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Pathogenic Variants in Complement Genes and Risk of Atypical Hemolytic Uremic Syndrome Relapse after Eculizumab Discontinuation

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Abstract

Background and objectives The complement inhibitor eculizumab has dramatically improved the outcome of atypical hemolytic uremic syndrome. However, the optimal duration of eculizumab treatment in atypical hemolytic uremic syndrome remains debated. We report on the French atypical hemolytic uremic syndrome working group's first 2-year experience with eculizumab discontinuation in patients with atypical hemolytic uremic syndrome.

Design, setting, participants & measurements Using the French atypical hemolytic uremic syndrome registry database, we retrospectively identified all dialysis-free patients with atypical hemolytic uremic syndrome who discontinued eculizumab between 2010 and 2014 and reviewed their relevant clinical and biologic data. The decision to discontinue eculizumab was made by the clinician in charge of the patient. All patients were closely monitored by regular urine dipsticks and blood tests. Eculizumab was rapidly (24–48 hours) restarted in case of relapse.

Results Among 108 patients treated with eculizumab, 38 patients (nine children and 29 adults) discontinued eculizumab (median treatment duration of 17.5 months). Twenty-one patients (55%) carried novel or rare complement genes variants. Renal recovery under eculizumab was equally good in patients with and those without complement gene variants detected. After a median follow-up of 22 months, 12 patients (31%) experienced atypical hemolytic uremic syndrome relapse. Eight of 11 patients (72%) with complement factor H variants, four of eight patients (50%) with membrane cofactor protein variants, and zero of 16 patients with no rare variant detected relapsed. In relapsing patients, early reintroduction (≤48 hours) of eculizumab led to rapid (<7 days) hematologic remission and a return of serum creatinine to baseline level in a median time of 26 days. At last follow-up, renal function remained unchanged in nonrelapsing and relapsing patients compared with baseline values before eculizumab discontinuation.

Conclusions Pathogenic variants in complement genes were associated with higher risk of atypical hemolytic uremic syndrome relapse after eculizumab discontinuation. Prospective studies are needed to identify biomarkers predictive of relapse and determine the best strategy of retreatment in relapsing patients.

hemolytic uremic syndrome | complement | eculizumab | Adult | Antibodies, Monoclonal, Humanized | Antigens, CD46 | Atypical Hemolytic Uremic Syndrome | Child | Complement Factor H | Complement Inactivating Agents | Complement System Proteins

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