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Stec-Triggered Deap-Hus in a Toddler: Successful Management with Eculizumab and Mycophenolate Mofetil Without Corticosteroids

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Abstract

DEAP-HUS (deficiency of CFHR proteins and autoantibody-positive HUS) is a rare autoimmune subtype of atypical HUS, distinct from typical Shiga toxin–producing Escherichia coli (STEC)-associated HUS. We report the case of a 30-month-old child initially presenting with STEC-associated HUS, whose severe clinical course prompted complement investigation despite confirmed STEC positivity. Markedly elevated anti–factor H antibody titers and a homozygous CFHR1–CFHR3 deletion led to reclassification as DEAP-HUS. The patient was treated with eculizumab without high-dose corticosteroids, followed by mycophenolate mofetil (MMF) introduced at month 5, allowing successful discontinuation of complement blockade at month 9. Anti–factor H antibody titers remained stable throughout follow-up without clinical relapse, suggesting that MMF monotherapy provides sufficient immunological stabilization even in the absence of significant antibody reduction.

What is new?

STEC positivity should not exclude complement-mediated disease. In DEAP-HUS, eculizumab can be successfully discontinued under MMF monotherapy, without high-dose corticosteroids.

1. INTRODUCTION

Hemolytic uremic syndrome (HUS) is a thrombotic microangiopathy defined by hemolytic anemia, thrombocytopenia, and acute kidney injury [1]. In its typical form, it most commonly follows infection with Shiga toxin–producing Escherichia coli (STEC), accounting for approximately 90% of pediatric cases [2]. In about 10% of cases, HUS is classified as atypical HUS (aHUS), resulting from dysregulation of the alternative complement pathway [3].

Among aHUS cases, a distinct autoimmune subgroup — DEAP-HUS (deficiency of CFHR proteins and autoantibody-positive HUS) —defined by deletion of the CFHR1 and/or CFHR3 genes combined with autoantibodies against complement factor H (anti-FH). The absence of these proteins, whose epitopes are highly homologous to factor H, promotes loss of immune tolerance and production of anti-FH autoantibodies. These autoantibodies impair factor H binding to endothelial surfaces, resulting in uncontrolled alternative pathway activation [4]. This entity accounts for approximately 10% of aHUS case and differs from classical genetic forms by its autoimmune components.

We report a child presenting with STEC-associated HUS whose severe clinical course led to the diagnosis of DEAP-HUS, and discuss the diagnostic and therapeutic implications of this rare association.

2. CASE REPORT

In April 2025, a 30-month-old child was admitted to the pediatric intensive care unit at Nancy University Hospital for severe acute kidney injury (AKI) requiring kidney replacement therapy.

HUS was suspected based on KDIGO stage 3 AKI (creatinine 288 µmol/L, Schwartz eGFR 11 mL/min/1.73 m²), mechanical hemolytic anemia (hemoglobin 9.1 g/dL, haptoglobin < 0.10 g/L, schistocytes 1.3%, LDH 2160 IU/L), and thrombocytopenia (70 G/L). Continuous kidney replacement therapy was initiated on day 1 and maintained for 29 days. Neurological manifestations developed shortly after admission, included focal seizures. Brain MRI demonstrated diffusion-weighted hyperintensities in the caudate nuclei, corpus callosum genu, and bilateral subcortical white matter, consistent with HUS-related encephalopathy. Extrarenal involvement included transient hepatic cytolysis (up to five times the upper limit of normal) and troponin elevation (peak 348 pg/mL), both resolving spontaneously.

Stool PCR identified STEC (Stx1 and Stx2 positive), initially orienting the diagnosis toward typical HUS. ADAMTS13 activity was normal (44%). Given the severity of the presentation, complement investigations were performed at a national reference laboratory and showed: slightly elevated CH50 (94 U/mL), normal C3 and C4, decreased factor H (59%), normal factor I (96%), and positive anti-FH antibodies at 686 UA.

Eculizumab was initiated (600 mg, then 300 mg at days 7 and 21) in view of multiorgan dysfunction and neurological involvement. High-dose corticosteroids were not administered. The markedly elevated anti-FH antibody titers, combined with the severity of the presentation, led to reclassification as aHUS triggered by STEC infection. Genetic testing confirmed a DEAP-HUS form with a homozygous deletion of CFHR1 and CFHR3.

Eculizumab was continued every two weeks after PICU discharge, with monitoring of complement parameters and anti-FH antibody titers. At month 5, mycophenolate mofetil (MMF) at 600 mg/m² was introduced. Eculizumab was discontinued at month 9; MMF monotherapy was continued thereafter. At 12-month follow-up, no clinical or biological relapse was observed. Kidney function showed partial recovery (Schwartz eGFR 80 mL/min/1.73 m²). Anti-FH antibody titers remained stable under MMF monotherapy. The clinical and biological course is illustrated in Fig. 1.

3. DISCUSSION

STEC positivity is classically regarded as sufficient to diagnose typical HUS and to defer complement investigation. Our case illustrates the limitations of this approach: severity prompted complement workup despite confirmed STEC infection, leading to reclassification as aHUS. This sequence demonstrates that STEC positivity and complement-mediated disease are not mutually exclusive, and that an underlying autoimmune predisposition may be entirely masked by an infectious trigger.

To our knowledge, only one previous case of STEC-triggered DEAP-HUS has been reported — Mortari et al. involving a 9-year-old child with a CFHR composite deletion and positive anti-FH antibodies, managed with eculizumab, later switched to ravulizumab, without corticosteroids, with a 14-week follow-up [5]. Our patient is younger (30 months), presented with comparable severity, and provides, a documented 12-month follow-up under MMF monotherapy after eculizumab discontinuation in this specific context.

The coexistence of STEC infection and DEAP-HUS is explained by a two-hit model. The first hit is genetic: homozygous deletion of CFHR1/CFHR3 promotes loss of immune tolerance and development of anti-FH antibodies, which impair complement regulation at the endothelial surface [4]. The second hit is STEC infection itself, providing the inflammatory trigger sufficient to precipitate overt complement dysregulation in this genetically primed host — consistent with the broader aHUS literature, in which infectious episodes frequently unmask latent complement vulnerabilities [5].

Typical STEC-HUS has no specific treatment; management is supportive. Eculizumab is increasingly used in severe neurological cases, though its benefit remains debated. For DEAP-HUS, no formal guidelines exist. Historically, treatment combined plasma exchange with immunosuppression (corticosteroids, cyclophosphamide, or rituximab) [6]. More recently, a multicenter retrospective study demonstrated significant reduction in anti-FH levels with eculizumab combined with immunosuppressive regimens including MMF alone, MMF plus steroids, or MMF plus rituximab [7]. A 2025 study reported similar findings using eculizumab with corticosteroids and MMF [8]. In our case, high-dose corticosteroids were withheld due to concomitant active STEC infection — initially circumstantial, later deliberate. This differentiates our case from previously published DEAP-HUS reports, in which corticosteroids were typically included in induction therapy [9; 10]. Despite their absence, clinical and biological remission was achieved without relapse at 12 months, suggesting that corticosteroids may not be an absolute prerequisite for remission — a clinically relevant observation for settings in which their use is contraindicated.

Our report also provides extended follow-up under immunosuppression alone after eculizumab discontinuation. Unlike genetic aHUS, DEAP-HUS has an acquired autoimmune component potentially amenable to immunosuppressive control. Ferri et al. demonstrated eculizumab discontinuation was achievable after a median of 11 months, with sustained remission despite elevated anti-FH antibody titers [7]. Coccia et al. reported similar outcomes, with discontinuation in 3 of 4 patients after a median of 6 months [8]. In our patient, eculizumab was discontinued at month 9; anti-FH antibody titers remained markedly elevated at discontinuation and did not significantly decline thereafter. This suggests that complement blockade is the primary determinant of short-term remission, and that MMF provides sufficient immunological stabilization to prevent relapse even without achieving antibody reduction. Longer-term follow-up is needed to assess whether MMF can reduce antibody titers and whether relapse risk increases over time.

Overall, this case highlights that STEC positivity should not be considered sufficient to exclude complement-mediated disease, particularly in the context of severe presentation. The coexistence of an infectious trigger and an underlying autoimmune predisposition represents a diagnostic and therapeutic challenge not addressed by current recommendations. Our observation supports the feasibility of eculizumab discontinuation under MMF monotherapy, without high-dose corticosteroids, with sustained remission at 12 months. Prospective multicenter registries are needed to better characterize the natural history, optimal immunosuppressive strategy, and long-term outcomes of STEC-triggered complement-mediated HUS.

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Oral informed consent was obtained from the patient's parents prior to publication of this case report. This retrospective description of the clinical case was approved by the local ethical committee (SAISINE 590)

CONFLICT OF INTEREST

The authors report no conflicts of interest.

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Figures

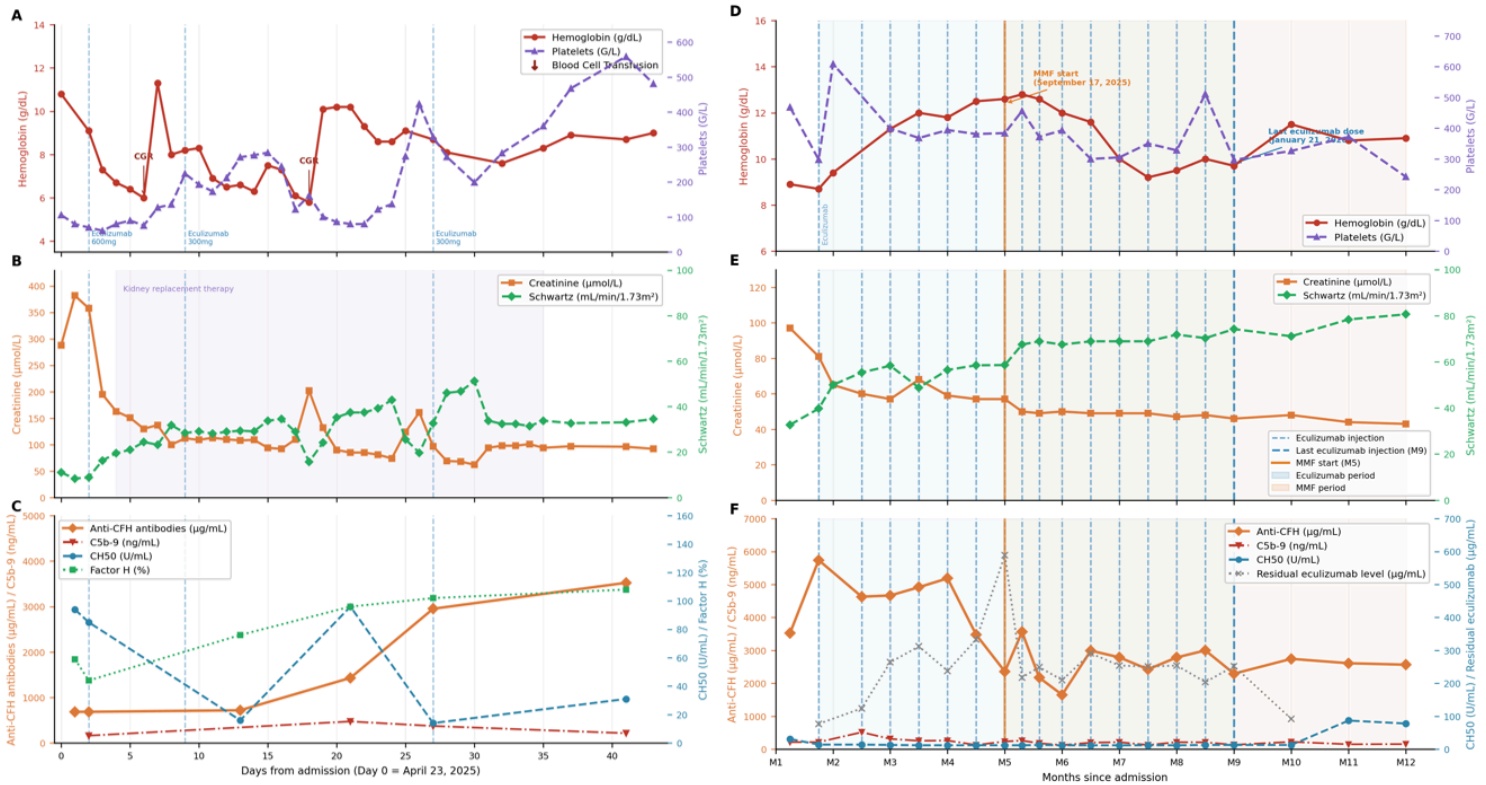


Figure 1

Clinical and biological course following STEC-triggered DEAP-HUS

Note:

. Hematological **(A)**, renal **(B)**, and complement **(C)** parameters during the acute phase (Day 0–Day 43)

. Haematological **(D)**, renal **(E)**, and complement **(F)** parameters during long-term follow-up under eculizumab and mycophenolate mofetil (Month 1–Month 12)