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LETTER TO THE EDITORS

Long-term renal function under plasma exchange in atypical hemolytic uremic syndrome

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Dear Sir,

In a paper by Waters and Licht published recently in *Pediatric Nephrology*, eculizumab is presented as the emerging drug to replace plasma exchange (PE) to treat and prevent atypical hemolytic uremic syndrome (aHUS) [1], allowing complications possibly associated with chronic PE use related to arteriovenous fistula and infusion of blood products (viral infections, allergic reaction) to be avoided. Eculizumab is an anti-C5 monoclonal humanized mouse antibody that binds to C5 and prevents the action of C5 convertase that splits C5 in C5a and C5b, impeding formation of the C5b-9 membrane-attack complex (or MAC) that binds to and permeabilizes cell membranes, thereby killing microorganisms but also damaging host endothelial cells, as in aHUS. Eculizumab treatment has been shown to be successful in several reported aHUS cases. However, the use of this drug over the long term is limited by extremely high cost, possible infectious complications by *Neisseria*, and by fetal morbidity in case of administration during pregnancy. Although it has not yet been demonstrated, the possibility of developing antieculizumab antibodies cannot be excluded.

Another recently proposed alternative to PE consists of combined kidney–liver transplantation, which remains, however, a high-risk procedure [1]. Because of the limitations of the latter techniques and the necessity of life-long treatment in a large number of cases, it seems important to us to emphasize the possibility that an adequate PE strategy could obtain long-term preservation of renal function in aHUS. In aHUS, *CFH* mutations are the most frequent. The prognosis in this group is poor, with most patients developing end-stage renal failure (ESRF) and a recurrence rate posttransplant of 80% [1] that, when not adequately treated, lead to graft loss in 100% of cases. Since our reports on successful aHUS treatment by intensive daily PE on native kidney and on kidney transplantation, followed by prophylactic PE pursued indefinitely and intensified during relapses [2, 3], this strategy has been widely recommended [4].

In this letter, we present the evolution of three sisters, two of whom are homozygote twins presenting with aHUS associated with *CFH* mutation (c.3572 C>T, Ser1191Leu) since data published in our previous paper [3]. These observations represent the longest successful prophylactic PE treatment used in aHUS. The oldest sister is more than 20 years old and received her third kidney transplant at the age of 17 under prophylactic PE initiated from before transplantation. Four months later, she experienced a severe relapse when the frequency of PE was reduced from two to one sessions per week. Immediate treatment by daily PE resulted in complete recovery of baseline renal function. Later on, due to severe reaction to plasma, PE had to be replaced with eculizumab treatment, which prevented HUS relapse and renal function deterioration (plasma creatinine 125 μmol/L 2 years after eculizumab initiation). Twin 1 [2, 3] presented an initial HUS episode at the age of 5 years. She reached ESRF 6 months later despite having received ten daily PE sessions initially and three courses of plasma infusion at the time of hematological exacerbation of the disease. She was transplanted with a cadaver kidney 2 years later under prophylac-

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tic PE (40 ml/kg of fresh frozen plasma) just before transplantation and then daily for 7 days, being progressively tapered and continued indefinitely once a week until now. Eight years posttransplantation, plasma creatinine was 145 μmol/L despite two relapses in the early posttransplantation period secondary to cytomegalovirus (CMV) infection, which responded well to daily PE sessions and ganciclovir. Twin 2 presented a first episode of HUS 6 months after her twin sister [3]. She was immediately treated with daily PE for 21 days until normalization of plasma creatinine and thereafter tapered to one session/2 weeks until now. Ten years after the first episode, plasma creatinine was normal (57 μmol/L), and the patient did not present any urinary abnormality. Long-term regular PE sessions did not worsen school performance and social life in that family.

All three patients presented reactions to plasma that indicated in each case the use of Octaplas instead of fresh frozen plasma. Octaplas is a plasma preparation that considerably reduces reaction risk by assuming complete removal of cells and cell debris by multiple size-exclusion filtration steps. The latter product is also submitted to virus inactivation by S/D methods.

In conclusion, in this family of patients with aHUS related to *CFH* mutation, intensive and prophylactic treatment with PE allowed long-term preservation of transplant and native renal function. However, because of the burden of this technique, the cost of eculizumab, and the high risk of liver transplantation, the best option for treating aHUS related to *CFH* mutation might be a human-plasma-derived CFH concentrate, presently being developed in France by the Laboratoire Francais du Fractionnement et des Biotechnologies.

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