

observed reduction in the plasma level of factor H to 180  $\mu\text{g}$  per milliliter (normal range, 284 to 528). Furthermore, we detected a homozygous deletion comprising at least exon 2 within the *CFHR1* gene.<sup>5</sup> No mutation was found in the *MCP* or *CFI* genes. Transplant biopsy specimens showed thrombotic microangiopathy (Fig. 1A through 1C).

Since recurrent atypical hemolytic–uremic syndrome leads to graft loss in more than 90% of patients, we decided to administer a single dose of 600 mg of eculizumab after renal function worsened in this patient despite four plasma exchanges. After the administration of eculizumab, the total complement activity was completely blocked, the hemolysis resolved, and the transplant function recovered (Fig. 1D). The patient's renal graft function has been stable for 8 months.

These findings show the positive effect of complement inhibition on the course of atypical hemolytic–uremic syndrome in our patient and, in our view, the use of eculizumab in atypical hemolytic–uremic syndrome warrants further investigation.

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Dr. Nürnberger reports receiving lecture fees from Novartis and Roche; Dr. Witzke, consulting and lecture fees from Novartis and Roche and lecture fees from Astellas and Wyeth; Dr. Zimmerhackl, grant support from Baxter and Novartis and lecture fees from Novartis and Roche; and Dr. Kribben, consulting and lecture fees from Novartis and Roche and lecture fees from Astellas. No other potential conflict of interest relevant to this letter was reported.

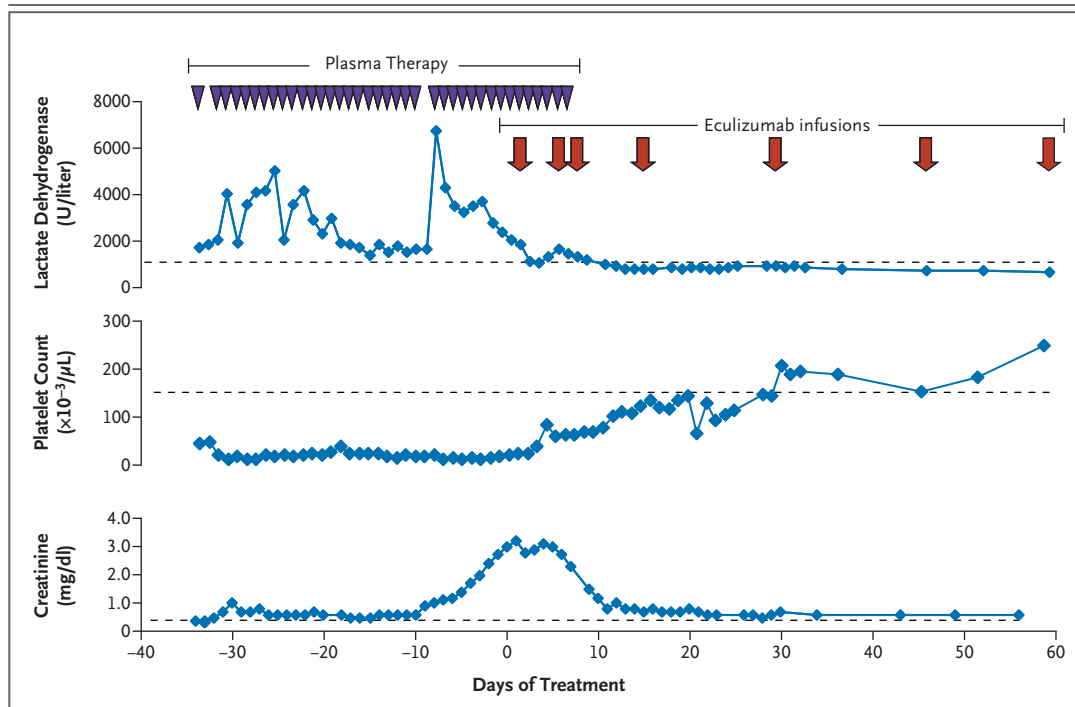
This article (10.1056/NEJMc0808527) was last updated on June 3, 2009, at NEJM.org.

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## Eculizumab for Congenital Atypical Hemolytic–Uremic Syndrome

**TO THE EDITOR:** Atypical hemolytic–uremic syndrome of infancy is a rare disorder that is associated with thrombotic microangiopathy and acute renal failure. It often involves complement dysregulation.<sup>1,2</sup> Plasma infusions have variable efficacy, and end-stage renal disease often develops in children who are unresponsive to plasma therapy.<sup>1,2</sup> We report on a patient with congenital relapsing atypical hemolytic–uremic syndrome who was unresponsive to plasma therapy but had a response to eculizumab, a humanized monoclonal antibody against terminal complement protein C5.<sup>3</sup>

An 18-month-old boy was admitted with a fourth relapse of congenital atypical hemolytic–uremic syndrome. He was born at 34 weeks' gestation, and thrombotic microangiopathy developed within the first 8 days after birth. The hemoglobin was 8.5 g per deciliter, the platelet count  $18 \times 10^3$  per microliter, and the blood urea nitrogen 34 mg per deciliter. The creatinine level was 1.0 mg per deciliter, and the lactate dehydrogenase (LDH) level was 6077 U per liter (normal value, <920 U per liter). A blood smear showed schistocytes. These findings were consistent with congenital atypical hemolytic–uremic syndrome.



**Figure 1. Response to Eculizumab Therapy in a Patient with Congenital Atypical Hemolytic–Uremic Syndrome.**

Eculizumab therapy was initiated in an infant with atypical hemolytic–uremic syndrome for the treatment of a thrombotic microangiopathic event that was unresponsive to 32 consecutive days of plasmapheresis. During the period before treatment with eculizumab, lactate dehydrogenase levels (as a measure of hemolysis) ranged from 1400 to 6800 U per liter (upper limit of the normal range, 920 U per liter [dashed line]) and platelet counts ranged from 11,000 to 38,000 per microliter (lower limit of the normal range, 135,000 per microliter [dashed line]). Creatinine levels began to increase 10 days before the initiation of eculizumab treatment and reached a level of 3.0 mg per deciliter (upper limit of the normal range, 0.4 mg per deciliter [dashed line]). Shortly after eculizumab therapy was initiated, hemolysis decreased (as assessed by levels of lactate dehydrogenase), platelet counts increased, and creatinine levels decreased. Within 1 week after initiation of eculizumab treatment, plasma therapy was discontinued. By day 20, the level of lactate dehydrogenase and the platelet count were normal, and the creatinine level was near normal (0.6 mg per deciliter). Clinical remission was maintained through day 60 with ongoing eculizumab treatment.

Levels of ADAMTS13 activity and complement proteins C2 through C9, factor H, and factor I were normal. Analysis of factor H, factor I, and membrane cofactor protein (MCP) genes did not detect a mutation.

The infant received four exchange transfusions followed by daily plasma infusions; he entered a clinical remission after 13 days. Relapses occurred at 3, 9, and 11 months of age, with remission occurring within 10 to 16 days after plasma infusions. After recovery from the third relapse, the remission was maintained during weekly plasma infusions for 20 weeks. A fourth relapse occurred at 18 months of age, 2 months after discontinuation of the plasma infusions. Despite 32 consecutive days of plasmapheresis, increased hemolysis and thrombocytopenia persisted and renal func-

tion worsened (Fig. 1). Eculizumab therapy was initiated on hospital day 35 in this 12-kg infant; 300-mg doses were given approximately weekly for 3 weeks, followed by 600 mg every 2 weeks. This treatment resulted in complete and consistent terminal complement blockade; there was no measurable serum hemolytic activity at any trough time point tested after the initiation of treatment.

Hematologic and renal improvement began within 48 hours after initiation of eculizumab, and a remission occurred within 10 days (Fig. 1). Plasma therapy was discontinued within the first week after eculizumab treatment. An eculizumab dosing regimen of 600 mg every 2 weeks has continued for 4 months, to date, with sustained clinical remission. These data suggest that C5a, C5b-9, or both contribute to the microangiopathic

process in congenital atypical hemolytic–uremic syndrome, and they provide impetus for the evaluation of eculizumab in controlled studies.

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