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CASE REPORT PEER REVIEWED | OPEN ACCESS

Treatment with chemotherapy plus brentuximab vedotin in anaplastic large cell lymphoma and pregnancy: A case report

Emma E Pride, Jacob P Calahan, Shannon M Collins Shaver, Brandi N Creel, John M Waples

ABSTRACT

Introduction: Brentuximab vedotin (BV) is a CD-30 directed antibody and microtubule inhibitor conjugate indicated for the treatment of multiple types of lymphoma, including anaplastic large cell lymphoma (ALCL). Consensus-based guidelines recommend BV with cyclophosphamide, doxorubicin, and prednisone (CHP) as first-line treatment in a patient with ALCL. Alternative treatment options for ALCL can be limited due to patient-specific factors. Lymphomas account for approximately 11% of cancers in pregnancy. Brentuximab vedotin has not been studied in pregnancy; therefore, making the use of an antibody drug conjugate in this patient the first documented use in pregnancy.

Case Report: A 26-year-old female was diagnosed with anaplastic large cell lymphoma at 14 weeks gestation. The patient has a past medical history of ALCL in 2004 at eight years old and a prior miscarriage. Consensus-based guidelines recommend BV with cyclophosphamide, doxorubicin, and prednisone (CHP) as first-line treatment in a patient with ALCL. Treatment with BV plus CHP was initiated at 15 weeks gestation for a total of 6 cycles during the antepartum period. At 33 weeks gestation, the patient delivered a 4-pound infant male without complications, birth defects, or health disparities. Two additional cycles of BV and CHP were administered during the postpartum period. Complete remission has been achieved in this patient.

Conclusion: The outcomes in this case indicate the potential safety of BV in patients after the first trimester of pregnancy.

Keywords: Anaplastic large cell lymphoma in pregnancy, Brentuximab vedotin in pregnancy, Brentuximab vedotin in pregnancy and lymphoma, Pregnancy and lymphoma

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INTRODUCTION

Brentuximab vedotin (BV) is a CD-30 directed antibody and microtubule inhibitor conjugate indicated for the treatment of multiple types of lymphoma, including anaplastic large cell lymphoma (ALCL) [1]. Consensus-based guidelines recommend BV with cyclophosphamide, doxorubicin, and prednisone (CHP) as first-line treatment in a patient with ALCL [1]. Alternative treatment options for ALCL can be limited due to patient-specific factors.

Lymphomas account for approximately 11% of cancers in pregnancy [2]. Brentuximab vedotin (BV) has not been studied in pregnancy; therefore, the use of this antibody-drug conjugate in this patient represents the first documented instance in pregnancy.

The following case report discusses a 26-year-old female diagnosed with ALCL at 14 weeks gestation. The patient has a past medical history of ALCL in 2004 at eight years old and a prior miscarriage. Treatment with BV plus CHP was initiated at 15 weeks gestation for a total of 6 cycles during the antepartum period. At 33 weeks gestation, the patient delivered a 4-pound infant male without complications, birth defects, or health disparities. Two additional cycles of BV and CHP were administered during the postpartum period. Complete remission has been achieved in this patient. The outcomes in this case indicate the potential safety of BV in patients after the first trimester of pregnancy.

CASE REPORT

A 26-year-old female presented to a primary care provider in November 2022 for an evaluation of painful lesions on the right upper arm and breast which was non-responsive to the patient's at home treatment with triamcinolone cream. The patient was referred to a general surgeon for lymphadenopathy evaluation. An ultrasound was performed which revealed multiple suspicious right axillary lymph nodes. Upon right breast evaluation, a tender axillary lymph node measuring 3×2 cm was identified.

In January 2023, a biopsy was performed that revealed abnormal cells that were large and had abundant amphophilic cytoplasm, indistinct cell borders, and irregular, pleomorphic nuclei with coarsely clumped chromatin and prominent eosinophilic macronuclei. There were frequent cells with eccentric, reniform nuclei that are "hallmark cells" for ALCL. The cytology report from the biopsy sample resulted in atypical lymphoid infiltrate, suspicious for lymphoma. Atypical cells were positive for CD30. Cells were negative for CD20, CD3, and ALK, as well as Reed-Sternberg cells which ruled out other types of lymphoma. Positron emission tomography (PET) scan was performed and revealed atypical metabolic activity of the right shoulder and axillary lymph nodes (Figure 1). Completion of diagnostic evaluation revealed a normal left ventricular ejection fraction, non-reactive hepatitis and human immunodeficiency virus (HIV) panel, normal protein electrophoresis, a complete blood count that showed leukocytosis, elevated neutrophil count, lymphopenia, and a left shift. An elevated glucose-6-phosphate dehydrogenase was noted, likely due to leukocytosis. Complete metabolic panel was unremarkable. Diagnosis was confirmed as ALCL, Ann Arbor stage III. At the time of diagnosis, the patient was 14 weeks pregnant with a past medical history of ALCL in 2004 at 8 years old and a prior miscarriage.

Prompt treatment of systemic ALCL is recommended to achieve adequate response due to the aggressive nature of the disease. In pregnant patients, the risk of rapid disease progression may be further increased due to associated maternal immunosuppression [3]. Prednisone 100 mg daily was initiated for 5 days while the treatment plan was being discussed. A multidisciplinary team including medical oncologists, an obstetrician that specializes in high-risk pregnancies, and a board-certified clinical oncology pharmacist evaluated the case.

The patient's medical history of ALCL and the associated treatment was considered. In 2004, the patient was treated with induction therapy including methotrexate, vincristine, and pegaspargase at an outside facility. Maintenance therapy including etoposide and cytarabine was prescribed for 13 months total. The patient's juvenile treatment regimen resulted in long-term neuropathy. Grade 1 neuropathy from the prior vincristine treatment persists.

After extensive consideration of the disease status and patient factors, the decision was made to initiate CHP and BV every 21 days for eight cycles. Counseling was provided to the patient and immediate family on the risks and benefits of chemotherapy. The discussion included the unknown risk of BV administration during pregnancy. The patient consented to treatment.

The patient was experiencing increased pain and edema to the right shoulder at the site of disease prior to treatment initiation. An ultrasound was performed which revealed a new thrombus. Enoxaparin was initiated.

The first chemotherapy cycle was initiated at 15 weeks gestation with prednisone 100 mg orally days 1–5, cyclophosphamide 750 mg/m² intravenous (IV) and doxorubicin 50 mg/m² IV on day 1, followed 1 hour later by brentuximab vedotin 1.8 mg/kg IV. Pegfilgrastim was administered on day 2 for neutropenia prophylaxis.

At the second cycle pre-treatment evaluation, the patient reported improvement in range of motion and diminished right shoulder pain. The patient reported no adverse events since the last infusion. The treatment plan remained on schedule and was tolerated without issue for cycles 3 and 4.

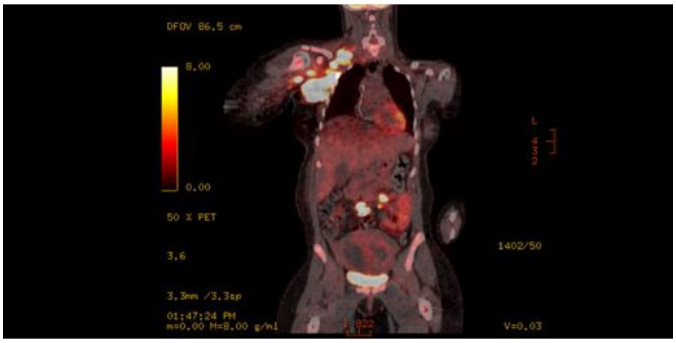

Figure 1: PET scan with atypical metabolic activity of the right shoulder and axillary lymph nodes that aided in diagnosis of ALCL.

During the fifth cycle pre-treatment assessment the patient demonstrated full range of motion of the right shoulder without pain. Complete resolution of the pre-existing thrombus was noted on Doppler ultrasound. Enoxaparin was decreased to prophylactic dosing. Computed tomography (CT) of the chest was performed; previous axillary nodal involvement was no longer noted. Imaging identified incidental pulmonary nodules which were characterized as insignificant and thought to be old granulomas (Figure 2). Cycle 5 was initiated at 31 weeks gestation. After cycle 6, the patient reported a thrush-like tongue reaction and sore throat. Fluconazole and nystatin oral solution was prescribed.

At 33 weeks gestation, the patient experienced premature rupture of membranes. The patient vaginally delivered a male infant weighing 4 pounds. No birth defects were noted; however, the infant was admitted to the neonatal intensive care unit due to premature delivery. The patient's postpartum period was uncomplicated. Due to the patient's ongoing chemotherapy, the patient elected not to breastfeed.

After delivery, the ALCL treatment plan was resumed. The patient received two additional cycles of the treatment course without dose modifications or delay. A total of 8 cycles of CHP and BV were administered: six cycles antepartum and two cycles postpartum.

Computed tomography scans were performed one month after the last treatment cycle of CHP and BV. Complete remission was evident by the absence of lymphadenopathy within neck, chest, abdomen, and pelvis; no measurable disease was noted. The patient was found to be in complete remission. Continued complete response was evident by CT scan at six months (Figure 3). The infant was also reported to be healthy and thriving with no deformities or developmental delays. Complete remission continues at the time of this writing.

DISCUSSION

Cancer during pregnancy is rare, accounting for approximately one in every 1,000 pregnancies [4]. Management of cancer during pregnancy requires specialized care due to the presence of a fetus which often requires alterations in the standard treatment. Lymphomas account for approximately 11% of cancers in pregnancy, with Hodgkin lymphoma being most prevalent [5]. Anaplastic large cell lymphoma only accounts for 1% of all non-Hodgkin lymphomas [5]. Due to the low incidence of ALCL, the diagnosis has rarely been reported during pregnancy. Prior to this case, only 11 cases of ALCL in pregnancy have been reported [5–7]. Consensus-based guidelines recommend BV and CHP as first-line treatment in patients with ALCL [1]. Chemotherapy is often contraindicated in the first trimester of pregnancy due to the high risk of teratogenicity [2]. Chemotherapy may be safely administered in the second and third trimester of pregnancy [3]. Cyclophosphamide, doxorubicin, and prednisone (CHP) have been studied within a pregnant population; however, BV has not.

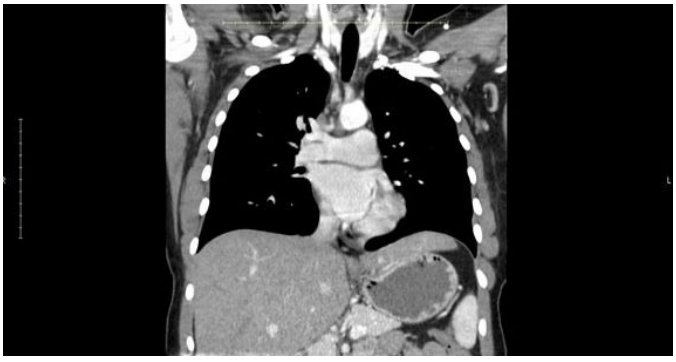

Figure 2: CT scan of the chest after the fifth cycle of BV + CHP with resolved axillary nodal involvement.

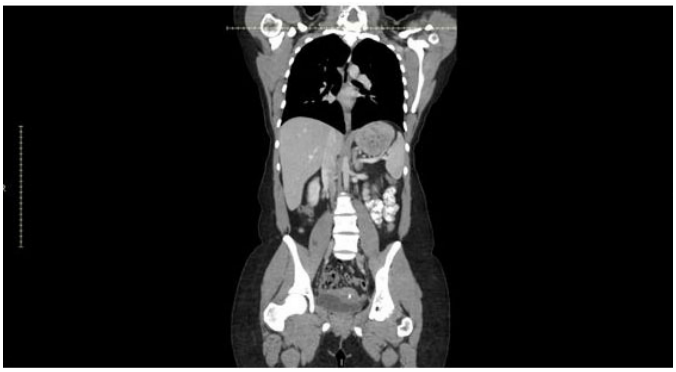

Figure 3: CT scan of the chest six months after completion of cancer treatment showing complete remission.

Drug therapy can be complex during pregnancy due to maternal physiologic changes and the potential for fetal harm due to placental barrier crossing [3]. Transfer of xenobiotics occurs through simple diffusion which is influenced by protein binding, ionization, lipid solubility, and molecular weight [8]. Medications that readily cross the placenta have low molecular weight, are lipid-soluble, ionized, and poorly protein-bound [8].

Brentuximab vedotin is a CD-30 directed antibody and microtubule inhibitor conjugate indicated for multiple lymphomas, including ALCL [9]. Brentuximab vedotin and other antibody drug conjugates have never been studied in pregnancy. The pharmacologic properties of BV indicate that this drug would not likely cross the placenta and cause fetal harm, especially in the second and third trimesters of pregnancy. The molecular weight of BV is 153,000 Daltons [9]. Typically, drugs and other xenobiotics greater than 500 Daltons do not cross the placenta [10]. The drug's molecular weight supports potential use of BV in pregnancy. Brentuximab vedotin is protein bound up to 82% [9]. Protein bound drugs have a more difficult time crossing the placenta [8]. A clinical concern requiring consideration was the composition of BV, including the microtubule disrupting agent vedotin, or monomethyl auristatin E (MMAE). Monomethyl

auristatin E is a nonpolar molecule, which means it could more readily cross the placenta [11].

Other recommended first-line treatments for ALCL include vincristine which can be safely administered in the second and third trimesters of pregnancy [3]. The patient declined vincristine due to a personal history of chronic neuropathy from prior vincristine treatment. The patient and family were counseled that peripheral neuropathy is a known side effect of BV. However, BV associated peripheral neuropathy is most commonly reversible upon discontinuation of the agent, although there is a risk of permanence [12]. The patient preferred the option to treat with BV over vincristine.

The medical team performed a risk-benefit analysis, including consideration of the molecular weight, protein binding properties of BV, the patient's stage of gestation, and the patient's preference. The standard of care treatment, CHP plus BV, was selected.

Kanj et al. 2015 provided a thorough literature review of ALCL cases in pregnancy and the associated treatments [5]. Positive and negative outcomes were reported in the review [5]. Subsequent research by Amante et al. describes a case of ALCL treatment in pregnancy [6]. This case reported a female who was treated with two cycles of CHOP therapy prior to delivery of a healthy infant [6]. Complete remission was achieved in this patient after completing four additional cycles of CHOP therapy postpartum [6].

CONCLUSION

Historically, many chemotherapy-based treatments have proven to be safe and efficacious in the second and third trimesters of pregnancy. Antibody-drug conjugate medications are a novel treatment option in several cancers. However, the use of antibody drug conjugates in pregnancy is not well-documented. The case outlined in this report documents the safety and efficacy of the use of BV with chemotherapy in a pregnant patient with ALCL.

REFERENCES

1. Horwitz S, O'Connor OA, Pro B, et al. Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): A global, double-blind, randomised, phase 3 trial. Lancet 2019;393(10168):229–40.
2. Dunleavy K, McLintock C. How I treat lymphoma in pregnancy. Blood 2020;136(19):2118–24.
3. Basta P, Bak A, Roszkowski K. Cancer treatment in pregnant women. Contemp Oncol (Pozn) 2015;19(5):354–60.
4. Anaplastic large cell lymphoma. Lymphoma Research Foundation. 2024. [Available at: https://www.lymphoma.org/understanding-lymphoma/aboutlymphoma/nhl/anaplastic-large-cell-lymphoma/#:~:text=Anaplastic%20large%20cell%20lymphoma%20(ALCL,of%20all%20T%20cell%20lymphomas]
5. Kanj RV, Gerber D, Frey MK, Rahmanou F, Hardy C. Anaplastic large cell lymphoma in pregnancy. A case report. J Reprod Med 2015;60(5–6):265–8.
6. Amante MA, Galagnara SJP, Ignacio J. Anaplastic large cell lymphoma in a pregnant Filipino woman successfully treated with prepartum and postpartum chemotherapy. BMJ Case Rep 2018;2018:bcr2018225576.
7. Yang S, Jiang WM, Yang HL. ALK-positive anaplastic large cell lymphoma of the thoracic spine occurring in pregnancy: A case report. World J Clin Cases 2019;7(18):2857–63.
8. Velasco R, Domingo-Domenech E, Sureda A. Brentuximab-induced peripheral neurotoxicity: A multidisciplinary approach to manage an emerging challenge in Hodgkin lymphoma therapy. Cancers (Basel) 2021;13(23):6125.
9. Adcetris (brentuximab vedotin) [package insert]. Bothell, WA: Seagen; 2023.
10. Pacifici GM, Nottoli R. Placental transfer of drugs administered to the mother. Clin Pharmacokinet 1995;28(3):235–69.
11. Bera D, Roy D. Brentuximab vedotin resistance in classic Hodgkin's lymphoma and its therapeutic strategies: A review. Futur J Pharm Sci 2024(10):15.
12. Feghali M, Venkataramanan R, Caritis S. Pharmacokinetics of drugs in pregnancy. Semin Perinatol 2015;39(7):512–9.

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Author Contributions

Emma E Pride – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Jacob P Calahan – Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Shannon M Collins Shaver – Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Brandi N Creel – Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

John M Waples – Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.