Burkitt Lymphoma in Pregnancy: Two Cases of Successful Treatment and Continued Fertility; With a Review of the Literature

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Clinical Practice Points

- Burkitt lymphoma (BL) can occur during pregnancy and be fatal within days if untreated.
- Standard treatment is multiagent chemotherapy that includes high-dose alkylating agents, a schedule of frequent, repetitive drug administration, and central nervous system prophylaxis.
- Pregnant women are no exception to requiring such treatment.
- High-dose alkylating agents are notorious for inducing infertility.
- We present 2 cases of pregnant women who underwent successful treatment for BL and maintained fertility; one continues to menstruate without hormonal supplementation and the other has birthed a child.
- Our experiences with these 2 patients suggest that pregnancy might provide protection from chemotherapy-related infertility.
- This provides hope for pregnant women faced with the prospect of undergoing intensive chemotherapy for treatment of malignancy.

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Introduction

Malignancy during pregnancy is more common than one might expect, affecting approximately 1 in 1000 pregnancies.[1] Burkitt lymphoma (BL) is a rare but aggressive malignancy that has been described in pregnant women. We provide a summary of the currently available literature of cases of BL during pregnancy which provides evidence that prompt treatment with aggressive multiagent chemotherapy is the best approach in these patients. Unfortunately, such chemotherapy is notorious for inducing infertility. We present 2 cases in which pregnant women underwent successful treatment of BL and maintained their fertility, suggesting that perhaps the pregnant state is protective against chemotherapy-induced infertility.

Case Reports

Case 1 is a 30-year-old previously healthy woman who presented at 26 weeks of pregnancy with dyspnea on exertion. The diagnosis of BL was not made on initial presentation. At that time she had a normocytic anemia (hemoglobin, 7.7 g/dL) and mild thrombocytopenia (platelet count, 120×10^9/L) with previously normal values during her second trimester of pregnancy. After evaluation, her anemia and thrombocytopenia were believed to be attributable to pregnancy. Three weeks later she presented to a clinic visit and complained of bilateral breast enlargement which was more prominent than in her previous pregnancies. Physical exam demonstrated bilaterally enlarged and indurated breasts with no focal lesions or skin changes. Ultrasound of the breasts showed bilateral hypoechoic lobulated breast tissue without focal abnormalities. Core biopsy of her breast demonstrated lymphoid cells that were intermediate-sized, monotonous, with small nucleoli and scant cytoplasm along with numerous macrophages giving the classic "starry sky" appearance. Immunostains were positive for CD10, CD20, CD79a, and PAX-5, and negative for CD5; the CD20, CD79a, and PAX-5 confirmed B-lineage, and the CD10 positivity suggested a B-cell lymphoma of germinal center origin (Fig. 1). The neoplastic cells were not associated with Epstein-Barr virus (EBV) infection, confirmed using in situ staining for EBV-encoded RNA. Cytogenetic analysis using fluorescent in situ hybridization (FISH) on the tissue block showed that 87.5% of the cells harbored a MYC gene rearrangement, but lacked a rearrangement of the BCL2 gene. Her bone marrow was involved by BL, with neoplasm involving 10% to 15% of cellularity. She was in tumor lysis syndrome with acute renal failure at the time of presentation. Laboratory tests revealed a serum

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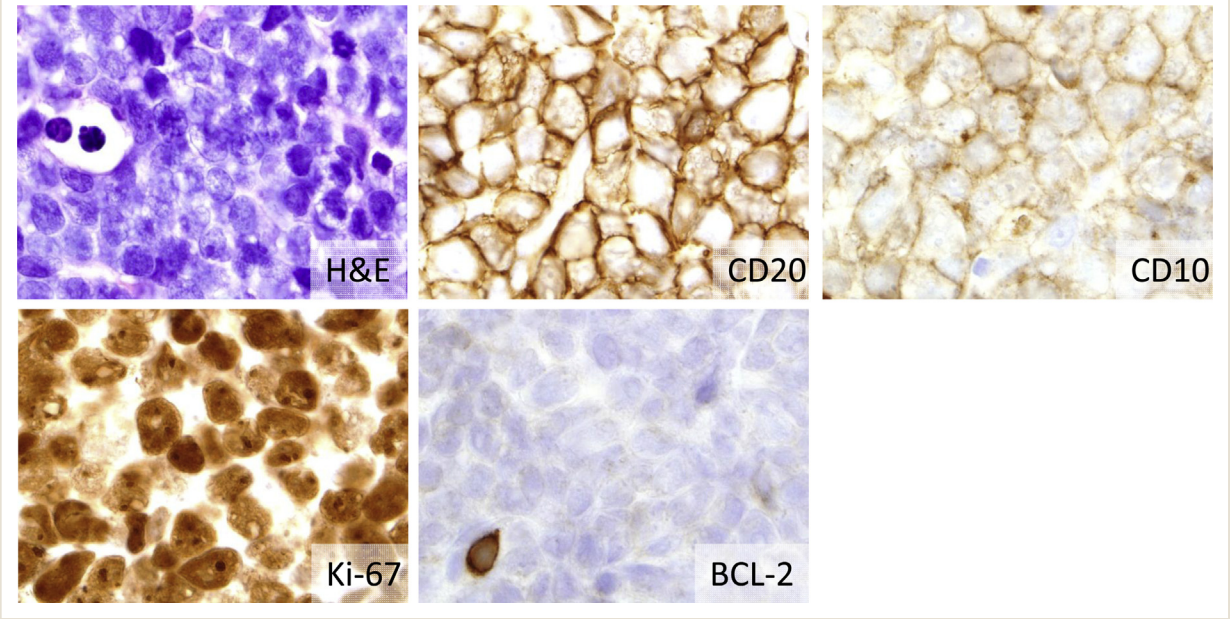
Figure 1 Diagnostic Pathology, Patient 1. A Needle Core Biopsy Demonstrates a Diffuse Infiltrate of Neoplastic Cells With Vesicular Chromatin, and Relatively Uniform Size. Cell Debris is Present. The Cells Uniformly Express CD20, Confirming B Lineage, and They Express CD10, Suggesting Germinal Center Origin. The Ki-67 Defined a Very High Proliferative Rate, Approaching 100% of Cells. The Cells do not Express BCL-2; a Nonneoplastic T Cell is Included as a Positive Control. FISH Demonstrated a Rearrangement of the MYC Locus, but not of the BCL-2 Locus, Confirming a Diagnosis of Burkitt Lymphoma



Abbreviations: FISH = fluorescent in situ hybridization; H&E = hematoxylin and eosin.

phosphorus level of 4.6 mg/dL, uric acid of 17.9 mg/dL, and creatinine 1.9 mg/dL. This did not resolve with hydration, urine alkalization, and allopurinol, but did with the administration of rasburicase. After discussion between the patient, the Maternal-Fetal-Medicine team, and the Oncology team, which provided information on the risks and benefits that treatment might have on the mother and fetus, it was decided to begin treatment without delay using the cancer and leukemia group B (CALGB) 10002 protocol (Table 1).[2] She started cyclophosphamide and prednisone. On day 2, she went into preterm labor. A Cesarian section was performed, which successfully delivered a 1480 g baby girl with Apgar scores of 4 and 6. A segmental resection of her bilateral fallopian tubes was performed at delivery; pathologic examination identified involvement by lymphoma. There was no evidence of disease in the placenta. She resumed cycle 1 of chemotherapy 2 days later. She was given a 5-day break between cycle 1 and cycle 2 to promote healing from her Cesarian section. She finished the full course of chemotherapy and achieved complete remission. The patient and daughter are alive and well 2 years later. The patient continues to menstruate regularly on a 28-day cycle without hormonal supplementation.

Case two is a 23-year-old woman with a history of HIV with a CD4 count of 190/mm^3 and undetectable viral load, who was 14 weeks pregnant and presented with complaints of back pain. She developed right lower extremity weakness and numbness 3 days before presentation. The neurologic deficits were confirmed on physical examination and a magnetic resonance imaging (MRI) scan of her spine showed an epidural mass at T5 to T7. She urgently underwent laminectomy, with material submitted to pathology. Morphologically, the specimen was a briskly mitotically active lesion hallmarked by uniform-appearing lymphocytes in association with tingible body macrophages. Concurrent flow cytometry identified a clonal aberrant CD10-positive B-cell population expressing CD19, CD20, and surface kappa light chains but lacking CD5 (Fig. 2). Cytogenetics confirmed the MYC translocation in 54% of the cells present. Staging using MRI revealed involvement of an axillary lymph node and no other disease. Bone marrow biopsy did not reveal any evidence of BL. After multidisciplinary consultation between Oncology, Maternal-Fetal Medicine, which provided information on the risk of treatment including possible fetal death, and the patient, chemotherapy with hyper-fractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone (Hyper-CVAD) was initiated (Table 1).[3] Unfortunately, she had a miscarriage at 18 weeks of gestation that was discovered when screening ultrasound showed a nonviable fetus. The patient went on to attain a complete remission with 7 cycles of chemotherapy. Her course was complicated by near-paraplegia (which resolved with intensive rehabilitation), neuropathy, and depression. Two years after the completion of her chemotherapy, she has delivered a healthy baby.

Discussion

The treatment of malignancy during pregnancy requires consideration of the effects of treatment on the mother and the unborn fetus. The focus of therapy should be on maternal survival,