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From the Clinic

Immunoadsorption for paediatric post-diarrhoea haemolytic-uraemic syndrome with severe neurological involvement

The haemolytic-uraemic syndrome (HUS), a thrombotic microangiopathy, occurs often secondary to an infection due to Shiga-toxin-producing *Escherichia coli* (*E Coli*), the most threatening complication being neurological involvement [1]. Plasmata exchange has been shown to have some efficiency [2, 3]. Use of complement cascade-blocking antibody eculizumab is becoming the first-line treatment in the severest cases [4]. At the onset of spring in Europe in 2011, IgG depletion through immunoadsorption was reported to be effective in treating the severe neurological complications of HUS in adults [5, 6].

In October 2011, a 26-month-old girl presented with HUS requiring dialysis, with hepatic, pancreatic and cardiac involvement, seven days after the onset of *E. coli* enteritis. Eculizumab was administrated to treat severe neurological symptoms (unresponsiveness, comatose state, hypertonic quadriplegia, Glasgow score 8/15) due to bilateral thalamic infarctions seen on MRI one day after the onset of HUS (Figure 1). On day 3, a session of plasmapheresis was performed followed by a second eculizumab infusion because of the absence of neurological recovery. Despite this treatment and a slight increase in the platelet count, the patient's neurological status worsened, with recurrent occipital seizures and the need for mechanical ventilation. A third eculizumab infusion was carried out on day 8. Diffusion MRI sequences showed new lenticular lesions associated with right occipital-cortex lesions. In this life-threatening situation, we decided to perform IgG depletion by immunoadsorption as a rescue therapy (six sessions over five days, starting on day 9). A moderate clinical improvement (cessation of seizures, extubation on day 14) was associated with a rapid improvement in the disease activity (platelet count $>150.10^9$/L on day 16). Dialysis was stopped on day 13. The patient was discharged on day 60 with severe neurological sequelae: absence of eye contact, quadriplegia and major cortical and subcortical atrophy on MRI. The creatinine clearance rate was 45 mL/min, with 2 g/L proteinuria. Screening for complement function abnormalities (CFH, CFI, MCP, C3 and C4) and anti-CFH antibodies was negative. Three months later, surprisingly, the patient recovered her previous level of motor function with an independent walk and previous language skills. The creatinine clearance rate stayed at 45 mL/min. Thus, in this child with severe neurological HUS, eculizumab and immunoadsorption treatment were associated with an unexpectedly favourable evolution in the medium term.

The effectiveness of plasmapheresis is controversial [2, 3], and despite encouraging results with eculizumab [4], this treatment is not effective in all forms of post-diarrhoea HUS with severe neurological involvement. We suggest that immunoadsorption, considered a therapeutic option in severe neurological HUS in adults, also be used as a rescue treatment in children. However, studies and protocols are needed to determine the relevance of the association between the two treatments and their timing in neurological forms of post-diarrhoea HUS in children.

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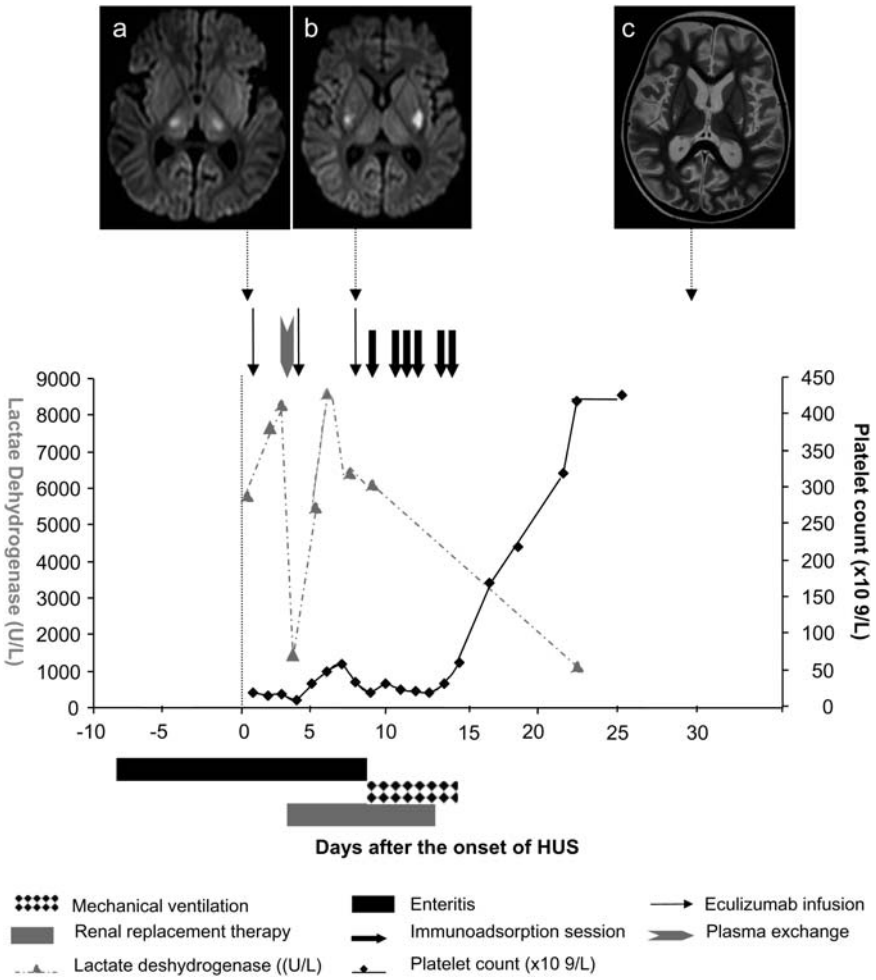

Fig. 1. Course of a 26-months-old girl with severe post-diarrhoea HUS treated by administration of eculizumab and by immunoadsorption. (a) day 1 MRI: diffusion-weighted image, axial view: marked bilateral hypersignal in thalami. (b) day 8 MRI: diffusion-weighted image, axial view: marked bilateral hypersignal in thalami, putamina and asymetrical hypersignal in right occipital lobe. (c) day 30 MRI: T2-weighted image, axial view: global cortical and basal ganglia atrophy with marked bilateral hypersignal in putamina.