common Terminology Criteria for Adverse Events.^{32,33}

Treatment monitoring with interim PET/CT after 3 cycles confirmed complete metabolic response, a predictor of long-term survival in DLBCL,^{34,35} at 60 months of follow-up, the patient remains in complete remission.

The case herein reported demonstrates that postpartum DLBCL, though rare, requires urgent diagnosis and individualized therapy. Key clinical lessons include the need to discontinue breastfeeding to prevent infant exposure to toxicity drugs, and the value of considering CNS prophylaxis in extranodal disease involving the Waldeyer's ring, even when the standard risk scores are low. The favorable long-term outcome in this patient highlights the importance of precise molecular diagnostics, multidisciplinary coordination, and tailored treatment strategies in the management of lymphoma in the postpartum setting.

Authors' Contributions

MBA: collection and assembly of data, data analysis and interpretation, manuscript writing, conception and design, final approval of the manuscript, and provision of study materials or patient care; ABAS: collection and assembly of data, data analysis and interpretation, manuscript writing, conception and design, and final approval of the manuscript; and AAS: collection and assembly of

data, data analysis and interpretation, and manuscript writing.

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Conflict of Interests

The authors have no conflict of interests to declare.

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