Eculizumab in the Successful Treatment of Postpartum Hemolytic Uremic Syndrome - A Case Report

Craig A. Mackaness DO
Lehigh Valley Health Network, Craig_A.Mackaness@lvhn.org

Frederick S. Fleszler MD
Lehigh Valley Health Network, Frederick_S.Fleszler@lvhn.org

Follow this and additional works at: http://scholarlyworks.lvhn.org/medicine
Part of the Bacterial Infections and Mycoses Commons, Digestive System Diseases Commons, Medical Sciences Commons, Nephrology Commons, Pathology Commons, and the Therapeutics Commons

Published In/Presented At

This Poster is brought to you for free and open access by LVHN Scholarly Works. It has been accepted for inclusion in LVHN Scholarly Works by an authorized administrator. For more information, please contact LibraryServices@lvhn.org.
Eculizumab in the Successful Treatment of Postpartum Hemolytic Uremic Syndrome - A Case Report

Craig A. Mackaness, DO and Frederick Fleszler, MD
Lehigh Valley Health Network, Allentown, Pennsylvania; Easton Hospital, Easton, Pennsylvania

INTRODUCTION:

- Preeclampsia, HELLP syndrome, and Pregnancy associated atypical hemolytic uremic syndrome (P-aHUS) represent a continuum of complex pathophysiologic processes which remain the subject of ongoing investigation.
- Preeclampsia occurs in approximately 3-9% of pregnancies1,2 and is characterized by new onset or worsening hypertension and proteinuria after 20 weeks gestation. HELLP syndrome, a severe variant of preeclampsia, affects 0.1-0.2% of pregnancies1,2 and is defined by the presence of hemolysis, elevated liver enzymes and low platelets.3
- Pregnancy-associated thrombotic microangiopathies (p-TMA) are rare, affecting 1-25 per 25,000 pregnancies3,4 accounting for 9%–18% of all cases of TMA. p-TMA is defined by the occurrence of thrombi of fibrin (and platelets) in the microvasculature (arterioles and capillaries) of various organs, mainly the kidney and brain.5
- Pregnancy-associated atypical HUS occurs mainly in the first 6 months after delivery.6
- Complement mediated injury has been implicated in severe preeclampsia.5,6
- Eculizumab is a monoclonal antibody that inhibits the terminal complement pathway.7
- Eculizumab is FDA-approved for the treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH), and more recently atypical hemolytic uremic syndrome (aHUS).8,9
- A case report has suggested Eculizumab may safely prolong pregnancy in patients with preeclampsia and it’s use has been suggested in the setting of post-partum TM.10

CASE PRESENTATION:

The patient is a 39 year old G2P1 woman admitted to the hospital at 37 weeks and 4 days after presenting with new-onset headaches at a routine prenatal visit. Her obstetric history is significant for preeclampsia with her first pregnancy with c-section delivery. She had developed gestational diabetes during this current pregnancy as well as hypertension. Her family history consists of a mother with a history of pulmonary emboli and fetus with a history of DVT. The patient had undergone a thrombophilia workup earlier in her pregnancy which revealed heterozygosity for MTHFR (677T/C), and homozygosity for FVIII (711G/G). On evaluation, She was found to be proteinuric with worsening hypertension. She was diagnosed with preeclampsia and subsequently underwent a successful emergent cesarean section delivery with no immediate complication. In her subsequent post-partum course, the patient demonstrated some vaginal bleeding which prompted laboratory studies which revealed a profound drop in her hemoglobin from 11.0 to 5.7g/dL, accompanied by a decrease in her platelet count from 200k to a nadir of 57k. The peripheral blood smear demonstrated the presence of schistocytes. AST rose from 17 to 210 U/L and ALT from 22 to 118 U/L. Laboratory studies also demonstrated an elevated LDH of 2011 U/L and normal PT/INR. The patient was diagnosed with preeclampsia syndrome. She became progressively oliguric with an elevation in serum creatinine from a baseline of 0.64 mg/dL to a peak of 5.15 mg/dL. In view of her acute kidney injury and out of proportion elevation of LDH, Atypical Hemolytic Uremic Syndrome (aHUS) was suspected.

Renal Ultrasound: The left kidney measures 12.1 cm and the right measures 11.1 cm. Low normal parenchymal thickness with modestly increased echogenicity - Suggestive of medical renal disease. She was treated with daily therapeutic plasma exchange (TPE) with fresh frozen plasma with improvement in hematologic parameters. Her renal failure progressively worsened, and she was placed on intermittent hemodialysis (HD) and continued on daily TPE.

Due to lack of renal recovery three weeks after delivery, the patient underwent a native renal biopsy which demonstrated active thrombotic microangiopathy involving the glomeruli and arterioles. She was treated with Eculizumab, and demonstrated rapid response to therapy, and was able to discontinue TPE and HD within 48 hours. She remains on Eculizumab with a serum creatinine of 1.4mg/dl.

Figure 1. Schematic representation of Eculizumab inhibiting the cleavage of C5, preserving the formation of C5a and the membranes attack complex.

Figure 2a. Light Microscopy demonstrating acute fibrin thrombus.

Figure 2b. Light Microscopy demonstrating organizing thrombus.

Figure 2c. Electron Microscopy.

Table 1. Laboratory Data Demonstrating Renal and Hematologic Parameters

<table>
<thead>
<tr>
<th>Date</th>
<th>Creatinine</th>
<th>Hemoglobin</th>
<th>Platelet</th>
<th>AST</th>
<th>ALT</th>
<th>LDH</th>
<th>Fibrinogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/22/2013</td>
<td>0.64</td>
<td>124</td>
<td>118</td>
<td>17</td>
<td>3.63</td>
<td>220</td>
<td>89</td>
</tr>
<tr>
<td>09/23/2013</td>
<td>1.2</td>
<td>3.60%</td>
<td>220</td>
<td>2011</td>
<td>124</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>09/25/2013</td>
<td>5.7</td>
<td>2011</td>
<td>124</td>
<td>2011</td>
<td>124</td>
<td>1.2</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION:

The pathogenesis of preeclampsia, HELLP, and p-TMA continues to be a focus of research.

The terminal complement system appears to play an integral role in mediating preeclampsia/HELLP/p-aHUS. Inhibition of the terminal complement pathway with Eculizumab led to rapid and durable improvement in renal function and hemolytic anemia in this patient with P-aHUS. This case demonstrates the effective use of Eculizumab in treating aHUS induced by pregnancy and highlights the utility of renal biopsy in diagnosis, prognosis, and management of post-partum renal failure following initiation of appropriate therapy with improvement in hemostatic parameters but lack of recovery of renal function.

Patients receiving Eculizumab are at an increased risk for infection from encapsulated bacteria, and require a meningococcal vaccine, and consideration for interim antimicrobial prophylaxis.

REFERENCES:


ACKNOWLEDGEMENTS:

We would like to thank Dina Holmer for her photography, and Bruce Maynard, MD for her support.

FOR FURTHER INFORMATION:

© 2014 Lehigh Valley Health Network