Case Report

Treatment of Hairy Cell Leukemia During Pregnancy: Are Purine Analogues and Rituximab Viable Therapeutic Options

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Clinical Practice Points

- The Occurrence of Neoplastic Diseases In Pregnant Women Can Present a Significant Diagnostic and Therapeutic Challenge for the Treating physician.
- We Describe the Case of a Pregnant Woman Who Presented With Hairy Cell Leukemia (HCL) In the Second Trimester of Pregnancy. In the 26th Week of Pregnancy She Started Treatment With Weekly Rituximab. She Remained Pancytopenic and Was Then Treated With Cladribine During the 32nd Week With Favorable outcome.
- We Found Scant Published Data Regarding Use of Rituximab Or Cladribine for the Treatment of Hcl In Pregnant women.
- We Further Discuss Potential Treatment Indications and Therapeutic Options for Hcl In pregnancy.

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Introduction

Approximately 1 in 1000 pregnancies in the United States are plagued by concurrent neoplastic diseases. These account for the second leading cause of maternal mortality in the United States.[1] The majority of these cases are related to solid tumors with only 25% of the cases related to hematologic malignancies.[2] Hairy cell leukemia (HCL) is a relatively uncommon lymphoproliferative disorder.[3] The outcome of patients with HCL has significantly improved with the introduction of purine nucleoside analogues including cladribine and monoclonal antibodies including rituximab. Remission rates of $>$ 90% have been documented after just 1 course of therapy.[4,5] The management of the pregnant patient with hematologic malignancies represents a diagnostic, therapeutic, and social challenge, requiring a multidisciplinary team approach.

There is scant published literature regarding treatment of HCL in pregnancy. The therapeutic efficacy, teratogenicity, and maternal toxicities of purine analogues and rituximab in pregnancy are poorly defined.[6,7] Orlowski published the first report of successful pregnancy outcome after treatment of HCL with cladribine, suggesting that fertility may be preserved in some female patients exposed to purine analogues.[8] However, to our knowledge this is the first report of a favorable outcome in a pregnant HCL patient treated sequentially with a monoclonal antibody (rituximab) followed by a purine analogue (cladribine).

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Case Report

A 28-year-old pregnant female (Gravida 5; Para 3) was in good health until the 23rd week of pregnancy; when routine blood testing revealed pancytopenia with a white cell count (WBC) of 1.3 K/μL, absolute neutrophil count (ANC) 0.25 $\times$ 10^9/L, hemoglobin 8.6 g/dL, and platelet count 65 $\times$ 10^9/L. Further work-up led to a diagnosis of marginal zone lymphoma and she was treated with prednisolone 100 mg by mouth daily for 5 days, to be repeated every 3 weeks. She was subsequently referred to the University of Texas M.D. Anderson Cancer Center (UTMDACC). Review of original bone marrow biopsy at our institution showed hairy cell leukemia. Bone marrow flow cytometry was positive for CD11c, CD20, FMC-7, CD103, CD19, CD22, CD23, CD25, and monotypic lambda light chains. Flow cytometry of peripheral blood was positive for CD11c, CD19, CD20, CD22, CD23, CD25, CD44, CD103, FMC7, and monotypic lambda light chain. On presentation to UTMDACC her WBC count was 1.0 K/μL, ANC 0.21 K/μL, hemoglobin 8.6 g/dL, and platelet count 35 K/μL. She had normal renal and hepatic function. Physical examination revealed an acneiform rash on the face

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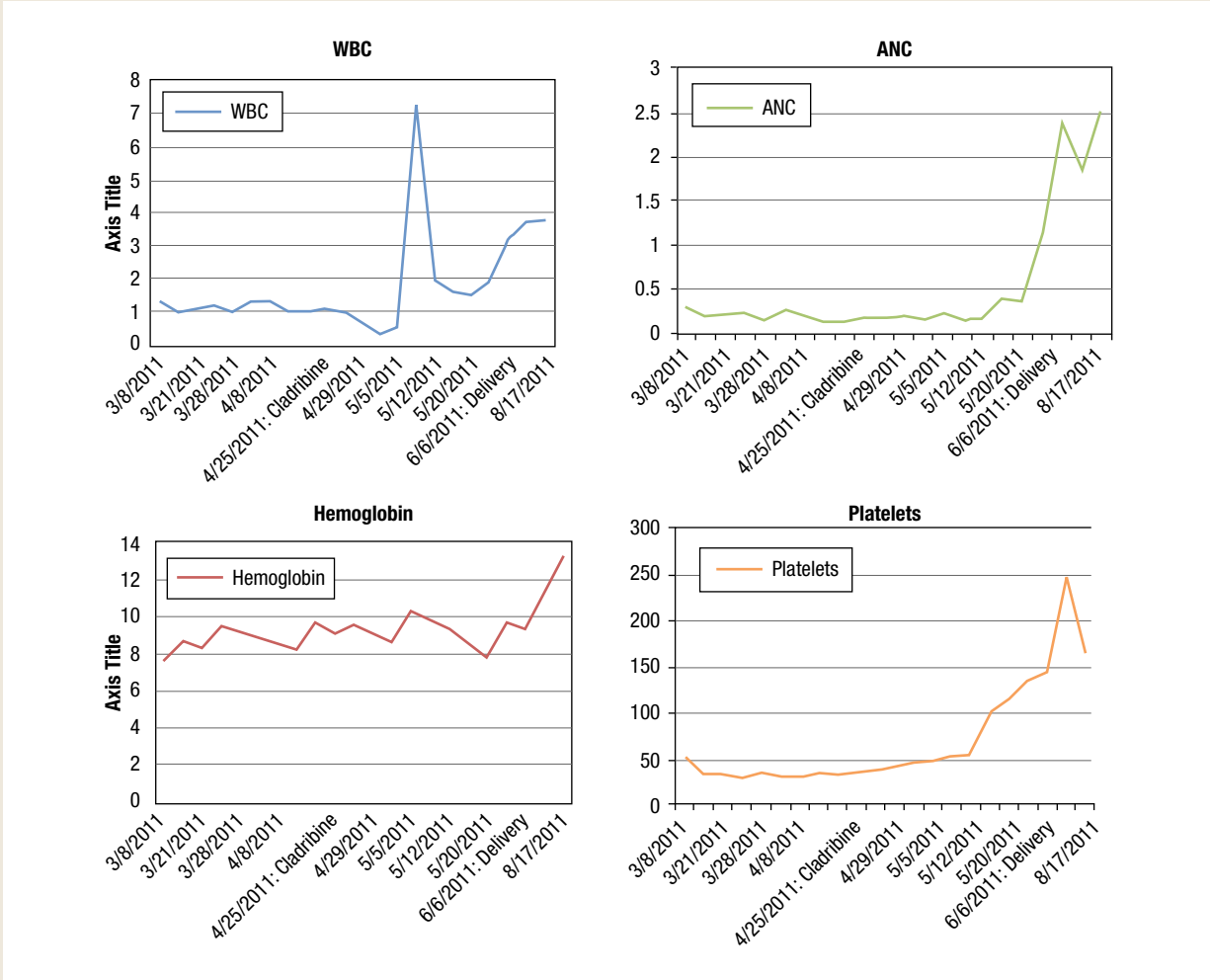
Figure 1 Trend of White Cell Count (WBC), Absolute Neutrophil Count (ANC), Hemoglobin, and Platelets, From Presentation at University of Texas M.D. Anderson Cancer Center Through Delivery



with no lymphadenopathy or hepatosplenomegaly. Ultrasound of the uterus showed a live fetus with appropriate size for gestational age. Laparoscopic splenectomy was considered, but deemed unfeasible given the advanced stage of pregnancy and the presence of significant thrombocytopenia. During the 26th week of gestation, she was treated with rituximab at a dose of 375 mg/m^2 intravenously; given weekly for 4 weeks with no improvement in her blood counts. She was monitored closely with blood and platelet transfusions as needed. Treatment with cladribine was considered. To minimize the risk of developing severe cytopenias at the time of labor, cladribine was initiated early—during the 32nd week of pregnancy. She received 5 consecutive days of cladribine at a dose of 5.6 mg/m^2 per day. She tolerated the therapy well and subsequently had improvement in her blood counts. She was monitored closely and eventually underwent spontaneous labor during the 40th week of gestation resulting in the delivery of a healthy baby. Her blood counts at delivery had significantly improved to WBC of 3.7 K/μL, ANC of 1.8 K/μL, hemoglobin (HGB) of 11.5 g/dL, and platelet (PLT) of 248 K/μL (Figure 1: Trend of WBC, ANC, platelet, and hemoglobin from presentation at UTMDACC through delivery).

Discussion

Hairy cell leukemia is a chronic lymphoproliferative disorder characterized by splenomegaly and pancytopenia. Pathologic diagnosis is based on characteristic 'hairy' appearance of white blood cells on peripheral blood film, presence of increased bone marrow fibrosis, and localized or diffuse infiltration of bone marrow with cells that have characteristic cytoplasmic halo. Confirmation is by means of immunohistochemistry with anti-CD20/DBA-44 and tartrate-resistant acid phosphatase (TRAP) stain. Immunophenotyping, showing strong expression of CD11c, CD25, HC2+, CD123, cyclin D1, annexin A^4, and lack of expression of CD5, CD10, CD23,[9] differentiates HCL from other lymphoproliferative disorders. Therapy is not recommended unless the patient develops significant cytopenias (HGB $<$ 10 g/dL, ANC $<$ 1.0 K/μL, PLT $<$ 100 K/μL), symptomatic splenomegaly, recurrent infections, extralymphatic involvement, autoimmune complications, or progressive disease.[4,5] Man-