WORKSHOP
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Delayed Graft Function and Immunosuppression Drugs in Kidney Transplant: Cytokine Release Syndrome successfully treated with adjuvant hemoadsorption therapy

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Background

Pre-emptive transplantation is associated with a longer survival and improved quality of life since it can avoid the need of dialysis and its complications. Notwithstanding the advantages, the related risk of delayed graft function (DGF) and acute rejection is not completely absent, especially considering high risk profiles donors and recipients. Furthermore, pharmacological immune suppression drugs, i.e. Anti-thymocyte globulin (ATG), might present critical adverse effects, above all the Cytokine Release Syndrome (CRS), impacting most organ systems. Therefore, cytokine levels modulation through blood purification could be a possible adjuvant strategy to limit CRS induced injuries and multi-organ dysfunction

Case Presentation

We present our experience of a young male patient, 23 yo, weight 60 kg, suffering from IgA nephropathy, known as Berger's disease, who underwent to a pre-emptive kidney transplant. In the immediate post-operative days, the occurrence of DGF was observed, firstly treated with Tacrolimus, Mycophenolic acid and subsequently with several administrations of ATG.

After 20 days post-transplant, the patient developed a CRS because of a recurrent ATG cycle, resulting in a worsening severe multi-organ dysfunction. The patient was immediately transferred to our ICU with a severe decline in kidney function (creatinine serum: 3.49 mg/dl), metabolic disorders with lactic acidosis (lactate: 4.8 mmol/l), progress to acute respiratory distress syndrome (ARDS) and cardiac dysfunction. An impairment of the hemodynamic status was observed (mean arterial pression, MAP: 60 mmHg), requiring the administering of Norepinephrine (0.26 µg/kg/min), Dopamine (5.55 µg/kg/min) and then also Levosimendan (0.05 µg/kg/min) to maintain an adequate perfusion and contractility. In the third day in ICU, the limited respiratory function deteriorated (P/F: 42) requiring mechanical respiratory support with pressure-controlled ventilation (PCV), whereas in front of the severe impairment of renal function (creatinine: 5.28 mg/dl), CVVH treatment (Amplya, Bellco) was started.
Cytosorb cartridge was additionally installed into the CRRT circuit with the aim of modulating the cytokine cascade involved in CRS and organ dysfunction, trying to control the organ damages and graft rejection. We performed 3 consecutive Cytosorb cycles, 24-h each until a hemodynamic and general clinical improvement was obtained.

Results

The combined treatment resulted in an important hemodynamic improvement (Figure 1), obtaining a quick MAP stabilization, accompanied by a reduction of inotropic support during the course of the treatment until its complete abolition. Renal function was restored and diuresis returned normal (Table 1) and, on day 9, the patient could be extubated.
The SOFA score improved from 17 to 12 at the end of the treatment and the patient was discharged from our ICU on day 13 in a general good clinical condition (SOFA 4).

Table 1: Clinical parameters during the ICU stay (Day 1: ICU admission)

	Day 1	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
SOFA score	11	17	15	15	15	12	11	9
WBC (x10³/ml)	2.99	17.34	9.56	9.65	7.95	5.75	3.69	3
PCT (ng/ml)	19.89	>100	>100	>100	87.3	69.7	50.18	18.12
Lactate (mmol/l)	37.8	10.4	11.1	12.4	11.1	-	-	-
Creatinine (mg/dl)	3.49	5.28	2.5	1.39	1.07	1.13	1.06	1.05
MAP (mmHg)	60	63	117	87	112	91	90	95
Norephineph rine (µg/kg/min)	0.26	0.2	0.13	0.06	0.06	0.03	0	0
P/F	181	42	289	396	467	494	722	-

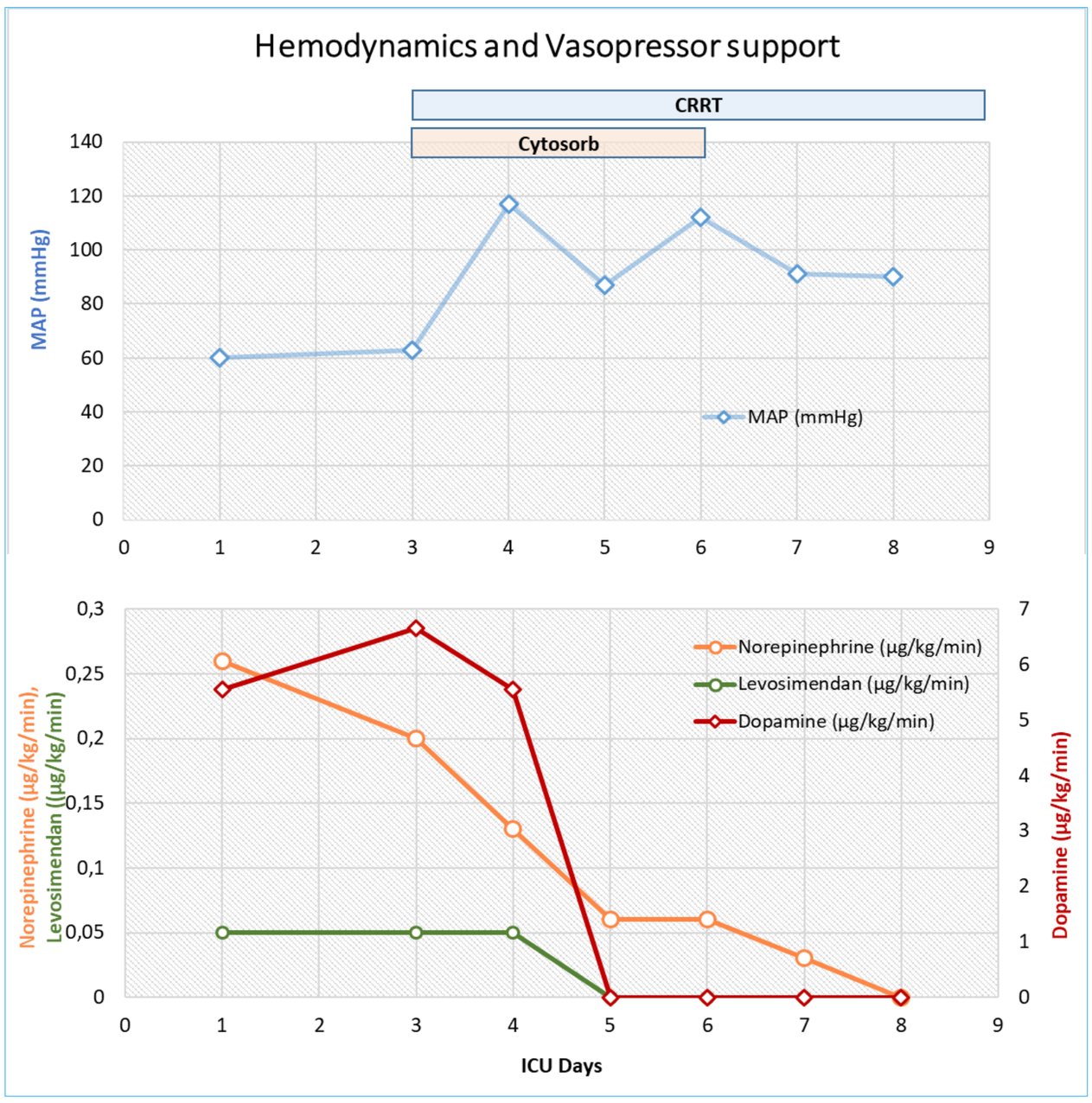

Figure 1: Hemodynamic improvement and ICU stay (Day 1: ICU admission)

Conclusions

Our preliminary experience underlines that the use of Cytosorb hemoadsorption cartridge may be helpful to control cytokines involved in CRS caused by DGF and immunosuppressant drugs in order to limit organ-related damages and eventually prevent graft rejection.